Resins and Resin Combinations

Resins are amorphous products with a complex chemical nature. They are usually formed in schizogenous or in schizolysigenous ducts or cavities and are end products of metabolism. Physically, resins are usually hard, transparent, or translucent and, when heated, they soften and finally melt. Chemically, they are complex mixtures of resin acids, resin alcohols, resinotannols, esters, and resenes. They are insoluble in water, and some investigators believe resins are oxidation products of the terpenes. Several resins are used in pharmacy and in the arts, among which rosin, guaiac, and mastic are typical examples.

Resins often occur in more or less homogeneous mixtures with volatile oils; the mixtures are known as **oleoresins.** Natural oleoresins are exemplified by turpentine and copaiba; pharmaceutic oleoresins are derived from ginger and capsicum. Oleoresins also occur in mixtures with gums; these mixtures are called **oleo-gum-resins.** Because gums are water-soluble carbohydrate derivatives, they can be separated from oleoresins rather easily. Oleo-gum-resins include asafetida and myrrh. The nomenclature of these resinous combinations is, at best, artificial because small amounts of volatile oil are often present in resins, and small amounts of gum are often present in oleoresins.

Balsams are resinous mixtures that contain cinnamic acid, benzoic acid, or both, or esters of these acids. Benzoin, Peru balsam, Tolu balsam, and styrax are typical balsams. The term "balsam" has been erroneously applied to some oleoresins, e.g., balsam of copaiba. This error has occasionally led to some confusion.

In a few cases, resins are found in glycosidal combinations; such combinations are called **glucoresins** or, more properly, **glycoresins.** Such glycoresins are found in jalap and podophyllum.

RESINS

When resins are separated and purified, they are usually brittle, amorphous solids that fuse readily when heated, after passing through a preliminary stage of softening. They are insoluble in water but dissolve in alcohol or other organic solvents. On evaporation these solutions deposit the resin as a varnishlike film. Resins burn with a characteristic, smoky flame.

Resins may be the final products in destructive metabolism. Many are believed to be oxidation products of the terpenes. They are usually more or less complex mixtures and their principal constituents may be classified as follows.

Resin Acids. These contain a large propor-

tion of oxyacids, usually combining the properties of carboxylic acids and phenols. They occur both in the free state and as esters. They are soluble in aqueous solutions of the alkalies, usually forming soap-like solutions or colloidal suspensions. Their metallic salts are known as resinates, and some of these resinates are used extensively in the manufacture of cheap soaps and varnishes. Examples of resin acids are abietic acid in rosin or colophony, copaivic and oxycopaivic acid in copaiba, and commiphoric acid in myrrh.

Resin Alcohols. Complex alcohols of high molecular weight, known as **resinotannols,** give a tannin reaction with iron salts. **Resinols** do not give such a reaction. The resin alcohols occur in the free state and as esters in combination with simple aromatic acids (benzoic, salicylic, cinnamic, and umbellic). The following resinotannols have been isolated: aloeresinotannol from aloe, peruresinotannol from balsam of Peru, siaresinotannol and sumaresinotannol from benzoin, and toluresinotannol from balsam of Tolu. The following are examples of resinols: benzoresinol from benzoin and storesinol from storax.

Resenes. Complex neutral substances devoid of characteristic chemical properties are called resenes. They do not form salts or esters and are insoluble in and resist hydrolysis by alkalies.

Glycoresins. These are complex mixtures yielding sugars and complex resin acids on hydrolysis, as with the resin of jalap.

Pharmaceutic Resins. Pharmaceutic resins are usually obtained (1) by extracting the drug with alcohol and precipitating the resin in water, as with resins of jalap and podophyllum; (2) by separating the oil from oleoresin by distillation, as with rosin from turpentine and copaivic resin from copaiba; or (3) by collecting the natural product that has exuded as oleoresin from the plant through natural or artificial punctures and from which the natural oil has partially evaporated into the atmosphere, as with mastic.

