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Cosmetics and Interactions with Superficial Epidermis

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INTRODUCTION

The superficial epidermis is the part of the skin that we see directly. Our appreciation of the condition of the skin, both as consumers and as medical professionals, is primarily dependent on visual inspection. Various examination techniques can be applied additionally [1–3]. Techniques that illustrate the skin condition, such as surface microscopy, assessment of color, scaling, and surface contour, are first-line methods in the evaluation of cosmetic products because of their direct relevance, whereas other methods such as electrical conductance, transepidermal water loss, and pH are second-line or surrogate methods that may only serve as tools in research with a special aim.

From a holistic point of view, consumer appreciation of a cosmetic product is highly complex, and only to a minor degree dependent on true and documented biological effects of the product on skin functions and structures such as the superficial epidermis. Every product has its own aura dependent on culture, society, personal aims, and habits. This is supported by marketing activities of companies in a broad range as well as specifically for a product promoted by the company with a special profile to make profitable business in a market with hundreds or thousands of competitors. The highly complex interaction between psyche, skin, and product is discussed later in this chapter.

EPIDERMIS: THE SUBLIME BARRIER

Barrier functions of various kinds is the sublime function of the epidermis [4]. The barriers of the skin are structurally located in the superficial epidermis. The interface between the superficial epidermis with stratum corneum and the profound epidermis with the stratum Malpighii is the important interface between ambient conditions and environment, including cosmetic product effects, and the internal milieu with many cellular and metabolic functions. The barriers in the superficial epidermis include a temperature moderator and barriers against evaporation of water, uptake of oxygen, expiration of carbon dioxide, penetration of chemicals from the environment (exposures related to occupation and lei-

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sure), chemicals contained in products (cosmetics, cosmeceuticals, and drugs), and the penetration of ultraviolet light, which is reflected or scattered in the superficial epidermis. The superficial epidermis also protects against microbes such as bacteria and fungi.

These critically important interfaces in the epidermis are not a simple structure that can be visualized by histology, but by functions and gradients. The epidermis and the skin is also a neurosensory perceptive organ where negative sensations (pain, itching, stinging, burning, hot, cold) and positive sensations (touch, sexual stimulation) are elicited. Cosmetics, cosmeceuticals, and drugs are designed to interact with the different layers of the skin. Cosmetics primarily aim to influence the visible, superficial epidermis, whereas drugs typically aim to influence the inner layers of the skin and heal disease. Some drugs, namely the transdermals, permeate the skin and are absorbed into the blood stream to exert their action at a distant target organ.

It is not clear if cosmetic products and the chemicals ingredient they contain respect epidermal barriers and remain in the superficial epidermis or if they penetrate to deeper layers of the skin. For example, cosmetic products have to penetrate to the dermis in order to smoothen coarse wrinkles. Being present in the dermis, such ingredients or chemicals are expected to be systematically absorbed and reach the blood stream, maybe after metabolism in the skin to some unknow breakdown chemical with unknown action. However, for safety reasons, cosmetic products are normally claimed not to penetrate the dermis to any significant degree.

The interaction between epidermis and the cosmetic product with its various constituents is, as it may be understood, of crucial importance both for the claimed efficacy and the safety of product. Of course, ingredients are selected carefully, and limited to those expected to be harmless.

NATURE OF INTERACTIONS BETWEEN PRODUCTS AND THE SUPERFICIAL EPIDERMIS

Cosmetic products are intended for interaction with the superficial epidermis, and ideally create objective and visible changes. The importance of such changes to be visible to the naked eye and appreciated as improvements was highlighted in the introduction.

The intended, beneficial interactions of cosmetic products with the epidermis are the traditional ones, namely improvement of scaling, improvement of skin color, improvement of wrinkles (fine and coarse), improvement of elasticity, and a range of beneficial effects on the specialized superficial epidermis, namely the hair and nails. These effects are well known. However, interactions of products with the epidermis may also be innocent or irrelevant or directly harmful, with adverse events such as irritant or allergic contact dermatitis or special events such as development of comedoes and acne. Fragrance allergy is now the number two allergy in industrialized countries, with increasing prevalence. Fragrances are, however, contained not only in cosmetic products, but also in a broad range of household products. Harmful effects on the epidermis may be direct or indirect, acute/short term or chronic/long term, predictable and dose dependent (AHA products, urea, and others), or idiosyncratic, occurring unexpectedly in special individuals. Moreover, effects may be objective or subjective, and if subjective, real (stinging, burning, itching, pain) or purely imaginative. The list of effect variables is not complete.

Products of topical pharmaceuticals, in principle, carry the heavy burden of complete preregistrational documentation, whereas cosmetic products reach the market with a small

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safety dossier only, mirabile dictu non–animal based, but no or very limited formal requirements regarding documentation of efficacy claims.

SELECTED TECHNIQUES FOR THE STUDY OF THE SUPERFICIAL EPIDERMIS

Techniques to study scaling, dryness, transepidermal water loss, skin elasticity, color, and wrinkles, among others, are already well covered in this book and in a number of recent monographs [1–3,5–7]. In each case, techniques need to be adopted and modified relative to the precise purpose of the study protocol. Errors in the use of biophysical methods were more or less the standard some years ago when these techniques were in their infancy, but nowadays the state of the art is to develop, e.g., standard operating procedures, and prestudy validation of the techniques and the design used [8]. Guidelines have been developed and the biophysical methods have today, as a result of this development, acquired acceptance and respect in research and academia.

There are certain study premises to consider:

- A primary claim should be defined, and this should be directly addressed in a study.
- Methods and techniques must be validated before study, and guidelines and proper conduct should be followed.
- The method should be concluded to be valid for the purpose, i.e., accurate, reproducible, linear, and display values within the clinically relevant range.
- The protocols should be orderly and designed with respect to inclusion of, e.g., individuals, blinding, randomization, product application, observation periods, controls, and regression study following active treatment.
- A statistician should be involved and a proper sample size calculation should be conducted.
- Criteria for success relative to the primary study objects should be predefined. Blinding and randomness should be used whenever applicable and despite the use of objective measuring systems.
- It should be clearly understood and defined before study whether a test is used as a first-line method directly to document primary claims or the primary object of clinical relevance, or if the test is used as an indirect or surrogate method, in which case special documentation or arguments are needed to support its relevance for the main claim. The pros and the cons of surrogate parameters should be displayed in an open and balanced discussion.
- In their core design, the conduct and conclusion of studies should not be biased by marketing interests.
- Results should be published irrespective of the outcome.

These modern principles of research are universal, and not only relevant for the study of the superficial epidermis. No good argument has been made for why studies of cosmetic products in humans shall not follow the standards for the study of products on humans as defined by the International Congress of Harmonization (ICH), standards now obligatory in the pharmaceutical industry [9]. In the real world, of course, there is a dilemma between resources and ideal demands, and the good clinical practice (GCP) system is

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mainly introduced to ensure validity of results and help public control. Studies can easily be high-quality and valid without following GCP, but the GCP remains a master class lesson one can learn from.

THE PSYCHE, SKIN, AND COSMETIC PRODUCT TRIANGLE

It was known for many years that skin well being correlates with physical, social, and mental well functioning. Consumer's use of a cosmetic product on their skin is overall in perspective, and not used by the consumer specifically to improve elastic fibers, electrical conduction, or transepidermal water loss, to maintain a pH of 5.5, or to give her or his kerotinocytes a bigger and rounder shape or whatever the intellectual or pseudointellectual argument for the product might be. Basic biology is a black box for the consumer. Likewise, the consumer does not apply an antiwrinkle cream to improve fine lines of micrometer width, which are only visible under a microscope, but she or he uses an antiwrinkle cream to directly treat visible coarse wrinkles with the overall aim to obtain a young or younger look. The consumer typically has almost no idea about the strong economic forces in the marketplace, where she or he is more or less a gambler in a beauty shop.

There is in cosmetic-product use a triangle with the psyche at the top and the skin and the product at the bottom (Fig. 1). The consumer spontaneously coexists with her or his skin and develops her or his degree of self-esteem relative to the skin depending on her or his intellect and society's coding of her or his psyche. There are many examples of how use of cosmetics vary in different cultures and in different historical periods, and this is, of course, not explained by a different biology of the skin.

Already the application of a cosmetic product is a venue of pleasure and relaxation. The person can for a brief period concentrate on herself or himself and relax, and the massage maneuvre, while spreading an elegant, fragrant scent, is coupled with pleasure and mental satisfaction. Such daily life dreamy meditation is often displayed in announcements for cosmetics where beautiful ladies apply wonderful creams, wordless in their happiness, almost flying in the cosmos. By promoting this way, the producers contribute to daydreams and quality of life, and actually meet with some true needs of the consumers. Cosmetics are used to an enormous degree, much more so than true biological or medical needs of the skin could ever explain or justify on rational grounds.

Thus, it is a difficult dilemma to use objective methods, including biophysical techniques in order to document cosmetics. The role of the methods is bound to be limited, but there remains to exist a distinction between fine and honest products with true claims and documented safety and efficacy, and those products that are just manufactured and sold and which may after all, with an unknown risk, also improve quality of life, despite their limited documentation.

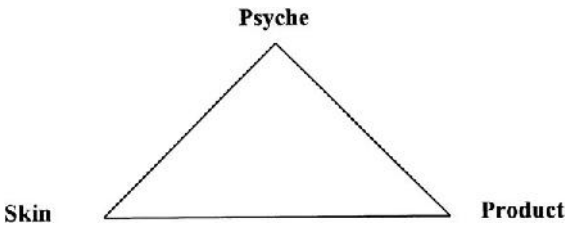

FIGURE 1 The psyche, skin, and cosmetic product triangle.

FIGURE 2 The professor's research project on cosmetics.

The dilemma between theory and subjective needs and practice and objective effects has no solution or answer (Fig. 2). There are different angles. This was elegantly expressed by a leading researcher in a French company who said, *''The cosmetic products do less than we say, but more than we think.''*

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Skin Cleansing Bars

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INTRODUCTION

Although the origin of soap is not very clear, it is widely accepted that some form of primitive soap-making methods existed several thousand years ago, dating as far back to 2000 BC. For many centuries, soaps were made by heating a mixture of animal fats (tallow) with lye, a basic solution obtained from wood ashes [1]. Until the late eighteenth century, soap was considered a luxury item available only to royalty and the social upper class. Today, soaps are produced using a variety of much more refined processes and different fats and oils, resulting in finished products that deliver consumer-relevant performance benefits with desirable aesthetics [1]. In this section, we will discuss the chemical and physical properties of commercial soap bars with a focus on skin cleansing, the raw materials needed, the manufacturing and process requirements, and the final finished product performance evaluations.

WHAT IS SOAP?

Soap is generally defined as an alkali salt of a long-chain fatty acid. When a fat or oil is saponified, the sodium or potassium salt formed from the long-chain fatty acids is called a soap. The term ''soap'' refers to a group of neutralized long-chain carboxylic acids, which result from two primary ingredients: an alkali and a triglyceride (fat or oil). The chain length of the aliphatic group is typically between 7 and 21 carbons with one carboxylate carbon, yielding a molecule containing 8 to 22 carbons. The cation associated with the carboxylate head group generally comprises sodium, potassium, or to a lesser extent other cations such as triethanolamine as well as heavy metals and alkali earth metals such as magnesium.

Soap cleans by altering the surface tension of water and emulsifying and suspending soils to be rinsed away. The two ends of soap have different polarities where the long carbon chain end is nonpolar and hydrophobic, whereas the carboxylate salt end is ionic and hydrophilic. When a soap is used to clean grease or dirt, the nonpolar ends of the soap molecules solubilize nonpolar fats and oils that accompany dirt. The water-loving (hydrophilic) salt ends of the soap molecules extend outside where they can be solubilized in water. The soap molecules coat the oil or grease, forming clusters called micelles. The

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hydrophilic end of the soap molecules provides polarity to the micelles, thus emulsifying them in water. As a result, small globules of oil and fat coated with soap molecules are pulled into the water layer and can be rinsed away.

SOAP RAW MATERIALS

Fats and Oils

The naturally occurring fats and oils used in soap making are glycerides with three fatty acid groups randomly esterified with glycerol (trihydroxy alcohol). The difference between fats and oils is merely one of their physical states: fats are solids and oils are liquids. Fats and oils typically comprise both saturated and unsaturated fatty acid molecules containing between 7 and 21 carbons randomly distributed on the glycerol backbone. Overall, the reaction of caustic (lye) with triglycerides yields glycerin and soap in a reaction known as saponification. This is the most widely used soap making process. The second major soap making process is the neutralization of fatty acids with an alkali. Fats and oils are hydrolyzed (split) with high-pressure steam to yield crude fatty acids and glycerin. The fatty acids are then purified by distillation and neutralized with an alkali to produce soap and water (neat soap) [2–7].

The properties of the resulting soap are determined by the quality and composition of the component fatty acids in the starting fat mixture. In general, chain lengths of less than 12 carbon atoms are more irritating to the skin; conversely, saturated chain lengths greater than 18 carbon atoms form soaps less soluble for ready solution and sudsing. Similarly, a higher proportion of unsaturated fatty acids (e.g., oleic and linolenic) yields soaps susceptible to undesirable atmospheric oxidative changes. For these reasons and the fact that fats and oils are treated as commodities in the open market, the number of fats and oils suitable for commercial soapmaking is limited. The selection of the appropriate starting fats and oils forming the base composition of a soap is key to its quality and performance. Among the fats and oils used throughout the world, beef and sheep tallow are the most common fats, and oils from coconut, palm, soy, and babassu are the most frequently used oils. Soap compositions containing fractions of oils such as palm stearin and other oils with hydrogenation or other upgrading are also in the formulators' arsenal for selection. In the United States, most toilet soaps are made from beef tallow and coconut oil. Some of the common fats and oils used in commercial soapmaking are discussed in the following sections (Table 1).

Tallow

Tallow, which is the principal animal fat in soapmaking, is obtained from the meat processing industry as a result of rendering the body fat from beef and in some cases sheep [8]. In the United States, most toilet soaps are made from beef tallow and coconut oil. The properties of these and other fats are dependent on the constituent fatty acids. Tallow from different sources may vary considerably in color (both initial and after bleaching), titer (solidification point of the fatty acids), free fatty acid content, saponification value (alkali required for saponification), and iodine value (measure of unsaturation). Tallow is composed of mostly long-chain saturated and unsaturated fatty acids—mostly C_{16} (palmitic, 28%), C_{18} (stearic, 18%), and $C_{18:1}$ (oleic, 44%)—providing hardness and thick and creamy long-lasting lather (Table 1).

TABLE 1 Fatty Acid Distribution and Characteristics of Soap Bases

Fatty acid distribution	Tallow	Coconut	Palm oil	Palm stearin	Palm kernel
Caprylic (C-8)		7.4			
Capric (C-10)		6.3			
Lauric (C-12)		47.8			49.7
Myristic (C-14)	2.8	18.3	1.1	1.5	15.7
Palmitic (C-16)	27.8	9.0	43.5	56.5	8.0
Palmitoleic (C-16:1)	3.8			0.2	
Stearic (C-18)	17.9	2.8	4.2	4.8	2.4
Oleic (C-18:1)	43.9	6.3	40.8	29.6	15.2
Linoleic (C-18:2)	2.3	2.0	10.2	7.2	1.5
Linolenic (C-18:3)				0.1	
Characteristics					
Iodine value (IV)	38–48	8–10	50–55	32–40	14–22
Titer, °C	40	26	40	49–51	25
Saponification value (SV)	193–200	251–263	196–209	196–209	240–250
Fatty acid average molecular weight (FA Ave mw)	272	213	270	268	221

Coconut Oil

Coconut oil is one of the most important vegetable oils used in soap making. As previously mentioned, most toilet soaps in the United States are made from tallow and coconut oil. Coconut oil is composed mostly of C_{12} (lauric, 48%) and C_{14} (myristic, 18%) fatty acids, reducing hardness and providing solubility and lather with large bubbles that do not last long (Table 1). Coconut oil is obtained from the dried fruit, copra, of the coconut palm tree.

Palm Oil

Palm oil, which often serves as a substitute for tallow, is obtained from the fruit of the palm tree. It is composed of mostly long chain–length fatty acids—such as C_{16} (palmitic, 44%) and $C_{18:1}$ (oleic, 41%)—providing properties and compositions more similar to tallow than other vegetable oils (Table 1).

Palm Kernel Oil

Palm kernel oil unlike palm oil, is obtained from the center of the nuts of the palm tree and is composed of mostly shorter chain–length fatty acids—such as C_{12} (lauric, 50%) and C_{14} (myristic, 16%)—providing properties and composition similar to coconut oil (Table 1). Palm kernel oil is commonly used as a substitute to coconut oil in the soap-making process.

Palm Stearin

Like palm oil or tallow, palm stearin is composed of mostly long chain–length fatty acids but with lower degree of saturation. Palm stearin is produced by splitting palm oil into palm olein (which is used in foods) and palm stearin. Palm stearin provides properties more similar to tallow than other vegetable oils.

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Although the five oils discussed are the most commonly used fats and oils in the soap-making industry, other sources such as lard (hog fat), Babassu oil, rice bran oil, palm kernel olein, and soybean oil are also used throughout the world.

SOAP PHASES

The physicochemical nature of soap has been shown to be critical for the in-use properties. It is generally accepted that four distinct sodium soap crystalline phases exist. These soap phases are referred to as the beta, delta, omega, and liquid crystalline phases. Today, radiographic diffraction (XRD) is considered the simplest and most reliable method for distinguishing the different phases. The phases designate the lattice spacing between the hydrocarbon chains and are predictive of physical properties such as lather, slough, use-up rate, and even the degree of translucency of a soap bar [9]. The large crystals of the omega phase with the liquid phase are formed when neat soap is cooled down (after the drying step). Beta-phase conversion in soap bars depends on several factors, including temperature, type of surfactant, moisture level and number of millings. Delta phase is formed by the recrystallization of saturated higher chain soaps under specific temperature conditions and moisture level. Ferguson et al. first linked XRD measurements to the physical properties and characteristics of soap bars as finished product. For instance, delta phase provides low slough and low wear rate, whereas beta phase has good lather, low wear rate, and high slough [9].

SOAP BASE COMPOSITION AND PERFORMANCE

Product performance profiles are critically dependent on the base composition selection. For example, the relatively less-soluble tallow provides for bar hardness and a dense, stable, small bubbled lather, whereas the more soluble coconut oil provides an easily generated lather consisting of large bubbles. In addition to bar hardness, color, odor, and lather considerations, the formulator must be concerned with the solubility of the soap as it impacts on the use-up and sloughing of the final product. A typical soap bar in the United States uses a tallow/coconut oil base and the ratio of the two components determines lather attributes such as speed, quantity, and richness. An increase of all of these attributes occurs with the increasing proportions of the coconut oil but the higher proportion of coconut oil also results in an increasing degree of irritation to the skin because of the high short-chain–length fatty acid composition. Furthermore, the behavior of the base can be determined not only by the fatty acid chain but also by the cation by which it is neutralized. The cation can also have a significant influence on the solubility and mildness properties of the base. For example, a sodium soap would be harder than a potassium soap of the same carbon chain length [1].

ADDITIVES

Soap manufacturers have developed a variety of formulation approaches to deliver products that better meet the consumer needs of today. Even though the base soap composition has not changed, consumer needs are met by the inclusion of various additives. As with any other product, the stability (physical and chemical state) of the soap-base–additive or even additive-additive mix must be considered during the formulation. There are a variety of additives that are formulated into soap bars to provide additional consumer

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benefits and/or to modify the performance and aesthetics of the final product. A complete list of functional additives can be found in The Cosmetic, Toiletry and Fragrance Association (CTFA) Cosmetic Ingredient Handbook [10].

Fragrance

Fragrance is by far the most important additive for consumer acceptance of a personal cleansing product. Even though the primary purpose of the selection of a fragrance is to target a specific user group, it is also used to mask the characteristic base odor associated with the fatty acids. Fragrances are compounded from several components including carboxylic acids, esters, aldehydes, ketones, and glycols where the selection of the components could adversely effect the stability and/or the processability of the final product. For instance, fragrances with solvents such as dipropylene glycol (glycol) and diethylpthlate (ester) tend to soften and cloud translucent soap bars [2]. The raw-material manufacturer's ability to provide cleaner base with significantly less base odor has greatly improved in the past two decades, thus allowing soap manufacturers to use less fragrance in the final product or even, in some cases, provide products that are fragrance free. Fragrances are also known to alter the mildness properties of soap bars. For example, a soap bar that targets consumers with sensitive skin has enough fragrance to mask the base odor of the fatty acid while providing some soft perfume that reinforces their mildness properties. The fragrance levels in the soap bar typically range from 0.3% (sensitive skin) to 1.5% (deodorant soaps). Long-term aging studies are always necessary in order to assess the stability of the fragrance in the soap base and its continued ability to mask the base odor.

Free Fatty Acid or Superfatting

Traditional soap bars are alkaline in nature with a pH of around 10. A manufacturing process with excess fatty acid beyond what is needed by the reaction yields a final product with free fatty acid, also known as ''superfatted'' soap. Conversely, a process with caustic in excess of what is needed by the reaction yields a base soap with a slight excess of free caustic. Excess caustic can be neutralized by the addition of excess free fatty acids such as coconut, palm kernel, or stearic acid, or by postaddition of weak acids such as citric or phosphoric acid. Superfatting enhances the lather profile of the soap bar, eliminates free alkali (lowers the pH), and can provide some improvement of skin mildness attributes [1].

Glycerin

Glycerin is a common ingredient formulated into soap bars that dates back to ancient times. As previously discussed, it is the by-product of saponification and thus has always been present in soaps in varying levels [2]. Glycerin is well known for its ability to absorb water (humectancy). This makes it an ideal additive for skincare (moisturization) benefits. Its humectant properties, even at low levels, can alter the rinsability of the soap bar, thus modifying the consumer perception of the product as clean rinsing product.

Colorants and Pigments

The visual appearance of a soap bar is known to influence the consumer acceptance of the product. Because of color differences of some of the base compositions, it is common for most manufacturers to alter the appearance of the final product. This is mostly accom-

plished by the addition of colorants and opacifying agents. Some of the common additives used to alter the appearance of a soap bar include food and/or cosmetic grade dyes and pigments, as well as lakes and opacifiers such as titanium dioxide and zinc oxide [10].

Preservatives

Soap bases with high proportions of unsaturated fatty acids (e.g., oleic, linoleic, linolenic) [11,12] and the presence of certain soap additives, such as fragrance, tend to be susceptible to undesirable atmospheric oxidative changes. Therefore, preservatives (chelating agents and antioxidants) are necessary to prevent such oxidation from occurring. Some commonly used chelating agents (for trace metals present) in soap bars include ethylenediaminetetraacetate (EDTA); diethylenetriamine pentaacetate (DTPA, also known as pentasodium pentate); sodium etidronate or ethane-1-hydroxy-1,1-diphosphonic acid (EHDP) [13]; citric acid; and magnesium silicate. The most commonly used antioxidants in conjunction with chelating agent in soap bars are butylatedhydroxytoluene (BHT) and, recently, the addition of tetradibutyl pentaerithrityl hydroxyhydrocinnamate [14]. Both of these antioxidants are soluble in fragrances.

Skin Conditioners

As previously mentioned, consumer demand for products that not only cleanse the skin but also provide skin mildness and moisturizing benefits is constantly changing. Therefore, it is common for manufacturers to add ingredients that are known to provide such benefits. We previously discussed two of the most commonly used additives, free fatty acid and glycerin. Other additives that are commonly used in soap bars include the following: vitamin E, aloe, jojoba oil, lanolin, glyceryl stearate, isopropyl esters, sodium cetearyl sulfate, cetyl esters, petrolatum, silicones, beeswax, ceresin, carbomer-934, sodium polyacrylate, cocoa butter, mineral oil, and polyethyleneoxideglycol-12, to name a few [10].

Antimicrobial Agents

Soap bars are very effective in removing microbial flora that are known to cause skin infections, pimples, and malodor during the washing/bathing process. The addition of antimicrobial actives to a soap bar extends this benefit for a longer period of time, mainly between washing/bathing. Because of safety concerns about the different actives used in soap bars, the number of antimicrobial agents used in soap bars has decreased from several in the 1970s to only three today. Trichlorocarbanilide (TCC), trichlorodiphenylhydroxyether (triclosan), and parachloro m-xylenol (PCMX) are commonly used in soap bars today. The selection of which active to use in different products is based on claims or product positioning, efficacy, and cost of the final product. TCC is effective mostly against gram-positive bacteria, whereas triclosan and PCMX have been shown to be effective against both gram-positive and gram-negative bacteria. The use levels of these actives are dependent on the claims associated with the final products and government regulations. For instance, in the United States the maximum use levels allowed for triclosan and TCC are 1.0% and 1.5%, respectively.

Synthetic Surfactants

The formulation of soap bars has become more complex because of the ever-increasing consumer demand of products that not only provide cleansing properties but also skin-

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conditioning/moisturization benefits. Synthetic surfactants are often used to enhance the performance of soap bars, resulting in improved skin feel, less irritation, and improved quality and quantity of lather. Synthetic surfactants are used at levels ranging from 5% (low-level combar) to 80% (Syndet), which will be discussed in detail in the later sections of this chapter. The selection of a good synthetic surfactant is critical for the performance of the final product. Some examples of commonly used synthetic surfactants in soap bars include sodium cocoyl isethionate, alkyl ether sulfonate and cocomonoglyceride sulfates [15,16].

Other Additives

Several other additives not mentioned in the previous sections are currently being used in soap bars. Some examples include processing aids, binders (gums and resins), fillers (dextrin, salt, talc, etc., for bar hardness), exfoliants, anti-acne actives, and anti-irritants.

SOAP-MAKING/MANUFACTURING PROCESS

The process of making soap begins with the receipt of fats and oils and ends with a soap bar pressed into a desired shape and packaged for sale. There are many unit operations involved in soap making, from distillation (glycerin recovery) to drying to pneumatic conveying. The soap-making process involves the production of neat soap (wet soap) from fats and oils. The soap then goes through drying and finishing steps in order to complete the process. There are two basic routes of commercial soapmaking [17], which are discussed in the following two sections.

Neutral Fat/Oil Route or Saponification

In the saponification process, neutral fats and oils (tallow, palm oil, palm stearin, coconut oil, palm kernel oil) are first upgraded to remove particulate dirt, proteinaceious materials, and other odor and color bodies, and then reacted with caustic (NaOH or KOH) yielding neat soap and free glycerin (Fig. 1a). Saponification can be done in either a batch (kettle) process or a continuous process [1,2].

Fat Splitting/Fatty Acid Route

In this method of soap production, the fats and oils (triglycerides) are hydrolyzed with high-pressure steam (fat splitting) to produce fatty acids and glycerin. The fatty acids are then purified by distillation and neutralized with an alkali to produce soap (neat soap) and water (Fig. 1b). This method of production is most suitable when lower grade fats and oils are used for soap production.

Drying and Finishing

Neat soap produced by one of the processes previously outlined contains over 30% moisture. The soap needs to be dried, typically by vacuum drying to a final moisture level of 8 to 16% for the final finishing steps. Once the neat soap is dried to soap pellets (soap chips), it is transferred into mixers (amalgamators) and the minor additives such as fragrance, color, preservative, antibacterial agents, and other formula additives are added. These additives are mixed with the soap pellets, refined, and extruded into long continuous billet. The billet is cut and pressed into the desired shape and packaged (Fig. 2). Some

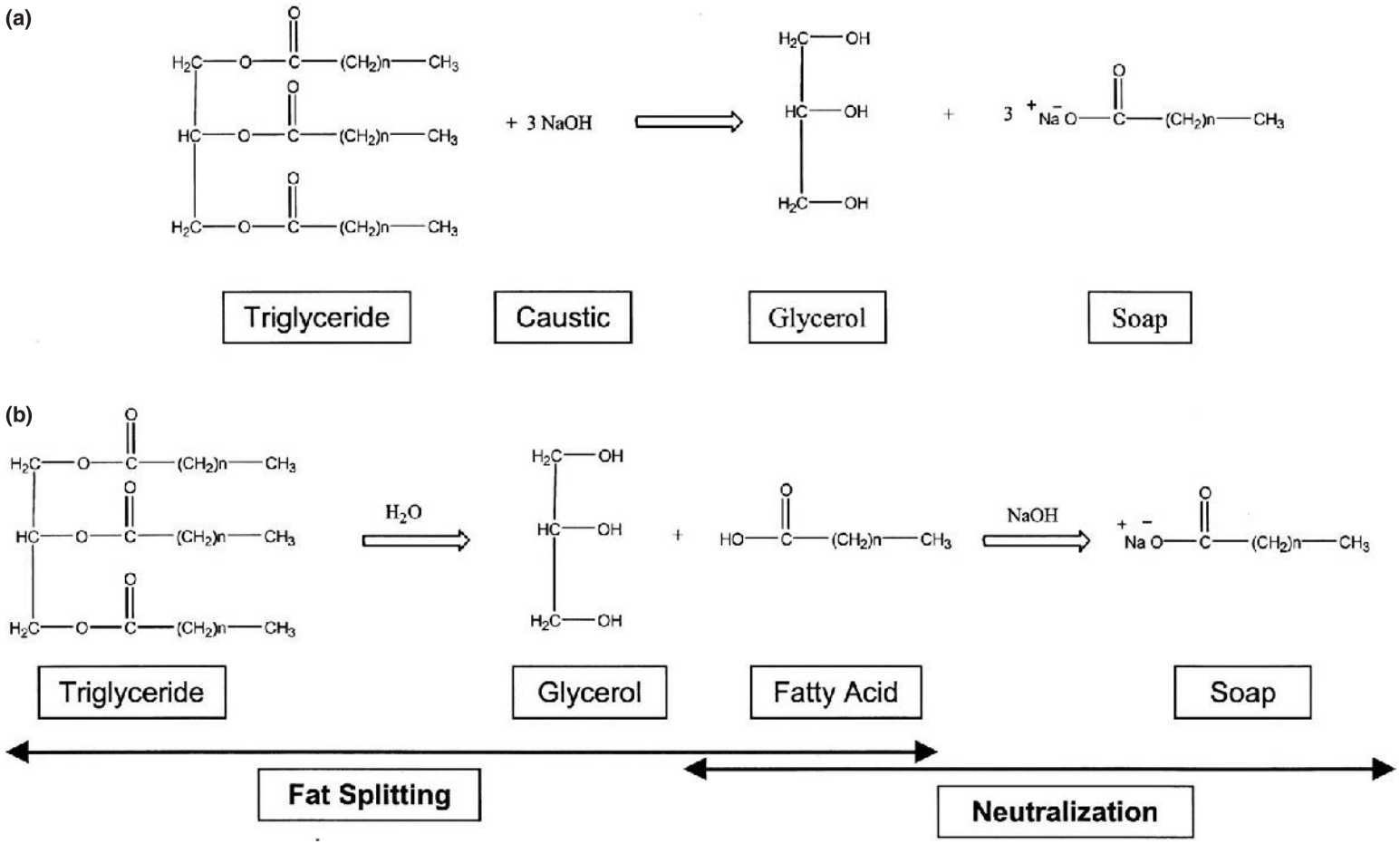

FIGURE 1 (a) Saponification of triglycerides; (b) fat splitting (glycerol as a by-product) and fatty acid neutralization reaction.

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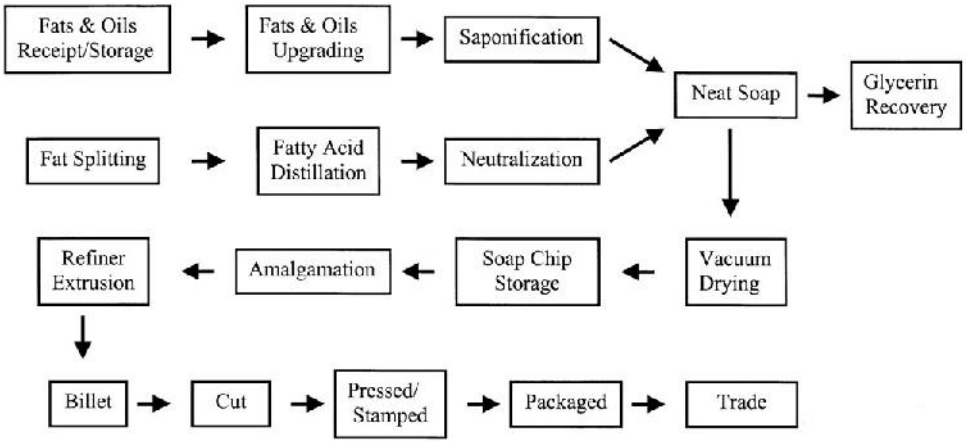

FIGURE 2 Flow chart of the soap manufacturing steps.

soaps are cast instead of cut into shapes. In this case the soap is poured into a mold of desired shape [1,2,18].

FORMULATIONS: REGULAR SOAPS, COMBARS, AND SYNDETS

Soap bars are formulated with a combination of longer carbon chain length fats (tallow, palm oil, palm stearin) and shorter carbon chain length oils (palm kernel oil, coconut oil). Common nomenclature for bar soaps is the ratio of the longer carbon chain length fat to the shorter carbon chain length oil. For example, a bar containing 80% tallow and 20% coconut oil as its soap base would be referred to as an ''80/20'' soap bar. Ratios used typically range from 90/10 to 60/40. The higher coco or palm kernel oil levels in a soap bar not only leads to a higher lathering profile [1] but also to a higher use-up rate due to the high portion of the shorter carbon chain length base. Regular soap bars generally contain approximately 75 to 85% soap. The remainder of the soap bar is made up of water, glycerin, salt, fragrance, and other additives that enhance its aesthetics and performance.

Soap bars are frequently superfatted to ameliorate the harshness of the soap and improve the sensory profiles of the products (see the Free Fatty Acid or Superfatting sections of this chapter). Superfat levels in soaps typically range between 1 and 7%.

Formulation of soap bars has become increasingly complex. As soaps have become more readily available to consumers, the demands on the product performance have increased. Consumer expectations have increased beyond basic cleaning to improved mildness, lathering, deodorant protection, antibacterial protection, and interesting product aesthetics and packaging [2]. Bars produced with synthetic surfactants have improved lathering and rinsing profiles, especially in hard water. At higher levels of synthetic surfactants, the bars exhibit superior mildness versus regular soap. Examples of synthetic bars (syndets) on the market are Dove, Oil of Olay, and Vel. The raw materials and hence the finished product cost of incorporating synthetic surfactants is higher versus soaps. Combination bars, or combars, are designed to incorporate the most desirable properties of plain soap bars and synthetic cleansing bars (Syndets) (Fig. 3). In general, their advantages over conventional soap are superior rinsability and latherability in hard water. Examples of combars on the market include Zest and Lever 2000.

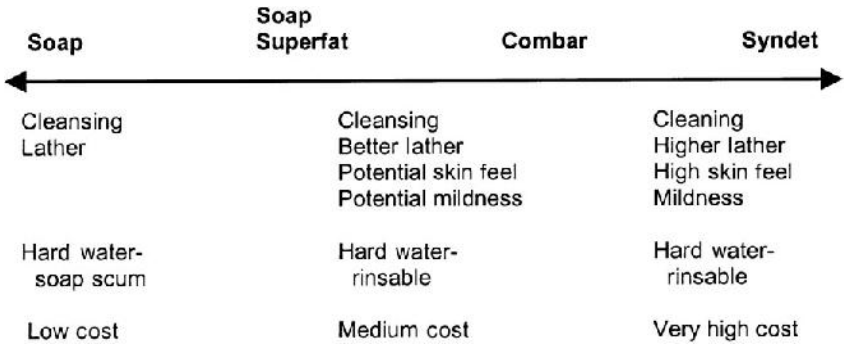

FIGURE 3 Skin cleansing bar formulations and attributes.

The benefits of conventional soap bars are good lathering, thorough cleaning, and low cost compared with bars containing synthetic surfactants (Fig. 3). Some of the shortcomings are: (1) performance dependence on water hardness conditions because of its reactions with calcium and magnesium salts in hard water causing difficulty to rinse ''soap scum,'' and (2) lack of clinical and consumer-perceived mildness benefits. Some people can experience irritation and excessive dryness, especially during periods of low temperature and humidity such as in winter. Synthetic cleansing bars (syndets) generally contain only low levels or no soap. Instead, syndets comprise synthetic surfactants (between 20–80% of the total bar composition), high concentrations of emollients and conditioners, and some fillers and binders [19]. They tend to cleanse and lather well in soft or hard water, and they are unaffected by calcium or magnesium salts which results in better rinsing properties from skin and hard surfaces. Also because of the presence of high levels of skin moisturizers and conditioners, syndets impart more skin after feel, leaving the skin feeling softer and more moisturized.

While all synthetic surfactants overcome the hard-water deficiencies of soap, not all of them are suitable for use in cleansing bars because their effects on skin can be markedly different than soap. Selection criteria that one needs to follow in order to choose a synthetic surfactant for use in soap bars are quite strenuous. In addition to being mild, the surfactant must possess acceptable properties such as surface activity, physical and chemical stability, good odor and color, processability into soap bars, quick lather, and clean skin feel [1]. Some can be too strong and irritating to the skin and can therefore leave the skin feeling dry and damaged. Common anionic synthetic surfactants used in syndets and combars include sodium cocoylisethionate, alkylglycerylether sulfonate, and alkylsulfate. Amphoteric surfactants such as cocamidolpropylbetaine or nonionic surfactants are also sometimes used at low levels. Translucent and transparent soaps incorporate high levels of solubilizers, which tend to control the crystal size and structure, thus allowing the transmittance of light through the product. Examples of solvents added to translucent and transparent soaps include glycerin, sorbitol, triethanolamine, and other sugars [20–22]. These specialty soap products frequently have altered lathering, rinsing and use-up rate characteristics because of the high level of solubilizers in the finished product. Other specialty soaps include the addition of unique aesthetics (marbleized and striated) or the addition of specialty abrasives (e.g., pumice, seaweed) and other botanical or natural ingredients.

BAR SOAP PERFORMANCE EVALUATIONS

Soap bars are evaluated for several characteristics to ensure that they meet consumer needs and expectations.

Lather

The amount of lather, how rapidly a product lathers, and the quality of lather can be judged by a trained panel. This trained panel rates the product on lather quantity, quality, and quickness by rating it on a numerical scale. Typically panelists are trained to rotate a soap bar a fixed number of times and evaluate it for attributes versus benchmark products. This is most useful in the analysis and comparison of formulation similarities and differences as well as competitive products. Variables affecting lather performance of a product include water temperature, water hardness, and method of washing. Trained panelists need to be trained and validated on a regular basis to ensure consistency of their evaluations.

Laboratory methods of lather evaluation include the Ross-Miles foam height test. This requires measuring the foam height of a soap solution that has been inverted in a cylinder for a fixed number of times. Results from this type of test can be misleading because the bar shape and solubility can affect the lather performance in use [1].

Wear Rate/Use-Up

The measurement of how long a bar lasts under normal use conditions is an important attribute to the consumer perceived value. The use-up rate is measured by first weighing the soap bar and then washing the bar for a set number and length of times (for example, 25 washings for 10 sec each). The bar is then dried and weighed again and the use-up or wear rate is reported as the percent weight loss. Soap bar shape and size impact the reported use-up rate. The use-up rate measurement must be controlled for water hardness and temperature. For formulation comparison purposes, it is best to compare soap bars with similar sizes and shapes. Bars can be shaved to the same sizes and shapes in order for the measurement to reflect the true formula influence. To compare how bars will perform in the hands of consumers, actual commercial sizes and shapes should be used.

Slough/Mush

Slough or mush is the undesirable soft part of the bar that results from the hydration of a soap bar as it sits in a wet soap dish. Slough is measured by placing a pre-weighed bar in a high humidity chamber for a fixed period of time, then removing the soft part of the bar and allowing the soap bar to dry. The weight taken before and after determine the slough or mush measured as the percent weight loss. Syndet bars tend to have high slough relative to regular soaps. High humidity conditions exaggerate typical home usage conditions, but help differentiate products and formulations. Slough can also be run at room temperature. Commercial soap bar shapes can be selected by manufacturers to minimize the formation of slough or mush in use conditions.

Cracking

Cracking is the splitting of a bar along the side seams or at any part in the bar during use. Cracking of a soap bar in use conditions is a perceived as a negative by consumers.

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Cracking is evaluated by partially submerging bars in water of fixed hardness and temperature for a set period of time. The bars are then dried and evaluated for cracking after one to two days. Ideally, there should be no cracks present in the soap bars.

Hardness

Bar hardness is a mechanical measure of how resistant the bar is to physical pressure. Bar hardness can be mechanically measured in finishing trials for machineability as well as during routine lab evaluations. Bars that are too soft may be difficult to extrude on the finishing line without significant surface defects.

Bar Feel and Sandiness

Bar soaps are typically evaluated for dry specks and drag. Specks of dry soap (insoluble soap) can occur during the manufacture of the base soap or syndet or from the additives in the soap bar. These specks show up as distinct bumps on the surface of the bar. The bar is washed under controlled water conditions with cooler water bringing out more obvious dry specks. The bar is both evaluated during wash and after drying for feel and appearance and rated against standard quality bars.

Sensory Skin Evaluations

Clearly, next to the fragrance preference at the point of purchase, skin feel and lather are the most important attributes for consumers. Various skin feel attributes from bar soaps are evaluated by a trained panel of experts. These groups of panelists are trained to evaluate small (or large) differences in products focusing on a set of defined attributes. Products are usually compared with a reference product. Examples of attributes evaluated by a trained panel for skin feel include time to rinse, skin slip, tightness of skin after drying, and smoothness of skin.

Clinical Evaluations

Clinical Evaluations of soap products are used to determine how effective the products are on certain attributes, primarily mildness/irritation, skin dryness/tightness, antibacterial efficacy, and deodorancy. There are several methods of measuring the clinical attributes of a soap bar ranging from trained panels to biophysical instrumentation [1,2,23].

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Skin Cleansing Liquids

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INTRODUCTION

Skin cleansing liquids are products that clean and refresh the skin by removing soil or dirty materials to help keep the skin's physiological condition normal. There are residual metabolites on the skin that are unstable and reactive with oxygen or deposited molecules by sun exposure or skin micro-organisms to form harmful materials to cause skin trouble. Thus cleansing is a necessary daily skincare practice even for normal skin. Furthermore, special care must be taken for sensitive skin or atopic skin because of its vulnerability. In these troubled types of skin, cleanliness must be attained without contributing to their susceptibility [1]. There are different types of cleansing products developed and commonly used depending on the types of materials to be removed from the skin or types of use conditions.

Typical types of commercial skin cleansing products are listed in Table 1 [2]. A most common cleansing product contains a relatively high concentration of surfactants and is applied with water to make foam before washing off thoroughly. Good lathering is the most important feature of these products because sensory feeling of the rich and fine foam is the key factor of repeated use by consumer, although amount and quality of foam are not directly related to the detergency from a physicochemical viewpoint. On the other hand, fine and thick lather serves an important function in shaving foam preparations for smooth razor application. Ease of quick rinse and after-feeling are other factors that rule the quality of skin cleansing products. Refreshed and moist feelings are typical elements that fulfill consumers' desires, and refreshing seems more important for body wash, especially for Japanese consumers.

In terms of formulations for surfactant-type skin cleansers, soap bars have been the most traditional skin cleansers but there are liquid-, paste-, or aerosol-type cleansers getting more popular on the market. Facial cleansing powder—a rather new and niche trend in Japan—contains enzymes to help the cleaning of protein-type deposits because of its anhydrous formula to preserve enzyme activities.

Solvent type is mainly used to remove oily cosmetics applied to the skin. This type is further categorized to cleansing creams, lotions, liquids, or gels. The use of makeup products, such as waterproof or nonstaining and long-lasting lipsticks, require use of spe-

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TABLE 1 Types of Commercial Skin Cleansing Products

Product type	Form (formula type)	Features
Surfactant-based type	Solid (soap, transparent soap, neutral soap)	Main type of cleanser: easy to use and feels good, but skin feels tight afterwards.
	Cream · paste (cleansing foam)	Special face cleanser with excellent feeling and lather. It is easy to use. Bases may be selected in the range weakly acidic to alkaline depending on the purpose.
	Liquid or viscous liquid type (cleansing gel)	Weakly acidic to alkaline. The weakly acidic base produces a weak cleanser but the alkaline base produces a strong one. The main type of cleanser for hair and body.
	Granule/powder form (cleansing powder, face cleansing powder)	Easy to use. As they contain no water, papain or other enzyme may be incorporated.
	Aerosol type (shaving foam type, after-foaming type)	There are two types—one that comes out like a shaving foam and the other as a gel which becomes a foam on use (after-foaming type). A double container is used for the after-foaming type.
Solvent-based type	Cream · paste (cleansing cream)	The emulsion type uses mainly O/W emulsion. The type in which oils are made into a gel has high cleansing power. For heavy makeup.
	Milky lotion (cleansing milk); liquid form (cleansing lotion)	O/W emulsion milky lotion. Lighter feeling after use than with cleansing cream. Easy to use. Cleansing lotion. Contains large amounts of nonionic surfactants, alcohol, and humectants. There is also a physical cleansing effect as it is wiped off with cotton. For light makeup.
	Gel (cleansing gel)	The emulsion and liquid crystal types containing a lot of oils have high cleansing power and are rinsed off. They give a light feeling after rinsing off. The water-soluble polymer gel type has low cleansing power.
	Oil (cleansing oil)	Ingredients like surfactants and alcohol are added to the oil in small amounts. Rinsed off. When rinsed off forms O/W emulsion. Soft and moist feeling after use.
Others	Pack (cleansing mask)	Peel-off mask using water-soluble polymers. Skin has strong feeling of being stretched. Removes dirt from skin surface and pores when peeled off.

Source: Ref. 2.

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TABLE 2 Main Surfactants Used for Cleansing Products

Type	Ingredients
Anionic Surfactants	Soap
	Polyoxyethylene alkyl ether sulfate
	Acylglutamate
	Acylglycinate
	Acylmethyltaurate
	Acylsurcosinate
	Acylisethionate
Ampoteric surfactants	Alkyl dimethylaminoacetic acid betaine
	Alkyl amidopropyl dimethylaminoacetic acid betaine
Nonionic surfactants	POE alkyl ether
	POE glycerol fatty acid ester
	POE-POP block copolymer

cial cleansers to remove them. Facial packs with cleansing gel that claim gentleness and sufficient cleansing power have been launched in Japan.

SURFACTANT-TYPE SKIN CLEANSERS

Main surfactants used for surfactant-type skin cleansers are listed in Table 2. Soaps are used as a primary surfactant for solid bar cleansers and paste-type cleansers. Sodium soaps are commonly used for solid bars and potassium soaps are mainly for paste-type cleansers or shaving foams. Opaque soft bar is made from triethanolamine soap as gentle facial cleanser. Soaps have excellent lathering properties and superior detergency but some deposit in hard water and cause skin tightness. Additional surfactants are combined with soap in order to improve tightness and give better mildness. Alkylethersulfate, acylisethionate, acylglutamate, acylmethyltaurate, and acylglycinate are commonly combined as a secondary or tertiary surfactant with soap. Acylglutamate has a unique feature as weakly acidic similar to skin pH surfactant and is thus often used as a primary surfactant to give superb mildness for different formulation types.

As of their physicochemical nature, surfactants not only remove soils but also tend to strip useful substances from the skin. Thus excessive solubilization and stripping of skin lipids and natural moisturizing factors (NMF) must be avoided, otherwise destruction of skin-barrier functions would happen. The composition of skin-surface lipids is listed in Table 3 [3] and composition of constitutive lipids in the stratum corneum is shown in Table 4 [4]. Detergency of surfactant should be good enough to remove surface lipid but not to strip minimally constitutive lipids, which are key components of skin-barrier function. Such selective detergency is found for several surfactants and acylaminoacids such as acylglutamate or acylmethyltaurate, which are relatively better in this regard than soap [5,6]. Composition of NMF is shown in Ref. [7]. Acylglutamate showed less stripping of NMF than soap. [8] Changes of skin pH are dependent on the type of surfactant used too. As shown in Figure 1 and 2, water-holding capacity and skin pH by repeated wash with acylglutamate was not affected much while soap changed these two properties seriously.

Formulations are designed to fit for the specific concept to which a product is aimed along with the general requirement as a skin cleanser such as detergency, feeling, viscosity,

TABLE 3 Composition of Human Skin Surface Lipids

Lipid	Average amount (wt%)	Range (wt%)
Triglycerides	41.0	19.5–49.4
Diglycerides	2.2	2.3–4.3
Fatty acids	16.4	7.9–13.9
Squalene	12.0	10.1–13.9
Wax esters	25.0	22.6–29.5
Cholesterol	1.4	1.2–2.3
Cholesterol esters	2.1	1.5–2.6

Source: Ref. 3.

TABLE 4 Composition of Constitutive Lipids in the Stratum Corneum

Lipid	Wt%
Cholesterol esters	1.7
Triglycerides	2.8
Fatty acids	13.1
Cholesterol	26.0
Ceramides	45.8
Glucosylceramides	1.0
Cholesteryl sulfate	3.9
Unidentified	5.7

Source: Ref. 4.

TABLE 5 Analysis of Commercial Paste–Type Facial Cleansers

Sample	Distribution of fatty acid (wt%)				Total fatty acid (wt%)
	C12	C14	C16	C18	
Sample A	5.9	16.8	1.4	6.4	30.5
Sample B	10.9	4.7	9.6	8.5	33.7
Sample C	0.0	15.0	6.9	4.0	25.9
Sample D	5.8	6.4	2.2	3.6	18.0
Sample E	4.9	13.3	3.5	5.8	27.5
Sample F	1.2	23.1	3.9	5.6	33.8

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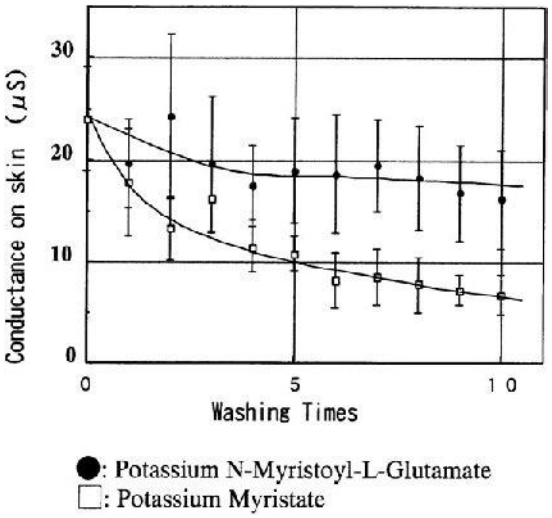

FIGURE 1 Effect of surfactant on the moisture content of the skin. Forearms were washed every 20 minutes with 5 mL of surfactant solution (10%) and skin surface conductance was measured by surface hygrometer (Skicon 200; IBS Japan, at 25°C, 40 RH%, n = 6) as indicator of the moisture of the skin.

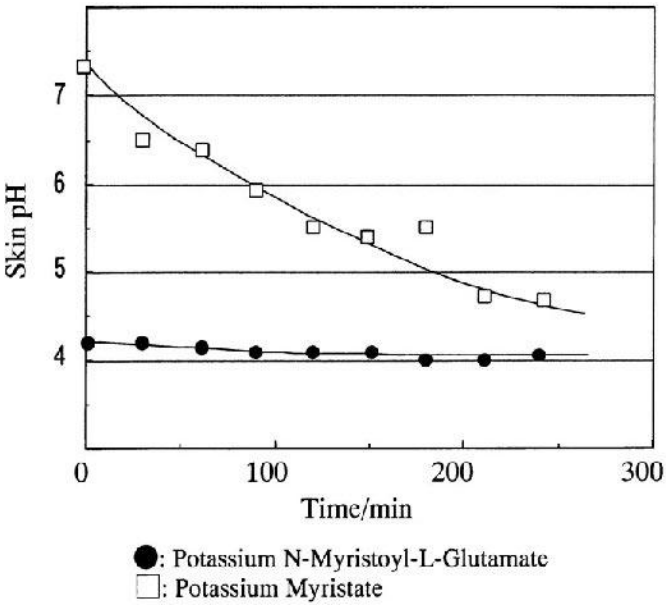

FIGURE 2 Effect of surfactants on the pH of human skin. Forearms were washed with 5 mL of surfactant solution (10%) and after that pH of the skin was measured every 20 minutes at 25°C, 40 RH%, n = 6.

stability, safety, and manageability or easiness of use, which are sometimes contradictory to fulfill all at once. Consumers' desire for a natural product requires not only that the ingredients used be natural but also that their appearance be natural-looking or transparent. Such requirements cause further difficulties for the formulation work [9].

Liquid-type skin cleansers have been developed mainly for facial use and diversified further to paste-type or gel-type formulations. Liquid-type body wash was developed first in Japan and spread widely to western markets with rapid growth even to replace significant share of soap bar market. This is among others because of their friendliness of use and added values as natural and mildness concepts.

Following are typical formulas of surfactant-type skin cleansers with their characteristics described:

Formula 1: Soap-Based Liquid Facial Cleanser (Excellent Lathering and Refreshing After-Feel)

Ingredients	%
Lauric acid	2.5
Myristic acid	7.5
Palmitic acid	2.5
Lauric acid diethanolamide	2.0
Propylene glycol	8.0
Potassium hydroxide	3.6
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Add all the ingredients together and heat to dissolve with stirring. Cool down to room temperature.

* q.s., quantum satis (in sufficient amount).

Formula 2: Laurylethersulfate (LES)-Based Liquid Facial Cleanser (Compatible with Hard Water)

Ingredients	%
Sodium polyoxyethylene(3)lauryl ether sulfate (30%)	40.0
Sodium N-lauroylmethyltaurate (30%)	10.0
Coconut acid diethanolamide	3.0
Glycerin	5.0
Sodium chloride	2.0
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Add all the ingredients together and heat to dissolve with stirring. Cool down to room temperature.

* q.s., quantum satis (in sufficient amount).

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Formula 3: Acylglutamate-Based Liquid Facial Cleanser Weakly Acidic, Leaves Skin Moist and Supple-Feeling

Ingredients	%
Triethanolamine N-cocoyl-L-glutamate (30%)	30.0
Cocoyl amide propyldimethyl glycine (30%)	30.0
1.3-butylene glycol	5.0
Sodium hydroxide	0.5
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Add all the ingredients together and heat to dissolve with stirring. Cool down to room temperature.

* q.s., quantum satis (in sufficient amount).

Formula 4: Acylglycinate-Based Liquid Facial Cleanser (Excellent Lather and Refreshed After-Feeling Without Tightness)

Ingredients	%
Potassium cocoyl glycinate (30%)	15.0
Potassium laurate	11.0
Potassium myristate	6.0
Glycerin	3.0
Sorbitol (70%)	2.0
Ethylene glycol distearate	2.0
Hydroxypropylcellulose	0.5
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Add all the ingredients together and heat to dissolve with stirring. Cool down to room temperature.

* q.s., quantum satis (in sufficient amount).

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Formula 5: Soap-Based Paste-Type Skin Cleanser [10] (Good Foaming and Cleansing Power)

Ingredients	%
Stearic acid	10.0
Palmitic acid	11.0
Myristic acid	12.0
Lauric acid	2.0
Squalane	2.0
Potassium hydroxide	6.0
PEG1500	10.0
Glycerin	20.0
Glycerol monostearate	2.0
POE(30)glycerol monostearate ester	2.0
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Heat fatty acids, emollient, humectants, and preservative together until melted and keep at 70°C (oil phase). Dissolve the alkali in the purified water and add this to the oil phase while stirring. Keep at 70°C until the neutralization reaction is completed. In Table 5, analytical results of the fatty acid compositions for the commercial soap-based paste-type facial cleanser are shown.

* q.s., quantum satis (in sufficient amount).

Formula 6: Acylglutamate-Based Paste-Type Facial Cleanser (Weakly Acidic, Moist and Supple After-Feeling)

Ingredients	%
Sodium N-lauroyl-L-glutamate	35.0
Potassium laurate	5.0
Coconut acid diethanolamide	2.0
1.3-butylene glycol	10.0
Dipropylene glycol	20.0
Polyvinyl pyrolidone	0.5
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Mix polyols and surfactants completely. Add other ingredients and water, then heat to dissolve. Cool to room temperature under reduced pressure with stirring.

* q.s., quantum satis (in sufficient amount).

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Formula 7: Acylglycinate-Based Paste-Type Facial Cleanser (Neutral pH, Fresh After-Feeling)

Ingredients	%
Potassium cocoyl glycinate	32.0
Potassium myristate	1.5
Behenyl alcohol	0.5
Citric acid	2.5
1.3-butylene glycol	15.0
Glycerin	17.0
Ethylene glycol distearate	2.5
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Mix polyols and surfactants completely. Add other ingredients and water then heat to dissolve. Cool to room temperature under reduced pressure with stirring.

* q.s., quantum satis (in sufficient amount).

SOLVENT-TYPE SKIN CLEANSERS

Solvent-type cleansers are designed to remove oily residues from cosmetics. Normally these cleansers are applied by hand to remove oily deposits of colors or pigments from the skin, and are then wiped out with tissue or cloth. Water-oil (W/O) emulsions or simple oils work satisfactorily for this purpose but leave skin oily. Thus surfactant-type cleansers are quite often applied after this treatment. The widespread trend of long-lasting cosmetics requires stronger and laborious cleansing with solvent-type cleansers. In order to avoid excess burden to the skin and achieve effective cleansing of oily deposits, (1) solubilization and dispersibility, and (2) washability with water are key properties of solvent-type cleansers, while mildness is mandatory requirement for the product. For the former need, the product should be more lipophilic, and on the contrary for the latter purpose it is better to be rather hydrophilic. To overcome these contradictory tasks, there are several different formulations developed that are W/O emulsions, gels, or liquid crystals with special selections and combinations of oil phase and aqueous phase. The principle of these formulas is to have potent oily phase, which can easily interact and solubilize liquid deposits, when applied to the skin. Thereafter, by the application of an excess amount of water, a mixture will form between the cleanser and the oily deposit, which will easily turn into a hydrophilic mixture (such as a W/O emulsion) [11,12].

Following are typical formulas of solvent-type skin cleansers with their characteristics described:

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Formula 8: Soap-Based Facial Cleansing Lotion (Soap Emulsion)

Ingredients	%
Stearyl alcohol	0.5
Hardened palm oil	3
Liquid paraffin	35
Cholesteryl/behenyl/octyldodecyl Lauroyl glutamate	2
Dipropylene glycol	6
PEG 400	4
Sorption sesquioleate	1.6
POE(20)oleyl alcohol ether	2.5
Carboxyvinyl polymer (1%)	15
Potassium Hydroxide	0.1
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Add the humectants and chelating agent to the purified water and heat to 70°C (water phase). Heat the oil component ingredients together to make solution, add the surfactants, preservative, and perfume, and keep heating to 70°C. Add this mixture to the water phase.

* q.s., quantum satis (in sufficient amount).

Formula 9: Facial Cleansing Cream (with Arginine to Neutralize Carbomer)

Ingredients	%
Stearic acid	2
Cetyl alcohol	3
Petrolatum	10
Liquid paraffin	38
Isopropyl myristate	10
Propylene glycol	5
Glycerin monostearate	2.5
POE(20)sorbitan monostearate	2.5
Arginine	0.3
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Add the humectant and alkali to the purified water phase. After heating the oil component ingredients together to make a solution, add the surfactants, preservatives, antioxidant, and perfume and keep heating to 70°C. Gradually add this to the water phase.

* q.s., quantum satis (in sufficient amount).

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Formula 10: Gel-Type Makeup Remover

Ingredients	%
(A) Glyceryl trictanoate	56.4
Cetyl octanoate	5.0
POE(25)octyldodecyl ether	16.0
Butyl paraben	0.2
(B) POE(10)methyl glucoside	4.0
Glycerin	1.7
Sorbitol (70%)	9.0
Water	7.3
Methyl paraben	0.1
(C) Perfume	0.3

Procedure: Mix (A) components at 80°C to dissolve completely. Mix (B) components separately and dissolve at 80°C completely. Add (A) to (B) with paddle stirring. Gradually cool down while stirring. Add perfume at 55°C; mixture turns to gel at 50 to 45°C.

Formula 11 Body Wash Based on LES

Ingredients	%
Sodium laureth sulfate	40.0
Cocoamidopropylbetain	10.0
Sodium cocoyl glutamate	3.0
Laulamide DEA	3.0
Sodium PCA	2.0
Glycerin	3.0
PEG(150)distearate	0.1
Water	q.s.* to 100
Perfume	q.s.
Preservative	q.s.

Procedure: Add all the ingredients together and heat to dissolve with stirring. Cool down to room temperature.

* q.s., quantum satis (in sufficient amount).

CONCLUSION

A hygiene consumer product must make skin clean and refreshed. There are industrial or heavy-duty cleansers available for skin, often with sufficient mildness but nothing especially elegant. With skin cleansing bars, skin cleansing liquids are the products categorized as cosmetics and personal care. Skin cleansing liquids are more and more chosen by consumers with highly perspective or emotional motives, which is why skin cleansing liquids must carry concepts that appeal to consumers' trendy desires. Cosmetic scientists will continue challenging such difficult tasks to make innovative products, with the encouraging findings that the mental effects of cosmetics use improves quality of life.

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Emulsion-Based Skincare Products: Formulating and Measuring Their Moisturizing Benefits

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AN OVERVIEW OF EMULSION-BASED SKINCARE PRODUCTS

A variety of skincare products exist in today's marketplace. They fulfill a variety of functions by either acting directly on the skin (e.g., moisturizers) or being a cosmetically elegant vehicle for the delivery of specific active ingredients (e.g., sunscreens or antipuretic or antiacne medicaments). In general, these products may be categorized into three functional groups:

- *Drugs*. To Prevent or ameliorate diseases by altering the structure and/or function of the body.
- *Cosmetics*. To beautify and improve the feeling or sensory aspects of normal and/or nondiseased skin. Dry skin would be included in this category.
- *Cosmeceuticals*. An intermediate classification for cosmetic products that may enhance the function of skin. Currently, this category is not recognized by the United States Food and Drug Administration (FDA) [1].

