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Personal Cleansing Products: Properties and Use

Keith Ertel
P&G Beauty, Sharon Woods Technical Center, Cincinnati, Ohio, U.S.A.

INTRODUCTION

> *"Let it be observed, that slovenliness is no part of religion, that neither this, nor any text of Scripture condemns neatness of apparel. Certainly this is a duty not a sin. Cleanliness, indeed, is next to Godliness."*
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> —John Wesley (1703-1791), Sermon XCII

> *"Cleanliness becomes more important when Godliness is unlikely."*
>
> —P. J. O'Rourke

In today's marketplace personal cleansing products are found on the shelves of mass retailers and behind cosmetic counters at prestige stores, where they are offered as part of a total skin care and beauty package. Nearly every shopping mall has a purveyor of specialty cleansing products and a simple search on the Internet reveals a number of suppliers whose distinctive personal cleansers are purported to remedy the deficiencies of the products made by large-scale manufacturers. New cleanser forms offer increased convenience and consumers can choose from myriad product scents, colors, and functional ingredients intended to help them achieve relaxation and escape from the cares of everyday life, and to improve their skin's health and appearance (1–4). Yet despite their increased variety and complexity, present day cleansers have the same basic function as their counterparts of times past: to cleanse the skin.

SKIN CLEANSING

Soil Removal

The skin is covered with a hydrolipid film that, depending on the area of the body, comprises secretions from sebaceous glands and from apocrine and eccrine sweat glands. Decomposition products from cornification (cellular debris and stratum corneum lipids) and corneocytes in the process of being shed are also present. This film provides a degree of waterproofing to the skin's surface, traps water to help maintain skin pliability, and provides a natural defense against pathogenic organisms. But this film also attracts

and holds dirt and pollutants from the environment. The skin's surface is also home to a variety of microorganisms. In most cases these organisms, the so-called resident flora, cause no harm and provide an additional defense against overgrowth by potential pathogens. But these organisms can act on components of the surface film and create undesirable by-products, such as those resulting from the metabolism of compounds found in apocrine sweat that create body odor. Thus, while the surface hydrolipid film is an important skin integument, periodic cleansing to remove dirt, debris, and odor is essential to maintaining skin health and in many cultures, social acceptance. Additionally, periodic cleansing is necessary to remove soil (including bacteria) from the skin surface that is acquired by incidental contact or by intentional application, e.g., medications or makeup and other cosmetic products.

Water alone is capable of removing much of the soil from the skin's surface (5). However, water has a limited ability to dissolve and remove oils; as the old adage goes, "oil and water don't mix." The surfactants that make up the bulk of most personal cleansing products aid this process. A surfactant, or surface active agent, is a material that lowers the interfacial tension of the medium it is dissolved in, and the interfacial tension with other phases. Said more simply, a surfactant increases the affinity of dissimilar phases for each other. This ability is based on surfactants' unique structure, which combines both hydrophilic and hydrophobic moieties at opposite ends of the surfactant molecule. In a dilute aqueous solution, surfactant molecules will arrange themselves such that the hydrophilic portion of the molecule is oriented toward the bulk solution while the hydrophobic portion orients itself in the opposite direction. For water in contact with skin the presence of surfactant molecules at the interface lowers the interfacial tension and aids wetting, which improves water's ability to spread over the skin's surface. This, along with the mechanical action of applying the cleanser, helps to remove soil. As the concentration of surfactant in solution increases a point is reached at which the surfactant molecules begin self-association into micellar structures. This point is known as the critical micelle concentration (CMC). Surfactants in aqueous micelles have their hydrophilic end oriented toward the bulk (water) phase and their hydrophobic end oriented toward the interior of the micelle. The hydrophobic interior provides a good environment for dissolving lipids, and micellar solubilization is an important mechanism by which surfactants remove oily soils from the skin's surface and help keep the soils suspended until they are rinsed away. Other factors may aid this process. For example, the skin's surface possesses a net negative charge at physiological pH and repulsive forces between the skin and anionic surfactants or their associated micelles help keep suspended soils from redepositing, making these surfactants particularly good cleansers.

Tests of Cleansing Efficiency

A personal cleanser's ability to clean the skin is dependent on a number of factors including its (surfactant) composition, its in-use concentration, the application time and method, the soil load, and the surface characteristics of the particular skin being cleaned. The past several decades saw a change in how personal cleansers are viewed, the focus shifting from their role as skin cleansing aids to their role as agents with a potential to damage skin (6). Thus, while numerous publications describing methods to assess and compare personal cleansers' skin compatibility appeared in this time frame, in-use cleansing performance was largely ignored. However, this question deserves consideration given the greatly expanded range of personal cleansing products now available, both in terms of forms and ingredients.

Weber described a method to assess cleansing that employed a device designed to wash forearm skin in a controlled manner (7). A colored model soil was applied to forearm skin of normal subjects and three subject groups with psoriasis, atopic dermatitis, or non-lesional skin disease. Four cleansing bars ranging from full soap to synthetic detergent (syndet) were tested on each subject group. The amount of color on skin was measured photometrically before and after cleansing. Weber found differences in cleansing, not only between the cleaner types but also between subject populations. Skin cleansing was in all cases best with the syndet bar, poorest with the soap. The measured cleansing response was greatest in psoriatics, which could reflect soil removal by detergency and the mechanical removal of stained psoriatic plaques by the washing process. Cleansing was poorest in atopics, which the author attributed to higher skin dryness (roughness) and greater adherence of the model soil.

Schrader and Rohr also used a device to assess personal cleansers' skin cleansing ability under controlled conditions (8). Their device was designed for use on the forearm, with a dual-chamber arrangement for simultaneous testing of two products. Agitators with felt inserts rested on the forearm surface at a controlled pressure and moved in a back-and-forth motion to effect washing. A mixture comprising oleaginous materials (including lanolin, petrolatum, and mineral oil) and lipid- and water-soluble dyes was used as a model soil. The published study compared soap-based and syndet-based liquid cleansers at 2% and 8% concentrations. Water and a 2% solution of sodium lauryl sulfate (SLS) were used as controls. The color (L^*-value) on skin before and after "washing" was measured with a chromameter. This work showed greater cleansing efficiency for the soap-based cleanser.

These authors conducted a separate experiment to assess the skin roughening effect of the test cleansers. Subjects used the test solutions for forearm washing over a two-week period. Skin roughness was assessed using silicon replicas taken at baseline and study end and analyzed by laser profilometry. The 2% solution of the soap-based cleanser produced greater roughening than did the 2% solution of the syndet-based cleanser. Changing the concentration of soap-based cleanser from 2% to 8% did not increase skin roughness. However, skin roughening for the syndet-based cleanser showed a concentration effect and at the higher concentration skin roughening was comparable to that produced by the soap-based cleanser. This illustrates the concentration-dependence of cleanser effects on skin and, since an 8% concentration is representative of cleansers' concentration on the skin during actual use (9), the importance of understanding test conditions when judging how a cleanser will affect skin. This is particularly important when attempting to predict cleansers' in-use skin effects.

Wolf and Friedman used a modification of Schrader's method to assess the skin cleansing effect of soaps (10). An oleaginous mixture (petrolatum, lanolin, mineral oil) was again used as a model soil but in this case it was applied to the dorsum of the hand. The soiled hand was immersed for five minutes in a beaker filled with a stirred, 1% solution of the test cleanser maintained at 37°C. Sebumeter® readings made before and 30 minutes after immersion were used to determine the amount of soil removed. The authors report that this method is a convenient and economical alternative to the method of Schrader that can reliably and reproducibly measure and discriminate the skin cleansing ability of different products. A study comparing a syndet to a mild cleanser containing "25% hydrating soothing cream" showed that the latter product removed less of the model soil from the skin, i.e., it was a poorer cleanser. The authors conclude that for a product to function as an effective cleanser it must also dry the skin to a certain degree.

Imokawa used a model soil consisting of a mixture of triolein, cholesterol, squalene, palmitic acid, and Sudan Black dye (11). This mixture was applied to six glass slides, which were placed into a beaker containing 40°C surfactant solution and stirred at

1300 rpm for 10 or 30 minutes. Cleansing efficiency was judged by spectrophotometrically or gravimetrically measuring the amount of soil removed from the slides.

Lockhart and Lazer presented work that examined the impact of various physical conditions on cleansing (12). Charcoal applied to the dorsum of the hand served as a model soil. Four "wash" conditions were examined: simple soaking and placing the hand in a whirlpool, a simulated shower, or in an ultrasonic bath. Water temperature was maintained between 32°C and 38°C in all cases. Cleansing efficacy was judged by measuring color at the charcoal-stained area with a chromameter before and after washing. The results showed that the conditions ranked, in order of increasing cleansing effectiveness, soaking < whirlpool < shower < ultrasonic bath. While this study did not involve a cleansing agent or oleaginous soil, it demonstrates the potential for physical conditions and mechanical action to influence removal of a simple soil from the skin's surface. Personal cleansers are used under a range of conditions and with a variety of implements, and these factors will affect overall cleansing efficacy.

The above methods all used a device in an attempt to reduce variability associated with the washing process. Other authors describe cleansing efficacy methods that more closely approximate in-use conditions. Sauermann et al. used mineral oil containing 0.1% anthracene as a model soil (13). The material was applied to the lower inner forearm, and the site was washed in a regular manner for 30 seconds with warm (32°C) water and then gently blotted dry. Cleansing efficacy was calculated based on fluorescence measured at the site before and after washing. These authors reported greater cleansing efficacy for soap bars than for syndet bars.

Puvvada et al. describe a method using makeup materials (e.g., lipstick or mascara) as model soils (14). Washing involved rubbing a (wetted) bar on the skin for one minute, rinsing with 35°C water for 30 seconds, and then patting dry. Cleansing efficacy was estimated from the difference in chromameter measurements taken before and after washing. While this method employs model soils that represent everyday cleansing needs, the wash conditions are exaggerated beyond expected use. Mills et al. also described a method using makeup (opaque camouflage cream) as a model soil (15). The makeup was applied to nine test sites on the ventral forearms, and then a technician washed each site in a controlled manner with a pad lathered with one of the test cleansers. The sites were rinsed to remove all traces of lather then rank-ordered based on the level of cleansing. Of the cleanser types tested, a bar soap product was ranked among those with the poorest cleansing efficacy, followed by a liquid soap marketed for sensitive skin. Cleansing products based on sugar surfactants (polyhydroxy fatty acid amides) were ranked as having the best cleansing efficacy. These products were also found to have the best skin compatibility in a chamber scarification test (16).

We also assess cleansing efficacy using a makeup removal model. Subjects are screened on the basis of skin tone (chromameter L^*-value); only subjects with sufficiently light skin are enrolled to assure good contrast with the model soil. A dark, oil-based makeup is applied to application areas marked on the volar forearms, and 30 minutes later the color at each site is measured again. Then a bar or liquid cleanser lather is generated, and a technician washes a randomly assigned site with lathered fingers for 10 seconds; the site is rinsed for 10 seconds with warm water and gently patted dry. A water-only wash is commonly included as a control. Thirty minutes after rinsing the color at the site is measured again. The color difference (ΔE) is calculated from the pre- and post-wash $L^*a^*b^*$ values as an indicator of cleansing efficacy. This method is useful for assessing the relative cleansing efficacy of a variety of personal cleanser types. For example, the makeup removal method was used to compare cleansing efficacy of traditional soap bars

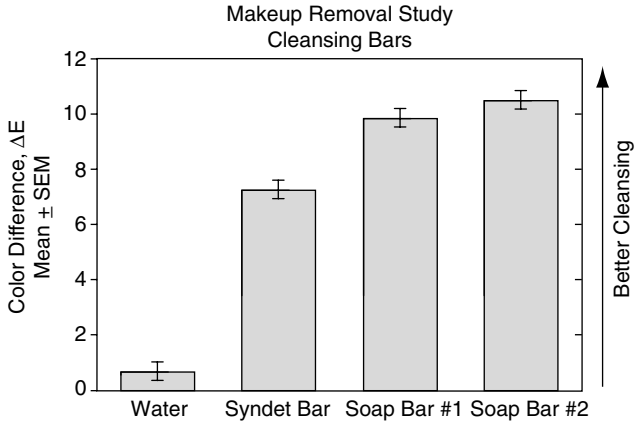

Figure 1 Results from a makeup removal study comparing two soap bars and a syndet bar. The soap bars cleaned significantly better than the syndet bar ($P < 0.05$), and all of the cleansing products removed significantly more of the model soil than water.

and a syndet bar. The cleansing efficacy for the soap bars was significantly better than that for the syndet bar under this method (Fig. 1).

Liquid personal cleanser forms are becoming increasingly popular, and some of these cleansers incorporate benefit agents such as petrolatum that deposit on skin during use. This product performance model seems inconsistent with a cleanser's purpose, i.e., how can products that are designed to deposit material onto the skin function effectively as cleansers? One strategy involves employing technology that takes advantage of varying conditions that exist at different stages of the wash process. The benefit agent remains suspended in the lather during cleansing but upon rinsing this lather becomes dilute and the emulsion suspending the benefit agent "breaks," depositing the benefit agent onto the skin. To demonstrate that this type of cleanser can effectively remove soil, we used the makeup removal test to assess the cleansing efficacy of two marketed liquid hand cleansers and three prototype liquid hand cleansers containing different levels of petrolatum (Fig. 2). The petrolatum-depositing products showed significantly better cleansing efficacy than the marketed cleansers under this model, and the results suggest that cleansing efficacy improved with increasing petrolatum level. Since the model soil is an oil-based makeup product this could reflect a "like dissolves like" phenomenon, which should translate to good removal of lipophilic soils from the skin in actual use. There are other examples of using lipophilic materials to aid soil removal. In ancient times the Romans applied oil to their skin during the cleansing process (17), and lipid-based washing products are again being promoted for use by patients with sensitive skin and atopic dermatitis (18,19).

Cleansing efficacy is important but for a product like a hand wash, which is used multiple times each day for washing, good skin compatibility is also necessary. We conducted a controlled application pilot study simulating in-use exposure to assess this parameter for the petrolatum-depositing hand wash (25% petrolatum). Healthy adult females were enrolled in a hand washing study comprising a seven-day pre-treatment period and a five-day treatment period. Subjects were provided with a regular liquid hand cleanser for hand washing and a syndet-based bar to use for showering. They were instructed not to apply cleansing products to the dorsal part of their hands and to avoid any activity that required hand immersion in a surfactant solution, e.g., washing dishes. Moisturizer use was prohibited. Ten subjects who exhibited a sufficient level of hand dryness entered the treatment phase. Treatment was conducted as a paired comparison.

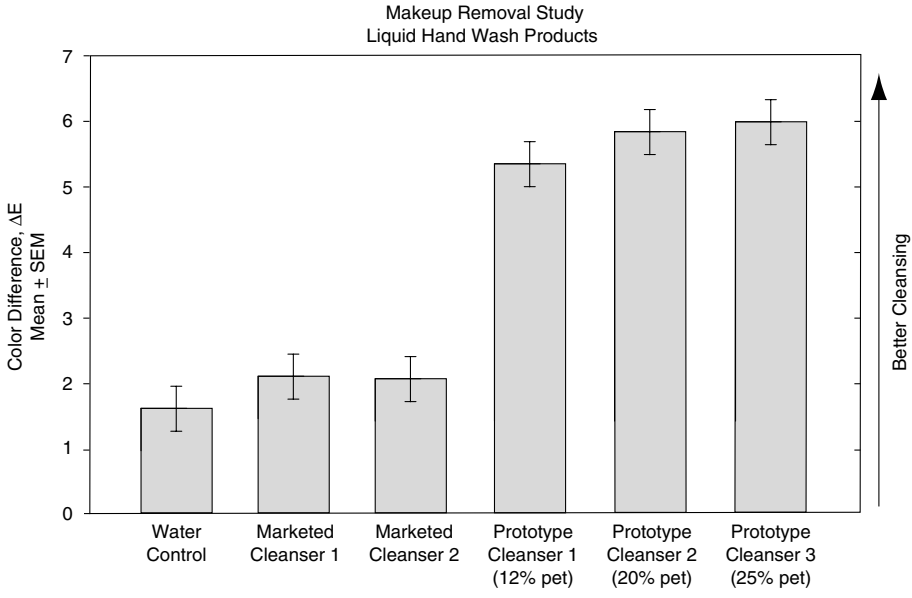

Figure 2 Results from a makeup removal study comparing three prototype petrolatum-depositing hand wash formulas to two marketed hand wash products. The percentages of petrolatum are shown in parentheses. The prototype formulas cleaned significantly better than the marketed hand washes and water ($P < 0.05$).

A technician washed one randomly assigned hand with the petrolatum-depositing hand wash product for 10 seconds following a prescribed procedure; the other hand was wet, rinsed, and patted dry. There were five wash visits each day, spaced by 30 minutes, with the washing procedure conducted four times in succession at each visit. Thus, subjects' hands were washed a total of 20 times each day. Hand condition was evaluated visually (20) and instrumentally (CM-825) at baseline, before washing, and two hours after the final wash each day. Subjects acclimatized for 30 minutes in a controlled environment room before each evaluation.