Biosynthesis of Resin Components. The exact chemical identity of most constituents of resin mixtures is unknown; thus, detailed information on the biosynthesis of these plant constituents is lacking. Many resin components are considered to arise by oxidation of polymerized terpenoid metabolites. Acetate and mevalonate are incorporated into some resins, and a surprisingly rapid rate of "resin acid" turnover in pine has been suggested by studies with $^{14}CO_2$.

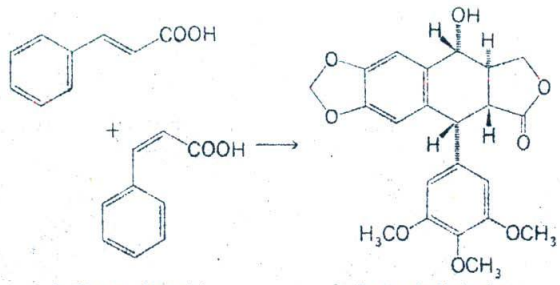
The aromatic acids in balsams are undoubtedly formed by way of the shikimic acid-phenylpropanoid pathway. It is also believed that phenylpropanoid precursors are involved in the formation of more complex resin components. The lignan, podophyllotoxin, which presumably arises via an oxidative coupling of 2 cinnamic acid residues (Fig. 6–1), is an example of this type of resin component. This belief is supported by the observed 1.4% incorporation of radioactivity into podophyllotoxin during preliminary feeding studies using phenylalanine-U-^{14}C and *Podophyllum emodi.*

Rosin

Rosin or colophony is a solid resin obtained from *Pinus palustris* Miller and other species of *Pinus* Linné (Fam. Pinaceae).

The commercial grades of rosin vary in color from light amber (the finest or "water-white" grade) to almost black (and very dirty); the latter is used principally for destructive distillation and the production of "rosin oils." Rosin has a great variety of technical uses. Only the light-colored transparent rosins are used medicinally.

Rosin usually occurs as shiny, sharp, angular fragments that are translucent, amber-colored, and often covered with a yellowish dust. Rosin is hard, brittle, and easily pulverized. Its fracture is shallow-conchoidal; its odor and taste are faintly terebinthinate. Rosin is soluble in alcohol, ether, benzol, carbon disulfide, acetic acid,



2 Cinnamic acid Podophyllotoxin

Fig. 6–1. Proposed biosynthetic origin of podophyllotoxin.

fixed and volatile oils, and in solutions of potassium or sodium hydroxide.

The alcoholic solution of rosin becomes milky white when added to water. When fragments of rosin are heated in water, they melt, flow together, and form a sticky mass.

Rosin contains from 80 to 90% of the anhydrides of abietic acid (which, on treatment with alcohol, are changed into crystalline abietic acid); sylvic acid, which is probably a decomposition product of abietic acid; sapinic acid; pimaric acid and other acids; and resene, a hydrocarbon.

USES. Rosin is used as a stiffening agent in cerates, plasters, and ointments. It is employed in veterinary medicine as a diuretic. Commercially, rosin is used in the manufacture of varnishes, varnish and paint dryers, printing inks, soap, sealing wax, floor coverings, and numerous other products. Rosin is frequently used as an adulterant of other resinous products.

Podophyllum

Podophyllum consists of the dried rhizome and roots of *Podophyllum peltatum* Linné (Fam. Berberidaceae) (Fig. 6–2). It is also known as **mayapple** or **mandrake.**

The generic name is Greek and means footlike leaf; *peltatum* means shieldlike. The plant is a perennial herb that has a long, jointed, and branching rhizome. The rhizomes are dug either early in the spring or in the autumn after the aerial parts have died down. Most of the commercial supplies come from the central United States and from Virginia and North Carolina. The drug was known to the Indians, who introduced it to the early settlers. The drug should not be confused with mandragora, referred to as mandrake by the ancient Greeks and Asiatics (see page 200).