There is a similar classification in the European Union.

The three product groups can also be classified by their physical properties. Most common forms of skincare products are emulsions. Emulsions are mixtures of two insoluble materials that are stabilized against separation. An example is oil and water, which will not mix unless an intermediate emulsifier is incorporated into the mixture.

Different Types of Emulsions

Emulsifiers can act as solubilizers as well as spreading or dispersing agents. Correct use of emulsifiers permits the formulation of homogeneous mixtures, dispersions or emulsions of oily, waxy substances with water. Solids may be dispersed in liquids or insoluble liquids within other liquids. Greasy anhydrous ointments can be designed to be more washable. These types of properties may be achieved by appropriate selection of emulsifiers, active ingredient, and other compatible ingredients in the vehicle.

Emulsions may be water-in-oil (w/o), oil-in-water (o/w), aqueous gel, and silicone in water. Other products may be formulated as semisolids containing oleaginous ingredi-

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TABLE 1 Examples of Vehicle Types

Type of emulsion	Examples
w/o	Cold creams, cleansing, evening, or overnight creams
o/w	Moisturizers, hand and body lotions
Oleaginous	Petrolatum
Water-soluble	Polyethylene glycol-based ointments
Aqueous gels	Lubricating jelly; gelling agents such as carbomers, hydroxyethylcellulose, and magnesium aluminum silicate may be used in the formulation
Absorption bases	Hydrophilic petrolatum; these vehicles may contain raw materials able to function as w/o emulsifiers permitting large quantities of water to be incorporated as emulsified droplets

Source: Ref. 3.

ents, absorption bases, and water-soluble types containing polyethylene glycol. Recently, there has been a growing interest in water-in-oil-in-water (w/o/w), also referred to as multiple emulsions.

Oil-in-water emulsions are the most commonly formulated. These types of emulsions tend to feel less greasy and have a lower cost than other forms because of a higher water content. Water-in-oil (w/o) emulsions have historically been less popular because of a characteristic greasy, oily feel on application to skin. However, the development of newer emulsifiers has enabled a skilled formulator to develop w/o emulsions of a lighter texture. Silicone formulation aids may also be used to form stable water in silicone (w/Si) or w/o emulsions. These silicones are polymeric surface active agents with long bond lengths and wide bond angles. This provides for free rotation of functional groups permitting formulation of w/o and W/Si emulsions with exceptional elegance and good coverage when applied to the skin [2]. This enables formulation of stable emulsions with medium to low viscosity. These different chemical-type emulsions are commonly referred to as vehicles when ''cosmetic'' active or drug active ingredients are incorporated into them (see Table 1).

Not all emulsifiers behave in the same way. Properties of the emulsifier will determine the emulsion type. Their compatibility with oils having different polarities is also a critical concern. Emulsifiers will impact the desired sensory properties of the product such as color, odor, and desired viscosity (e.g., lotion or cream consistency).

Different Types of Emulsifiers

Emulsifying agents, which are surface active agents (surfactants), are available in a wide range of chemical types. These include nonionic, hydrophilic, lipophilic, ethoxylated, and nonethoxylated. A recent trend is to lower or even eliminate surfactants in an effort to minimize the already low irritation potential of the formulation. It is possible to formulate emulsifier-free emulsions with cross-linked acrylic polymer derivatives. These materials are hydrophilic polymers that are hydrophobically modified by adding an alkylic chain. These molecules, known as polymeric emulsifiers provide additional formulation options for new product development [4].

FORMULATING HYDRATING CREAMS AND LOTIONS

The continuing development of biophysical instrumentation and test techniques has enabled formulation of highly effective skincare formulations. Formulators now have several

options with respect to formulating new products. When initiating formulation development, it is important to understand project/product requirements, type of product(s), performance and aesthetic needs, formulation cost constraints, packaging needs, product claims, and formulation safety. To what part of the body will the formulation be applied? What time of day, morning or overnight? Will makeup be applied over the product, and will clothing come into contact with the product? Will the targeted consumer apply a fragrance to the body after application of the product, and if so, will the fragrances conflict? Once these requirements are defined, the formulator can consider active ingredients, emulsion systems, preservative systems, color, and fragrance.

Emulsions allow the formulating chemist to combine otherwise incompatible ingredients into an effective, commercially desirable cosmetic product. Key in product development is the technique used to select appropriate raw materials. Commonly used emulsifying agents are ionic (anionic or cationic) or nonionic. The function of the emulsifying agent is dependent on the unique chemical structure of the emulsifier. Each emulsifier has a hydrophilic (water-loving) and lipophilic (oil-loving) part. Examples of hydrophilic moieties are polyhydric alcohols and polyethylene chains. Lipophilic parts may be a long hydrocarbon chain such as fatty acids, cyclic hydrocarbons, or combination of both. Nonionic agents may have hydrophilic action generated by hydroxyl groups and ether linkages, such as polyoxyethylene chains. Nonionic emulsifying agents can be neutral or acidic, giving formulators greater flexibility regarding pH requirements for cosmetic actives. Nonionics can be used in formulating w/o- or o/w-type emulsions and will help to mitigate the characteristic oily feel of w/o emulsions.

Thousands of emulsifying agents are available on the world market today. Choosing the best agent is the key responsibility of the formulator. Many agents used in the cosmetic and drug industry are classified by a system known as Hydrophilic-Lipophilic Balance (HLB) number. This system, developed in the mid-1950s, is a useful starting point in emulsifier selection. In this system, each surfactant having a specific HLB number is used to emulsify an oil phase having an HLB required for a stable emulsion. Using an emulsifier or combination of emulsifiers matching the required HLB of the oil phase will form a stable emulsion. Limitations to this method include incomplete data for required HLBs of many cosmetic ingredients. Combinations of or single emulsifying agents giving the appropriate theoretical HLB may not be the optimal combination for emulsion stability or product performance. Other emulsifying agents may work better, providing a more elegant formulation with greater efficacy. In addition, theoretical HLB numbers of complex mixtures may not follow a linear additive rule specified in the calculation [2].

In this classification system, emulsifying agents with an HLB of 10 would indicate a more water-soluble agent compared with one having an HLB of 4.

For nonionic detergents of the ester type:

HLB = 20(1-s/a)

s = saponification number of the material

a = acid number of the fatty acid moiety of the product

For ethoxylated esters and ethers when the saponification value is not known:

HLB = E + P/5

E = Percent of ethylene oxide

P = Percent of polyalcohol in the molecule

When the hydrophobic portion contains phenols and monoalcohols without polyalcohols, the equation can be simplified to

$$HLB = E/5$$

Most nonionics fall into this category. Manufacturers who provide HLB values in their product specifications most frequently use the latter formula (see Table 2).

Mixtures of anionic and nonionic agents obtain the best emulsion, whereas mixtures of cationic and nonionic emulsifiers may not be as elegant. Examples of nonionic emulsifiers are alcohol ethoxylates, alkylphenol ethoxylates, block polymers, ethoxylated fatty acids, sorbitan esters, ethoxylated sorbitan esters, and ethoxylated castor oil. The solubility of nonionic surfactants in water can often be used as a guide in approximating the hydrophilic-lipophilic balance and usefulness.

Oil-in-Water Emulsions

Oil-in-water emulsions typically contain 10 to 35% oil phase, and a lower viscosity emulsion may have an oil phase reduced to 5 to 15%. Water in the external phase of the emulsion helps hydrate the stratum corneum of the skin. This is desirable when one desires to incorporate water-soluble active ingredients in the vehicle. Oil droplets in emulsions have a lower density than the phase they are suspended in; to have a stable emulsion it is important to adjust the specific gravity of the oil and water phases as closely as possible. Viscosity of the water phase (external phase) may be increased to impede the upward migration of the oil particles. Addition of waxes to the oil phase will increase specific gravity but have a profound effect on the appearance, texture, and feel on application to skin of the product. Increasing water-phase viscosity is one of the most common approaches. Natural thickeners (alginates, caragenates, xanthan) and cellulosic (carboxymethyl cellulose) gums are used for this purpose.

Carbopol® resin is perhaps the most popular gum thickener for contributing towards emulsion stability, especially at higher temperatures. The addition of a fatty amine to a Carbopol resin will further enhance stability by strengthening the interface of the water

TABLE 2 Relationship Between HLB Range and Water Solubility

Water solubility	HLB Range
No dispensability in water	1–4
Poor dispersion	3–6
Milky dispersion after agitation	6–8
Stable milky dispersion	8–10
Translucent to clear dispersion	10–13
Clear solution	13+

HLB	Application
4–6	w/o emulsifier
7–9	wetting agent
8–18	o/w emulsifier
13–15	detergent
15–18	solublizer

Source: Ref. 5.

and oil phases through partial solubilization into the oil droplets. Electrolytes and cationic materials will have a destabilizing effect on anionic sodium carboxymethyl cellulose and should not be used together. Veegum, an inorganic aluminum silicate material, is also commonly used to thicken emulsions. Carbopol and Veegum may be used together to modify the characteristic draggy feel of Carbopol when used at the higher levels.

Emulsifier blends with HLBs ranging from 7 to 16 are used for forming o/w emulsions. In the blend, the hydrophilic emulsifier should be formulated as the predominate emulsifier to obtain the best emulsion. A popular emulsifier, the glycerol monostearate and polyoxyethylene stearate blend is self-emulsifying and acid-stable. Emulsifiers are called self-emulsifying when an auxiliary anionic or nonionic emulsifier is added for easier emulsification of the formulation. Formulating with self-emulsifying materials containing nonionic emulsifiers permit a wide range of ingredient choice for the formulator, especially with acid systems. In alkaline formulations, polyoxyethylene ether–type emulsifiers are preferred with respect to emulsion stability.

An alternative to glycerol monostearate self-emulsifying emulsifier is Emulsifying Wax, National Formulary (NF). This emulsifier, when used with a fatty alcohol will form viscous liquids to creams depending on the other oil-phase ingredients used. Use levels may vary from 2 to 15%; at lower levels a secondary emulsifier such as the oleths or PEG-glycerides will give good stability. This system is good for stabilizing electrolyte emulsions or when other ionic materials are formulated into the vehicle. Polysorbates are o/w emulsifiers, wetting agents, and solubilizers often used with cetyl or stearyl alcohol at 0.5 to 5.0% to produce o/w emulsions [6].

Water-in-Oil Emulsions

Although less popular than o/w emulsions, these systems may be desirable when greater release of a medicating agent or the perception of greater emolliency is desired. Emulsifiers having an HLB range of 2.5 to 6 are frequently selected. When multiple emulsifiers are used, the predominant one is generally lipophilic with a smaller quantity of a hydrophilic emulsifier. These emulsions typically have a total of 45 to 80% oil phase.

During the last few years, formulators have become interested in more elegant w/o emulsions. This has been achieved by formulating with new emulsifying agents, emollient such as esters, Guerbet alcohols, and silicones. Selection of a suitable emollient depends on ability of the material to spread on skin with low tack, dermal compatibility, and perceived elegance by the user. In achieving this elegance, some researchers suggest a correlation of emollient and molecular weight of the emollients. In these studies, viscosity of w/o creams has correlated with molecular weight of the emollients used in test formulations. High–molecular-weight co-emulsifiers formulated with high–molecular-weight emollients gave more stable w/o emulsions. The polarity of the emollients used was found to be important as well. Emollients or mixtures of emollients with medium polarity gave test lotions the most desirable stability results [7]. Anionic emulsifiers are generally inefficient w/o emulsion stabilizers, because more surface active agents are often needed to stabilize these emulsions. Sorbitan stearates and oleates are effective emulsifiers when used at 0.5 to 5.0% sorbitan isostearates, being branched chain materials, give a very uniform particle size for w/o emulsions.

Multiple Emulsions

Multiple emulsions are of interest to the skincare formulator because of the elegant appearance and less greasy feel of these formulation types. Two types of multiple emulsions are

encountered in skincare: (w/o/w), where the internal and external water phases are separated by oil, and oil-in-water-in-oil (o/w/o) where the water phase separates the two oil phases. The method of preparation for each multiple emulsion type is similar. Benefits of these types of formulations are the claimed sustained release of entrapped materials in the internal phase and separation of various incompatible ingredients in the same formulation.

A suggested technique for forming a w/o/w emulsion is to first create a w/o primary emulsion by combining water as one phase with oil and a lipophilic emulsifier as the second phase in the traditional method. Next, water and a hydrophilic emulsifier are combined with the w/o primary emulsion at room or warm (i.e., 40°C) temperature with mixing forming a w/o/w multiple emulsion. These emulsions typically contain about 18 to 23% oils and 3 to 8% lipophilic emulsifier. The continuous oily phase is stabilized with about 0.5 to 0.8% magnesium sulfate. Water-in-oil emulsifiers have an HLB less than 6 and are frequently nonionic or polymeric. Oil-in-water emulsifiers have an HLB greater than 15 and are ionic with high interfacial activity. For o/w/o multiple emulsions, w/o emulsifiers have an HLB less than 6 with similar properties as a w/o/w w/o emulsifier. Oil-in-water emulsifiers have an HLB greater 15 and are nonionic with lower interfacial activity.

Water-in-Silicone Emulsions

Silicone compounds have evolved into a class of specialty materials used for replacements, substitutes, or enhancers for a variety of organic surface-active agents, resulting in the ability to formulate products with unique properties. Previously, silicone compounds were available as water-insoluble oily materials almost exclusively. Newer silicone compounds such as polyethylene-oxide bases grafted to polydimethylsiloxane hydrophobic polymers, known as dimethicone copolyol emulsifiers, have been developed. These types of emulsifiers permit formation of water-in-cyclomethicone emulsions. Further work in this field led to adding hydrocarbon chains to silicone polyether polymers. This resulted in improved aesthetics to o/s emulsions. Silicone copolyols exhibit high surface activity and function similarly to traditional emulsifiers. Unlike hydrocarbon emulsifiers with higher molecular weights, high–molecular-weight silicone emulsifiers can remain fluid. This gives very stable viscoelastic films at the w/o interface. The ability to make silicones more formulator-friendly has led to development of several new silicone-based surfactants. Both a water-soluble and an oil-soluble portion are needed to make a surface-active molecule. Silicone surfactants substitute or add silicone-based hydrophobicity, creating a distinctive skin feel and other attributes of typical silicones as well as attributes of fatty surfactants. These emulsions may be prepared in a traditional two-phase method, e.g., 2 to 3% w/w of laurylmethicone copolyol in 23% w/w oil phase can be mixed in a separate water phase with electrolyte to form a hydrating cream. [8]

Water-Soluble Ointment Bases

Polyethylene glycol polymers (PEGs) are available in a variety of molecular weights. These materials are water-soluble and do not hydrolyze or support mold growth. For these reasons, PEGs make good bases for washable ointments and can be formulated to have a soft to hard consistency. Polyethylene glycols dissolve in water to form clear solutions. They are also soluble in organic solvents such as mineral and produce formulations that are more substantive on skin. Polyethylene glycol ointment USP is a mixture of polyethylene glycol 3350 and polyethylene glycol 400 heated to 65°C and cooled and mixed until

congealed. To formulate a water-soluble ointment base, water and stearyl alcohol may be incorporated into this base.

Absorption Bases and Petrolatum

Absorption bases can serve as concentrates for w/o emollients, and water may be added to anhydrous absorption bases to form a cream-like consistency. Petrolatum, a component of some absorption bases, has been shown to be absorbed into delipidized skin and to accelerate barrier recovery. Bases can be made washable by addition of a hydrophilic emulsifier. For example, formulation with polysorbate-type emulsifiers with polyoxypropylene fatty ethers will improve washability. These surfactants will form o/w emulsions with rubbing on skin. Water-in-oil petrolatum creams can be formulated by mixing 50 to 55% petrolatum with a sorbitan sesquioleate at 5 to 10%, having an HLB of about 3 to 7 in one phase and water in a second phase. Both phases are blended at 67 to 70°C with mixing.

Other Ingredients

Consumer-perceived benefits of a cream or lotion are often a result of ingredients remaining on the skin after water and other volatile materials have evaporated. Emollients and other skin conditioners are commonly used for this reason. Table 3 lists ingredients frequently used to modify the feel of the emulsion on skin.

Preservative Systems

Most formulations, especially those containing a significant proportion of water, require preservative systems to control microbial growth. Microbial contamination with pathogenic micro-organisms can pose a health risk to the consumer, especially from *Pseudomo-*

TABLE 3 Examples of Moisturizer Ingredients and Their Functions

Ingredient	Use level	Comments
Emollient esters	5–25%	Modify the oily, greasy feel of mineral oil and petrolatum; light to moderate feel on skin
Triglyceride oils	5–30%	Light to heavy feel; often used as spreading agents
Mineral oil/petrolatum	5–70%	Heavy, oily feel; provides occlusion for appropriate vehicles
Silicone oils	0.1–15.0%	Helps to prevent soaping of formulations; improves spread on skin; water-repellent and skin-protective properties
Humectants (glycerin, propylene glycol, sorbitol, polyethylene-glycol)	0.5–15.0%	Moisture-binding properties; helps retard evaporation of water from formulation; viscosity control; impacts body and feel of emulsion
Thickeners (Carbopol, Veegum)	0.1–2.0%	Help obtain viscosity; enhances stability, bodying agents

TABLE 4 Examples of Emulsifiers

Emulsifiers	Properties
Nonionic	
Polyoxyethylene fatty alcohol ethers	Very hydrophobic to slightly hydrophobic
Polyglycol fatty acid esters	Very hydrophobic to slightly hydrophobic
Polyoxyethylene-modified fatty acid esters	Very hydrophilic to slightly hydrophilic
Cholesterol and fatty acid esters	Slightly lipophilic to strongly lipophilic
Glyceryl dilaurate	Secondary emulsifier
Glycol stearate	Secondary emulsifier
Anionic	
Disodium laureth sulfosuccinate	
Sodium dioctyl sulfosuccinate	
Alcohol ether sulfate	
Sodium alkylaryl sulfonate	
Cationic	
PEG-Alkyl amines	
Quaternary ammonium salts	
Self-Emulsifying Bases (Form O/W Emulsions)	
PEG-20 stearate and cetearyl alcohol	
Cetearyl alcohol and polysorbate 20	
Glyceryl stearate SE	
Absorption Bases	
Lanolin alcohol and mineral oil and octyldodecanol	
Petrolatum and ozokerite and mineral oil	

nas infection in the eyes, or from an existing illness. Microbial contamination may cause an emulsion to separate and/or form off-odors. Contaminated products are also subject to recall, which is undesirable from a commercial view point.

Preservatives can be divided into two groups: formaldehyde donors and those that cannot produce formaldehyde. The former group includes DMDM hydantoin, diazolidinyl urea, imidazolidinyl urea, Quaternium 15, and the parabens (esters of p-hydroxybenzoic acid), whereas preservatives such as Kathon GC, phenoxyethanol, and iodopropynyl butylcarbamate work by alternate mechanisms. The formulator is advised to consult appropriate preservative manufacturers to select the optimal preservative system for the emulsion.

ASSESSING MOISTURIZER EFFICACY

Overview of Lotion Function

Hand and body moisturizers have two primary functions. The traditional view of moisturizer function is that they alleviate pre-existing dry skin and prevent its return. Recently, however, reports in the scientific literature have shown that moisturizers can prevent the induction of some signs of irritant contact dermatitis [9,10].

The ability to prevent irritant contact dermatitis has relevance to a significant segment of the population. Epidemiological studies have shown that the prevalence of diagnosable hand and forearm eczema can be as high as 5.4% of the population at any one time, and from 8 to 11% in the preceding year [11,12]. This often has an irritant component especially from repeated exposure to surfactant solutions. Being able to prevent irritation may provide a significant benefit to these individuals, as well as those with dry skin (xerosis), which frequently affects the arms and legs of consumers. Although symptoms are usually less intense than eczema, dry skin probably affects a larger proportion of the population.

Measuring lotions' effects on dryness and primary irritation is key to assessing moisturizer efficacy. Clinical methods have been developed that assess dry skin or its absence via visual scoring by a trained observer and by using biophysical measurements of the skin. Similarly, erythema and stratum corneum barrier damage associated with primary irritation can be measured clinically. Clinical efficacy alone is not sufficient to make a product commercially successful. To appeal to consumers, the lotion must be both efficacious and aesthetically pleasing, i.e., pleasantly scented (or unscented) and have acceptable tactile characteristics during and immediately after application.

Clinical Evaluation of Moisturizer Efficacy

To effectively assess the clinical efficacy of moisturizers, it is important to assess several parameters that relate to skin condition. As lotions can have multiple effects on the skin, using only one modality such as observer scoring may be misleading. For instance, visual observation suggests that Lotion ''E'' is as effective as Lotion ''C'' at reducing skin dryness. Skin that was not treated also showed a reduction in visually scored dryness, indicating the effect of prevailing weather conditions. DeSquame® sticky tape (Cuderm Inc, Dallas, TX) and its quantification by image analysis was able to differentiate between the three test sites. DeSquames show that at day 4 (end of treatment phase), Lotion E did not remove corneocytes from the skin's surface as effectively as Lotion C. At day 7, Lotion E was similar to the ''No product'' site. This suggests that Lotion E may mask the dryness. In contrast, Lotion C caused corneocyte removal at days 4 and 7 (Fig. 1). Visual assessment of skin dryness is useful because it is a direct link to the benefits of moisturization that consumers readily recognize, such as skin flaking, scaling, ashiness, and cracking. These visual assessments should be supplemented with instrumental measures of skin flaking, hydration, surface topography, or elasticity. These instrumental measurements yield a more complete understanding of how moisturizers affect the skin, and can be more easily standardized than observer assessments.

Alleviating Dry Skin

The majority of clinical studies that measure the relief of dry skin after lotion application use either the Kligman regression protocol or a modification [13–17]. Typically these studies start out with dry skin, which is treated for an extended period, followed by a short regression phase during which product usage is discontinued. Kligman originally studied the effect of ingredients and products on the lower legs of 12 to 30 female panelists (Fig. 2). These dry skin sites were treated with an ingredient or lotion (2 mg/cm^2) twice daily for up to 3 weeks. The visual dryness was assessed before treatment (baseline) and at the end of each week. Panelists started with dry skin and the improvement in dryness from baseline was the measure of moisturizing efficacy, or the relief of dryness.

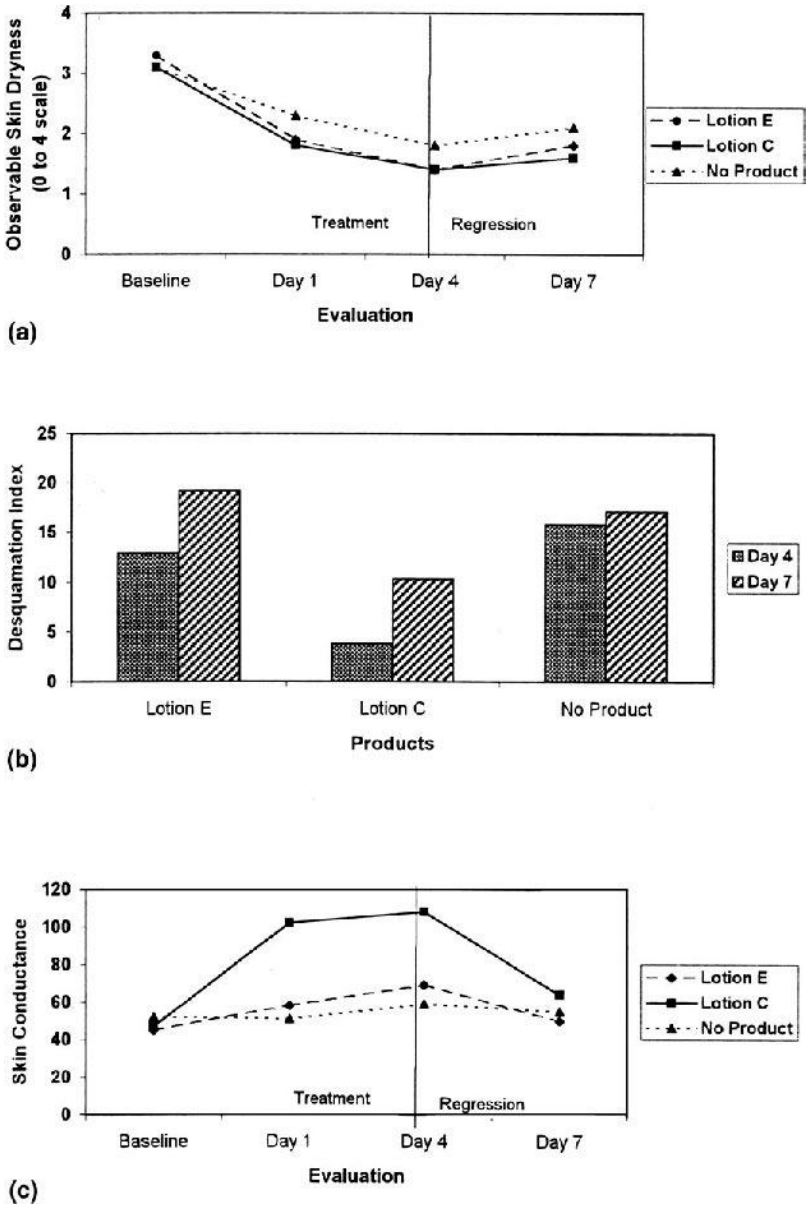
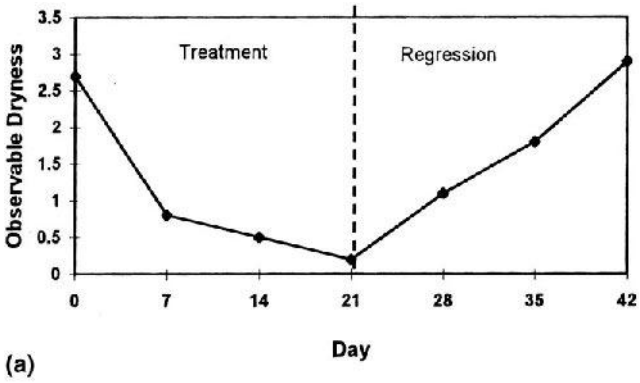


FIGURE 1 Assessing the ability of two commercially available lotions to alleviate skin dryness using a mini-regression test. (a) Assessment by a trained observer; (b) Assessment of Desquamation Index: harvesting of skin flakes with sticky tape, then quantitation using image analysis; and (c) Evaluation of skin hydration using a Skicon 200 to measure conductance.



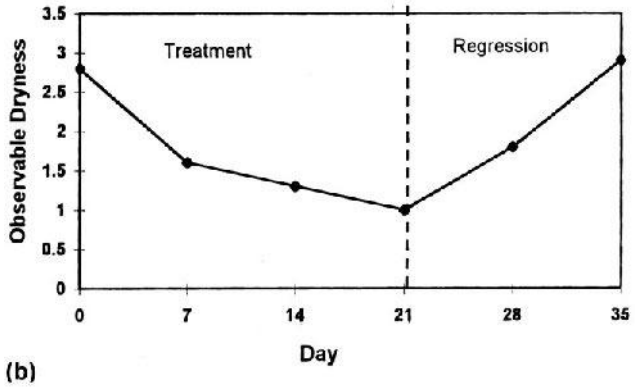


FIGURE 2 Petrolatum is more effective than lanolin in alleviating dry skin and preventing its return. Methodology: Kligman Regression Test (see Ref. 5). Test material is applied to the lower leg daily for 3 wks. After treatment stops, the legs are followed until the skin's condition regresses to its original level of dryness. Regression takes longer for petrolatum (a) than for lanolin (b).

The prevention of the return of dryness is measured during the regression phase immediately after the treatment period. A slow return to baseline is indicative of an efficacious product with lasting effects. Figure 2 shows the data obtained by Kligman for two cosmetic moisturizing ingredients, petrolatum and lanolin. The data clearly show product efficacy during the treatment and regression phases. During the regression, persistent moisturizing effects are shown 21 days after the last treatment with petrolatum but only 2 weeks for lanolin. Using the regression test, Kligman showed that hydrophobic oils—such as mineral oil or olive oil—alone had little ability to alleviate dry skin. The efficacy of these oils was enhanced when they were formulated with hydrophilic materials into cold creams. Kligman's data suggested that the moisturizer's composition could have a greater influence on its efficacy than the number of applications (dosage). He showed a large range in the ability of ingredients to alleviate dryness, but increasing the dosage had limited effects, especially beyond four applications a day.

The Kligman regression protocol has been modified by several groups to meet different assessment needs. For instance, treatment time can be reduced to 5 days to yield a more rapid assessment of moisturizer efficacy [14,16]. The mini-regression assay is able to show clear differences between two marketed moisturizers and between the treated sites and the untreated site were observed (Fig. 3). Additional assessment methods such as conductance and image analysis of DeSquame sticky tapes should be used to confirm observer scored dryness.

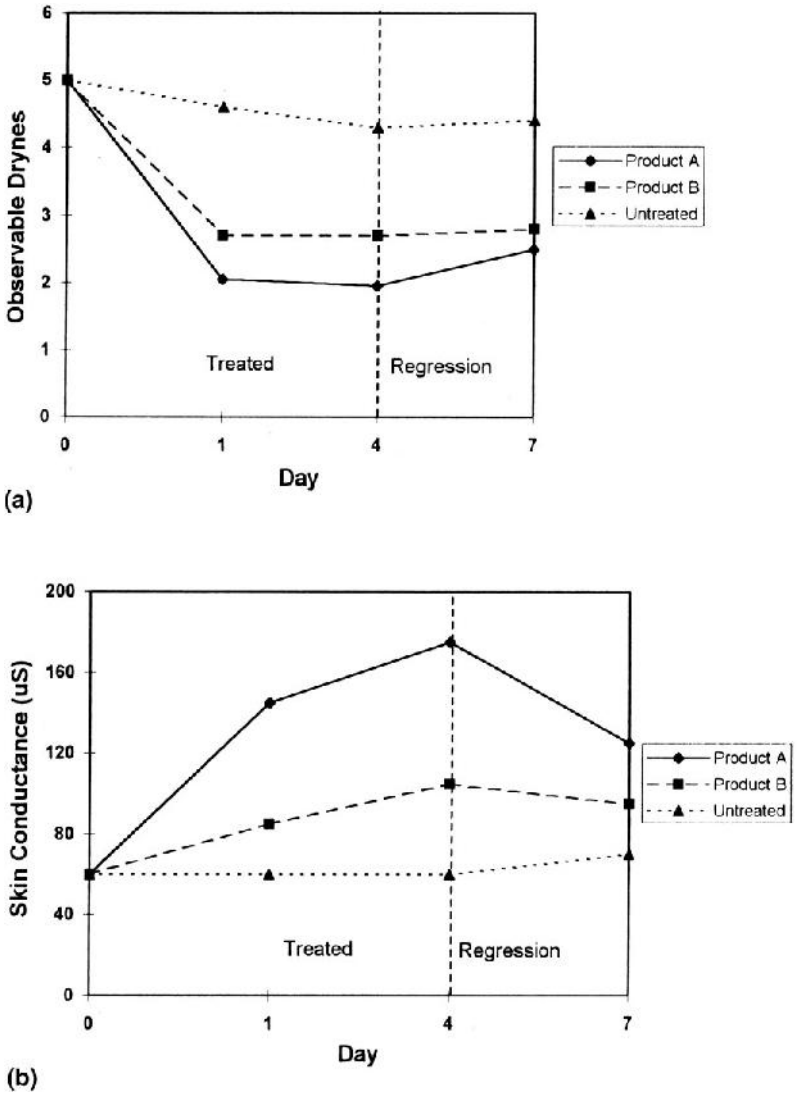
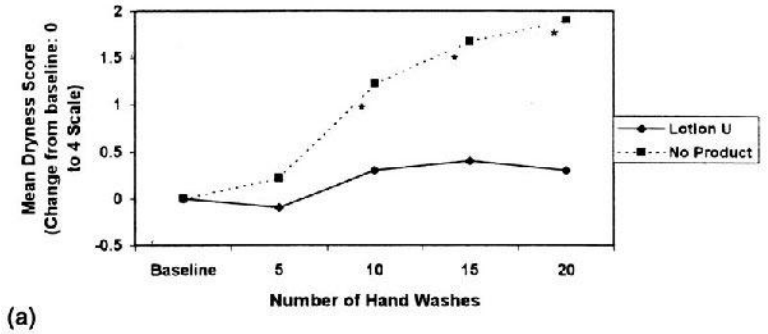
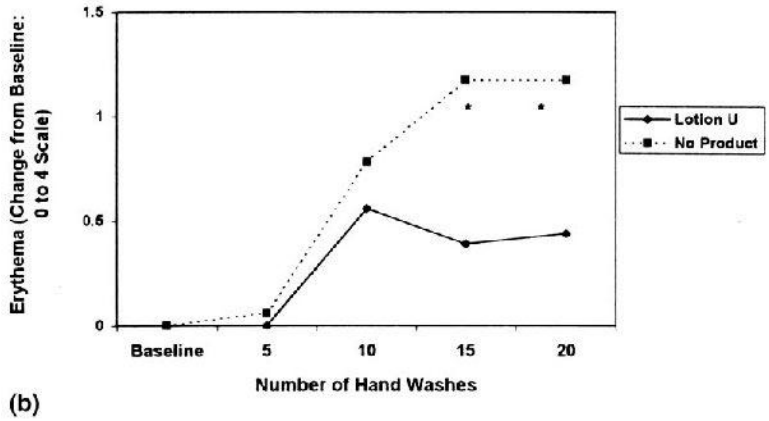


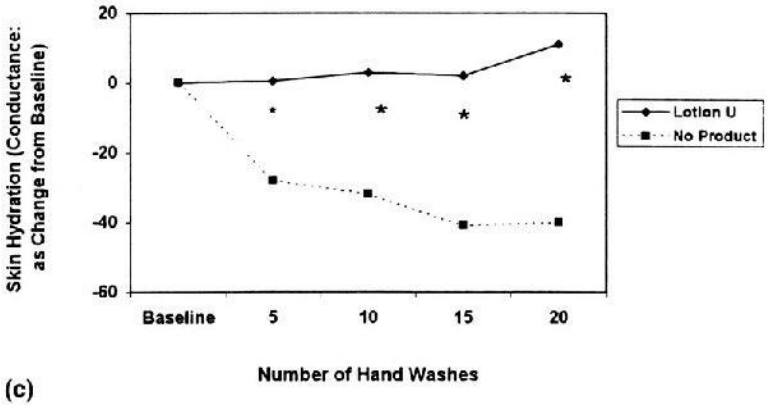
FIGURE 3 Effect of two lotions on: (a) observable skin dryness and (b) skin hydration, as assessed in a mini-regression test. (Data from Ref. 9.)



(a)



(b)



(c)

FIGURE 4 Ability of a commercially available lotion to prevent dryness induced by repeated hand washes with an aqueous detergent solution. (a) Lotion U prevents the induction of skin dryness, as assessed by a trained observer; (b) Lotion U prevents the induction of erythema, as assessed by a trained observer; and (c) Lotion U prevents the reduction of skin hydration, as measured by a Skicon 200 conductance meter.

TABLE 5 Bioengineering Methods Currently Used for Assessing Skin Condition

Methodology	Instruments Available*	Parameters Measured	Limitations/Sources of Error	References
Quantification of scaling/flaking	Desquame/sticky tape followed by comparison to a numerical scale or image analysis	Number and thickness of skin flakes	Reproducible application of tape onto skin; materials that interfere with the tape's adhesion to the skin	19
Skin conductance/ capacitance	Skicon 200 Nova Dermal meter Corneomter DermaLab moisture meter	Skin conductance/capacitance, which is a function of water content	Many moisturizer ingredients can affect conductance, either increasing (salt, glycerin) or decreasing it (mineral oil); should be used in environmentally controlled room	20–23
Evaporimetry	Evaporimeter Tewameter DermaLab TEWL probe	Rate of water loss from the skin; measure of stratum corneum barrier function; a critical parameter in anionic surfactant-induced primary irritation	Measures water regardless of source—water evaporating from a lotion immediately after application or subject's sweating, can cause artifacts; should be used in environmentally controlled room	24–28
Skin elasticity	Dermal Torque meter Cutometer Dermaflex Tactile sensor Ballistometer DermaLab elasticity module Gas Bearing Electrodynometer	Viscoelastic properties of the skin; measurements in plane of skin—Dermal Torque meter; the other instruments measure effects perpendicular to skin	Which skin layers are affected, depth of effect; how to relate the parameters measured to skin condition	29–32

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Blood flow	Laser Doppler Velocimeter	Measures blood flow near skin's surface	Must be positioned exactly at same place at each measurement; due to use of lasers, cannot be used in eye area	33
Skin color	Minolta Chromameter Erythema meter Mexameter DermaSpectrometer	Measurements of skin color—either of whole color space—Minolta Chromameter, or at specific wavelengths; frequently used to measure primary irritation or tanning/hyperpigmentation	Best used when observable color changes occur on skin	34–37
Skin surface texture	(1) Silicone replicas followed by analysis by mechanical or optical profilometry; (2) Optical profilometry of the skin—either directly or from photographs		Silicone replicas can damage skin; data is reported as mathematical parameters which can be difficult to interpret	38

* New instruments that may prove useful in the future include:

1. *Magnetic Resonance Imaging*. Specially adapted instrumentation can visualize whole skin and can delineate epidermis. Currently resolution is not sufficient to assess stratum corneum where skin dryness usually manifests itself. Equipment is large and expensive.
2. *Ultrasound*. Measures thickness of skin layers. Use requires hydrating gel on skin's surface to maintain good contact. Currently resolution is not sufficient to assess stratum corneum where skin dryness usually manifests itself.
3. *Confocal Microscopy*. Capable of visualizing cell patterns near skin's surface. Currently pictures are not sufficiently distinct for routine measurements or assessment of stratum corneum effects.

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The legs are not the only site that can be used in regression testing. The groups working with both Prall and Grove have used the lower arms to assess moisturizer efficacy. The regression phase of the clinical evaluation may be used to examine the persistence of the moisturization efficacy when skin is stressed by winter weather or washing with soap.

Preventing Skin Dryness and Irritation

There are two main approaches to assessing the ability of a lotion to prevent the induction of skin dryness. First, the rate at which dry skin returns after treatment ceases can be assessed from the regression phase of the Kligman regression test. It is evident that many effective moisturizers and moisturizing ingredients do have a residual effect on the skin and will maintain it in good condition for several days, despite prevailing adverse conditions such as winter weather.

An alternate approach to measure the prevention of dry and irritated skin was developed by Highley et al. [18]. In the Highley Hand Wash protocol, the analysis begins with nondry, healthy skin. The panelists wash their hands with a detergent based cleanser for 1 minute, 5 times a day for several days. Lotions are applied to test sites after the first four washes each day. There are control areas of skin that are washed, but to which no moisturizer is applied. The dryness of the hands are assessed by a trained observer and by instrumental methods, before the first wash of the study (baseline) and approximately 1 hour after the last (fifth) wash each day. Results show that ingredients such as petrolatum and commercial lotions can prevent the induction of dry skin, which can be considerable on the untreated skin (Fig. 4). Products and ingredients can be compared by determining the difference between the sites treated with moisturizers and nonmoisturized skin. Although panels as small as 5 have been used, it is more usual to use panels of 10 or more to enable the data to be statistically analyzed.

Hannuksela and Kinnunen [10] also showed that moisturizers could prevent surfactant induced irritation and speed skin's recovery. Arms were washed with dishwashing liquid for 1 minute, twice a day, for 7 days. The investigators evaluated cleanser-induced irritation using transepidermal water loss (TEWL) as a measure of stratum corneum integrity and Laser-Doppler flowmetry to assess blood flow. They showed that moisturizer application could prevent surfactant induced skin damage and accelerate repair compared with no treatment, but were unable to differentiate between products.

The ability of moisturizers to prevent detergent induced skin dryness has important public health implications. In Denmark, dermatitis is the third leading cause leading occupational disease, and it is reasonable to assume that it has a high incidence in other countries. Such dermatitis which is frequently expressed as hand or forearm eczema, can last for many years as patients are exposed to irritants such as cleansers in both the workplace and at home. Professions that involve frequent hand washings, such as healthcare workers, day-care workers, and cleaners and food preparers, are at particular risk. Frequent, effective moisturization may provide a significant preventative benefit.

Instrumental Evaluations of Moisturizer Efficacy

Instrumental evaluation of skin condition should be used to supplement visual assessments in clinical moisturization studies. They will provide a more complete measure of skin condition that visual scoring alone. Conversely, because each instrumental method measures a physical parameter, care must be taken in using the data to interpret the biological

response. For example, conductance is used as a measure of skin hydration, but is reduced when hydrophobic materials such as petrolatum, silicones or mineral oil are applied to the skin. These materials can be effective emmollients and moisturizers, despite the reduction in conductance. Thus multiple bioinstrumental measures should be used simultaneously together with observer scoring, to build a more complete picture of the lotion's effects on the skin.

Table 5 summarizes some of the bioinstrumental methods frequently used in moisturizer studies. This table includes what physical parameters the method assesses, its relationship to skin condition and limitations, and possible artifacts.

Consumer Evaluation of Moisturizer Performance

Consumer testing is a vital tool by which the personal-care industry assesses lotion acceptability. Usage testing provides the most consumer-relevant information available. Not only can moisturization performance be assessed, but information concerning product aesthetics, such as fragrance, appearance, and tactile properties including greasiness and spreadability, is obtained. Such studies yield data on both the intensity of various attributes and whether they are acceptable to the target consumers.

Consumer studies use large panels, frequently hundreds of consumers who use the test moisturizer(s) for a designated period according to their normal routine. Once consumers have tried the product for themselves, they are debriefed with interviews and written questionnaires or in focus groups. Feedback on product attributes such as greasiness, stickiness, and after-feel enables the cosmetic formulator to optimize the products to the needs of the target consumers.

Product Evaluation by a Trained Expert Sensory Panel

Because large-scale consumer testing is time consuming and expensive, product attributes including stickiness, greasiness, and after-feel can be rapidly evaluated by a trained expert sensory panel. One such method is the Skin Feel Spectrum Descriptive Analysis (Skinfeel

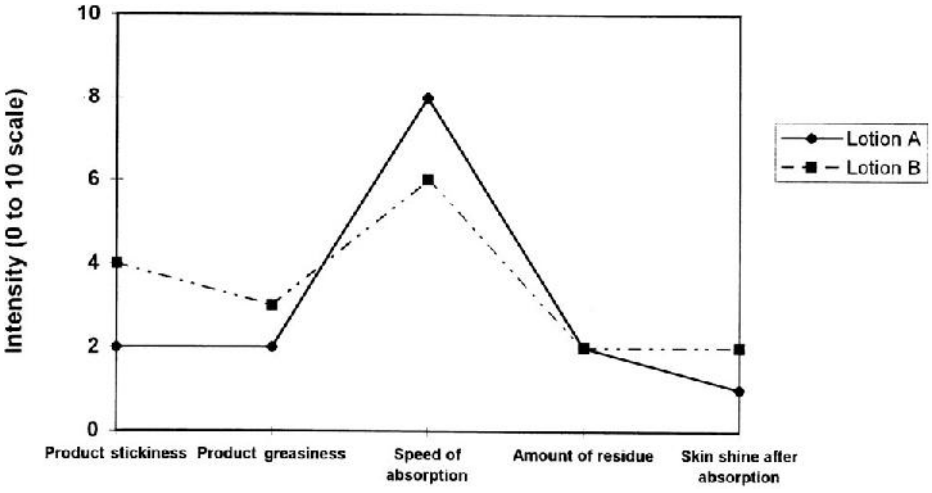

FIGURE 5 Prototypical results for the sensory profile of two lotions.

SDA) used by Meilgaard et al. [19]. This method outlines the product attribute descriptors and scoring scales used to evaluate moisturizers. An expert panel of 8 to 15 persons is required to complete over a 100 hours of training to ensure they can reproducibly quantify moisturizer and skin attributes such as spreadibility, amount of residue, and absorbency, which are scored using a 0-to-10 scale (Fig. 5.) Once the panel is calibrated, they can be used to evaluate competitors' products and optimize new formulas. Validation requires that the sensory panel correctly predict the intensity of attributes from a large-scale consumer test. It should be noted that sensory panels measure attribute intensity only, and do not assess the preference of distinct types of consumer for different products.

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Anticellulite Products and Treatments

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INTRODUCTION

Cellulite is a localized condition of subcutaneous fat and connective tissues with the typical visual appearance of the orange-peel look of the skin. Cellulite, or more correctly local lipodystrophy affects mostly women and rarely men, and is considered to be a common aesthetic problem for many women. Cellulite generally appears after puberty and worsens with age. There are preferential places of cellulite: buttocks, thighs, upper part of the arms, knees and more rarely the lower parts of the legs and the back of the neck (Fig. 1). The aims of this chapter are to describe (1) the histological, physiological, and biochemical characteristics of subcutaneous lipodystrophy, (2) the different objective evaluation methods of lipodystrophy, and (3) the different anticellulite treatments available and their efficacy.

CLINICAL VISUAL AND TACTILE SYMPTOMS OF CELLULITE

Upon clinical examination of cellulite, the following symptoms of lipodystrophy can be noticed [1–11].

- Presence of orange-peel skin upon normal visual examination and after pinching of the skin.
- Deep palpation of the skin reveals differences in the mobility of fat tissue: presence of micro- and macronodules and fibrosclerosis.
- Irregularities in skin-surface temperature: touching the skin reveals the presence of cold spots.
- Sometimes presence of painful subcutaneous nodules through deep palpation.

There are different stages in the evolution of cellulite with age. It is difficult to detect cellulite by visual examination and palpation at the first stages: orange-peel skin is not permanently present, and is only visible after pinching the skin.

The clinical symptoms are clearly more visible at later stages of cellulite: permanent orange peel, colder skin areas, diminution in mobility of fat tissue upon palpation and increased skin sensibility.

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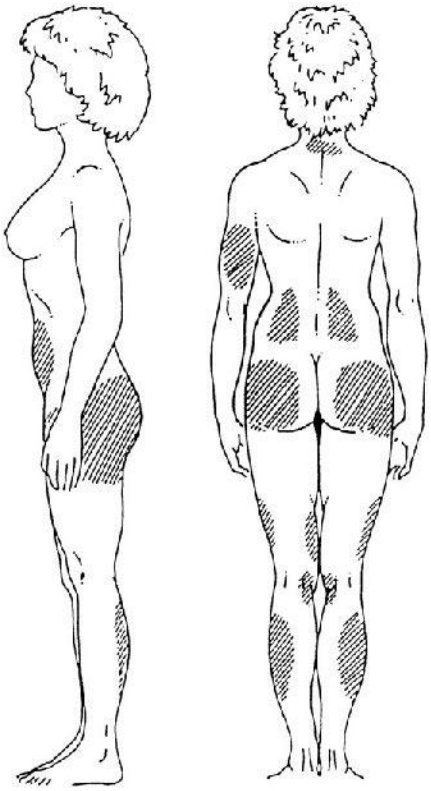

FIGURE 1 Preferential localizations of subcutaneous lipodystrophy in women.

As a consequence of this, there is a need for sensitive noninvasive bioengineering methods for the detection and evaluation of the degree of cellulite at early stages, and for the objective evaluation of the efficacy of various cosmetic treatments [12,13].

CAUSES OF CELLULITE

Cellulite is probably a multicausal condition and many hypotheses have been proposed regarding the origin of fat lipodystrophy [1–11].

- Sexual differentiation in the histological distribution of subcutaneous fat lobules in women and in men. The differences between the sexes can be found in the structure of the septal connective-fat tissue: the fat lobules in women are larger and more rectangular, whereas men have diagonal septa and smaller lobules. Because cellulite is widely present in women, some investigators consider cellulite to be a secondary sexual characteristic.
- Alterations in the microvascular network (mostly venous blood circulation) in the fat tissue: venous stasis.
- Presence of plasmatic exudate in the subcutaneous connective tissue: noninflammatory edema.

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- Alterations in the reticular fibrillar network surrounding the blood vessels and adipocytes: fibrosclerosis. Stiffening and decrease in mobility of fibers.
- Alterations in the interstitial fundamental substance (proteoglycans).
- Modifications and hypertrophy of adipose tissues. Although cellulite is not always synonymous with obesity (skinny persons can sometimes present symptoms of cellulite), there is a relation between cellulite and hypertrophy of fat tissues. Formation of, first, micronodules and, later, of macronodules in adipose tissues.

The combined effect of modifications and hypertrophy of adipose tissues, alterations in the fibrillar connective tissue, and alterations in the microvascular venous network always leads to the presence of cellulite.

HISTOLOGICAL DESCRIPTION OF THE DIFFERENT STAGES OF LIPODYSTROPHY OF FAT TISSUES

Skin-surface contact thermographic pictures using thermographic foils give an indication of the degree of cellulite, because the skin-surface temperature correlates to some extent with the clinical symptoms of cellulite. Based on these thermographic patterns and clinical symptoms, Curri and coworkers proposed a classification of cellulite in four stages [4,5,14,15]. In normal adipose tissues, a fine mesh of blood vessels and lymph vessels supplies this adipose tissue with the necessary nutrients and oxygen, and takes care of the removal of metabolized products. In the early stage of cellulite (stage I), the capillary blood-vessel walls become more permeable, causing leakage of blood plasma from the vessels in between the adipose tissues, which cause an edema in the adipose tissues. In addition, probably, problems with the lymph circulation hampers removal of accumulating fluids. The aggregation of adipose cells and the amplification of the fibrillar network of collagen bundles interconnecting the adipose cells hampers blood circulation leading to some hemostase (stage II).

Adipose cells aggregate into ''micronodules'' surrounded by less-mobile collagen fibers (stage III). The size of these ''micronodules'' is on the order of millimeters. Finally, many of these ''micronodules'' aggregate into ''macronodules'' with larger sizes (2–20 mm) (stage IV). As nerves may be squeezed by this larger nodules, persons with severe cellulite often suffer from sensitive to painful skin.

Stages I, II, and III of lipodystrophy are not considered clinically as pathological symptoms but more as aesthetic–cosmetic problems of the skin. Only in stage IV are clinical symptoms such as an increased skin sensitivity, extensive fibrosclerosis of connective tissue and very advanced edema considered to be light pathology symptoms. Furthermore it is believed that the first stages are more or less reversible, whereas the latter stages are irreversible. However, it must be said that the microscopic description of cellulite and the different stages in the evolution of lipodystrophy, as described by Curri, are not universally accepted [16,17].

OBJECTIVE EVALUATION OF THE SYMPTOMS OF LIPODYSTROPHY OF THE SKIN

In addition to the visual and tactile clinical evaluations of the symptoms of cellulite, various noninvasive bioengineering measurements may be used [11,12].

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However, the clinical evaluation of cellulite remains important. The clinical evaluation of cellulite is based on visual examination and palpation of the orange-peel skin with a diminution of the mobility of the hypodermis (appearance of nodules of fat tissues and fibrosclerosis), appearance of differences in skin surface and temperature and patient complaints of hypersensitive skin and pain.

The different noninvasive bioengineering measurements are as follows:

- Contact skin-surface thermographic measurements using liquid crystals
- Non–contact skin-surface thermography of skin surface using infrared video camera
- Microblood circulation using Laser Doppler image analysis
- Ultrasonic skin analysis of skin density
- Measurement of thickness of the hypodermis at 10 to 14 MHz
- Measurement of the surface of the interface between dermis and hypodermis at 20 MHz
- Skin-surface topographical imaging
- Macroscopic normal and digitalized photographic pictures of the skin surface

DESCRIPTION AND VALIDATION OF THE DIFFERENT BIOENGINEERING MEASUREMENTS USED FOR OBJECTIVE EVALUATION OF CELLULITE

Skin-Surface Contact Thermography Using Encapsulated Liquid Crystals in the Evaluation of Cellulite [14,15,18]

The principle of the encapsulated cholesteric liquid-crystal contact thermography consists of different color plates presenting a pattern of different colors corresponding to a temperature range of about 3°C. Application of the color sheet with uniform pressure on the skin surface and photographic recording of the thermographic pattern using a Polaroid camera are carried out. A qualitative global analysis of the thermographic pictures in relation with the different stages of cellulite can be made. A cellulite-free skin-surface thermography shows a uniform color pattern without hypothermic and hyperthermic areas. A cellulite skin-surface thermography shows a nonuniform color pattern with the presence of hypothermic (cold spots) and hyperthermic (warm spots) areas. Quantitative analysis of the thermographic pictures can also be carried out by image analysis. Computerized color-image analysis gives the mean temperature of the thermogram and the number and percent area of the hypo- and hyperthermic areas, respectively, present on a well-defined skin area. As experimentally observed, an anticellulite treatment will induce an increase of the mean temperature of the skin surface and a decrease of the percent hypothermic zones (with a concomitant increase of the percent hyperthermic zones).

This method is rapid, easy to use and inexpensive for screening subjects for cellulite and for confirmation of the clinical diagnosis. However, considering the low accuracy and reproducibility of the photographic pictures, quantitative image analysis of the thermograms is very difficult. One observes large interindividual variations in skin-surface temperature (a large number of subjects is necessary in a study) and long acclimatization time for temperature equilibrium of the skin (influence of external temperature). This method remains a qualitative test of cellulite at different stages.

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Validation of Skin-Surface Thermography Using Infrared Thermal Imaging System in the Evaluation of Cellulite

Using an infrared video camera, an infrared thermal image of the skin surface is obtained in a noninvasive manner. The thermographic picture can be quantitatively analyzed [12,13].

In the validation of this infrared video-imaging technique the same problems are encountered as with the contact thermography with liquid crystals such as large interindividual variations in skin-surface temperature, long acclimatization time for temperature equilibrium of the skin, and influence of external temperature.

Validation of Laser Doppler Imaging System in the Evaluation of Cellulite

Using a Laser Doppler Perfusion Imager, an image of the superficial blood circulation can be obtained [12,13]. The He–Ne laser light emitting at 633 nm has a penetration power in the skin of only about 300 μm. This instrument measures the superficial blood flux of the skin (papillary dermis). The blood perfusion of the deeper layers of the skin, such as the hypodermis, cannot be measured with this technique. However, a high correlation is obtained between the skin-surface thermographic pictures and the Laser Doppler imaging system when studying skin with cellulite. However, the measurements are delicate (long measuring times during which the volunteer must remain immobile).

Validation of the Ultrasonic Imaging of the Skin in the Evaluation of Cellulite

A promising method appears to be high-frequency ultrasound C-mode imaging (10–20 MHz). This noninvasive method has been frequently used both clinically and in research for studying the epidermis, dermis and hypodermis [19–21].

Different investigators have used the technique of measuring the thickness of the subcutaneous fatty layer using ultrasound imaging at 10 to 14 MHz [22–26]; however, the determination of the echographic border line between subcutaneous fat and connective tissues/muscles is very delicate. As a consequence, the determination of the mean thickness of the hypodermis is not very accurate. Measurement of the interface between the dermis and the subcutaneous fat using ultrasound imaging at 29 MHz is possible [27,28]. The interface between the echogenic epidermis–dermis and the hypoechoic subcutaneous fat is clearly visible, allowing measurements of skin thickness and of the surface of this border.

Quantification of the surface of the interface between the dermis and the hypodermis (fat tissue) is possible [27,28]. In normal cellulite-free skin, the interface between the dermis and the fat tissue is irregular but rather smooth. In skin with cellulite, this surface is not smooth and very irregular. The surface of this interface is quantified and can be used as a measure of the degree of cellulite.

Measurement of Skin-Surface Topography

Cellulite skin surface presents irregularities (orange-peel skin) and in principle the classic skin-surface roughness measurements, which are used in cosmetic research, can be applied for studying cellulite. It involves stylus profilometry, image analysis by shadow method

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and optical focus laser profilometry [29–31]. These measurements are carried out on soft or hard skin replicas of general small size (2–3 cm^2 area) and have a limited vertical range of roughness capability (maximum 400–500 μm). These techniques are well suited for the determination of the microrelief of the skin surface (50–200 μm) but not for assessing the skin surface with cellulite. The skin-surface topography of skin with cellulite can be evaluated using photographic pictures, skin-surface contour measurements, and other optical measurements such as Fringe Projection Topography [28,32–34].

The macrorelief of the skin surface can also be evaluated using an optical triangular Laser profilometry. This method involves measurements on large-size soft replicas with an extended vertical range of skin irregularities (up to 8–10 mm). Quantification of the skin surface macrorelief involves a computerized correction for the curvature of the skin surface with cellulite [32].

Normal and Digitalized Macroscopic Photographic Pictures of the Skin Surface

The macrorelief of the skin can be evaluated by taking photographic pictures (classic or digitalized) under standardized experimental conditions. These photographic pictures are then visually graded in a double-blind manner by expert oberservers for the intensity of cellulite (photograding with numerical scales). It has been known for many years that the standardization of classic photographic pictures is not easy, considering the problems of reproducibility of the processing of color film. In addition double-blind visual scoring of these photographic pictures remain subjective. However, some investigators have used photographic pictures in order to evaluate the efficacy of anticellulite treatments [35].

The use of digitalized photographic pictures is aimed to overcome the standardization problems of classic processing of the color film. Macroscopic digitalized photographic pictures (with the use of a CCD camera) of the external part of the thighs were taken after application of a gripping system around the thigh in order to increase the orange-peel look of the skin. The degree of cellulite was photograded by experts using a 0 to 7 scale of intensity of cellulite [24,36].

TREATMENTS OF CELLULITE

Different anticellulite treatments are available [12,13], such as manual and electromechanical deep massage (''pincer-rouler''), manual lymph drainage, sequential pneumatic compression (lymph drainage), electrolipolysis, mesotherapy, and topical applications of dermatocosmetic products with and without massage.

Physiotherapeutic treatments such as deep massage and manual and pneumatic lymph drainage, stimulate the blood and the lymph microcirculation and increase the removal of extra fluid in the adipose tissues. In addition, these massage techniques will retard the further development of fibrosclerosis and the aggregation of fat cells in nodules. These physiotherapeutic treatments are generally combined with the topical use of anticellulite dermatocosmetic products (during massage or pre- or postmassage).

Electrolipolysis and mesotherapy are invasive medical treatments of cellulite; these techniques will not be described in this chapter.

Various topical dermatocosmetic products have been used, generally with massage, in the treatment of cellulite and/or as slimming for many years [37]. A list of the ''active''

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TABLE 1 List of Dermatocosmetic Ingredients Most Frequently Used in Anticellulite Treatments

Caffeine
Barley (*Hordeum vulgare*)
Butcher's broom (*Ruscus aculeatus*)
Centella (*Centella asiatica*)
Cola (*Cola nitida*)
Gingko (*Gingko biloba*)
Green tea (*Thea sinensis*)
Horse chestnut (*Aesculus hippocastanum*)
Horsetail (*Equisetum arvensis*)
Ivy (*Hedera helix*)
Thistle (*Cnicus benedictus*)
Witch hazel (*Hamamelis virginiana*)
Algae
Fucus vesiculosus, Garcinia combogia, Laminaria flexicaulis, and *Ascophyllum nodosum*

ingredients mostly used for this purpose [37–38] is given in Table 1. The main purpose of these topical slimming/anticellulite products is to influence the metabolism of the adipocytes. In vitro metabolism studies on fat cells have shown that it is possible to slow down the lipogenesis and to stimulate the lipolysis in different ways [37,39]:

- Diminution of the uptake of glucose by interfering with the membrane-bound glucose transport proteins (e.g., rutin plant flavonoids, Ruta graveolens)
- Stimulation of the hydrolysis of the triglycerides by blocking the enzyme (fosfodiesterase) that hydrolyzes cAMP (e.g., caffeine) and by binding of the membrane-bound beta receptors (Gingko biloba and horse chestnut)
- Inhibition of lipogenesis by binding with the alpha receptors (gingko biloba and horse chestnut).

In addition some of these slimming/anticellulite ingredients present properties of stimulation of the blood and lymph circulation and further inhibit the fibrosclerosis of the fat surrounding collagen matrix. A few examples of typical slimming ingredients are:

- Ivy (*Hedera helix*) stimulation of the lymph circulation
- Butcher's broom (*Ruscus aculeatus*) vasoconstrictive and anti-inflammatory properties
- Horse chestnut (*Aesculus hippocastanum*) and witch hazel (*Hamamelis virginiana*) are also used for their supposed beneficial effects on venous circulation
- Various algae species, such as *Fucus vesiculosus, Laminaria flexicaulis*, and *Ascophyllum nodosum*, are incorporated in anticellulite cosmetic preparations for their hypothetical beneficial effect on the skin surface.

CRITICAL REVIEW OF CLINICAL ANTICELLULITE STUDIES

Very few anticellulite studies that were performed under well-controlled experimental conditions (i.e., double-blind, vehicle-controlled) and under medical and paramedical supervision are published.

A clinical study on 27 female subjects with cellulite at the thighs involving a daily massage with a commercial preparation containing caffeine, *Hedera helix* and Butcher's broom (massage carried out by the subjects themselves) showed after 1 month a significant diminution of the thickness of subcutaneous fat tissues as examined by ultrasonic echography, skinfold and by visual and tactile examination [40].

However, these findings were not confirmed by a similar clinical study carried out on 15 female subjects with cellulite at the thighs using the same cosmetic product in a double-blind vehicle-controlled manner [41]. After 21 days treatment, no significant modifications were observed in skin-surface color (Chromameter), superficial blood flow (Laser Doppler), skin-surface topography (profilometry on skin replicas), and in anthropometric parameters such as thigh perimeter and skinfold.

A double-blind vehicle-controlled clinical study on 15 female volunteers with moderate cellulite at the upper and middle thighs, involving a topical application of a commercial preparation containing mixture of algaes (a 30-min topical application under plastic foil with a thermal electrical blanket) has been published. This typical balneotherapeutic treatment was carried out every 3 days during 3 consecutive weeks under the medical and physiotherapeutic control [42]. A significant decrease in thigh perimeter was observed equally for the vehicle alone and the vehicle with the ''active'' algaes extract, probably because of the combined effect of plastic foil occlusion and heating with the blanket. No significant modifications were observed in skin-surface color (Chromameter), and superficial blood flow (Laser Doppler) after 3 weeks treatment with the vehicle and the algaes extract.