Expert visual evaluation showed little difference in erythema production between the hand wash and control (Fig. 3). In fact, the hand wash generally produced somewhat *less* erythema than the control. In addition, the hand wash produced marked dryness improvement compared to control at the post-wash evaluations, and there was progressive improvement in dryness observed at the pre-wash evaluations over the course of treatment (Fig. 3). Trends in the skin capacitance measurements, which provide an indirect assessment of stratum corneum hydration, paralleled the expert dryness scores. These results demonstrate that this petrolatum-depositing hand wash shows good skin compatibility and can actually improve dry skin condition, even under exaggerated exposure conditions.

PERSONAL CLEANSER EFFECTS ON SKIN

Surfactant Types Commonly Used in Personal Cleansers

While some new cleanser technologies can combine effective cleansing with the potential to improve skin condition, the focus for the majority of personal cleansing products remains on minimizing the potential for skin damage. Surfactants make up the bulk of most personal cleansing products and are primarily responsible for a product's in-use

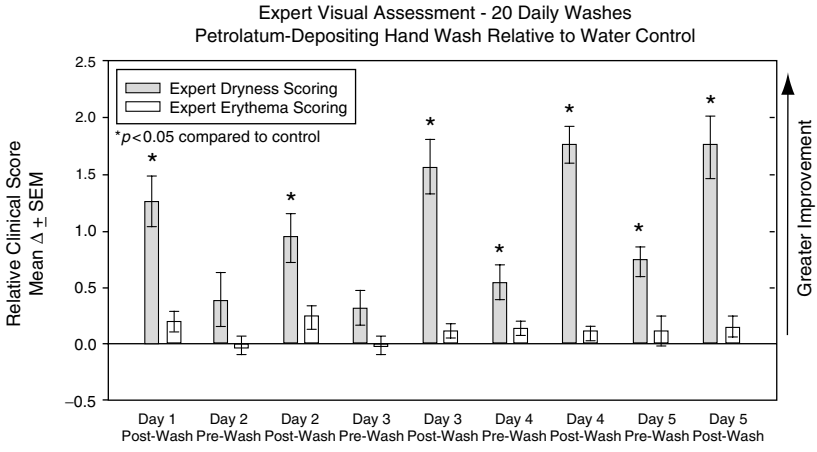

Figure 3 Expert visual dryness and erythema results from a hand washing pilot study comparing a petrolatum-depositing hand wash product to a water control. The hand wash product improved dry skin condition, even when used for washing hands 20 times daily.

properties, e.g., lather, and for its effects on skin. While all surfactant molecules are amphiphilic, there are distinct surfactant types. A surfactant's dissociation behavior in water provides a convenient basis for classification.

Anionic Surfactants

These surfactants dissociate in water to yield a surfactant with a negatively charged hydrophilic group and a cation that is usually an alkali metal (sodium or potassium) or a quaternary ammonium species. Anionic surfactants are used in a wide variety of bar and liquid personal cleansing products and account for about 50% of worldwide surfactant production (21,22). Soap, which is chemically the alkali salt of a fatty acid, is the best-known anionic surfactant, but a variety of synthetic (i.e., non-soap) anionic surfactants are commonly used in personal cleansing products, including the acyl isethionates, alkyl sulfates, and alkyl ether sulfates (AES). The acyl isethionates have good skin compatibility and are good detergents and lime soap dispersants, viz they inhibit the formation of hard water scum. Sodium cocoyl isethionate is an example; this surfactant is a common primary surfactant in "mild" cleansing bars. The alkyl sulfates are widely used in cosmetic products ranging from skin cleansers to toothpastes. They have good foam-forming properties and produce creamy lather but do not perform well in hard water. Alkyl sulfates have a marked potential to irritate skin. Sodium lauryl sulfate (SLS), an alkyl sulfate found in many personal care products, is often used as a model irritant. The AES are similar to the alkyl sulfates but their hydrophobic portion comprises ethylene oxide units rather than a straight-chain hydrocarbon. This gives AES a number of advantages over alkyl sulfates, including better lather formation in hard water and better lime soap dispersion. AES are also less irritating than alkyl sulfates, and their skin compatibility is improved by increasing the degree of ethoxylation (23,24). Sodium laureth sulfate is an example of an AES that is commonly found in personal cleansing products.

Cationic Surfactants

These surfactants dissociate in water to yield a surfactant with a positively charged hydrophilic group and an anion. Fatty amine or ammonium salts and quaternary ammonium salts are examples. Cationic surfactants are generally not good detergents or

foaming agents, and they are usually incompatible with anionic surfactants. However, being positively charged they adsorb to biological (and other) surfaces, which tend to have a net negative charge at a neutral pH. This property makes cationic surfactants useful as antistatic agents in hair conditioning products. The quaternary ammonium compounds have marked antibacterial activity and are often found in toiletries such as deodorants and mouthwashes.

Nonionic

These surfactants do not dissociate in water. Instead, their hydrophilic group is commonly an alcohol, phenol, ether, ester, or an amide. Alcohol ethoxylates and alkylphenyl ethoxylates are two common examples of this type of surfactant. A "new" class of nonionic surfactants employs various sugars as hydrophilic groups. The uncharged nature of nonionic surfactants makes them compatible with other surfactant types, and they also show reduced sensitivity to conditions such as water hardness or salinity and to formulation pH. Common examples are the sorbitan esters (marketed as SPAN) and their ethoxylated counterparts (marketed as TWEEN). As a class, nonionic surfactants tend to exhibit good skin compatibility (15,25), but they still have a potential to interact with and negatively impact the stratum corneum (26).

Amphoteric Surfactants

These surfactants have two functional groups, one anionic and one cationic. Their character is determined by the pH of their environment; amphoteric surfactants are anionic under alkaline conditions and cationic near or below their isoelectric point, i.e., the point at which the surfactant molecule carries no net charge. Betaines, which actually carry a positive charge in both acidic and alkaline media (27), are among the most widely used amphoteric surfactants and are found in both bar and liquid cleanser formulations. Betaines are used to improve lather quality or to increase the viscosity of liquid formulations. They generally show good skin compatibility and can decrease the skin irritation potential of harsher anionic surfactants when used in combination with them (24,28). But betaines are not without issues. There are a number of reported cases of contact allergy to cocamidopropyl betaine (29–32), one of the most commonly used surfactants in this group, and this surfactant was named the contact allergen of the year in 2004 (30). However, the effective incidence of issues is low given the widespread use of this surfactant in personal care products. Still, manufacturers may be able to reduce the risk of contact allergy by using a higher grade of betaine material as data suggest the allergic response is caused by impurities rather than by the surfactant itself (32–34).

Surfactant Interactions with the Skin

Personal cleansing products are complex systems that often contain several surfactants. Even a seemingly simple cleanser such as a soap bar comprises a mixture of soap species. Several of the mechanisms believed to drive surfactant interactions with the skin are discussed below. These are presented separately for convenience but the mechanisms are undoubtedly interdependent to some degree.

Surfactant Structural Considerations

The surfactant composition of a personal cleanser in large part determines the product's potential to impact skin, and there are numerous published studies that compare and

contrast the skin effects of individual surfactants and full formula cleansers. But skin compatibility can vary even within a given surfactant type. Soap provides a good example. As defined previously, soap is the alkali salt of a fatty acid. The regulatory definition of soap is quite narrow and only a few true soaps remain on the market in the United States (35–37), but products based on soap-syndet mixtures (so-called combo bars) persist in the U.S. market, and soap remains a popular cleansing form in many other countries. The raw material used in soap manufacture is often a mixture derived from tallow, vegetable oils, and their processed derivatives (38,39). Being derived from natural sources, these raw materials comprise a mixture of fatty acid species. The fatty acid compositions of triglycerides from several different sources that are used in soap manufacture are shown in Figure 4 (21).

The varying composition of the raw materials used in soap manufacture means that saponfication, i.e., reacting triglyceride with alkali to form soap and glycerin, yields a mixture of soap species. The chemical composition of the finished soap product determines its skin compatibility. For example, Dahlgren et al. used soap bars prepared with different relative amounts of tallowate and cocoate soaps to demonstrate that the level of dryness and erythema following controlled washing is dependent on the ratio of these soap species (40). In this work a bar based entirely on coconut-derived soap was harshest to skin, while a bar based entirely on tallow-derived soap was mildest. The mildness of bars based on intermediate combinations of cocoate and tallowate soap fell between these extremes. These results, and the differences in the fatty acid compositions of the raw materials (Fig. 4), indicate that the distribution of soap species in a personal cleansing product is an important determinant of its skin compatibility.

Studies conducted with pure fatty acids demonstrate this effect at a more fundamental level. Blank conducted patch tests using coconut oil and pure fatty acids commonly found in soap (41). Patches were applied for 24 hours to intact skin on the upper arms of normal (healthy) subjects, subjects who previously exhibited a reaction to soap (pruritus or vessiculation), and subjects with evidence of contact or atopic dermatitis. Reactions were read one hour after patch removal. The results are summarized in Fig. 5. The percentage of positive reactions in each test group shows clear fatty acid chain length dependence, with the incidence decreasing as the chain length increases. Kellum

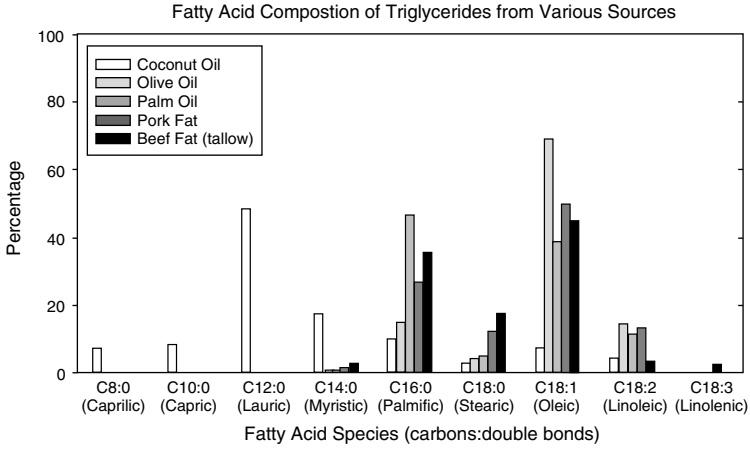

Figure 4 Typical fatty acid composition of some triglycerides commonly used to manufacture soap. *Source*: From Ref. 21.

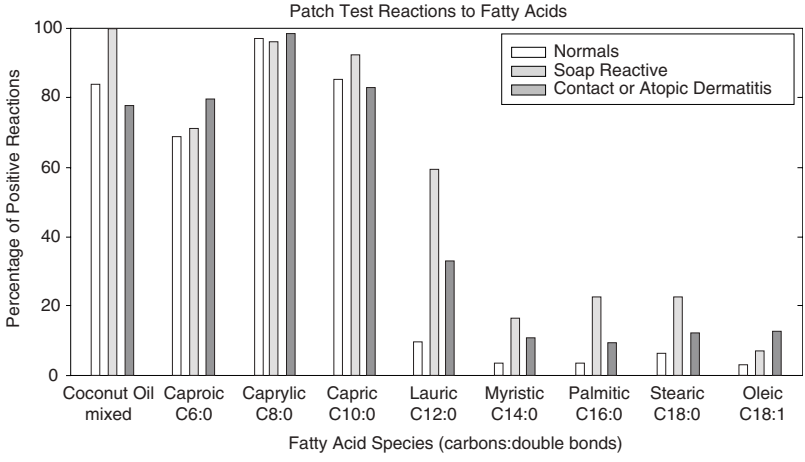

Figure 5 Results from a patch test study conducted among normals, soap reactive individuals, and individuals with contact or atopic dermatitis. There is a decreased irritation potential with increasing fatty acid chain length. *Source*: From Ref. 41.

conducted a similar study, patching saturated fatty acids with even-numbered chain lengths from C_2-C_{16} on the backs of healthy volunteers for up to 15 days (42). Response was greatest to the C_8-C_{12} acids, with the C_{12} homologue producing the most severe reactions. The author hypothesized that the C_{12} chain length might be optimum for incorporation into or passage through biological membranes. Stillman et al. conducted patch testing with even- and odd-numbered saturated fatty acids ranging from C_3-C_{18}; several unsaturated C_{18} species were also tested (43). The results again showed the greatest reaction to the C_8-C_{12} acids. Of the unsaturated species tested, only linoleic acid (C18:2) produced irritation.

García-Domínguez and coworkers proposed a five-step model to account for the increased irritancy of C_{12} ionic surfactants (44). The model involves both ionic and hydrophobic interaction between the surfactant molecule and proteins at the skin surface, ultimately leading to migration of the charged and hydrophobic portions of the surfactant molecule into the protein. Irritation results from localized environmental changes within the protein structure induced by the presence of surfactant. Thus, the higher irritancy of C_{12} surfactants is again attributed to structural characteristics that favor their interaction with the skin.

These studies show that soap composition, in particular the chain length distribution of fatty acids in the soap, is an important determinant of soaps' skin compatibility. Using tailored mixtures of fatty acid starting material, in which the longer chain length species predominate, is one approach that is used to effectively improve the skin compatibility of soap bars (45,46).

The skin compatibility of many synthetic detergents exhibits a structural dependence similar to that of soap. Kligman and Wooding used patch testing to estimate the ID_{50}, the concentration needed to produce a discernible irritant reaction in 50% of the study population in 24 hours, and the IT_{50}, the number of days of continuous exposure to produce a threshold reaction in 50% of the study population, for a series of sodium alkyl sulfates (47). They observed minimum values for both parameters, i.e., greatest irritancy, for the C_{12} chain length (SLS). Dugard and Scheuplein measured the effect of C_8-C_{16} homologues of the sodium salts of primary aliphatic acids (soap), sodium *n*-alkyl sulphates, and *n*-alkylamine hydrochlorides on the permeability of human epidermal

membranes (48). They observed the greatest permeability increase with the C_{12} and C_{14} members in each series. Robbins and Fernee reported a maximum in the swelling behavior of epidermal membrane, a parameter reported to parallel anionic surfactants' ability to elicit erythema in vivo, for the C_{12} homologue in a series of alkyl sulfates (49). They note that surfactant binding to keratin is also optimal at this chain length. Rhein et al. used a similar experimental procedure and reported maximal swelling for the C_{12} or C_{14} homologues of alpha olefin sulfonates, paraffin sulfonates, linear alkylbenzene sulfonates, and alkyl sulfates (23). Increases in swelling response with time suggested surfactant effects on keratin secondary and tertiary structure. Imokawa and co-workers conducted experiments using a surfactant solution circulation apparatus to assess the skin roughening potential of C_8-C_{14} soaps and of homologous series of various synthetic surfactants (50,51). The C_{12} soap and synthetic surfactants produced the greatest skin roughening effect within each homologous series.

These examples illustrate a common surfactant feature that reduces skin compatibility, namely, a chain length of about C_{12}. Thus, one way to improve skin compatibility of syndet-based cleansers is to minimize their content of short-chained surfactants, especially C_{12} species, analogous to the soap bar example given earlier. Using a modified surfactant can also improve skin compatibility. For example, Rhein et al. reported a reduction in stratum corneum swelling produced by C_{12}-C_{14} alkyl ethoxy sulfates as the degree of ethoxylation increases (23). Finally, personal cleansers' skin compatibility is often improved by using mixtures of different synthetic surfactants (23,24,28,52).

Removal of Skin Lipids (Delipidization)

As noted earlier, the hydrolipid film on the surface of the skin is important for maintaining skin health. Epidermal lipids, which serve as the "mortar" between the corneocyte "bricks" in the stratum corneum, are also important to maintaining skin health and stratum corneum barrier function (53–55). Patient populations that exhibit heightened sensitivity to personal cleansing products, such as individuals with atopic dermatitis, often exhibit aberrant epidermal lipid composition or structure (56,57), and di Nardo et al. found an inverse relationship between susceptibility to irritation from SLS and levels of certain stratum corneum ceramides in normals (58). Visscher et al. reported an increase in transepidermal water loss rate, consistent with stratum corneum barrier compromise, following acetone/ether extraction of lipid from the skin surface and upper stratum corneum (59). Findings such as these, coupled with surfactants' natural ability to emulsify oils and lipids, suggest that surfactants' negative impact on skin could result from delipidization or selective removal of lipid components from the stratum corneum.

Kirk examined the amount of casual lipid, i.e., lipid on the skin surface, removed by one minute of controlled hand washing (60). Results from washing with water and with several bar cleansers are summarized in Figure 6. As expected, water is relatively inefficient at removing skin surface lipid. The surfactant bars are more efficient but still do not completely strip the skin surface of lipid. However, even partial removal of the hydrolipid film may effect changes in skin condition. Morganti reported that washing the skin with water decreases surface lipids by about 24%, while washing with soap reduces surface lipids by about 36% (61). Surprisingly, using a syndet bar to wash the skin reduced surface lipids by about 50%. Removal of skin surface lipids was hypothesized to decrease the skin's ability to retain natural moisturizing factors (NMF), ultimately leading to dry skin. Sauermann et al. also reported removal of NMF by exposure to water and to soap or syndet solutions, but these authors did not measure lipid removal (13).