Mayapple is an important American botanical drug; the annual production is several hundred tons and supplies both domestic and export demands.

Podophyllum contains 3.5 to 6% of a resin whose active principles are lignans. These include podophyllotoxin (20%), α-peltatin (10%), and β-peltatin (5%). A number of lignan glycosides are in the plant, but because of their water solubility, they are lost during the normal preparation of the resin.

The antimitotic and purgative properties of these compounds depend on a lactone ring in the *trans* configuration. Treatment with mild alkali produces epimerization with formation of the stable *cis* isomers, which are physiologically inactive. Picropodophyllin is an inactive *cis* isomer produced in this way from the active *trans* podophyllotoxin.

Podophyllum yields not less than 5% of podophyllum resin.

USES. Podophyllum possesses drastic purgative properties. Its resin is also employed as an antimitotic and caustic.

ALLIED PLANTS. Indian podophyllum, the rhizome of *Podophyllum emodi* Wallich, a plant growing on the lower slopes of the Himalayas, is larger and yields 11.4 to 12% of resin that contains about twice as much

Fig. 6–2. A typical stand of mayapple (*Podophyllum peltatum*) plants growing in Indiana. (Photo courtesy of Dr. Thomas M. Zennie.)

podophyllotoxin as the resin obtained from *P. peltatum*.

Podophyllum resin is also known as **podophyllin** and is the powdered mixture of resins removed from podophyllum by percolation with alcohol and by subsequent precipitation from the concentrated percolate when added to acidified water.

The precipitated resin is washed twice with water and is dried and powdered. It is an amorphous powder that varies in color from light brown to greenish yellow and turns darker when subjected to temperatures exceeding 25° C or when exposed to light. It has a slight, peculiar, bitter taste and is highly irritating to the eye and to mucous membranes in general.

USES AND DOSE. Podophyllum resin is a caustic for certain papillomas. It is applied topically as a 25% dispersion in compound benzoin tincture or in a 70 to 96% solution of alcohol. Podophyllum resin has also been used as a drastic purgative and as a hydragogue cathartic. The dose employed was 10 mg.

A number of lignans with lactone rings in the *trans* configuration are the tumor-inhibiting constituents of podophyllum resin. Such compounds include podophylloxtoxin, several podophyllotoxin derivatives, and α- and β-peltatin. The peltatins are responsible for most of the purgative effects of the drug.

PROPRIETARY PRODUCTS. Bilstan®, Pod-Ben-25®, and Podoben®.

Eriodictyon

Eriodictyon or yerba santa is the dried leaf of *Eriodictyon californicum* (Hooker et Arnott) Torrey (Fam. Hydrophyllaceae). *Eriodictyon* is Greek and means woolly, referring to the hairy leaves. The plant is an evergreen shrub indigenous to the mountains of California and northern Mexico. The drug has been employed by the Indians of California for many years.

Eriodictyon contains a resin, eriodictyol (the aglycone of eriodictin), xanthoeriodictyol, chrysoeriodictyol, homoeriodictyol, eriodictyonic acid, formic acid, butyric acid, volatile oil, and tannin.

USES AND DOSE. Eriodictyon is a flavor used to disguise the bitterness of certain preparations, such as those containing qui-

nine. It has also been used as a stimulating expectorant in doses of 1 g.

Jalap

Jalap or jalap root is the dried, tuberous root of *Exogonium purga* (Wendoroth) Bentham (Fam. Convolvulaceae). Jalap yields not less than 9% of resins. *Exogonium* is Greek and means "outside" and "offspring," referring to the exserted stamens and pistils; Jalapa is the name of the city in Mexico from which the drug was first obtained. The plant is a perennial, twining herb indigenous to the mountains of Mexico and cultivated in Mexico, India, and, to some extent, in the West Indies. The plant possesses thin, horizontal, underground runners. The tuberous roots arise from the nodes of the runners. The roots are usually dug in the fall, placed in nets, and dried over open fires. This latter process accounts for their empyreumatic odor. Our nation's supply comes entirely from Vera Cruz.