A double-blind vehicle-controlled clinical study was carried out on 15 female volunteers with cellulite at the upper and middle thighs, involving a manual massage with a cream containing various plant extracts every 3 days during 3 consecutive weeks (massage carried out by a physiotherapist), showed after this period of treatment a significant diminution of the extent of cellulite as examined by skin-surface thermography using liquid crystal sheets [43]. However, no significant differences were obtained between massage treatment with the vehicle containing ''active'' plant extracts (e.g., ivy, thyme, centella, nettle, horse chesnut, bark, witch hazel) and with the placebo vehicle alone. Recently, a clinical anticellulite study was published consisting of a massage treatment with the help of a hand-held electromechanical apparatus consisting of a low-pressure chamber (200 mBar) and two rollers. The duration of the treatment was 3 months, (three times a week, during 15 minutes on each upper leg (thigh region), on 19 healthy female volunteers with moderate symptoms of cellulite on the thighs. The efficay of this treatment was evaluated using ultrasound measurements at 20 MHz [27].

This electromechanical treatment induces a significant smoothening of the dermis/hypodermis surface after 1, 2, and 3 months treatment. After the treatment was stopped, the dermis/hypodermis surface gradually increased again, which indicates that the effect of this massage on the skin is not permanent.

This modification of the interface structure (smoothening) after this mechanical treatment of the skin can be interpreted as the result of the diminution of the venous stasis (positive effect on the venous microcirculation) and an improvement also of the lymph circulation and prevention of further fibrosclerosis and of aggregation of fat micro- and macronodules. Similar positive improvements as measured by ultrasound echography were obtained after comparable manual-massage treatments and lymph drainage with pressotherapy of cellulite skin located at the thighs [44].

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A clinical study was carried out on 55 healthy female volunteers with lipodystrophy on the hips and thighs. The topical anticellulite treatment (massage with a cream containing caffeine, rutin, horse chestnut, and gingko) consisted of a twice daily light massage during 28 days of both legs [40]. The intensity of cellulite was rated by visual skin-surface roughness scoring, skin thickness using a caliper, and the thickness of subcutaneous fat layer. Significant decreases were observed for these 3 experimental parameters after 28 days treatment.

In a double-blind placebo-controlled clinical study, 30 healthy female volunteers with cellulite on the thighs were twice daily treated during 2 months with a massage product containing various plant extracts [24,25]. The intensity of lipodystrophy was rated using photographic digital pictures and thickness of subcutaneous fat tissue by echography. Significant decreases of the mean score of cellulite intensity (photogradation) and the thickness of subcutaneous fat were observed after 2 months treatment only with the active product.

The critical analysis of the efficiency of the different anticellulite treatments generally indicate that similar if not identical improvements of cellulite were observed with the inert massage product and the massage product with the ''active ingredients.'' These findings substantiate the hypothesis that almost all cellulite improvements are attributable to physiotherapeutic treatments such as massage, lymph drainage or thermal occlusion of the skin, and not to the so-called active anticellulite dermatocosmetic ingredients. As a consequence, we must at present time admit that there are very few cosmetic products with a clearly scientifically proven anticellulite activity.

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Antiwrinkle Products

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INTRODUCTION

Skincare products that affect wrinkles are a reality and are well established in consumer, practitioner, and corporate perspectives. In the broadest definition, ''products'' range from classic and simple cosmetic preparations through vitamins, antioxidants, topical and oral cosmeceutical and pharmaceutical preparations, and even to surgical and laser interventions. Substantiation of product effect ranges from user testimonials through rigorous consumer testing and claim substantiation to classical pharmaceutical trials. Methodologies vary from casual visual and tactile observations to elaborate scoring of specific clinical parameters, and may be enhanced and embellished by use of many sensitive, accurate, reproducible, and validated instrumental techniques. The topic is currently exceptionally rich and expansive.

BACKGROUND

Definition of Wrinkles

Although intuitively obvious, the strict scientific definition of a wrinkle has been somewhat elusive. The consumer easily observes the fine and coarse indented lines of the skin of the face and attributes them to ''aging.'' Although many cultures of the past recognized the damaging effects of sun exposure, only recently, in fact, has science verified the exceptionally strong link between wrinkles and repetitive, chronic, even suberythrogenic ultraviolet irradiation (UVR). Difficult as it is to histologically identify or quantify individual wrinkles, there is much scientific evidence of distinct dermal structural alterations of collagen and elastin that correlate generally with wrinkled skin. Easily conceptualized, the underlying ''weaknesses'' caused by this damaged infrastructure of the skin allows various length and depth infoldings of the skin to occur as a result of repetitive and chronic contractions of the exceptionally varied superficial musculature of facial expression.

Causes of Wrinkles

All scientific evidence points to UVR as the primary cause of wrinkles and other stigmata of ''photoaging,'' and plausible mechanisms of pathogenesis have been elucidated. The

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pleotropic effects of UVR on many different cellular and subcellular systems make it difficult however to establish a strictly linear sequence of events, and it is likely that as in most biological systems, interrelated damage and reparative pathways interplay to establish progression, regression, or equilibrium. It is most helpful in rationalizing the potential of various products for prevention or reversal of wrinkles to understand the underlying molecular events. UVR has long been thought to damage skin partly through its generation of reactive oxygen species and subsequent damage to membrane lipids, various cellular proteins, and DNA. It has recently been shown that, within minutes of suberythrogenic UVB exposure, there is induction in human skin of matrix-degrading metaloproteinase messenger RNAs, their translated proteins, and consequent activities, possibly through a complex process involving signal transduction, transcription factors, and cytokine release [1]. Because the metalloproteinases are a large group of zinc-requiring enzymes that includes collagenases, elastases, and several other other proteinases, their induction, required cofactors, and potential inhibitors are logically of considerable interest in wrinkle causation, prevention, and treatment. Repetitive UVR radiation, presumably by chronic production of matrix damage attributable to this mechanism, would then, if inadequately repaired, lead to dermal ''scars'' and thus wrinkle formation [2]. This theory logically leads to many diverse, possible therapeutic interventions to prevent, stabilize, or reverse photoaging, along with its characteristic and prominent stigmatum of wrinkles.

PREVENTION OF WRINKLES OF PHOTOAGING

Quite apart from specific products, elimination of UVR exposure essentially prevents wrinkles. The effect of lifelong UVR avoidance is easily shown by comparison of the never-exposed skin of the buttocks to even suberythrogenic exposed skin of the face in any individual of types I to III skin. Although wrinkles usually appear only after some years of exposure and are noticeable beginning in the second or third decade of life, other seemingly benign yet insidious signs of photoaging, such as freckling, can be shown even in young children, especially those with light skin and high solar exposure as in Australia [3]. Complete avoidance of UVR is impractical, but avoidance during peak solar flux of midday is frequently possible. Protective hats and clothing are practical and highly desirable. Sunscreens of various types have definite utility in reducing UVR damage. Less well established is the potential role of a host of purported preventatives and treatments such as vitamins and antioxidants, many of which would appear to have a theoretical basis for consideration.

SUBSTANTIATION OF ANTIWRINKLE CLAIMS

Clinical Methodologies

Adequate methodologies of many and varied types now exist to accurately, precisely, reproducibly, and validly examine and quantitate the effects of products on wrinkles [4]. Consumers can judge for themselves if a product meets their needs in wrinkle effacement and, even if objective proof of efficacy is lacking, this positive perception is sometimes sufficient. There is a human tendency to estimate the age of other adults primarily by casual estimate of the degree of wrinkling of the skin of the face and, whether applied to others or the self, this quick estimate is fairly accurate [5].

Consumer-panel testing of many types can be quite rigorous and can quantify effect surprisingly effectively. Global grading of overall appearance is performed by using photographically derived scales of severity, with 0 = none, 1 to 3 = mild, 4 to 6 = moderate, and 7 to 9 = severe photodamage [6]. Specific grading of wrinkling and other parameters using visual analogue scales is simple and reproducible when used alone, and can be combined in very elegant clinical-panel testing [7]. The scale may be continuous, rating from 0 to 100 the condition as absent to severe to balanced, with a score of 0 designating no change from baseline, improvement recorded to the right side of 0 (to a maximum of +50 mm), and worsening recorded to the left side of 0 (to a minimum of 50 mm). Pharmaceutically oriented trials have successfully used similar methodologies with good correlation between subject and investigator evaluations.

Instrumentation

The evolving ''gold standard'' is doubtlessly the area of bioengineering devices. For wrinkling, optical profilometry is the most useful technology and has been widely and successfully used even in large clinical trials [8]. Most commonly, skin replicas of representative areas of wrinkling are evaluated by using image-analysis computer software that reflects wrinkle width and depth [9].

REPRESENTATIVE PRODUCTS FOR WRINKLES

Adequate sun avoidance and sunscreen use are partially prophylactic in the prevention of wrinkle formation. Purely cosmetic and emolliating products may substantially reduce the appearance of wrinkles without change in structure or function of the skin, whereas a number of cosmeceutical and pharmaceutical products fulfill both criteria.

Sunscreens

UVR, even in suberythrogenic doses, is damaging to skin. Prevention of wrinkles, especially in those most genetically predisposed, requires early initiation and lifelong minimization of exposure by sun avoidance and correct use of sunscreens. As multiple wavelengths of UVR are incriminated, it is prudent to use the most complete chemical block that the consumer and physical activity will permit. Substantial block of UVB and UVA is now available in many products, and with the addition of zinc oxide or titanium dioxide, nearly complete block of all damaging wavelengths is achieved.

Cosmetics

Innumerable cosmetic products exist, many of which claim to affect wrinkles and some of which may considerably minimize the appearance of wrinkles. Cosmetics of a simple, occlusive nature may essentially ''fill in'' the wrinkle valleys; others are of a color or substance that changes reflected light from the wrinkle sufficiently to minimize its appearance. Some products currently regulated as cosmetic contain ingredients such as alpha-hydroxy acids or retinol with potential pharmacological actions, and could more logically be designated cosmeceutical. The effect of removing dead, loosely coherent surface keratinocytes, or of stimulating epidermal or dermal processes, may significantly improve the appearance of wrinkles. It is important to remember that, at least in the United States, if

pharmaceutical claims are not stated, the product is legally cosmetic in nature and thus its ingredients and marketing claims may vary considerably and creatively.

Moisturizers

Definite effects on skin appearance, and potentially on structure and function, can be achieved with moisturizers, especially those currently available, many of which are of sophisticated and elegant composition. Improvement in stratum-corneum structure and hydration, and decrease in transepidermal water loss (TEWL) can be quickly achieved and may result in improvement in the appearance of wrinkles.

Alpha- and Beta-Hydroxy Acids

There is substantial evidence that meaningful improvement can be obtained in multiple signs and symptoms of photodamaged skin by the sustained topical application of alpha-hydroxy acids. Specifically, wrinkle effacement has been shown in multiple well-designed and executed clinical trails using clinical and instrumental endpoints [10,11]. Fewer published trials are available that document a similar effect by use of alpha-hydroxy acids, but they nonetheless appear to have utility [12].

Retinoids

Incontrovertible evidence of wrinkle effacement by topical application of retinoids has been extensively shown in numerous large, published clinical trials. Tretinoin (all transretinoic acid) has been the most studied [13,14], but results with topical isotretinoin (13 cis-retinoic acid) appear comparable [15,16]. Retinol, the parent compound, may require metabolism to the purported active transretinoic acid for pharmacological effect and is increasingly incorporated in cosmetic products claiming benefit in wrinkle appearance. Similarly, retinaldehyde has been shown to be active in wrinkle effacement [17]. The most recently marketed retinoids, adapalene and tazorotene, will most likely be studied for similar effect.

Vitamins

Many vitamins, including vitamins A, C, D, and E, are vital in normal metabolic processes, and clinical skin changes resulting from their deficiencies were identified in many cases even in the 1800s. Some of these changes have been shown to be secondary to abnormal keratinization, altered differentiation, or impaired collagen synthesis. Nevertheless, it has been difficult to scientifically confirm cosmeceutical activity or utility of these vitamins under the conditions of normal nutritional status. Retinoids (vitamin A class), which were previously discussed, at pharmaceutical concentrations are the most thoroughly substantiated class in their general effect in photoaging and specific effect on wrinkles.

Vitamin E is an exhaustively studied antioxidant in many systems and could therefore logically be studied in photoaging [18]. Some evidence for pharmaceutical effect in treatment of wrinkles is available. A 4-week study of 5% RRR alpha tocopherol naturally occurring oil-in-water (o/w) cream applied to the crows feet area showed, by optical profilometry, decreased skin roughness, length of facial lines, and depth of wrinkles compared with placebo [19].

An increasing number of vitamin C–containing topical products are being marketed with claims of improvement in skin wrinkling.

Vitamin D analogues have been highly successful in treatment of psoriasis and because of their modulating effect on keratinization, should be studied in photoaging.

Hormones

Estrogens and their diminution at menopause have profound effects, especially on epithelium of the skin and vagina. Wrinkle effacement has been convincingly shown in at least one controlled clinical trail of topical application of 0.01% estradiol or 0.3% estriol-containing preparations [20]. Other studies have shown beneficial changes in skin thickness and texture with topical estrogen application [21,22].

Minerals

That many minerals, such as sodium, potassium, calcium, magnesium, selenium, and zinc, are critical in normal mammalian physiology is well established. A potential cosmeceutical role in improvement of skin appearance has been suggested and requires confirmation [23].

Miscellaneous Agents

Hyaluronic acid is a normal component of epidermis and especially dermis. Stimulation of hyaluronic-acid production in skin by a device that produces a specific pulsed electromagnetic field (electrorydesis) produced improvement in appearance of wrinkles in a small study [24].

Natural cartilage polysaccharides as oral formulations derived from cartilage of marine fish have purported to improve dermal thickness and elasticity [25].

SUMMARY AND CONCLUSIONS

Skincare products now exist that have various degrees of utility for preventing, minimizing the appearance of, or treating wrinkles caused by UVR. Conscientious use of sunscreens can minimize photoaging and wrinkle formation. Rigorous consumer-panel testing can show consistent improvement of the appearance of wrinkles with many products of a purely cosmetic nature. Application of well-established clinical methodologies and increasingly sophisticated instrumental techniques have conclusively shown pharmacologically mediated wrinkle improvement, especially with topical use of retinoids or alpha-hydroxy acids.

In conclusion, the substantial scientific progress that has driven the development of elegant cosmetic and pharmaceutically active products to ameliorate skin wrinkles warrants optimism for the future. Can the day be far in the future when present cosmetic and cosmeceutical treatments will be eclipsed by specific genetic manipulations to rejuvenate aging skin [26]?

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Artificial Tanning Products

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INTRODUCTION

The desire for tanned skin alongside increasing awareness of the hazards of ultraviolet (UV) light exposure has led to renewed interest in artificial tanning products. Better formulations of sunless or self-tanners with improved aesthetics are more widely available. As consumer experience with the newer products has grown this category has become more popular, resulting in an increasing proportion of overall suncare sales. Dihydroxyacetone (DHA) is the active ingredient in sunless or self-tanners, and is responsible for darkening the skin by staining. DHA is classified in the International Cosmetic Ingredient Dictionary and Handbook [1] as a colorant or a colorless dye. Tan accelerators containing tyrosine and other ingredients and tanning promoters containing psoralens require UV exposure and will not be discussed here.

HISTORY

The first mention of DHA as an active ingredient in medicine appeared in the 1920s, when it was proposed as a substitute for glucose in diabetics. In the 1950s the oral administration of DHA was restudied as a diagnostic procedure for glycogen storage disease when it was given in large doses orally [2]. When children in the study spit up this sweet concentrated material, the skin became pigmented in splattered areas on the skin without staining clothing. Aqueous solutions were then applied to the skin directly and the pigmentation reproduced [3]. In the late 1950s, cosmetic tanning preparations first appeared in the marketplace. Cosmetic acceptance of these initial products was limited because of the uneven orange-brown color they imparted to the skin.

CHEMISTRY

Dihydroxyacetone ($C_3H_6O_3$) is a white, crystalline, hygroscopic powder. This 3-carbon sugar forms a dimer in freshly prepared aqueous solution (Fig. 1). With heating to effect a solution in alcohol, ether, or acetone, it reverts to the monomer. The monomeric form is more important in the browning reaction, which leads to the skincolor change [4]. DHA

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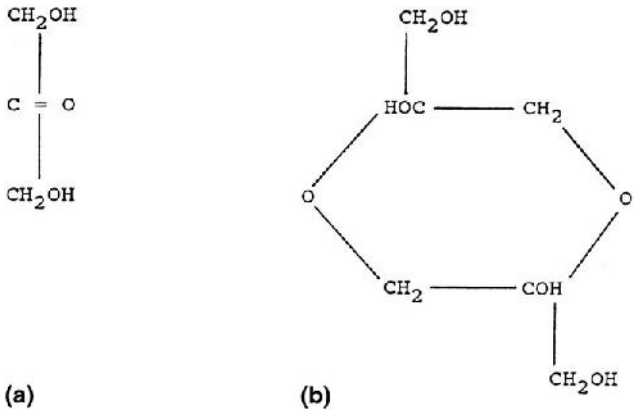

FIGURE 1 The chemical structure of DHA: (a) monomer, (b) dimer.

is stable between pH 4 to 6, but above pH 7 efficacy is lost with the formation of brown-colored compounds. A buffered mixture at pH 5 is most stable. Heating above 38°C for long periods of time will also effect stability. DHA needs to be stored in a cool, dry place. Glyceraldehyde, the isomer of DHA, is also present in solution [4]. Glyceraldehyde may degrade into formaldehyde and formic acid. In acidic solution (pH 4), this isomerization and consequently these latter undesirable ingredients are minimized.

The Maillard or browning reaction has been defined as the reaction of an amino group of amino acids, peptides, or proteins with the glycosidic hydroxyl group of sugars. DHA in the context of this reaction may be considered a 3-carbon sugar, reacting with free amino groups available as amino acids, peptides, and proteins supplied by the keratin to form products or chromophores referred to as melanoidins [5]. Melanoidins have some physicochemical properties similar to naturally occurring melanin [6].

FORMULATION

The concentration range of DHA in self-tanning products can range from 2.5 to 10%. Lower-concentration products allow the consumer greater latitude with application because they tend to be more ''forgiving'' of uneven application or rough surfaces. Labeling products as light, medium, or dark can be particularly helpful with the depth of shade a function of DHA concentration.

DHA is predominantly formulated in oil-in-water emulsions. Oils and waxes may reduce the color. Formulating with silicones allows the formulator to obtain the spreadability of oils, which potentially reduces streakiness with application to the skin. Minimizing particle size of the micelles in the chosen emulsion also improves uniformity of spreading on the skin's surface. Based on the chemistry of DHA, formulations should be buffered to an acidic pH (4 to 5) and not heated in manufacturing to temperatures higher than 40°C.

DHA can react with oxygen- and nitrogen-containing compounds, collagen, urea derivatives, amino acids, and proteins. They should be avoided in the formulation of the DHA-containing vehicle. Attempts have been made to take advantage of this effect by using a sulfur-containing amino acid, methionine sulfoxide, in an excipient applied before the application of the DHA-containing cream [7]. Two compartment systems have been patented based on this reaction.

As will all cosmetic products, aesthetics are determined by vehicle formulation. Products may be formulated for dry skin types by the addition of emollients and humectants. Products formulated in gel or alcoholic vehicles may be more suitable for oily skin.

MECHANISM OF ACTION

The site of action of DHA is the stratum corneum. Tape stripping of the skin quickly removes the color [8], as does mechanical rubbing. Deeper staining in areas with thicker stratum corneum and no staining of mucous membranes without a stratum corneum is also consistent with this being the site of action. DHA may be used as a substitute for dansyl chloride as a measure of stratum corneum turnover time [9]. Microscopic studies of stripped stratum corneum and hair reveal irregular pigment masses in the keratin layers [10] known as melanoidins. These melanoidins are formed via the Maillard reaction with DHA as a sugar reacting with the amino groups supplied by the keratin.

APPLICATION

After application of a typical DHA-containing self-tanning lotion, color change may be observed within an hour [11]. This color change may be seen under Wood's light (black light) within 20 minutes. Maximal darkening may take 8 to 24 hours to develop. Individuals can make several successive applications every few hours to achieve their desired color. Color may last as long as 5 to 7 days with a single application. Depending on anatomical application, the same color can be maintained with repeat applications every 1 to 4 days. The face requires fewer applications but more frequent reapplication to maintain color than the extremities. Depth of color varies with the thickness and compactness of the stratum corneum. Palms and soles stain deepest, necessitating washing of hands after application to avoid staining. Hair and nails will color, but not mucous membranes lacking a stratum corneum or keratin layer. Rougher hyperkeratotic skin over the knees, elbows, and ankles will color more unevenly as will older skin with keratoses and mottled pigmentation. Color will also be maintained longer in these areas.

As in the formulation, the pH of the skin before application may have an effect on the tonality of the skin color [4]. Alkaline residues from soaps or detergents may interfere with the reaction between DHA and the amino acids on the skin surface. Wiping the skin surface with a hydroalcoholic, acidic toner just before DHA application may improve results.

Careful directions provided with these products are, therefore, quite important in determining consumer satisfaction. The skin may be prepared with a mild form of exfoliation. Even application is required with lighter application around elbows, knees, and ankles to avoid excessive darkening in these areas. Care also needs to taken around the hairline where lighter hair may darken. Hands need to be washed immediately after use to avoid darkening of the palms, fingers, and nails. Clearly, care, skill, and experience are necessary when using these products.

ADDITIVES

As commonly occurs, growth in this category has compelled both formulators and marketers to seek points of differentiation between their product and that of their competitors. Besides formulating for specific skin types, active treatment ingredients may be incorpo-

rated into DHA-containing formulations. Vitamins, botanical extracts, antioxidants, antiirritants, and even alpha-hydroxy acids may be added to broaden the claims made by a given product. The addition of sunscreen ingredients to self-tanners warrants a more detailed discussion.

SUNSCREEN ACTIVITY

In the United States, the FDA Tentative Final Over-the-Counter Monograph on Sunscreens (Fed Reg. 1993) lists DHA as an approved sunscreen ingredient when used sequentially with lawsone (2-hydroxy-1, 4-napthoquinone). The European Economic Community Directive does not list DHA as a permitted UV filter. DHA itself has at most a modest effect on SPF [12], providing perhaps SPF 3 or 4 protection. The brown color obtained on the skin does absorb in the low end of the visible spectrum with overlap into long UVA and may provide some UVA I protection [13].

Individuals using DHA-containing tanning products need to be cautioned that, despite visible darkening of their skin, these products provide minimal sun protection. Confusion may be compounded by the addition of UV filters to the formulation providing significant sun protection. The stated SPF for the product is applicable for a few hours after application, but not for the days during which the skin color change may remain perceptible.

INDICATIONS

Even with recent improvement in DHA formulations, the color achieved remains dependent on skin type. Individuals of medium complexion with skin phototypes II or III [14], as opposed to those who are lighter or darker, will obtain a more pleasing color. Individuals with underlying golden skin tones will achieve better results than individuals with rosy, sallow, or olive complexions. Older consumers with roughened, hyperkeratotic skin or mottled pigmentation with freckling may be less pleased with their use. Dermatologists regularly recommend these products for tanning as a safe alternative to UV exposure. They may be used to camouflage some skin irregularities such as leg spider veins. Light- to medium-complected patients with vitiligo who show increased contrast with the vitiliginous areas with natural or unavoidable tanning in their normal skin may also benefit. They may even provide some protection for individuals with certain photosensitivity disorders [15].

SAFETY

The visible color change associated with the use of artificial tanning products might suggest to some users that these products are hazardous. Based on the chemistry of DHA and its toxicological profile, it can be considered nontoxic. It reacts quickly in the stratum corneum minimizing systemic absorption. The acute toxicity of DHA was investigated for diabetics in the 1920s with their oral intake well tolerated [6]. The phosphate of DHA is found naturally as one of the intermediates in the Kreb's cycle. Contact dermatitis to DHA has only rarely been reported [16]. As with other topical products with active ingredients, such as sunscreens, much of the reported sensitivity is secondary to other ingredients in the vehicle [17]. Adverse reactions are more likely to occur on the basis of irritation

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and not true allergy. Ultimately all claims related to product safety are based on testing the final formulation.

ALTERNATIVE TANNING AGENTS

Lawsone found in the henna plant and juglone (5-hydroxy-1,4,-napthoquinone) derived from walnuts also stain hair, skin, and nails. They have been used for centuries for hair coloring. Both substances lack skin substantivity and readily discolor clothing [18]. The skin color they produce does not resemble a natural tan.

Based on the underlying principle of the Maillard reaction, other molecules with a ketone function have been investigated [19]. An alpha-hydroxy group with attaching electron withdrawing groups can also increase reactivity. Substances such as glyceraldehyde and glyoxal [20] have been described but found ineffective. Mucondialdehyde as described by Eichler [21] is an effective agent but is also associated with toxicity, which mitigates against its use [19]. Although several other aldehydes have been shown to have better color properties, stability issues limit their use [19].

CONCLUSION

Increasing consumer awareness as to the hazards of UV light should fuel ongoing interest in self-tanning products. The benign toxicological profile of DHA reinforces the notion that these products represent a safe alternative to a UV-induced tan. The results obtained with these products are dependent on the final formulation, individual application technique, and consumers' complexion type. Greater experience in formulation combined with increasing sophistication on the part of the consumer should lead to continuing growth and satisfaction with the use of these products.

Consumers need to be clearly informed that these products do not offer significant protection against UVB. If formulated with standard sunscreens, consumers should be cautioned that the duration of UV protection is more short-lived than the color change.

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Barrier Creams

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INTRODUCTION

The expression ''barrier cream'' is used most often to indicate those creams that are used in the context of prevention of irritant contact dermatitis (ICD) [1]. The use of this type of product, however, is much broader than the medical care circuit (diagnosed patients by dermatologists, general practitioners, or other healthcare professionals), and in fact the major sales of barrier creams is in the segments of skincare and occupational use. In these segments there is quite some mix-up between ''barrier creams,'' ''emollients,'' and ''moisturizers,'' both in use and marketing. However, contemplating on insights gained during the last one and a half decades in both the causes and prevention of ICD [2–6], a more consummated view on treatment options can be given [7,8]. Repeated exposure of the skin to low concentrations of irritants, low temperatures, or friction during daily wear and tear of the skin, may lead to a gradual lowering of treshold for disruption of the skin barrier, and consequently to ICD. This means that it makes sense to distinguish prevention and treatment options for people who are at risk for developing ICD. In this respect persons with a history of (skin) atopy should be considered, along with those whose occupational environments create the aforementioned conditions. It will be evident that prevention of skin barrier problems has two aspects, namely risk avoidance, e.g., by minimizing contact time with irritating conditions and fluids, and protection of the skin, e.g., with gloves or protective products. If despite these measures the skin gets abrogated, it is important to apply products that have the capacity to aid or accelerate skin repair.

Consequently, these principles should be reflected in the definition and choice of topical products used in the management of skin-barrier problems in general and ICD in particular. It is therefore proposed to classify such products as ''barrier protective'' (BP) and ''barrier restorative'' (BR) products. In this view, BP products are considered products that guard the skin against the deleterious influences of exogenous stimuli leading to barrier disruption and consequently to the development of ICD. On the other hand, BR products are defined as being intended to restore a disrupted skin barrier. Both types of products can appear as ointments, creams, milks, and foams.

Because of the different functions of BP and BR products in the management of skin-barrier problems, it is noteworthy to consider that this has an impact on the properties that are expected from such products. In this respect it is important to realize that protective

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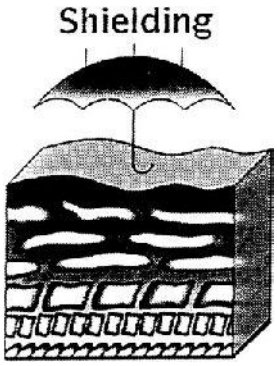

FIGURE 1 The primary function of a protective product.

products have the primary function to shield the skin (Fig. 1), but that this should be accomplished under conditions where people are working in a household or occupational environment. This implies that not only the shielding properties of such preparations, but also whether or not these products can be used under daily working conditions are important. Because occupational conditions may vary tremendously, it is not surprising that this has an impact on what can be called the ''secondary properties'' of BP products, which mean that BP products for e.g., hairdressers, kitchen workers, and slaughterhouse workers should offer the same level of protection but with different wash and wear resistancy as well as cosmetic properties. This requires special products for specific user groups.

In contrast, for BR products there is, in principle, no need for differentiation on the user's occupation, because these products are intended to be used after work. However, because different irritants cause differential structural alterations in e.g., the horny layer of the skin [9], this may require different types of BR formulations. Figure 2 depicts the differences between protective and restorative products. Consequently, product properties can be defined and criteria can be set to comply with.

PROTECTIVE PRODUCTS

Properties

The ideal BP product should be effective, nonsensitizing, nonirritating, easily applied and removed, cosmetically acceptable, and cost efficient. Importantly, BP product characteristics should be designed taking into account both the nature of the irritant and the required

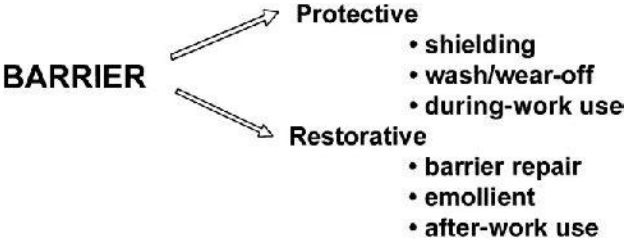

FIGURE 2 Properties of protective and restorative products.

cosmetic properties (e.g., compatible with daily life activities) to guarantee use suitability. This implies that in order to define properties, one should first identify user-group specifications and make an inventory of property—user combinations. An attempt at this is shown in Table 1. Accordingly, product profiles can be defined and assessed as product requirements after testing the product. It is particularly important to realize that the use suitability of BP products is dependent on the fulfillment of all different types of product requirements at the same time. This is not easily accomplished, however. Unfortunately there is an almost inverse relationship between shielding properties and cosmetic acceptability for ointments, creams, and foams, as is depicted in Figure 3.

Formulations

To date, very few preparations have characteristics that make them especially suited for any of the user groups given in Table 1 [10], although some general remarks can be made: current protective products against water-based irritants (soap, alkaline, acids) act in a rather nonspecific way by depositing mineral oils, isopropylmyristate, long-chain alcohols, fats, or waxes on top of the skin or into the outer stratum corneum cell layers in order to create a physical lipids barrier. Water repellants, like silicone oils or perfluoroether, are sometimes included. However, because these are highly inert molecules, high percentages of emulsifier are required to stabilize such formulations. This means that the net increase in protective properties with these supplements is disappointing (water-dragging effect), while high emulsifier concentrations may also cause irritation. More successful attempts have been made by including chemicals that are intended to bind to skin constituents, such as Eucoriol (sodium bischlorophenyl sulfamine), which is included in a water-in-oil (W/O) ointment. A disadvantage is that the product is rather greasy on the skin. The emulsion type of preparations against water-based irritants is usually W/O, although there are some exceptions: a high-fat product in an oil-in-water (O/W) fatty cream*, and a product with petroleum jelly and silicone oil in a gel structure. The latter products have better cosmetic properties. Despite the fair-to-good protective properties offered by W/O products, their poor cosmetic properties make these products less suitable for use by, e.g., hairdressers and hospital nurses.

Recently, O/W emulsions, including CM glucan, a polysaccharide isolated from baker's yeast, was proposed and tested for its protective properties in surfactant-challenged skin [11]. The clinical value of this type of formulation has not been shown, however. In order to increase cosmetic properties for BP products, foam-based products have been developed. An example is a foam containing stearic acid and dimethylpolysiloxane. Unfortunately, comparative tests have shown that the apparent advantage in cosmetic properties for this product does not extend to acceptable protective properties [12].

Cream and gel preparations for the prevention of nickel-induced ICD with ethylene diamine as a chelator have been made and tested in in vitro tests and patch tests [13]. Despite encouraging results in these types of tests, clinical efficacy of this type of preparation has not been shown. For protection against organic solvents, O/W creams are recommended [14], although in efficacy tests using toluene, or poison ivy extracts, this is not well accomplished with currently marketed products [1,10,15], thus casting doubt on this recommendation. Unfortunately, it can be stated that despite the many technological ad-

* Product protected by, e.g., Canadian patent 1200504.

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TABLE 1 Product Users and Properties Needed to Fulfill Users' Needs for Protective Formulations

	Product properties*								
	Protective properties against						Wash/Wear		
Usergroup	Soap solutions	Aggressive chemicals	Diluted acid	Diluted alkali	Dehydrating polar solvents	Apolar solvents	Wash-off	Friction	Cosmetic properties
Cooks, sandwich makers, meat-industry workers	+								
Hairdressers	++	++	+	++			++		++
Packers								++	−/+
Mechanics	+	+	+			++		+	−
Confectionary workers								++	++
Laboratory technicians			+	+	+	+	+		+
Farmers							+	++	−
Graphic-industry workers		++			+	+		+	−/+
Hospital nurses	+		+	+	+		++		+

* On a scale of −, not important/needed; +, important/needed; ++, very important.

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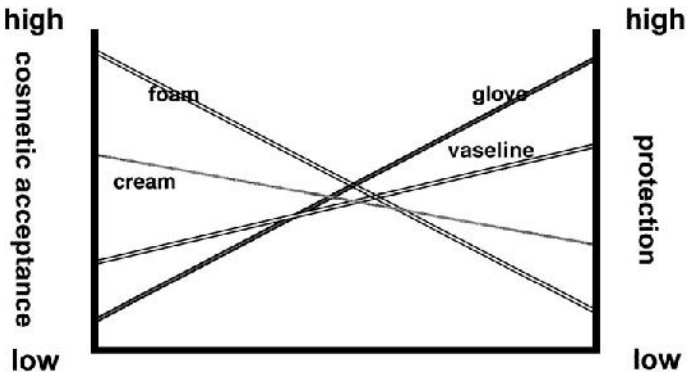


FIGURE 3 Skin-protective properties and suitability in daily-use characteristics for differential topical protective formulations.

vancements that have been made in pharmaceutical and cosmetic topical formulation science, and that have brought a better understanding of composition–properties relationships [16,17,18], this has not yet been translated into efficacious BP products for all user groups.

Test Methods

Sufficiently large field studies proving the efficacy of BP products under real-life conditions are scarce. In fact, the only study that shows the efficacy of a product in this respect is a field study in kitchen workers and cleaners, which showed protective properties of the O/W fatty cream previously mentioned [19]. The availability of reliable laboratory test methods is, therefore, essential, both for classification of products and for the development of new products. Suitable tests should give quantitative read-outs, include appropriate standard preparations and controls, and mimic wear-and-tear conditions when applicable.

Hallmarks for tests with a good predictive clinical value in this respect are the use of low, subtoxic doses of the irritant and repetitive application for 1 to 2 weeks, in absence or presence of pretreatment with test products thus mimicking real-life conditions. If wash-off is important for the target user groups of certain products, modifications can be made, which include washing schemes. After pioneering work by Lachapelle and coworkers [20], Frosch and colleagues have validated a test schedule in human volunteers where pretreatment of the skin with BP products was followed by repetitive treatment with a panel of irritants consisting of diluted solutions of sodium lauryl sulphate, sodium hydroxide, lactic acid, and undiluted toluene [1]. Other groups have used similar approaches on the back or forearm of human volunteers [10,21,22].

In vitro tests for assessing the protective ability of topical products generally have a poor predictive value for the in vivo situation [23]. However, for candidate selection in large-scale industrial development programs, such tests are indispensable to cut time-consuming product-screening procedures. In this respect, a method to test the water-repellent properties of formulations applied on slides dipped into a 1% eosin solution and evaluated for the absorption of color with a chromameter was found valuable as a preselection tool in a development program to identify products against water-based irritants, whereas another test where penetrating dye was assessed after application of the products

on a filter paper was of very limited value in this respect (author: unpublished observations). Although some animal tests may be worthwhile because of an obvious good clinical predictability of the results, e.g., the repetitive irritation test in guinea pigs [12], similar information can be obtained in human volunteer studies, avoiding sacrifice of animals.

In an industrial program aimed to develop an O/W cream that should protect against water-based irritants, maintain activity after washing, and with acceptable cosmetic properties, we have used a series of in vitro and human volunteer tests in serial and parallel combination. The test sequence was composed of high-capacity (in vitro) tests as the first selectors, and more laborious tests later on. Firstly, the in vitro eosin dip test was used as mentioned above. Secondly, formulations were tested into an in vivo eosin penetration test (see Fig. 4) and a cosmetic properties test [24]. Formulations that complied with predefined activity and cosmetic standards were taken into a repetitive-irritation test with sodium lauryl sulphate (SLS). The protocol for this test was based on procedures as published by Frosch's group [1], but including a wash-off scheme and with SLS as the only irritant. Typical results for a test run with the eosin penetration test and the repetitive irritation test are given in Figures 4 and 5.

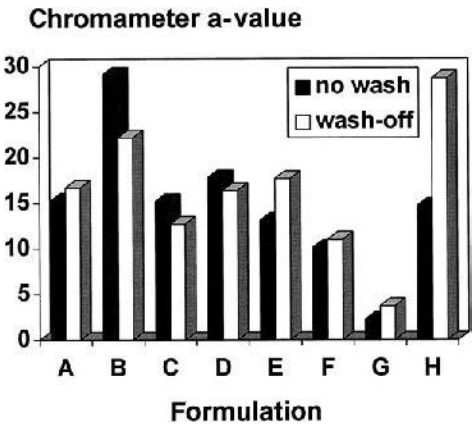


FIGURE 4 Results from a comparison of six experimental protective products (prepared by Yamanouchi Europe B.V., Leiderdorp, The Netherlands). (A, C, D, F, G, H) and two reference products (B, E) in an eosin dye penetration test *with* (first column) and *without* (second column) wash-off schedule. In eight healthy males, 50 μl of the test formulations was applied on 4 areas/arm of 4 × 5 cm. After rubbing in, the left sites of the spots were washed off gently with water. Accordingly, at all sites small paper disks, soaked in 1% eosin solution, were applied. After washing all sites, colorimetry (a* parameter) was performed with a Minolta CR300 colorimeter, and the difference with untreated was noted. (A low value for a* denotes good protective properties.) Preparations used: (A) 45% liquid paraffin/10% carnauba wax/3% glycerin W/O cream; (B) commercial hand cream including among others (a.o.) alcohols, waxes, paraffin, W/O and O/W emulsifiers, glycerin, dimethicone, and water; (C) 25% petroleum jelly in Carbopol 1382 O/W gel; (D) 10% ceresine wax added to an O/W fatty cream; (E) commercial W/O ointment containing mineral oil, petrolatum, Eucoriol, lanolin, Ozokerite; (F) 38% beeswax/34% Miglyol812 O/W oleogel; (G) 100% petroleum jelly; (H) 45% liquid paraffin/3% glycerin W/O cream.

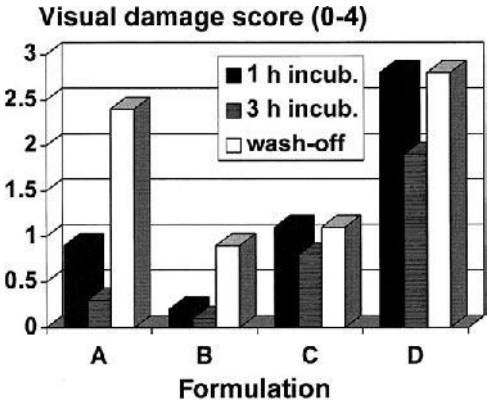
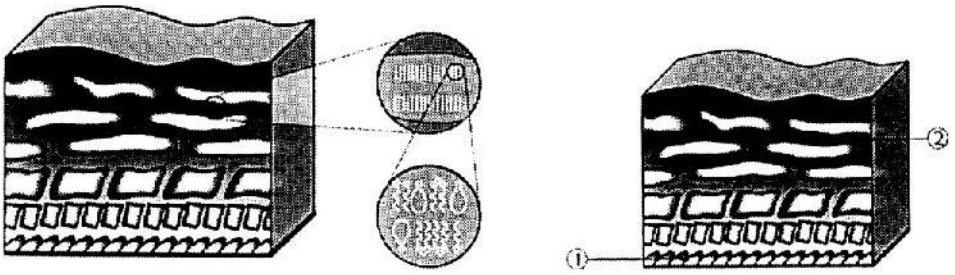


FIGURE 5 Results from a comparison of three experimental protective products (prepared by Yamanouchi Europe B.V., Leiderdorp, The Netherlands) (A, C, D) with a reference product (B) in a repetitive irritation test after five treatment days with SLS and incubation time of 1 h (first bar), 3 h (second bar), and with wash-off treatment (third bar). In this test eight healthy males were treated on 12 spots on the back with rubbing in 50 μl of the four formulations, applied in each column. Each row was allocated to one of the schedules: 1 h incubation, 3 h incubation, or wash-off after 30 min, whereas at 1 h after application 50 μl patches filled with 10% SLS were applied for 30 min. Erythema was scored with a chromameter (Minolta CR300) using the a* scale. Visual damage was scored on a scale from 0–4 (Frosch PJ, Kligman AM. The soap chamber test. J Am Acad Dermatol 1979; 1:35–41). The visual damage scores after five treatment days are given. Preparations used: (A) 4% perfluoroether (Fomblin HC) added to an O/W fatty cream; (B) commercial W/O ointment containing a.o. mineral oil, petrolatum, Eucoriol lanolin, Ozokerite; (C) 4% Fomblin HC/15% octyl, stearate W/O cream; (D) 4% Fomblin HC/18% Miglyol812/15% propyleneglycol O/W cream.

Properties

Based on studies that have been initiated by the group of Elias in San Francisco [25,26], and taken further by others as well [8,27,28], insight has been gathered into mechanisms and components involved in skin repair. Although the body of experiments in this direction was carried out on murine skin, evidence is accumulating that qualitatively similar mechanisms are operative in humans [29,30]. This leads to the view that BR products should have properties directed at re-establishing the broken skin barrier, which is accommodated by restoration of the physical integrity via application of missing basic components of the intracellular lipid matrix in combination with occlusive materials to stimulate repair mechanisms (Fig. 6). The function of the skin barrier is reflected by its ability to prevent excessive water loss. Consequently, transepidermal water loss (TEWL) is the parameter of choice to define the status of the skin barrier in this respect [31]. In this respect, criteria for BR products to comply with are based on the ability to accomplish a significant reduction of TEWL, thus stimulating ''early'' and ''late'' recovery [8], e.g., in mouse models [32], and finally in man [30], which go beyond the effect of occlusive products, like petroleum jelly. It should be noted that BR products share some of their purposes with ''emollients'' [33,34,35], although no strict criteria have been defined for the latter products.



(a) (b)

FIGURE 6 Schematic representation of the structure of the skin and strategies for restoring the barrier.

Formulations

For BR products, formulations containing ceramides, cholesterol, and fatty acids in vehicles that allow the formation of lamellar structures have been proposed [36,37]. Test results for this type of formulation are encouraging [36]. However, clinical results with the first marketed product of this kind* that are underway have to show whether this approach will result in better treatment options for dry skin and damaged skin due to ICD.

Test Methods

Because of the fact that BR products as such are an upcoming category of products, there is not an established view on test methods that should be used to identify and label such products. However, based on the arguments given in this chapter, test methods using mice where recovery of TEWL is studied following breaking of the skin barrier with acetone [26,32] are proposed, whereas human volunteer models using *treatment* instead of *pretreatment* schedules following damaging the skin with irritants [38,29] seem to be appropriate.

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* Containing petrolatum, water, paraffin, liquid paraffin, glycerin, sorbitan oleate, carnauba, cholesterol, ceramide-3, oleic acid, palmitic acid, tromethamine, and covered by US patent 5667800.

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Skin-Whitening Products

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Skin-whitening products have been widely used in the cosmetic field and clinic therapy. They are supposed to either lighten skin (individuals who wish to change or modify their skin color) or depigment skin (treatment for abnormal-hyperpigmentation skin such as melasma, freckles, and senile lentigines). Whitening agents, such as hydroquinone, kojic acid, and ascorbic acid derivatives have shown efficacy in a variety of hyperpigmentary disorders [1–14] but with varying success [1,2,7–9]. Their mechanism of action has been studied in vitro and in vivo [3,10–17]. Recently, their safety of application have been extensively investigated [18–32]. This chapter includes the most popular active ingredients of whitening agents and emphasizes their efficacy and safety.

HYDROQUINONE (1,4-DIHYDROXYBENZENE)

Hydroquinone is a nonvolatile chemical used in the photographic, rubber, chemical, and cosmetic industries. In the late 1930s, it was observed that a chemical used in rubber manufacture, monobenzyl ether of hydroquinone, caused depigmented skin in some workers [1]. The efficacy of hydroquinone (1,4-dihydroxybenzene) as a skin-lightening agent has been established in both human and animal studies. The chemical structure of hydroquinone is shown in Figure 1. Clinically, hydroquinone is applied topically in the treatment of melasma, freckles, and senile lentigines, as well as postinflammatory hyperpigmentation. In the United States, hydroquinone is readily available in concentrations up to 2.0% as an over-the-counter (OTC) drug and by prescription at higher concentrations [1,2]. Thus, hydroquinone is readily applied to the skin for medical and cosmetic reasons [33].

Hydroquinone inhibits the conversion of dopa to melanin by inhibiting the tyrosinase enzyme [1–3]. Other proposed mechanisms are inhibition of DNA and RNA synthesis, degradation of melanosomes, and destruction of melanocytes [2]. Electron microscopic studies of black guinea-pig skin treated with hydroquinone show the anatomic consequences of this action: (1) the melanosome structure is disturbed, resulting in decreased production or increased degradation of these organelles, or both; (2) hydroquinone exposure can ultimately lead to the degradation of the melanocyte; and (3) keratinocytes are spared, showing no apparent injury [1].

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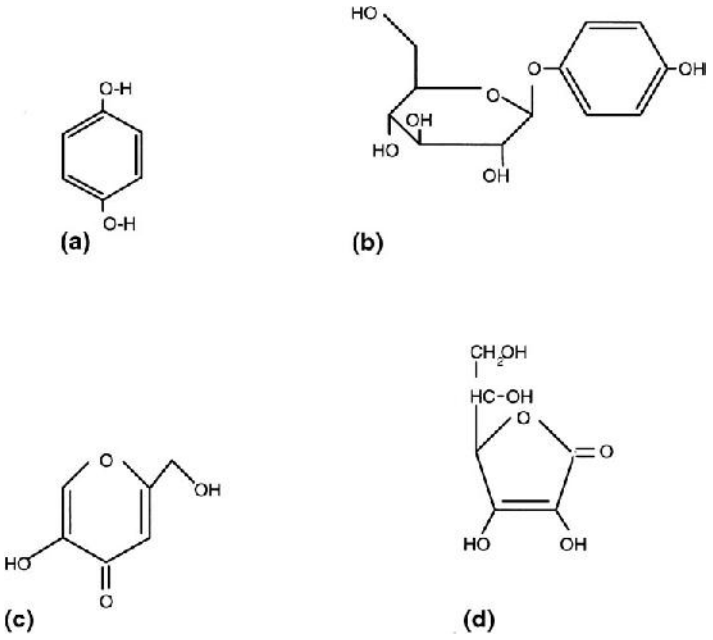

FIGURE 1 Chemical structures of (a) hydroquinone, (b) arbutin, (c) kojic acid, and (d) L-ascorbic acid (vitamin C).

Arndt and Fitzpatrick [4], in a non–placebo-controlled study, compared the efficacy of 2% and 5% hydroquinone cream for treatment of various pigmentary disorders in 56 patients. Results showed that hydroquinone was a moderately effective depigmenting agent in 80% of cases and that there was no difference between the two concentrations in therapeutic efficacy. Two percent hydroquinone was less irritating than 5%. Fitzpatrick et al. [5], in a non–placebo-controlled study, evaluated the efficacy of a 2% cream of stabilized hydroquinone in 93 patients. Sixty-four percent of them showed decreasing hypermelanosis without untoward effects. Sanchez and Vazquez [6] treated 46 patients with melasma using two versions of a 3% hydroalcoholic solution of hydroquinone. In this non–placebo-controlled study, overall improvement was noted in 88% of the patients and moderate-to-marked improvement in 36%. Side effects were minimal. The usage of a sunscreen agent was necessary for therapeutic efficacy. The efficacy of hydroquinone may be improved when it is used in combination with other chemicals as well as tretinoin, salicylic acid, or corticosteroid [1,2]. Kligman and Willis [7] noted an enhanced efficacy with 5% hydroquinone, 0.1% tretinion, and 0.1% dexamethasone in hydrophilic ointment for the treatment of melasma, ephelides, and postinflammatory hyperpigmentation in a non–placebo-controlled study. In contrast, they experienced poor results with each of the aforementioned as monotherapies. However, senile lentigines were resistant to this therapy. Gano and Garcia [8] conducted a 10-week clinical trial in 20 women with melasma. Topical applications of 0.05% tretinoin, 0.1% betamethasone valerate, and 2% hydroquinone were used in a non–placebo-controlled study. There was an objective improvement rate of 65% and a subjective improvement rate of 95%. Side effects were frequent but minimal. Caution is necessary when using potent fluorinated corticosteroids for prolonged periods on the face, because telangiectasia, atrophy, or acne rosacea can develop.

Pathak et al. [9] clinically tested the efficacy of hydroquinone in varying concentrations supplemented with corticosteroids or retinoic acid (tretinoin) in 300 Hispanic women with melasma in a non–placebo-controlled study, and concluded that cream or lotion formulations of 2% hydroquinone and 0.05 to 0.1% retinoic acid provided the most favorable results. In addition, avoidance of sun exposure and constant use of broad-spectrum sunscreens are necessary for the best therapy effects. Recently, Clarys and Barel [34] tested the efficacy of an ascorbate-phytohydroquinone complex in 14 patients with lentigo senile lesions in a non–placebo-controlled study. Objective skin-color changes were evaluated with a chromameter. After 1 month of treatment, a clear depigmentation of the macules was measured. None of the patients reported adverse effects.

Gellin et al. [35] established a reliable in vivo method to predict the depigmenting action of chemicals on mammalian melanocytes. They used black guinea pigs and black mice as animal models to screen the depigmenting capacity of several phenols, catechols, and organic antioxidants. Results showed that complete depigmentation on all test sites was achieved with monomethyl ether of hydroquinone and tertiary butyl catchall in the black guinea pig. Less-pronounced pigment loss was noted with these chemicals in black mice.

To treat some cases, higher concentrations of hydroquinone may be used. The formulations contain concentrations as high as 10% combined with nonfluorinated corticoid creams with or without the additional use of tretinoin or salicylic acid. Extemporaneously compounded preparations are often effective in patients that have failed to respond to lower concentrations of hydroquinone. With controlled use and monitoring, side effects from these preparations have proved minimal [2]. Note, however, that hydroquinone may be quickly oxidized in such formulations.

Hydroquinone occurs in nature as the beta-glucopyranoside conjugate arbutin. Arbutin is a safe and mild agent for treating cutaneous hyperpigmentation disorders, including melasma and UV-induced ephelides [10]. Arbutin is an active ingredient of the crude drug Uvae Ursi Folium-traditionally used in Japan and contained in the leaves of pear tees and certain herbs. The chemical structure of arbutin is shown in Figure 1. Maeda and Fukuda [10] determined the arbutin's inhibitory action on the melanin synthetic enzyme and its effects on melanin intermediates and melanin production in cultured human melanocytes. They indicated that the depigmentation effect of arbutin works through a inhibition of the melanosomal tyrosinase activity, rather than suppression of the expression and synthesis of tyrosinase in human melanocytes. Arbutin was much less cytotoxic than hydroquinone to cultured human melanocytes.

Adverse reactions associated with hydroquinone use include acute and chronic complications. Acute reactions include irritant dermatitis, nail discoloration, and postinflammatory hyperpigmentation [1]. Although commonly assumed to be a common allergen, the documentation of hydroquinone allergic contact dermatitis is weak [1]. Hydroquinone use can also induce hypopigmentation and, rarely, depigmentation of treated surrounding normal skin. However, these changes are temporary and resolve on cessation of hydroquinone treatment, in contrast to monobenzone use, which can cause permanent depigmentation [36]. Hence, the only indication for monobenzone therapy is in the treatment of severe vitiligo.

A more recent concern regarding the use of hydroquinone is the occurrence of hydroquinone-induced ochronosis, a chronic disfiguring condition resulting, in general, from the prolonged use of strong concentrations of hydroquinone [36]. Hydroquinone's acute and chronic toxicity toward higher terrestrial organisms appears to be minimal in humans

[20,21]. An epidemiologic investigation in 478 photographic processors has shown no significant excess mortality, sickness absence, or cancer incidence [20]. The reported nephropathy and cell proliferation, as evidence of carcinogenicity, observed in Fischer 344/N rats [22,23] appear to be strain and sex specific [23]. Hydroquinone was negative in the Ames/Salmonella and Drosophila genotoxicity assays [24]. Others suggest that carcinogenic and teratogenic potentials have been, at present inadequately studied [20,25], and that both hydroquinone and benzoquinone produce cytotoxic effects on human and mouse bone-marrow cells [26]. Hydroquinone readily penetrates human forehead skin in vivo following a single topical exposure in an alcoholic vehicle of 24-hour duration. Elimination was complete within 5 days [19]. Wester et al. [18] determined the topical bioavailability, metabolism, and disposition of hydroquinone on humans in vivo and in vitro; dose recovery in urine was 45.3%, of which the majority was excreted in the first 24 hours.

KOJIC ACID

Kojic acid, a fungal metabolic product, is increasingly being used as a skin-lightening agent in skincare products marketed in Japan since 1988. It was first isolated from Aspergillus in 1907 [31]. The structure is shown in Figure 1. The mode of action of kojic acid is to suppress free tyrosinase, mainly attributable to chelation of its copper [11,16,31], and it has been shown to be responsible for therapy and prevention of pigmentation, both in vitro and in vivo [11,31].

In Japan it is used in nonprescription skincare products up to a concentration of 1%. To increase percutaneous absorption and thus therapeutic activity, it is usually used at the highest concentration allowed [31]. Because it is used intensively in foods (e.g., bean paste, soy, and sake) in some countries, particularly Japan, its oral safety has been studied. Shibuya et al. [28], investigating the mutagenicity of kojic acid by the Ames test, forward mutation test in cultured Chinese hamster cells, and dominant lethal test in mice, concluded that, although kojic acid is a weak mutagen in bacteria, it is nonmutagenic in eukaryotic system either in vivo or in vitro. Abdel-Hafez and Shoreit [30] tested the mycotoxins using the dilution-plate method. Results showed that kojic acid may induce some toxins. Fujimoto et al. [32] examined the tumorigenicity of kojic acid in $B6C3F_1$ mice. Three groups of animals were given 0, 1.5, and 3.0% kojic acid–containing food for 6 weeks; kojic acid groups significantly induced thyroid tumors in $B6C3F_1$ mice. But true adverse effects after human oral ingestion have not been shown. Nakagawa et al. [31] noted that there were no signs of relapse of dermatitis or any other adverse effects on sensitized patients upon ingestion of foods containing kojic acid. However, they reported that topical application of kojic acid may induce allergic contact dermatitis with sensitized patients. They postulated that kojic acid was considered to have a high sensitizing potential, because of the comparatively high frequency of contactsensitivity in patients using 1 or more kojic acid–containing products. Recently, Majmudar et al. [37] used an in vitro model to evaluate the efficacy, stability, and cytotoxicity of whitening agents. They also conducted a non–placebo-controlled clinical study that indicated that kojic acid in an anhydrous base can induce more skin lightening than in the aqueous base.

ASCORBIC ACID (VITAMIN C) AND ITS DERIVATIVES

Ascorbic acid may inhibit melanin production by reducing *o*-quinones [12] so that melanin cannot be formed by the action of tyrosinase until all vitamin C is oxidized. The chemical

structure of vitamin C is shown in Figure 1. Although the lightening effect of vitamin C is considered, it is quickly oxidized and decomposes in aqueous solution and is thus not generally useful as a depigmenting agent. Numerous stable derivatives of vitamin C have been synthesized to minimize this problem [12–14,17]. Magnesium-L-ascorby-2-phosphate (VC-PMG) is a vitamin-C derivative that is stable in water, especially in neutral or alkaline solution containing boric acid or its salt [12]. VC-PMG is hydrolyzed by phosphatases of liver or skin to vitamin C and thus exhibits vitamin C-reducing activity [12]. Kameyama et al. [12] investigated the effects of VC-PMG on melanogenesis in vitro and in vivo. Results from this non–placebo-controlled study suggested the topical application of VC-PMG was significantly effective in lightening the skin in 19 of 34 patients with chloasma or senile freckles, and in 3 of 25 subjects with normally pigmented healthy skin.

OTHER AGENTS

Various systemic drugs and natural products may be used as protective agents, such as chloroquine, indomethacin, vitamin C and E, fish oil, and green tea, etc. Topical agents include azelaic acid and melawhite except where previously described [38]. Recently, Kobayashi et al. [39] reported that neoagarobiose could be useful as a novel whitening agent as it has shown moisturizing and whitening effects with low cytotoxicity. Ando et al. [40] evaluated the effects of unsaturated fatty acids on UV-induced hyperpigmentation of the skin in a placebo (vehicle)-controlled study. Skin hyperpigmentation was induced on the backs of guinea pigs by UVB exposure. Oleic acid, linoleic acid, and α-linolenic acid (0.5% in ethanol), or ethanol alone as a control, were then topically applied daily five times per week for 3 successive weeks. Results suggest that the pigment-lightening effects of linoleic acid and α-linolenic acid are, at least in part, attributable to suppression of melanin production by active melanocytes as well as to enhanced desquamation of melanin pigment from the epidermis.

CONCLUSIONS

In general, skin-whitening products are considered modestly effective. High concentrations are not recommended except under a physician's supervision. The application as a combination with certain chemicals (retinoic acid and alpha-hydroxy acids) may enhance lightening. Optimal whitening agents remain a future goal.

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Interactions with Hair and Scalp

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PSYCHOSOCIAL FACTORS INVOLVED IN HAIR COSMETICS

Haircare and psyche reciprocally reflect each other both positively and negatively (bad hair days). Contrary to the bad haircare and negligence of a depressed person or a man in grief, generally people tend to offer themselves the best of haircare when they are feeling happy or when they want to show their internal feelings to others through body language. This is particularly obvious during public appearances and important social gatherings (e.g., parties, marriage ceremonies). Haircare by itself can induce a state of self-confidence and may reflect social status. This may explain significant differences in shampooing regimens, which range from once or twice a week to once a day.

Hair is midway between nature and culture [1]. Haircare attitudes are different from one society to another regardless of economic differences, and from one person to another within societies; e.g., hair loss is not equally perceived by everybody in all societies in the same manner [2–5]. Some people are seriously psychologically affected and ready to spend a fortune in order to cope with the problem, whereas others just do not care at all. In the former group, styling is of high significance as is the selection of cosmetic agents.

The intersocial and interpersonal attitude of adult males towards greying of hair is quite evident, added to the difference in attitude between men and women toward the same problem. However, this is not an exclusivity of mankind; the social significance of hair/pelage/beard/crown is very pronounced in other mammals (e.g., primates, lions). Grooming in humans is specifically a private activity or limited to one professional body (hair stylists).

NATURAL PROPERTIES OF HAIR AND THEIR IMPORTANCE FOR HAIR APPEARANCE

Physical Properties of Hair as a Basis for Appearance and Perception

Optical properties (absorption and reflection of visible light); the role of pigmentation in inducing a contrast between skin and hair; and the role of cuticle, cortex, and medulla are some physical properties playing an important role in hair appearance and perception [6]. Apart from albinos, all normal subjects have melanin. The production of these pig-

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ments is genetically determined and results in the production of various proportions of the following: (1) eumelanin, which gives colors from brown to black; and (2) pheomelanin, which gives colors from yellow-red to red. The hair color of each individual depends on the preponderant type of melanin as well as its quantity and distribution in the skin and hair. Melanin is a polymer of high molecular weight, insoluble in water and most solvents. It originates from melanocytes located in the basal cell layer of the hair matrix. Melanogenesis involves a complex sequence of chemical reactions corresponding to an oxidative polymerization catalyzed by certain enzymes; these complex processing phases occur in small vesicles named melanosomes. An intimate relationship must exist between the factors controlling melanocytes and matrix cell activity, because melanosome and pigment transfer from the melanocyte to the hair matrix occur only during the anagen phase of the hair cycle. Hair color also varies with age. There is first an intensification and then a slowdown, or sometimes even a halt, in pigment formation despite the rather constant number of melanocytes. This points to functional and regulatory aspects.

Melanin granules are distributed throughout the hair cortex but in greater concentration towards the periphery [6]. The color of hair is an optical phenomenon attributable to the reflection and refraction of incident light from various interfaces, especially the bulk of melanin contained in the cortex. Newly formed unpigmented hair with no medulla appears yellowish rather than white. This is probably the intrinsic color of dense and well-organized arrangement of keratin fibers [6]. Another important physical factor that helps the ease with which hair can be styled and given a desired shape is the elimination of static electricity, which causes repulsion between individual hairs and is an obstacle to styling and arranging hair [7]. The development of electrical charges on hairs during combing and brushing is a complicated phenomenon that varies according to hair type, surface state, and the humidity of the surrounding environment. A product's antistatic properties can be assessed in vitro by measuring the electrical potential build-up of hair during combing. If opposed electric charges are face to face, matting of hair may occur. There is no way of untangling it and a substantial haircut is the only solution.