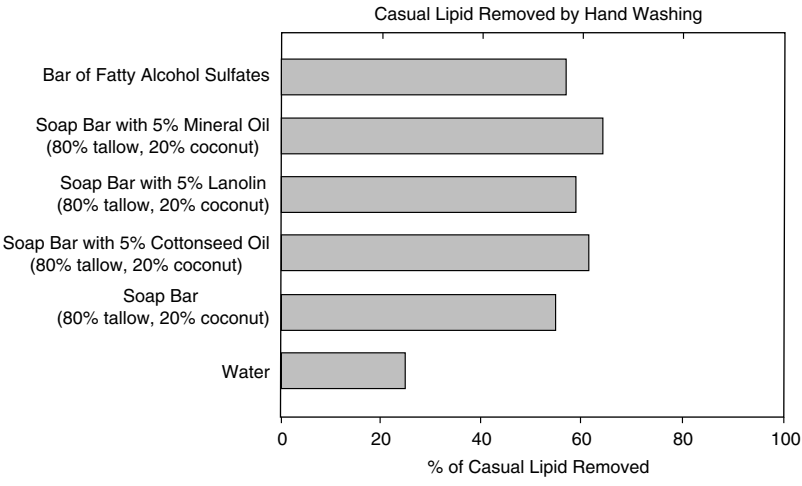

Figure 6 Percentage of casual lipid removed by 1 minute of hand washing. Washing with water alone removes about 25% of casual lipid; the amount of casual lipid removed increases to 50%–60% when a cleanser is used. *Source*: From Ref. 60.

Bechor et al. reported $>70\%$ relative change in casual sebum levels after washing the cheek for 30 seconds with water or various personal cleansing products (62). Sebum removal was not linked with clinical symptoms in this study, and sebum levels returned to baseline values in about one to two hours. Gfatter et al. examined the effect of washing on skin surface lipid content in a group of infants aged two weeks to 16 months (mean age 3.2 months) (63). Treatment consisted of a one-minute wash performed on each child's chest and buttock with tap water (control), a synthetic detergent liquid, a synthetic detergent bar, or a soap bar. Skin surface lipid content and several other parameters were measured 10 minutes after washing. All of the washes removed a significant amount of skin surface lipid. Not unexpectedly the least removal was observed for the control group ($-0.93\ \mu g/cm^2$), the greatest removal for the soap bar group ($-4.81\ \mu g/cm^2$). The authors conclude that removal of surface lipid might reduce stratum corneum hydration and lead to dryness and scaling.

Personal cleansers can also induce changes in epidermal lipids, which are responsible for maintaining the skin's barrier function. Imokawa et al. reported that the stratum corneum lipid lamellar structure of forearm skin was disrupted following a 30-minute exposure to 5% aqueous sodium dodecyl sulfate (64). Post-exposure analysis showed a selective loss of various lipid components including cholesterol, cholesterol ester, free fatty acids, and sphingolipid. The authors noted that surfactant exposure produced an enduring chapped, scaly appearance and reduced hydration. Recovery studies conducted by applying isolated lipid fractions to surfactant-treated skin suggested a role for sphingolipids in helping to restore the skin's ability to retain water. Rawlings et al. examined lipid structure and composition in the normal skin of adult females and in xerotic skin induced by soap washing (65). Xerotic skin samples were obtained by tape stripping the backs of subjects' hands following one week of three-times-daily washing with soap; normal skin samples were obtained from a control group of subjects. The authors noted an apparent perturbation of desmosomal degradation, with intact desmosomes persisting to higher levels in the stratum corneum in soap-treated skin. The lipid bilayer structure in the outer stratum corneum was degraded in both skin types, but the normal and soap-treated structures had a different appearance. The authors found a decreased stratum corneum

ceramide content in soap-treated skin, with a progressive, deeper loss accompanying more severe dry skin grades. However, the relative levels of the various ceramide species were not different in the two skin types. The authors concluded that alterations in stratum corneum lipid composition and organization, along with reduced desmosomal degradation, are responsible for the scaling that accompanies soap washing.

Fulmer and Kramer compared lipid content in normal and surfactant-induced dry skin in a paired, dry leg study (66). Subjects washed one randomly assigned leg three times daily with 4% sodium dodecyl sulfate solution for a period of two weeks; the other leg remained untreated as a control. At the end of treatment shave biopsies were taken for lipid analysis. In contrast to the results reported by some other groups, no alteration in the total amount of lipid per gram of stratum corneum protein resulted from the surfactant washing. In particular, the total ceramide level was not changed. However, ceramide, cholesterol, and free fatty acid profiles were altered in the surfactant-treated skin compared to control. The authors concluded that surfactant washing affects the quality, but not the quantity, of stratum corneum lipids, suggesting that surfactants' role in the dry skin process is related to perturbation of the stratum corneum formation process, not lipid extraction.

Other studies also call the hypothesized relationship between lipid extraction and surfactant-induced skin damage into question. Scheuplein and Ross examined the effect of three classes of compounds on human epidermal membrane permeability to tritiated water: lipid solvents (e.g., chloroform:methanol), hydrogen-bonded solvents (e.g., water, DMSO), and surfactants (sodium laurate, SLS) (67). Lipid extraction decreased the dry weight of the stratum corneum by up to 20% even though its gross appearance remained unchanged. Solvent extraction of epidermal lipids resulted in a large increase in membrane permeability; this effect was irreversible. Hydrogen-bonded solvents also increased permeability, which was attributed to resolvation and membrane expansion. Unlike solvent extraction, the increase in permeability from hydrogen-bonded solvents was largely reversible. Exposure to surfactant caused visible expansion in the plane of the tissue, suggesting that the anionic surfactants initiate uncoiling of alpha-keratin molecules to form beta-keratin. The effect was reversible for mild surfactant exposures but irreversible for more severe exposures. Follow-up work by Dugard and Scheuplein again showed reversible changes in human epidermal membrane permeability following exposure to surfactants belonging to three *n*-alkyl homologous series (48). They concluded that extraction of lipids or other epidermal components was not the primary mechanism responsible for the increased membrane permeability, and instead suggested that surfactants act on membrane proteins. Rhein et al. reported that the swelling response of stratum corneum exposed to surfactant solutions was reversible, again suggesting a limited role for lipid extraction in surfactant interactions with skin (23). Froebe et al. examined in vitro stratum corneum lipid removal by SLS and linear alkyl benzene sulfonate (68). Both materials removed detectable levels of lipid only above their CMC, demonstrating that lipid removal is a micellar phenomenon. The primary lipid species involved were cholesterol and free fatty acids; little or no ceramide was extracted. Even at the highest surfactant concentration used (2%), the amount of lipid material removed from the skin represented less than 7% of the total stratum corneum lipid, indicating that delipidization, or at least the removal of sizable amounts of stratum corneum lipid, is not a primary mechanism for surfactant-induced irritation.

Surfactant Binding to Stratum Corneum Proteins and Surfactant Penetration

Other studies also support a role for surfactant-protein interaction in the development of skin irritation. Imokawa et al. measured the specific rotation of bovine serum

albumin (BSA) in the presence of surfactant to assess surfactant-protein interaction (69). Changes in the specific rotation were the result of conformational changes in BSA due to interactions with surfactant. Studies conducted with a range of surfactants suggested that both ionic and hydrophobic interactions between the surfactant molecule and BSA determine the extent of denaturation. For example, the authors proposed a stepwise interaction between ionic surfactants and BSA that would ultimately lead to complete denaturation of the protein molecule. They reported an excellent correlation between surfactant-protein interaction, as determined by the BSA specific rotation method, and skin roughness measurements made with a circulation apparatus (69).

Imokawa also used a technique based on indigo carmine dye displacement to examine binding of surfactant to stratum corneum and reported that the skin roughening effects of surfactants are related to their ability to adsorb onto skin (11,51,70). Keratin denaturation was believed to follow surfactant adsorption, as in the BSA model, ultimately leading to skin roughness. Kawai and Imokawa later extended this model to explain the sensation of tightness (71). Their work showed that lipid removal from skin was related to tightness induction; however, delipidization of the skin with ether did not result in marked tightness, and surfactants' ability to remove lipids did not always parallel their potential to induce tightness. There was, however, a strong correlation between surfactant adsorption and tightness, and removal of skin surface lipids enhanced tightness upon subsequent surfactant exposure. The authors proposed a model in which stratum corneum lipid extraction by surfactant is a necessary step to induce skin tightness, but is itself not sufficient to cause tightness.

Prottey et al. analyzed tape strip or cup scrub samples collected from the backs of hands following immersion in surfactant solutions or water for acid phosphatase activity (72). They found a decrease in enzyme activity following surfactant exposure, which was attributed to acid phosphatase denaturation and subsequent enzymatic inactivation resulting from surfactant interaction with the protein. The authors reported an inverse relationship between remaining acid phosphatase activity and hand dryness, and proposed this enzyme as a marker for monitoring interactions between surfactants and stratum corneum proteins. Ananthapadmanabhan et al. examined the binding behavior of several surfactants to isolated guinea pig or human stratum corneum and reported that the extent of surfactant binding to stratum corneum correlated well with the irritation potential predicted by in vitro and in vivo methods (73). Rhein et al. noted a time-dependent effect on stratum corneum swelling for SLS, which was attributed to the interaction of surfactant with keratin and disruption of the keratin's secondary and tertiary structure (23). As noted earlier, swelling induced by this and other surfactants studied exhibited a maximum for C_{12}-C_{14} chain lengths. The swelling response was for the most part reversible except following exposure to soap concentrations $>1\%$ or prolonged (>24 hours) soap exposure. In a later review Rhein proposed a model by which surfactants interact with stratum corneum proteins that explains the observed swelling behavior (74). This model incorporates ionic and hydrophobic binding interactions and accounts for the effect of pH on both stratum corneum proteins and on anionic and cationic surfactants.

Mukherjee et al. examined the interaction of pure anionic surfactants and cleansing bars based on anionic surfactants with isolated stratum corneum in vitro by measuring displacement of 1-anilinonaphthalene-8-sulfonic acid (ANS), a fluorescent probe known to bind to stratum corneum proteins (75). Their results showed agreement between surfactants' ability to displace ANS from stratum corneum samples and their potential to irritate skin as predicted by in vitro and in vivo methods, suggesting that surfactants' potential for binding to stratum corneum proteins determines their in-use skin

compatibility. López et al. exposed porcine stratum corneum to solvent (chloroform-methanol) and nonionic surfactant (octyl glucoside) solutions (26). Solvent exposure removed stratum corneum lipids but did not affect stratum corneum adhesion. In contrast, surfactant exposure preserved epidermal lipids; however, the lipid domain structure was disrupted. The surfactant also damaged corneocyte envelopes and caused corneocyte dishesion, suggesting that surfactant-protein interaction plays a role in irritation development. Shukuwa et al. studied the impact of pure surfactants and 1% solutions prepared from full formula bars on corneocyte disaggregation and swelling, and on morphologic deterioration using stratum corneum disks isolated from forearm suction blisters (76). The test materials' tendency to induce corneocyte disaggregation did not correspond well with induced swelling behavior, e.g., SLS caused significant corneocyte disaggregation but only slightly greater swelling than water. The ranking of the test soaps based on corneocyte swelling was consistent with irritation potential predicted by the soap chamber test (77), and the authors propose corneocyte swelling as an in vitro model for predicting cleansers' skin effects. One caution with the extrapolations made in several of these studies, however, is that the results generated under controlled exposure protocols that are used to "validate" the in vitro test data are themselves not always predictive of consumer experience with personal care products (9,78,79).

Factors related to the personal cleanser use environment will also influence surfactant-skin interactions. For example, Berardesca et al. examined irritation resulting from 5% SLS applied to the forearm at temperatures of 4°C, 20°C, and 40°C (80). Measurements made after four days of once-daily treatment showed that barrier compromise and erythema production increased with temperature. Desquamation and reflectance (L^*-value) also exhibited temperature-dependent behavior. Clarys et al. demonstrated a temperature-dependent increase in the irritant response to two dish washing liquids over a much narrower temperature range: 37°C and 40°C (81). In both of these studies the increase in irritation with temperature was attributed to greater fluidity of the epidermal lipids and enhanced irritant penetration.

Water hardness is another variable that varies in different use situations. We showed that water hardness impacts the absolute and relative skin compatibility of commercial personal cleansing products; soap-containing bars being more affected than syndet-based cleansers (82). Fujiwara and coworkers conducted arm immersion experiments using solutions of sodium laurate to examine the relationship between water hardness (calcium ion) and calcium soap-deposition onto skin (83). They found that hardness in water increased soap deposition, driven especially by the presence of calcium in the rinse water. We extended this work using marketed cleansing bars tested under a consumer-relevant arm wash protocol (84,85). A syndet bar, a triethanolamine (TEA) soap bar, and a sodium soap bar were tested. Washing was divided into two phases: a wash phase and a rinse phase conducted with various combinations of deionized water and hardened water (11 grains/gallon calcium). The syndet and TEA soap bars produced significantly less dryness and erythema than the sodium soap bar in the presence of calcium, but the difference between the products was negligible in deionized water ($P \geq 0.48$ for inter-product comparisons). Greater deposition of calcium soap onto skin occurred under the hard water conditions. As reported by Fujiwara, the rinse step was particularly important in determining the compatibility of these cleansing bars with the skin. Although the specific interaction between the calcium soap and skin was not examined in either of the above studies, both provide an example of the role surfactant-skin interaction (i.e., calcium soap deposition) plays in determining personal cleansers' skin compatibility.

Effect of Personal Cleanser pH

The pH is thermodynamically defined as the negative logarithm of the hydrogen ion activity in aqueous solution. The pH is often defined in more practical terms as the negative logarithm of hydrogen ion *concentration*. Strictly speaking the hydrogen ion activity and concentration are not identical but in dilute solution this is a reasonable assumption. Many publications refer to the pH of the skin, but since the skin is not an aqueous solution it clearly does not have a pH. When a wet pH electrode is placed onto the skin, water-soluble materials on the skin surface dissolve; the pH of this solution is what is actually measured. Also, personal cleansing products, and even the preparations made from them, are usually not dilute solutions. In what follows, "pH" is used to remain consistent with the original references, even though in many instances what is measured is more correctly called an apparent pH.

Soap dissolves in water to form free fatty acid and strong base, e.g., sodium soap will react with water to produce small quantities of free fatty acid and sodium hydroxide. As a result soap-based cleansing bars usually produce lather with a higher pH than do products based on synthetic detergents. The inherent tendency for soap-based cleansers to produce lather/solutions with pH values in the range of about 9–10, coupled with their generally poor skin compatibility, frequently forms the basis for a hypothesized cause-and-effect relationship between a cleanser's pH and its potential to irritate the skin.

At a fundamental level, Ananthapadmanabhan et al. reported a pH dependence for sodium lauroyl isethionate adsorption to skin, showing a minimum from pH 7 to pH 9, suggesting that pH might play a role in determining surfactant-skin interactions (73). However, van Scott and Lyon examined the potential for tap water with its pH adjusted from 4.5-10.5 or 1% solutions of various soap and detergent products to denature keratin (86). Water had no effect on the denaturation of defatted keratin or keratin plus 1% sebum over the pH range studied. Similarly, there was no significant relationship between product pH values, which ranged from pH 6.7 to pH 10.1, and denaturation of any of the keratins studied. Robbins and Fernee reported no significant in vitro swelling change when stratum corneum was exposed to water with pH values adjusted to between 3 and 9 (49). They also examined the effect of pH on stratum corneum swelling response to three different surfactants: SLS, linear alkylbenzene sulfonate (LAS), or dodecyl trimethyl ammonium bromide (DTAB). SLS and LAS are anionic; DTAB is cationic. Decreasing the pH value from 9 to 3 reduced the swelling responses for SLS and LAS. However, the swelling response was unchanged or increased when the pH was lowered from pH 9 to 6, a range that is relevant to many personal cleansers. The swelling response for DTAB increased when the pH was lowered from pH 9 to pH 3. Dugard and Schueplein observed that buffer in the pH range 3.0–9.5 produced no increase in stratum corneum permeability in the absence of surfactant (48). These authors found no change in the rate of permeability increase as a function of pH for the three surfactants studied: sodium dodecanoate (pH range 7.5-9.5), sodium dodecyl sulphate (pH range 5.0–9.0), and sodium dodecylamine hydrochloride (pH range 3.0–7.5). Bettley and Donoghue also performed water permeability experiments using isolated human stratum corneum (87). Their work showed that water, pH 10 buffer, and "Teepol" (2° alkyl sulphate detergent) at its natural pH or buffered to pH 10 had a minimal effect on membrane permeability. However, membrane permeability was markedly increased by exposure to 1% or 5% solutions of sodium palmitate. Membrane permeability gradually recovered upon removal of the soap, which as mentioned earlier argues against epidermal lipid extraction as a mechanism of irritation. The authors instead suggested that irritancy is related to a surfactant's ability to penetrate the stratum corneum.

In vivo studies show a similar trend. Bettley and Donoghue also conducted patch testing with toilet soap and TEA soap (88). The TEA soap was less irritating than the toilet soap even though the solutions prepared from each product had a comparable pH value. This may reflect a counterion effect; Rhein et al. also reported reduction in swelling response, i.e., a reduced potential for skin irritation, from TEA salts of surfactants (23). Frosch reported the relative skin irritation potential of 23 cleansing bars marketed in the United States and Germany determined using a soap chamber test (9). These products represented a range of surfactant compositions and covered a pH range from 5.4 to 10.7. The published results do not support a cause-and-effect relationship between a cleanser's potential to irritate skin and its pH value. Van der Valk et al. conducted a similar experiment and assessed the skin compatibility of 13 marketed personal cleansers (89). Irritation from 2% aqueous solutions of the products applied to subjects' volar forearms on stratum corneum barrier function was assessed by evaporimetry. All of the cleansers significantly increased transepidermal water loss (TEWL) compared to control, but the results showed no relationship between cleanser pH and irritation TEWL. In a similar study, van der Valk conducted patch testing with pure surfactant solutions on unaffected forearm skin of healthy subjects and subjects with irritant contact dermatitis or atopic dermatitis (90). The results again did not support a relationship between surfactant pH and irritation. Van Ketel et al. examined the irritation potential of several liquid hand cleansers spanning a pH range from 3.5 to 10.0 by applying 8% aqueous solutions of each product under patch (91). These authors concluded that the pH value of a cleanser is not a useful parameter for predicting its irritancy. Murahata et al. used a modified soap chamber test to study the skin irritation from a series of buffer solutions covering a pH range from 4.0 to 10.5, 8% (w/w) detergent solutions prepared from marketed syndet and soap bars, and 8% solutions prepared from altered soap base in which low molecular weight free fatty acids were added to the bars during processing (92). The buffers altered the skin surface pH but did not produce irritation. Likewise, the cleanser preparations changed the skin surface pH, but there was no correlation between pH and irritancy. One seeming exception is a patch test study by Baranda et al. conducted with 27 cleansing bars (tested as 8% emulsions), two undiluted liquid cleansers, and water (93). These authors reported a significant correlation between irritation and cleanser pH. However, the coefficient of determination calculated from the reported results is $r^2 = 0.244$. Thus, only about 25% of the variability in irritation that was observed in the study is explained by differences in cleanser pH.

Taken together, these in vitro and in vivo results suggest that the skin irritation potential of a personal cleansing product is primarily driven by differences in the chemical and physical properties of its component surfactants rather than by the pH value. However, personal cleansing products could affect skin condition in other ways. For example, Ananthapadmanabhan et al. conducted experiments to study the effect of pH on the physical properties of the stratum corneum (94). A series of in vitro experiments was conducted using Yucatan piglet skin as a model substrate. Sections of isolated stratum corneum were placed into the wells of microtiter plates and buffer or buffered surfactant solutions were added. Samples intended for swelling analysis (optical coherence tomography) were soaked for five or 21 hours at 37°C. Samples intended for lipid fluidity analysis were soaked for about 16 hours at room temperature. These experiments showed an increase in stratum corneum swelling at pH 10 compared to the other pH values; this effect was increased by the addition of surfactant. Lipid fluidity decreased at pH 10 relative to the other pH values; surfactant again increased this effect. The authors conclude that there is a direct effect of pH on stratum corneum protein swelling and lipid rigidity; both are greater at pH 10 than at pH 6.5 or pH 4.

Sznitowska et al. studied the effect of pH on the lipoidal route of stratum corneum penetration (95). Suspensions of two model compounds, hydrocortisone and testosterone, were prepared at pH values ranging from 2.0 to 10.0 (hydrocortisone) and from 1.0 to 12.0 (testosterone). Penetration was studied using full thickness cadaver skin mounted in flow-through diffusion cells. The studies were conducted with untreated skin and with skin pretreated with methanol-chloroform (11) or Azone, a material that alters stratum corneum lipid organization. The results from the experiments conducted with intact skin showed no significant effect of pH on the penetration of the model compounds in the range from 1.0 to 11.0. Removal of skin lipids with methanol-chloroform increased penetration, as did pretreatment with Azone. However, no significant pH effect on penetration was found for either pre-treatment method. A follow-up study was conducted to examine the effect of pH on lipid and free fatty acid extraction, lipid packing, and keratin conformation (96). Human stratum corneum samples were shaken for 24 hours with buffers ranging from pH 1 to 12. Buffer pH had no large impact on the amount of sterols or ceramides extracted, but free fatty acid extraction was pH-dependent, being maximal at pH 11 and 12. Differential scanning calorimetry showed some disordering of lipid packing in alkaline-treated samples. The changes were not instantaneous and required >1 hour exposure, becoming maximal after about eight hours. Fourier transform infrared spectroscopic analysis showed that the stratum corneum was largely unaffected by exposure to the buffer solutions, with no major changes to lipid packing motifs. Keratin conformation also appeared to be largely unaffected by buffer exposure, though there was some evidence that intracellular keratin took on a more ordered conformation at alkaline pH values. These authors concluded that the stratum corneum is remarkably resilient to extended exposure to both highly acidic and highly alkaline environments.

In adults the skin surface is normally slightly acidic, giving rise to the concept of the so-called "acid mantle." Healthy adult skin exhibits a very good ability to recover from pH changes even when challenged with alkaline solutions having a pH value around 13 (97). Literature indicates that personal cleansing products can transiently affect the skin surface pH in both adults and infants. As was mentioned previously, Gfatter et al. examined the effect of washing infants' skin with synthetic detergent and soap-based cleansing products (63). Washes were conducted with water (pH 7.9–8.2), a synthetic detergent bar (pH 5.5), a liquid synthetic detergent cleanser (pH 5.5), or a soap bar (pH 9.5). Skin surface pH measurements were made 10 minutes after washing. All washes increased the skin surface pH, with the water control producing the smallest increase ($+0.20$ units). Both synthetic detergent cleansers increased the skin surface pH by $+0.29$ units, significantly greater than the control. The soap produced the greatest skin surface pH increase, $+0.45$ units. This increase was significantly greater than that produced by the control or the synthetic detergent cleansers.

Changes in the skin surface pH resulting from washing with personal cleansing products can persist for longer periods. Bechor et al. examined the time course of changes in skin surface pH following controlled washing (62). Adult volunteers washed their faces for 30 seconds with one of 41 cleansing products covering the surfactant composition range from soap to synthetic. The skin surface pH was measured at defined times for up to 200 minutes after washing. The results from this study show that cleanser-induced elevation of skin surface pH persisted for as long as 94 minutes after washing.

Korting et al. conducted eight-week crossover studies to demonstrate the potential for personal cleansers to alter skin surface pH. Liquid syndet cleansing preparations adjusted to pH 5.5 or 8.5 were used as test products. Subjects washed sites on their forehead and the ventral forearm twice daily for one minute. One cleanser was used for the first four weeks, the other for the remaining four weeks. Skin parameters were assessed at

various times during each period, at least six hours after the previous wash. Both studies showed that washing with the pH 8.5 product resulted in a higher skin surface pH than washing with the pH 5.5 product. The cleansers produced no consistent difference in TEWL or skin surface roughness (98) but did influence the skin's microflora (99). No cleanser effect was observed on coagulase-negative Staphylococci populations, but Propionibacteria counts were increased when the cleanser at pH 8.5 was used. A similar effect on bacterial populations was demonstrated in a crossover study in which subjects used a full syndet bar or a soap bar for cleansing (100). The authors report that overall the skin surface pH was higher by 0.3 units and that Propionibacteria counts were elevated during the period of soap washing. These products were later compared in a three-month use study conducted among adolescents and young adults with acne (101). Fewer inflammatory lesions were observed in the group using the full syndet bar product. The authors extrapolate results from the earlier study conducted with liquid cleansers to rule out an effect due to differences in cleanser composition.

Alteration of skin surface pH might also effect more fundamental changes in the stratum corneum. For example, Fluhr et al. examined the impact of pH on stratum corneum acidification and integrity in a murine model (102). The backs and flanks of hairless mice were treated twice daily for three days with secretory phospholipase inhibitor (bromphenacylbromide or 1-hexadecyl-3-trifluoroethylglycero-sn-2-phosphomethanol) or vehicle control. Free fatty acid (palmitic, stearic, or linoleic acid) was co-applied to some animals. The effect of pH was examined by immersing flanks of anesthetized mice in bffer solution (pH 5.5 or pH 7.4) for three hours. The authors found that treatment with secretory phospholipase inhibitor increased skin surface pH and decreased barrier function (TEWL) and integrity (tape stripping), demonstrating a role for phospholipid metabolism in both these processes. Co-application of free fatty acid or exposure to pH 5.5 buffer normalized these effects. However, exposure to pH 7.4 buffer alone produced barrier alterations similar to the inhibitors, and exacerbated barrier effects in inhibitor-treated mice.

Barel et al. compared the skin effects resulting from use of a syndet bar (pH of 2% solution = 6.9) or a soap bar (pH of 2% solution = 9.6) in a blinded home-use test (103). Subjects washed their entire body with the assigned product at least once daily for a period of 10 weeks. Skin surface pH, TEWL, redness (chromameter a^*-value) and stratum corneum hydration were measured at baseline and endpoint on the hand, forearm, upper arm, neck, and leg. The skin surface pH after using with soap was significantly higher than after using the syndet bar on the upper arm, neck, and leg. The difference between the mean pH values measured at study end was ≤ 0.4 unit, and the mean skin surface pH was in all cases ≤ 6.0. None of the other instrumental measurements showed a difference between the two treatment groups, and expert evaluation of dryness and erythema showed that daily use of the products did not induce visible skin changes. Subjective ratings of overall irritation/mildness showed a trend favoring the syndet bar at the end of the 10-week use period, but it seems likely based on the earlier discussion (e.g., the work of Imokawa) that this was due to a factor other than the product pH. The results of this study again highlight the difficulty of predicting in-use experience with controlled exposure models.

Other Ingredient Considerations

Surfactants determine many of the actions personal cleansing products have on the skin, but other ingredients can also have an effect. For example, certain polymers are used in personal cleansing products as formulation aids, to alter skin feel, or are substantive on skin, providing skin-protective properties (104–106). Glycerin is a

humectant ingredient used in many leave-on moisturizers that can also facilitate desmosome degradation (107). But being water soluble, it is difficult to deposit an effective level of glycerin on the skin in the rinse-off context that applies to most personal cleansers. However, glycerin can have other effects when used in personal cleansers. For example, Dahlgren et al. showed that incorporating glycerin into a soap bar improved the product's perceived moisturization benefit even though clinical endpoints are unchanged (40). As was mentioned earlier, some personal cleansers can now deposit effective levels of petrolatum onto the skin during use. These new petrolatum-depositing cleansers can produce marked improvement in dry skin condition; the prototype hand wash products described earlier are an example. Beyond this, there is evidence that topically applied petrolatum permeates the stratum corneum and improves barrier function (108), and that petrolatum deposited from a body wash can improve lipid bilayer structure in the outer stratum corneum (109) and improve stratum corneum barrier function (110).

Ancillary ingredients can also negatively impact skin condition. Fragrances are widely used in personal cleansing products. These materials often serve a functional role, covering the base odor of other formula components, and enhance product aesthetics and the cleansing experience. However, fragrances are frequently implicated as a cause of contact dermatitis and as a potential triggering factor in disease conditions such as atopic dermatitis. Since manufacturers rarely identify specific fragrances or fragrance components, identifying an offending agent is difficult. Using a cleanser that is labeled as "unscented" or "fragrance-free" does not guarantee that fragrance will not be an issue. Fragrance-free, for example, implies that a product has no perceptible odor, but these products can contain a low level of fragrance, smaller than the amount needed to impart a noticeable scent, to mask the odor from raw materials (111). A complicating factor is that some fragrance-free products contain ingredients such as preservatives or natural oils that provide scent as a secondary function, but that can also be a covert source of dermatitis (112,113).

SOME PRACTICAL CONSIDERATIONS WHEN CHOOSING A PERSONAL CLEANSER

Dermatologists and consumers are faced with a variety of choices when recommending or selecting a personal cleansing product. The previous sections of this chapter reviewed some of the available literature that examines factors governing the interaction between surfactants and the skin from a theoretical standpoint. While many of the studies presented were not conducted under in-use conditions, and some of the conclusions differ, they demonstrate that personal cleansers can impact skin in a number of ways and produce a range of skin effects. What does this mean from a practical standpoint?

Facial Cleansing

Facial cleansing is a primary need for most individuals. Apart from being a key interface for social interaction ("put your best face forward"), the face is a prime location for the accumulation of endogenous and exogenous soils. Sebaceous gland size and density are greatest on the face, upper back, and chest. The secretions from these glands, in conjunction with applied cosmetic products, help create a hydrolipid film on the skin surface that can effectively trap environmental pollutants (e.g., dust, and cigarette smoke). But while the accumulation of soil necessitates effective facial cleansing there are also

considerations that argue against excessive cleansing. For example, the facial stratum corneum has fewer cell layers than other parts of the body, except for the genitalia (114). A thinner stratum corneum barrier could increase susceptibility to irritation. The face is a site commonly associated with "sensitive skin," which by definition is based on subjective irritation and excludes individuals with pre-existing skin disease (115). This condition, which is estimated to affect about 50% of females, is reportedly associated with a defective stratum corneum barrier and to improve with a controlled skin care regimen (116). Facial skin is also moveable and rich in sensory nerves, so sensations such as tightness or tautness are more easily noticed. A retrospective study conducted by de Groot showed that the face far exceeded other body sites as an area for adverse effects from cosmetics among both females and males surveyed (117). Both sexes identified cleansers (soaps) as the agents most often responsible for these effects.

Bars are a convenient and popular facial cleansing option. These cleansers are available in a wide range of compositions. Traditional soaps provide effective cleansing and results presented previously indicate that with normal washing even soap bars do not completely strip the hydrolipid layer from the skin surface. However, soap may still induce or predispose the skin to sensations of tightness. Cleansing in adolescents or acne-prone populations requires special consideration. Acne is not caused by dirt on the skin surface, but regular cleansing is important. While soap is an effective cleanser, some evidence suggests that soap washing may predispose the skin to acne (101). More importantly, soap can irritate already inflamed acne lesions. Washing with a mild cleanser and warm water is recommended (118).

Exfoliating agents help to physically remove dirt and cellular debris from the surface of the skin, provide a rejuvenated look, stimulate the skin through a massage effect, and smooth the skin surface (119). The latter can increase the cleansing efficacy of personal cleansers. Exfoliating agents take several forms. There are exfoliating implements; those intended for use on the face are often made of a non-woven polyester material and are used to apply a cleansing product to the skin; some incorporate a cleanser that is activated by wetting. Proper use is important to avoid damaging the stratum corneum barrier, which will increase the likelihood of cleanser irritation, and manufacturers' directions for use should be followed. Some bar and liquid cleansers incorporate particles intended to act as exfoliating agents. Materials such as polyethylene, silica, various ground seeds (e.g., apricot, almond, or walnut seed), jojoba esters, loofa powder, cross-linked polymethacrylate, or calcium carbonate are used for these beads. The effectiveness of these exfoliating products and their potential to impact the skin is dependent on the concentration of the exfoliating agent and the properties of the particular agent used (119–121). As with exfoliating implements, manufacturers' directions for use should be followed to avoid damaging the skin when using these products.

Cleansing cloths are a relatively new introduction into the personal cleansing market. These cloths are available in dry and wet forms. The former, like the cleansing sponges mentioned above, incorporate cleansers that are activated when the cloth is wet. The textured surface of these cloths provides exfoliation and, in conjunction with the integrated surfactants, effective cleansing (122). These cloths can incorporate additional agents, such as petrolatum, that are transferred to the skin during use to provide skin benefits such as improved hydration. A four-week study conducted among a subject population with stage 1 or stage 2 rosacea showed good in-use tolerance for a dry lathering facial cleansing cloth with petrolatum (123). Thus, these facial cleansing cloths may provide a good cleansing option for individuals with sensitive skin.

Astringents and toners are sometimes used after cleansing to remove soap residue or remaining oil. These products may contain water, alcohol, propylene glycol, witch hazel,

or salicylic acid (124). Astringents and toners can dry the skin and leave it with a tight feeling, a cleansing endpoint that is considered desirable by some consumers. However, Wortzman reported that using a toner after cleansing increases irritation (125), either by a direct effect for toners with high alcohol content, or paradoxically for toners with moderate to low alcohol content. Propylene glycol that is found in some products is a mild irritant that may cause stinging in some individuals, and is also a potential contact allergen.