Mechanical Properties of Hair Appearance

Hair fibers are generally elliptical, with cross sections having minor and major axis ratio in the range of 0.63 to 0.91, the most elliptical being black hair, the most circular Asian hair. Resistance to longitudinal deformation, bending and torsion stiffness, and hold of set hair are related to fiber diameter. The relationship between the constraint and elongation obtained follows a curve of three regions (preyield, yield, and postyield) according to the stretching force [7]. Fiber breakage occurs mainly in the postyield region. The load values depend on the cohesion of α-keratin. All factors diminishing this cohesion bring the load value down, e.g., wet hair. Examination of load elongation curves helps in studying how hair behaves in the course of various hairdressing procedures including the wide range of temperature, humidity and chemical agents involved.

The hair shaft is a strong enough fiber. It behaves like reinforced wire. Curled black hair is fairly fragile because of the highly twisted configuration and flattening as opposed to Asiatic hair [7]. The disruptive load for hair varies with age, peaking at about 20 years of age.

The length of hair plays a role in perception. A typical example is when the hair is cut short, people usually interpret the perception of stubbles as thickening of the newly

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produced hair fiber. Instead of the soft feel of a nonchanging full head of hair, one now feels hair growing from day to day. Another misconception among lay people may be so explained: a haircut does not influence hair growth, it is just becoming noticeable.

SPECIFIC ACTIONS OF HAIR COSMETICS ON HAIR SURFACE (CUTICULA), CORTEX, AND MEDULLA

Desirable Actions

The intended desirable effects of cosmetics on hair are very wide and variable. Cleansing, dyeing, perming, bleaching, straightening, dressing, setting, and removing are some of the innumerable aims and claims of hair cosmetics. Some desirable actions are not achievable without inducing some kind of damage to the hair fiber itself, e.g., in permanent or oxidative hair dyeing a degree of damage to the hair cuticle is necessary to introduce the dyes that are targeting the hair cortex. The same is true for bleaching and perming. When the hair cuticle is weakened it cannot be fully restored (Fig. 1), but some cosmetic agents may decrease the abnormal fragility and the rough feel of damaged hair. No better results can be achieved than by cutting away the damaged fibers and letting new hair growth proceed without new harsh procedures (Fig. 2).

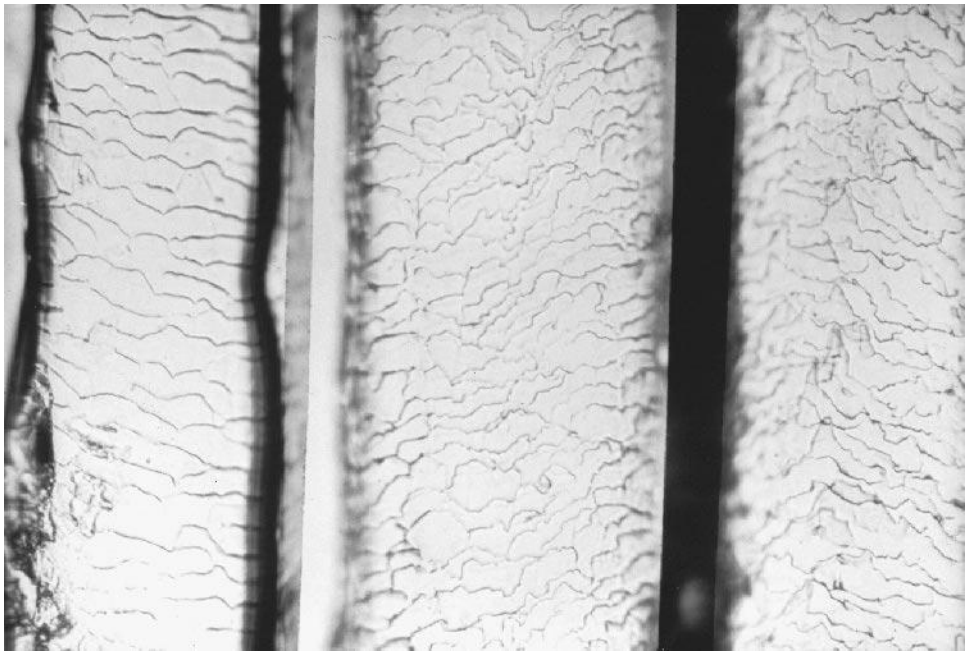

FIGURE 1 The condition of the cuticle on three hair segments taken at the merger of the scalp (left), 1 cm away from it (middle), and 3 cm away (right). Damage of the cuticular scale edges clearly occurs within 3–4 months of exposure to the environment.

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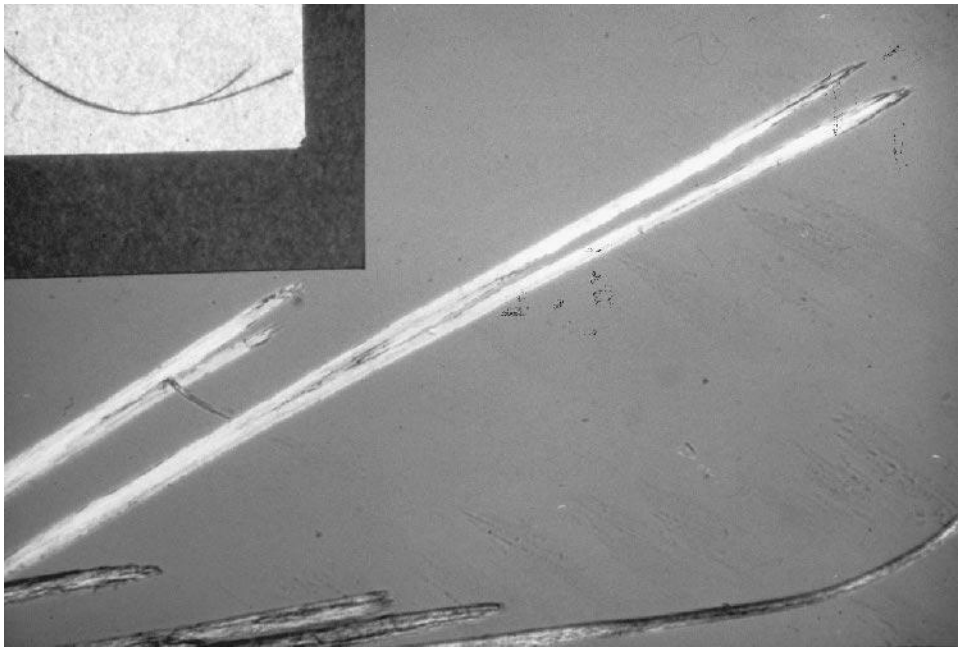

FIGURE 2 Trichoptilosis or split ends. These damaged hair tips frequently occur on long hairs. Lack of cuticle, which normally envelopes the hair fibers, exposes the cortex, a much weaker part of the hair shaft.

Undesirable Action

Hair cosmetics and shampoos in particular are formulated to be nontoxic, nonirritant, and nondamaging to the hair, skin, and eyes. These formulae should not of course, include substances that are systemically toxic following their percutaneous absorption. The integrity of the cuticle is degraded by perming, bleaching, and permanent dyeing, which lead to raising and softening of the cuticle thereby making it vulnerable to mechanical abrasion, e.g., during combing.

Scalp hair may be under excessive physical traction determined by fashion, e.g., tight rollers and tight hairstyles. This can result in temporary hair loss, and if continued over a long period will result in permanent hair loss (thinning). Some examples of this condition have been described by medical literature as chignon alopecia and frontoliminal alopecia.

The hair shaft can be damaged by previous permanent waving or bleaching and thus made more permeable to certain dyes, leading to some unexpected effects, e.g., greencolor from azo dyes, green hair from copper metallic salts, and red hair from chino form. The so-called Bird's Nest hair is a physical phenomenon of felting. This occurs when frictional forces are applied to physically damaged hair especially after the use of a cationic shampoo. A large tangled mass of hair is produced and defies all attempts to unravel it, and the mass has to be cut off. The process can be reproduced experimentally with normal hair. There is no evidence that subjects affected have especially susceptible hair [7].

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SPECIFIC ACTIONS OF HAIR COSMETICS ON THE SKIN

Intended Contact with the Skin

Many cosmetic compounds target the skin rather than the hair. Antidandruff and antiseborrehic cosmetic compounds target the scalp skin, not the scalp hair. Many other cosmetics intend to modify the hair/skin system, e.g., preshave and aftershave lotions, along with depilatories, where the effect on hair is always associated with some effect on the skin.

Nonintended Contact with the Skin

Ideally, hair cosmetics should not have contact with the skin, but in practice this is hardly achievable. In some procedures, such as hair dyeing and hair bleaching, skin contact is unnecessary to perform the procedure itself but hardly avoidable during such a procedure.

Many consumers report hair shedding with changes in the shampooing regime. This is not because of a biological process in particular but because of a detachment of telogen hairs, which may modify the usual daily shedding of hair. Another reason for this is that when consumers change products, they tend to be more attentive to the condition of their hair and scalp and attribute any perceived change to the new product, especially if viewed as negative. Properly conducted trials showed that shampooing regimes did not modify hair shedding [8].

The aim of wet and dry shaving is to cut facial hair without harming the skin, which is a frequent adverse side effect of these procedures. These side effects vary in intensity, from a slight irritation—that is going to disappear with time during a process of adaptation—to a very severe and persistent reaction. This will mostly force the consumer to give up using that particular method and select a more ''friendly'' alternative.

Permanent wave solutions or their neutralizing chemicals can cause chemical burn or necrosis of the scalp epidermis if allowed to contact the scalp skin in certain concentrations for too long. The chemical burn may affect the skin of the scalp, forehead, face, and neck.

Physical burn can result from heated rollers or other apparatus that can cause damage to the superficial layers of the epidermis. The risk of burn also exists during or just after the use of flammable vehicles (e.g., alcoholic lotions) in close proximity to a fire or heat source.

Contact dermatitis to cosmetics in general and to hair cosmetics in particular is not uncommon in clinical dermatology. Following are leading examples from a long list of hair cosmetics reported to be skin sensitizers: hair dyes (p-phenylenediamine, resorcinol), shampoos (surfactants, zinc pyrithione, hydroxyquinolines), hair creams and gels (lanolin, parabens), hair lacquers (benzoin, cyclohexanone-formaldehyde resin), hair lotions (quinine, resorcinol), deodorants (hydroxyquinolines, Irgasan DP 300), bleachers, and shaving lotions (musk ambrette, antimicrobial agents) [9]. Acute and chronic allergic contact dermatitis have been associated with significant though usually transient or reversible hair loss [6]. This is a very often neglected or even unrecognized cause of diffuse hair loss [10].

The irritant effect of cleansing agents is attributable to the removal of surface lipid film and water-holding substances in the stratum corneum. They may denature protein and damage the cell membrane as well. The risk of irritant and allergic contact dermatitis induced by deodorants is greatly enhanced by the natural occlusive properties of body sites such as the armpits.

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Hair Cosmetics

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INTRODUCTION

Throughout recorded history, hair has always been an important element of personal adornment. From the beautifully regular beard curls of the Assyrian kings to the elegant hair cuts of Egyptian pharaohs to the carefully coiffured wigs of the European nobility, hair has been shown, admired, and envied. Over the years, what had been the privilege of the affluent few has become an almost consuming passion of many. The explosive growth of the haircare market since the middle of the twentieth century is the result of deep, socioeconomic changes combined with an increasing focus on personal aesthetics, assisted by affordability of products. The attempt to satisfy the genuine needs of the consumer and the drive for competitive advantage among marketers has led to a variety of grooming aids and products, such as shampoos to cleanse the hair, hair conditioners to make it soft and combable, hair colorants and permanent waves to impart to hair properties it does not have, and hair sprays to keep hair in the desired style. Hair products are in the cosmetic category and, as such, are subject to all laws and regulations that control the labeling and claims of all cosmetic products.

The Structure and Properties of Hair

Hair follicles, which in tens of thousands are deeply invaginated in the scalp tissue, are the essential growth structures of hair. At the base of each follicle, the cells proliferate and, as they stream upwards, the complex and intertwined processes of protein synthesis, structural alignment, and keratinization transform the cytoplasm into the tough fibrous material known as hair. Hair is unique in that its structural and growth characteristics are different between races, sexes, individuals of the same race, areas in the same individuals, and even within the same follicle. The development of hair is a dynamic, cyclical process in which duration of the growth cycle depends not only on the body site, but also on such variables as the individual's age, nutritional habits, and hormonal factors. In the scalp, each hair grows steadily (about 1 cm per month) and continuously for 3 to 5 years (anagen phase); growth then stops and is followed by a brief transient stage (catagen) and a 2- to

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4-month resting stage (telogen) during which the old hair is shed. With the onset of the anagen, the new hair starts to grow from the same follicle. The growth process functions independently in each follicle, so hairs are not shed simultaneously as they are in most animals. At any given time, some hairs are growing, some are resting, and some are being shed. Normally, of about 150,000 scalp hairs, 90% are in the anagen phase and the remaining 10% are in the catagen and telogen phases, with 50 to 100 hairs being shed daily. Scalp hair is a fiber of 50-80 μm in diameter and its exterior consists of a layer of flat, imbricated cuticle cells pointing outward from root to tip. This ratched-like structure of the cuticle scales serves as an effective self-cleaning feature and, by interlocking with the scales of the inner root sheath of the follicle, helps to hold the hair firmly in place. The cuticles are thin (0.5 μm), 50 to 60 μm square sheets, attached at their approximal ends to the underlying cortex. Their longitudinal overlap is substantial resulting in an average separation of scale edges of approximately 5 μm. This overlap generates a multilayered shield 3 to 4 μm thick around the hair fiber. The structure of the cuticle fulfills well the role of a protective barrier for hair. A thin film of covalently-bounded lipid on the exterior of the cuticle assures a low friction surface, together with water repellency. Just underneath, the highly cross-linked lamellae of the A-layer and exocuticle augment the mechanical stability of the scales, whereas the soft and water-absorbing endocuticle cushions effects of mechanical impact. The high water swellability of the endocuticle is the likely source of pronounced cuticle lifting on wetting of hair.

Enveloped by this formidable protective sheath of the cuticle layer is hair cortex, which constitutes the bulk of the fiber and is mainly responsible for the mechanical properties of hair. The spindle-shaped cortical cells are arranged parallel to the fiber axis, overlapping each other with frequent interdigitation. They have a unique arrangement of the constituent proteins, comprising intermediate filaments (IF), traditionally termed microfibrills, aligned in the direction of fiber growth and are surrounded by a matrix of IF associated proteins (IFAP). The filaments are composed of high–molecular weight protein chains of low sulfur (cystine) content and possess a high degree of molecular organization (α-helical), whereas the surrounding matrix of IFAP is made up of proteins more extensively cross-linked by cystine lacking definite structural pattern.

During the process of keratinization, the cell plasma membranes are modified to establish a strongly adhesive layer between the adjacent cells known as the cell membrane complex (CMC). This is the only continuous phase in the hair fiber providing adhesion between the cortical cells as well as between and with the cuticle cells.

Dispersed throughout the structure of cortex are melanin pigment particles. Their number, chemical characteristics, and distribution pattern determine the color of hair. In some hairs, coarse hairs in particular, vacuolated medulla cells are present in the central region of the fiber.

Although hair of different racial origin differs in shape, degree of curliness, and color, there is little difference in the underlying chemical properties and fiber structure. The amino-acid composition of the constituent proteins and most physical properties are similar [1,2]. The differences between hair of different ethnic groups are often smaller than the variation in the properties of hair taken from different individuals within one ethnic group.

Compared with Caucasian or Asian hair, African hair is more irregular in the shape of its cross-section. The sharp kinks seen in such hair are often associated with random unevenness of fiber diameter, resulting in weak spots along the fiber length. These are likely to cause problems during combing or chemical treatments.

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SHAMPOOS

General Comments

Cleansing is clearly a dominant element of personal hygiene and, when reinforced by the aspect of attractive appearance, translates into a powerful and highly marketable stimulus. Shampooing has become, thus, a factor *sine qua non* in maintaining the aesthetics of hair.

The cleansing task is formidable. A mass of 100,000 to 150,000 flexible fibers has to be cleansed of oily deposits of sebum, sweat, entrapped desquamated scalp cells, along with the residues of mousses, gels, and hair sprays. All this has to be done within the span of a few minutes, leaving the individual hairs clean and free of tangles to which the ratched structure of hair cuticles makes it particularly vulnerable. It should also be kept in mind that although cleansing action is the fundamental assignment of a shampoo formulation, it is by no means the only goal. The promise of hair shine, softness, body, and manageability is inherently tied to product performance. Furthermore, one must not ignore the process of shampooing itself. It is expected to provide a pleasurable experience in working up a rich and lubricous lather that seems almost to caress the hair and leave it, after rinsing, with a touch of refreshing fragrance.

Hair Soiling and Soil Removal

In the course of its residence on the scalp, hair is exposed to a variety of events that contribute to its soiling. Among them are the innate processes of scalp desquamation, sweating, and sebum secretion, which are supplemented by deposition of extraneous substances arising either from environmental pollution (dust and other airborne contaminants) or from hair-grooming preparations, such as oils, waxes, hair spray, and mousse residues. Of all these, sebum, because of to its steady replenishment, greasy characteristics, high adhesiveness to hair, and ability to cement the other soil particulates together and to the hair surface, appears most insidious and thus it is not surprising that its efficacious removal is key in hair cleansing.

The sebaceous glands attached to each of the hair follicles provide a continuous supply [3] of this oily substance to the surface of hair. There are seasonal variations in the amount of sebum secreted [4], but more importantly its output is under hormonal control [3], reaching a maximum at puberty. Oily hair of adolescents is the obvious and often annoying consequence of the high activity of the sebaceous glands, and this at a time in one's life when personal adornment is particularly important. Sebum secreted from the sebaceous ducts spreads within the mass of hair primarily via physical contact between the fibers [5]. Brushing and combing (as well as contact with a pillow) further redistributes the sebum and partly assists in its removal. The quantity of sebum on hair at a particular moment thus reflects the relative efficacy of these two processes (sebum secretion and removal). The term ''oily hair'' often connotes a highly undesirable image of stringy and dull hair with little body and greasy feel. It is, however, worth bearing in mind that such a perception is not universal being strongly influenced by fiber texture and geometry. Thus, a visual appearance of curly African hair can visibly benefit from an increase in oiliness, a fact that is exploited in grooming products for such hair.

Because of the adhesiveness and sticky consistency of sebum-containing soil, its adequate removal by simple mechanical means is virtually impossible, and satisfactory cleansing can only be attained by use of aqueous solutions of detergents. In the broadest sense, all materials used in cleansing that are water and other solvents, soaps and synthetic

surfactants, salts, and abrasives may be considered as detergents. However, more specifically, the term ''detergent'' is limited to those surface-active agents that, in addition to the property of lowering surface tension, are effective in deflocculating soil and dirt clumps and keeping them in suspension so that they can be washed away before redepositing on the surface that is being cleaned. This property is exhibited by compounds that contain both a hydrophilic group and a hydrophobic tail that serves as an emulsifying agent. In essence, the removal of soil from hair is governed by the same basic processes that had been previously identified as being involved in laundering of fabrics [6]. Without elaborating on theories underlying the detergency, one should allude to the three fundamental mechanisms that have been proposed to account for the cleansing action of detergents.

1. The ''roll-up'' mechanism [6], particularly relevant to oily deposits in which the progressive wetting of the fiber surface leads to rapid detachment of oil droplets;
2. In the micellar solubilization mechanism [7] the soil is solubilized into micelles that come into contact with the soiled surface. The efficacy of this cleansing mode depends on the availability of sufficient quantity (concentration) of micelles, which does not usually present a problem with conventional shampoo formulations; and
3. The third mechanism [8] invokes the dispersion and emulsification of soil particles penetrated by the diffusing detergent. The amphiphilic components of sebum might enhance cleansing by direct interaction with the molecules of the surfactant.

There is no precise information presently available as to which mechanism is dominant in hair cleansing. Quite possibly all three might be involved, depending on the characteristics of the soil. In any case, the vast majority of shampoo products are formulated to be operative under diverse conditions of detergent action, thus assuring their cleansing efficacy.

Shampoo Ingredients

Almost without exception, shampoos consist of an aqueous solution, emulsion, or dispersion of one or more surfactants together with some additives to enhance performance and aesthetic properties of the product. Additives are used to provide fragrance and color, thicken, opacify, and convey specific tactile attributes. They include stabilizers, foam modifiers, preservatives, conditioning, and antidandruff agents.

Surfactants

Surfactants are long-chain electrolytes and are usually classified according to the nature of their hydrophilic group, which may be anionic, nonionic, amphoteric, or cationic.

Anionic Surfactants

Soaps are salts of fatty acids and, not in the distant past, were the mainstay of shampoo products. In soft water, they lather copiously, cleanse well, and leave the hair in a well-conditioned style. Unfortunately, in hard water the lather is poor, and as the soap combines with calcium or magnesium salts present in hard water it deposits on hair a dulling film. The introduction of synthetic surfactants brought about the end of soap-based shampoos,

although some products still contain a small quantity of soap to exploit its conditioning property.

Alkyl sulfates are the most widely used anionic in shampoos, displaying excellent foaming and cleansing properties unaffected by hard water. Lauryl sulfate is the dominate ingredient being present in most shampoo formulations in the form of its ammonium or triethanol ammonium salt at a level of 6 to 18% w/w. Although very effective cleansers, the alkyl sulfates, particularly at high concentrations, have a tendency to irritate the scalp and remove some lipid constituents of hair cuticle. To make the alkyl sulfate-based shampoos milder, they are frequently modified by incorporation of less-irritating alkyl ether sulfates or amphoteric surfactants.

Alkyl ether sulfates are sulfated products of ethoxylated fatty alcohols. They are more water soluble than alkyl sulfates, are excellent solubilizers for fragrances and other oleophilic additives, and are particularly suitable for formulations of clear shampoos. As alluded to earlier, these surfactants are less irritating than the alkyl sulfates and are used, at a higher degree of ethoxylation, in baby shampoos.

Alpha-olefin sulfonates are complex mixtures resulting from sulfonation of alpha-olefins. These detergents exhibit excellent foaming in the presence of sebum, are effective over a wide range of pH, and compare favorably with other surfactants in dermal and eye irritation [9].

Other anionic surfactants worthy of note include alkyl monoglyceride sulfates and alkyl sulfosuccinates. Both are very mild to the skin and, although the former are good foamers and can be used in shampoo formulation in their own right, the latter are primarily used in combination with alkyl sulfates.

Nonionic Surfactants

They are considered to be the mildest of surfactants. Although poor foamers, owing to their good solubilizing and dispersing properties, they have been extensively utilized to supplement the action of the primary cleanser.

Alkanolamides are prepared by condensation of fatty acid (usually lauric) and primary or secondary alkanolamines. Their presence in a shampoo formulation can have a pronounced effect on stabilizing the foam level and improving lather consistency. *Amino oxides* are formed by oxidation of tertiary fatty amines and are used in shampoos primarily as foam modifiers and as antistatic agents to improve the overall manageability of hair.

Polyethoxylated surfactants represent the largest group of nonionics and include the ethoxylated derivatives of alkylphenols, fatty alcohols, fatty esters, and diglycerides. They exhibit excellent detersive power and cleansing properties, but because of poor foaming, their use has been restricted to solubilizing of shampoo fragrances and other oleophilic additives.

Amphoteric Surfactants

Often referred to as ampholytic, these surfactants contain both cationic and anionic groups in one molecule. Because the charge of these surfactants are pH dependent, their properties, such as foaming potential, solubility, and CMC, also vary with the change in pH. Most amphoterics are derivatives of imidazoline or betaine. They are quite compatible with anionic, nonionic, or cationic surfactants, and have been extensively used to formulate mild (baby) shampoos or as mollifying agents in the more irritating anionic compositions.

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Shampoo Additives

These are materials incorporated into a shampoo formulation to enhance its aesthetics as well as improve its performance.

Thickeners comprise a broad variety of compounds that are used to increase viscosity of the formulations, modifying their consistency from viscous liquids to thick gels. Among the most frequently used are electrolytes, such as sodium chloride, alkanolamides and water-soluble cellulose derivatives, such as carboxymethylcellulose, hydroxyethylcellulose, carboxy vinyl polymers of the Carbopol type, polyvinyl alcohols, and natural gums, such as tragacanth. Magnesium aluminum silicates have found application as thickeners and suspending agents in antidandruff shampoos.

Opacifiers serve to impart to shampoo a pearlescent or opaque appearance. For this purpose, high-melting, wax-like materials are blended into formulations. Of particular utility in this respect are cetyl and stearyl alcohols and their esters as well as the latex emulsions of vinyl-, styrene-, and acrylic polymers.

The shampoo milieu offers itself as an ideal ground for microbial growth, particularly of the aerobic gram-negative organisms of Pseudomones. This may have a deleterious effect on the shampoo properties, posing at the same time a health hazard to the consumer. The function of preservatives is to inhibit such bacterial development. Although formaldehyde has been one of the most popular and effective preservatives, its use has declined as other compounds have come to the fore. Examples include methyl and propyl parabenes, DMDM hydantoin, quaternium-15, imidazolidynyl urea and others. The selection of a suitable preservative is made through a challenge test in which the product is subjected to the worst possible conditions anticipated during manufacture, shelf storage and actual use.

Other additives. Fragrance is an essential ingredient, often deciding the market appeal and success of the product. Addition of alcohols (ethanol, isopropanol) or glycols may be required to maintain the clarity of clear shampoos, while the presence of sequestering agents like EDTA prevents the formation of insoluble calcium or magnesium soaps when the shampoo is rinsed off the hair. FD&C and D&C dyes are commonly added to enhance the aesthetics of shampoo formulations. ''Squeaky'' clean feel of shampooed hair is frequently accompanied by difficult combing and substantial ''fly away.'' To overcome this, the shampoos contain ''conditioning'' additives that are substantive to hair remaining adsorbed on the surface after rinsing. A plethora of materials has been used to this end. To these belong amine oxides, protein hydrolysates, cationic surfactants, cationic polymers, lanolin and its derivatives, as well as natural materials, such as beer, honey, and egg.

Shampoo Formula

It must have become clear from the foregoing that a shampoo product, although straight forward in its purpose, is a complex blend of ingredients carefully chosen and attuned to effectively address the need of individual consumers. Table 1 shows the nature and relative concentration of materials contained in a typical shampoo formulation:

Specialty Shampoos

Baby shampoos place stringent requirements for nonirritancy of the scalp and eye. The majority of products are based on amphoteric detergent systems. Thus, derivatives of

TABLE 1 Typical Shampoo Formulation

Ingredient	Weight %	Function
Ammonium lauryl sulfate	10–20	Primary cleanser
Lauramide DEA	3–5	Foam stabilizer
Methyl paraben	0.08	Preservative
Propyl paraben	0.05	Preservative
Sodium chloride	0.5–1.5	Thickener
Disodium EDTA	0.2	Sequesterant
Fragrance	0.5	Fragrance
FD&C Yellow No. 5	0.001	Colorant
D&C Orange No. 4	0.002	Colorant
Water	to 100.00	Dilutent

imidazoline, betaine, and sulfobetaine are usually combined with nonionic surfactants of the polyoxyethylated alcohol esters class to procure sting-free formulations.

Medicated dandruff shampoos are designed to lessen and alleviate the excessive desquamation of the scalp via inclusion of specific ingredients. These include antimicrobials, such as quaternary ammonium salts; keratolytic agents, e.g., salicylic acid and sulfur, or antiseborrheic compounds like coal tar and resorcinol. Over the past 20 years, the shampoos containing selenium sulfide or zinc pyrithione as anti-dandruff actives have greatly risen in popularity, reflecting both the efficacy of the products and aesthetics of the formulations.

Although so-called conditioning shampoos, or *two-in-one shampoos*, have been on the market for a number of years, offering the feature of hair cleansing and conditioning in a single step, the early versions of such products did not perform to consumers' satisfaction leaving the hair often undercleansed and overconditioned. It was not until the mid-1980s that significant improvements in performance were achieved by emulsifying silicones into an anionic shampoo base. Such products have proved to be efficacious cleansers, and the shampooed hair feels soft and silky and is easy to comb. In some recent renditions of two-in-one products, the silicones have been replaced by quaternized guar gums, cationic polymers, and guaternaries.

Product Forms

In general, the shampoo formulations are relatively simple aqueous systems and, as such, quite amenable to modulation of their physical forms. The latter are often the consequence of market considerations of consumer preferences. Thus, the clarity of clear liquid shampoos conveys the impression of superior cleansing whereas opaque formulations of similar or slightly higher viscosity are suggestive of conditioning qualities. Clear gels are usually sold in compact flexible tubes that are convenient for storage and travel. A class apart are the aerosol dry shampoos that continue to occupy a small niche in the shampoo category. They consist of oil-absorbing powders, such as starch, talc, or clay, which are sprayed on to the hair and after a short while removed by brushing or combing.

Evaluation and Safety

As the work progresses at the formulator's bench, the efficacy of developed shampoo prototypes is being evaluated in the laboratory using established testing procedures. Thus,

foamability and lather characteristics are measured in the presence and absence of sebum, gaining some insight into the detersive aspects of the formulas. The properties of shampooed hair, with respect to its luster, combability, body, and fly-away, are instrumentally assessed together with the subjective evaluation of hair appearance. The ultimate proof, however, of the potential success of the formulation is in the practical use. Thus, the consumer evaluation of the product either with outside panelists or in-house testing facility is imperative. The preference of consumers for a particular fragrance is of vital importance and their comments as to the aesthetic characteristics of shampoo and the feel of shampooed hair when combined with the results of laboratory tests provide firm ground for potential product claims.

Shampoo ingredients do not pose a particular hazard with regard to skin or eye safety. The contact time is short and a water rinse follows. The irritation potential of some surfactants has already been alluded to. It is a common practice for most of the manufacturers to make provisions to evaluate their product for skin and eye irritation.

HAIR CONDITIONERS

It is worth noting that the subject of hair ''condition'' appears to be restricted almost entirely to the domain of women's hair. Although, as a woman's ''crowning glory'' the hair evokes in her a particularly profound concern for its beauty, there are at work some more mundane factors. Unlike men's hair, that of a woman's is subject to more frequent and diverse assaults that are injurious to its properties. It is perhaps ironic that except for environmental effects (weathering), most of these are associated with what we call the ''haircare'' practices. Thus, the handling of hair in the course of its daily shampooing, combing and brushing, and blow drying cause, even in the case of intact hair, gradual abrasion of the hair cuticle signaling the onset of hair damage. This process of cuticle loss is particularly evident in longer hair leading often to the generation of split ends. Hair coloring, bleaching, waving, or straightening, although imparting to hair a much sought after different or novel appearance, impair the surface lipid layer of the cuticles, further aggravating the abrasive effects of daily hair regimens. Although gradual, these deleterious effects are additive and further exacerbated by sun exposure.

Clearly, by the use of conditioning shampoos, avoiding practices singularly injurious to the cuticle, such as teasing, and keeping the hair relatively short and shielded from sun, one might, for a considerable length of time, maintain the intact hair in satisfactory condition. Alternatively, one can go a step further and by the use of products designed explicitly for conditioning supplement the benefits obtained from a shampoo and significantly extend their range. A good conditioner eliminates tangling, makes the hair easy to comb and style, eliminates static charge, and, by fostering fiber alignment, enhances the luster and shine of hair. The soft feel of hair and improved manageability are additional important attributes of conditioned hair. It is important to stress that these effects are universal, i.e., irrespective of cosmetic history of hair, whether the hair is intact, waved, colored, or bleached, the conditioner delivers its benefits.

Two general forms of conditioners are currently in use: 1) hair rinses and 2) leave-in products, often referred to as ''deep'' conditioners. Both are applied to freshly shampooed hair. True to their name, the rinse product is rinsed off after a few minutes, whereas the leave-in product is left on the hair for up to 30 minutes, after which it is rinsed off. The purpose of the longer time is to allow the product to penetrate further (thus the name ''deep'') into the hair shaft thereby extending the conditioning effects.

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The active ingredients in most conditioners are based on quaternary ammonium salts (cationic surfactants) such as steartrimonium chloride and, cetrimonium chloride, and the like. Because of their great affinity for hair, these compounds bind strongly to the cuticles, providing a low-friction surface, thus making the cuticles slick and less prone to abrasion. Other components present in the conditioning formulations, such as fatty amines, fatty alcohols, and amine oxides, supplement the action of cationic surfactants, adding primarily to the tactile benefits. The leave-in conditioners that are recommended for use on damaged hair frequently contain protein and lanolin derivatives.

Conditioning effects are usually lost in shampooing, and a reapplication is recommended to reinforce the protective effect. Conditioning formulations containing cationic polymers are somewhat longer lasting. The same is true for conditioners based on emulsions of polymeric silicones.

HAIRDRESSINGS

Hairdressing is a broad term describing products applied for final grooming. Including brilliantines, tonics, and gels, this category follows new fashions, hairstyle trends, and is attuned to progress in styling techniques. Hairdressings are applied by spreading the product through the hair with the fingers and then combing through for an even distribution. As they are not rinsed off after application, care must be taken to avoid excessive build-up.

The primary purpose of brilliantines is to add sheen to hair. Thus, the main constituent of these products is oil—usually mineral oil—which is spread on fiber strands increasing their luster and providing grooming effects. Solid brilliantines (pomades) are based on petrolatum to which various waxes are added to attain the desired consistency and texture. Tonics might be viewed as lighter versions of brilliantines and usually consist of alcoholic solutions of various oils. The alcohol wets the hair and after evaporation leaves a thin film of oil. By using synthetic, rather than natural oils, much less greasy formulations can be obtained. Using a high concentration of ethoxylated emulsifiers, grooming oils can also be readily blended into clear gels. On the other hand, setting gels based on hydroalcoholic solutions of carboxyvinyl polymers or methylcellulose ethers are oil free. They range in consistency from liquid to rigid gels and provide a good range of textures, volume, and hold.

Styling Products

Whereas most of the styling needs of short hair are satisfactorily met by a good haircut, those with longer hair require more effort which is, however, well rewarded by the diversity of styles that can be imparted. The underlying principle of all styling processes is hair setting and a few comments on the subject seems appropriate. Hair fibers are flexible and elastic, and when dry bounce back immediately to their original configuration (straight or curly) when bent, extended, or twisted. On wetting, however, they become pliant and malleable and can be readily molded (set) to almost any desired form. On drying, they retain the new shape until exposed to water (moisture) again.

The primary function of all styling products is to assist in the setting process and/or to ensure the stability of the newly imparted configuration. Depending on the type of styling product, different mechanism of action are operative.

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Styling Aids

As the name implies, the role of these products are first to facilitate styling the hair and second to keep it in a newly styled shape. Three general product forms represent this category: styling gels, mousses, and styling sprays. Most of the formulations are based on synthetic film-forming polymers and contain a variety of additives to improve film properties and performance. Thus, phtalates and glycols are used as plasticizers. Lanolin derivatives and silicones are added to improve feel and impart some resistance to moisture. The products are applied to wet hair which is styled with fingers or a comb. Usually the more viscous the product, the easier it is to style the hair. As the hair dries and sets in the desired configuration, a polymeric film forms on the surface of hair, cementing adjacent fibers together and thus further stabilizing the newly imparted style.

Table 2 serves as an example of typical styling formulations for a styling gel and a styling mousse.

Hairsprays

Also in this category, polymeric film formers are the backbone of the formulations, although both the intended use and the mode of action are somewhat different from those of styling aids.

These products are applied to dry and already styled (set) hair in the form of fine mist or spray. The spray droplets collide with and become deposited on hair fibers. As they spread on the hair surface, they tend to migrate and accumulate at the points where adjacent fibers are very close or intersect with each other. This results in the formation of minute joints distributed throughout the hair mass. As the solvent evaporates, these joints become rigid bonds welding the fibers together and, thus, preventing the motion of individual hairs relative to each other. This cumulative restraining action of hundreds of

TABLE 2 Typical Formulas of Styling Aids

Ingredient	Weight %	Function
Styling Mousse		
Polyquaternium-11	1.4	Styling ease
Polyquaternium-4	0.6	Film former
Lauramide DEA	0.2	Foam stabilizer
Isosteareth-10	0.2	Foam stabilizer
Dimethicone copolyol	0.15	Styling ease
Fragrance	0.2	Fragrance
DMDH hydantoin	0.2	Preservative
Methyl paraben	0.1	Preservative
Isobutane/propane blend	7.0	Propellant
Water	to 100.00	Solvent
Styling Spray		
Ethylester of PVM/MA copolymer	2.5	Film former
Dimethicone copolyol	0.3	Styling ease
Isopropyl alcohol	5.0	Solvent
Fragrance	0.3	Fragrance
Ethanol	45.0	Solvent
Water	to 100.00	Solvent

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such microscopic welds throughout the hair assembly accounts for the style-stabilizing performance of hair sprays, protecting the hair from mechanical deformation,wind, and humidity.

The strength of these hairspray bonds depends on a number of factors, of which the nature of the polymeric resin is of paramount importance. Most of the polymers used form adequately strong bonds at low relative humidity (RH). As the RH increases beyond 80%, however, most resins begin to absorb moisture from the environment, softening the welds. At the same time, water absorption by hair causes rapid relaxation of the set configuration of the fibers and it is the tenacity of the hairspray welds alone that stabilizes the imparted style. Clearly, the polymers that are least sensitive to the plastizing effect of water are likely to be the better performers and are thus preferred for a hairspray product.

It should be stressed that in addition to the intrinsic strength of the resin, other factors may affect bond formation and/or bond toughness. For example, the characteristics of the solvent system used to deliver the resin to hair plays an important role. Efficient weld formation depends on the wetting and spreading properties of the resin droplets on the hair surface. As mentioned earlier, the welds are formed by the accumulation of liquid spray at contact points between fibers. Thus, an aerosol formulation with 30% alcohol and 70% highly volatile propellant will dry much faster than a solvent vehicle with 50% or more alcohol. As the solvent evaporates, the viscosity of droplets increases and mobility decreases. This reduced mobility results in relatively small bonds between adjacent or intersecting fiber which might negatively affect the product performance. One might be led to a conclusion that the spray that stays ''wetter'' longer generates better performing welds. This may hold true for nonaqueous systems as the organic solvents used in hair formulation do not have any adverse effect on the set of the styled hair. With the hydro-alcoholic systems, however, and the water content of over 20% the long ''residence'' time of hairspray droplets on hair may lead to a significant loss of set caused by the selective water absorption by hair fibers.

Although a number of hairspray resins have been developed over the years and many of them have been in use, the combination of regulatory restrictions and increased demands on the aesthetics of product performance has narrowed the field somewhat. Thus the butyl and ethyl esters of poly (vinyl methyl ether/maleic anhydride) copolymers, which for years have been the most widely used polymers in hair sprays, have suffered a rapid decline, being surpassed by octylacrylamide/acrylates/butylaminoethyl methacrylate copolymer. The latter provides excellent holding properties at relatively low resin concentration. For the aerosol hairsprays, the resin of choice is vinyl acetate/crotonates/neodecanoate, which, by modulation of the extent of its neutralization, can substantially modify the film properties.

Essential as it is, the set holding is not the only attribute that has to be considered in formulating hair sprays. Clearly, the aesthetic aspect of sprayed hair cannot be neglected. Thus, the resin film should add shine (gloss) and not dull the hair, nor should the hair become tacky in humid weather. It should resist flaking, but be readily removed by shampoo. By selection of appropriate additives and solvents, both the holding and aesthetic goals can be readily attained. Table 3 provides ingredient listings for typical aerosol and pump sprays.

Safety and Regulatory Issues

All aerosol hairsprays, whether containing hydrocarbon or carbon dioxide propellant, are classified as flammable by virtue of their flame propagative properties. The same is true

TABLE 3 Typical Hair Spray Formulas

Ingredient	Weight %	Function
Aerosol Hairspray		
Poly(vinyl methyl ether)-maleic anhydride ethyl ester	5.0	Film former
Amino methyl propanol	0.2	Neutralizing agent
Dimethyl phthalate	0.4	Plasticizer
Fragrance	0.2	Fragrance
Ethanol	70.0	Solvent
Isobutane/propane	24.2	Propellant
Pump Hairspray		
Octylacrylamine/acrylates/butyl amino ethyl methacrylate copolymer	3.5	Film former
Amino ethyl propanol	0.5	Neutralizing agent
Cetearyl octanoate	0.1	Plasticizer
Fragrance	0.15	Fragrance
Ethanol	80.00	Solvent
Deionized water	15.75	Solvent

of pump sprays on account of their high alcohol content. Appropriate warnings should be displayed on the package informing of potential eye irritancy of the product.

Federal regulation in 1978 that banned the use of chlorofluorocarbons in hairsprays brought about a drastic change in the technology of aerosol hairsprays. New propellants had to be evaluated and formulations developed to accommodate their different properties. The hydrocarbon gases, such as propane, butane, and isobutane have been found to generate the most consistent hairspray pattern, being at the same time compatible with alcohol and current hairspray resins. However, in 1990, both California and New York introduced the concept of volatile organic component (VOC) placing strict limits on allowable VOC content in hair sprays. As the VOC is defined as any organic compound having between 1 and 12 carbon atoms, the VOC restrictions also affect the nonaerosol hairsprays where the ethanol is both the resin solvent and propellant. The decrease in VOC levels is primarily compensated for by the increase in water content of the hairspray, making it wetter, less efficacious, and sticky leaving aside the less aesthetic delivery characteristics. A search is underway to develop new resins that accommodate the high–water content formulas with performance standards equal or approaching those of current sprays.

Permanent Waving

It was perceived a long time ago that wavy hair not only surpasses straight hair in opportunities for more diverse styling, but because of its geometry, it appears more luxurious and, thus, highly desirable. Early records show that the ancient Assyrians wore a mass of curls falling over their shoulders and the beards of men displayed exquisite and highly uniform wave patterns. The earliest recorded methodology of hair waving can be traced to Egyptians who curled their hair with mud and then dried it in the hot sun. The elaborate coiffures of Roman women relied on prototypes of the curling iron. Then, with the advances of the Middle Ages, hair virtually disappeared from view and did not make its reemergence until the time of the Renaissance. But then shortly it hid again—this time

under wigs. The latter, made of human hair, were processed to desired configurations by techniques not greatly different from those developed by Egyptians and Romans. It was not until the early 20th century and the pioneering work of Nessler on hot waving that generated stimuli for affordable and simple waving procedures. Basic precepts of modern permanent waving were developed in the 1930s. Over the years, these principles have been further explored and creatively utilized to yield safe and efficacious products.

Hair-Waving Process

The immediate objective of waving is to impart to hair a durable configuration that is different from what the hair exhibits in its native form. Each hair has a geometry that is the result of processes of keratinization and follicular extrusion that transforms a viscous mixture of proteins into strong, resilient, and rigid keratin fiber. In principle, waving can be viewed as a combination of reversal and a stepwise restaging of these processes, as it entails softening of keratin, molding it to a desired shape, and annealing the newly imparted geometry. The underlying mechanism of waving is, thus, essentially molecular and involves manipulation of physicochemical interactions that stabilize the keratin structure.

It might be useful at his point to emphasize the essential difference between waving and setting of hair. Although both cases involve the impartation of new geometry to hair, only water-labile bonds are manipulated in setting, and thus the imparted geometry is moisture sensitive and lost on shampooing. In waving, both the covalent and secondary bonds are involved and the new geometry is stable to repeated washing cycles. The cleavage of covalent bonds (disulphide cross-links of cystine) is conveniently attained by reducing agents that convert them to cysteine residues that can be relinked in the last phase (neutralization step) of the waving process.

In a typical waving procedure, freshly shampooed, damp (but not wet) hair is separated into 30 to 60 tresses. Each tress is wetted with the waving lotion and wound onto plastic rods or curlers with the help of a porous end paper or sponge. The size of the curler determines the character of the resulting wave; the smaller the curler, the tighter the wave. After 10 to 20 minutes, the hair is rinsed thoroughly and, while still on rods, wetted with the neutralizing lotion. The hair is then unwound, rinsed again, and either freely dried or set in the desired style. The waving procedure depends on the type of the waving product used and the desired end result. Thus, instead of wrapping with lotion, the hair can be wound wet and the lotion applied to curled hair. Sometimes a suggestion for a ''creep'' step is made to obtain a tighter and longer lasting curl. This involves an approximate 30-minute wait between rinsing off the lotion and application of the neutralizer.

The tight curl produced by permanent waving is frequently not the configuration desired for the final hairstyle. Often a water set of a larger curl configuration is superimposed on the wave. Then, as the temporary set begins to relax under the influence of moisture, the change of the hair form towards the tighter, waved configuration counterbalances the forces to straighten the hair with the net result of a greater set stability and more body than if the hair had not been waved.

Waving with Mercaptans as the Active Ingredients

European, American, and large segments of the Asian markets are dominated today by the formulations based on thioglycolic acid (TGA) and its derivatives. The popularity of TGA stems from a number of factors. The long history of use has built an impressive evidence of adequate medical safety. The incidence of injury has been extremely low and

so has been the frequency of sensitization. High adaptability of TGA to various formulation types that provided markedly different end benefits coupled with performance reliability and a low price all contributed to its success. The unpleasant odor of TGA has remained it most perceptible drawback. Although some progress has been made in the fragrancing of TGA-based lotions, the results so far are at best mediocre.

Conventional waving lotions contain 0.5 to 0.8M TGA adjusted to pH 9.1 to 9.5. The neutralizing base can be ammonia, alkanol amines, sodium carbonate, or a mixture thereof. Ammonia appears to be more effective than the other bases in facilitating diffusion of TGA through hair. It is also preferred over nonvolatile amines because it escapes during processing and the resultant drop in pH reduces the activity of the lotion with time and thus minimizes the danger of overprocessing.

Over the years, several TGA derivatives (primarily amides and esters) have been tried, but as of now, only one—glyceryl monothioglycollate (GMTG)—is of practical importance and used in so-called acid waves. In terms of waving performance, GMTG works better than TGA at *low pH* under such conditions, however, the resulting wave lacks the crispness and durability of the conventional alkaline TGA wave. This is somewhat compensated for by less hair damage. To increase the efficacy of GMTG, the waving process is often carried out with the aid of heat.

Apart from the weaker waving performance of GMTG, when compared with TGA there are several other disadvantages associated with the use of this mercaptan. Its low water solubility and propensity for hydrolysis necessitates a separate package (container), which represents inconvenience for the consumer and additional cost. Occasional reports of skin sensitization has limited the use of GMTGA to salon applications. Finally, its rather pungent odor has a tendency to stay on the hair even after the neutralization step. Perhaps because of its hydrophobic character, GMTGA may be tightly bound to the apolar domains of the keratin structure, and therefore be more resistant to rinsing.

There are on the market several types of TGA-based formulations that claim point of difference from the conventional lotions. One is called a ''self-timing'' wave, the other a ''self-heating'' or ''exothermic'' wave. Both use TGA under alkaline conditions. The self-timing wave contains, however, dithiodiglycollic acid (DTDGA), which is the oxidation product of TGA. The function of DTDGA is to prevent hair overprocessing without negatively affecting the waving performance. In the United States self-timing formulations command approximately 20% of the market share.

The exothermic wave product contains a small vial of aqueous H_2O_2 (separate from the neutralizer), which is to be added to the waving lotion just before its use. Oxidation of TGA (which in this case is in excess of concentration required for waving), generates some heat as well as small quantities of DTDGA. Although the warmth can be readily perceived on mixing, the heat dissipates quickly as the lotion is applied to hair and equilibriates itself with that of the environment.

The acid wave based on TGA is a conventional TGA formulation adjusted to a lower pH (6.8-8). Unlike the acid wave with its esters (GMTGA), these formulations perform poorly and often require heat to improve the result.

In the Far East, particularly in Japan, the use of cysteine as a waving agent is widespread. This amino acid is claimed to provide a 'natural' and nonodorous alternative to TGA and to wave the hair without damage. Although some of these assertions are doubtlessly true, the waving efficacy of cysteine is mediocre. One can significantly increase its efficacy by the incorporation of a high concentration of urea (2-3M). Most of the Japanese

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formulations contain, apart from cysteine, hefty amounts of TGA as the effective ingredient.

Waving Formulations with Sulfite as the Active Ingredient

Sulfite, as a permanent setting agent, has found wide application in the wool industry (pleating, lustering, flat setting) well ahead of TGA on account of its effectiveness and lack of odor. Sporadic attempts to use it as a waving agent had not been very successful until the late 1970s when it was successfully introduced. The rapid rise of sulfite products appeared initially to spell demise for conventional TGA formulations. Readily consumer-perceptible attributes, such as lack of odor and low hair damage, combined with the then preference for softer hairstyles greatly favored sulfite systems. A number of companies rushed to the market with offerings of formulations for tight curls, body waves, and hair straighteners. However, attractive as these formulations appeared to be, they could not match the waving efficacy or durability aspects of TGA systems. The TGA-based products regained their ubiquity, although the sulfite product held on to a stable, though small, market share.

It appears appropriate at this junction to re-emphasize that the current methodology of hair waving (ambient temperature, medically safe reagents, short treatment time) relies heavily on the disulfide bond reactivity as the cornerstone of the process. The reductive cleavage of disulfide cross-links is as essential to fiber softening as is their reformation to the stability of newly imparted configuration. Needless to say, throughout the waving process, secondary interactions (hydrogen bonds, salt links, Van der Waals interaction) participate therein, and their more or less intense contributions reflect themselves in the overall efficacy of the process. Nevertheless, so far it is the disulphide bonds that represent the *sine qua non* condition for waving.

Over the years, there have been numerous attempts to explore the ways of permanently altering the configuration of keratin fibers by exclusive manipulation of secondary bonds. Some success has been shown in fibers modified by inclusion of bulky apolar residues, high-temperature steam setting, or by blocking cysteine side chains with hydrophobic maleimides. Except for high-temperature steam setting of wool (in the crimping process), these approaches found little, if any, practical applications either because of the complexity and severity of treatment conditions or because of less-than-acceptable results.

Neutralizing Compositions

The principal active ingredient in most of the neutralizing formulation is acidic hydrogen peroxide at a concentration of 1 to 3 %. Sodium bromate and sodium chlorite are occasionally used on account of their good stability and absence of bleaching power. H_2O_2-compatible conditioning agents, such as cationic surfactants or silicone emulsions, are often included to ensure easy combing, smooth texture, and control of fly-away of the waved hair.

Evaluation of Waving Efficacy

Although ''permanent'' is the defining adjective of the imparted wave, there are many other considerations that are important in the assessment of wave quality. Among them are tightness of curl, its springiness, feel of the hair, its luster, and combability. Ultimately, the most reliable way of judging the characteristic of a wave is on the head of the consumer, and thus it is not surprising that this subjective approach has always been used as the final evaluative tool of product prototypes. The importance of using the consumer

as the testing probe is of particular importance in assessing the wearing characteristics of the imparted wave. So far, no satisfactory laboratory procedures have been developed to accurately mimic this important aspect.

The objective laboratory measurements on both hair tresses and single fibers are the backbone of the development of new prototypes, screening processes, and further evaluation of competitive products.

Single-fiber technique is particularly useful in differentiating between different chemical systems (e.g., TGA vs. sulfite, alkaline vs. acid wave) providing rapid information as to the efficacy of the process. Some measure of the durability can be gained by submitting these microsprings to the action of hot water, detergents, and stress. Using calibrated fibers, the mechanical measurements can provide the first impression of process aggressiveness.

Clearly, hair tresses are required for evaluation of assembly characteristics—combability, fly-away, luster, and feel—as well as for porosity determination by liquid retention. The curl appearance, both wet and dry, can be assessed and appropriate recordings (photographs) made. The tresses are also required for water-setting evaluations where the imparted wave is used as a background to the consequent hair-setting experiments. In this case, conventional techniques of set impartation and durability evaluation in the humidity chamber are used.

The cosmetic history of hair (before waving, straightening, color, bleaching, weathering) influences not only the degree of damage that the waving lotion can inflict, but also the quality of wave it can impart. Both single-fiber techniques and tresses should be used in the manner previously described.

Prevention and/or Masking of Damage

Hair damage has become a constant companion and by-product of most of our hair care practices (e.g., combing, brushing, heat setting, coloring, bleaching), with hair waving making its own contribution. Because the problem of damage is so widespread, there has been vigorous activity over the years to develop some general specific ways of damage repair. So far, none that are effective and reliable are available. A more promising route is that of damage prevention (the word ''alleviation'' would be more appropriate) or damage masking.

Taking a somewhat detached view, one should add that there is no evidence for the epidemic of hair damage with almost any of the cosmetic treatments of hair, and the damage reflected is usually well tolerated by the consumer for the benefits gained. Nevertheless, even from the discussion presented, some measures can be taken to at least limit the damage inherent in the process. Thus, if a gentle wave is required, an acid type of a thiowave or one based on sulfite might be an alternative. With alkaline waving, the potential of acid-buffered salt solution before water rinsing should be considered, primarily for fine or weathered hair. Recovery of disrupted membrane structures can apparently be attained in the use of sulfite waves by using a cysteine after-treatment (a genuine harbinger of damage repair?). Consumers considering combined treatments (e.g., waving and bleaching or haircoloring) should wave the hair first–as the reduction step, irrespective of whether sulfite or TGA is used, is much more damaging to hair with an oxidative cosmetic history.

To mask and/or limit the damage after waving (and hair combing comes here to the fore), the use of both conditioning shampoos and conditioners is imperative. Clearly, the waving formulations containing effective cationic polymers are at an advantage, as

every anionic detergent used in the shampoo (and the shampooing process can be quite abrasive to the wave-sensitized cuticle) forms a lubricating complex with the surface-adsorbed polymer.

Finally, as previously indicated hair undergoes faster weathering and sun lightening after waving than before it. Here, sunscreens would come in handy as long as they are delivered from an effective vehicle, such as a hairspray or mousse. The protection attained from sunscreen-containing shampoos or conditioners has been virtually nil up to now.

Hair Straightening

Although the molecular mechanism underlying hair-straightening parallels that of waving or setting of hair, there are some distinct differences in the composition of formulations and, naturally, in the mode of their application. There are essentially two different categories of straightening preparations; 1) those that aim at temporary straightening and 2) those designed to accomplish permanent effects.

Temporary Hair Straightening

The most frequently used technique in this category is hot combing. An oily material (pressing oil) is applied to hair, which is then combed under slight tension with a heated comb. The straightening effect is produced by the combined action of heat and the moisture present in hair. The function of the pressing oil is threefold: 1) to act as a protective heat-transfer agent between the comb and the hair 2) to serve as a lubricant reducing the drag of the comb, and 3) to function as a barrier slowing diffusion into the hair of moisture from the scalp and environment, and thus delaying reversal of the straightening effect. Pressing oils are mostly based on petrolatum and mineral oil blended with some wax and perfume. Frequent combing dulls and damages the hair, leading ultimately to hair breakage.

Permanent Hair Straightening

The most effective class of permanent straighteners (relaxers) is that based on alkali as an active ingredient. Sodium or potassium hydroxide or sodium carbonate in combination with guanidine are used at concentrations of 1.5 to 3% in a heavy cream base. Even though the recommended treatment time is only 5 to 20 minutes, the straightening effects in general, surpass those obtained with either thioglycollates or bisulfites because of the different chemistry of the process and the greater aggressiveness of alkaline relaxers. A 15-minute treatment irreversibly decreases the cystine content of hair to two thirds of its initial value.

The damaging action of strong alkali on hair is not restricted to disulfide bonds alone. Apart from the potential of mainchain scission (peptide bond hydrolysis), the very nature of the base (high pH) leads to a build-up of negative charges in hair that results in increased swelling, which is intensified by concurrent breakdown of the disulfide bonds. Great care must be exercised in the use of alkaline relaxers because even brief contact with skin can cause blistering. It should be pointed out that the chemistry underlying the hair-straightening process with alkaline relaxers is fundamentally different from the systems based on thioglycollates or sulfites. The alkalis (irrespective of their nature, i.e., sodium hydroxide [lye], calcium hydroxide, or guanidine) cleave the disulfide bonds, and this cleavage is almost instantly followed by formation of new (monosulfide) cross-links. The efficacy of this secondary process varies between 50 and 70%, and this, to a great

extent, accounts for the observed alkali damage. If the cross-linking step is not accomplished at that time, there is no known way of cross-link reformation at a later stage of the process. The so-called neutralization step in alkaline relaxing should never be confused with that used in thio or sulfite processes, where its main function is bond rebuilding. In the case of alkaline relaxing, the neutralization aims at removing the excess alkali from hair, which is accomplished by acid-containing (or acid-buffered) shampoo.

Alkaline thioglycollate has also been used as the active ingredient in relaxers, although in somewhat different form from that encountered in conventional waving lotions. The latter are always thin, promoting a fast lotion penetration into the tightly wrapped hair on the curler. Relaxers, on the other hand, are formulated into thick (viscous) oil-and-water (o/w) emulsions or creams using a high concentration of cetyl and stearyl alcohols and high–molecular weight polyethylene glycols together with fatty alcohol sulfate as an emulsifier. The cream is worked into the hair while it is combed straight. The high viscosity of the formulation helps to maintain the extended configuration of the hair during processing, which may take from 30 minutes to 2 hours depending on the initial curliness of the hair. In the course of the treatment, the hair is often recombed to assure its straight configuration. Upon thorough rinsing, conventional oxidizing neutralizers (hydrogen peroxide, bromates, or perborates) are used as a final step of the process.

In recent years, hair-straightening compositions based on mixtures of ammonium bisulfite and urea have been introduced and found to be of some use, primarily in the Caucasian hair-straightening market. The recross linking of bisulfite-treated hair is more effectively accomplished with an alkaline rinse (pH 8–10) than with oxidizing agents, although the latter can also be used to destroy the residual sulfite reductant.

Hair Coloring

Not belittling the importance of hair texture and its geometry, it is perhaps not surprising that the quintessence of hair beauty manifests itself in its color. This has been well recognized as much in the distant past as it is now. It is truly remarkable how nature, using the melanin pigment (a substance without an identifiable chromophore) as its primary colorant, has been able, via clever manipulation of physics and chemistry, to generate hundreds of shades ranging from the Scandinavian blondes through Scottish redheads to the intense black hair of Africans and Asians. Still, the need for color enhancement, or indeed its change, continues to exist and is clearly the driving force of the hair-coloring market as reflected by the variety of products available to the consumer.

Setting aside the diversity of claims and application techniques, hair-coloring products fall into two general categories: 1) those that are based on materials that are inherently colored, and 2) those that use colorless precursors and develop their hair coloring characteristics only on interaction with an oxidant. Dyes of the first category are used in temporary (or shampoo-removable) products and semipermanent color formulations (color stable to several shampooings). The second category forms the mainstay of so-called permanent or oxidative hair colors. Their importance lies not only in the durability of the effect, but also in that the natural color of hair can be modified, almost at will, to any desirable hue or shade, whether darker or lighter than the original. This is accomplished in one step through a combination of bleaching of the natural pigment present in the hair and simultaneous color development. Such shade manipulation is clearly not available in the temporary or semipermanent products, the function of which is primarily restricted to the build-up of color intensity. Although semipermanent colorants lack the versatility of oxidative

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dyes, they are recognized as being gentler to hair because no peroxide is required. In each hair-coloring category, a sizeable number of dyes (or precursors) is required to attain a viable palette of shades. These dyes differ not only in their chromophoric characteristics, but also in their affinity to hair, water solubility, and overall photostability. In color impartation, a delicate balance of constituent dyes is essential to obtain uniform and desirable results. However, subsequent exposure of dyed hair to shampooing, sunlight, perspiration, and simple wear and tear often highlights the differences in properties of dyes that can result in unpredictable color changes.

Temporary Hair Colorants

As the name itself implies, the dyes of this class are scheduled for only a fleeting residence on hair being removed at the first shampoo opportunity. Although the postulate of fast removing precludes the use of low–molecular weight colorants that could penetrate the hair shaft, it nevertheless extends the palette to almost any toxicologically acceptable dye that can be aesthetically formulated into a cosmetic vehicle. In general, food colors, cosmetic colors, pigments, or even textile dyes can be considered. To be avoided are strongly basic dyes that have a tendency toward intensive skin staining and a high affinity for chemically damaged and weathered hair. Table 4 lists some of the dyes currently used in temporary hair products.

Temporary color formulations are of the ''leave-on'' type, which means that they are applied to hair usually after shampooing and left there to dry. They can be simple solutions of dyes incorporated into a styling mousse, or can be complexed with surfactants whereby more color can be deposited on hair. By the very nature of the application, the intensity of the coloring effect is low, but sufficient, to produce aesthetically pleasing effects. Exposing the colored hair to heat (whether from a blow dryer or bonnet) may bring about some increase in durability of the imparted color to shampooing.

Semipermanent Hair Colorants

This class of dyes, initially designed exclusively for gray-hair coverage, has progressively grown in importance as the formulation changes extended the color palette and improved the durability of the imparted color.

The majority of products features a blend of low–and medium–molecular weight dyes that are capable of penetrating into the hair shaft, thus assuring a moderate degree of fastness. A blend is necessary to achieve the desired color and obtain a match between the roots and the more permeable ends. The dyes that are used are generally nitrophenyldiamines, nitroaminophenols, and, to a lesser extent, aminoantraquinones. Table 5 lists some of the dyes in use.

TABLE 4 Temporary Hair Colorants

Name	Type
FD&C Blue No. 1	Triphenyl methane
D&C Red No. 22	Xanthene
Ext. D&C Yellow No. 7	Nitro
D&C Brown No. 1	Disazo
D&C Green No. 5	Antraquinone
D&C Red No. 33	Azo

TABLE 5 Semipermanent Hair Colorants

Name	Color
4-nitro-o-phenylenediamine	Yellow
1,4,5,8-tetra amino anthraquinone	Blue
1,4-diamino anthraquinone	Violet
N′-(2-hydroxy ethyl)-2-nitro-p-phenylene diamine	Red

Several product forms are available: lotions, shampoo-in formulations, or mousses. In all cases, the dyes are dissolved or dispersed in a detergent base that contains a thickener so the product stays on the hair without running or dripping. Application time of 20 to 40 minutes is common, after which time the product is rinsed off and frequently followed by a conventional shampoo.

Recently, formulations providing more durable (color stability up to 20 shampoos) effects have become available. They consist of the conventional semipermanent dyes blended with oxidative dye precursors, which in conjunction with dilute hydrogen peroxide produces longer-lasting color moieties. Such products are occasionally referred to as ''demipermanents.'' Unlike the conventional semipermanent products that are sold in single containers, they, in addition to the dye mixture, contain a separate package of the oxidant.

Often included in the semipermanent category is also the only vegetable dye that is permitted to be used in the United States: henna. Henna consists of the dried leaves of the plant *Lawsonia alba*, which grows in North Africa, the Middle East, and India. The active ingredient, lawsone (2-hydroxy-1-4-naphtoquinone), constitutes about 1% of the dried leaves [10]. Using henna, only limited reddish shades can be achieved. In some products, henna is mixed with other dyes to obtain more variety in color. Such products are then subject to the label warnings used for coal-tar dyes.

A mention should also be made of metallic dyes, which are still popular with men. These products usually contain dissolved lead acetate and elemental sulfur. After application to hair and subsequent air exposure, the lead salt reacts to form a mixture of insoluble sulfides and oxides imparting to the hair a darker color, thus providing a gradual gray coverage.

Permanent Hair Colorants

Unmatched by other colorants in the shade palette, durability to shampooing, resistance to fading, and absence of skin staining, the permanent (oxidative) hair colorants have justifiably carved off the largest market share in hair dyes worldwide. Available in a variety of forms (e.g., lotions, gels, shampoos, creams.), these products deliver reliable results that last until the new hair grows out. Most often, the colorant is supplied as a two-component kit consisting of a mixture of colorless dye precursor and of a stabilized solution of hydrogen peroxide. Occasionally, the peroxide is provided in the form of a powder, such as urea peroxide or sodium perborate. The two components are mixed immediately before use, applied to hair, and left for 20 to 40 minutes before being rinsed out with water.

The color formation commences upon mixing and involves complex reactions between precursors and the oxidant. The precursors consist of two classes of reactants: 1) primary intermediates, comprising o- and p-aminophenols and phenylenediamines, which

upon oxidation by peroxide form colored quinone imines; and 2) secondary intermediates (couplers). The latter condense with the imines to yield the final dye molecules. While the color-forming reactions take place in the dye mixture, a significant fraction of the dye precursors diffuse rapidly into the hair together with the hydrogen peroxide forming the colorant moieties throughout the hair fiber. The process is carried out at alkaline pH which also favors the bleaching of the melanin pigment by H_2O_2. Table 6 lists some of the primary and secondary intermediates and colors they produce.

Depending on product form, the formulation of the dye base varies. Ammonia and ethanol amines are preferred alkalizing agents, and a mixture of surfactants and solvents are used to solubilize the dyes and assure wetting of hair. A small quantity of reducing agents are added to prevent the auto-oxidation of the dyes during storage. It is important to realize that hydrogen peroxide, which so effectively assists in both the color development and lightening of hair pigment, also displays a less desirable role in causing oxidative hair damage. Although the damage associated with a single application is slight, the cumulative effect of subsequent treatments is quite perceivable.

Hair Repigmenting

The idea of dyeing the hair by melanin has always been alluring. The ''natural'' aspect of the colorant implied durability of the coloring effect and its insensitivity to haircare regimens, or shade fading—all these have been factors providing continuous incentive to use the potential of such process. Apart from intense patenting in this field, several papers have recently appeared [11,12] that describe such coloring systems as well as the characteristics of repigmented hair. Recently, products based on the principle of melanin repigmentation of hair have appeared on the market, but the information available to date is too scanty to offer a reliable judgment as to the market viability of these products.

Bleaching

The bleaching action of hydrogen peroxide has been already alluded to in the context of permanent hair coloring, and quite satisfactory levels of lightening can be obtained with such products.

To attain a significantly greater level of bleaching, hydrogen peroxide is combined with bleach accelerators or ''boosters.'' The latter are mixtures of ammonium, potassium, or sodium persulfates. The salts are packaged as dry powders and mixed with hydrogen peroxide just before use. Thickeners and alkalizers (usually sodium silicates) are included in the booster package. Processing time depends primarily on the initial hair color and the desired level of lightening. The pH of these formulations is usually much higher than

TABLE 6 Oxidation Dye Colors

	Colors on hair with	
Coupler	PPD	p-Aminophenol
Recorcinol	Greenish-brown	Yellow-brown
m-Phenylenediamine	Blue purple	Violet
m-Amino phenol	Red-brown	Light orange
1-Naphtrol	Blue violet	Red-violet
2-Methyl resorcinol	Yellow brown	Yellowish-beige
2-Amino pyridine	Dark grayish-blue	Light grayish-green

that of the permanent hair-color products and so is the concentration of H_2O_2. All of these factors—high concentration of peroxide, presence of oxidizing salts, and high pH of the process—connote significant oxidative damage of hair. After thoroughly rinsing off the bleaching mixture, the hair should be given an acidic ''bath'' (lemon juice or solution of citric acid or diluted vinegar) followed by a 5 to 10 minute treatment with a ''deep'' conditioner.

Hair-Color Safety and Regulatory Issues

Because of the allergenic potential of some of the materials used in hair dyes (primarily p-phenylenediamine, or PPD), hair colorants in the United States display on the label as a legal requirement a warning, plus instructions for a 24-hour patch test with the precursors and hydrogen peroxide mixed in the same manner as in use. As required by Section 601(a) of the Federal Food, Drug and Cosmetic Act, the warnings reads as follows:

> This product contains ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should be made. This product must not be used for dyeing the eyebrows or eyelashes; to do so may cause blindness.

It should be noted that allergic contact dermatitis to hair dyes appears to be far less common today than decades ago. It has been suggested that PPD, although a strong sensitizer, is not likely to produce skin sensitization because of the short contact time with skin and rapid reaction of PPD with the oxidizing agent and couplers [13].

Concerns as to the possible carcinogenicity of some hair ingredients arose in 1975 when these were reported to be mutagenic for bacteria in bioassays [14]. Presently, it is not clear how significant a risk this poses to users of hair dyes. Because hair dyes have been in common use for over 50 years, epidemiological studies on cancer rates in occupationally exposed groups or the users of hair dyes are of particular value. So far, the results of most of these suggest that hair dyes do not pose a carcinogenic risk [13].

CONCLUDING REMARKS

Available space limits this chapter on hair cosmetics to only a brief overview of what is used and practiced in this broad and important segment of personal-care products. Many aspects of hair chemistry and physics have only been fleetingly discussed, including properties of single hair fibers and their assemblies. The whole area of claim substantiation has been left out, together with the description of physicochemical techniques that are relevant to this subject. For a fuller account on these topics, the reader is referred to an excellent book by Zviak [15] and recent publications on haircare [16] and cosmetic-claim substantiation [17].

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Ethnic Differences in Haircare Products

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INTRODUCTION

Hair is undoubtedly one of the most important personal features of people in all cultures. For the past several centuries hair has played an important role. Style, length, and color changes are influenced by fashion trends. Hair often allows for feelings of health and beauty, and thus its influence is of great importance. Therefore hair has been studied greatly as cited in numerous publications. Three major types of hair are known: African, Asian, and Caucasian. The differences between these hair types are related to diameter, geometry, and other physical parameters [1,2]. Closely related to these parameters are biophysical factors, tensile strength, and combing forces, which might be influenced by cosmetic formulations that are applied to hair. Caucasian hair is also called European hair and African hair is also called Negroid hair. The names only summarize the complexity of hair types, e.g., Asian hair is the sum term for Japanese, Chinese, and other Asian ethnic groups. And furthermore, even in such ethnic subgroups we do not really see a single hair quality. Therefore, taking Asian, Caucasian, or African hair is an overall example for the corresponding hair types of these regions. Table 1 shows an overview about the most important hair fiber characteristics [3,4].

The demand for hair care is closely related to the condition and length of the hair and fashion trends. Hair is exposed daily to a wide variety of influences that can damage it to a greater or lesser degree. Especially the surface of hair that has been exposed to environmental influences (e.g., sunlight, combing, blow drying, etc.) or chemical treatments (e.g., cold waving, dyeing, bleaching) carries a stronger negative charge than the surface of untreated hair.

The resulting change in the hair's structure may reduce its natural gloss or cause a mild build-up of static charge, and in extreme cases the hair may break, especially in the region of the tip.

Such changes in the hair's appearance can be avoided by, in the first place, using mild hair-cleansing products or conditioning shampoos. The second protection step, however, is provided by hair aftertreatment products such as hair conditioners or rinses.

The effect of conditioning preparations is restricted to the part of the hair shaft that projects out of the epidermis. Both the cortex and the cuticle of the hair shaft can be negatively affected by the aforementioned influences.

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TABLE 1 Hair Fiber Characteristics

	Caucasian	Asian	African
Thickness	fine	coarse	coarse
Curvature	straight to curly	straight to wavy	wavy to wooly
Cross sectional shape	nearly round to slightly oval	nearly round to slightly oval	slightly oval to elliptical
Color	blond to dark brown	dark brown to brown-black	brown-black to black
Cross section area (μm^2)	~70	~90	~70

Chemical hair treatments such as cold waving, bleaching, or the use of straighteners and relaxers have a particularly unfavorable effect on the cortex, because they influence or change, e.g., the disulfide bonds between and in proteins. This generally results in a loss of mechanical strength, a more marked tendency to absorb moisture and therefore to swell, a greater susceptibility to alkalines, and an increase in electrostatic charge [5].

Mechanical stresses such as frequent combing and brushing, blow drying, and intensive exposure to sunlight cause damage to the cuticle; scales either break off completely or along their edges. This makes the hair rougher and reduces its natural gloss [6,7]. An overview of the properties of damaged hair is shown in Figure 1. The requirements to be satisfied by an optimally formulated hair-treatment preparation derive from the listed hair-damaging processes.

Objective test methods are developed to investigate all the effects. Some of the most important methods to understand the actions of hair-treatment preparations are listed in Table 2 [8]. In addition to these tests, cosmetic assessment is usually obtained from the half-head test, the panel test, and the home-use test.

AFRICAN HAIR

The biophysical properties of African hair are more closely related to wool fibers than to the other hair types. African hair shows some special properties as a result of its very curly structure [9–11]. These properties are listed in Figure 2. African hair is treated with hair relaxers, perms, or straighteners in order to get a straight to light curled style. This

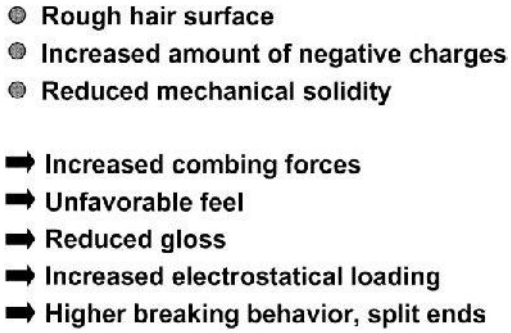

FIGURE 1 Properties of damaged hair.

TABLE 2 Objective Measuring Methods

Term	Objective measuring methods	Measurement parameter
Combability, detangling	Resistance to combing	Wet combing work Dry combing work
Strength	Resonance frequency	Modulus of elasticity
	Tensile strength measurement	Elastic range (range of Hooke's law)
	Breaking strength of single hair	Breaking force
	Breaking strength of hair tress	Breaking force
Charging capacity	Faraday cage	Charge difference
Splitting	Electron-scanning microscope	
Gloss	Goniophotometer	Reflection

has an influence on the hair structure. We measured the wet tensile strength of hair tresses after the application of typical hair relaxers. As expected, straighteners and relaxers have a strong influence in decreasing the tensile strength. Relative to untreated hair we found a residual tensile strength of only 60% depending upon the relaxing agent. Thioglycolate (7.5% active at pH 9.3) is milder than sodium hydroxide (2.0% at pH 13.5) and this is better than calcium hydroxide (0.6% active at pH 13.5). A more detailed description of the physical properties and differences of African hair relative to Caucasian hair is reported in the literature [9–11].

Influence of Surfactants and Protein Hydrolysates on African Hair

The use of mild surfactants in shampoos is necessary and avoids additional damage. Applying 2% sodium hydroxide (pH 13.5) to kinky hair resulted in a residual strength of about 73%. Shampooing this hair with a 12% active solution of sodium laureth sulfate (SLES) gave a further decrease of the tensile strength to 64%. If we choose decyl glucoside as surfactant, there is no further damage and a significantly higher wet tensile strength relative to the SLES result.

Adding protein hydrolysates to relaxers or straighteners strongly increases tensile strength. Using 2% active hydrolysed collagen in a 0.6%-containing calcium hydroxide straightener at pH 13.5 resulted in an increase of the wet tensile strength up to 142% relative to the same straightener without hydrolyzed collagen. This is important for the formulation not only for these products, but for shampoos and conditioners in general. The addition of protein hydrolysates to restructure the hair is strongly recommended.

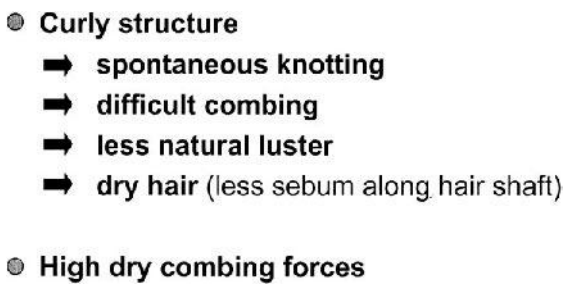

FIGURE 2 Characteristics of African hair.

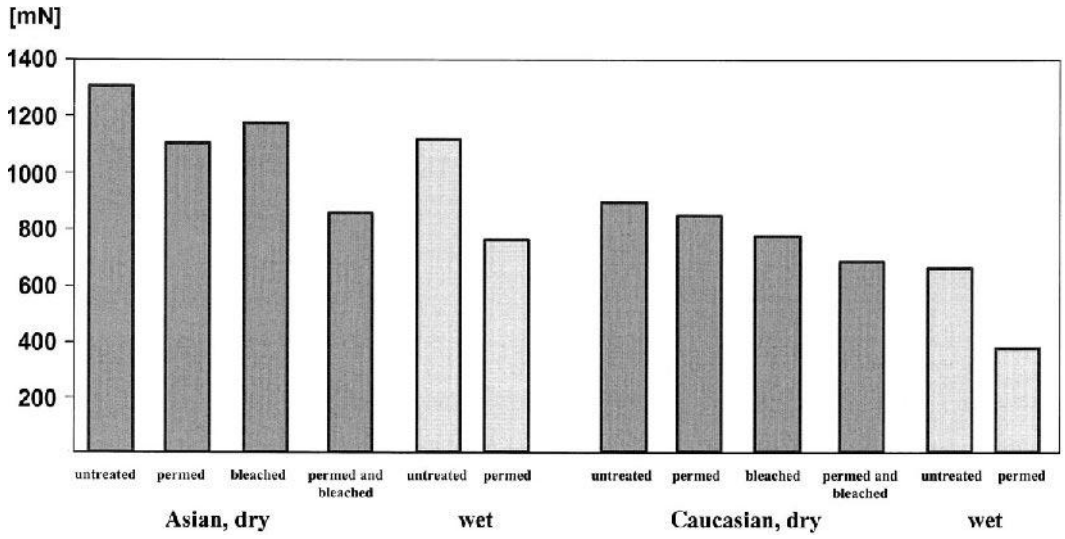

FIGURE 3 Dry and wet tensile strength of single fibers.

DIFFERENCES OF UNTREATED ASIAN AND CAUCASIAN HAIR

Because of the differences in cross-section, we found different wet and dry tensile strengths of single hair fibers. Asian hair shows higher values than Caucasian hair. The application of a perm, bleach, or both results in decreasing tensile forces for both hair types (Fig. 3). The higher values for dry combing forces are found again for Asian hair (Fig. 4). The wet combing work shows comparable results for the untreated hair types.

In addition to these results we measured the bounce of curls. For a natural appearance of hair the physical parameters attenuation, maximum zero amplitude and force of elonga-

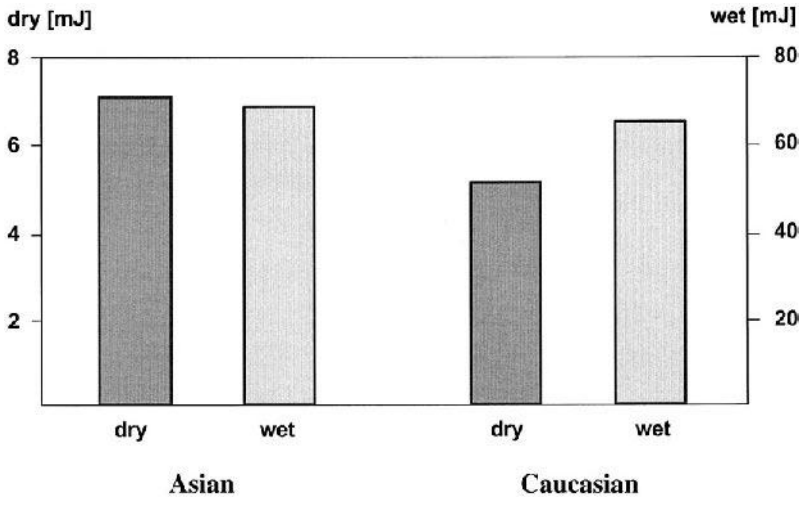

FIGURE 4 Combing work of Asian and Caucasian hair.

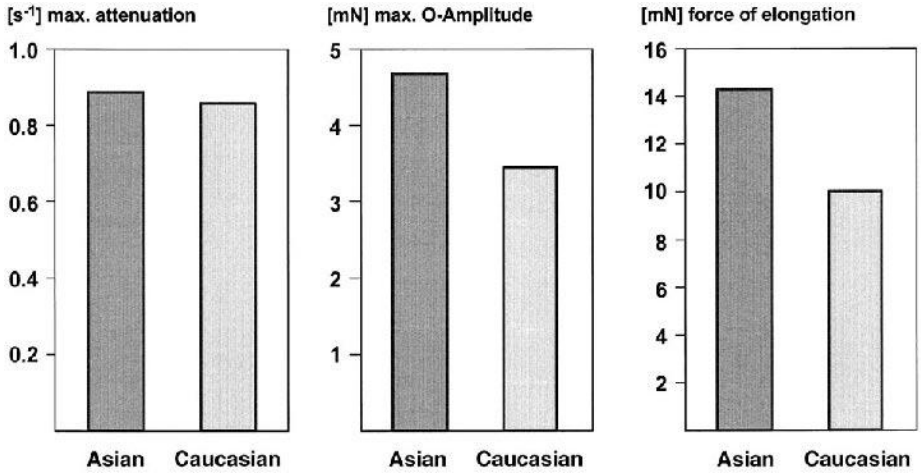

FIGURE 5 Bouncing of Asian and Caucasian hair.

tion are important. If these values are too low, the single hair fibers are not connected to each other. A natural swinging behavior of hair tresses needs entanglements of hair fibers. Therefore, styling products as well as products for fine hair are formulated with polymers. Figure 5 shows the bouncing behavior of untreated hair tresses. Water is used as standard. Differences between Asian and Caucasian hair are detected for the 0-amplitude and the force of elongation. This may be considered a result of the difference in the cross-section of these hair types.

A further difference is split-end generation. As a simulation for the building of split ends 10 washing cycles followed by 3000 combing cycles with a rough comb has been used. Asian hair has a higher tendency for generating split ends by applying this method.

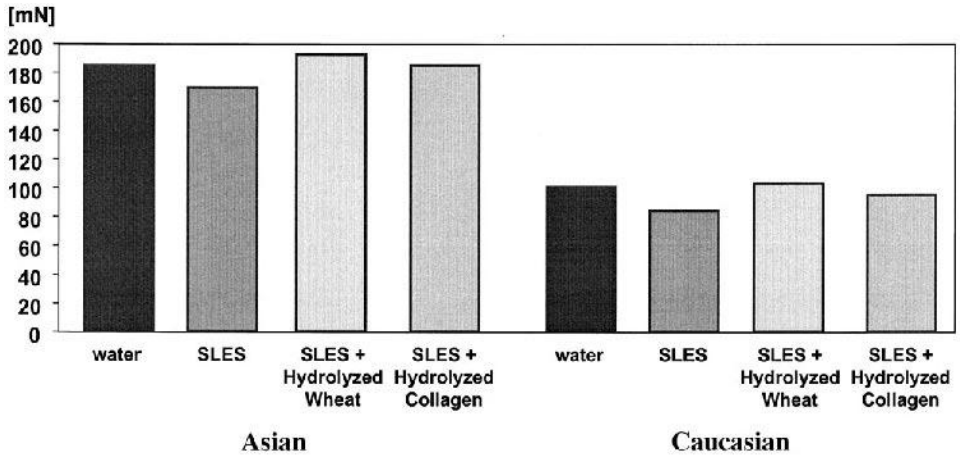

FIGURE 6 Influence of protein hydrolysates and surfactants on the wet tensile strength of permed hair tresses.

TABLE 3 Types of Shampoos and Their Use

Shampoo type	Hair type
Baby shampoo	All baby hair
Shampoo for dry hair	Caucasian, African
Shampoo for fine hair	Caucasian, African
Shampoo for greasy hair	Caucasian, Asian
2-in-1 shampoo	All
Antidandruff shampoo	All
Detangling shampoo	African
Neutralizing shampoo	African
Protective shampoo (after perms, colors, etc.)	All

INFLUENCE OF SURFACTANTS AND PROTEIN HYDROLYSATES

The influence of single surfactants to the tensile strength of Asian and Caucasian hair is tested (Fig. 6). We chose sodium laureth sulfate (2 mol EO—type) as one example for surfactants. First, the hair was permed and then washed with the surfactant. Finally, the tensile strength of the hair tresses was determined. The differences in the absolute values are related to the differences in the cross-section of the hair types. Relative to water, SLES decreases the tensile strength of the hair tresses. This is observed for both hair types.

In a further experiment we added protein hydrolysates to the SLES. The addition of hydrolysates increased the tensile strength of the hair tresses relative to the SLES values. The source of the hydrolysate, animal-based or vegetable-derived, shows no difference in this effect (see Fig. 6). Therefore protein hydrolysates are useful to strengthen hair fibers [12].

EFFECTS OF SHAMPOO

A surfactant plus a protein hydrolysate is not a complete shampoo formulation. Depending on the type of hair they are formulated according to the needs of the different hair qualities. In addition to the ethnic hair quality, hair can be fine, greasy, pretreated etc. Therefore a complete range of different products exists in the market. Table 3 shows various types of shampoos. The following is only a short overview of some formulations and concepts. A basic formulation is shown in Table 4.

TABLE 4 Basic Structure of a Shampoo

Amount (%)	Ingredient	Use
1–3	Preservative	Microbiol, stability
	Color	Sensorial acceptance
	Perfume oil	Sensorial acceptance
0–10	Thickener/auxiliaries	Appearance/product claims
3–5	Cosurfactant	Cleaning, foam
10–15	Basic surfactant	Cleaning, foam
q.s. 100	Water	Handling

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TABLE 5 Frame Formulations for a Daily-Use Shampoo

DE/96/161/15 (wt%)		DE/96/161/23 (wt%)	
Decyl glucoside	20.0	Lauryl glucoside	4.8
Ammonium lauryl sulfate	6.5	Sodium laureth sulfate	20.0
Cocamide DEA	3.0	Ammonium lauryl sulfate	11.5
Panthenol (50%)	1.0	Cocamidopropyl betaine	6.7
Polyquaternium-10	0.3	Laurdimonium hydroxypropyl	
Propylen glycol (and) PEG-55	2.5	Hydrolysed wheat protein	3.0
Propylen glycol oleate		Polyquaternium-10	0.3
		Sodium chloride	0.2
Water	q.s. 100		
pH	5.5	Water	q.s. 100
		pH	5.5
		viscosity (mPa.s)	5000
Residual wet combing work Asian hair:	42%		28%
Residual wet combing work Caucasian hair:	40%		52%
Residual dry combing work Asian hair:	40%		104%
Residual dry combing work Caucasian hair:	40%		95%

Daily-Use Shampoos

A daily-use shampoo has to cleanse and condition the hair. It is used frequently, and therefore must be mild. An example for a formulation is listed in Table 5. The influence of this formulation on both hair qualities with respect to dry and wet combing was the same. The reduction of the wet combing forces was sufficient to have an easy combing. The dry combing forces were comparable to the untreated hair. In addition to the objective test results a half-head test on 10 European volunteers was done and a good performance was achieved.

Special Shampoo Products

Fine and Greasy Hair

The appearance of fine hair is described as poor shining, low volume, poor manageability, as well as low tensile strength and problems in the dry combability. In addition to a mild-surfactant base, additives must be incorporated into the formulation to provide easy conditioning, increase dry combability, and thus improve manageability. Furthermore, formulation ingredients must be used that improve the tensile strength of the hair [13]. Cationic protein hydrolysates, specific cationic surfactants compatible with anionic surfactants or pseudo cationics (amphopolymers) are used as slightly conditioning additives. The texture is improved with glucose, alkyl polyglycosides, protein hydrolysates, cationic protein-hydrolysates, or polymers. This formulation concept is summarized in Figure 7.

European hair is finer than Asian hair. If this fine hair type takes up sebum it sticks together. Often greasy hair is also fine hair. Therefore special formulations for this hair type are developed [14]. The formulation concept has to include active ingredients to avoid either the production or uptake of sebum. Often-used ingredients are sulfur products or plant extracts. In formulation DE/94/145/11 (Table 6), the potassium abietoyl hydrolysed collagen is the product that reduces the sebum uptake. The effects with respect to increase the dry

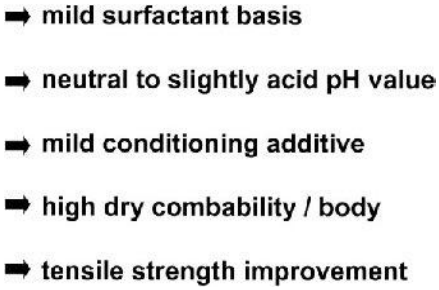

FIGURE 7 Formulation concept for fine hair.

combing work as well as the wet combing work is sufficient for Caucasian but not Asian hair. By applying this formulation to Asian hair the amount of quaternary polymer has to be slightly increased. This formulation also reduces the uptake of sebum. The action and mechanism for the reduction of sebum uptake is described in the literature [14].

2-in-1 Shampoos

This type of shampoo is very popular. Washing and conditioning is only one step. Therefore these products are well accepted by the consumer. The formulation concept is not so different from the others (Fig. 8). In this case silicones are mostly formulated to achieve the special conditioning effect. New concepts are using monoglycerides in combination with alkyl glucosides and cationic polymers to get this conditioning effect. With such a concept, the build-up effect can be avoided [15]. Formulation DE/94/005/25 is one example tested on Asian and Caucasian hair and one example formulated without the use of silicones. Important is the reduction of wet-combing forces and the increase of the dry-combing forces in order to get a style and volume. The formulation and the results are shown in Table 7. The performance is best on Caucasian hair. For Asian hair the amount of cationic polymer has to be increased.

AFTER HAIR TREATMENTS

Modern preparations are divided into rinse-off types, which are rinsed off after being left to take effect for a certain time, possibly with the help of a slight increase in temperature,

TABLE 6 Shampoo for Fine and Greasy Hair

	DE/94/145/11 (wt%)
Decyl glucoside	10.0
Sodium laureth sulfate	14.3
Cocamidopropyl betaine	10.0
Potassium abietoyl hydrolyzed collagen (PAHC)	5.1
Polyquaternium-10	0.2
Laureth-3	1.0
Sodium chloride	1.0
Water	q.s. 100
pH	5.5

FIGURE 8 Formulation concept for 2-in-1 shampoo.

and leave-on types, which remain in the hair. In Figure 9 an overview about the hair aftertreatments is listed. We studied the effects of typical conditioners (Table 8). After treatments are used to restructure and improve the hair quality. Such preparations must be effective not only superficially but also below the surface of the hair. Changing the properties of the hair surface can cause improvements in properties such as combability, feel, and manageability, and can reduce the build-up of static charge. Moreover, a protective action can be achieved with chemical hair treatments, and special additives that penetrate inside the hair can improve its mechanical strength. Therefore a schematic formulation makeup is based on the described general requirements derived from hair-damaging processes described in the introduction [16,17].

Cationic surfactants act by being adsorbed onto the surface of negatively charged hair [19,20]. In contrast, active agents such as cationic protein hydrolysates, protein hydrolsates, panthenol, and glucose penetrate at least partially below the surface of the hair.

In order to evaluate differences between conditioners we applied several formulations containing 1.0% active distearoylethyl hydroxyethylmonium methosulfate and 2.5% cetearyl alcohol to Asian and Caucasian hair. The combing work was measured before and after the application of the conditioner. The absolute values for the combing work of Asian and Caucasian hair are different as shown previously in Figure 4. For testing the efficacy it is not important to see the absolute values of combing work; it is more important to know the degree of reduction. This means a residual combing work of 40% is a relative reduction of 60%. All formulations have the same efficacy on Asian and Caucasian hair. There is no significant difference in the relative change of the combing work.

TABLE 7 Example of a 2-in-1 Shampoo

		DE/94/005/25 (wt%)
Sodium laureth sulfate (and) lauryl glucoside		21.0
Glycol distearate (and) glycerin (and) laureth-4 (and) cocamidopropyl betaine		2.0
PEG-7 glyceryl cocoate		1.0
Guar hydroxypropyl trimonium chloride		0.5
Water		q.s. 100
pH		5.5
residual combing work	dry	wet
Asian hair	87%	87%
Caucasian hair	87%	60%

Pretreatments for waving preparations	Prophylaxis
Intermediate treatments for waving prep.	Prophylaxis
Keratin hardeners	Repair
Hot-oil treatments	Repair
Leave-on conditioners	Repair / Prophylaxis
Thermal conditioners	Repair
Rinse-off conditioners	Repair
Hair tip fluids	Repair
Sunscreens	Prophylaxis
Blow-drying lotions	Hair styling
Hair-setting lotion	Hair styling
Hairspray, lacquer	Hair styling
Hair gels	Hair styling
Hair tonic	Hair styling

FIGURE 9 Overview of hair treatment preparations.

TABLE 8 General Conditioner Formulation

Use	Hair rinses	Amount %
Formulation auxiliary	Emulsifier	0–2
Consistency, conditioning agent	Consistency factors	1–5
Emollient, care component	Oily components, auxiliaries	0–3
Conditioning agent	Cationic components	0.5–1.5
Sensorial acceptance	Perfume oil	0–2
Microbiological stability	Color	
	Preservative	
	Water	
	pH value: 3–5	

DE/92/197/6 (wt.-%)	
Lauryl glucoside	2.0
Cetearyl alcohol	3.0
Cetrimonium chloride	4.0
Emollient	2.0
Water	q.s. 100

Emollients:	
G:	Octyldodecanol
GTEH:	Octanoic Triglyceride
NPC:	Neopentylglycol Dicaprate
302:	Propylenglycol Dicaprylate/Dicaprate
SN-1:	Cetyl Isooctanoate
TPEH3:	Trimethylolpropane Triisooctanoate
PEEH4:	Pentaerythritol Tetraisooctanoate

FIGURE 10 Formulation with emollients in conditioners.

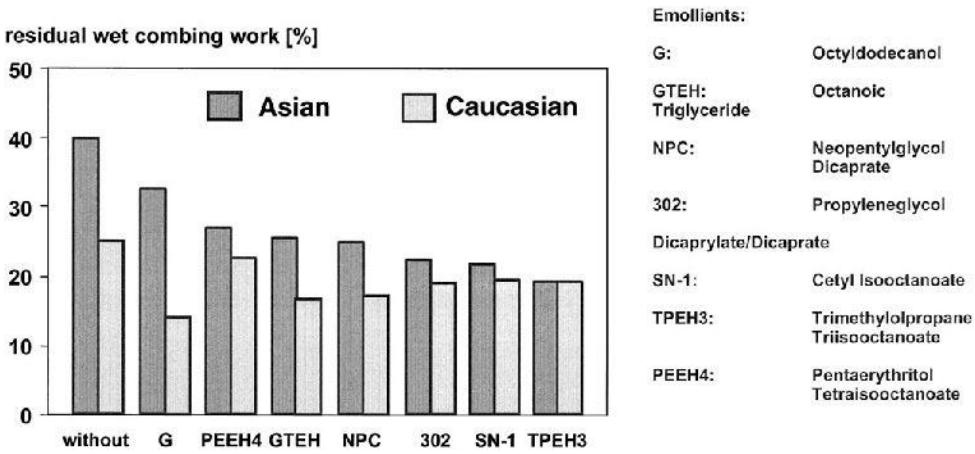

FIGURE 11 Wet combing work/emollients in conditioners.

Further improvements in wet combability properties of hair rinses or hair conditioners can be achieved by adding suitable emollients [18]. The influence of emollients on the conditioning effect of hair aftertreatment preparations was studied with the help of the model formulation DE/92/197/6 shown in Figure 10.

Various emollients were blended into the formulation so that they formed 2% of the total components. The effect of these emollients on wet combability was determined. It can be seen from Figure 11 that the addition of emollients can facilitate a further enhancement of hair-conditioning action.

Relative to emollient-free formulations, a further reduction of 10 to 20% is achieved in the combing work of wet hair. The most marked reduction in wet combing work is

TABLE 9 Conditioners with Active Ingredients

	DE/94/038/43 wt%	DE/94/038/44 wt%	DE/94/038/45 wt%
Distearoylethyl hydroxyethylmonium methosulfate (and) cetearyl alcohol	1.0	1.0	1.0
Cetearyl alcohol	2.1	2.1	2.1
Glyceryl stearate	0.5	—	0.5
Ceteareth-20	0.8	0.8	0.8
Soya sterol	0.7	—	0.7
Hydrolyzed collagen	—	—	2.0
Methyl hydroxypropyl cellulose	0.5	—	0.5
Hydroxypropyl methylcellulose (1% swelling)	—	20.0	—
Laurdimonium hydroxypropyl hydrolyzed wheat protein	—	2.8	—
Water, preservation	q.s. 100	q.s. 100	q.s. 100
Tensile strength of tresses		42.4 (Ncm/g)	51.9 (Ncm/g)
Significance (t-test)		>99.9%	>99.9%

TABLE 10 Leave-On Conditioner

	DE/96/099/4 wt%
Polyacrylamide (and) C13-14 isoparafin (and) laureth-7	3.0
Cocamide DEA	1.0
Glycerin (86%)	5.0
Lauryl glucoside	0.5
Oleyl erucate	0.5
Tocopherol	0.2
Hydrolyzed sweet almond protein	3.0
Laurdimonium hydroxypropyl hydrolyzed wheat protein	0.8
Ethanol (96%)	10.0
Water, preservation	q.s. 100
pH	7.0
Viscosity (Brookfield RVF, 23°C, spindle 4, 10 rpm)	ca. 3000 mPa.s

brought about by high molecular emollients. When the influence of these emollients on the combability of dry hair was studied, it was found that they cause almost no changes.

Not only the hair's characteristics were favorably influenced by the oils in hair rinses, but the physicochemical properties of hair rinses that contain fatty alcohol were also improved. Emollients generally have the effect of stabilizing viscosity during storage.

EXAMPLES OF FORMULATIONS AND EFFECTS

Some further examples of different formulations are listed. If any effects have been measured, these are mentioned. Conditioners for colored, permed, bleached, or straightened hair are given in Tables 9 to 12. These formulations may be used on all ethnic hair types. The listed examples are rinse-off (Tables 9, 10) as well as leave-on (Table 11) conditioners. The so-called liquid hair (Table 12) is a special leave-on product that acts as a restructuring agent for damaged hair. Pretreatments (Table 13) are used to reduce the effects caused by the following application of a perm, bleach, or coloring. They are useful for all ethnic hair types. The last two formulations are shampoos for African hair (Tables 14, 15).

TABLE 11 Hot Oil Treatment

	DE/91/303/11 wt%
Cetrimonium chloride	8.0
Hydroxyethyl cellulose (2% swelling)	20.0
Polysorbate-20	1.5
Hydrolyzed collagen	0.3
D-panthenol (50%)	0.2
Water, preservative, perfume, etc.	q.s. 100

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TABLE 12 Liquid Hair (Leave-On)

	DE/94/211/6 wt%
Decyl glucoside	4.0
Laurdimonium hydroxypropyl hydrolyzed collagen	2.0
Hydrolyzed keratin	3.0
Glycerin (86%)	20.0
Ethanol (96%)	5.0
Water, preservative	q.s. 100
pH	5–5.5

TABLE 13 Pretreatment Preparation

	Wt%
Hydrolyzed keratin	2.0
Citric acid	0.1
PEG-hydrogenated castor oil	1.0
Fragrance, preservative, water	q.s. 100

TABLE 14 Detangling Shampoo for African Hair

	Wt%
Ammonium lauryl sulfate	30.0
Cocamidopropyl betaine	10.0
Coco glucoside (and) glyceryl oleate	5.0
Hydrolyzed wheat protein	3.0
Laurdimonium hydroxypropyl hydrolyzed wheat protein	3.0
Water, preservative	q.s. 100
pH	5.5

TABLE 15 Neutralizing Shampoo for African Hair

	Wt%
Ammonium lauryl sulfate	35.0
Cocamidopropyl betaine	10.0
Coco glucoside (and) glyceryl oleate	2.0
Laurdimonium hydroxypropyl hydrolyzed wheat protein	1.0
Hydrolyzed wheat protein	1.0
Polyquaternium-10	0.4
Guar hydroxypropyl trimonium chloride	0.2
Water, preservative	q.s. 100
pH (adjusted with citric acid)	5.5

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Oral-Care Products

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THE TEETH AND ORAL ENVIRONMENT

Like all mammals, humans generally have two sets of teeth during a lifetime. The first set, known as deciduous, primary, or ''milk'' teeth, begins to appear in infants between the age of 5 and 9 months. All 20 of these ''baby'' teeth are generally in place by age 2½ years. The second set, or permanent teeth, forms within the gums during the period from infancy to puberty. These teeth, also known as succedaneous teeth, begin to erupt at around age 5, displacing the deciduous set as they appear. There are 32 permanent teeth. An individual will spend 91% of his or her lifetime chewing with these permanent teeth if they are properly cared for. Of the 32 permanent teeth, 16 are located in the upper jaw, or maxillary dental arch, which is part of the cranium, or skull, and is immoveable. The other 16 are located in the mandibular dental arch which is part of the lower jaw and is the moveable part of the skull. Each type of tooth is equally divided between these two dental arches (Figs. 1 and 2).

The Parts of a Tooth

Each tooth consists of three parts: the area above the gum that can be seen, the area below the gum that is not visible, and the constricted portion, or neck, between the other two parts. The crown is the enamel-covered portion of the tooth. The root is the portion of the tooth which, by means of the periodontal ligament, relates to the osseous (bony) structures of the jaw. The root makes up about two thirds of the total length of a tooth (Fig. 3).

The Tissues of a Tooth

A tooth is made up of five different tissues, each with a specific and important function. Serious disease in any of these tissues can affect the entire tooth and result in its decay and/or destruction. These tissues are as follows:

1. Enamel, which is a hard white outer covering surrounds the crown of the tooth and protects it from wearing away as a result of the pressure of chewing. It consists largely (96 to 98 percent) of inorganic substances, mainly calcium and phosphate.

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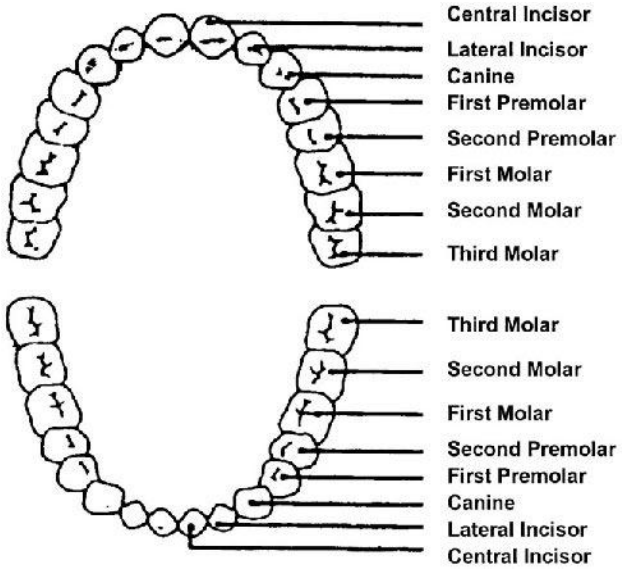

FIGURE 1 The permanent teeth showing the orderly arrangement of the various types in the upper and lower dental arches.

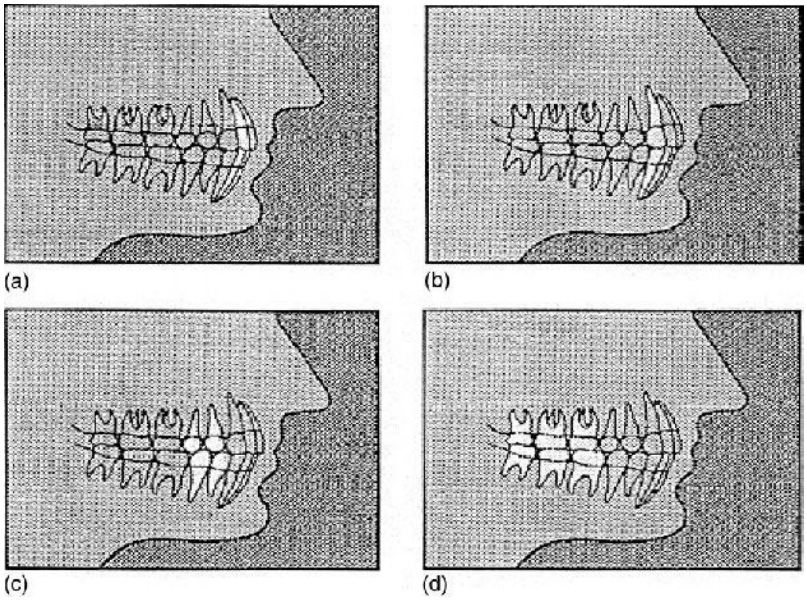

FIGURE 2 Lateral or side view of the permanent teeth showing the four types of teeth, their arrangement in the dental arch, and differences in size and shape.

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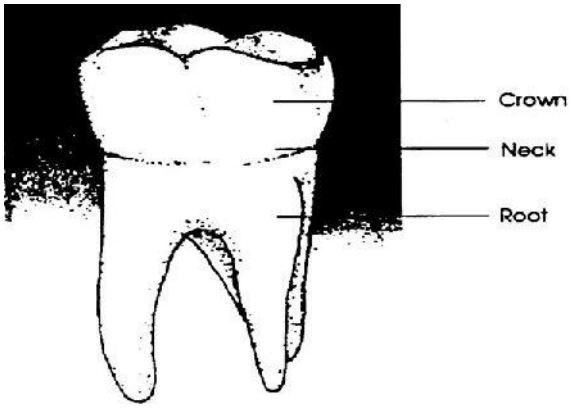


FIGURE 3 The parts of a tooth.

2. Dentin, a yellowish bone-like tissue under the enamel, provides support and forms the bulk of the tooth structure, extending almost to its entire length. It is covered by the enamel on the crown and the cementum on the root. Chemically, dentin is composed of 20% organic and 75% inorganic matter, or collagen and calcium phosphate, respectively. The remaining five % is mainly water and other mucosubstances.
3. Pulp, a soft tissue within the center of the crown and root, contains nerves, blood vessels and lymph vessels that produce dentin and provide nourishment for the tooth throughout its life. Because of its rich supply of blood and nerves, the pulp also functions as a defense system against bacterial invasion and as a sensory signal of injury by causing toothache.
4. Cementum, a thin, bone-like tissue that covers the root, serves as a means of attaching the tooth to the surrounding bone.
5. Periodontal ligament, a layer of connective-tissue fibers, stretches between the cementum and the bone connecting the tooth root to the jawbone. It also cushions the tooth from the pressures exerted during chewing (Fig. 4).

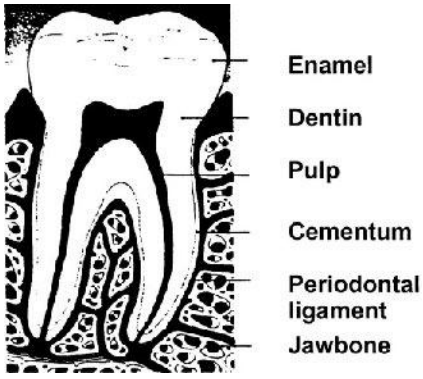


FIGURE 4 The five tissues of a tooth.

The Periodontium

The periodontium (from the Greek ''peri,'' meaning ''around,'' and ''odous,'' for ''tooth'') is a functional system consisting of several different tissues that surround and support the teeth. This system is also called the ''attachment apparatus'' or the ''supporting tissues of the teeth.'' Anatomically, the term refers only to the connective tissue between the teeth and their bony sockets (Fig. 5).

The tissues that make up the periodontium include the gingiva, the periodontal ligament, the cementum, and the alveolar bone or jawbone. Their good health is of great importance to the overall health of your mouth and the survival of your teeth.

The Gingiva

The gingiva, commonly called the ''gums,'' is the most external part of the periodontium. It is composed of dense fibrous tissue which forms a close ring-like attachment around the necks of the teeth and connects with the epithelial covering (oral mucosa) that lines the mouth. The gingiva is firm in consistency and does not move from its underlying structures. It is covered by a smooth vascular mucous membrane which is tender to the touch and bleeds easily when penetrated or bruised. It also overlays the unerupted teeth, and the pain which occurs during the teething process is the result of the new tooth pushing through this sensitive tissue. Clinically the gingiva is divided into following:

1. Free marginal gingiva which is about 1.5 mm wide and forms the skin-like soft-tissue fold around the teeth. The narrow shallow groove present between the tooth and the free gingiva is known as the gingival sulcus. It is approximately 0.5 mm deep and 0.15 mm wide and surrounds the tooth on all sides. The bottom of the sulcus is made up of cells from the junctional epithelium. The size of this groove or ''pocket'' is of great importance when determining the health of the periodontium and the stability of the teeth.

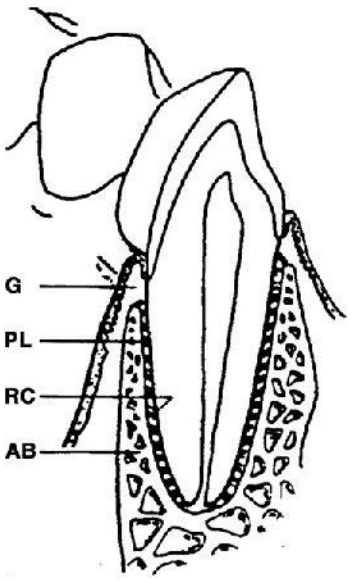


FIGURE 5 A healthy tooth with its periodontium.

2. Attached gingiva which is firmly connected to the hard surface of the tooth by means of a ring of specialized tissue known as the junctional epithelial attachment. The attached gingiva becomes wider with age and may vary considerably among individuals and from tooth to tooth.
3. The cells in the junctional epithelium are continuously being renewed during life and have a turnover rate of every 4 to 6 days. This results in a very permeable tissue which serves as a pathway for the metabolic products produced by the bacteria present in the mouth. This area plays a key role in the maintenance of periodontal health.
4. Interdental gingiva which varies in depth and width and occupies the area between adjacent teeth.

The Periodontal Ligament and the Cementum

The periodontal ligament occupies the space between the root surface of the tooth and the alveolar bone or jawbone. It is composed of connective tissue fibers, blood vessels, nerves and other cells. Its function is to provide the connection between the cementum layer of the tooth and the jawbone, the teeth and the gingiva, and between each tooth and its neighbor. Anatomically the cementum is a part of the tooth, but functionally, it belongs to the tooth-supporting apparatus because the gingival and periodontal ligaments are anchored in it.

The Alveolar Bone

Alveolar bone, also referred to as the jawbone, develops along with the formation of the teeth throughout pregnancy and continues to grow during the eruption of the teeth in childhood. Three types of alveolar bone have been defined: compact bone, trabecular bone, and alveolar bone proper. The trabecular bone provides the major support structure of the teeth and is composed mainly of fatty marrow in adults.

Other Parts of the Mouth

There are several other areas in the mouth which are important. These include the tongue, palate, salivary glands, and the oral mucosa or lining of the mouth or oral cavity itself.

Palate

The palate forms the roof of the mouth and consists of two portions: the hard palate in the front area behind the upper teeth and soft palate at the back at the entrance to the pharynx or throat area. The hard palate separates the mouth from the nasal cavity and serves as the roof of the mouth and the floor of the nose. The soft palate aids in swallowing and sucking functions.

Tongue

The tongue is the main organ of the sense of taste and an important organ of speech. It also assists the teeth in the chewing and swallowing of food. The tongue is situated in the floor of the mouth and is connected to various muscles in the epiglottis and pharynx, or throat. It is covered by mucous membranes, and numerous mucous and serous glands as well as taste-buds. Internally, it consists of fibrous tissue, muscles, blood vessels and nerves (Fig. 6).

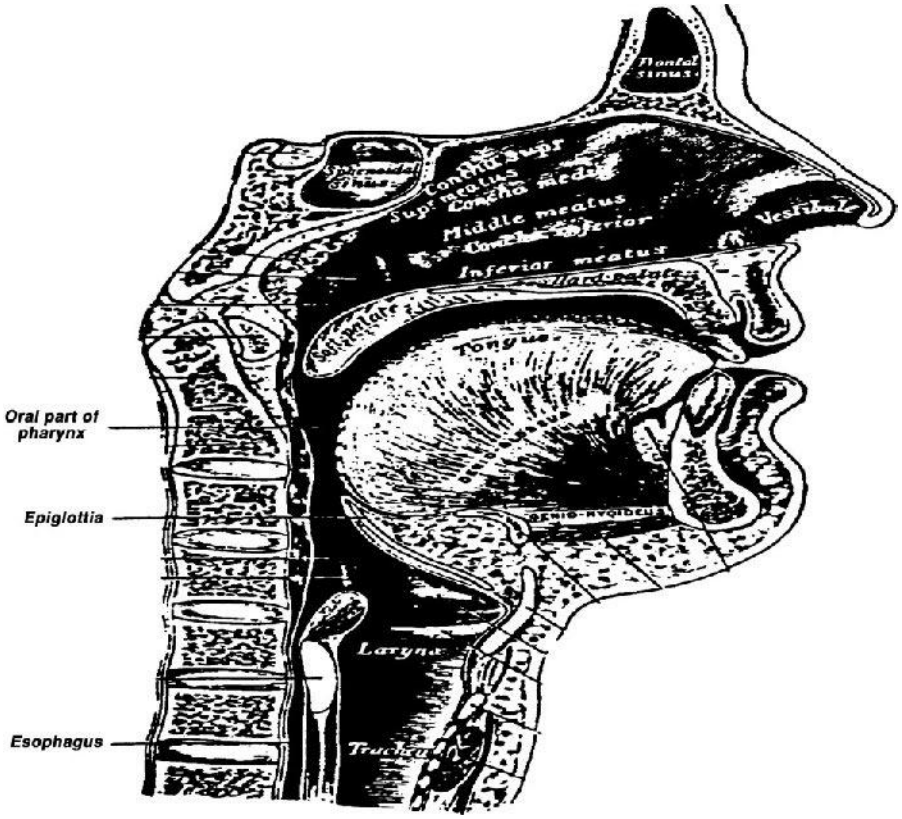


FIGURE 6 The anatomical location of the palate and tongue within the oral cavity.

Saliva and the Salivary Glands

Saliva is a fluid containing water, mucin, protein, salts and enzymes. It is produced and secreted into the oral cavity by three pairs of salivary glands: the submaxillary, sublingual (or submandibular), and parotid glands (Fig. 7).

The submaxillary glands are located beneath the floor of the mouth on the inner side of the jaw. Saliva secreted from these glands enters the mouth through a duct or opening beneath the tongue known as the duct of Wharton. The sublingual glands also are located below the floor of the mouth, but closer to the mid-line and pour their saliva into the mouth through a number of small ducts—the duct of Bartholin and the duct of Rivinus. The parotid glands lie below the ears and along the sides of the jaws. The ducts from these glands enter from the inner cheek opposite the second upper molars.

The salivary glands contain both serous and mucous cells. The secretion from the serous glands is thin and watery while that from the mucous glands contains mucin and is, therefore, thicker and more slimy. These glands are controlled by the autonomic (or involuntary) nervous system and react by reflex to both direct and indirect stimulation. For example, saliva is automatically and directly produced when you take a mouthful of food, but it also can be indirectly produced when you talk about or see some food you particularly like.

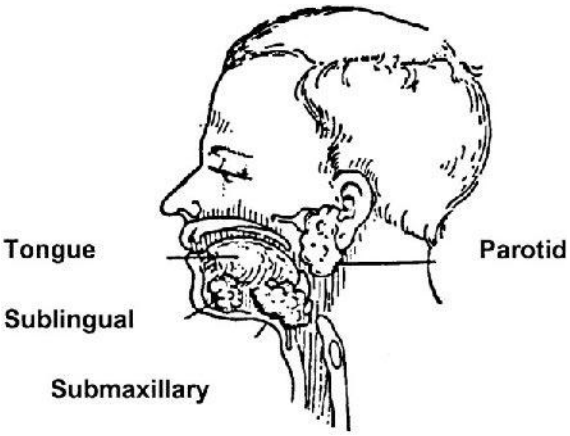


FIGURE 7 The location of the salivary glands.

Saliva has the following important functions:

- to assist in the digestion of food,
- to prepare food for swallowing by altering its consistency,
- to moisten and lubricate the mouth and lips,
- to cleanse the mouth and teeth from food debris and other foreign materials, and
- to excrete organic and inorganic substances from the body.

The latter function especially can result in serious inflammation of the oral mucosa (the lining of the mouth) and the gums.

Oral Mucosa—The Lining of the Mouth

The oral mucosa, or ''mucous membrane'' lining of the mouth, also has special functions that are important to oral health. This thin, freely movable lining is composed of several layers of epithelial cells. These are the same type of cells found on the outer layers of your skin and which serve as a protective covering. However, within the mouth, this covering lies on a thick layer of ''mucous membranes'' which secrete mucus.

As discussed earlier, mucus contains a protein material known as mucin which is formed within the cytoplasm of these epithelial cells. As the mucin accumulates,the cells become distended until they finally burst, discharging their contents onto the surface of the mouth. The mucus coats the epithelial surface serving as protection against injurious substances in the mouth or as a means to trap small foreign particles.

The production of mucus can be greatly increased by stimulation caused by infection, allergy or temperature. We are all familiar with the increased production of mucus caused by a cold or sore throat. Often, ''cold sores'' or ''canker sores,'' which are small painful ulcerations on the oral mucosa, appear during these illnesses. Therefore, the oral mucosa can also be used as a mirror that reflects the general health of the body.

DENTAL DISEASES WORLDWIDE

Dental diseases including cavities (caries), tartar (calculus), sore gums (gingivitis), and periodontitis (loss of teeth supporting the tissue) are worldwide problems. The annual cost

of all dental care in the U.S. exceeds $37 billion, out of which roughly $6 billion is spent to repair the ravages of decay [1]. However, the cost of dental disease cannot simply be measured in monetary terms. Other factors also need to be considered; for example, the loss of teeth leading to impaired chewing ability, speech problems, and changes in facial aesthetics which can cause embarrassment. The well-being of a person may also be compromised due to the associated dental pain, inability to chew properly, and potential of the infection spreading from the mouth to other parts of the body [2].

Currently, a tremendous amount of time is spent by dentists and hygienists to clean the teeth and associated structures to prevent dental disease. Alternative methods to prevent dental diseases which can be used by the general population are being developed to reduce the amount of time spent with the dental professional.

Factors Affecting Delivery of Actives in the Mouth

Before discussing specific product technologies for the prevention and treatment of oral disease, we need to understand the general principles underlying the efficacy and delivery of therapeutic agents in the oral cavity (Fig. 8).

The effective use of active ingredients in oral products is depending upon several factors; some of the major ones are depicted schematically in Figure 8. Normally a therapeutic toothpaste or mouthrinse contains an active ingredient or drug which must be dissolved in the formulation. Mouthrinses currently on the market are aqueous-based formulations but contain numerous other ingredients which must be compatible with the drug. The potential for undesirable interactions between ingredients is a major concern of formulators and manufacturers. Some interactions are specifically designed, such as the increased solubility of poorly water soluble drugs (e.g., triclosan) by adding surfactants and other ingredients to form a microemulsion. However, incompatible ingredients are sometimes unknowingly used, especially in complex formulations where there is an incomplete understanding of the chemistry [3].

The packaging material can also be a source of compatibility problems. Any number of possible interactions can affect, either directly or indirectly, the availability of the drug in the formulation. This can usually be evaluated in the laboratory on new and aged samples of the product. Drugs which are complexed with other materials, although still soluble in the formulation, may exhibit reduced bioavailability in vivo. The term bioavailability is usually used to express a temporal relationship of free drug concentration at the target site. In this case, after mouthrinsing or toothpaste use, the bioavailability is the concentra-

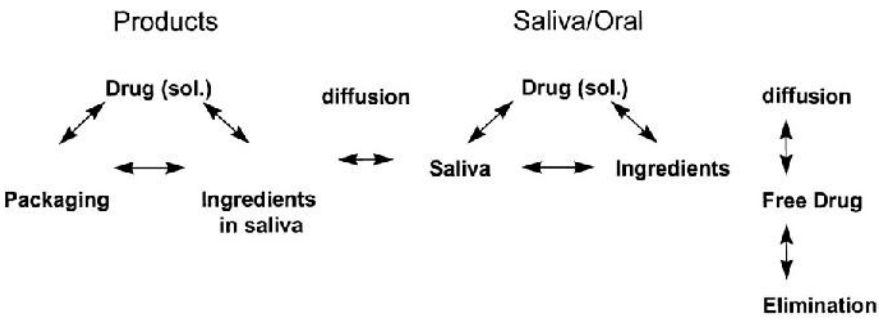


FIGURE 8 Factors affecting delivery of active agents in mouth.

tion of free drug in the environment of the target site and the rapidity at which it disappears. This can be determined providing the site can be sampled and the drug concentration measured in the medium contacting the target site (i.e., saliva, plaque fluid, crevicular fluid).

The duration of exposure may be important. Since most of the dose in the oral product is expectorated, the time in the mouth should be long enough for optimal retention of the drug. This has been determined for some orally used antiseptics such as chlorhexidine and triclosan. In general, 30 to 45 seconds is usually sufficient. Once introduced into the oral environment via a toothpaste/gel/mouthrinse, the residual drug must diffuse in saliva before it can reach its intended site of action. In saliva the drug is then free to interact with salivary components before reaching oral surfaces. In theory, only free available drug can interact optimally with target sites. Such sites include plaque, enamel, the gingival sulcus, gingival tissue, and the mucous membranes.

The amount of drug retained on oral surfaces after use is also thought to be important since subsequent desorption of the drug into the microenvironment of the target site could provide a sustained effect. This will be determined mainly by the substantivity of the particular drug used. Because of the long dosage interval commonly practiced with the product (once or twice a day), highly substantive drugs may have a distinct advantage because of their longer presence in the oral cavity. Superimposed upon this is the normal clearance process by which materials are removed from oral surfaces by salivary flow. The longer a drug can be retained in the environment of the target site in active form, the better chance there is to exert a therapeutic effect.

Evolution of Technologies in Oral Products

Historically, dentifrices or toothpastes were developed to keep the teeth clean and free of stains. The essential ingredients of a toothpaste are: a thickening agent, an abrasive cleaning agent, a surfactant, a humectant, flavor, and active therapeutic agents. One of the first dentifrices contained an abrasive (precipitated calcium carbonate) and a small amount of powdered soap. This toothpaste was irritating to the tissues of the mouth because the pH was relatively high due to its soap content [4]. After the Second World War, many companies undertook scientific research to develop dentifrices which were milder, gentler, and also had therapeutic properties. Instead of soap, a synthetic detergent—sodium lauryl sarcosinate—was introduced in toothpaste. Besides preventing irritation, the synthetic detergent improved the taste and was also shown to control plaque acids which cause cavities. Figure 9 provides an overview of the evolution of technologies in oral products. The category is driven by scientific advances and consumer benefits which have been broadly classified as a good smile (Fig. 9).

Stain Removal and Whitening Toothpastes

There are two types of stains on teeth: (1) stain on teeth (extrinsic stain); and (2) stain in the tooth (intrinsic stain). The extrinsic stain may originate from chromogenic materials from food or drink, while the intrinsic stain could be caused by therapeutic agents, such as tetracycline, or excessive fluoride exposure during teeth development (below age of 5). Several investigators have studied mechanisms of stain formation and developed methods to remove dental stain (Fig. 10) [5].

The evolution of whitening/cleaning technologies in toothpaste and gel is depicted in Figure 10. The most commonly used procedure for removing stains on teeth is the use

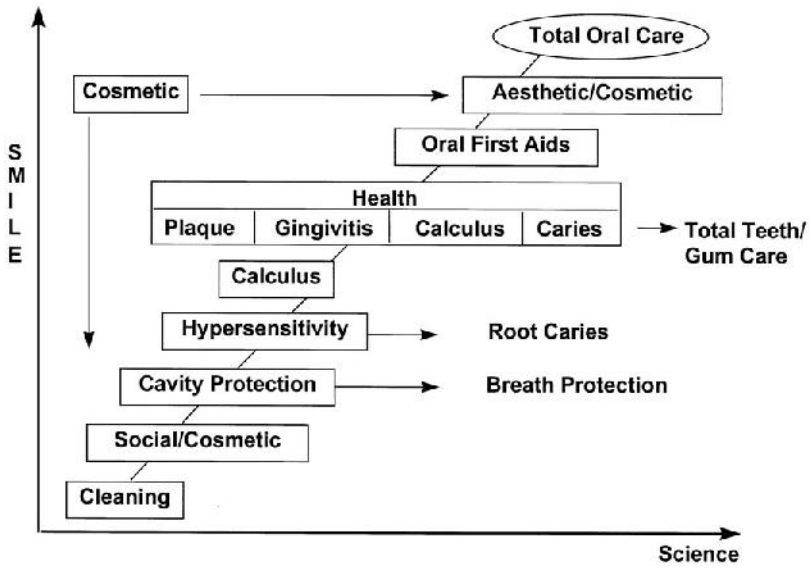


FIGURE 9 Evolution of technologies in oral products.

of abrasives such as silicon dioxide, dicalcium phosphate dihydrate, and aluminum salts such as calcined alumina. All these are used in combination with detergents to remove stains. In the early eighties, calcined alumina or enzymes with or without tartar control ingredient, such as pyrophosphate, were added. Later on, fluoride preparations such as hydrogen peroxide, urea peroxide, or calcium peroxides were added to remove both intrinsic and extrinsic stains. To assess performance, several laboratory tests were developed but none of them correlate with in vivo stain removal on teeth. Therefore, in vivo clinicals are the best way to assess stain removal. Typical results from in vivo studies are depicted in the table below (Table 1).