Body Cleansing

The number of cleansing forms available for use on the body is more limited than for the face, but the range of surfactants used in these products is no less varied. Soap is a cleanser used since antiquity, and it remains a popular cleanser despite much negative press and the introduction of syndets. In fact, soap is an effective, economical, and acceptable cleansing alternative for many people. The large number of soap-based products sold by large-scale and specialty manufacturers attests to this, and results from studies like the one conduced by Barel et al. suggest its effects on healthy skin may be limited in normal use (103). But numerous controlled application studies demonstrate the *potential* for soap to negatively impact skin and for this reason prudence dictates choosing an alternative cleanser in certain situations. For example, while some studies suggest that soap is well-tolerated in and may actually benefit conditions such as atopic dermatitis (126,127), there are better options for cleansing diseased skin. For patients who prefer a bar form, syndet cleansing bars provide good cleansing and are usually well-tolerated. Those who prefer a liquid cleanser form can benefit from using one of the newer body wash technologies, such as a product that will deposit petrolatum on the skin during use (128). An added benefit to using a body wash product is that they are applied with a polyethylene mesh "cleansing puff." This type of implement provides a mild exfoliation benefit (129) that can help remove the dry skin that accompanies many dermatoses.

There are situations were personal cleanser choice can be important, even for individuals with healthy skin. As mentioned above, the stratum corneum is thinnest on the genitalia (114), and the presence of a thin barrier in this intertriginous area seems a formula for personal cleanser issues. Cleanser irritation of the external genitalia is a greater issue for females than for males (130), and cleansing residue may also be a source of discomfort in females (131). In both sexes, cleansing with water only is advised, or if a cleanser must be used, a syndet-based product followed by thorough rinsing (130).

Aged skin also presents a cleansing challenge. The skin undergoes many changes with age, some of which can impact the response to personal cleansing products: the microvasculature that supplies the epidermis degrades and circulation decreases (132,133), the stratum corneum lipid content decreases (134), the stratum corneum turnover rate decreases (135), and the skin becomes drier and rougher (136). Resting TEWL values are lower in aged skin than in young skin, (134,137) which is usually associated with better barrier function. Aged skin does show a decreased response to irritants (133,137), but it also shows altered permeability to a variety of topically applied materials, suggesting that the decreased irritation reflects an attenuated inflammatory response rather than an improved barrier. Once perturbed, barrier recovery occurs more slowly in old than in young skin (134).

Cleanser choice can impact the elderly in a number of ways. The natural decrease in stratum corneum lipids and increased dryness can predispose aged skin to the drying effects of cleansers. Apart from its affect on skin appearance, increased dryness can worsen pruritus that commonly accompanies aging, which can lead to scratching, excoriation, and

infection (138). The loss of hydration and elasticity also makes the stratum corneum more susceptible to mechanical damage; a study conducted among residents of a long-term care facility showed an increased incidence of skin tears during periods when a non-emollient soap was used, compared to periods of emollient soap use (139). Regular skin cleansing remains important, but decreasing bathing or showering frequency and using a non-soap cleanser is recommended (140,141). Emollient cleansers can help, but their benefit must be balanced with the potential for slipping in the tub or shower (140). Since water temperature impacts skin-cleanser interactions (80,81), bathing in warm rather than hot water can help reduce drying and irritation. If a cleanser is used, thorough rinsing is important to assure that the cleanser residue is removed from the furrowed skin surface (142).

Race can also be a consideration when recommending or choosing a personal cleansing product. There are numerous published works describing physiological differences between different racial groups and controlled exposure studies that examine differences in irritant susceptibility (143–149), but the practical implications of the reported results in terms of susceptibility to in-use irritation remain unclear. Regardless of whether there are differences in the magnitude of the physiological response to personal cleansing products, the potential to induce some level of dryness or irritation undoubtedly exists for all skin types and this could have different implications for different groups. For

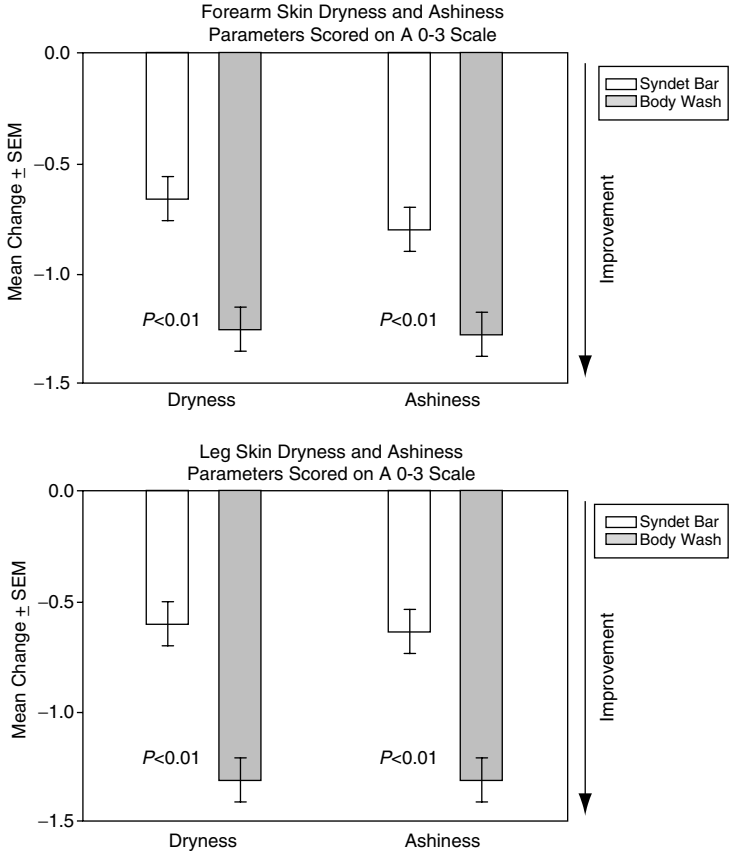

Figure 7 Change in dryness and ashiness on African American subjects' arms (*top*) and legs (*bottom*) assessed by the dermatologist investigator during a four-week home use study.

example, dry skin flakes are more visible when viewed against a dark background and light scattered by dry skin gives dark skin a dull, gray, "ashy" appearance, a condition that is considered undesirable or even disturbing to individuals with skin of color. Moisturizers are often used to mitigate skin dryness and the ashy appearance, but proper cleanser selection is also important to help minimize dry skin production.

To demonstrate the potential impact of personal cleanser choice on dryness and ashiness, we conducted a blinded, parallel group study among African American women with self-perceived dry/ashy skin, especially on their legs (150). Approximately half of the 83 women enrolled were randomly assigned to use a petrolatum-depositing body wash for daily showering for four weeks, and the remainder of the subjects were assigned to use a syndet bar. Moisturizer use was prohibited to eliminate this variable as a potential confounding effect and tub bathing was restricted. The dermatologist investigator scored dryness and ashiness on the lateral surface of subjects' arms and legs at baseline and study

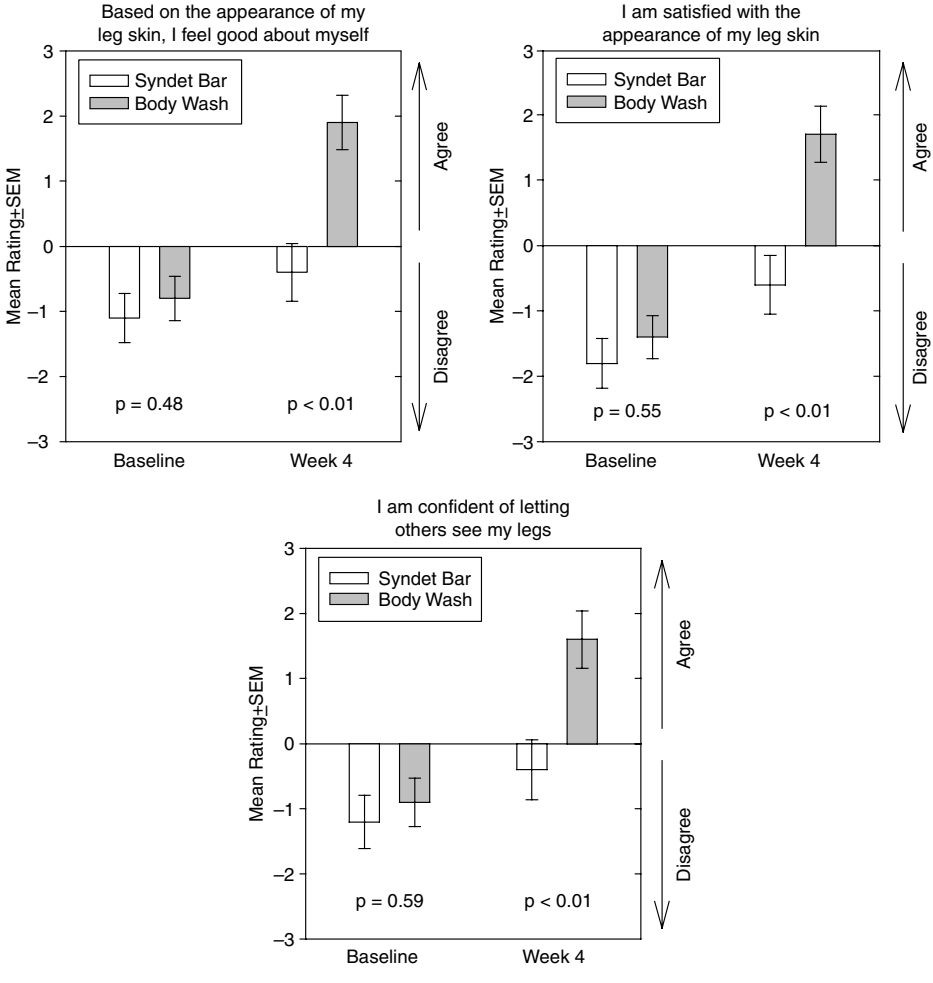

Figure 8 African American subjects' responses to a psychosocial questionnaire administered at baseline and after four weeks of using a petrolatum-depositing body wash or a syndet bar. The responses from subjects who used the body wash showed a marked improvement over the course of the study.

end. Subjects also completed a brief psychosocial questionnaire at these times to assess the impact of their dry/ashy leg skin on self-image. The dermatologist's evaluations showed that both personal cleansing products reduced dryness and ashiness over the course of treatment; a significantly greater reduction was observed for those subjects using the petrolatum-depositing body wash (Fig. 7). Weather conditions were reasonably consistent during the study, but a baseline habits and practices questionnaire showed that a high percentage of the enrolled subjects used a soap or combo bar (soap + syndet) as their usual cleanser. Since the study did not include a pretreatment period, some improvement in dryness and ashiness was expected as a result of switching to a less drying (i.e., non-soap) cleanser. While the test cleansers had a positive impact on these clinical parameters, an even more striking effect was shown on subjects' self-image (Fig. 8). Mean responses to these questions were relatively poor at baseline. Responses for subjects using the syndet bar exhibited a shift toward neutrality over the course of the study. However, responses for subjects who used the petrolatum-depositing body wash exhibited a strong positive shift, demonstrating that modern personal cleansing products can have a much broader impact than simply providing a means to remove soil from the skin.

REFERENCES

1. Fellingham C. Soaps that fight skin problems. Glamour 1997; September:135.
2. Dyett L. The super cleansers. Glamour 1998; August:192–197.
3. Kintish L. Soap: it's not just for cleansing anymore. Soap/Cosmet/Chem Spec 1998; October:50–54.
4. Bronner A. The energizing shower. An alternative to the morning cup of coffee. Self 1998; August:145–146.
5. Kuehl BL, Fyfe KS, Shear NH. Cutaneous cleansers. Skin Ther Lett 2003; 8:1–4.
6. Wolf R. Has mildness replaced cleanliness next to godliness? Dermatology 1994; 189:217–221.
7. Weber G. A new method for measuring the skin cleansing effect of soaps and detergents. Acta Derm Venereol (Stockh) 1987; 134:33–34.
8. Schrader K, Rohr M. Methods for measuring the skin-cleansing effect of surfactants in comparison with skin roughness and compatibility. Clin Dermatol 1996; 14:57–65.
9. Frosch PJ. Irritancy of soaps and detergent bars. In: Frost P, Horwitz S, eds. Principles of Cosmetics for the Dermatologist. St. Louis: CV Mosby, 1982:1–12.
10. Wolf R, Friedman M. Measurement of the skin-cleaning effects of soaps. Int J Dermatol 1996; 35:598–600.
11. Imokawa G. Comparative study on the mechanism of irritation by sulfate and phosphate type of anionic surfactants. J Soc Cosmet Chem 1980; 31:45–66.
12. Lockhart L, Lazer W. A novel technique for assessing cleansing efficacy, 53rd Annual Meeting of the American Academy of Dermatololgy, New Orleans, LA, 1995, Schaumburg, IL: American Academy of Dermatology.
13. Sauermann G, Doerschner A, Hoppe U, et al. Comparative study of skin care efficacy and in-use properties of soap and surfactant bars. J Soc Cosmet Chem 1986; 37:309–327.
14. Puvvada S, Post AJ, Subramanyan KK, et al. (inventors), Unilever Home & Personal Care U.S.A. (assignee), Exfoliating and moisturizing toilet bar, U.S. Patent 6,764,991, July 20, 2004.
15. Mills OH, Rizer RL, DeRosa A. Using sugar surfactants for cleansing and soothing sensitive skin. 63rd Annual Meeting of the American Academy of Dermatology, New Orleans, LA, Feb 18–22, 2005, Schaumburg, IL: American Academy of Dermatology.
16. Frosch PJ, Kligman AM. The chamber-scarification test for irritancy. Contact Dermatitis 1976; 2:314–324.

17. Routh HB, Bhowmik KR, Parish LC, et al. Soaps: from the Phoenicians to the 20th century—a historical review. Clin Dermatol 1996; 14:3–6.
18. Subramanyan K, Johnson AW, Leyden J. Skin care regimen with emollients benefits patients with sensitive facial skin. J Am Acad Dermatol 2005; 52:P72.
19. Msika P, Piccardi N, Choulot JC, et al. Washing oil: a new concept for the management of atopic dermatitis., 63rd Annual Meeting of the American Academy of Dermatology, New Orleans, LA, February 18–22, 2005, Schaumburg, IL: American Academy of Dermatology.
20. Lukacovic MF, Dunlap FE, Michaels SE, et al. Forearm wash test to evaluate the clinical mildness of cleansing products. J Soc Cosmet Chem 1988; 39:355–366.
21. Accessed June, 2005 at http://www.firp.ula.ve/cuadernos/E300A.pdf.
22. Accessed July, 2005 at http://www.kcpc.usyd.edu.au/discovery/9.5.5-short/9.5.5_anionic.html.
23. Rhein LD, Robbins CR, Fernee K, et al. Surfactant structure effects on swelling of isolated human stratum corneum. J Soc Cosmet Chem 1986; 37:125–139.
24. Speiss E. Raw materials. In: Williams DF, Schmitt WH, eds. Chemistry and Technology of the Cosmetics and Toiletries Industry. London: Blackie Academic & Professional, 1996:1–35.
25. Simon P, Veyrat S, Piquemal P, et al. Surfactants and the skin. The revival of sugar esters. Cosmet Toilet 1998; 113:69–72.
26. López O, Walther P, Cócera M, et al. Structural modifications in the stratum corneum by effect of different solubilizing agents: a study based on high-resolution low-temperature scanning electron microscopy. Skin Pharmacol Appl Skin Physiol 2000; 13:265–272.
27. Thau P. Surfactants for skin cleansers. In: Rieger MM, ed. Surfactants in Cosmetics, Vol. 16. New York: Marcel Dekker, Inc., 1985:349–376.
28. Domínguez JG, Balaguer F, Parra JL, et al. The inhibitory effect of some amphoteric surfactants on the irritation potential of alkylsulphates. Int J Cosmet Sci 1981; 3:57–68.
29. de Groot AC, van der Walle HB, Weyland JW. Contact allergy to cocamidylpropyl betaine. Contact Dermatitis 1995; 33:419–422.
30. Fowler JF, Jr. Cocamidopropyl betaine. Dermatitis 2004; 15:3–4.
31. Fowler JF, Jr., Zug KM, Taylor JS, et al. Allergy to cocamidopropyl betaine and amidoamine in North America. Dermatitis 2004; 15:5–6.
32. Moreau L, Sasseville D. Allergic contact dermatitis from cocamidopropyl betaine, cocamidoamine, 3-(dimethylamino)propylamine, and oleamidopropyl dimethylamine: co-reactions or cross-reactions? Dermatitis 2004; 15:146–149.
33. Fowler JF, Fowler LM, Junter JE. Allergy to cocamidopropyl betaine may be due to amidoamine: a patch test and product use study. Contact Dermatitis 1997; 37:276–281.
34. Vilaplana J, Mascaro JM, Trullas C, et al. Human irritant response to different qualities and concentrations of cocoamidopropylbetaines: a possible model of paradoxical irritant response. Contact Dermatitis 1992; 26:289–294.
35. Wood TE. Regulatory considerations for soap products in the U.S.A. Cosmet Toiletries 1989; 104:75–79.
36. Hopkins H. All that lathers is not soap. FDA Consum 1979; 13:12–13.
37. Bachrach EE. Federal regulation of soap products. Soap Cosmet Chem Spec 1981; 57:35–38. See also page 64.
38. Kuntom A, Kifli H. Properties of soaps derived from distilled palm stearin and palm kernel fatty acids. J Surfact Detergent 1998; 1:329–334.
39. Friedman M, Wolf R. Chemistry of soaps and detergents: various types of commercial products and their ingredients. Clin Dermatol 1996; 14:7–13.
40. Dahlgren RM, Lukacovic MF, Michaels SE, et al. Effects of bar soap constituents on product mildness. Proceedings of the Second World Conference on Detergents, Montreux, Switzerland, October 1986, Champaign, IL. Am Oil Chem Soc 1987:127–134.
41. Blank IH. Action of soap on skin. Arch Derm Syph 1939; 39:811–824.
42. Kellum RE. Acne vulgaris. Studies in pathogenesis: relative irritancy of free fatty acids from C_{12} to C_{16}. Arch Derm 1968; 97:722–726.