It can be seen that the addition of calcined alumina with pyrophosphate gave good stain removal in vivo. Another procedure for stain removal in vivo is by reflective spectros-

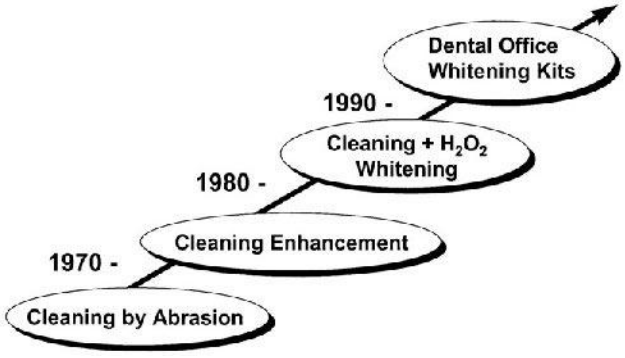


FIGURE 10 Evolution of cleaning/whitening technologies.

TABLE 1 In Vivo Stain Reduction 6 Weeks After Brushing

Dentifrice treatment	% Stain reduction
SiO_2/NaF toothpaste	No change
SiO_2/NaF/tripolyphosphate	14.0
SiO_2/Calcined Alumina/Pyrophosphate	49.0

copy using a Minolta chromameter. The color change is measured by $\triangle E$ (difference in color). The higher the positive value, the whiter the teeth. Using $\triangle E$ in vivo, one would get $\triangle E$ of 2 to 4 with above technologies (in Table 1). If one adds peroxide, the value could reach as high as 6. For the reference, an in-office treatment by a dentist would provide $\triangle E$ of 7 to 8 following two weeks procedure.

Dentifrices to Reduce Offensive Bad Breath

Local mouth odor is caused by oral bacteria reacting with salivary proteins to form volatile sulfur compounds (VSC). Tonzetich has shown that hydrogen sulfide, methyl mercaptan, and dimethyl sulfide [H_2S, CH_3SH and $(CH_3)_2S$, respectively] are the major components of mouth odor. A gas chromatographic method was developed to objectively measure VSC directly from mouth air as an alternative to the organoleptic/sensory method. This instrumental method has, in turn, permitted investigators to carry out studies in a number of areas relevant to human malodor [6]. There are two methods currently available to assess the magnitude of oral malodor. The first is the organoleptic or sensory rating approach, and the second is the GC instrumental method. A study was conducted to determine the correlation between these two methods in a controlled clinical study. An excellent correlation ($r = 0.78$) has been established between the instrumental method and sensory evaluation. Using the analytical technique, the effect of dentifrices on mouth odor has been evaluated in a variety of clinicals. A baseline reading is taken in the morning. The subjects then brushed with a placebo or an active dentifrice, and then readings are taken three or 12 hours post-treatment to assess the effects. A dentifrice containing the antibacterial triclosan and a copolymer polyvinyl methyl ether maleic acid (PVM/MA) has been developed. This provides sustained reduction in mouth odor. The typical clinical results are summarized in Figure 11 [7].

Therapeutic Dentifrices

Dentifrices to Control Caries (Cavity)

It is well-known that the formation of dental caries is a result of interactions between the tooth enamel, environment (saliva), plaque fluid and ingestion of dietary carbohydrates. These interactions are also important in the formation of dental plaque on teeth. Dental plaque plays an important role in the formation of caries since it is the plaque bacteria which produce acids from sugars. However, the production of acids by plaque bacteria and subsequent dissolution of tooth enamel is not a constant process. Instead, it appears to be cyclical. At a given time, plaque acids attack the enamel surface and deplete it of minerals, creating a small microtrauma at the surface. These areas are actually called incipient caries or white spots and occur long before caries can be detected by dentists or hygienists. If left unchecked, the process eventually results in destruction of the teeth.

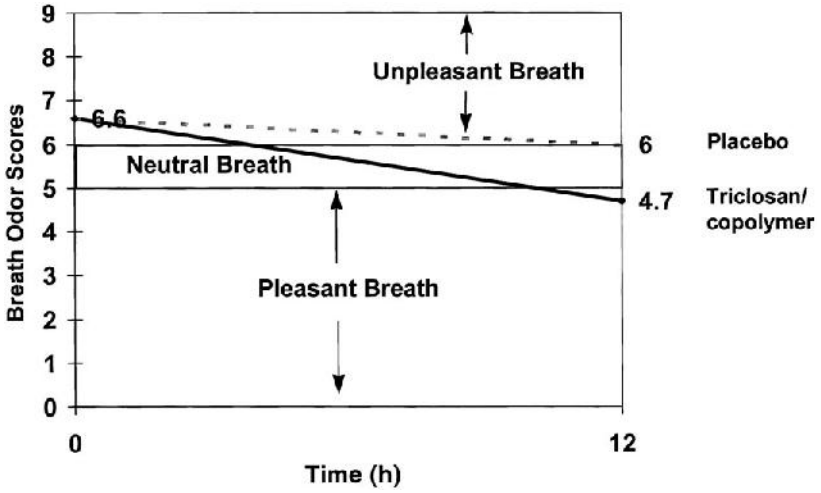


FIGURE 11 Plot of breath odor scores.

Since caries is not a continuous process, early lesions can be repaired through interactions of various elements in the oral environment, that is, supersaturation with respect to calcium phosphate in saliva, fluoride and pH of the plaque fluid [8].

Tooth enamel is not a smooth impervious surface, instead it is porous, and an apparent lack of activity on the surface may mask actual activity below. In order to create a caries lesion, the acids must penetrate the enamel structure, which consists of hydroxyapatite (HA) crystals surrounded by an organic matrix consisting of water, protein and lipid materials and this they do by removing some of the mineral from the crystalline rods below the surface of the teeth. This demineralization weakens the structure and, if unchecked, eventually results in a subsurface lesion often called a white spot which will appear to be chalky and whiter than the normal surrounding tooth surface. Continuation of the demineralization process results in the creation of cavities. This occurs when the surface enamel collapses as the underlying structure of mineral rods can no longer maintain the tooth structure. However, not all white spot lesions progress to cavities, and one of the prime reasons being the process of remineralization which occurs when minerals are redeposited into the enamel that has been weakened by bacterial acids. Remineralization can, therefore, only take place when there has been loss of tooth structure through demineralization. Thus, demineralization and remineralization are continuous processes with loss from, and replacement of, minerals into enamel within the oral environment. The most soluble mineral in the teeth is thereby replaced by the most insoluble calcium phosphate, such as dicalcium phosphate dihydrate (DCPD). If the environment is rich in DCPD, the process of remineralization occurs. This process is greatly enhanced by fluoride ions which convert DCPD into fluorohydroxyapatite which forms onto, and within, the tooth increasing resistance to acid attack [9].

Fluoride increases remineralization by increasing the rate of crystal growth, but to restore tooth structure a supersaturation of calcium phosphate in the environment is also necessary. The process of remineralization has been shown to be controlled by the presence of fluoride and a supersaturation of calcium and phosphate in plaque fluid. Thus, the tooth and environment are in a seesaw battle. Under healthy conditions when supersaturation is high and plaque acids are low, the ambient calcium phosphate (DCPD) in plaque fluid

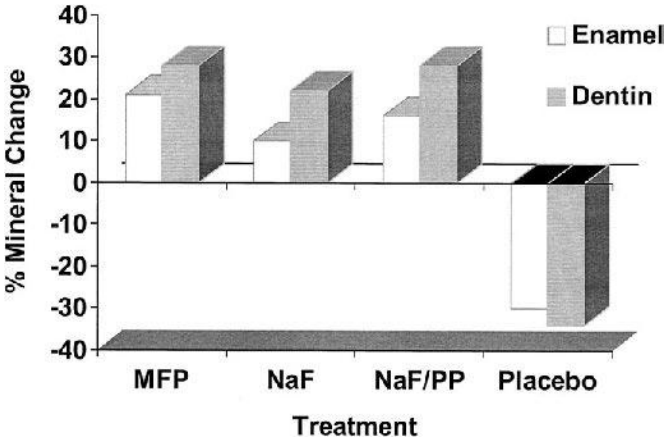


FIGURE 12 Average percent mineral changes for enamel and dentin.

is sufficient to maintain healthy enamel. When the caries challenge is high and plaque is producing more acids, supersaturation with respect to DCPD decreases and demineralization occurs. Fluoride inhibits lesion formation by enhancing the process of remineralization, and this enhancement is greatly influenced by supersaturation of the plaque fluid with respect to HA.

Fluoride dentifrices are capable of adding minerals (remineralization) to early caries lesions. This process can be measured in vivo by using the model of intra-oral remineralization. A dose response effect of fluoride is shown in Figure 12 which shows the percent mineral gains in either enamel or dentine following two weeks use of either 1100 ppm F from MFP (sodium monofluorophosphate) or sodium fluoride, NaF. Both fluoridating systems extend the same degree of mineralization as an equal concentration. Human clinical studies for caries (cavity) prevention require 3 years to document anti-caries effect. In those studies, mean reduction in caries varies from 25 to 40% depending upon the population used in the study and whether or not the study area had water fluoridation. Current efforts are to enhance efficacy of 1000 to 1500 ppm of fluoride in dentifrices with additives such as xylitol, a non-fermentable sugar, or the antibacterial triclosan. These additives have been shown to boost the effectiveness of fluoride in toothpaste (Figs. 12, 13) [10].

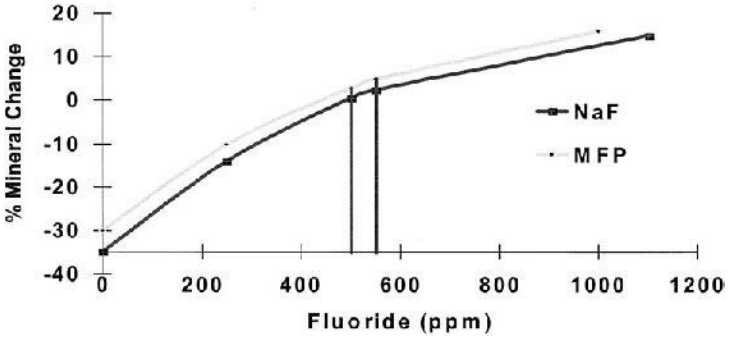


FIGURE 13 Fluoride dose response for MFP and NaF dentifrices.

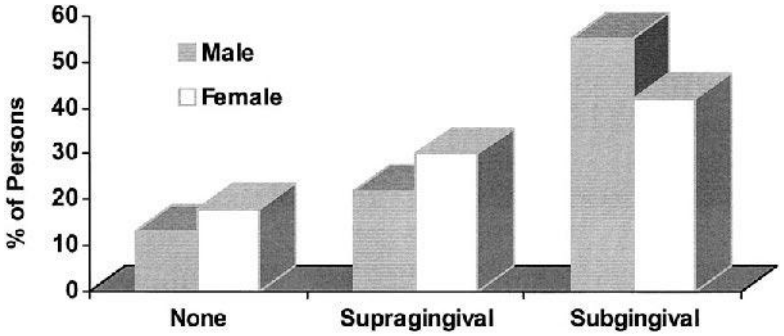


FIGURE 14 Data from "Oral Health of U.S. Adults," NIDR, 1985.

Anticalculus and Anticavity Technologies

Calculus build-up on teeth is a worldwide problem. For nearly 5,000 years since the time of the Sumerians, calculus has been considered an important factor in the etiology of periodontal diseases. Although it is not considered to be a principle cause of periodontal diseases today, calculus is an important contributor to the formation of dental plaque which is implicated in periodontal disease. At a given time, hundreds—even thousands—of hygienists around the world are removing calculus build-up by mechanical cleaning. These procedures are very labor-intensive and may cause a great deal of discomfort to the patient.

The extent and incidence of calculus in the general U.S. population has been shown in a comprehensive oral health survey by the National Institute of Dental Research [11]. The data shown in Figures 14 and 15 indicate the incidence of calculus. Calculus was observed in 34% of school-aged children. In adults, 25 to 30% had calculus build-up above the gingival margin, but 60–65% had deposit below the gingival margin. Older adults showed an even higher incidence. The extent of calculus in the population indicates a need to develop an effective but safe chemical means to prevent calculus build-up on the teeth. This is especially important for the countries where the dentists and hygienists are not readily available (21). Therefore, the development of the technologies to prevent calculus is important around the world from a public health point of view (Figs. 14, 15).

Chemical Composition of Dental Calculi on Teeth and Dental Materials

Dental calculus consists of both organic and inorganic components. The organic portion is a combination of epithelial cells, leukocytes, micro-organisms, and polysaccharides.

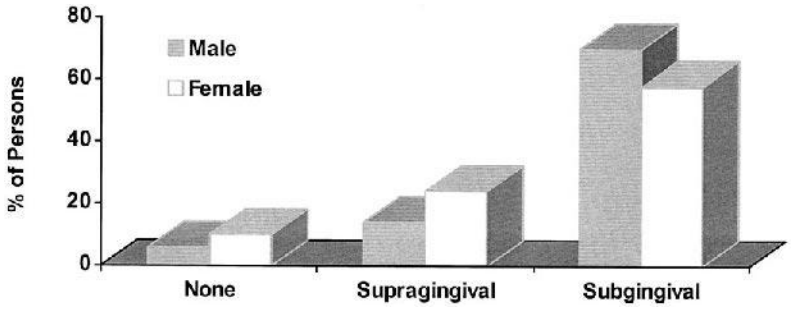


FIGURE 15 Calculus in U.S. population (seniors, "Oral Health of U.S. Adults," NIDR, 1985).

The inorganic part is primarily calcium phosphate salts which include: carbonated hydroxyapatite (CHA), dicalcium phosphate dihydrate (DCPD), and octacalcium phosphate (OCP). The x-ray diffraction patterns and infrared absorption spectra of human dental calculi and the samples obtained from the dentures and tooth surfaces show that the inorganic component of calculus from dentures is principally carbonated hydroxyapatite (CHA), while material from tooth surfaces is a mixed calcium phosphate phase β-TCPC Mg-substituted), CHA, and OCP. The deposits then are primarily basic calcium and phosphate salts [12].

Technologies for the Prevention of Calculus Formation

A general method of removing calculus is by mechanical means. The mechanical means are labor-intensive and painful. Another approach is to develop a chemical way of preventing the formation of the basic phases of calcium phosphates. A large number of agents have been proposed to retard the formation of calculus on to surfaces. These agents are usually compounds which inhibit the formation of calcium phosphate salts to the crystalline phases. Among the most effective inhibitors are pyrophosphate, pyrophosphate plus polymer and zinc salts. In general, agents usually work via a surface effect. The inhibitors adsorb to the growing (calcium phosphate) crystals and they reduce the formation of crystalline phases allowing calcium phosphate to remain in an amorphous phase. In general, two types of tests have been used to evaluate the inhibitors. One test follows the spontaneous formation of HA (Fig. 16) using a supersaturation environment which stimulates the plaque fluid. The second test is a seeded crystal growth for hydroxyapatite which uses the driving force equivalent to saliva environment (Fig. 17). Using these tests, the relative value of efficacy of these inhibitors is summarized, shown in Table 2. It shows that the most active inhibitor is pyrophosphate. Also a combination of pyrophosphate and the copolymer of pyrophosphate and the copolymer (PVM/MA) provides an enhanced efficacy. Zinc salts, on the other hand, require a higher concentration for effectiveness. The relative clinical efficacy of these agents in various dentifrices are summarized in Table 3. Available data from the composite of several clinical studies indicate that calculus inhibition with the pyrophosphate and sodium fluoride combination is roughly in the range of 26%; with the copolymer/pyrophosphate (1.3% soluble pyrophosphate to 3.3%) the

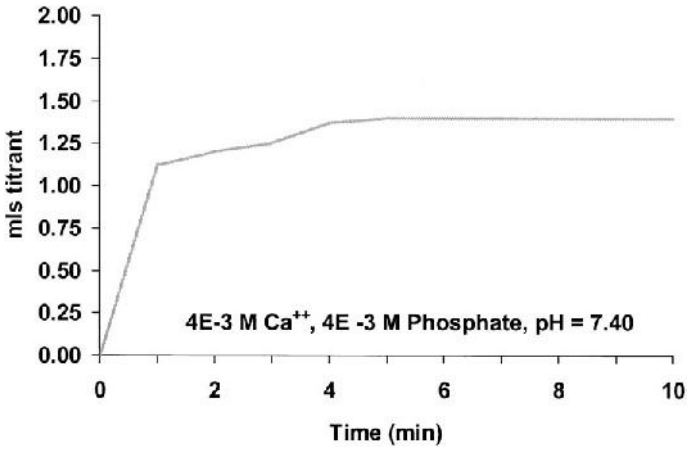
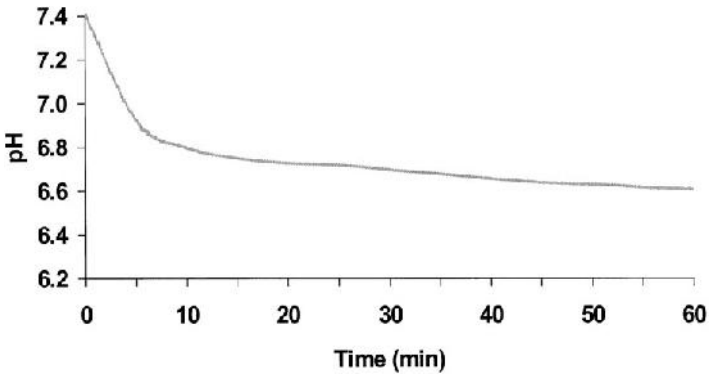


FIGURE 16 HAP formation.



$$5Ca^{2+} + 3HPO_4^{2-} + H_2O \rightarrow Ca_5(PO_4)_3OH + 4H^+$$

FIGURE 17 Crystal growth.

calculus reduction ranged as high as 50%; zinc salts require higher concentration for efficacy (2% or above). With a lower concentration (0.5%), the efficacy against supergingival calculus formation is very poor [13].

Mechanisms of Action of Anticalculus Agents

The mechanism for the inhibition of calculus formation by anticalculus agents are schematically illustrated. The calcium and phosphate from saliva or from plaque fluid precipitate and form a precrystalline phase which matures to crystal phase in the absence of inhibitor. In the presence of inhibitor that amorphous phase is stabilized and the conversion of the crystalline phase is delayed. This is clearly evident from the electronmicrographs of calculus formed in the presence and the absence of inhibitor. In the absence of inhibitor, the crystal size was very large and well-defined; in the presence of an inhibitor, the deposit was very small and has morphology of amorphous calcium phosphate (Fig. 18).

The current technologies used for inhibiting calculus formation also contains fluoride. When the application of a potent inhibitor of calcium and phosphate crystal growth coexists with fluoride, a crystal growth promoter, we need to understand how they work together. The inhibitor prevents the formation of HA. Then how do two agents coexist in the same system and exert the respective effect? Our early data indicated that crystal growth inhibitors work on tooth surfaces while fluoride ion works within teeth. The effect can be explained by the fact that the calculus formation occurs on the teeth (above) where the demineralization occurs in the subsurface region of the enamel (under pellicle). The presence of pellicle on the tooth allows the selective transport of fluoride and the inhibitor. This mechanism has been elucidated by studies of natural inhibitors of crystal growth in

TABLE 2 Calculus-Control Technologies: Relative Efficacy

Compound	Inhibition (ppm)
Pyrophosphate	4.0
Pyrophosphate + copolymer	3.0
Zinc	60.0

TABLE 3 Clinical Efficacy of Toothpastes in Humans

Toothpaste	Mean reduction in calculus vs. placebo
3.3% pyrophosphate + NaF	26%
3.3% pyrophosphate + 1% PVM/MA/NaF	50%
1.3% pyrophosphate + 1.5% PVM/MA/NaF	47%
0.5% zinc citrate + MFP	14%
2% zinc + sodium fluoride	38–50%

Abbreviation: PVM/MA, copolymer polyvinymethyl maleic acid.
Source: Ref. 13.

saliva. The study indicated that the crystal growth inhibitory effect of the natural inhibitor can be overcome by the addition of fluoride. This effect was neither due to displacement of an adsorbed inhibitor by fluoride nor the activation of secondary growth sides. Rather the effect was explained on the basis of increased driving force of precipitation and incomplete blockage of crystal growth sites on the basis of steric effect. This has now been confirmed via in vivo studies.

Technologies to Reduce Tooth Sensitivity

The next evolution of toothpaste chemistry was developed as a means to prevent pain caused by sensitive teeth; i.e., hypersensitivity. Dentinal hypersensitivity is defined as an acute, localized tooth pain in response to thermal, tactile, or air blast stimulation to exposed dentine surfaces. Normally, the roots of teeth are covered by the gingival or gum tissue but when the gum recedes, the underlying tooth surface is exposed. Once exposed, with time, abrasion and erosion will remove the thin layer of cementum, thus exposing underlying porous dentine. Exposure of the dentine surface to dietary or bacterial acids can expose

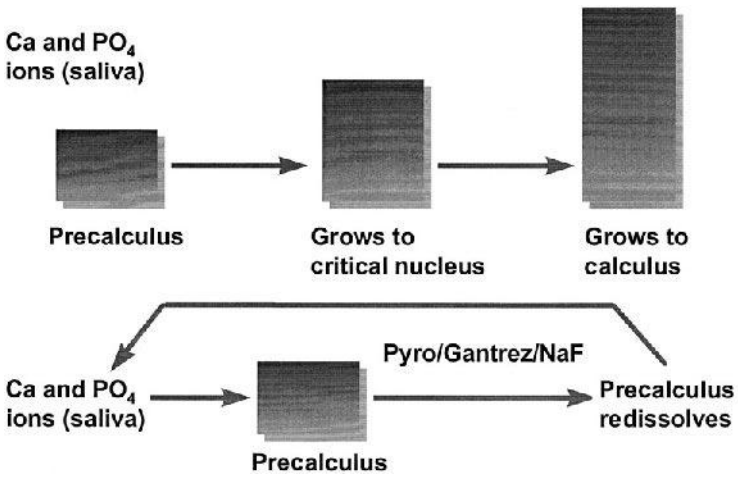


FIGURE 18 Mechanism of pyrophosphate/copolymer/NaF on tartar formation.

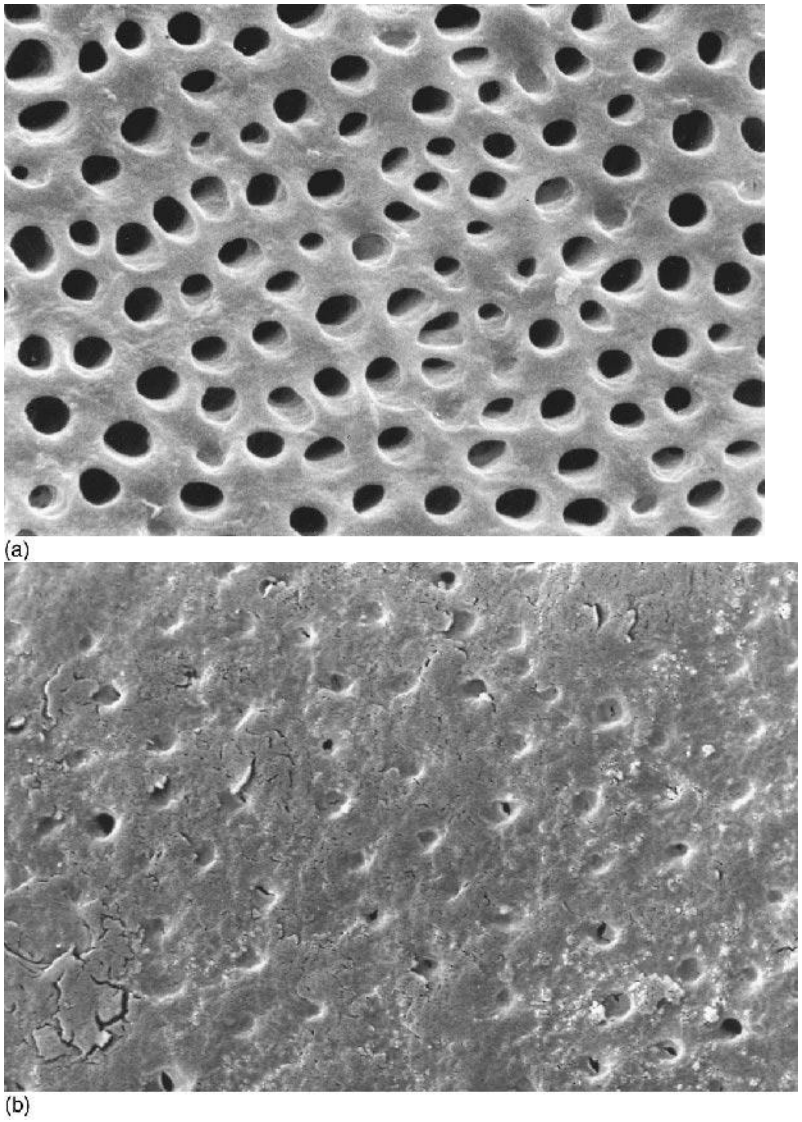


FIGURE 19 (a) Open dentinal tubules. (b) Occluded dentinal tubules.

the dentine pores or tubules at the surface. It is well known that exposure and the presence of open tubules (Fig. 19a) on the surface is associated with increased dentinal hypersensitivity. The dentine tubes contain fluid.

Mechanistically, hot or cold stimuli can cause this fluid to expand or shrink, stimulating underlying pulpal nerve resulting in pain. Currently, salts of potassium are available as preventive therapies in OTC toothpaste. Various other agents such as potassium nitrate are believed to cause reduction in nerve activity by altering the threshold of pulpal nerve excitation. These approaches have been combined in a single toothpaste containing potassium nitrate and copolymer which adhere to tooth surfaces. Figure 19b shows occlusion

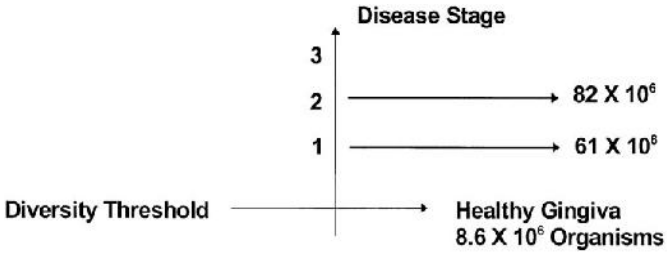


FIGURE 20 Microbiota (health vs. disease).

which can result from in vitro treatment of dentine with such a toothpaste. Unfortunately, this therapy requires two to three weeks treatment before a reduction in sensitivity is observed. Therefore, there is currently a strong need for a fast reactive material in toothpaste which could rapidly reduce dentinal hypersensitivity (Figs. 19a,b) [14].

Multibenefit Technologies in Dentifrices

The next development in dentifrice technology was to incorporate antibacterial agents with fluoride and tartar reducing compounds.

Microbiota of Dental Plaque: Health Versus Disease

The basic research within the past 30 years clearly established the role of dental plaque at the interfaces of tooth/gingiva as the main cause of gingival inflammation, which could lead eventually to periodontitis. The previous studies by Löe et al. [15] and subsequent studies by Syed [16] and Loesche indicated that there was threshold level of bacteria which was compatible with gingival health. When that threshold level of bacteria increased by at least two or three orders of magnitude, then gingival inflammation was initiated. Therefore, the prime purpose of chemical antiplaque agents is to bring the microflora to a healthy level at the gingival interfaces, primarily by reducing the total mass of microbiota at the surface, or by reducing the total number of pathogens at the surface (Figs. 20, 21).

Since dental plaque is principally composed of microorganisms, it is logical to use antibacterials to reduce or prevent plaque formation. The rationale is that the antibacterials will either inactivate bacteria in the existing plaque or prevent colonization. However, early studies clearly showed that 99% of bacteria in the oral cavity must be killed in order to inhibit plaque formation for only 6 hours, provided teeth are brushed twice daily. Since

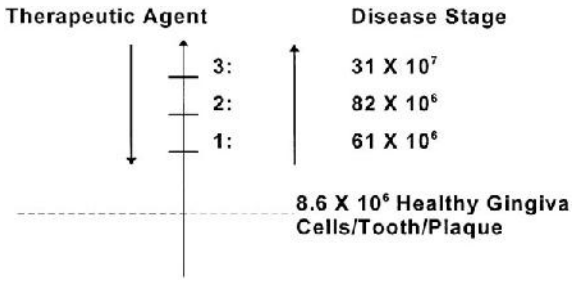


FIGURE 21 Therapeutic strategies.

TABLE 4 Characteristics of Antibacterials for Plaque Effects

Broad spectrum antibacterial activity
Substantivity to oral surfaces
Good taste
Compatible with toothpaste ingredients
Low toxicity
No disturbance of oral ecology

the oral cavity is an open system, the chance of continued reinfection is ever present. Based on recent studies, the general characteristics of antibacterial agents useful for an antiplaque effect can be summarized in Table 4. For an antibacterial antiplaque agent to be effective, a broad-spectrum activity against oral microflora is required, since the microbial composition of the plaque is complex. With cationic antibacterial agents, a minimum inhibitory concentration in the range of 0.1 to 0.5 μg/ml against oral pathogens has been noted. However, the current understanding of the pharmacology of antibacterial antiplaque agents indicates that there are factors other than antibacterial activity in determining sustained antiplaque effect on teeth. These factors include the retention and release of antibacterials on oral surfaces, as well as their efficacy in the presence of the salivary environment. Furthermore, it is important that a given antibacterial does not disturb taste, otherwise the patient's compliance would be very poor. Another consideration for use in oral products is compatibility with polishing agents and surfactants, since both of these ingredients are important for controlling stain on teeth, as well as emulsifying flavor oils, which are incorporated in the oral hygiene products for compliance. Other important considerations are a low toxicity and a minimum potential to disturb the normal microbial oral ecology [17].

Cationic Antibacterial Agents

Among the widely studied agents are cationic antibacterials such as chlorhexidine digluconate (CHDG), benzethonium chloride (BTC), and cetyl pyridium chloride (CPC). CHDG is more effective than BTC or CPC and has higher retention in the oral environment. They also differ with respect to their reaction with salivary protein, which is an important parameter for the retention of cationic antibacterials on oral surfaces; increased retention provides a sustained release of concentrations active against oral pathogens.

Long-term clinical studies have demonstrated the efficacy of cationic antibacterials against plaque, gingivitis and plaque microflora. However, these agents cause unacceptable staining of teeth and an increase in calculus formation. Therefore, their use in oral hygiene products clearly is limited [17].

Noncationic Antibacterial Agents

More recently (during the past 10 years), there has been tremendous interest in non-cationic antibacterials which provide multi-benefits such as plaque, gingivitis, calculus, and caries reduction. This is primarily based on a non-ionic antibacterial agent, triclosan, which has broad-spectrum antibacterial activity against gram-positive and gram-negative bacteria. For triclosan to be effective, a delivery system is required to increase its residence time in the oral cavity. A copolymer of polyvinyl methyl ether (PVM) and maleic acid (MA) has been shown to accomplish that. This copolymer was well-suited for improving the delivery of triclosan, since PVM/MA has been shown to react with hard and soft

TABLE 5 Noncationic Antibacterials: Comparative Study for In Vivo Plaque Inhibition

Treatment	Mean P on all surfaces ± SD	SNK group
Placebo	1.46 ± 0.12	A
0.12% CHDG	0.53 ± 0.17	B
0.2% SnF_2 (rinse)	1.10 ± 0.16	C
0.06 Triclosan	1.00 ± 0.14	C
0.06 Triclosan + Gantrez	0.72 ± 0.17	B
0.06 Triclosan + PVPA	0.67 ± 0.16	B

Abbreviations: Gantrez, PVM/MA, polyvinyl methyl/maleic acid; PVPA, polyvinylphosphonic acid; SNK, Student Neuman Keuls test; P, plaque index.

surfaces in the oral cavity. In a four-day short-term study of de novo plaque formation, we evaluated a series of different antibacterial agents. We found that triclosan actually needs an improved delivery system, primarily a copolymer, to enhance its retention to both tooth and oral epithelial surfaces [18].

One of the important principles developed is that retention per se is not the only factor in antiplaque activity; the retained concentration has to be active biologically. To demonstrate this principle, we conducted a series of studies to understand how much triclosan was retained post-brushing. In one of the studies, we compared three triclosan formulations, each having a different enhancing system (Table 5). As can be seen in Table 6, even after 14 hours, a significant amount is retained in plaque, a concentration above the MIC's of triclosan for oral bacteria (MIC being 0.3-4 μg/mL). The next important step was to determine whether this retained amount was active biologically. A plaque viability assay was used, in which we exposed the plaque to two fluorescent dyes to discriminate between live and dead bacteria by measuring the ratio of green to red fluorescence. In this study, one could quantitatively measure the ratio and ascertain whether the retained amount was active biologically. In one of the typical studies shown here, brushing with the placebo toothpaste gave some reduction of plaque viability; the triclosan copolymer system gave the highest reduction in viability, and the other systems, such as triclosan/pyrophosphate and triclosan/zinc citrate, were not significantly different from the placebo (Fig. 22). These results have been corroborated by an independent six-month clinical study by Renvert and Birkhed (Table 6) [19].

The mechanism by which the copolymer enhances the delivery of triclosan has been elucidated (Fig. 23). The polymer has two groups: one is the attachment group and the other is the solubilizing group. The solubilizing group retains triclosan in surfactant mi-

TABLE 6 Plaque Triclosan Levels After Brushing (μg/mL)

After brushing	0.3% Triclosan/ copolymer n = 12	0.3% Triclosan/ pyrophosphate n = 12	0.3% Triclosan/ 1% zinc n = 12
2 h	38.83 ± 18.28*	20.90 ± 14.14	30.60 ± 13.6
14 h	4.14 ± 1.72	2.74 ± 2.11	3.95 ± 1.79

* P = 0.05, compared with a placebo toothpaste.

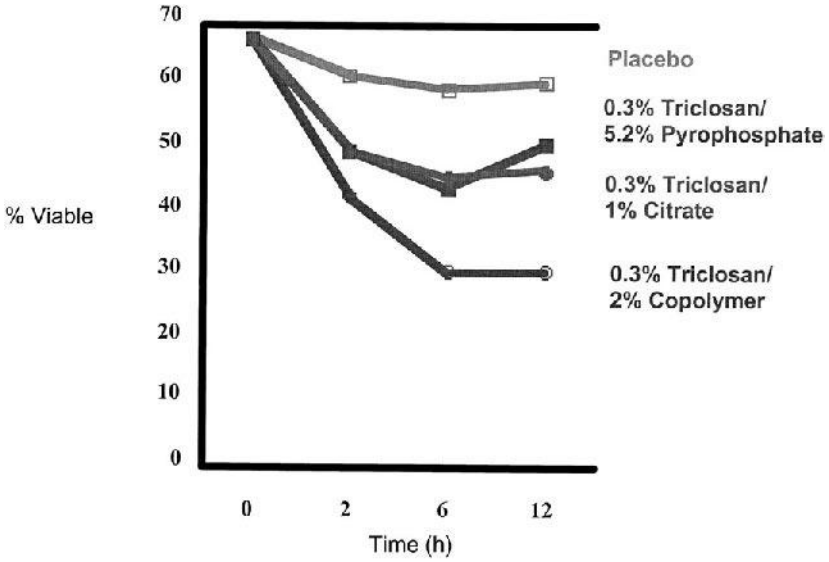


FIGURE 22 Plaque viability study determined via a fluorescent-dye technique.

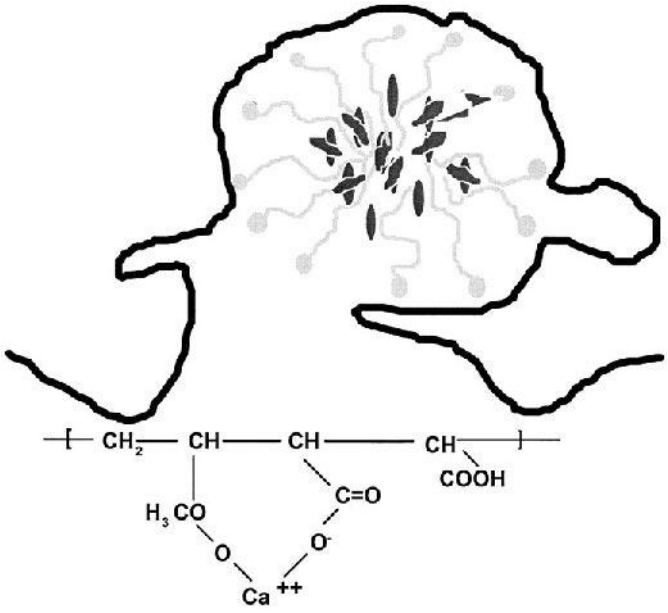


FIGURE 23 Mechanism of retention of triclosan on oral surfaces by the copolymer. The solubilizing group (methoxyether) traps triclosan/surfactant micelle while the attachment group (COOH) binds to calcium in an adherent liquid layer on tooth/enamel interface.

TABLE 7 Therapeutic Mouthrinses

Mouthrinse	Active agents	Typical reduction in the diseases vs. placebo
Fluoride rinses	225 ppm F	50% reduction in caries, children (3 years)
Tartar + calculus	1% pyrophosphate amion; 100 ppm F plus a copolymer of PVM/MA (0.5%)	30–35% reduction in tartar formation after 6 months use
Antiplaque/antigingivitis	0.03 to 0.06 Triclosan + 1% copolymer PVM/MA + fluoride	20–30% reduction in plaque/gingivitis after 3 months of use

celles, and the attachment group reacts with the oral surfaces via calcium in the liquid adherent layer. Triclosan is then slowly released via interactions with salivary environment. In terms of long-term clinical trials, this technology has now been evaluated around the world in 12 six-month plaque/gingivitis studies, three calculus studies, three caries clinical trials, and five long-term studies monitoring the oral microbial population. The results of all these studies indicated that this technology was effective against plaque, gingivitis, calculus, and caries. No side effects of staining or calculus increase were seen. There was also no disturbance of the oral microbial ecology.

One of the most exciting aspects of triclosan is its ''double-barrel'' effect. This unique antibacterial not only kills bacteria, but also neutralizes the products of bacteria which could provoke inflammation. We have shown that triclosan was a potent inhibitor of both cyclo-oxygenase and lipoxygenase pathways. It not only inhibited these enzymes in vitro but also inhibited the release of their products (prostaglandins and leukotrienes) in gingival fibroblasts which were stimulated by interleukin 1-β. These data were clinically confirmed in a study in which we blocked the antibacterial effect of triclosan but maintained its anti-inflammatory effect. Thus, triclosan has a ''double barrel'' effect—both antibacterial and anti-inflammatory. This unique feature is not provided so far by other antibacterial, anti-plaque agents [20].

MOUTHWASHING

Mouth rinses currently on the markets are aqueous-based formulation where the therapeutic agents are at lower concentrations than toothpaste. For example, the general population uses toothpaste at 1 g or 1 mL on the brush, but the rinses are used in 10 to 15 mL and some lower concentration of the actives are incorporated. Also, the rinses do not contain polishing agents or thickeners. A typical therapeutic rinse contains surfactants, flavor, active agent, and water. The general principles of active agent delivery which were outlined above also apply for the active agent delivery in the mouthwash. Table 7 summarizes the typical clinical performance vs. a placebo rinse of therapeutic rinse (Table 7).

STRATEGY FOR CLINICAL STUDIES IN ORAL-CARE PRODUCTS

Preclinical Evaluation → Pilot Studies → Controlled Studies → Field Trials

To document the effectiveness of oral products against dental diseases, the strategy for clinical studies is outlined in the above chart. The preclinical studies include laboratory and animal tests. For example, for fluoride efficacy a test would include fluoride uptake in teeth or hydroxyapatite, reduction in enamel solubility following fluoride treatment, followed by an acid challenge. The effectiveness in rats include the effects of topical application of fluoride solution in reducing caries. The pilot studies in humans are done to assess the effectiveness of fluoride to promote mineral deposition or prevent dissolution of artificially created lesions in enamel slabs implanted in partial dentures. Such studies are of 2 to 4 weeks duration and conducted in 20 to 30 subjects per group. If the pilot study significantly enhance remineralization of artificial lesions, control studies in 30 to 60 subjects for 3 to 6 months are conducted with the final formula for efficacy. The parameters could include promotion of mineralization, regression of early cavity lesions, and fluoride uptake in dental plaque and saliva. The field trials are conducted in children (1000 per group) for a period of 3 years to assess the effects on cavity development. For prevention of plaque and gingivitis formation, such trials are conducted for 6 months. The calculus reduction field trials are also conducted for a period of 6 months. Such field trials are of parallel/double-blind design.

FUTURE TRENDS

The global needs for prevention of dental diseases can be met by the development of knowledge in academia and industry and its subsequent applications. With a better understanding of processes occurring in the mouth, we will be able to design better actives and active agent delivery systems for the control of oral diseases. The technological trends are leading toward the goal.

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Decorative Products

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INTRODUCTION

Decorative cosmetics are principally concerned with beautifying and decoration rather than functionality. No discussion of decorative products can be complete without a full understanding of the importance of color, a prime component of every decorative cosmetic. Conventional pigments create color by absorption of certain wavelengths of incident light. The color perceived corresponds to that of the wavelengths reflected. Formulation of decorative cosmetics has been an exciting challenge for cosmetic chemists. Before formulating any color cosmetic product, one must check the current regulations in the country where the proposed product will be sold to make sure all the colors conform to those regulations. The following is a practical guide for the formulator and covers a maximum of technical and regulatory issues in an easy-to-use format.

COLOR

Color-Additive Regulation

In the past, colorants had been used in cosmetics without any consideration being given to their possible toxicity. Today, all countries have regulations that control the type and purity of colors that may be used in cosmetics.

United States: U.S. Food and Drug Administration (FDA)

21 CFR 73, 74; Positive List [1]: Colors listed for general cosmetic use, including eye area only if stated specifically, or external only, meaning no contact with mucous membranes. Hair dyes and true soaps are exempt.

European Union (EU): European Commission (EC)

Directive 76/786, Annex IV [2]; Positive List: Colors listed for ingested use, general, including eye area, external, or rinse-off.
Annex II: Negative List

Japan: Ministry of Health and Welfare (MHW)

MHW Ordinance No. 30 [3]; Positive List, Coal-Tar Colors: Premarket approval by MHW for all other cosmetic ingredients, including inorganic and natural colorants.

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Color-Additives Definitions

Primary/Straight Color: A color that is pure, containing no extenders or dilutents.
Dye: A color that is soluble in the medium in which it is dispersed. (e.g., FD&C Blue #1).
Pigment: A color that is insoluble in the medium in which it is dispersed. (e.g., FD&C Blue #1 Al lake, Black iron oxide).
Lake: A water-insoluble pigment composed of a water-soluble straight color strongly absorbed onto an insoluble substratum through the use of a precipitant (e.g., FD&C Blue #1 Al Lake). Generally, 10 to 40% color.*
Toner: A pigment that is produced by precipitating a water-soluble dye as an insoluble metal salt (e.g., D&C Red #6 barium salt, D&C Red #7 calcium salt).
True Pigment: A pigment that, based on its chemistry, precipitates as it is formed (e.g., D&C Red #36).
Extender: A pigment diluted on substrate
1. during manufacture by precipitation, or
2. postmanufacture by intimate milling or mixing.

U.S. Regulations

21 CFR Part 73 [4]: Listing of Color Additives Exempt from Certification

Inorganic pigments, powdered metals, and naturally derived colorants approved for food, drug, and/or cosmetic use. Listed permitted uses are as follows:

- Food
- Ingested/externally applied drugs
- General cosmetic
- Eye area only if mentioned
- External (no mucous membrane), i.e., ultramarines, ferric ammonium ferrocyanide not permitted in lip or bath products

21 CFR Part 74 [5]: Listing of Color Additives Subject to Certification

Synthetic organic dyes and pigments. Each batch must be submitted by the manufacturer to the FDA for certification that specifications are met. Permitted uses as in Part 73.

Four certified organic dyes and their lakes are now permitted for eye-area use:

1. FD&C Blue #1
2. FD&C Red #40
3. FD&C Yellow #5
4. D&C Green #5

21 CFR Part 82 [6]: Listing of Certified Provisionally Listed Colors

Lakes:

FD&C: Aluminum or calcium salt on alumina.

---

* FDA has considered any certified colorant mixed with a diluent to be a lake; e.g., D&C Red 30 Plus talc, and D&C Red #7 CA lake on calcium carbonate.

D&C: Sodium, potassium, barium, calcium, strontium, or zirconium salt on alumina, blanc fixe, gloss white, clay, titanium dioxide, zinc oxide, talc, rosin, aluminum benzoate, calcium carbonate.

A salt prepared from straight color, i.e., D&C Red #6, by combining the color with a basic radical.

Proposed Permanent Listing of Color Additive Lakes (FR Vol. 61 #43), March 4, 1996 [7]

- List substrate, e.g., D&C Red #27 aluminum lake on alumina
- Extenders of insoluble straight colors will no longer be called lakes, e.g., D&C Red #30
- Permit blends of previously certified straight colors in a lake, e.g., FD&C Blue #1 and Yellow #5 aluminum lake
- All lakes to be prepared from previously certified batches of straight color would necessitate process changes for D&C Reds #6, #7, and #34
- Abbreviations permitted for cosmetic ingredient labeling, omitting FD&C, precipitate and substrate designation e.g., Blue 1

European Community

Directive 76/786, as amended [8].

Annex IV

This is a list of coloring agents allowed in cosmetic products.
List by color index number:

Part 1: Permanently listed
Part 2: Provisionally listed

Four fields of application:

1. All cosmetic products
2. All cosmetic products, except those intended to be applied in the vicinity of the eyes, in particular eye makeup and makeup remover
3. Allowed exclusively in cosmetic products intended not to come into contact with mucous membranes (including the eye area)
4. Allowed exclusively in cosmetic products intended to come into contact only briefly with skin (not permitted in nail preparations)

Lakes and Salts

If a color index number is listed in Annex IV, then the pure color plus its salts and lakes are allowed, unless prohibited under Annex II (the list substances that cosmetics may not contain). Exceptions include barium, strontium, and zirconium.

Prohibited under Annex II, but where Footnote 3 appears in Annex IV, ''the insoluble barium, strontium, and zirconium lakes, salts, and pigments . . . shall also be permitted.'' They must pass the test for insolubility which will be determined by the procedure in Article 8. (Insoluble in 0.1 N HCl).

Purity Criteria

Only colors designated by an ''E,'' those also permitted for food use, must meet the general specification for food colors.

<5 ppm	As
<20 ppm	Pb
<100 ppm	Sb, Cu, Cr, Zn, $BaSO_4$ separately
<200 ppm	Of those together
None detectable	Cd, Hg, Se, Te, Th, U Cr^{+6}, or soluble Ba

Sixth Amendment to the directive is currently adopted. Update of purity criteria is being considered, test methods may be stipulated.

Japan

MHW ordinance No. 30 (1966) as amended by MHW ordinance No. 55 (1972) [9].

Positive List

83 Coal-tar colors:

- Must be declared on cosmetic product label
- Fields of application: oral, lip, eye area, external, rinse-off

Inorganic/Natural Colorants

Listing, specifications, test methods:

- Japan standards of cosmetic ingredients (JSCI)
- Comprehensive licensing standards of cosmetics by category (CLS)
- Japan cosmetic ingredient dictionary (CLS)

U.S. Colorants Not Permitted/Restricted in Japan

Pigments

D&C RED #6	Ba Lake
D&C RED #21	Al Lake
D&C RED #27	Al Lake
D&C RED #33	Zr Lake
D&C ORANGE #5	Al Lake

Substrates

Aluminum benzoate	0.5% maximum in lipstick
Rosin	7.0% maximum in lipstick
Calcium carbonate	Not permitted

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Inorganic Pigments

In general, inorganic colors are more opaque, more light fast, more solvent resistant, but not as bright as organic colors. They may be affected by alkali and acid. Inorganic colorants are formed from compounds of the transition elements. Color is produced as a result of the ease with which the outer ''d'' electrons can absorb visible light and be promoted to the next higher energy level.

Iron Oxides		
Good stability, opacity	Red	Fe_3O_4
	Brown	
	Burgundy	Fe_2O_3
	Black	Fe_3O_4
	Yellow	FeOOH
Chromium Oxide		
Good stability, opacity	Green	Cr_2O_3
Chromium Hydroxide		
Good stability, lower tinting strength	Aqua	$Cr_2O_{3X}H_2O$
Ultramarines		
Good light stability, lower tinting strength, unstable to acid	Blue Violet Pink	$Na_x(AlSiO_4)_yS_z$
Manganese Violet		
Good light stability, lower tinting strength, unstable to water	Violet	$NH_4MnP_2O_7$
Ferric Ammonium, Ferrocyanide		
Lower light stability, high tinting strength, unstable to alkali and salts, difficult dispersion	Deep Blue	$FeNH_4Fe(CN)_6$
Ferric Ferrocyanide		
Physical/chemical stability as above, precipitated on a substrate (i.e., mica)	Deep Blue	$Fe[Fe(CN)_6]_3$ XH_2O
Titanium Dioxide		
Medium light stability, good chemical stability, high opacity	White	TiO_2 Anatase Rutile

Organic Pigments

Organic pigments are characterized by:

- Transparency
- Variable chemical and physical stability
- ''Clean,'' bright colors

Color is produced by chromophoric groups, generally electron acceptors.

—N=N—	—C=O
$—NO_2$	—C=S
—NO	

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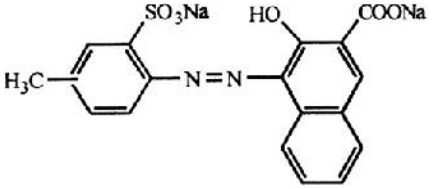
Shade is modified or intensified by auxochromes, generally electron donors.

$-NH_2$	$-OH$
$-NHR$	$-OCH_3$
$-NR_2$	

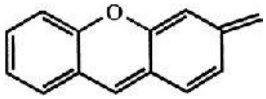
Categories of Organic Colorants

AZO Colorants: —N═N—



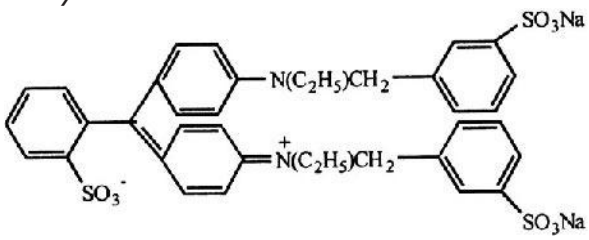
Insoluble (unsulfonated): D&C Red #36; light stable
Soluble (sulfonated): D&C Red #33, FD&C Red #40, FD&C Yellow #5, FD&C Yellow #6; stable to acid, alkali, light, bleed in water
Slightly soluble (sulfonated/insoluble salt): D&C Red #6; D&C Red #7, D&C Red #34; color shift in acid and alkali; light fast; resistant to oil bleed
Oil soluble (unsulfonated): D&C Red #17

Xanthenes



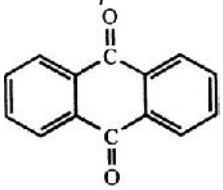
D&C Orange #5; D&C Red; D&C Red #21; D&C Red #27. ''Staining dyes'': structure changes with pH, poor light stability, bleed in solvent

Triarylmethane



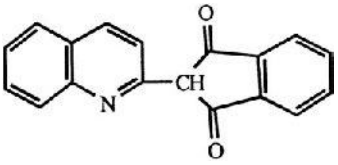
FD&C Blue #1, FD&C Green #3 water soluble; poor light stability

Anthraquinone



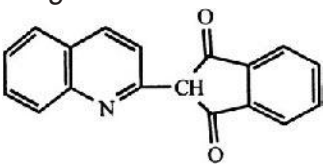
D&C Green #5; good light stability

Quinoline



D&C Yellow #10, D&C Yellow #11; oil soluble

Indigoid



D&C Red #30; good chemical, light, bleed resistance; exception: acetone soluble

Stability of Organic Pigments

True pigments > Toners > True Lakes
Light: Anthraquinone > Quinone > Indigoid > Azo > Triarylmethane > Xanthene
Heat: True pigments stable to heat.
Toners: D&C Red #7 Ca lake changes reversibly
Lakes: D&C Red #27 Al lake changes irreversibly
pH: 4–9
Metal ions: Unstable
Solubility: True lakes tend to bleed in water,
Fluorescein lakes bleed in solvent

Natural Dyes [10]

Generally used in foods, there is no restriction on their use in cosmetics. For the most part, the resistance of natural dyes to heat, light, and pH instability is much inferior to their synthetic counterparts. A further disadvantage is that they often tend to exhibit strong odors.

Color	Description	Source
Yellow	Curcumim	Turmeric
Yellow	Crocin	Saffron
Orange	Capsanthin	Paprika
Orange	Annatto	Annatto
Orange	Cartenoids	Carrots
Red	Cochineal	Coccus cactii
Red	Betanine	Beetroot
Red	Anthocyanins	Red berries
Green	Chlorophylls	Lucerne grass
Brown	Caramel	Sugars

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All of the above are of vegetable origin, with the exception of cochineal which is extracted from the crushed insects *Coccus cactii*.

Color Chemistry and Manufacture

The property of a colorant that makes it absorb more in one part of the visible spectrum than another is its chemical constitution. Molecules, like atoms, exist in different electronic states. Because molecules contain two or more nuclei, they also possess energies of rotation and vibration. This theory applies to both organic and inorganic colorants. With the inorganic colorants, colored compounds are obtained with the ions of the transition elements that have atomic numbers 22 to 29.

Inorganic Pigments

Titanium Dioxide

A brilliant white pigment. Two crystal types occur: anatase and rutile. Two manufacturing processes are used:

1. Sulfate—either crystal may be produced.
2. Chloride—only rutile crystals are formed properties. Crystals of both rutile and anatase are tetragonal, rutile having greater hiding power because of the closer packing of the atoms in the crystal. Refractive indices are 2.55 for anatase and 2.71 for rutile. Opacity is the result of the light-scattering ability of titanium dioxide. Light, heat and chemical stability are excellent. Additionally, in the United States, titanium dioxide is a Category I sunscreen.

Zinc Oxide

Zinc ore is roasted and purified at 1000°C. Two methods of manufacture are used: 1) French (indirect) and 2) American (direct).

Properties. Zinc oxide forms transparent hexagonal crystals; whiteness is attributable to the light scattering of the extremely fine particles. Refractive index is 2.0. Hiding power is less than titanium dioxide. Primary use is for antibacterial and fungicidal properties. Heat and light stability are good. It is soluble in acid and alkali. Zinc oxide in the United States is a Category I skin protectant and a Category III sunscreen.

Iron Oxides

These are used in all types of cosmetic products. By blending black, red, and yellow in certain properties, brown, tans, umbers and sienna may be produced. Yellow iron oxide is hydrated iron II (ferrous) oxide, $Fe_2O_3XH_2O$. It is produced by the controlled oxidation of ferrous sulfate. Red iron oxide is chemically Fe_2O_3 and is obtained by the controlled heating (at about 1000°C) of yellow iron oxide. Black iron oxide is Fe_2O_4 and is a mixture of ferrous and ferric oxide and is prepared by controlled oxidation of ferrous sulfate under alkaline conditions.

Ultramarines

Theoretically they are polysulfide sodium/aluminum sulfosilicates. They range in color from blue to violet, pink, and even green. A mixture is calcined at 800°C to 900°C, for 4 to 5 days. Shades are determined by reaction time, formula variations, and particle size,

whereas ultramarine violets and pinks are obtained by treating ultramarine blue with HCl at 275°C, removing some sodium and sulfur from the molecule.

Manganese Violet

Chemically this is $MnNH_4P_2O$. Manufactured by heating manganese dioxide with ammonium dihydrogen phosphate and water. Phosphorus acid is added and the mixture is heated until the violet color develops.

Iron Blue

Chemically ferric ammonium ferrocyanide. $Fe[Fe(Cn)_6]_3$. Sodium ferrocyanide and ferrous sulfate are reacted in the presence of ammonium sulfate. Pigments prepared with sodium or potassium salts are called ferric ferrocyanide.

Chromium Oxide (Cr_2O_3)

A dull yellow green pigment may be prepared by blending an alkali dichromate with sulfur or a carbonaceous material. Reduction to chrome (III) oxide is achieved in a kiln at 1000°C.

Chromium Hydroxide ($Cr_2O(OH)_4$)

A bright bluish green pigment prepared by the calcination of a bichromate with boric acid at 500°C. During cooling, the mass is hydrolyzed with water, yielding a hydrate.

Hydrated Alumina

Chemically Al_2O_3 X H_2O gives little opacity and is almost transparent.

Barium Sulfate

It is relatively translucent and may by used as a pigment extender.

Organic Pigments

These are chiefly conjugated cyclic compounds based on a benzene ring structure, although some heterocyclic ones exist. There are three main types: lakes, toners, and true pigments. Organic pigments are seldom used without a diluent or substrate in order to maintain color consistency from batch to batch. A true pigment is an insoluble compound that contains no metal ions, examples of which are D&C Red #30 and D&C Red #36. They are the most stable. A lake is essentially an insoluble colorant, produced by precipitating a permitted soluble dye to a permitted substrate. In cosmetics, most lakes are based on aluminum, although zinconium lakes are also found. Stability-wise, true aluminum lakes can be affected by extremes of pH, resulting in reforming of the soluble dye or ''bleeding.'' They are fairly transparent and not particularly light-fast. Toners are colorants made with other approved metals besides aluminum, such as barium and calcium. Generally, they are more resistant to heat, light and pH, although extremes of pH can result in shade changes. Generally, many organic colorants are unsuitable for certain cosmetics because of their chemical nature. D&C Red #36 is a typical nonsoluble azo color is not recommended for lipstick because of its very slight solubility in oils and waxes it tends to crystallize upon continual reheating of the lipstick mass. Soluble azo dyes such as FD&C Yellow #5 and #6 Red #33 lakes are often used in lipstick and nail lacquer. Sparingly soluble types such as D&C Red #6 are not highly soluble but the barium lake of Red #6 and the calcium

lake of Red #7 are the most popular colors for cosmetics. Colors in this group do not need a substrate to make them insoluble. The D&C Red #6 and #7 lakes are widely used in lipstick and nail lacquer because of high strength, bright hues, good light fasteness, as well as chemical and heat stability. Non–azo-soluble dyes such as D&C Red #21, Orange #5, and Red #27 are all fluoresceins and act as a pH indicator and will change accordingly. They all strain the skin and D&C Red #27 gives the strongest blue stain.

Quality Control of Colorants

Establishment of Standards

- Ensure that product development is performed with material representative of supplier's production
- Before purchase, evaluate at least three lots, establish standard in consultation with the supplier
- Supplier and end user should agree on specifications, standard, and test methods

Test Methods

Shade Evaluation. Methods should predict performance of the colorant under use conditions.

Light Source for Visual Evaluations to Be Specified.

- Dyes: Visual or spectrophotometric evaluation of solutions.
- Pigments: Cannot be evaluated as received due to variable degree of agglomeration. Visual or instrumental evaluation is made of wet and dry dispersions prepared under defined conditions to a defined degree of dispersion.

Vehicles:	Dispersion equipment:
Talc	Osterizer
Nitrocellulose lacquer	Hoover muller,
Acrylic lacquer	Three roll mill, or
Castor oil	Ball mill

Heavy Metals:

Wet chemical
Atomic absorption spectroscopy (AAS)
Inductive coupled plasma (ICP)

Particle Size:

Wet/dry sieve analysis
Optical microscopy
Laser diffraction
Sedimentation

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Bulk Density:

Fischer-Scott Volumeter
pH

Pearlescent Pigments and Other Specialty Pigments

Pearlescent Pigments:

The most important requirement for a substance to be pearlescent is that its crystals should be plate-like and have a high refractive index. A thin, transparent, platy configuration allows light to be transmitted. A pearlescent material should have a smooth surface to allow specular reflection and be nontoxic. Generally, when using pearlescent pigments one must use the most transparent formulation, avoiding grinding or milling the pearl pigments and blend pearls complement one another.

1. **Organic Pearls**. These pearls produce a bright silver effect and are obtainable from fish scales as platelets or needles, which are highly reflective. The materials responsible for the pearl effect are crystals of a purine called guanine. Guanine is chiefly used in nail-enamel.
2. **Inorganic Pearls**.

(A) Bismuth oxychloride:

Bismuth oxychloride produces a silvery-grey pearlescent effect and is synthesized as tetragonal crystals. Crystal sizes vary from approximately 8 microns, which give a soft, opaque, smooth luster, and 20 microns, which give a more brilliant sparkling effect. Its major disadvantage in use is poor light stability, which may cause darkening after prolonged exposure. UV absorbs in the finished products are used to overcome this defect. BioCl is chiefly used to pearl nail enamels, lipsticks, blushes, and eye shadows. BioCl may be modified by deposition on mica, titanium dioxide and mica, or talc. Inorganic pigments may be bonded to BioCl then deposited on mica. All these alter the final effect on the finished product.