43. Stillman MA, Maibach HI, Shalita AR. Relative irritancy of free fatty acids of different chain length. Contact Dermatitis 1975; 1:65–69.
44. García-Domínguez J, Parra JL, Infante MR, et al. A new approach to the theory of adsorption and permeability of surfactants on keratinic proteins: the specific behaviour of certain hydrophobic chains. J Soc Cosmet Chem 1977; 28:165–182.
45. Kefauver PJ, Tollens FR, Syfert SW. (inventors), The Procter & Gamble Company (assignee), Personal cleansing bar with tailored fatty acid soap, U.S. Patent 5,540,852, July 30, 1996.
46. Tollens FR, Kefauver PJ, Syfert SW. (inventors), The Procter & Gamble Company (assignee), Personal cleansing bar with tailored base soaps and mixed with counterions for improved mildness and processability without lather negatives, U.S. Patent 5,387,362, Feb 7, 1995.
47. Kligman AM, Wooding WM. A method for the measurement and evaluation of irritants on human skin. J Invest Dermatol 1967; 49:78–94.
48. Dugard PH, Scheuplein RJ. Effects of ionic surfactants on the permeability of human epidermis: an electrometric study. J Invest Dermatol 1973; 60:263–269.
49. Robbins CR, Fernee KM. Some observations on the swelling of human epidermal membrane. J Soc Cosmet Chem 1983; 34:21–34.
50. Imokawa G, Sumura K, Katsumi M. Study on skin roughness caused by surfactants: I. A new method in vivo for evaluation of skin roughness. J Am Oil Chem Soc 1975; 52:479–483.
51. Imokawa G, Takeuchi T. Surfactants and skin-roughness. Cosmet Toilet 1976; 91:32–46.
52. White IR. Skin tolerance to cleansing agents. Wien Med Wochenschr Suppl 1990; 108:13–16.
53. Brod J. Characterization and physiological role of epidermal lipids. Int J Dermatol 1991; 30:84–90.
54. Grubauer G, Feingold KR, Harris RM, et al. Lipid content and lipid type as determinants of the epidermal permeability barrier. J Lipid Res 1989; 30:89–96.
55. Wertz PW. Lipids and barrier function of the skin. Acta Derm Venereol Suppl (Stockh) 2000; 208:7–11.
56. Pilgram GS, Vissers DC, van der Meulen H, et al. Aberrant lipid organization in stratum corneum of patients with atopic dermatitis and lamellar ichthyosis. J Invest Dermatol 2001; 117:710–717.
57. Melnik B, Hollmann J, Hofmann U, et al. Lipid composition of outer stratum corneum and nails in atopic and control subjects. Arch Dermatol Res 1990; 282:549–551.
58. di Nardo A, Sugino K, Wertz P, et al. Sodium lauryl sulfate (SLS) induced irritant contact dermatitis: a correlation study between ceramides and in vivo parameters of irritation. Contact Dermatitis 1996; 35:86–91.
59. Visscher MO, Tolia GT, Wickett RR, et al. Effect of soaking and natural moisturizing factor on stratum corneum water-handling properties. J Cosmet Sci 2003; 54:289–300.
60. Kirk JF. Effect of hand washing on skin lipid removal. Acta Derm Venereol (Stockh) 1966; 46:24–68.
61. Morganti P. Natural soap and syndet bars. Cosmet Toilet 1995; 110:89–97.
62. Bechor R, Zlotogorski A, Dikstein S. Effect of soaps and detergents on the pH and casual lipid levels of the skin surface. J Appl Cosmetol 1988; 6:123–128.
63. Gfatter R, Hackl P, Braun F. Effects of soap and detergents on skin surface pH, stratum corneum hydration and fat content in infants. Dermatology 1997; 195:258–262.
64. Imokawa G, Akasaki S, Minematsu Y, et al. Importance of intercellular lipids in water-retention properties of the stratum corneum: induction and recovery study of surfactant dry skin. Arch Derm Res 1989; 281:45–51.
65. Rawlings AV, Watkinson A, Rogers J, et al. Abnormalities in stratum corneum structure, lipid composition, and desmosome degradation in soap-induced winter xerosis. J Soc Cosmet Chem 1994; 45:203–220.
66. Fulmer AW, Kramer GJ. Stratum corneum lipid abnormalities in surfactant-induced dry scaly skin. J Invest Dermatol 1986; 86:598–602.
67. Scheuplein R, Ross L. Effects of surfactants and solvents on the permeability of epidermis. J Soc Cosmet Chem 1970; 21:853–873.

68. Froebe CL, Simion FA, Rhein LD, et al. Stratum corneum lipid removal by surfactants: relation to in vivo irritation. Dermatologica 1990; 181:277–283.
69. Imokawa G, Sumura K, Katsumi M. Study on skin roughness caused by surfactants: II. Correlation between protein denaturation and skin roughness. J Am Oil Chem Soc 1975; 52:484–489.
70. Imokawa G, Mishima Y. Cumulative effect of surfactants on cutaneous horny layers: adsorption onto human keratin layers in vivo. Contact Dermatitis 1979; 5:357–366.
71. Kawai M, Imokawa G. The induction of skin tightness by surfactants. J Soc Cosmet Chem 1984; 35:147–156.
72. Prottey C, Oliver D, Coxon AC. Prediction and measurement of surfactant irritation upon human skin under realistic conditions. Int J Cosmet Sci 1984; 6:263–273.
73. Ananthapadmanabhan KP, Yu KK, Meyers CL, et al. Binding of surfactants to stratum corneum. J Soc Cosmet Chem 1996; 47:185–200.
74. Rhein LD. Review of properties of surfactants that determine their interactions with stratum corneum. J Soc Cosmet Chem 1997; 48:253–274.
75. Mukherjee S, Margosiak M, Ananthapadmanabhan K, et al. Interactions of cleansing bars with stratum corneum proteins: an in vitro fluorescence spectroscopic study. J Soc Cosmet Chem 1995; 46:301–320.
76. Shukuwa T, Kligman A, Stoudemayer T. A new model for assessing the damaging effects of soaps and surfactants on human stratum corneum. Acta Derm Venereol (Stockh) 1997; 77:29–34.
77. Frosch PJ, Kligman AM. The soap chamber test. A new method for assessing the irritancy of soaps. J Am Acad Dermatol 1979; 1:35–41.
78. Ertel KD, Neumann PB, Keswick BH, et al. A comparison of two antecubital fossa tests with personal care products. J Toxicol Cut Ocular Toxicol 1997; 16:19–30.
79. Mills OH Jr., Swinyer LJ, Kligman AM. Assessment of irritancy of cleansers, 43rd Annual Meeting of the American Academy of Dermatololgy, Washington, DC, Dec 1–6, 1984, Schaumburg, IL: American Academy of Dermatololgy.
80. Berardesca E, Vignoli GP, Disante F, et al. Effects of water temperature on surfactant-induced skin irritation. Contact Dermatitis 1995; 32:83–87.
81. Clarys P, Manou I, Barel AO. Influence of temperature on irritation in the hand/forearm immersion test. Contact Dermatitis 1997; 36:240–243.
82. Ertel KD, Knight EA, Rains GY et al. A body wash personal cleansing option to provide mild cleansing under a wide range of water hardness conditions, Academy ’97 Meeting, New York, NY, Jul 30–Aug 3, 1997, Schaumburg, IL: American Academy of Dermatology.
83. Fujiwara N, Toyooka I, Ohnishi K, et al. Absorbed residue of fatty acid soap on human skin. Analysis of human skin surface in situ using infrared spectroscopy. J Soc Cosmet Chem Jpn 1992; 26:107–112.
84. Warren R, Ertel KD, Bartolo RG, et al. The influence of hard water (calcium) and surfactants on irritant contact dermatitis. Contact Dermatitis 1996; 35:337–343.
85. Ertel KD, Keswick BH, Bryant PB. A forearm controlled application technique for estimating the relative mildness of personal cleansing products. J Soc Cosmet Chem 1995; 46:67–76.
86. van Scott EJ, Lyon JB. A chemical measure of the effect of soaps and detergents on the skin. J Invest Dermatol 1953; 21:199–203.
87. Bettley FR, Donoghue E. Effect of soap on the diffusion of water through isolated human epidermis. Nature 1960; 185:17–20.
88. Bettley FR, Donoghue E. The irritant effect of soap upon the normal skin. Br J Dermatol 1960; 72:67–76.
89. van der Valk PGM, Crijns MC, Nater JP, et al. Skin irritancy of commercially available soap and detergent bars as measured by water vapour loss. Dermatosen 1984; 32:87–90.
90. van der Valk PGM, Nater JP, Bleumink E. Vulnerability of the skin to surfactants in different groups of eczema patients and controls as measured by water vapour loss. Clin Exp Dermatol 1985; 10:98–103.

91. van Ketel WG, Bruynzeel DP, Bezemer PD, et al. Toxicity of handcleaners. Dermatologica 1984; 168:94–99.
92. Murahata RI, Toton-Quinn R, Finkey MB. Effect of pH on the production of irritation in a chamber irritation test. J Am Acad Dermatol 1988; 18:62–66.
93. Baranda L, González-Amaro R, Torres-Alvarez B, et al. Correlation between pH and irritant effect of cleansers marketed for dry skin. Int J Dermatol 2002; 41:494–499.
94. Ananthapadmanabhan KP, Lips A, Vincent C, et al. pH-induced alterations in stratum corneum properties. Int J Cosmet Sci 2003; 25:103–112.
95. Sznitowska M, Janicki S, Baczek A. Studies on the effect of pH on the lipoidal route of penetration across stratum corneum. J Control Release 2001; 76:327–335.
96. Sznitowska M, Janicki S, Williams A, et al. pH-induced modifications to stratum corneum lipids investigated using thermal, spectroscopic, and chromatographic techniques. J Pharm Sci 2003; 92:173–179.
97. Hostynek JJ, Wilhelm KP, Cua AB, et al. Irritation factors of sodium hypochlorite solutions in human skin. Contact Dermatitis 1990; 23:316–324.
98. Korting HC, Megele M, Mehringer L, et al. Influence of skin cleansing preparation acidity on skin surface properties. Int J Cosmet Sci 1991; 13:91–102.
99. Korting HC, Greiner K, Hübner K, et al. Changes in skin pH and resident flora by washing with synthetic detergent preparations at pH 5.5 and 8.5. J Soc Cosmet Chem 1991; 42:147–158.
100. Korting HC, Kober M, Mueller M, et al. Influence of repeated washings with soap and synthetic detergents on pH and resident flora of the skin of forehead and forearm. Acta Derm Venereol (Stockh) 1987; 67:41–47.
101. Korting HC, Ponce-Pöschl E, Klövekorn W, et al. The influence of the regular use of a soap or an acidic syndet bar on pre-acne. Infection 1995; 23:89–93.
102. Fluhr JW, Kao J, Jain M, et al. Generation of free fatty acids from phospholipids regulates stratum corneum acidification and integrity. J Invest Dermatol 2001; 117:44–51.
103. Barel AO, Lambrecht R, Clarys P, et al. A comparative study of the effects on the skin of a classical bar soap and a syndet cleansing bar in normal use conditions and in the soap chamber test. Skin Res Technol 2001; 7:98–104.
104. Faucher JA, Goddard ED. Sorption of a cationic polymer by stratum corneum. J Soc Cosmet Chem 1976; 27:543–553.
105. Faucher JA, Goddard ED, Hannan RB. Protection of the skin by a cationic cellulose polymer. Cosmet Toilet 1977; 92:39–44.
106. Pugliese P, Hines G, Wielinga W. Skin protective properties of a cationic guar derivative. Cosmet Toilet 1990; 105:105–111.
107. Rawlings A, Harding C, Watkinson A, et al. The effect of glycerol and humidity on desmosome degradation in stratum corneum. Arch Dermatol Res 1995; 287:457–464.
108. Ghadially R, Halkier-Sorensen L, Elias PM. Effects of petrolatum on stratum corneum structure and function. J Am Acad Dermatol 1992; 26:387–396.
109. Warner RR, Boissy YL. Effect of moisturizing products on the structure of lipids in the outer stratum corneum of humans. In: Lodén M, Maibach HE, eds. Dry Skin and Moisturizers. In: Chemistry and Function. Boca Raton: CRC Press, 2000:349–369.
110. Ertel KD, Focht HL, Plante JE, et al. Challenging the personal cleanser paradigm: a body wash that provides skin improvement benefits, 63rd Annual Meeting of the American Academy of Dermatology, New Orleans, LA, Feb 18–22, 2005, Schaumburg, IL: American Academy of Dermatololgy.
111. Lewis C. Clearing up cosmetic confusion. FDA Consum 1998; 32:6–11.
112. Scheinman PL. Is it really fragrance-free? Am J Contact Dermat 1997; 8:239–242.
113. Scheinman PL. The foul side of fragrance-free products: what every clinician should know about managing patients with fragrance allergy. J Am Acad Dermatol 1999; 41:1020–1024.
114. Ya-Xian Z, Suetake T, Tagami H. Number of cell layers of the stratum corneum in normal skin—relationship to the anatomical location on the body, age, sex, and physical parameters. Arch Derm Res 1999; 291:555–559.

115. Christensen M, Kligman AM. An improved procedure for conducting lactic acid stinging tests on facial skin. J Soc Cosmet Chem 1996; 47:1–11.
116. Muizzuddin N, Marenus KD, Maes DH. Factors defining sensitive skin and its treatment. Am J Contact Dermat 1998; 9:170–175.
117. De Groot AC. Adverse effects of cosmetics and toiletries: a retrospective study in the general population. Int J Cosmet Sci 1988; 9:255–259.
118. Accessed August, 2005 at http://www.aad.org/public/Publications/pamphlets/Acne.htm.
119. Morea-Swift G. Looking Good. New skin cleansing particles improve personal care formulations. Soap Cosmet 2003; 79:17–18. See also pp. 20,24.
120. Wigger-Alberti W, Fischer T, Greif C, et al. Effects of various grit-containing cleanser on skin barrier function. Contact Dermatitis 1999; 41:136–140.
121. Mills OH, Jr., Kligman AM. Evaluation of abrasives in acne therapy. Cutis 1979; 23:704–705.
122. Doughty DG, Blatz BA, Ertel KD, et al. Clinical and technical characterization of a breakthrough option for daily facial cleansing, 58th Annual Meeting of the American Academy of Dermatology, San Francisco, CA, Mar 10–15, 2000, Schaumburg, IL: American Academy of Dermatololgy.
123. Plante JE, Ertel KD, Amburgey MS, et al. Novel facial cleansing cloth provides a new daily cleansing option for sensitive skin, Academy 2000 Meeting, Nashville, TN, Aug 2–6, 2000, Schaumburg IL: American Academy of Dermatology.
124. Accessed August, 2005 at http://www.aad.org/NR/exeres/7430E3C2-E0E9-4C3D-A8A3-4E25CB1E48AB.htm? NRMODE=Published.
125. Wortzman MS. Evaluation of mild skin cleansers. Dermatol Clin 1991; 9:35–44.
126. Breneman DL, Hanifin JM, Berge CA, et al. The effect of antibacterial soap with 1.5% triclocarban on *Staphylococcus aureus* in patients with atopic dermatitis. Cutis 2000; 66:296–300.
127. Uehara M, Takada K. Use of soap in the management of atopic dermatitis. Clin Exp Dermatol 1985; 10:419–425.
128. Draelos ZD, Ertel K, Hartwig P, et al. The effect of two skin cleansing systems on moderate xerotic eczema. J Am Acad Dermatol 2004; 50:883–888.
129. Ertel KD, Werchowski KM, Rains GY, et al. Potential for enhanced clinical mildness from a body wash plus cleansing puff system, Academy '98 Meeting, Chicago, IL, Jul 31–Aug 4, (1998), Schaumburg, IL: American Academy of Dermatology.
130. Nürnberger F. Skin cleansing of the mucous membrane and skin borders. Wien Med Wochenschr Suppl 1990; 108:27–28.
131. Lindell ME, Olsson HM. Personal hygiene in external genitalia of healthy and hospitalized elderly women. Health Care Women Int 1990; 11:151–158.
132. Montagna W, Carlisle K. Structural changes in aging human skin. J Invest Dermatol 1979; 73:47–53.
133. Kligman AM. Perspectives and problems in cutaneous gerontology. J Invest Dermatol 1979; 73:39–46.
134. Ghadially R, Brown BE, Sequeira-Martin SM, et al. The aged epidermal permeability barrier. Structural, functional, and lipid biochemical abnormalities in humans and a senescent murine model. J Clin Invest 1995; 95:2281–2290.
135. Roberts D, Marks R. The determination of regional and age variations in the rate of desquamation: a comparison of four techniques. J Invest Dermatol 1980; 74:13–16.
136. Manuskiatti W, Schwindt DA, Maibach HI. Influence of age, anatomic site and race on skin roughness and scaliness. Dermatology 1998; 196:401–407.
137. Cua AB, Wilhelm KP, Maibach HI. Cutaneous sodium lauryl sulphate irritation potential: age and regional variability. Br J Dermatol 1990; 123:607–613.
138. Kligman AM. Perspectives in cutaneous geriatrics: skin care for the old-old. J Geriatr Derm 1993; 1:A18–A20.
139. Mason SR. Type of soap and the incidence of skin tears among residents of a long-term care facility. Ostomy Wound Manage 1997; 43:26–30.
140. Graham-Brown R. Soaps and detergents in the elderly. Clin Dermatol 1996; 14:85–87.

141. Accessed August, 2005 at http://www.aad.org/NR/exeres/5C8EABAB-1380-4BDF-9DF1-378951AC3B09.htm?NRMODE=Published.
142. Swanbeck G. Cleansing problems in senile skin. Wien Med Wochenschr Suppl 1990; 108:23.
143. Berardesca E. Racial differences in skin function. Acta Derm Venereol (Stockh) 1994; 185:44–46.
144. Berardesca E, Maibach HI. Racial differences in skin pathophysiology. J Am Acad Dermatol 1996; 34:667–672.
145. Corcuff P, Lotte C, Rougier A, et al. Racial differences in corneocytes. A comparison between black, white, and Oriental skin. Acta Derm Venereol (Stockh) 1991; 71:146–148.
146. Ertel KD, Werchowski KM, Rains GY. Irritation potential of personal cleansers: response of different skin types to a range of cleanser compositions, 60th Annual Meeting of the American Academy of Dermatololgy, New Orleans, LA, February 22–27, 2002, Schaumburg, IL: American Academy of Dermatology.
147. Montagna W, Carlisle K. The architecture of black and white facial skin. J Am Acad Dermatol 1991; 24:929–937.
148. Robinson MK. Population differences in skin structure and physiology and the susceptibility to irritant and allergic contact dermatitis: implications for skin safety and risk assessment. Contact Dermatitis 1999; 41:65–79.
149. Warrier AG, Kligman AM, Harper RA, et al. A comparison of black and white skin using noninvasive methods. J Soc Cosmet Chem 1996; 47:229–240.
150. Grimes PE. Double-blind study of a body wash containing petrolatum for relief of ashy, dry skin in African American women. Cosmet Dermatol 2001; 14:25–27.

5
Toners and Astringents

Melanie Smith
Mary Kay Inc., Dallas, Texas, U.S.A.

INTRODUCTION

Skin care sales continue to grow globally, driven by innovative new product forms, multifunctional products, consumer interest in reducing the signs of aging, a rise in disposable income, and the availability of foreign product lines in formerly less-developed countries. Most of the increase in sales is generated by anti-aging/nourishing products. Dermatologists' skin care lines with scientific-sounding names and minimalist packaging are increasingly popular with the consumer who feels these lines may provide efficacy at an affordable price without a prescription. Euromonitor (1) reported toner sales worldwide in 2004 at $4.7 billion, growing at a lower rate than other skin care categories. Growth in toner sales in 2004 came from Asia-Pacific, Western Europe, Eastern Europe, and Latin America where multistep regimens are well received. In the U.S., where convenience is a key factor in product usage, sales peaked at $384.7 million in 1999 and then began a gradual decline which is forecasted to continue. The perception among some consumers that toners are unnecessary or harmful because they "strip" the skin, the lack of innovation in the product form, and inconvenience are among the reasons toner sales have declined. Toners are often perceived as harmful because consumers tend to associate them with drying of the skin and high alcohol levels. At one time toners were touted as pH balancers and necessary to remove the highly alkaline, drying, irritating residue of cleansers and soaps of the past. Most cleansers marketed today are mild and well formulated so as not to disrupt the skin's pH level, thus minimizing the perceived need for toners. In addition, toners have not advanced from the traditional solution form. Consumers prefer the convenience of facial cleansing wipes and multifunctional products, such as two-in-one cleanser/toner and three-in-one cleanser/toner/mask products, rather than the additional step of a toner. Despite this, there are opportunities for the dermatologist, aesthetician, and consumer to use a toner that is cosmetically acceptable, provides a sensorial experience, is suitable as a delivery vehicle, and is formulated appropriately for skin type.

PRODUCT NOMENCLATURE

Toners, astringents, skin fresheners, skin lotions, softeners, tonics, balancers, cleansing waters and other terms are used for products in this category. The choice of nomenclature

can vary by manufacturer and even within product lines. Also, the product name does not necessarily indicate strength or inclusion of a particular ingredient. For this chapter the term toners will be used to cover all these nomenclatures unless specified. Toners may be categorized as cosmetics or over-the-counter (OTC) drug products, depending upon the claims and ingredients. There is an astringent category under the Food and Drug Administration's (FDA's) Skin Protectant Drug Products for Over-the-Counter Human Use (2) defining astringents as "… (products) applied to the skin or mucous membranes for a local and limited protein coagulant effect." This definition covers the use of aluminum acetate, aluminum sulfate, and witch hazel. Active ingredients and labeling claims in astringent drug products are dictated by the FDA OTC Monograph (2). Except for witch hazel (*hamamelis water*) USP, these actives are reserved for OTC uses and are not typically used in cosmetic toners and, therefore, will not be considered for purposes of this chapter. To add to this confusion, there are products branded as toners and astringents containing cosmetic ingredients as well as toners and astringents containing salicylic acid that are sold in accordance with the FDA's OTC Acne Drug Monograph (3).

FUNCTION AND ORDER OF APPLICATION WITHIN A SKIN CARE REGIMEN

Toners are leave-on products. They are the second cleansing step within a skin care regimen designed to freshen and tone, and they also prepare the skin for the application of moisturizer. After cleansing, toners are typically applied by saturating a cotton ball or pad and wiping this across the face. Men may use them as a splash-on after shaving. Toners remove any makeup residue, and oily skin patients find them beneficial to remove excess sebaceous secretions. Toners can provide a mild exfoliating action and a stimulating or cooling sensation. Toners may also serve as a delivery vehicle for active or cosmeticeutically important ingredients such as anti-acne, anti-aging, and whitening/lightening. Although toners are typically designed for facial use, they may also be used for the upper chest and back in acne treatment.

FORMULATION CONSIDERATIONS

Product Forms and Ingredients

Toners are typically clear to translucent aqueous or hydroalcoholic solutions. The choice of ingredients, function of these ingredients, and claims determine the product's appearance and type of solution. A generic base formulation is shown in Table 1. Water is typically the major component and main vehicle or delivery system for active or other cosmetically important ingredients. Ethanol may be added as part of the vehicle as desired for skin type and/or ingredient solubility. Ethanol is generally not used in toners formulated for dry or sensitive skin or in the Asia-Pacific market, but it is found at varying levels in normal, combination, oily, and acne-prone skin types. Ethanol also serves as a preservative when used at levels of 20% or higher. Various types of denatured ethanol are used in toners, depending on country regulations on the denaturant. Isopropanol was used years ago, but it is now out of favor because of its strong odor.

Humectants are added to attract moisture to the skin, mitigate the drying effects of alcohol, lower the freeze point to ensure stability in cold temperatures, solubilize other

Table 1 Skin Toner—Base Formula with Typical Concentration Ranges

Ingredients	%
Water	Qs to 100.00%
Ethanol	0.00–65.00
Humectants	1.00–5.00
Key ingredients	0.10–10.00
Emollients	0.10–3.00
Cosolubilizers	0.10–0.50
Thickeners/film formers	0.05–0.20
Preservatives	As needed
Color, fragrance	Qs

ingredients, and adjust the aesthetics. Glycerin and sorbitol are the most cost effective humectants, but they can lend a tacky afterfeel. Sodium polycarboxylic acid (PCA) is less tacky, but more importantly, it is similar to the PCA which is found in the skin's own natural moisturizing factor (NMF). When additional solubility and an elegant, smooth, non-tacky feel is desirable, propylene glycol, butylene glycol, polyethylene glycols, and the ethoxylated glycerins, such as methyl gluceth-10 or methyl gluceth-20, are used. Sodium hyaluronate and other water-soluble moisturizing agents may be added.

Emollients, such as dimethicone copolyols and small amounts of natural oils, are beneficial for skin lubricity and soothing. They require the use of cosolubilizers to assure ingredient solubility to maintain product clarity and stability. Cosolubilizers include ethoxylates and propoxylates, such as PEG-40 hydrogenated castor oil, PPG-5-ceteth-20, or polysorbate 20. They are added at concentrations of 0.10–0.50%, depending on the oil-soluble ingredient and level used. The ethoxylated and proproxylated humectants are also useful but less efficient cosolubilizers.

Botanical extracts are added for a variety of reasons (4–6). The concentration is dependent on many factors, including the type of extraction and the percent solids of the extract. For example, aloe extract and witch hazel distillate are often used as vehicles. Frequently, several botanicals will be incorporated into a toner. Some extracts are more suitable for specific skin types; some offer multiple benefits. They are frequently touted as the key ingredient that offers benefits such as astringency, anti-inflammation, antioxidant, exfoliating, soothing, and cooling. It is the extracts' polyphenolic content that offers one or more of these benefits. Especially popular and beneficial are the polyphenolic bioflavinoids found in green tea, rosemary, blueberry, raspberry, strawberry, red wine, grapeseed, and pine bark extracts. They provide antioxidant and anti-inflammatory benefits. The anti-inflammatory benefits equate to soothing the skin by reducing skin stinging, itching, and redness. Extracts of honey, mallow, soy, aloe, lavender, green tea, algae, licorice, and chamomile may be added for their soothing and conditioning effects on the skin. The high tannin levels in botanical extracts such as witch hazel, sage, horsechestnut, and *quercus lusitanica* oak provide astringency. In addition to its astringency, the distillate of witch hazel, which contains 14% ethanol, also provides a cooling effect on the skin. It may be claimed as an OTC drug product astringent under the Skin Protectant Monograph (2), but both the distillate and extracts forms are more frequently used as a cosmetic ingredient in skin toners. Isoflavones, such as soy extract, known for their phytoestrogen content, are beneficial to more mature and dry skins.

Other beneficial ingredients used in toners are allantoin and panthenol for conditioning and soothing of the skin, and free radical scavenging antioxidants, such as alpha lipoic acid, superoxide dismutase, and vitamins A, C, and E. Vitamin E and its derivative, tocopheryl acetate, can also be used to protect the product and its constituents from oxidization.

Alpha-hydroxy acids (AHAs) such as glycolic, lactic, malic, citric, and mixed fruit acids are used for exfoliation and/or pH adjustment. While they are not marketed as toners, the toner product form has been used by aestheticians and dermatologists to deliver high levels of hydroxy acids in chemical peels for years, and more recently chemical peels with lower levels of AHAs have been introduced through the retail market. AHAs at efficacious exfoliating levels of pH <5 may cause skin stinging and redness, so the addition of anti-inflammatory and soothing botanical extracts is recommended. Although neutral pH ranges offer less irritation potential, they do not offer the same exfoliation activity. Polyhydroxy acids (PHAs), larger molecular weight variants of AHAs, are designed to be less irritating (7). Both AHAs and PHAs may be used in both aqueous and hydroalcoholic solutions. When used as a pH adjuster, AHAs are added at levels of 0.01–0.20%. The beta hydroxy acid (BHA), salicylic acid, is used for its keratolytic/exfoliating activity and is monographed as an OTC anti-acne drug (3).

Whitening agents have a long history of use in Asia. They are highly regulated in Asia as quasi-drugs. They have gained popularity in the rest of the world for the cosmetic claim of even skin tone, where the term whitening is considered a drug claim. Licorice, mulberry, and bearberry are popular skin lightening botanical extracts. The oil-soluble form of licorice at 0.05% is regulated as a functional drug in Korea (8). The water-soluble vitamin C derivatives, magnesium ascorbyl phosphate (MAP) used at 3%, and ascorbyl glucoside at 2%, are recognized as quasi-drugs in most of Asia (9). MAP is highly unstable and turns brown readily with time, high temperatures, and exposure to light. Ascorbyl glucoside is preferred for its acceptable stability profile.

Thickening ingredients are added when a slightly viscous and/or film forming property is desired. They also provide a more lubricious application and afterfeel than a solution. Xanthan gum, polyacrylic acids such as carbomer, and cellulose gum derivatives, such as methylcellulose, hydroxypropylcellulose, and hydroxyethylcellulose, are used.

Fragrance oils or naturally derived extracts and oils may be added to impart a pleasant scent to the formula or cover off-odors that develop when the product is exposed to excessive heat, light, or other parameters associated with shelf life. They also can be used to support a toner's marketing position and enhance the message that the toner is soothing or refreshing or, in the case of anti-acne toners, medicinal. Rose and lavender extracts can be used for soothing and dry skin formulas. Rosemary, peppermint, and citrus extracts may be added to toners designed for oily and combination skins or when a refreshing, stimulating signal or scent is desired. Menthol, peppermint, and eucalyptus odors are associated with a medicinal benefit.

Like fragrance, color is included to deliver a sensorial signal, such as soothing, refreshing or therapeutic, or to enhance the product's appearance, or to cover product color stability issues. Water-soluble Food, Drug, and Cosmetic (FD&C) and Drug and Cosmetic (D&C) colorants are used.

New and Patented Ingredients/Applications

Toners have historically contained plant-derived key ingredients. With recent controversies in the cosmetic industry concerning the use of animal-derived ingredients, the use of collagen and other animal-derived ingredients has diminished, and they are very

rarely found in toners outside of Japan. A recent U.S. patent discloses the use of extensions, plant-derived hydroxyproline-rich glycoproteins that can be incorporated into toners as substitutes for animal collagen (10). The use of *Morinda Citrifolia* or Noni from the Indian Mulberry plant in a toner is disclosed in a recent patent. Noni provides antioxidant benefits and is high in linoleic acid to nourish the skin (11). *Sanguisorba,* a plant native to Korea, China, and Japan, produces a root extract widely used in Asian cosmetics for its astringent effect. It is said to offer antimicrobial and anti-inflammatory effects as well, and it functions much like superoxide dismutase as an antioxidant (12). A recent patent discloses the preparation zinc glycyrrhizinate for use as an astringent in medical and cosmetic preparations (13). A mixture of butylene glycol and mushroom extract is used as an astringent additive for its skin tightening benefits (14). Pycogenol or pine bark extract and blueberry extract exhibit potent antioxidant and anti-inflammatory actions. They are useful as soothing and antioxidant agents in toners (15). Another recent patent (16) discloses the use of solvent extracts of plants including *Spondias mombin, Maprounea guianesis, Waltheria indica, Gouania blanchetiana, Cordia schmoburgkii, Randia armata*, and *Hibiscus furcellatu*s to stimulate autosynthesis of reduced glutathione. A skin toner formulation patent (17) covers the use of butylene oxide-based ethers and propylene oxide-based ethers. It is purported to remove sebum from the skin without significant removal of moisture-retaining intercellular lipids.

Formulation Challenges

Skin Types

Toners have two key formulating challenges—formulating for specific skin types and vehicle/ingredient stability and compatibility. Varying skin types, including dry, normal, oily, combination, sensitive, and acne-prone, require different and skin-type specific ingredients and vehicles. Free radical scavenging antioxidants are used regardless of skin type. Most toners are used within a skin care regimen. The patient's concern about toners being drying or harmful may be mitigated by using a regimen and toner appropriate for skin type.

Alcohol-free formulas with humectants, emollients, and soothing agents are most suitable for the dry and sensitive skin patient (Table 2). This, in conjunction with the use of a moisturizer, allays the concern of a toner being drying. The addition of humectants and emollient agents will help maintain moisture balance. Soothing ingredients are beneficial to alleviate the redness and irritation often experienced with these skin types. Sensitive

Table 2 Skin Toner for Dry Skin

Ingredients	%	Function
Water	QS to 100%	Vehicle
Sodium PCA	5.0	Humectant
Green tea extract	3.0	Botanical extract with soothing, anti-inflammatory, mild astringency, free radical scavenger benefits
Soy extract	2.0	Botanical extract with moisturizing benefits
Xanthan gum	0.2	Film former, thickener
Fragrance, color, preservative	As needed	

skin toners are formulated similar to dry skin formulas with the addition of anti-irritants such as allantoin, green tea, or licorice extract.