(B) Titanium dioxide–coated micas:

Titanium dioxide–coated micas are extensively used in decorative cosmetics. They exist in several different forms: (1) silver-titanium dioxide uniformly coats platelets of mica, rutile crystals give a brilliant pearl effect because of a higher refractive index than the anatase grade; and (2)interference pearlescent products can be made by altering the thickness of the film. At a certain thickness, interference of light can take place so that some wavelengths of the incident light are reflected and others transmitted. The colors created are complementary to each other. As the layers become thicker, the reflection goes from silvery white, then yellow-gold, red, blue, and green. Additionally, colorants such as iron oxides can be laminated with this interference film, providing a two-color effect.

3. **Pigment Pearls**. Colored pearls are produced by laminating a layer of iron oxides on titanium dioxide–coated mica, producing a color and luster effect.
4. **Specialty Pigments**. In addition to BioCl and the titanium dioxide–coated mica systems, polyester foil cut into regular shapes, which have been epoxy coated with light fast pigments, have been used for nail enamels and body makeup. Finally, aluminum powder and copper/bronze powder have been used as reflective pigments, especially in eye shadows. For cosmetic-use aluminum powder, 100% of the particles must pass through a 200 mesh screen, and 95% must pass through a 325 mesh (44 millimicron) screen.

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Treated Pigments

Surface-treated colors and substrates allowed chemists to enhance the aesthetic and functional qualities of their formulations. The benefits of using these treatments may be divided into two categories: those evident in the finished cosmetic product, and the benefits derived from process improvements. Consumer benefits include hydrophobicity yielding greater wear, improved skin adhesion, smoother product feel, improved optical appearance, moisturization, and ease of application. Processing benefits include ease of dispersion, pressability, less oil absorption, uniformity, and less moisture absorption. The following surface treatments are commercially available:

- Amino Acids (N-Lauroyl lysine, acyl amino acid [11])
  - Natural
  - Good skin adhesion
  - pH balanced
  - Heat sensitive
- Fluorochemical (Perfluoropolymethylisopropyl ether perfluoroalkyl phosphate)
  - Hydrophobic and lipophobic greatly enhance wear
  - Heat and shear resistance
- Lecithin [12]
  - Natural
  - Exceptionally smooth, silky skin feel, particularly in pressed products
  - Heat sensitive, slightly soluble in water
- Metal Soaps (ZnMg Stearate)
  - Good skin adhesion
  - Enhanced compressibility
- Natural Wax
  - Natural
  - Moisturizing skin feel
  - Good skin adhesion
  - Heat sensitive (low m.p.)
- Nylon (pure mechanically coated)
  - Smooth skin feel
- Polyacrylate
  - Enhanced wetting in aqueous systems
  - Feel is not very good
  - but is usually used in dispersion
- Polyethylene
  - Hydrophobic
  - Waxy, smooth skin feel
  - Enhanced compressibility
  - Heat sensitive
- Silicone (Polymethylhydrogensiloxane; methicone will be chemically bonded and cannot be removed later)
  - Hydrophobic
  - Achieves full color development
  - Main use is to improve wetting
- Other Silicones (No potential for hydrogen evolution)
  - Dimethiconol

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  - Absorbed dimethicone
  - Silicone/lecithin
- Silane
  - Extremely hydrophobic, lipophilic
  - No hydrogen potential
- Titanate Ester Isopropyl triisosteryl titanate [13]
  - Enhances wetting in oil
  - Smooth skin feel
  - High pigment loading
  - Lowers oil absorption of pigments

Microfine/Ultrafine/Nanosized Pigments

These pigments have a primary particle size below 100 nm; larger agglomerates/aggregates can be present. Properties such as surface area, bulk density, vehicle absorption, and UV absorption differ significantly from those of conventional pigment. Microfine titanium dioxide, zinc oxide, and iron oxides can be used in a range of color cosmetics to provide unique visual effects as well as UV protection. In pressed powders and anhydrous and emulsified formulations, significant SPF values can be achieved in formulations having a translucent, natural-looking finish. With microfine pigments, formulations for darker skin tones can be formulated that avoid the ''ashy'' or ''made-up'' appearance caused by conventional opaque pigments.

Light-Diffusing Pigments

Some of the requirements for light-diffusing pigments include a high refractive index, reflection to be diffused, translucency, and its transmission must be primarily diffuse. Skin has a refractive index of 1.60. Examples of light diffusers include $BaSO_4$, silica, silica spheres coated on mica, $TiO_2/BaSO_4$-coated mica, Al_2OH_3/mica, ultrafine TiO_2/mica, ultrafine TiO_2/polyethylene, ethylene acyrates copolymer, polymethyl methacrylate, among others. These products are chiefly used in powders to create illusions and hide wrinkles.

MAKEUP TECHNOLOGY

- Types of Color Cosmetics
  - Foundation
  - Blushers
  - Mascara
  - Eyeliner
  - Eye shadow
  - Lip color
  - Nail color
- Purpose
  - Improve appearance
  - Impart color
  - Even-out skin tones
  - Hide imperfections
  - Protection

- Types of Formulations
  - Suspensions
    - Aqueous
    - Anhydrous
- Emulsions
  - Oil-in-water
  - Water-in-oil
- Powder
  - Pressed
  - Loose
- Anhydrous (wax, solvent)
  - Stick
  - Pan
  - Tube

Powder

Powdered cosmetics are generally used to describe face powders, eye shadows, and blushers. When the product is applied to the skin, the shade must not significantly change as it is worn; must feel smooth in use, making it easy to apply; and adhere well for a reasonable time, without reapplication.

Face Powders

Some of the attributes of a satisfactory face powder are the following: (1) gives smoothness to overall texture, (2) gives added skin translucency when excess is buffed, (3) makes the skin appear more refined and finer textured, (4) helps set the makeup base and adds longevity to the makeup overall, and (5) suppresses surface oil and shine. Generally there is a wide range of raw materials used in powdered cosmetics and many of these carry over into the formulation of other decorative cosmetics.

Talc

Talc is the major component of most face powders, eye shadows, and blushers. Chemically it is a hydrated magnesium silicate. Cosmetic talcs are mined in Italy, France, Norway, India, Spain, China, Egypt, Japan, and the United States. Typically, talcs are sterilized by gamma irradiation. Particle size should pass through a 200 mesh sieve. Cosmetic talc should be white, free of asbestos, and have high spreadibility or slip with low covering power. Micronized talc is generally lighter and fluffier but less smooth on the skin than regular grades. Although talc is fairly hydrophobic, treated talcs have been used to enhance its texture. In some products, talc is present up to 70% of the formulation.

Kaolin

Kaolin, or china clay, is a naturally occurring, almost white, hydrated aluminum silicate. It does not exhibit a high degree of slip. Kaolin has good absorbency, is dense, and sometimes used to reduce bulk densities in loose-powder products. It provides a matte surface effect that can reduce slight sheen left by some talc products.

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Calcium Carbonate

Calcium carbonate, or precipitated chalk, has excellent absorption properties. It provides a matte finish and had moderate covering powder. High levels should be avoided; otherwise an undesirable, dry, powdery feel can result.

Magnesium Carbonate

Magnesium carbonate is available in a very light, fluffy grade that absorbs well and is often used to absorb perfume before mixing into face powders.

Metallic Soap

Zinc and magnesium stearate are important materials for imparting adhesion to face powders. They are usually incorporated at 3 to 10% of the formulation. Stearates add some water repellency to formulas. They are although too-high levels give a blotchy effect on the skin. Zinc stearate, besides imparting adhesions, gives a smoothing quality to face powders. Aluminum stearate and lithium stearates have also been used. High levels can make pressed formulations too hard.

Starch

Starch is used in face powders to give a ''peach-like'' bloom and to provide a smooth surface on the skin. One problem attributed to rice starch is that, when moistened, it tends to cake. Also, the wet product may provide an environment for bacterial growth.

Mica

Mica is chemically potassium aluminum silicate dihydrate. Cosmetic mica is refined and ground to particles of 150 microns or less. It imparts a natural translucence when used up to 20% in formulations of face-powder blushes. Mica is available as wet ground, which is creamy, or dry ground, which is matte. Sericite is a mineral, similar to white mica in shape and composition. It has a very fine grain size and silky shine. It is soft and smooth and has a slippery feel on the skin. Sericite may be coated with silicone and other treatments for better water repellency and skin adhesion.

Polymers

Polymers are chiefly texture enhancers used at levels of 3 to 40%, depending on whether they are to be included in a loose or pressed powder. Among these polymers, we find Nylon-12 and Nylon-6, lauroyl lysine, boron nitride (makes active ingredients spread more uniformly on inactive bases), polyethylene, polypropylene, ethylene acrylates copolymer (very sheer, will not affect binder in pressed powders, processing temperature less than 85–90°), polymethyl methacrylate (PMMA) and silica beads (can carry oily ingredients into a system, increase wear on oily skin), polyurethane powders, silicone powders, borosilicate, microcrystalline cellulose, acrylate copolymers, Teflon® and Teflon® composites (effective at low concentrations, 1–5%), polyvinylidene copolymers (very light, ultra-low density), and composite powders that are coated on inexpensive beads to reduce costs and increase effectiveness, like nylon/mica, silica/mica, lauryl lysine/mica and boron nitride/

mica. Many of these polymers are treated with silicones, titanates, lecithin, etc. for increased effectiveness.

Colorants

Titanium dioxide and zinc oxide, both pigmentary and ultrafine organics, inorganics, carmine, and pearlescent pigments either predispersed or treated are found in all face powders because the textures of these colorants are not very satisfactory.

Perfumes

The use of perfumes is important for face powder, which requires them because most of the raw materials used are earthy smelling and should be masked. Perfumes should show stability and low volatility.

Preservatives

Preservation of face powders are usually not a problem because they are used dry, but small amounts of antibacterials are recommended. Powdered eye shadows should always contain antibacterials such as parabens, imidazolidinyl urea, and others.

Loose Face Powders

This type has declined in popularity in favor of pressed face-powder products. The smoothness of loose face powder can be enhanced by use of the aforementioned texture enhancers. In the manufacturing process, all ingredients except the pearls, if required, are combined in a stainless steel ribbon blender. Mixing time can be as long as 1 or 2 hours, depending on the size of the batch and evenness of the color. The perfume, if required, is slowly sprayed into the batch, blended until homogenous. The batch is then pulverized through a hammer mill and the color is checked. Color adjustments are made, if necessary, in the ribbon blender, and the batch is repulverized. Any pearl or mica is then added for a final mix. Batch is then stored and made ready for filling into appropriate containers.

Pressed Face Powders

Pressed face powders are more popular than loose powders because of their ease of application and portability. The basic raw materials are the same as loose powder except that one must use a binder to press the cake into a tin-plate godet. If water-based binders are used, aluminum godets should be considered to prevent corrosion. The properties of a binder is as follows: provides creaminess to the powder, aids in compression and adhesion, develops colorants, and enhances water resistance, pick-up, and deposit. If the binder level is too high, it may be difficult to remove the powder with a puff. Also, high levels may lead to glazing of the powder surface, making it waxy looking, with little or no pay-off. Fatty soaps, kaolin, polyethylene, Teflon® synthetic wax, and calcium silicate are some of the binder systems used. Use levels of binder are between 3 to 10%, depending on formulation variables. Silicone-treated pigments have given rise to pressed face powders that may be used wet or dry. When used dry, they are usually smoother than regular pressed powders. When a wet sponge is applied to the cake, no water penetrates the cake; the water is repelled. These ''two-way'' cakes can be used either as a foundation or face powder. When formulating pressed powders, one must be careful that the raw materials

used do not corrode the godets or attack the plastic packaging materials. The manufacture of pressed powders, including the mixing and color-matching process, is similar to loose powders. Sometimes the powder mix is pulverized without binder and then again after its addition. Pearls are usually added during the blending process and preferably without the milling operation which can damage the pearl. If milling a batch containing pearl becomes necessary, it should be done with the mill screen removed. Powder pressing is often times more successful if the powder is kept for a few days to allow the binder system to fully spread, especially when pearls are present. The most common used pressed for face powder are the ALITE-high speed hydraulic press and the KEMWALL, CAVALLA, or VE. TRA. CO. presses. The pressures used and the speed of pressing depends on the characteristics of the individual formulation and the size of the godet.

Powder Blushers

The attributes of blushers are as follows: (1) add color to the face; (2) can give more dimension to the cheekbones; (3) harmonizes the face-balance between eye makeup and lipstick; and (4) creates subtle changes in the foundation look when lightly dusted over the face. Pressed powder blushers are similar to face-powder formulations, except that a greater range of color pigments is used. The three basic iron oxides and one or more of the lakes are used to achieve various blusher shades. Blushers are usually applied with a brush. Manufacture and pressing is similar to face powders. Care should be taken that only nonbleeding pigments be used to avoid skin staining. Total pigment concentration ranges from 2 to 10%, excluding pearls. Pressed-powder rouges were once popular and contained high levels of colorants (10–30%). Usually they are applied from the godet with the finger, so glazing may frequently occur if the rouge is improperly formulated.

Pressed-Powder Eyeshadows

Eye shadows in general have the following functions: (1) adds color and personality to the face; (2) sharpens or softens the eyeball itself; (3) creates the illusion of depth or brings out deep set eyes; (4) creates light and dark illusions for subtle character changes; and (5) can be used wet or dry for different illusions. The technology is similar to other pressed-powder products, but the permitted color range is limited. In the US the only synthetic organic pigments that may be used in eye products are FD&C Red No. 40, FD&C Blue #1, FD&C Yellow #5, and Green #5. Carmine, N.F. is the only natural organic pigment allowed, and all of the inorganic pigments and a wide range of pearls may be used. Preservation is very important in eye-makeup products. Problems of poor adherence to the skin, color matching, and creasing in the eyelid are common when the binder formulation is ineffective with the type and level of pearls used. High binder levels may result in uneven pressing of the godets. In manufacture, formulas with high pearl content should be allowed to settle to remove entrapped air before pressing.

Quality Assurance on Powder Products

Color

Production batch and standard are placed side by side on white paper and pressed flat with a palette-knife. Shades are compared with one another. Shades of eye shadows and blushers are checked on the skin using a brush or wand.

Bulk Density

Carried out on loose powder to ensure that no entrapped air is present so that incorrect filling weights are minimized.

Penetration and Drop Tests

Are carried out on pressed godets. A penetrometer is used to determine the accuracy of the pressure used during filling. A drop test is designed to test the physical strength of the cake. Normally, the godet is dropped on to a wooden floor or rubber matte (1–3 times) at a height of 2 to 3 feet to note damage to the cake.

Glazing and Pay-Off

The pressed cake is rubbed through to the base of the godet with a puff, and any sign of glazing is noted. Pay-off must be sufficient and the powder should spread evenly without losing adhesion to the skin.

Foundation

In general, foundation makeup's chief functions are to hide skin flaws, even-out various color tones in the skin, act as a protectant from the environment, and make the skin surface appear smoother. Requirements for an ideal makeup foundation's application are as follows: (1) should be moderately fast drying to allow for an even application; (2) should be nonsettling, pour easily, be stable in storage; (3) should not feel tacky, greasy, or too dry; (4) it should improve appearance, not artificially; and (5) should have proper ''play time'' and slip. Depending on the formulations, several contain treated pigments and volatile silicones to add water-resistance properties. There should be shade consistency between the bottle and skin tone. Products should be uniform. Coverage or capacity will vary with skin types; finish on the skin may by matte, shiny, or ''dewy.'' Wear is extremely important—product should not peel-off, go orangy on the skin or rub-off on clothes.

Foundation makeup is available in the following forms:

- **Emulsions**. O/W, anionic, nonionic, and cationic. W/O; became more popular for water-proofness and contains volatile silicone, hydrocarbones, mineral oil, and light esters.
- **Anhydrous**. Cream powder and stick.
- **Suspensions**. Oil and aqueous.

Emulsified Foundations

Composition can vary widely depending on degree of coverage and emolliency desired. Although nonionic (usually not stable), cationic (difficult to make, not on market), and W/O systems have been marketed, most emulsified foundations are anionic O/W emulsions because of the ease of formulation. Anionics possess the following properties:

- emulsion stability
- pigment wetting and dispersion
- easy spreading and blending
- good skin feel
- slippery (soap-like) feeling

Formulation Considerations

1. Prolonged skin contact. Minimize emulsifier levels to avoid irritation.
2. Choose oils based on low *comedogenicity*.
3. Preservation—foundations may be difficult to preserve containing such ingredients as water and gums.

Emulsion Makeup Manufacturing Equipment

- *Pigment Extenders*: hammer mill and jet mill
- *Internal Phase*: propeller mixer/SS steam–jacketed kettle
- *External Phase*: colloid mill, homogenizer/sidesweep, and SS steam–jacketed finishing kettle
- *Emulsification*: sidesweep, homogenizer, and recirculating mill, i.e., colloid mill
- With *high-viscosity systems* planetary mixer is needed

Manufacturing

The coloration of the emulsion base may be handled in different ways: direct pigment, pigment dispersions, mixed pigment blender, and monochromatic color solutions [14]. Each has its advantages and disadvantages. In the direct pigment method, the pigments are weighed directly into the aqueous phase and dispersed or colloid milled; then the emulsion is formed in the usual manner. The major problem is that there are too many color adjustments needed and accurate color matching is difficult. With the pigment dispersion method, the pigment is mixed with talc as a 50:50 dispersion and pulverized to match a standard. This reduces the number of color corrections needed but storage may be a problem as well as the time taken to make these dispersions. During the mixed-pigment blender method, the pigments and extenders are premixed, pulverized, and matched to a standard; it is then dispersed in the aqueous phase of the emulsion and the emulsion is formed in the normal way. The finished shade is color matched at the powder blender stage. Chances of error are reduced. The last method—the monochromatic color solutions—required one to make color concentrates of each pigment in a finished formula. It is easy to color match by blending finished base, but much storage space is needed and the possibility for contamination is increased.

Anhydrous Foundations

Anhydrous foundations are generally powdery, not fluid, and easy to travel with. Ingredients needed include:

1. Emollients. Often texturally light and low viscosity; include oils, esters, and silicones.
2. Waxes.
   (A) Natural: Beeswax, jojoba, orange, carnauba, candelilla, and castor.
   (B) Beeswax derivatives: Dimethicone copolyol beeswax, polyglyceryl-3 beeswax, butyloctanol, and hexanediol beeswax (nice texture, compatibility with silicone material).
   (C) Synthetic: Paraffins, microcrystalline, polyethylene, and ''synthetic wax'' (highly branched olefin polymers).
   (D) Fatty alcohols and fatty alcohol ethoxylates: Unithox and unilin.

(E) Fatty esters: Croda (syncrowaxes), koster keunen (kester waxes), Pheonix Chemical, Scher, Flora Tech, and RTD.

3. Pigments. Often surface treated.
   (A) TiO2: Pigmentary and ultrafine.
   (B) ZnO: Pigmentary and ultrafine.
   (C) Iron Oxides: Pigmentary and ultrafine (enhances SPF value).
4. Texturizing Agents. Often surface treated; include nylon, PMMA, sericite, talc, mica, boron nitride, Teflon®, borosilicates copolymer, polyvinylidene copolymer, spherical silica, starches (oats, rice, wheat, corn, dry flo-starch), BiOCl, microcrystalline cellulose, polyurethane powder, and silicone powder.
5. Wetting Agents. Small amount to be used; include low HLB emulsifiers, polyglyceryl esters, e.g., polyglyceryl-3 diisostearate, hydrogenated lecithin, lanolin alcohols, polyhydroxy stearic acid, and soya sterols.

Basic Formulation	
Emollients (fluids, low melting point waxes, gel-like raws)	30–60%
Waxes	5–10%
Wetting agents	0.50–1.00%
Texturing agents	30–60%

Surface-treated raw materials are frequently used in these types of formulations for the following reasons:

- Improves dispersibility
- Enhances solids loading
  provides drier texture
  creates matte appearance
  improves wear
  overall improved aesthetics

Manufacturing Procedure

1. Emollients, waxes, and wetting agent(s) are introduced into a jacketed kettle and heated until phase is clear and uniform.
2. Pigments and texturizing agents are slowly introduced into the oil phase with higher shear mixing. Continue high shear mixing until dispersion is uniform and colorants are completely ''extended.''

If surface treatments are temperature-sensitive, care must be taken to prevent the displacement of that treatment from the surface of the powder into the oil phase itself.

EYE MAKEUP

Mascara

1. Brings out the contrast between the iris and the white of the eye, sharpens white of the eye

2. Thickens the appearance of the lashes
3. Lengthens the appearance of the eye
4. Adds depth and character to the overall look
5. Sharpens the color of the eye shadow when worn.

Mascara's performance is usually judged by application, appearance, wear, and ease of removal. It is critical that the proper brush is supplied for the chosen formulation. Generally, mascara and eyeliners consist of one or more film formers, pigment, and the vehicle that mostly evaporates to allow the film to set.

Three Types of Formulations Are Currently in Use

In the past, cake or block mascara was popular. This was basically a wax base with a soap or nonionic emulsifier present so that color could be applied with a wetted brush. Mascara and eyeliners consist of one or more film formers, pigment, and the vehicle that mostly evaporates to allow the film to set.

- Anhydrous solvent based suspension: waterproof but not smudge-proof and difficult to remove
- W/O emulsion: also waterproof but not smudge-proof and can be removed with soap and water
- O/W emulsion: water-based if the film is sufficiently flexible, can be flake-proof and smudge-proof. Water resistance can be achieved with the addition of emulsion polymers, i.e., acrylics, polyvinyl acetates, or polyurethanes.

Oil-in-Water (O/W)

Water Phase
  Water
  Suspending agent: hydroxyethylcellulose
  Film former/dispersing agent: polyvinylpyrrolidone
  Pigment
  Hydrophilic emulsifier: alkali, high HLB nonionic
Wax Phase
  High melting point waxes
  Lipophilic emulsifier: fatty acid, low HLB nonionic, co-emulsifier
  Plasticizer: lanolin or derivatives, liquid fatty alcohol
  Petroleum solvent (optional) as extender for water phase
  Preservative: propyl paraben
Additional Film Former
  Solution polyacrylate (improves flake resistance)
  Emulsion polyacrylate
  Polyurethane
  Polyvinyl acetate
  Rosin derivatives
  Dimethiconol
  Proteins: wheat, soy, corn, keratin, oat, silk
Preservative
  Formaldehyde releaser (not for use in Japan)

Manufacturing

Procedure is generally o/w emulsification procedure except that iron oxides are first wet and milled in the water phase before emulsification and final product goes through a colloid mill, roller mill, or homogenizer.

Solvent-Based

Hard, high melting point waxes
Rosin derivative (optional)
Wetting agent
Pigment
Suspending agent (organoclay)
Volatile solvent (to achieve wax solubility)
  Petroleum distillate
  Cyclomethicone
Preservatives: parabens
Plasticizer: lanolin or derivative, liquid fatty alcohol

Water-in-Oil (W/O)

Wax Phase
  High melting point waxes (carnauba, candellila, polyethylene)
  Rosin derivative (optional)
  Lipophilic emulsifier (lanolin acids, low HLB nonionic)
  Pigment
  Preservative: propyl paraben
  Petroleum solvent, some cyclomethicone
Water Phase
  Hydrophilic emulsifier (alkali, medium HLB nonionic)
  Preservative: methyl paraben
Additives
  Emulsion polymer (optional)
  Preservative: formaldehyde donor (not for use in Japan)

Anhydrous Mascara

Ingredients

- Solvents: Branched chain hydrocarbons and petroleum distillates, isoparaffinic hydrocarbons, and volatile silicones
- Waxes: Beeswax and its derivatives, candelilla, carnauba, paraffin, polyethylene, microcrystalline, castor, synthetic, ceresin, and ozokerite
- Resins: (could be introduced, but do not have to be); Include aromatic/aliphatic, hydrogenated aromatics, polyterpene, synthetic, rosin, acrylics, and silicones
- Gellants: Clays (stearalkonium hectorite, quaternium-18 bentonite, quaternium-18 hectorite), metal soaps (Al, Zn stearates)
- Colorants: Most often use a classic iron oxide without any surface treatment
- Functional Fillers: Spherical particles (PMMA, Silica, Nylon), boron nitride, starches, Teflon®

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Purpose

- Provides body to film to enhance thickening properties
- Improves transfer resistance
- Improves deposit on lashes

Basic Formulation:

Solvent(s)	40–60%
Waxes	10–20%
Resin(s)	3–10%
Gellant	3–7%
Colorant(s)	5–15%
Filler(s)	2–10%

Procedure

1. Heat waxes, solvents, and resins in a jacketed kettle until uniform and clear. Slowly add pigments under high shear and mill until dispersion is uniform.
2. Under high shear, add gellant and mill until uniform. Activate gellant with polar additive like propylene carbonate. Under high shear, add fillers and mill until uniform. Cool to desired temperature.

Mascara Componentry

Bottle

PVC-polyvinyl chloride for solvent based and H.D. polyethylene/polypropylene for water-based types.

Brush/Rod/Wiper

Works complementary with each other to deliver required product attributes.

Required for a Thickening Mascara

Larger diameter rod
Larger diameter wiper
Larger brush with significant spacing between the bristles

Suggested for a Defining Mascara

A smaller diameter rod
Smaller diameter wiper
Brush with minimal spacing between the bristles

Brush materials, fiber diameter, brush shape, fiber shape, fiber length, wire diameter, and the number of turns in the wire all affect performance.

Cream Eyeshadows

Generally, cream eye shadows are another form of eye shadow not as popular as the pressed form. Care must be taken in formulation to avoid creasing and other wear problems. In the past, stick eye shadows were popular. They are similar to cream eye shadows

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but contain high melting point waxes to make them moldable. The ingredients used are as follows.

Ingredients:

- Volatile solvents: Cyclomethicone, hydrocarbons, isoparaffins
- Waxes: Similar to those used in the anhydrous waterproof mascaras, although at lower concentrations
- Emollients: Esters, oils, silicones
- Gellants: Bentonite derivatives, hectorite derivatives
- Colorants and Pearls: Classical
- Fillers: Mica, talc, sericite
- Functional fillers: Boron nitride, PMMA, nylon, starches, Silica, Teflon, Lauroyl lysine

For enhanced textural properties, higher solids loading, and improved application and coverage, use surface-treated raw materials whose coatings are neither temperature nor solvent sensitive. Balance the absorption of fillers to maintain similar textures throughout the shade range.

Basic Formulation

Solvent	35–55%
Gellants	1.50–3.50%
Waxes	7–12%
Emollients	3–8%
Colorants/pearls	5–20%
Fillers	10–20%
Functional fillers	5–15%

The *manufacturing procedure* is identical to that of anhydrous mascaras.

Eyeliners

Eyeliners frame the eye while adding shape to or changing the shape of the eye. They give the illusion of a larger or smaller eye bringing out the color contrast between the iris and white of the eye. Lastly, eyeliners assist in making the lashes appear thicker. Generally, liquid eyeliners are the most popular and will be chiefly outlined. Cake eyeliner was popular in the past and was a wettable pressed cake applied with a wet brush. It contained powder fillers, waxes, resins, and a soap or nonionic. Liquid eyeliners include the following list of ingredients:

- Solvent: Water
- Gellant: Gums (magnesium aluminum silicate and bentonite)
- Wetting agents: Water-soluble esters, and high HLB emulsifiers
- Polyols: Propylene glycol, butylene glycol, and 2-methyl-1, 3 propanediol
- Colorants: Surface treatment is not essential but will enhance ease of dispersibility, maintain fluidity, improve adhesion and may also enhance water resistance. Chiefly, iron oxides and other inorganic are used

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- Alcohol: Can solubilize resins and improve dry time
- Film Formers: PVP, PVA, Acrylics, PVP/VA, PVP/Urethanes

Basic Formulations

Water	50–70%
Gellant	0.50–1.50%
Wetting Agent(s)	1–3%
Polyol	4–8%
Colorants	10–20%
Alcohol	5–10%
Film former	3–8%

Manufacturing Procedure

Gellant is premixed with the polyol and added to a heated water phase which also contains the wetting agent. Disperse with high shear until uniform. Add colorants and disperse until uniform. Cool and add alcohol and film former with low shear.

Pencils

Pencils are used in general for coloring the eyebrows and eyelids, although they are now popular as lipsticks, lip liner, and blushers, depending on the hardness of the pencil and the color composition.

Products are nearly always manufactured by a handful of contract manufacturers. The chemists' responsibility is to evaluate the finished product, rather than create one. Evaluation includes shade, texture, sharpenability, wear, application, stability (freeze-thaw and at 40–45°C), and penetration. Generally, extruded pencils are less stable than the molded ones.

Raw Materials

- Oils, esters, silicones
- High–melt point triglycerides
- Stearic acid–helps the extrusion
- Synthetic waxes
- Japan wax
- Bright colorants and pearls in leads increase the variety available in cosmetic pencils
- Fillers, Mica, talc, sericite
- Functional Fillers, boron nitride, Teflon, PMMA, Silicas

Product Types

Product types include eyeliner, lipliner, eyeshadow, lipstick, brow, blush, and concealer *Manufacturing Procedure*:

Molded and extruded; significant differences exist in how these products are evaluated initially after manufacturing. Molded pencils set up within a few days. Extruded pencil set up slowly over a few weeks. The molded or extruded lead is placed in a slat

of wood grooved lengthwise. A second grooved slat, is glued onto the first slat and pressed together.

LIPSTICKS

Lipsticks add color to the face for a healthier look, shape the lips, and sometimes condition. They Harmonize the face between the eyes, hair, and clothes. Created the illusion of smaller or larger lips depending on the color.

There are two types of lipsticks; classical and volatile based.

The Ingredients in a Classic Lipstick

- Emollients. Castor oil, esters, lanolin/lanolin oil, oily alcohols (octyl dodecanol), organically modified silicones (Phenyltrimethicone and alkyl dimethicones), Meadowfoam seed oil, jojoba oil and esters and triglycerides
- Waxes. Candelilla, carnauba, beeswax and derivatives, microcrystalline, ozokerite/ceresein, alkyl silicone, castor, polyethylene, lanolin, paraffin, Synthetic and Ester
- Wax Modifiers. Work in conjunction with the waxes to improve texture, application and stability include cetyl acetate and acetylated lanolin, oleyl alcohol, synthetic lanolin, acetylated lanolin alcohol, and petroleum (white and yellow)
- Colorants Widely Used.
  - D&Cs
    - Red #6 and Ba Lake
    - Red #7 and Ca Lake
    - Red #21 and Al Lake (stains)
    - Red #27 and Al Lake (stains)
    - Red #33 and Al Lake
    - Red #30
    - Red #36
    - Yellow #10
  - FD&Cs
    - Yellow #5,6 Al Lake
    - Blue #1 Al Lake
  - Iron Oxides
  - TiO_2
  - ZnO
  - Pearls
  - No Fe Blue, Ultramarines, Mn Violet
- Actives. Raw materials are added for claims and moisturization; tocopheryl acetate, sodium hyaluronate, aloe extract, ascorbyl palmitate, silanols, ceramides, panthenol, amino acids, and beta carotene
- Fillers (Matting and Texturizing Agents). Mica, silicas (classic and spherical), nylon, PMMA, teflon, boron nitride, BiOCl, starches, lauroyl lysine, composite powders, and acrylates copolymers

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- Antioxidants/Preservatives BHA, BHT, rosemary extract, citric acid, propyl paraben, methyl paraben, and tocopherol

Classic Lipstick

Formula	*Gloss*	*Matte*
Emollients	50–70%	40–55%
Waxes	10–15%	8–13%
Plasticizers	2–5%	2–4%
Colorants	0.5–3.0%	3.0–8.0%
Pearl	1–4%	3–6%
Actives	0–2%	0–2%
Fillers	1–3%	4–15%
Fragrance	0.05–0.10%	0.05–0.10%
Preservatives/Antioxidants	0.50%	0.50%

Procedure

1. Pigments are premilled in either one of the emollients (e.g., castor oil) or the complete emollent phase either by a 3-roller mill, stone mill, or a type of ball mill.
2. Grind phase is added to complete emollient phase and waxes, heated and mixed until uniform (approx. 90–105°C).
3. Pearls and fillers are added to above phases and mixed with shear (if necessary) until homogenous.
4. Add actives, preservatives, fragrance and antioxidants and mix until uniform.
5. Maintain a temperature just above the initial set point of the waxes and fill as appropriate.

Volatile Nontransfer Lipstick

The proper balance of solvents and emollients prevent transfer and prevent lipstick from becoming too dry on the lips [15].

- Solvents. Isododecane, alkyl silicones, cyclomethicone
- Emollients. Phenyl trimethicone, esters, alkyl silicones (fluids, pastes), vegetable/plant oils
- Waxes. Polyethylene, synthetic, ceresin, ozokerite, paraffin (not compatible with some silicones), beeswax, alkyl silicones
- Fixatives. Silicone resins (MQ type from G.E.), silicone Plus Polymers (SA 70-5, VS 70-5)
- Colorants/Pearls. Identical to classic lipstick
- Fillers. Identical to classic lipstick
- Actives. Identical to classic lipstick
- Preservatives/Antioxidants: Identical to classic lipstick

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Solvent Lipstick

Formula	
Solvent	25–60%
Emollient	1–30%
Waxes	10–25%
Fixatives	1–10%
Fillers	1–15%
Colorants/Pearls	1–15%
Fragrance	0.05–0.10%

Procedure. Identical to classic lipstick except product should be prepared in a closed vessel to prevent loss of volatile components.

NAIL COLOR

Nail lacquers form the largest group of manicure preparations. They should be waterproof, glossy, adherent, dry quickly, and be resistant to chipping and abrasion. The main constituents include a film former, modifying resin, plasticizer and solvents. Additionally, pigments, suspending agents, and UV absorbers are usually included. Nitrocellulose is the chief film-forming ingredient. Nitrocellulose is derived from cellulose, a polymer made of several anhydroglucose units connected by ether linkages. Nitrocellulose by itself will produce a hard brittle film so it is necessary to modify it with resins and plasticizers to provide flexibility and gloss. The most commonly used modifying resin is paratoluenesulfonamide formaldehyde resin, which is contained at 5 to 10% levels. This resin provides gloss, adhesion, and increases the hardness of the nitrocellulose film. The formaldehyde resin has caused allergies with a small number of consumers so that other modifiers such as sucrose benzoate, polyester resin, and toluene sulfonamide epoxy resin have been used in its place with varying results. Plasticizers used include camphor, glyceryl diesters [16], dibutyl phthalate, citrate esters and castor oil. Other resins such as polyurethanes and acrylics have been used as auxiliary resins. Variations of plasticizers and resins will change the viscosity, dry time, and gloss of the lacquer. Colorants include titanium dioxide, iron oxides, most organics, and pearlescent pigments. Soluble dyes are never used because of their staining effects on skin and nails. In order to reduce settling of the heavier pigments, treatments, such as silicone [17] and oxidized polyethylene [18] have been utilized. Modified clays derived from bentonite and/or hectorite are used to suspend the pigments and make the nail enamel thixotropic and brushable. Solvents, which constitute approximately 70% of nail lacquers, include n-butyl acetate, ethyl acetate, and toluene. Generally, those are cream and pearl nail lacquers. Cream shades may be shear or full coverage with titanium dioxide as the chief pigment. Pearlescent nail polish usually contains bismuth oxychloride and/or titanium dioxide–coated micas and may even contain guanine-natural fish scales. The manufacturing of nail lacquer is usually carried out by specialty manufacturing firms which are familiar with the hazards of working with nitrocellulose and solvents. The manufacture consists of two separate operations: (1) manufacture and compounding of the lacquer base, and (2) the coloring and color matching of shades. Top coats, which are used to enhance gloss, extend wear, and reduce dry time, are usually made with high solids and low boiling point solvents. Cellulose acetate butyrate (CAB) has been used as a substitute for nitrocellulose in nonyellowing top coats but does not

adhere as well to the nail [19]. Most top coats are nitrocellulose based. Base coats function to create a nail surface to which nail lacquer will have better adhesion. Different auxiliary resins, such as polyvinyl butyral, have been used in nitrocellulose systems. Fibers, polyamide resins, and other treatment items have been added in order to provide advertising claims, and some may actually alter the effectiveness of the film. In the evaluation of nail enamels the following criteria are used: color, application, wear, dry-time, gloss, and hardness.

FACE PRODUCTS: MAKEUP FORMULARY

Loose Face Powder [20]

Ingredients	W/W%
Zinc stearate	8.00
Magnesium carbonate	1.00
Iron oxides	q.s.
Bismuth oxychloride and mica	25.00
Fragrance	q.s.
Talc to 100.00	
Preservative	q.s.

Procedure

1. Mix ingredient #3 with a portion of ingredient #6; pulverize.
2. Add the other ingredients; mix in a ribbon or double-cone blender until uniform.

Pressed Powder Foundation [21]

Ingredients	W/W%
Part A:	
Talc	6.60
Titanium dioxide	19.20
Mica (and) titanium dioxide	4.80
Iron oxides	11.20
Zinc oxides	6.20
Barium sulfate	13.70
Part B:	
Dimethicone	5.50
Lanolin	8.20
Petrolatum	1.40
Mineral oil	1.40
Isopropyl myristate	1.40
Part C:	
Fragrance	q.s.
Preservative	q.s.

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Procedure

1. Mix all of the pigments in Part A together.
2. Add Part B, Part C, Part D with high shear mixing.
3. Press into suitable container.

Two-Way Powder Foundation (Wet and Dry)

Ingredients	W/W%
Sericite	35.0
Talc	24.0
Mica	10.0
Nylon-12	10.0
Titanium dioxide	8.0
Zinc stearate	3.0
Iron oxide pigments, silicone treated	2.0
Cetyl octanoate	q.s.
Squalane	2.0
Octyldodecyl myristate	2.0
Mineral oil	2.0
Dimethicone	2.0
Propyl paraben	0.05
Butyl paraben	0.05
Perfume	q.s.

Procedure

Mix all ingredients except liquid oils and perfume in a blender. Spray or add liquid oils and perfume. Mix and pulverize. Press into pans.

Pressed Face Powder

Ingredients	W/W%
Part A:	
Polymethyl methacrylate	12.00
Talc (and) polyethylene	q.s. to 100.0
Sericite	10.00
Mica (and) polyethylene	5.00
Magnesium stearate	3.00
Mica (and) titanium dioxide	5.00
Kaolin	8.00
Color	q.s.
Part B:	
Dimethicone	6.00
Glyceryl diisostearate	2.00
Tocopherol	0.10
Butyl paraben	0.05
Propyl paraben	0.05

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Procedure

Mix A well. Heat B to 80°C. Mix until uniform. Add B to A. Mix well until uniform. Pulverize and sieve. Press into pans.

Liquid Compact Foundation

A hot-pour solid cream foundation that seems to ''liquefy'' when touched. Easy to blend to a sheer finish.

Ingredients	W/W%
Part A:	
Titanium dioxide (and) isopropyl titanium triisostearate	12.99
Yellow iron oxide (and) isopropyl titanium triisostearate	0.33
Red iron oxide (and) isopropyl titanium triisostearate	0.33
Black iron oxide (and) isopropyl titanium triisostearate	0.10
Aluminum starch octenyl succinate (and) isopropyl titanium triisostearate	15.00
Sericite	6.25
Silica	2.00
Part B:	
Squalene	6.50
Dimethicone (5 centistoke)	11.00
Octyl palmitate	18.00
Polyglycerol-3 diisostearate	5.50
Mineral oil	3.00
Hydrogenated coco glycerines	2.00
Microcrystalline wax	4.00
Carnauba	1.00
Part C:	
Nylon-12	12.00
	100.00

Procedure

Micronize Part A until the color is fully developed. Heat Part B with stirring to 195 to 200°F. Continue to stir for ½ hour. Add Part A to Part B and mix until homogenous. Cool to 180°F. Add Part C and mix until homogenous. Pour into pans at 165–170°F.

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Blusher (Pressed) [22]

Ingredients	W/W%
Talc	65.70
Zinc stearate	8.00
Titanium dioxide	3.50
Iron oxides (russet)	12.00
Iron oxides (black)	0.20
D&C Red No. 6 barium lake	0.30
Titanium dioxide (and) mica	6.00
Methyl paraben	0.10
Imidazolidinyl urea	0.10
Fragrance	0.10
Pentaerythritol tetraisostearate	4.00
	100.00

Procedure

Mix ingredients 1 through 9 well. Pulverize. Place into ribbon blender. Spray into batch number 10 then into number 11. Repulverize. Sieve. Press into pans.

Eye Shadow (Pressed) [23]

Ingredients	W/W%
Mica (and) iron oxides (and) Titanium dioxide	40.5
Talc	32.4
Cyclomethicone (and) dimethicone	13.6
Oleyl Erucate	13.5
	100.00

Procedure

1. Mix and mill all ingredients through a 0.027″ herringbone screen.
2. Press into a suitable container.

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Eye Shadow (Pressed) [24]

Ingredients	W/W%
Talc	4.20
Bismuth oxychloride	10.00
Fumed silica	0.50
Zinc stearate	5.00
Titanium dioxide (and) mica	65.00
Methyl paraben	0.10
Propyl paraben	0.10
Imidazolidinyl urea	0.10
Lanolin alcohol	3.75
Mineral oil	9.75
Isostearyl neopentanoate	1.50
	100.00

Procedure

Mix 1 through 8 in a ribbon blender. Mix binders 9 through 11 in a separate container. Spray binders into 1 through 8. Mix until uniform. Pulverize, if necessary, without a screen. Press into pans.

Solvent Mascara [25]

Ingredients	W/W%
(A)	
Petroleum distillate	q.s. to 100.00
Beeswax	18.00
PEG-6 sorbitan beeswax	6.00
Ozokerite 170-D	4.00
Carnauba wax	6.00
Propylparaben	0.10
Glyceryl oleate (and) propylene glycol	1.50
(B)	
Iron oxides	15.00
(C)	
Petroleum distillate (and) quaternum-18 hectorite (and) propylene carbonate	12.50
(D)	
Deionized water	15.00
Methylparaben	0.30
Sodium borate	0.60
Quaternium-15	0.10

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Procedure

Mill pigment (B) into (A), which has been heated to 90°C. After (C) has been added slowly and heated with (A), emulsify by adding (D) at 90°C to (A), (B), and (C) mixtures. Continue mixing until cool.

Emulsion-Resistant Mascara [26]

Ingredients	W/W%
(A)	
Deionized water	41.00
Hydroxyethyl cellulose	1.00
Methylparaben	0.30
Aqueous 0.10% phenyl mercuric acetate	4.00
Triethanolamine	1.00
Ammonium hydroxide, 28%	0.50
(B)	
Iron oxides	10.00
Ulltramarine blue	2.00
(C)	
Isostearic acid	2.00
Stearic acid	2.00
Glyceryl monostearate	1.00
Beeswax	9.00
Carnauba wax	6.00
Propylparaben	0.10
(D)	
Quaternium-15	0.10
(E)	
30% Acrylic/acrylate copolymer solution in ammonium hydroxide	20.00
	100.00

Procedure

Mill the pigments of (B) in the water phase (B). Heat to 80°C. Heat the oil phase (C) to 82°C. Emulsify. Cool to 50°C. Add (D), then (E). Cool to 30°C.

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Waterproof Eyeliner [27]

Ingredients	W/W%
Beeswax	16.50
PVP/Eicosene copolymer	5.00
Petroleum distillate	35.00
Petroleum distillate (and) quaternium-18 hectorite (and) propylene carbonate	33.50
Preservative	0.20
Titanium dioxide (and) mica (and) ferric ferrocyanide	9.80
	100.00

Procedure

1. Heat ingredients 1 and 2 to 70°C and blend in (3) (n.b. flammable).
2. Blend in (4) with low shear mixing.
3. Cool to 50°C while continuing to mix.
4. Blend in ingredients (2), (5), and (6) and mix until uniform.

Aqueous Eyeliner [28]

Ingredients	W/W%
Part 1	
Ammonium vinyl acetate/actylates copolymer	55.00
Polysorbate 80	1.00
Isopropyl myristate	4.00
Part 2	
Propylene glycol USP	2.50
Methylparaben USP	0.25
Water, deionized	29.50
Hectorite (and) hydroxyethylcellulose	0.25
Iron oxides	7.50
	100.00

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Makeup Pencil [29]

Ingredients	W/W%
Part 1	
Cyclomethicone	40.0
Bis phenylhexamethicone	40.0
Diphenyl dimethicone	40.0
Part 2	
Beeswax	15.0
Carnauba	7.0
Ozokerite	7.0
Paraffin	20.0
Mineral oil	q.s. to 100.0
Cetyl alcohol	1.0
Part 3	
Pigments	q.s.
Titanium dioxide	q.s.

Procedure

1. The ingredients of Part 2 are melted and homogenized at 78–82°C, then maintained by a thermostatic bath regulated to 58–62°C.
2. The ingredients of Part 3 are dispersed in Part 1; the mixture is placed in a thermostatic bath at 58–62°C.
3. Part 3 is then added.
4. After homogenization, the whole is cooled in a silicone-treated mold (with dimethicone).

Classic Lipstick [30]

Ingredients	W/W%
Carnauba wax	2.50
Beeswax, white	20.00
Ozokerite	10.00
Lanolin, anhydrous	5.00
Cetyl alcohol	2.00
Liquid paraffin	3.00
Isopropyl myristate	3.00
Propylene glycolricinoleate	4.00
Pigments	10.00
Bromo acids	2.50
Castor oil	q.s. to 100.00

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Solvent Lipstick [31]

Ingredients	W/W%
Synthetic wax	6.00
Ceresin	4.00
Isododecane	10.00
Paraffin	3.00
Cetyl acetate/acetylated lanolin alcohol	5.00
Methylparaben	0.30
Propylparaben	0.10
BHA	0.10
D&C Red No. 7 calcium lake	4.00
FD&C Yellow No. 5 aluminum lake	3.00
Titanium dioxide/mica	5.00
Titanium dioxide/mica/iron oxides	3.00
Bismuth oxychloride	10.00
Cyclomethicone	41.50
Isostearyl trimetholpropane siloxy silicate	5.00
	100.00

Procedure

Mix the dry ingredients with the volatiles and silicone ester wax. The waxes and oils are added with heating. The powders are added next. The mixture is then stirred before pouring into molds and allowed to cool.

Cream Nail Enamel [32]

Ingredients	W/W%
n-Butylacetate—solvent	28.23
Toluene—diluent	24.54
Nitrocellulose ½ sec wet—film-former	12.00
Ethyl acetate—solvent	11.00
Toluene sulfonamide/formaldehyde resin—secondary resin	10.00
Acrylates copolymer—resin	0.50
Dibutyl phthalate—plasticizer	5.00
Isopropyl alcohol, 99%—diluent	4.25
Stearalkonium hectorite—suspending agent	1.00
Camphor—plasticizer	1.50
D&C Red No. 6 barium lake—color	0.08
Titanium dioxide	0.75
Iron oxides	0.15
	100.00

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Pearlescent Nail Enamel [33]

Ingredients	W/W%
n-Butyl acetate	34.04
Toluene	30.00
Nitrocellulose ½ sec. wet	14.90
Toluene sulfonamide/formaldehyde resin	7.10
Dibutyl phthalate	4.80
Camphor	2.40
Stearalkonium hectorite	1.20
Benzophenone-1	0.20
D&C Red No. 7 calcium lake	0.08
D&C Red No. 34 calcium lake	0.05
FD&C Yellow No. 5 aluminum lake	0.08
Iron oxides	0.15
Bismuth oxychloride (25%)	5.00
	100.00

Acrylic Nail Hardener [34]

Ingredients	W/W%
Ethyl acetate	41.20
Butyl acetate	30.00
Nitocellulose ½ sec. wet	14.00
Toluene sulfonamide/formaldehyde resin	10.00
Dibutyl phthalate	4.00
Camphor	0.50
Acrylates copolymer	0.20
Benzophenone-1	0.10
	100.00

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Cosmetics for Nails

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The purpose of this chapter is to present the cosmetics used for the decoration of the nail, of which the nail coating is of prime importance. Fingernail coatings consist of two types [1–3]:

1. Coatings that harden upon evaporation: these products include nail polishes, topcoats and base coats.
2. Coatings that polymerize: nail enhancements are a special type of coating used to create artificial fingernails.

EVAPORATION COATINGS

Base coat, top coat, and nail enamel have similar basic formulas.

They consist of the following:

1. *A film former such as nitrocellulose*. This organic polymer creates a continuous coating over the nail plate. Other nonnitrated cellulosic materials are also used with varying degrees of success, namely cellulose acetate and derivatives. Polyurethanes, polyamides, and polyesters have also been used. However, these cannot match the toughness and surface hardness of nitrocellulose. One of the most commonly used, nitrocellulose has several disadvantages: the surfaces produced by this polymer have low gloss and the films are brittle and adhere poorly to the nail plate. Upon evaporation, nitrocellulose films shrink excessively, which leads to poor adhesion. To overcome these drawbacks, additional film modifiers will offset some deficiencies of the primary film form.

2. *Film modifiers*. They are specifically used to improve adhesion and gloss. The most commonly used modifier is toluene sulfonamide/formaldehyde resin (TSFR), which is considered to be the heart of the product. This thermoplastic resin improves nail-plate adhesion while producing water-resistant, glossy surfaces with improved flexibility. Unfortunately, this resin is the main culprit of users' sensitization. Use of this resin imparts between 0.05 to 0.1% free formaldehyde (as impurity) into the formulation. Therefore, many alternate modifiers have been tried, including toluene/sulfonamide/expoxy resin,

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polyester sucrose benzoate, polyesters, acrylic ester oligomers, SAIB, arylsulfonyl methanes, and glyceryl tribenzoate.

3. *Plasticizers*. Plasticizers are chemical flexibilizers for polymer films that improve their durability. They may also improve adhesion and gloss. Dibutyl phthalate and camphor are the most common examples of low–molecular weight, high–boiling point plasticizers. Other examples of plasticizers are castor oil, glyceryl tribenzoate, acetyl tribenzoate citrate PPG-2 dibenzoate, glycerol, citrate esters, triacetin, and a polyether urethane.

4. *Solvents/diluents*. The solid film-forming polymers, upon evaporation, are deposited on the nail plate. The most commonly used solvents are alkyl esters and glycol ethers. Coupling agents (aliphatic alcohols) are useful in varnishes to increase the overall solubility and flow of the system. Diluents are usually nonpolar compounds that will not dissolve nitrocellulose. Toluene was commonly used until the appearance of California Proposition 65. Most companies are now developing toluene-free formulas.

5. *Viscosity modifiers or thixotropic agents*. Ideally, a nail enamel should be gel-like when sitting on the shelf but significantly thin when brushed on. Both consistencies are possible in one bottle by using thixotropic agents such as stearalkonium hectorite.

6. *Color additives*. Colorants should be nonsoluble pigments to prevent staining of the nail plate. Guanine, derived from scales of Atlantic herring, produces pearlescent pigment. Bismuth oxychloride and mica coated with titanium dioxide are used to create iridescent shades.

7. *Base and top coats*. Base coats contain a high percentage of TSFR. They are applied to the nail before application of nail varnish. They are adhesion promoters that improve retention and coating toughness. Top coats use higher levels of film formers, such as nitrocellulose, to maximize surface gloss and hardness. Often the top coat contains UV-absorbing materials.

POLYMERIZING COATINGS

Sculptured Artificial Nails

Liquid-and-powder systems are based on methacrylates. They consist of a liquid monomer (ethyl methacrylate) mixed with a polymer powder (polyethyl and/or polymethyl methacrylate), the latter carrying only the heat-sensitive initiator (usually benzoyl peroxide) to the monomer. UV absorbers are polymer additives that prevent sunlight yellowing. Catalysts speed up polymerization.

Light-Curing Gels

UV or visible light-curing gels are made primarily of urethane acrylate and other acrylated oligomers. Associated with initiator, the catalyst and oligomers are combined into a single product; they come premixed and ready to use. They may be considered a variant of sculptured artificial nails.

Preformed Artificial Nails

These are usually made of ABS plastic, nylon, or acetate, and are adhered to the natural nail with cyanoacrylate monomer. Home-use, retail versions of these tips may be used as temporary natural overlays, not worn for longer than 48 hours on any one occasion. They are more often used as permanent nail-tip extensions. Professional nail technicians usually

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coat these tips with artificial nail products to create longer lasting nail extensions. Most nail technicians feel it is too time consuming to sculpt nails, and these tips speed the process. The tip can be coated or overlaid with wraps or liquid-and-powder or gel products.

Wraps

Wraps can be used to coat the nail plate or add strength to thin, weak nails. The monomers used to create wraps are cyanoacrylates. In nail wrapping, the free edge of the nail should be long enough to be splinted by the various types of fabrics providing support and added strength to the coating. There are three fabrics in wide use: fiberglass, silk, and linen.

No-Light Gels

These products are wrap monomers that have been thickened to have a gel-like appearance. They should be used and handled as any other wrap product.

Removal of Fingernail Coatings

The most commonly used solvent for removal of nail products is acetone. Warming the solvent with great care can cut product removal time in half. However most gels are difficult to remove because they are highly cross-linked and resistant to many solvents. Therefore, if gel enhancements have to be removed, slowly file (do not drill) the enhancement with a medium-grit file, leaving a very thin layer of product. Soak in warm product remover and, once softened, scrape the remaining product away with a wooden pusher stick [1].

Cuticle Removers

These are lotions or gels containing approximately 0.4% sodium or potassium hydroxide. The lotion is left in place for 1 to 3 minutes and then washed off. Creams containing 1 to 5% lactic acid (pH 3–3.7) are also used.

Nail Whitener

This is a pencil-like device with a white clay (kaolin) core used to deposit color on the undersurface of the free edge of the nail.

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Antiperspirants

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GENERAL INTRODUCTION

This chapter presents an overview concerning the current knowledge of antiperspirant actives and their interactions with the human axilla. It is my intention to give the interested reader a short introduction about formulation work, drug delivery systems, and application forms developed for antiperspirant actives. The final section lists references that should be useful for anyone who wants to learn more about a specific topic of antiperspirant technology.

BIOLOGY OF SWEAT GLANDS IN THE HUMAN AXILLA

The axilla region of humans contains apocrine, eccrine, and sebaceous glands. Approximately 25,000 sweat glands/axilla can produce up to 12 g sweat/h [1]. The current understanding concerning structure and function of sweat glands is that thermoregulation is only one aspect of the body participating in immmunological, metabolic, and hormonal aspects of human life [2].

Eccrine Glands

This is the organ responsible for the majority of sweat production. It has a sensory and excretory function and can be stimulated by emotional and thermal stimuli [3]. It produces a clear, colorless and odorless liquid containing 98 to 99% water and 1 to 2% inorganic and organic compounds [4]. Inorganic components include NaCl, traces of K^+, Ca^{2+}, Mg^{2+}, Fe^{3+}, and Cu^{2+} ions. Organic components include: lactic acid, citric acid, formic acid, propionic acid, butyric acid, urea, and ammonia. Underarm wetness comes mostly from the secretion of eccrine glands. Antiperspirants reduce the amount of sweat only from eccrine glands.

Apocrine Glands

Apocrine glands are apparently a relict from the phylogenetic development of man. These glands start to produce a milky, viscous fluid during puberty on special locations of the body, especially the underarm pit [5]. In contrast to eccrine glands, the openings of the

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glands are not at the skin surface but appear at the hair follicle. Decomposition of apocrine sweat by skin bacteria are responsible for the characteristic malodor of human sweat. Apocrine sweat consists among water of proteins, carbohydrates and ammonium salts [6]. Other investigators have reported that these glands secrete lipids, cholesterol, and steroids [7]. Furthermore, it has been shown that androgen-converting enzymes in the apocrine glands are responsible for circulating androgens to dihydrotestosterone [5].

ANTIPERSPIRANTS

Antiperspirants are topically applied products designed to reduce underarm wetness by limiting eccrine sweat production. In the United States these products are regulated by the FDA as over-the-counter (OTC) drugs because they are intended to affect a ''function of the body'' (in this case, perspiration). Products containing antiperspirant actives have to reduce perspiration to minimum 20% by 50% of the test population under validated test conditions. Test protocols (in vivo clinical trials) to develop a safe and effective product have been designed to substantiate the desired claims [8–14].

Comparative quantitative determination of the activity of sweat glands on the forearm after application of aluminum chlorohydrate solutions is now possible by combining the classic starch iodine visualization technique with digital image analysis [15]. A noninvasive optical technique that allows the analysis of the function of a number of glands simultaneously in vivo was recently reported [16]. A new method for parallel testing of up to eight formulations on the backs of volunteers allows a very fast evaluation of product prototypes [1].

Sweat Reduction by Antiperspirants: Current Model/Theory

The reader should be aware that theories concerning the action of sweat-reducing agents depend strongly on the type of actives (aluminum salts, nonionics, ionic agents). The efficacy of antiperspirants based on aluminum and/or aluminum zirconium salts (see discussion p. 691) can be understood by the formation of an occlusive plug of metal hydroxide in the eccrine duct [17]. Tape-stripping experiments followed by analysis of transmission electron micrographs of an ACH-treated eccrine sweat-gland duct (see discussion p. 691) shows an obstructive amorphous material supporting the theory of a mechanical blockage of sweat glands from diffusion of the soluble ACH solution into the sweat gland and subsequent neutralization to a polymeric aluminum hydroxide gel [18,19]. There seems to be no correlation concerning efficacy of aluminum salts and the location of the plug in the duct because it is known that, compared with ACH, the more effective Al-Zr compounds do not penetrate as deep as the also highly effective $AlCl_3$ solutions [17]. The reader is referred to the literature concerning other theories of sweat reduction by aluminum salts [20].

Active Ingredients for Controlling Underarm Wetness—State of the Art

Buffered Aluminum Salts (ACH)

The first antiperspirant, Ever Dry, based on $AlCl_3$, was introduced to the market in 1903 [21]. The first cream-containing aluminumsulfate was introduced during the 1930s. The acidic pH value (2.5–3.0) was a drawback of these products, leading to skin irritation in the underarm pit. History tells us that the development of actives with a higher pH value,

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so-called buffered aluminumchlorides (aluminum chlorohydrate, ACH, pH = 4.0–4.2) was an appropriate step with the additional benefit of reduced destruction of fabric clothes. The formula of this buffering salt is $\{Al_2(OH)_5\}^+ + \{Cl^-\}$, or more conveniently $Al_2(OH)_5Cl$.

The historical development from $AlCl_3$ to $Al_2(OH)_5Cl$ can be easily understood by the following consideration:

$$AlCl_3 = \tfrac{1}{2}\, Al_2Cl_6 \qquad \text{Substitute 5 } Cl^- - \text{ ions against } OH^- - \text{ ions}$$
$$\Rightarrow Al_2(OH)_5Cl$$

$Al_2(OH)_5Cl$ is a 5/6 basic aluminumtrichloride. The accepted definition of ACH is the ratio of Al to Cl = 2.1 to 1.0. Lower levels lead to aluminum dichlorohydrate ($Al_2(OH)_4Cl_2$) or to aluminum sesquichlorohydrate ($Al_2(OH)_{4.5}Cl_{1.5}$—both actives are also generally regarded as safe (GRAS). ACH is supplied as a powder or a 50% solution in water. It can be formulated up to 25% calculated on an anhydrous basis. The 20% aqueous solution reduces perspiration by 35 to 40% on average [22]. Some dyes used in clothing may be acid sensitive and will change color when in contact with an antiperspirant.

The structure of the Lewis acid ACH is very complex because ACH in water forms so-called isopolyoxo-cations with chloride ions as couterions [23–25]. There exists several polymer equilibria of the polycationic aluminum species in water-based systems. Short-chain polycationic species are more effective in reduction of sweat.

Aluminum Zirconium Chlorohydrate-Glycine Complexes (AZG or ZAG)

Aluminum zirconium chlorohydrate is obtained by reaction of ACH with zirconylchloride. Reaction of the former ingredients in the presence of glycine leads ZAG complexes. Glycine is used as a buffering agent. These antiperspirant actives form very complex polymeric structures in water. The actives are defined by the ratio of Al + Zr metal–to–chloride ratio and the Al to Zr atomic ratio. The interested reader is referred to the literature concerning available actives [26,27] and nomenclature of the Al-Zr complexes [21,22]. These antiperspirant actives were developed especially for anhydrous formulations because they show, compared with ACH, enhanced sweat reduction [28–30]. The maximal concentration of ZAG calculated on an anhydrous basis is 20%. They are not allowed to be formulated for use in aerosols.

New Concepts for Controlling Underarm Wetness

Titanium Metal Chelates

The understanding of the complex solution chemistry of aluminum-based antiperspirants gave input to the search for alternative antiperspirant salts. Titanium derivatives like partially neutralized ammonium titanium lactate (ATL) salts were shown to be effective in in-vitro efficacy tests [31]. The titanium metal chelates can be synthesized from the corresponding titanium alkoxides and organic acids followed by neutralization with ammonia. Under acidic to neutral pH conditions the ATL active seems to be relatively stable to hydrolysis and therefore probably a suitable antiperspirant active in water-based or anhydrous drug delivery systems.

Film-Forming Antiperspirant Polymers

So-called polybarrier technology is another approach to reduce perspiration by using a polymer that forms an insoluble occlusive film barrier on the underarm skin [32]. It was

mentioned that the occlusive film is a barrier to the passage of moisture. The main advantage of this technology has been described as reduced skin irritation, applicable after underarm shaving, and higher sweat reduction compared with today's classic antiperspirant salts. The preferred polymer is an olefinic acid amide/olefinic acid or ester copolymer–like octylacrylamide/acrylate copolymer (Versacryl™-40). This copolymer can be used alone or in combination with PVP/eicosene-copolymer in sticks, roll-ons, or alcohol-based products [33]. The reduction of sweat depends on the choice of vehicle and exceeds in some formulations 40%.

Lyotropic Liquid Crystals

Certain surfactant/cosurfactant combinations in water form depending on the variables of concentration/temperature instead of micelles lamellar, hexagonal, inverted hexagonal, inverted micellar, or even cubic phases. The cubic phases can be of micellar or bicontinous type [34]. The water domains in lamellar or cubic phases can swell to a certain degree while taking up water. The use of this swelling behavior is the basis of a patent where a surfactant/cosurfactant combination is applied to the underarm pit [35]. Sweat (water) transfers the applied composition to a lyotropic liquid crystal of cubic structure, thus creating a sweat-absorbing system in the axilla. Oleic acid/glycerol monolaurate is one of the surfactant combinations in the patent. Both components are also well known as deodorizers.