Toners designed for normal to combination skin types typically contain low levels of ethanol, humectants, and appropriate key ingredients. Botanical extracts with high tannin levels offer skin tightening effects without stripping the skin of its natural oils to mitigate the potentially drying effect of ethanol. It is recommended that soothing agents and humectants be added and that toner use be followed by a moisturizer designed for normal skin.

Oily skin toners, such as the formula in Table 3, are designed to provide a high degree of astringency and to control and/or remove excess sebum. This is achieved by using higher levels of ethanol and highly astringent and oil-absorbing ingredients. Levels of 20–50% ethanol may be used. The sebum removing and cooling effects of ethanol are highly desirable to the oily skin patient. High tannin-containing ingredients provide astringency. Astringent botanicals to consider include extracts of witch hazel, rosemary, lemon, grapefruit, horse chestnut, and stinging nettle. Natural sources of glycolic acid found in sugar cane extract, lactic acid found in milk, and salicylic acid found in willow bark extracts are often added for exfoliation. If a stimulating sensation is desired, peppermint, menthol, or eucalyptus is added. Kaolin, polyamides (nylon-6 and -12), methylmethacrylate crosspolymer, and silica absorb skin oil and minimize the appearance of oily shine on the skin. Silica settles slowly and gives the product a hazy appearance. The other oil-absorbing particulates settle readily, so a shake-well instruction prior to use is required. Soothing botanical agents and allantoin may be added to lessen any irritating dryness associated with higher ethanol concentrations.

Toners formulated for acne-prone skin typically contain high levels of ethanol, salicylic acid, and naturally derived antibacterials such as cinnamon, neem, and tea tree oil. Recently, there have been several references on the allergenic characteristics of tea tree oil (18–21). The ethanol level should be kept to the minimum necessary to solubilize the salicylic acid in order to minimize excessive drying to the skin. The FDA OTC Acne Monograph (3) dictates levels of salicylic acid from 0.5–2.0% as well as the acne treatment claim that may be listed on the product. A pH <4 is needed to assure delivery of the acid form. Formulations containing salicylic acid typically use 35–60% ethanol to maintain its solubility and stability. Levels as low as 20% ethanol in conjunction with the humectants glycerin and butylene glycol as cosolvents have been shown to provide acceptable salicylic acid solubility at room-temperature and low-temperature (5°C) conditions (22). To further enhance the perception of medicinal benefits of an anti-acne toner, scent and skin sensorial-stimulating agents such as menthol, eucalyptus, peppermint, or camphor may be added. Soothing botanical extracts and humectants are beneficial to minimize the potentially irritating and drying effects of high alcohol levels.

Table 3 Skin Toner for Oily Skin

Ingredients	%	Function
Water	QS to 100%	Vehicle
Ethanol	20.0	Vehicle, astringent, preservative, oil removal
Witch hazel distillate	20.0	Astringent, cooling and soothing effect
Glycerin	5.0	Humectant
Fragrance, color	As needed	

Alcohol-free toners may be used as a last step in cleansing, a preparation step to moisturizing, or as a whitening treatment product in the Far East. Toners are frequently sold under the "softener" nomenclature in Asia. Asian consumers have a negative perception of alcohol in terms of both skin reactions and odor of ethanol. They exhibit a higher degree of sensitivity to the skin effects of alcohol (23). It is advisable to avoid the use of alcohol and sensorial-stimulating agents to minimize the chance of irritation. Botanical extracts and the quasi-drug ascorbyl glucoside are used for whitening effects in toners. Another popular toner form in Asia is the lightweight, low-viscosity milky lotion. These are frequently used to prepare the skin as the first step of the moisturizing regimen. The milky lotions are alcohol-free. Collagen, hyaluronic acid, and whitening agents are popular in these products.

Ingredient and Vehicle Stability and Compatibility Considerations

Requirements of pH, ingredient solubility and compability, and product stability influence the choice of ethanol-to-water ratios, humectants, and cosolubilizers. Hydroxy acids require low pH to be effective as exfoliants. Fortunately, they also act as pH adjusters when a low pH is desired. This low pH limits the choice of film formers and thickeners. There are also pH and concentration limitations when using AHAs in retail products sold in the U.S. The Cosmetic, Toiletry, and Fragrance Association's Cosmetic Ingredient Review (CIR) Expert Panel recommends that cosmetic products containing glycolic and lactic acids and their salts and esters be formulated at pH ≥ 3.5 and at concentrations $\leq 10\%$ (24). Oil-soluble ingredients such as emollients, fragrance oils, and vitamins A and E require cosolubilizers to assure ingredient solubility to maintain product clarity and stability. The use of these cosolubilizers may cause product foaming during production filling and consumer use. This foaming can be minimized by adding an ingredient such as simethicone to reduce surface tension. Tea tree oil, found in many anti-acne and oily skin toners for its antibacterial activity, requires solubilizing agents for a clear solution, has a distinctive odor and its terpene constituents are highly susceptible to oxidation. The oxidation potential impacts the safety of the product (18–21); therefore, a recent European Cosmetic Toiletry and Perfumery Association (COLIPA) report recommended that manufacturers add antioxidants and/or packaging that minimizes the product's exposure to light (25).

High levels of ethanol in a toner can solubilize oil-soluble ingredients without the need for additional cosolubilizers. Easier to use water-soluble botanical extracts are more commonly used to provide antioxidant, anti-irritant, and soothing benefits, thus negating the need for cosolubilizers and mitigating any drying effects of alcohol. Alcohol-free toners or toners with less than 20% alcohol require preservatives to maintain microbiological quality.

PRODUCT CLAIMS

Toners on the market tout a plethora of skin benefit claims. It is these benefits that offer a prime opportunity for toner acceptance. The benefit most frequently associated with toners is a reduction of apparent pore size. Although no cosmetic product can alter the actual size of the pores, this claim is achieved because the pores appear less prominent due to an astringent effect that results in swelling of the skin surrounding the pore or removal of oil and dirt from the pore. "Purifies skin by removing dirt and oils" and "removing (or)

controlling oil" are claims used in oily skin toners. The toner claims, "restores the acid/alkali balance of the skin" and "pH balanced," still resonate well with consumers although they go back to the days of highly alkaline cleansers. Sensorial claims include "skin looks healthy," "even skin tone," "softens," "soothes," "refreshes," "energizes," "cools skin," "warms skin," and "tightens." Lightening and whitening claims such as "whitens (or lightens) the skin" and "reduces dark spots" are popular in Far East whitening toners. These claims may be quasi-drug or cosmetic depending on the country, ingredient, and claims. The "evens skin tone" claim is gaining popularity in the rest of the world.

CLAIMS TESTING METHODS

Toner claims are substantiated by subjective and objective measurements. Many claims are substantiated by using both measurements. These tools are useful in the screening of ingredients and final product efficacy. Subjective measurements include consumer perception testing and panelists self-assessment on clinical trials. These tests include yes/no, like/dislike, agree/disagree, and point scales to rate consumer perception. Point scales may be a three-, five-, seven-, or 10-point scale. For example, using a five-point scale of "much worse," "slightly worse," "no change," "slightly improved," or "much improved" would offer the panelists the option to rate the skin's appearance and condition. Another method is the use of a line marked in units from one to 10 designating least to most, where the panelists mark product attribute agreement.

Objective measurements include expert grading, photography, and instrument measurements. The expert grader is trained in visually assessing the skin for changes in color for evenness of skin tone, reduction of pore size for tightening and astringent claims, and reduction of the appearance of fine lines and wrinkles for anti-aging claims. Photography and more recently VISIA CR™ is used to capture these same measures on a permanent record. Instrumental measures include the Sebumeter™ and Sebutape (CuDerm Corporation, Dallas, TX) (Fig. 1) to measure oil control. The Gas Bearing Electrodynamometer™ assesses skin softness, and the Minolta chromameter measures skin tone and color. Chromameter measurements are useful in measuring skin tone and color in products claiming evenness of skin tone or skin whitening as well as the reduction of redness when measuring anti-irritant and anti-inflammatory benefits.

USES IN DERMATOLOGY

Until recently, the use of astringents and toners in dermatology was primarily limited to their anti-acne and astringent properties, although some also functioned as mild antiseptic agents suitable for mild or limited bacterial infections of the skin surface (24). Today soothing toners are increasingly being used by dermatologists and aestheticians for their anti-inflammatory and anti-irritant benefits as part of a post-cosmetic surgery regimen such as laser, chemical peel, or light-modulated procedures. The perceptual attributes of clean and refreshing for oily and acne-prone skins and soothing and calming for dry and sensitive skins in a cosmetically acceptable toner formulation assure patient compliance when compared with traditional drug vehicles that lack the aesthetic characteristics preferred by patients (26).

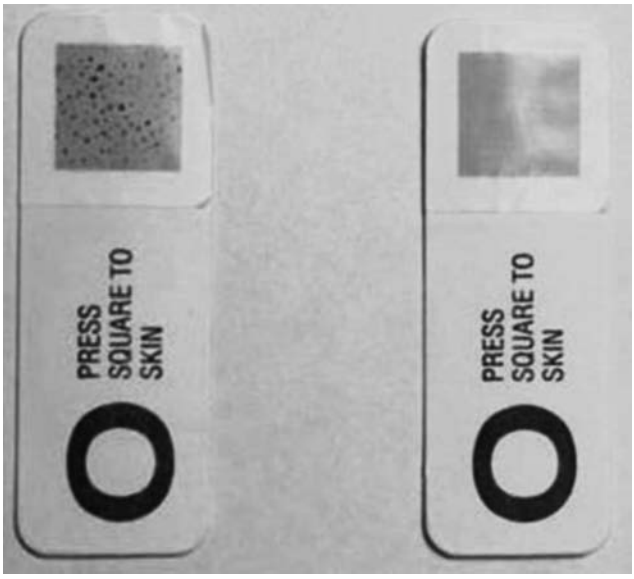

Figure 1 Macroscopic view of Sebutapes taken from oily skin surface before (*left*) and after (*right*) toner treatment. The fewer and smaller black spots on the right indicate a reduction in sebum after treating the skin with an oily skin toner. The number of pores and amount of sebum secreted can also be determined via image analysis.

ADVERSE REACTIONS

Adverse reactions in toners include transient contact irritation, contact allergy, and sensitization. Contact allergy is most often seen with more pharmacologically complex products, such as those containing multiple botanical extracts and penetration enhancers (27). Propylene glycol is often used as a humectant and sometimes as a solvent in toners. It is approved for use in concentrations up to 50% by the CIR (28), but caution is advised in using it above 10% as it can act as a penetration enhancer and cause irritation which, in patch testing, is often confused with comedones. Although tea tree oil is not recognized by the FDA as an anti-acne, antiseptic or antibacterial active ingredient, it is found in many anti-acne and oily skin toners. It also has a distinctive odor, and recently there have been several reports on the allergic, sensitization, and irritation potential of tea tree oil (18–21,29). COLIPA recommended that it not be used in cosmetic products at concentrations greater than 1% (25). Increased sun sensitivity occurs from topical application of AHA-containing products. Recently, the FDA issued industry guidance for labeling these products with a sunburn alert to minimize this risk (30). Toners have very low rates of reported adverse reactions compared to other skin care products. FDA statistics for the years 1991–1994 show 7.07 reported adverse reactions to toners and fresheners per million units sold, (31) and no consumer complaints were reported from 1995–2003 (32).

SUMMARY

Toners have a beneficial role in a patient's skin care regimen. They reduce the appearance of pore size; exfoliate; remove or control sebum; soothe skin aggravated by the environment,

dryness, or dermatological procedures, and provide a clean, refreshing skin feel. When properly formulated for skin type and skin benefits, they offer a cosmetically acceptable vehicle for delivery of ingredients used in cosmetic, cosmetology, post-cosmetic surgery, and acne treatment applications.

ACKNOWLEDGMENTS

The author is grateful to Dawn Burke-Colvin of Mary Kay Inc., and Laurie Pan, PhD, for their technical expertise, Gopa Majmudar, PhD, for providing Figure 1, and to Regina Lee, Mary Kay Inc., for research assistance.

REFERENCES

1. Skin Care: Cosmetics and Toiletries, In: Integrated Marketing Information System, Euromonitor® International: London, 2005.
2. Skin Protectant Drug Products for Over-the-Counter Human Use: Astringent Drug Products; Final Rule, Federal Register, 2004.
3. Topical Anti-microbial Drug Products for Over-the-Counter Human Use: Acne Drug Products; Final Rule, Federal Register, 1991.
4. Dweck A. Natural extracts and herbal oils: concentrated benefits for the skin. Cosmet Toilet 1992; 107:89–98.
5. Accessed April, 2005, at http://www.drugdigest.org/DD/DVH/Herbs/0,3913,,00.html.
6. Accessed April, 2005, at http://www.mskcc.org/mskcc/html/11571.cfm?search=tannin&tab.
7. Draelos Z. Topical Agents Used in Association with Cosmetic Surgery. Semin Cutan Med Surg 1999; 18(2):112–118.
8. Notice No. (2000-33) of the Korea Food and Drug Administration [Functional Cosmetic Regulations]: Attachment A, 2000.
9. Taiwan: Law for the Control of Cosmetic Hygiene in the Republic of China. Bureau of Pharmaceutical Affairs, Department of Health, The Executive Yuan, Republic of China, 2004.
10. Wolf B, Tietjen M. Patent US5443855-A (to Revlon), 1995.
11. Patent 2002187168 (to Jensen C, Robinson H.), 2002.
12. Lee O, Kang H, Han S. Oriental herbs in cosmetics. Cosmet Toilet 1997; 112:57–64.
13. Patent JP7149787-A (to Toyo Beauty), 1995.
14. Patent 6803032 (to Cognis Corporation), 2004.
15. Baumann L. Cosmeceutical Critique: Pycnogenol. Skin and Allergy News, 2004.
16. Patent 6,406,720 (to Pauly G, Fleury M.), 2002.
17. Patent 5133967 (to The Dow Chemical Company), 1992.
18. Southwell IA, Freeman S, Rubel D. Skin irritancy of tea tree oil. J Essent Oil Res 1997; 9:47–52.
19. Crawford GH, Sciacca JR, James WD. Tea tree oil: cutaneous effect of the exracted oil of Melaleuca alternifolia. Dermatitis 1992; 27:279–280.
20. Knight TE, Hausen BM. Melaleluca oil (tea tree oil) dermatitis. J Amer Acad Dermatol 1994; 30:423–427.
21. Rubel DM, Freeman S, Southwell IA. Tea tree oil allergy: What is the offending agent? Report of three cases of tea tree oil allergy and review of the literature. Aust J Derm 1998; 39:244–247.
22. Herrera L. Solubility of salicylic acid with and without co-solvents. Unpublished data presented to Mary Kay Inc., Dallas, TX, in fulfillment of the University of Texas College of Pharmacy internship, 1999.
23. Stephens TJ, Oresajo C. Ethnic sensitive skin: a review. Cosmet Toilet 1994; 109(2):75–79.
24. Cosmetic Ingredient Review Expert Panel (CIR), Andersen FA, ed. "Final Report on the Safety Assessment of Glycolic Acid, Ammonium, Calcium, Potassium, and Sodium Glycolates,

Methyl, Ethyl, Propyl, and Butyl Glycolates, and Lactic Acid, Ammonium, Calcium, Potassium, Sodium, and TEA-Lactates, Methyl, Ethyl, Isopropyl, and Butyl Lactates, and Lauryl, Myristyl, and Cetyl Lactates." Int J Toxicol 1998; 17:1–241.
25. SCCP Opinion on Tea Tree Oil. Scientific Committee on Consumer Products Adopted by the SCCP during the 2nd plenary meeting of 2004.
26. Barker MO. Masks and astringents/toners. In: Baran R, Maibach H, eds. Textbook of Cosmetic Dermatology. 3rd ed. London; New York: Taylor and Francis, 2003:229–237.
27. Pittz E. Skin barrier function and use of cosmetics. Cosmet Toilet 1984; 99:30–35.
28. Cosmetic Ingredient Review Expert Panel (CIR). Final Report on the Safety Assessment of Propylene Glycol and Polypropylene Glycols. J Am Coll Toxicol 1994; 13:437–491.
29. Human studies Draize method, study no. DT-029. Skin and Cancer Foundation Australia, 1997.
30. Guidance for Industry: Labeling for Topically Applied Cosmetic Products Containing Alpha Hydroxy Acids, U.S. Department of Health and Human Services. College Park, MD: Food and Drug Administration, 2005.
31. Participation Status Report for Cosmetic Voluntary Registration Program, Office of Cosmetics and Colors, Division of Program and Enforcement Policy. Washington, DC: Food and Drug Administration, 1995.
32. Accessed April, 2005, at http://www.cfsan.fda.gov/~dms/cos-comp.html. Consumer Complaints about Cosmetic Products, 1995-2003, Office of Cosmetics and Colors, U.S. Department of Health and Human Services. College Park, MD: Food and Drug Administration.