DRUG-DELIVERY SYSTEMS AND APPLICATION FORMS FOR ANTIPERSPIRANT ACTIVES

Antiperspirant actives can be formulated in a variety of delivery systems like anhydrous suspensions, water- or hydroalcoholic-based solutions, and emulsions. Typical application forms for antiperspirants are sticks, roll-ons, creams, pump sprays, aerosols, gels, and powders. A new technology for pump sprays is discussed in the chapter 57. On a global basis, the three most important product forms are sticks, roll-ons, and aerosols.

Formulation Work

After the decision for the desired application form has been made the formulator has to decide on the vehicle system for the antiperspirant active. It is the intent of this section to summarize some of the current knowledge concerning influence of actives with the formula, efficacy of different delivery systems, and the function of the ingredients used in antiperspirants.

Antiperspirant actives like ACH or ZAG complexes are soluble in water. Application of a concentrated aqueous solution of an antiperspirant active gives a rather tacky feeling [36]. Reduction of tackiness can be best achieved by silicone oils (cyclomethicones) or ester oils like Di-(2 ethylhexyl) adipate [27]. The acidic pH value (pH 4.0–4.2) has to be taken into account by selecting additional components for the desired drug delivery system. Loss of viscosity and problems of a final formula with color stability are often a hint to change the gellant and/or perfume. Aluminum powders in anhydrous systems (aerosols, suspension sticks) often leave visible white residues on skin or clothing. Liquid emollients, like PPG-14 butylether or the aforementioned adipate ester, minimize these residues. Another approach is to use the solid emollient isosorbide monolaurate (ICI, Arlamol ISML) [37]. In anhydrous aerosol formulations the ACH powder settles down and

forms a hard to redisperse cake at the bottom of the aerosol can. Suspending aids like Quaternium-18 Hectorite or Quaternium-18 Bentonite prevents settling of the active and additionly thickens the cyclomethicone oil phase. Usage of fine powders of ACH is another approach to overcome natures law of gravity.

The reader should be aware that hydrophobic ingredients like emollients have an influence on the effectiveness of an antiperspirant active because a cosmetic oil phase or wax can cover the pores of the eccrine duct. The efficacy of an antiperspirant active like ACH is higher in water-containing systems compared with anhydrous formulations. The following rules concerning efficacy might be helpful:

1. Efficacy: Aqueous solution > Anhydrous suspension
2. Since diffusion of an active in the vehicle and from the vehicle to the skin after application has to considered one can further differentiate the expected efficacy trends.
   Efficacy: Aqueous solution > Sprayable O/W emulsion > O/W-emulsion roll-on > O/W-emulsion cream
3. It is accepted that antiperspirant actives in the outer phase of an emulsion have a higher efficacy than in dispersed phase.
   Efficacy: O/W-emulsion > W/O-emulsion
4. In water-free systems the viscosity of the drug delivery system might be of relevance. Suspended ACH in anhydrous vehicles needs to be solubilized after application to the axilla by sweat (water). The effectiveness of suspension sticks depends on the rapidity of active solubilization. The usage of ultrafine powders of ACH is expected to boost efficacy compared with fine powders.
   Efficacy: low viscous suspension > suspension stick

The interested reader is referred to the literature concerning vehicle effects on antiperspirant activity [7,38,39].

Not only lipophilic ingredients might have an influence on the efficacy of a product because it is known that the water-soluble propylene glycol can form complexes or hydrogen bonds with aluminum polycationic species thereby altering the efficacy of the salt [40]. Additionally propylene glycol in high concentrations may result in skin irritations [41]. Successful formulation work aims at finding the right viscosity for the product in the desired application form, a lower viscosity during flow into the underarm pit and a higher viscosity after application so that the product stays where it was applied. Conventional shear shinning flow curves are characteristic for antiperspirant products. The reader is referred to the literature concerning rheology aspects of cosmetic products [42].

Deodorant/Antiperspirant Sticks

It is at present not easy to give the reader an overview about sticks because nowadays there exists many technologies to develop this solid delivery system. In Figure 1 an attempt was made to summarize this area. In the following section only systems of major importance are discussed.

Sticks can be divided into different classes like suspension sticks, gel sticks, and emulsion sticks. Soft sticks have some properties of all three categories (Fig. 1).

Suspension Sticks

Dry deodorants, or antiperspirant solids, are synonyms for an application form where the active in the form of a powder is suspended in a silicone oil phase. Stearyl alcohol is

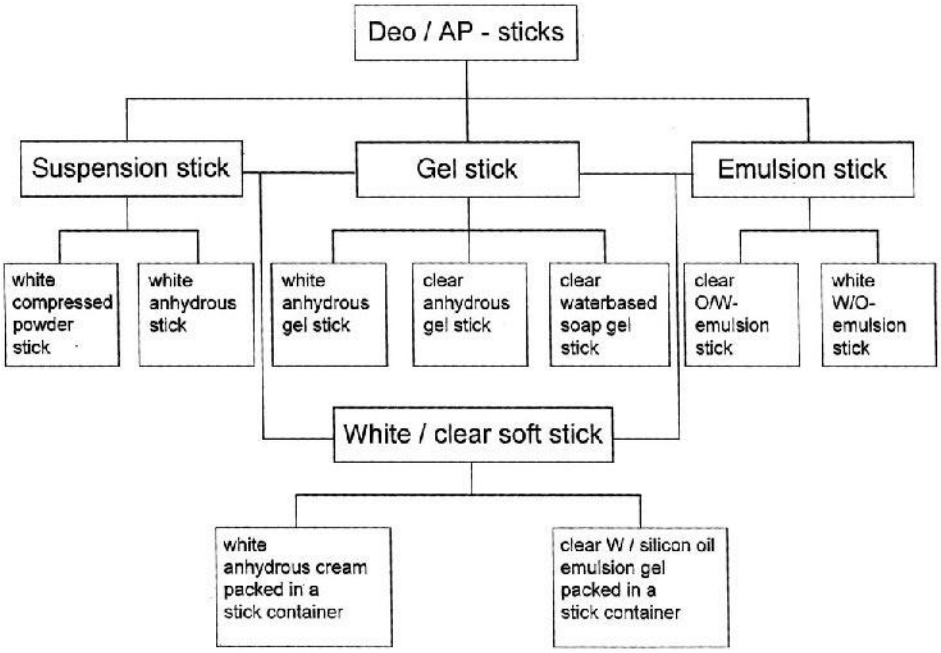

FIGURE 1 Overview of cosmetic Deo/AP-sticks.

usually used as the hardening agent. The molten mass crystallizes into a matrix of stearyl alcohol saturated with the silicone oil and suspended particles [43,44]. Settling of the actives can be reduced by Quaternium-18 Hectorite. Cyclomethicones give the stick a dry, silky feel, and nonvolatile oils like PPG-14 butylether minimize white residues on skin [43]. Low-residue sticks can be obtained by using a combination of high-melting and low-melting waxes and a volatile and nonvolatile silicone-oil combination [45].

Suspension stick	Wt%
Stearyl alcohol	20.0
Cyclomethicone	54.0
PPG-14 butylether	2.0
Hydrog. castor oil	1.0
Talc	2.0
Antiperspirant	20.0
Fragrance	1.0

Gel Sticks

This classes can be subdevided into the groups white anhydrous gel sticks, clear anhydrous gel sticks, clear water-based soapgel sticks. The last mentioned is discussed in the deodorant chapter.

White Anhydrous Gel Sticks.

Shear solids or ultra-clear solids are synonyms for sticks with improved wash-out performance compared with the classic suspension sticks. They contain N-acyl aminoacid amides (N-lauroyl-L-glutamic acid dibutylamide) and 12-hydroxyacid as gelling agents for an oil-phase mixture (e.g., silicone oil/mineral oil). The wash-out agent is an ethoxylated solubilizer like Ceteareth-20. These white sticks turn clear after application to the skin (no-residue stick) [46].

Clear Anhydrous Gel Sticks.

They are quite popular in the United States because clarity is associated by the consumer with a lack of white residue on skin, no dangerous ingredients, and high efficacy. A typical gelling agent is dibenzylidene sorbitol (dibenzyaldehyd monosorbitol acetal, DBMSA). This acetale is not stable in an acidic aqueous environment [47]. The sticks usually contain a high level of alcohol and/or polyols. At high polyol concentration the active is regarded to be solubilized instead of suspended in the gel matrix [48]. An alternative gelling agent is a polyamide [49].

White anhydrous gel sticks	Wt%	Clear anhydrous gel sticks	Wt%
N-Lauroyl-glutamic acid dibutyl amide	5.0	Dibenzylidene sorbitol	2.0
12-Hydroxystearic acid	5.0	Dimethicone copolyol	2.0
Cyclomethicone	40.0	Diisopropyl sebacate	2.0
Hydrog. polyisobutene	15.0	Glycine	1.0
Diisopropyl myristate	15.0	Dipropyleneglycol	10.0
Antiperspirant powder	20.0	Propyleneglycol	33.0
		Antiperspirant powder	50.0

Source: Ref. 58.

Emulsion Sticks:

They can be grouped into clear o/w emulsions, white w/o emulsions, and clear w/s: emulsion gels. The last mentioned is will be discussed shortly.

Clear O/W Emulsions.

They contain a high surfactant combination with the active solubilized in the external water phase. The high concentration of surfactants is a disadvantage; no products based on this technology are known to the author [47].

W/O-Emulsion Sticks.

The water phase containing the active is solubilized by a surfactant like Polyglycerol-4 Isostearate. A typical example for an oil/wax-phase combination is a mixture of silicone oil/stearylalkohol [50].

W/O Emulsion Stick	Wt%
Stearyl alcohol	19.0
Volatile silicone	26.0
Mineral oil	1.0
2-Methyl-2,4 pentandiol	2.0
Polyglyceryl-4 isost.	2.0
ACH solution (50%)	50.0

Source: Ref. 50.

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Soft Sticks (Soft Solids, Smooth-Ons)

These sticks can be differentiated into two subgroups: white, anhydrous creams (suspensions) and clear water-in-silicone emulsion gels. Both delivery systems are packed in a container that gives the impression of a stick. The suspension or gel is extruded onto the skin from holes in the top of the stick container to a wide smooth area around the holes.

White, Anhydrous Creams. These creams contain an antiperspirant active, a volatile and nonvolatile silicone oil and a thickener (N-acyl glutamic acid amide).

Clear Water-in-Silicone Emulsion Gels. These formulations can be achieved by adjusting the refractive index of the water and silicone-oil phase. Silicone formulation aids (Dow Corning 3225 C) are mixtures of cyclomethicone and dimethicone copolyol helping to solubilize the active [7,46,48,51]. Low surface tension of cyclomethicones facilitates good spreading of a product on the skin and reduces the tackiness of antiperspirant actives.

Antiperspirant Roll-Ons

Roll-on products can be differentiated into several categories (see Fig. 2). O/W emulsion–based delivery systems are quite popular in Europe, whereas anhydrous suspension roll-ons or transparent water-in-silicone emulsions are preferred in the United States. A new trend concerning the size of the roll-on applicator has been identified. Consumers prefer the big-ball format (3.0–3.5 cm) because of the ease of applying the product to the underarm pit [52]. The popularity of roll-ons in general is due to the nongreasy and nonoily feel in the axilla and the good spreadability of the content on the underarm skin.

Clear Hydroalcoholic Roll-On

This delivery system contains a water/alcohol solution of the antiperspirant active thickened with a water-soluble polymer like hydroxyethylcellulose. The alcohol in the formula gives, compared with the clear aqueous solution–based roll-ons, a fresh sensation in the

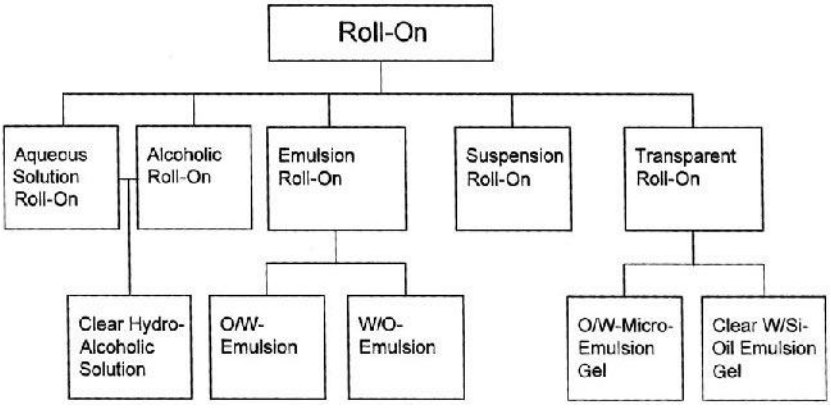

FIGURE 2 Overview of cosmetic Deo/AP-roll-on types.

axilla and faciliates drying of the product. Excellent antiperspirant efficacy is another benefit of hydroalcoholic roll-ons.

O/W Emulsion Roll-On

This delivery system uses ethoxylated surfactants like PEG-40 stearate to solubilize an oil phase like mineral oil. The active is dissolved in the outer phase, allowing the formulation of a highly effective product. In alcohol-free formulated systems microbiological stability has to be checked.

O/W emulsion roll-on	Wt%	Hydroalcoholic roll-on	Wt%
PEG-40 stearate	5.0	Antiperspirant active	20.0
Cetyl alcohol	3.0	PPG-5 ceteth 20	2.0
Mineral oil	2.0	Water	35.4
Polysorbate-80	1.0	Ethanol	42.1
Glycerin	1.5	Hydroxyethylcellulose	.5
Mg-aluminum silicate	.8		
Antiperspirant active	20.0		
Water	66.7		

W/O Emulsion Roll-On

They are weaker in efficacy because the actives are encapsulated and the external oil phase often gives a sticky feeling.

W/Si Emulsion Roll-On

Silicone oils allow to formulate products based on a ''W/O-technology'' because the skin feeling is not comparable to traditional oily components like ester oils or triglycerides. The concentration of the thickener is reduced compared with sticks based on this type. The technology is discussed under soft sticks (see p. 696).

O/W Microemulsion Gel

An alternative approach to transparent products uses the PIT technology. A suitable mixture of surfactants, oils, and water is heated to 60 to 90°C to give a w/o emulsion above the phase inversion temperature (PIT). During cooling the mixture shows phase inversion to give white or transparent o/w emulsions. o/w Microemulsion gels are obtained in the presence of hydrophobically modified water-soluble polymers [53]. The technology is explained in more detail in the deodorant chapter.

Suspension Roll-On

The antiperspirant active in powder form is suspended in cylomethicone. The roll-on can be formulated with or without ethanol. Quaternium-18 Hectorite is used as a thickener to prevent settling of the active. Consumers in the United States prefer this delivery system since it does not give a wet feeling after application and because of the easy drying [39]. Actives like ZAG-complexes give high efficacy underarm products.

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Suspension roll-on	Wt%
Volatile silicone	65.0
Quaternium-18 hectorite	13.5
Silica	.5
Antiperspirant powder	20.0
Fragrance	1.0

Antiperspirant Aerosols

Aerosols in Europe and Asia are popular delivery systems for consumers who prefer a hygienic and easy-to-use application form. Typical ingredients for aerosols include isopropylmyristate, isopropylpalmitate, volatile silicone, dimethicone, silica, clays, propylene carbonate, and ethanol. Propellants include propane, butane, and isobutane.

Antiperspirant aerosol	Wt%
Volatile silicone	13.4
Quaternium-18 hectorite	.8
Ethanol	.8
Antiperspirant powder	10.0
Propellant (butane/propane)	75.0

Because acidic aqueous ACH solutions lead to corrosion of the aerosol can, current aerosol antiperspirant products are formulated as water-free suspensions. The active is suspended as a powder in an oil phase like cyclomethicone or in a mixture of ester oils/cyclomethicone. Agglomeration of solid particles and settling of actives can be minimized by usage of suspending agents like fumed silica (amorphous silicon dioxide) or clays (bentonite, hectorite). The clays form a weak gel in the presence of an oil phase that can be destroyed by shaking the aerosol can before usage. The gel structure is reformed on standing, thereby holding the active in suspension. Because the organoclays are agglomerated, shear is needed to deagglomerate the platelets, and a polar activator like propylene carbonate or ethanol is used to disperse them and induce the gelation of the oil phase.

The steps involved to prepare an aerosol product can be summarized in the following sequence [7]:

1. Preparing a bentonite or hectorite clay with the emollient in the presence of the polar activator and shearing the mixture
2. Adding the antiperspirant active until a uniform agglomeration-free suspension is obtained
3. Filling the concentrate into the aerosol can and adding the propellant (pressure filling)

Efficacy studies of aerosols including comparison with other drug delivery systems have been reported in the literature [30]. ZAG-complexes (see discussion p. 691) are not allowed to be used in aerosols.

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Environmental Issues

Aerosols contain volatile organic compounds (VOCs) usually in a weight ratio propellant/concentrate of 75/25 [54]. The environmental impact of VOC like the reaction with NO_x in the presence of sunlight causes formation of unwanted ozone in the lower atmosphere. U.S. antiperspirant companies especially were forced to reduce VOC emissions by reformulating and/or exchanging of hydrocarbon propellants to the fluorohydrocarbons 1,1 difluorethane (Propellant 152 a) or 1,1,2,2 tetrafluorethane (Propellant 134 a). The water-soluble dimethoxyethane (DME) is another propellant that is thought to have no impact on the damage of the ozone layer [55].

The current trends in the aerosol market can be summarized as follows:

- Higher ratio of concentrate/hydrocarbon propellant
- Higher amount of silicone oils
- Usage of 1,1 difluorethane (Propellant 152 a)
- Formulations with lower vapor pressure
- Usage of smaller aerosol cans

Aerosols containing 20 to 50% propellants with a concentrate/propellant ratio from 1.0 to 1.0 to 2.3 to 1.0 have been patented [56].

FUTURE TRENDS

Some new trends in the antiperspirant field concerning new actives and delivery systems have been described in this chapter. Improvements of current formulations and innovative concepts will need the ongoing investigation and better understanding of the interaction active/vehicle and vehicle/skin. Improving efficacy and skin compatibility is another major trend in the antiperspirant field. New packaging concepts like the extrudable gels, the big ball applicator for roll-ons, and reduced size aerosol cans with ozone-friendly propellants are probably in a few years state of the art. The influence of perfume components to the skin, the increasing rate of contact allergies attributable to fragrance ingredients have to be closely monitored [57].

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57

Deodorants

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INTRODUCTION

It is the intention of this chapter to give an overview on the current knowledge about the origin of underarm odor, the biology of the underarm microflora and its interaction with deodorizing agents. The contents of this chapter have been arranged in particular sequence to facilitate the understanding of rational deodorant product development.

BIOLOGY OF THE UNDERARM MICROFLORA

The resident microflora of the human underarm skin consists of up to $10^6/cm^2$ organisms, eg. aerobic cocci, lipophilic diphteroids and varying species of gram-negative bacteria [1]. In the axillae two types of bacterial flora exists—coryneform bacteria and micrococcaceae like *Staphylococus epidermidis*. Coryneform- or *St. epidermidis*-dominated populations are characteristic for human beings. The resident microflora is a quite stable population not varying a lot between both axillaes [2]. The organisms are perfectly adapted to their ecological niche with its higher pH value and higher moisture content compared to other skin areas [3]. Hair in the axilla is according to the literature not a good substrate for bacterial growth, the bacteria prefer to reside on the underarm skin [2]. Moisture is required for bacterial proliferation and is secreted especially from the eccrine sweat glands [4]. The origin of strong compared to low underarm odor is associated with a numerical dominance of Coryneform bacteria [5]. Components of apocrine secretion like e.g. isovaleric acid and androstenone, were proposed to contribute to axillary odor. Hydrolytic exoenzymes of skin bacteria cleave the ester bonds of odorless water soluble precursors of androstenol to the corresponding volatile steroid [6]. Other studies proposed that the key odorants are branched, straight-chain and unsaturated C_6-C_{11} fatty acids [7]. (E)-3-methyl-2-hexenoic acid (E-3M2H) is the most abundant fatty acid compared to the rest of C_6-C_{11} fatty acids that contribute to the axillary odor bouquet. Apocrine sweat extracts have been analyzed and concentrations of 0.5 ng/µl for androstenone and 357 ng/µL for E-3M2H were detected [8]. Volatile odor molecules of E-3M2H found in sweat secretions are transported according to the authors in a nonvolatile fashion to the skin surface. Two apocrine secretion odor binding proteins ($ASOB_1$ and $ASOB_2$) were identified, carrying

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3M2H-molecules to the skin surface. Coryneform bacteria liberate the odor molecules from the protein precursor/odorant-complex [8].

The reader should be aware that occurrence of these chemical compounds does not mean that all of us can smell them. Individual differences in odor perception for both isomers of 3M2H [9] and for the steroid androstenone are well known [8]. Approximately 50% of the adult population are not able to smell androstenones, this anosmia to androstenone—or to 3-methyl-2-hexenoic acid—is genetically determined.

DEODORANTS

Deodorants are topically applied products designed to reduce underarm odor. They are considered in the United States as being cosmetics while antiperspirants are treated by the FDA as drugs. Deodorants tend to be less irritating than antiperspirants. In continental Europe the consumer today prefer deodorants compared to antiperspirants. In the United States the trend is approximately reversed.

Concepts for Controlling Underarm Odor: State of the Art

The current knowledge of the biology of the underarm microflora and the origin of underarm odor is the basis for developing strategies against odor formation. Numerous patents and literature articles disclose the incorporation of chemical compounds for their deodorizing properties. It is the intention here to describe and exemplify major strategies, but not all deodorant actives that were developed in the past.

Strategies to reduce underarm odor include the following:

- Antiperspirant active–containing deodorants
- Odor-masking deodorants
- Odor-neutralizing deodorants
- Odor-quenching deodorants
- Esterase inhibitors
- Antimicrobial active-containing deodorants

Antiperspirant Active–Containing Deodorants

Antiperspirant actives like aluminum chlorohydrate or the Al-Zr complexes (see Chapter 56) reduce the secretion of eccrine sweat. Their excellent antimicrobial properties against *St. epidermidis* and coryneform bacteria have been published [10]. The acidity of the aluminum salts may be a major factor in bacterial growth inhibition.

Odor-Masking Deodorants

Fragrance compositions (such as perfumes) have been used to mask odors since ancient times. It is conventional to incooperate 0.2–1.5% of a perfume in body deodorants [11]. They are designed to blend with the underarm odor and thus act as a masking agent. The perception of a perfume may differ significantly between individuals because of different interactions with the skin, washing habits and specific underarm odor. The fragrance materials are blended in order to achieve what is known as ''top note,'' ''middle note,'' and ''bottom note'' components. The first is the refreshing note upon application while the last are the olfactoric components which stay on after application to the underarm skin.

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Perfumes with antimicrobial properties have been described in patents and in the literature [12–14]. An additional benefit, especially for emulsion-based products, is that they might also act as a preservative. The increasing rate of contact allergies against fragrance ingredients should be taken into account using this approach to combat underarm odor [15].

Odor-Neutralizing Deodorants

In Chapter 56 it was mentioned that odorous C_6-C_{11} fatty acids contribute to underarm odor. Chemical neutralization with sodium bicarbonate ($NaHCO_3$) yields the corresponding odorless soaps [16]. This active however is not stable for a long time in aqueous compositions. Patents for deodorant applications and usage of sodium bicarbonate in the presence of antiperspirant actives have been filed [17,18]. Zinc carbonate containing deodorants are also content of a patent [19].

Odor-Quenching Deodorants

Zinc Ricinoleate

Zinc salts of ricinoleic acid have no bacteriostatic or antiperspirant effect [20]. They strongly bind odorous fatty acids, amines and mercaptanes. Ligand-exchange reactions of ricinoleic acid for odor molecules are probably the reason for the quenching properties of zinc ricinoleate [21]. Interactions with perfume components in a deodorant formulation may weaken the desired quenching effect of the odor molecules after topical application to the underarm.

Metal Oxides

The oxides of calcium, magnesium, and zinc form in the presence of fatty acids the corresponding metal soaps [22]. Zinc oxide particles aggregate to form a massive lump. This leads to clogging of aerosol products [23]. Hybrid powders were developed in which the metal oxide covers the surface of a spherical nylon powder [23]. The advantage of this technology is the increased surface area of zinc oxide and thus enhanced odor quenching efficacy and the reduced particle aggregation in aerosols.

Esterase Inhibitors

Zinc Glycinate

The inhibition of exoenzymes from the underarm bacteria (see discussion p. 703) should also result in odor reduction. Zinc glycinate has been described as a suitable active [24]. Antimicrobial tests showed no inhibitory effect against *St. epidermidis* or against the lipophilic diphtheroid bacteria supporting the suggested mechanism against microbial exoenzymes.

Triethylcitrate

The optimal pH value for development of underarm odor caused by coryneform bacteria is approximately about pH 6 in axillary extracts [25]. Shifting the skin surface pH to the acidic side should decrease the activity of skin esterases, proposed to be responsible for degradation of underarm secretions. Triethylcitrate was proposed to form citric acid by an enzymatic process on the underarm skin. In 1991 it was shown that this active has no

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pH-reducing effect after application to the underarm skin [26]. Nevertheless deodorants containing this active are still in the market.

Antimicrobial Active–Containing Deodorants

This approach is currently the most commonly used strategy to prevent underarm odor. Ethanol is probably one of the best known actives for deodorization [27]. Additional efficacy is normally required for a long term deodorization and this can be achieved by the additional usage of fragrance, an antiperspirant active or other antimicrobial actives (farnesol, phenoxyethanol, etc.).

Triclosan (2,4,4′-Trichloro-2′-Hydroxydiphenylether)

This active has a broad-spectrum antimicrobial activity against most gram-positive and gram-negative bacteria, molds and yeasts. The presence of triclosan in antiperspirant sticks and roll-ons leads to a higher reduction of the bacterial microflora versus the triclosan free antiperspirant composition [28]. Triclosan is also used in skincare products, hand disinfectants and household products [29].

Glyceryl Fatty Acid Ester

Mono- and oligoglyceryl fatty acid ester like glyceryl monocaprylate, -moncaprinate, -monolaurate and diglyceryl monocaprinate are effective deodorizers [30]. Combinations of glyceryl monolaurate with farnesol and phenoxyethanol showed synergistic efficacy effects against coryneform bacteria [31]. The advantage of this ingredient combination over the first generation deodorant actives like triclosan is attributed to their higher biodegradability and their selective bacterial action. These actives are all natural occurring in plants and animal species. In addition, it could be demonstrated that combinations of mono- and oligoglyceryl fatty acid esters with a variety of natural antimicrobials (e.g., wool wax acids) displayed a synergistic antimicrobial efficacy against underarm bacteria and serve as highly effective deodorant actives [32–35]. Products containing such actives have been successfully marketed for a number of years.

Sucrose Fatty Acid Ester

The fatty acid ester of sucrose are well known as emulsifiers in food products [36]. Sucrose can be substituted on eight hydroxyl groups with fatty acids. The antimicrobial potential depends strongly on the substitution degree of the sucrose. Sucrose monostearate and sucrose monolaurate have been described as deodorizers in the literature and in patents [37–39].

Glycerolether

2-Ethylhexyl glycerolether (octoxyglycerol) is a clear liquid with good solubility in cosmetic oils, polyols and alcohol but only moderate solubility in water (0.2%). Synergistic antimicrobial activity with other ingredients has been described [40]. This active has become popular recently in European deodorant formulations.

New Concepts for Controlling Underarm Odor

Ongoing research activities focussing on a better understanding of the interaction between underarm skin/skin microflora and skin microflora/odor formation, in combination with

the discovery of highly selective actives allows today more specific designs for deodorant products. In the next sections some of the new trends are discussed in detail.

New concepts for controlling underarm odor include the following:

- Chitosan
- Bacterial enzyme inhibitors
- Odor-inhibiting precursor mimics
- Product- and skin-mediated perfume transformations
- Antiadhesives

Chitosan

Chitin is a natural occurring polysaccharide (e.g., in insects, lobster, crabs, or fungi) containing N-acetylated D-glucosamin units. Deacetylation of the amino group leads to the slightly water soluble chitosan. The deodorizing properties of chitosan and the combination of this active with aluminum salts have been the subject of a patent [41].

Bacterial Enzyme Inhibitors

The enzyme amino acid β-lyase is, according to a patent filed in 1990, a catalyst for the formation of underarm odor [42]. This enzyme is located in odor-releasing bacterial cells and cleaves the apocrine precursors of sweat components, like amino acids with the structure unit COOH-CH-(NH_2)-CH_2-S-R, to the corresponding odorous sulfur products. Several classes of enzyme inhibitors like derivatives of hydroxylamines, β-substituted aminoacids, cycloserine and pyridoxal were identified.

Odor-Inhibiting Precursor Mimics

Another approach to the inhibition of the above-mentioned enzyme β-lyase is to provide an alternative substrate for the bacteria that cleave the structure unit CH(NH_2)CH_2-O-C(O)-R instead of the sulfur-containing amino acid sequence [43]. This approach leads to the corresponding non-odorous ingredients, like benzoic acid, or to pleasant odor generating substances, like phenylacetic acid.

Product- and Skin-Mediated Perfume Transformations

The physical and chemical interaction of a perfume with the underarm skin is a very complicated matter. Research activities in this area focused on the question which components of a perfume stay on and above the skin after topical application [44]. Headspace analysis is one of the techniques to gain more informations concerning skin/perfume interactions. It could be demonstrated that the long lastingness of a fragrance can be achieved by using a prodrug (ester, acetale) of a perfume ingredient [45]. The esters or acetales of a fragrance composition hydrolyze on human skin due to the slightly acid pH value. The hydrolysis products (acids, alcohols, aldehydes) impart a pleasant smell to the underarm skin. These product and skin-mediated perfume transformations are especially suitable for alkaline formulations like soap-based deodorant sticks. The advantage of the perfume precursor approach is attributed to a prolonged fragrance impression of a deodorant after topical application to the underarm skin.

Antiadhesives

An alternative concept to reduce the amount of skin bacteria in the underarm skin is the anti-adhesion approach. The understanding of the adhesion mechanisms of the resident

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underarm microflora to the skin surface is the basis for developing strategies against bacterial adhesion. Numerous skin microorganism adhere preferentially to specific sites on various body surfaces. For example, *S. aureus* and *P. aeruginosa* adhere to collected nasal epithelial cells [46]. *C. xerosis* binds to epidermal cells whereas yeasts species like *Candida albicans* bind to corneocytes. Structures of the skin specifically involved in adherence to the underarm bacteria are thought to be proteins, oligosasccharide structures, lipids and hydrophobic surfaces. Imitation of these adhesion motifs by saccharides, oligosaccharides, polysaccharides and glycoproteins allows to inhibit the bacterial adherence to the skin. Additionally it was discovered recently that among others sucrose ester like sucrose myristate and sucrose laurate have anti-adhesive properties to various microorganism including the typical microflora of the underarm skin [47].

DRUG-DELIVERY SYSTEMS AND APPLICATION FORMS FOR DEODORANT ACTIVES

Products designed to reduce underarm odor can be formulated in a variety of delivery systems such as suspensions, water or hydroalcoholic solutions, and emulsions. Typical application forms are sticks, roll-ons, creams, pump sprays, aerosols, and gels. Sticks, roll-ons, and aerosols are discussed in detail in the antiperspirant chapter. Lowering the amount of an antiperspirant active, like aluminum chlorohydrate, in an antiperspirant is one option to formulate a deodorant. In this case the antiperspirant active has only deodorizing properties and nearly no impact on the eccrine sweat glands. Deodorants can be formulated in acidic, neutral or alcaline environment. Designing a deodorant the formulator should have in mind the following points:

- Long-term deodorization
- No irritation potential
- Good solubility of the active in the delivery system
- Selection of a stable fragrance
- Viscosity control of the product
- Good skin feeling of the product

Protocols for the in vitro and in vivo evaluation of deodorants have been designed. The reader is referred to the literature [48]. A new method for in vivo evaluation of antimicrobial agents was recently developed where the underarm bacteria were translocated to the forearm allowing the simultaneous evaluation of multiple deodorizers in a single individuum [49].

Deodorant Sticks

Deodorant sticks are solidified by 6 to 8% of sodium stearate. The deodorizing agent and a fragrance are dissolved in a hydrophilic carrier. Two stick categories can be differentiated, the ethanol based and the propylene glycol based sticks [50].

Transparency is usually achieved by usage of a high polyol content. Clarifying agents for sticks like PPG-14 butylether, Cocamide DEA, Lauramide DEA, Steareth-100 have been patented [51,52]. Ethanol based sticks are preferred if it is the intent of the formulator to create a cooling sensation for the consumer. Shrinkage of the stick has to be taken into account because of evaporation of the alcohol. Propylene glycol based sticks

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tend to be more resistant to shrinkage, and solubilization of a fragrance is easier in some instances [53].

Deodorant stick	Wt%	Deodorant stick	Wt%
Water	16.0	Water	3.0
Ethanol	75.5	Propylene glycol	10.0
Deodorizer	1.0	Deodorizer	1.0
Sodium stearate	6.5	Sodium stearate	8.0
Fragrance	1.0	PPG-3 myristyl ether	77.0
		Fragrance	1.0

Deodorant Aerosols

Spray products containing a solution of an antimicrobial active in an ethanol and/or propylene glycol carrier blended with a liquidified propellant are typical for deodorant aerosols. The difference from an antiperspirant active containing aerosol is that the deodorizer is solubilized in an alcohol- or polyol-based formulation and not suspended. Deodorant sprays provide a dry skin feeling to the underarm skin since they are anhydrously formulated.

Typically, 20 to 60% of the sprayable contents of an aerosol reach the skin, since the liquidified hydrocarbon propellant vaporizes as it is sprayed [54]. Propane, butane and isobutane are the most commonly used propellants. They condense to form a clear, colorless and odorless liquid with densities of 0.51 to 0.58 g/mL at 20°C [55]. These propellants are inflammable in the presence of air or oxygen. Labelling of cosmetic aerosols concerning flammability risks of volatile organic compounds (VOCs) and volatile solvent abuse (VSA) is discussed in detail in a recently published review [56]. Aerosol containers can be fabricated from tin-coated steel, tin-free steel (chromium-coated steel) or aluminum. Numerous types of aerosol can corrosion and testing for it was recently discussed in the literature [57]. The environmental issues of aerosols are explained in greater detail in the antiperspirant chapter.

Deodorant aerosol	Wt%
Alcohol	42.0
Laureth-4	0.5
Deodoriser	1.0
Fragrance	0.5
Isobutane	47.6
Propane	8.4

The formulator of an aerosol has to optimize the following parameters to get a dry deodorant product:

- Spray rate
- Spray shape
- Particle size
- Concentrate/propellant ratio
- Fragrance/deodorizer concentration
- Pressure of the aerosol can

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Deodorant Pump Sprays

Hydroalcoholic Pump Sprays

An alternative to aerosols are pump sprays. This category is quite popular in Europe whereas it is of lower interest for the consumers in the United States, since they tend to prefer a dry application form, like the anhydrous sticks. Pump sprays allow a good dosage of the formulation to be delivered to the underarm skin in a hygienic way. They consist of low vicosity hydroalcoholic solutions of a deodorizer and a perfume. Usually a solubilizer, like PEG-40 hydrogenated castor oil, is incorporated into the formulation to maintain a clear and homogeneous solution.

Pump spray	Wt%
Water	35.6
Alcohol	60.0
PEG-40 hyd. Castor oil	2.0
Deodorizer	2.0
Fragrance	0.4

PIT-Emulsion Pump Sprays

A disadvantage of hydroalcoholic pump sprays is the alcohol content in the formulation that may contribute to unwanted side reactions especially in the shaved axilla. Beiersdorf AG in Hamburg, Germany introduced into the European market under the brand name ''Nivea'' a new pump spray based on an emulsion in 1995. The sprayable low viscous deodorant is based on the PIT technology. Suitable mixtures of ethoxylated surfactants, oils and water in the presence of antiperspirant and deodorizing actives are heated to 60–90°C. Cooling the resulting W/O emulsion to room temperature yields via a phase inversion temperature (PIT) process a finely dispersed bluish-white O/W emulsion [58–60]. The droplet size distribution of such PIT emulsions is in the range from 80–250 nm. The above-mentioned pump spray contained a skin-friendly deodorizing combination of glyceryl monocaprinate and wool wax acids (see discussion p. 706) in an alcohol-free delivery system.

PIT-emulsion pump spray	Wt%
Glyceryl stearate, ceteareth-20, ceteareth-10, cetearyl alcohol, cetyl palmitate (Emulgade SE)	4.5
Ceteareth-20	1.0
Dioctyl cyclohexane	5.0
Dicaprylylether	5.0
Deodorizer	2.0
Aluminum chlorohydrate	5.0
Water	77.5

Source: Ref. 60.

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Microemulsion Pump Sprays

Hydroalcoholic pump sprays are usually transparent, whereas sprayable PIT-emulsions are white or bluish-white products. Sprayable alcohol-free and additionally transparent pump sprays were recently introduced into the European market (e.g., Basis pH; Beiersdorf AG, Hamburg, Germany). Transparency of an emulsion is achieved when the size of the droplets is below 100 nm. This O/W microemulsion can be obtained with and without the PIT technology but needs careful selection of ingredients and considerable fine-tuning [61]. The main advantage compared to classical microemulsions is the low surfactant concentration (<10%). Furthermore it could be demonstrated that, in the presence of hydrophobically modified water-soluble polymers, the above-mentioned technology allows the formulation of gels, sprayable gels, roll-ons, sticks, and aerosol products [62].

FUTURE TRENDS

The deodorant market has undergone some remarkable changes concerning the principles to reduce underarm odor in the last years. It is expected that the search for effective, skin-friendly actives with a highly selective action against the cutaneous underarm microflora will lead to long-lasting and safe deodorants. Improvements in understanding how micro-organism adhere to human skin should facilitate the development of new strategies to reduce underarm odor. Improvements of aerosols with no/low impact to the environment or aerosol alternatives, like sprayable emulsions, are probably in a few years in the portfolio of every deodorant-selling company.

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Baby Care

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INTRODUCTION

Skin undergoes an extraordinary development. It must grow rapidly and expand dramatically in size to cover the entire developing body. It is exposed to both internal and external environmental influences throughout the entire phase of its existence. However, despite the multitude of regionally specific influences that play a role in the development of skin, there is a remarkable similarity in its developmental pattern and in the ultimate end product of differentiation in every part of the body. The purpose of this chapter is to outline what is known about the development and physiology of baby skin and its implications on our daily care regime of skin at this early stage of life.

THE DEVELOPMENT OF BABY SKIN

The development of skin usually begins 7 to 8 days after fertilization, during which an outer blastodermic layer, the ectoderm, is formed. During the embryonic phase of development, two layers evolve from the ectoderm, the underlying basal layer from which the uppermost skin layer—the epidermis—and the cutaneous appendages develop, along with the periderm, which faces the fetal cavity. When the epidermis is keratinized between week 22 and 24 of pregnancy, the periderm separates itself from most parts of the body. In the third trimenon all cell layers in the epidermis that are typical for mature skin are developed. However, until birth, the stratum corneum has still not developed a significant barrier function. This is made clear when premature babies are observed. One of the biggest problems in preemies is high transepidermal water loss (TEWL), although this decreases exponentially with increasing gestation age. High TEWL in turn may lead to hypothermia and difficulty in fluid balance [1–6].

The mesoderm, a middle layer, develops at day 18 or 19 after fertilization. The mesoderm, with its mesenchymal cells, forms the dermis (corium). Epidermis and dermis are connected by a membrane (basal lamina). Within the third trimenon this contact area (the dermo-epidermal junctional zone) between the dermis and epidermis can now be clearly identified by commencing undulations and by the development of epithelial crests and papillae. The development of the dermis also continues until the birth of the baby. In newborns it is about 60% as thick as in adults [1].

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In the embryonic phase the dermis and the underlying subcutis cannot be differentiated from one another. In week 15 of gestation the subcutis can clearly be recognized. The lobuli network, in which the adipocytes (fat cells) spread, is formed. Within the third trimenon large fat lobuli develop in the subcutis, which protect the organism from heat loss in cold conditions. Today it is still not clear what exactly stimulates the adipocytes to produce fat. The subcutis does not become thicker until after birth, depending on the baby's nutritional condition [1,2].

The sweat glands begin forming on the palms of the hands and the soles of the feet between weeks 10 and 12 of gestation. A portion of the excretory glands, however, remains closed until the end of month 7 of gestation. This is the reason why babies born prematurely have developed, if at all, a limited ability to sweat [2]. They also show a limited ability to regulate body temperature as well as an increased TEWL, both of which need to be considered when setting up a daily skincare regime [7]. In contrast, the skin of preterm and full-term infants usually shows no signs of a physiological deficit.

THE PHYSIOLOGY OF BABY SKIN

Protection Against Water Loss

The following two basic mechanisms account for fluid transport through the skin:

1. Perspiration: active process in which water is excreted through the openings of the sweat glands. (Perspiration plays an important role in thermoregulation) [8].
2. TEWL: passive diffusion of water through the skin [9,10].

Gestation age plays an essential role in the birth of a baby [11]. The TEWL decreases with increasing gestation age. In a fully developed newborn, a TEWL of 6 to 8 g water per m^2 of skin per hour is low. However, the TEWL is considerably higher in prematurely born babies, especially those born before week 30 of pregnancy. In the first months of life, water loss in infants increases slightly. The explanation for this is that the babies begin to perspire slightly [12].

As the body temperature rises, the permeability of the skin also increases, leading to higher water loss. As environmental temperatures rise, water evaporates faster. This fact must be considered especially when caring for newborns. Creams and ointments with occluding effect can lower TEWL. The application of liquid paraffin on the skin can reduce TEWL by up to 50%.

Protection Against Percutaneous Absorption of Harmful Substances

In addition to providing protection against water loss, the skin barrier function ensures that chemical agents, which could harm the organism, cannot penetrate percutaneously (through the skin). The permeability rate in prematurely born babies is 5 to 50 times higher than in fully developed newborns. The ratio between body surface and body weight is almost 2.5 times higher in newborns than in adults. This surface volume ratio is one of the essential points that must be considered in the application of topically affective therapeutics. Particularly with treatment of large areas, e.g., of dermatologicals containing corticoids, there is the danger of increased systemic absorption [13].

With increasing maturation, the epidermal cells develop increased metabolic activity. This means that the activation of enzymes can render potentially harmful substances harmless. They are modified through oxidation, hydrolysis, reduction, deamination, or

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conjugation and thereby inactivated. This enzyme activity is very restricted, especially in prematurely born babies, so that potentially harmful substances can enter the blood stream in an unaltered state if absorbed percutaneously [13].

Protection Against Pathogenic Micro-Organisms

After birth, the body of the baby is exposed to numerous germs. The skin barrier not only protects mechanically against invading micro-organisms, but also through the slightly acidic milieu of the hydrolipidic film on the surface of the skin. The surface of the skin is physiologically populated by specific germs (saprophytes), which are not pathogens but rather a vital microbial defense system on the skin's surface. For optimal living conditions, the saprophytes require an acidic milieu. Directly after birth, however, alkaline values prevail on the surface of the body of the newborn. It can be assumed that these alkaline values result from the vernix caseosa residue. Neither weight at birth nor gestation age seem to have an influence on the pH value. Within the first 24 hours after birth, the pH value drops noticeably. In the first month of life, the pH value then stabilizes at a slightly acidic range (slightly below a pH value of 6) [14].

The natural acid mantle of the skin on the newborn is already developed in the first few days of life, so that pathogenic micro-organisms generally find the conditions unsuitable for their survival. However, the alkaline-neutralizing properties of the skin of newborns and small children is restricted. After contact with alkaline substances (e.g., alkaline soaps), the skin requires a longer time to restore its slightly acidic physiological pH value as compared with adult skin [15].

FREQUENT SKIN PROBLEMS IN NEWBORNS

Diaper Dermatitis

At the beginning of this century, in 1905, a French pediatrician by the name of Jacquet gave the peculiar frequently occurring skin rash in the diaper area the name diaper dermatitis [16]. The skin alterations subcategorized under the diagnosis diaper dermatitis can have a variety of causes. They can be directly related to the contact dermatitis, which is diaper dermatitis in a narrow sense. The occurence can also be unrelated to the use of diapers. Today the factors that enhance this irritating contact dermatitis are known:

1. Diapers that have an occluding effect in an already moist environment, which results in an increased hydration of the stratum corneum.
2. The increased hydration facilitates penetration of xenobiotics.
3. The still very thin epidermis of the newborn reacts sensitively to mechanical stress and friction.
4. The skin barrier function is weakened, and the skin shows an increased irritability.

In addition, an increase of the pH value in the diaper area can also encourage an outbreak of diaper dermatitis. The alkaline urine activates enzymes (lipases and proteases) in the feces, which irritate the skin [17–19].

Boys and girls are equally afflicted with diaper dermatitis. It mainly occurs between 3 and 10 months of age, with a frequency peak between 6 and 9 months. Typically, a skin erythema can be found on the inside of the thighs and on the baby's bottom. The

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skin is increasingly reddened, has a shiny, glassy appearance, and is wrinkled on the surface.

Corticosteroids are used occasionally in the treatment of diaper dermatitis. In the follow-up treatment, emollients containing zinc oxide are mainly used. Zinc oxide has an astringent, slightly disinfectant effect and offers the skin protection against urine and feces [17–21].

Protective creams containing zinc oxide are usually used to cover the skin of the diaper area with a highly viscous film, which inhibits the penetration of xenobiotics without fully occluding the skin. In order to accomplish this goal, usually water-in-oil (W/O) creams are used, which contain one or more of the following ingredients: petrolatum, lanolin, lanolin alcohol, paraffin oil, natural oils, waxes, zinc oxide, and possibly cod liver oil, vitamins, plant extracts, and titanium dioxide.

Diaper candidiasis is a fungal-infected diaper dermatitis. The most common causative agent is a yeast fungus called *Candida albicans*. It is a known fact that extensive use of antibiotics in newborns and small children increases that incidence of diaper candidiasis. Initially, diaper candidiasis can be treated with a specific antimycotic therapy (nystatin, clotrimazole), then followed up with the healing methods for basic diaper dermatitis as previously described [22].

Neurodermatitis

Neurodermatitis, also called atopic dermatitis, is a skin disease that may occur at a very early age. It can be identified by the so-called milk crust on the reddened, damp skin of the head and cheeks of the newborn. As the first indication of an outbreak of neurodermatitis, the milk crust often provides the starting point for other skin disorders. The skin becomes cracked and transparent, and the permeability increases. Once the skin is damaged, the risk of infection is higher. The skin becomes increasingly dry, transparent, and irritated, with intensified itchiness. The temptation to keep on scratching the skin is usually almost irresistable for small children. Atopic dermatitis is an immunological reaction that affects the skin to an especially large extent. More than 10% of children in industrialized countries are already afflicted, with a rising tendency. The combination of the genetic predisposition and environmental influences as well as psychological and neurovegetative factors can result in an outbreak of this disease [23–25].

Adequate skincare, which reinforces the skin's vital barrier, is a meaningful prophylaxis for avoiding a first outbreak of neurodermatitis in high-risk allergy children. The following measures can help:

- Mild cleansing agents
- Moisturizing emulsions to support the skin's barrier function
- Skincare products with proven skin tolerability
- Skincare products and cleansers with few, carefully selected ingredients, in order to keep the risk of allergies as low as possible [23–25]

THE CARE OF BABY SKIN

The effects of baby-care products can usually be divided into the following categories: cleansing, caring, and protection. Currently, a multitude of product types can be found in the market. Although the shear number of products is overwhelming, there are features

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they all have in common. The following three sections will deal with product characteristics and general usage advice in the various segments of baby care.

Cleansing

Bath Additives

As soon as the umbilical cord has fallen off, the baby can be bathed [26–29]. However, daily bathing of the baby is not advisable, as this would dry out the skin too much. A bath every 2 to 3 days is sufficient. The bath temperature should lie between 36 and 37°C.

Bath additives usually contain a mixture of various anionic (e.g., fatty alcohol ether sulfates, protein fatty acid condensates), nonionic (e.g., ethoxylated fatty alcohols, fatty acid glycerides), and amphoteric (e.g., betaines) surfactants. Numerous protein hydrolysates, superfatting agents, solubilizing agents, plant extracts, colorants, and perfumes are also found in this product category. In general, bath additives contain mild surfactant mixtures, which neither dry out the skin nor burn in the eyes.

Cleansers for the Diaper Area

Baby oils containing mineral oils as well as oil-impregnated towelets are widely used. (Towelets are usually supplied in dispenser boxes securing product hygiene up to the last towelet used.) Liquid petrolatum is a very desirable ingredient in view of its stability, touch, barrier function, and cost. Liquid petrolatum also has a remarkable occlusivity. Intertrigo areas should therefore be frequently cleansed (1–3 times daily) with oil or oil-containing towelets.

Soft towelets containing mild oil-in-water (o/w) cleansing milks or, alternatively, clear cleansing lotions are also frequently found. They normally contain anionic and/or nonionic surfactants in low concentrations as well as varying amounts of skincare ingredients like plant extracts and protein hydrolysates. These towelets are also offered in dispenser boxes.

Whereas the irritating effect of soaps mainly results from their alkalinity, the use of alkaline-free soaps has shown that all detergents induce a significant delipidizing effect, which can also contribute to skin irritation [26–29].

Liquid cleansers are usually used for cleansing of the face, arm pits, and the genital area. Normally alkaline free, their composition resembles the composition of baby shampoos, whereas the concentration of surfactants is normally higher. The reasoning behind the higher surfactant level lies in the smaller product amount used for cleansing [26–29].

Shampoos

Baby shampoos are usually formulated to be nonirritating to the eyes. This guarantees extraordinary product safety and also ensures that babies do not object to shampooing. Although basically the ingredients used are comparable with the ingredients found in bath additives, the concentration of surfactants is normally lower. Viscosity is adjusted to about 1000 centipoise (cps) to make it hard for the shampoo to migrate into the eyes.

Care

Face and Body Creams/Body Lotions

Face creams are especially important for the protection against environmental influences like sunlight, wind, and cold temperatures, which may dry out baby skin. The composition

resembles that of the body-care creams, although the moisturizer content is often higher. The ingredients used are often more compatible with the mucous membranes (especially in the area of the eyes) than in the case of body creams. Body-care creams are frequently used for their excellent superfatting properties. Both o/w and w/o emulsions are found on the market.

Body-care lotions are normally used for large-area body care, e.g., after baby bath. Both o/w and w/o emulsions are found in the market. Classic ingredients used are lanolin, lanolin alcohol, paraffin oil, vaseline, natural and synthetic wax esters, natural oils, fatty alcohols, and emulsifiers (e.g., fatty acid glycerides, ethoxylated fatty alcohols). Many skin-caring, soothing active ingredients are also found.

Protection

Sun Protection

Spending summer vacation at the seashore is a tradition of many families. Unfortunately, the beach is a high-risk environment for future skin cancer because it allows for maximum sunlight exposure. Heat, wind, and humidity are often present. These factors can enhance or intensify UV injury. With or without topical sun-protection measurements, babies and small children should be kept out of direct sunlight. As soon as children begin to explore their environment, it usually becomes impossible to confine them to the shade. In such cases, sunscreens need to be applied.

A wide variety of different o/w and w/o emulsions, hydrogels and oleogels are found in the market using a variety of UV-filter systems. Many products contain broad spectrum (UVA and UVB) sunscreens with a moderate SPF. Products with a water-resistant SPF are favorable at the seashore [30–33].

Cold Protection

Mild facial creams are especially important in the winter for protection against the harsh effects of a dry, cold climate. At freezing temperatures, significant protection against frost bite is obviously helpful. Specific petrolatum-based water-free formulations, which optionally contain zinc oxide and skin-soothing agents like panthenol, can protect the skin at temperatures below freezing.

QUALITY MANAGEMENT IN BABY CARE

Despite careful research with respect to the good skin tolerability of each individual ingredient in baby-care formulations, it should be made certain that this data will also apply to the final product after these ingredients are integrated into the formula. In order to rule out the possibility of contact allergies or sensitizing skin reactions, products are frequently tested using the repeated-insult patch test (RIPT). This test is a validated, recognized method for the testing of skin sensitization. The test preparations are repeatedly applied to the same localization for 3 weeks. After a 2-week break, the test materials are applied once again on another location and the skin is assessed for any allergic reaction that could possibly have been induced [34]. Exposure to sunlight can cause certain ingredients to trigger photoallergic or phototoxic skin reactions. Photopatch or phototoxicity tests enable the detection of UV-induced irritant or allergic skin reactions.

In the elbow-wash test, the skin tolerability of cleansing formulas is tested in the sensitive crease of the elbow under controlled and extreme washing conditions, and com-

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pared with a skin-friendly standard product. The evaluation of the skin reaction is performed after repeated washings over a period of 5 days, based on subjective and objective reports [35].

In a clinical application test, skin tolerability as well as the skincare properties of baby products can be tested. At the start, and again after 4 weeks of practical application of baby-care products, dermatological examinations are carried out. Parents are given diaries for the daily evaluation of product properties. Children known to have skin allergies to ingredients in the test products are excluded from the testing.

SUMMARY

Normal baby skin shows no natural inborn deficits that need special treatment. However, the elevated skin permeability in newborns needs to be considered when establishing a routine skincare regime. The sensible use of skin-cleansing and caring products surely needs to be remembered.

However, there is a growing demand for specific dermatological treatments of newborns, as the number of skin disorders (e.g., neurodermatitis) in this age group are on the increase.

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Cosmetics for the Elderly

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INTRODUCTION

Aging is a basic biological process common to all living organisms. Its biochemical mechanisms have yet to be elucidated in detail. Aging is usually understood as an irreversible, progressive loss of homeostatic capacity. By definition, aging affects everyone, but at a variable rate. At present, aging is widely assumed to result partly from a genetically determined program and partly from endogenous and exogenous insults. Both processes occur at the level of individual cells.

At the organ level generally and in the skin specifically, aging is manifested by a loss of maximum metabolic activity and increasing sensitivity or susceptibility to certain diseases and environmental factors. The purpose of this chapter is to outline what is known about morphological and physiological aging of the skin and its implications for a tailored skincare of the elderly.

AGE-ASSOCIATED CHANGES IN HUMAN SKIN

Morphological and Histological Changes

The major aging changes in the morphology of the skin include dryness (roughness and scaliness), wrinkling, and laxity [1]. The most striking and consistent change is a flattening of the dermal-epidermal junction [2]. This results in a considerably smaller surface between the two compartments. This presumably leads to less nutrient transfer and may cause the relatively smaller proliferative compartment in the epidermis. It is also responsible for the lower resistance to shear forces [1]. However, most of the apparent clinical changes associated with advanced age are attributable to chronic sun damage [3,4].

Physiological Changes

An age-associated decrease in the epidermal turnover rate of approximately 30 to 50% between the third and the eighth decade has been determined by a study of desquamation rates at selected body sites [5]. The thymidine labeling index of the epidermis in vivo has been reported to decline nearly 50% during the human life span [6].

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Recent studies using highly sensitive techniques for the measurement of sebum secretion rates have documented a decline of approximately 23% per decade [7]. The physiological consequences of decreased sebum production in old age, if any, are unknown [1].

Clinical studies showed that eccrine sweating is markedly impaired with age. Spontaneous sweating in response to dry heat, measured on digital pads, was reduced by more than 70% in healthy old subjects [8], primarily attributable to a decreased output per gland.

The decreased vascular reponsiveness in elderly skin has been documented by clinically assessing vasodilation and transduction after application of standard irritants like histamine [9]. The intensity of erythema after UV exposure also decreases with age [10].

An age-associated decrease in delayed hypersensitivity reactions in human skin is manifested by a relative inability of healthy elderly subjects to develop sensitivity to dinitrochlorobenzene (DNCB), and by their lower rate of patch-test reactions to standard recall antigens. The cutaneous manifestations of immediate hypersensitivity similarly declines with age [1].

Langerhans cells are the epidermal cell population, which is largely responsible for recognition of foreign antigens. An approximately 25 to 50% reduction in the number of epidermal Langerhans cells occurs between early and late adulthood [11] and substantially contributes to the age-associated decrease in cutaneous immune responsiveness. The amount of dermal mast cells likewise decreases with age. The resulting consequences beyond the reduced rate of immediate hypersensitivity reactions, such as a positive ''prick-test'' [12] or acute urticaria, are unknown.

Photoaging

Photoaging is a term used to describe the array of clinical and histological findings in the chronically sun-exposed skin of middle-aged and elderly adults. It has also been called dermatoheliosis [13] and heliodermatitis [14], the latter term reflecting the low-grade inflammatory nature of the process.

Clinical features of actinically damaged skin include coarseness, wrinkling, irregular pigmentation, telangiectasia, and scaliness, as well as a variety of premalignant and malignant neoplasms. The relative severity of these changes varies considerably among individuals. This undoubtedly reflects strong differences in past sun exposure and marked individual differences in vulnerabilities and repair capacities for solar insults. Photoaging usually involves most severely the face, neck, or extensor surface of the upper extremities [15].

THE COSMETIC CARE OF ELDERLY SKIN

Cosmetics for elderly skin can usually be divided into the categories of facecare and bodycare. Currently, a multitude of product types can be found. Although the number of products is overwhelming, there are common features to be mentioned. The following two sections will deal with product characteristics in various segments for the cosmetic care of elderly skin.

Facecare

Skincare

Concepts for cosmetics suited for elderly people are often based on the dry skin conditions typical for elderly skin. Many skincare formulations contain humectants, which enable

excellent transient hydrational/moisturizing effects. While lessening the prominence of undesirable surface defects, these formulations have only minor influence on dermal losses. However, evidence is accruing that the following groups of topically applied actives do seem to reverse the degenerative skin changes seen with aging.

By far the most exciting discovery in cutaneous gerontology during the past decade is the effect of tretinoin (all-trans retinoic acid) on the clinical and histological appearance of photoaged skin. Kligman first realized that topical tretinoin improved the appearance of middle-aged women using the drug to control facial acne. Support for the concept was provided by a double-blind vehicle-controlled trial documenting tretinoin's effectiveness on human photoaging. After 4 months of daily application, 0.1% tretinoin cream produced statistically significant improvement in fine and coarse wrinkling, sallowness, and roughness of sun-damaged facial and arm skin [16].

Tretinoin was the first agent shown to reverse age-associated changes in any tissue. This statement must be qualified in that it is unclear whether tretinoin truly reverses aging changes or simply produces new changes that mimic a reversal. It is unclear whether tretinoin affects exclusively sunlight-induced pathologies or a combination of sun damage and intrinsic aging changes [1].

In the past years, estrogen supplementation of the climacteric women has opened new aspects on the wide variability of estrogen effects in various tissues. In skin, estrogens increase vascularization and show effects at various levels of dermal tissue [17,18].

Several attempts have been made to check the skincare efficacy of estriol (0.3%) or estradiol (0.01%) in perimenopausal women. Daily application of a cream over a period of 7 months resulted in a significant increase of skin parameters like skin firmness, wrinkles, and skin moisture content. Hormonal levels showed a slight increase in the prolactin level, whereas the estradiol level was unchanged. Side effects were not found [19,20].

Many further topical actives with excellent antiaging potential are currently used in marketed formulations, the number of which is increasing year after year [21–23].

Skin Cleansing

Active detergent substances contained in cleansing agents for human skin inevitably result in a degreasing of the keratinous layer, so that natural, moisture-retaining substances are also rinsed out in the process. It is, however, possible, by selecting the proper cleansing agents and reducing the frequency and intensity of their application, to reduce the unfavorable influence of various washing procedures on the skin of such elderly persons to a considerable extent.

Facial skin cleansers for elderly skin are usually particularly mild and superfatting. Both surfactant-based and oil-in-water (o/w) emulsion-based formulations are currently found. In the surfactant-based formulations, surfactants like ampholytes, betaines, sulfosuccinates, and various types of alkylpolyglucose are frequently used, whereas o/w emulsion-based formulas frequently contain superfatting agents and various humectants, which secure good cleansing efficacy without drying out the skin.

Bodycare

Skincare

For active care by means of humidity and lipid substitution, mainly o/w and water-in-oil (w/o) emulsions are used, which combine occlusive effects and moisturizing action. In addition to pyrrolidone carboxylic acid salt and urea, other humectant substances such as

alpha-hydroxy acid and hyaluronic acid, a highly efficient moisturizer, are frequently found. It is self-evident that such formulation ingredients as glycerine, propylene glycol, and other glycols also contribute to their humectancy.

Polar and unpolar lipids are frequently used in bodycare formulations. They act as emollients, as protective lipids, and as structure formers of the liquid crystalline bilayers between the corneocytes. These three functions are usually performed by fatty alcohols, fatty acids, and short- and long-chain esters, along with triglycerides and waxes. Special effects are frequently delivered by liposomes containing phospholipids, sphingolipids, and ceramides, and lead to the desired long-term effects. This is attributable to special binding mechanisms in the skin, an anchor capacity of transported and/or encapsulated active ingredients, and their slow release.

Skin Cleansing

Bath additives usually contain a mixture of various anionic, nonionic, and amphoteric surfactants. Numerous superfatting agents, solubilizing agents, plant extracts, and perfumes are also found in products within this category. However, only an oil bath for elderly skin may provide skin cleansing and conditioning at the same time. For serious dry-skin conditions, oil baths are indispensable.

A variety of shower products, meanwhile, also contain high amounts of superfatting agents, thus securing their good skin compatibility and low drying-out potential.

SUMMARY

There is an increasing demand for face- and bodycare formulations tailormade for the cosmetic treatment of elderly skin. Modern topical formulations not only deliver excellent moisturizing and superfatting capabilities, but many products, especially facecare products, contain one or more actives counteracting the signs of intrinsic and/or photoaging. However, it is still not clear whether these actives reverse the signs of aging or induce other effects on the skin that mimic a reversal of skin aging.

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