Jalap contains resin, 8 to 12%; volatile oil; starch; gum; and sugar. The resin contains a number of glycosides, such as ipurganol, a phytosterol glycoside (also found in certain *Ipomoea* species) and jalapin, a mixture of acidic glycosides. It also contains β-methyl esculetin and palmitic and stearic acids.

USE AND DOSE. Jalap is a cathartic and is generally considered a hydragogue and a drastic purgative. The usual dose is 1 g.

Jalap resin is prepared by extracting powdered jalap with an alcohol-water mixture. The percolate is concentrated to one fourth the weight of drug used and is then slowly poured into water and constantly stirred. The precipitated resin is washed with hot water, collected, and dried.

Jalap resin occurs as yellowish brown masses or powder. It is a cathartic possessing hydragogue activity. The usual dose is 125 mg.

Mastic

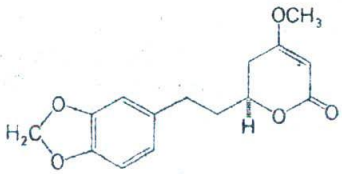
Mastic, mastiche, or mastich is the concrete resinous exudate from *Pistacia lentiscus* Linné (Fam. Anacardiaceae). Mastic is Greek and means to chew; *Pistacia* is from the Persian *pistah*, the name of the pistachio tree; *lentiscus* refers to the lenticular cavities into which the resin is secreted. The plant is a shrub or small tree indigenous to the Mediterranean region and cultivated in the Grecian archipelago, especially on the island of Chios. The resinous juice collects in cavities in the inner bark. Long incisions are made in the trunk and in larger branches, through which the resin exudes. The resin finally collects in small tears on the outside. The origin of the use of mastic is lost in antiquity; it is mentioned by both Theophrastus and Pliny. Mastic has long been chewed by Oriental women as a breath sweetener and is a common article in Oriental bazaars. Its employment in medicine dates back to about the 13th century.

Mastic contains about 90% of a resin, consisting of α-resin (mastichic acid), which is soluble in alcohol, and β-resin (masticin), which is insoluble in alcohol, and a volatile oil, 1 to 2.5%, which has the balsamic odor of the drug and consists chiefly of (+)-pinene. A bitter principle is also present.

USE. Mastic is used in the form of a dental varnish to seal cavities.

Kava

Kava or kava-kava is the dried rhizome and roots of *Piper methysticum* Forster (Fam. Piperaceae). The plant is a large shrub widely cultivated in Oceania; its underground parts have been extensively used by the natives of these islands in the preparation of an intoxicating beverage.



Dihydromethysticin

In addition to large quantities of starch, the drug contains about 5 to 10% of a resin

from which 6 different, closely related styrylpyrones have been isolated in pure form: yangonin, desmethoxyyangonin, kawain, dihydrokawain, methysticin, and dihydromethysticin. Pharmacologic studies have shown that all of the kava pyrones are more or less potent, centrally acting skeletal muscle relaxants. In addition to inducing changes in motor function and reflex irritability, they possess antipyretic and local anesthetic properties. Differences in action are largely quantitative. The central nervous and peripheral activities of the kava pyrones are sufficient to account for the native use of the drug.

Cannabis

Cannabis. Indian hemp, marihuana, or **pot** consists of the dried flowering tops of the pistillate plants of *Cannabis sativa* Linné (Fam. Moraceae).

The plant is an annual herb indigenous to central and western Asia and is cultivated in India and other tropical and temperate regions for the fiber and seed. *Cannabis* is the ancient Greek name of hemp.

Cannabis was used in China and India, spread slowly through Persia to Arabia where the resin was known as **hashish,** and probably was introduced into European and American materia medica about the time of Napoleon.

Through long years of selective cultivation, 2 genetic types of cannabis have evolved. One, designated the drug type, is rich in THC. The other, referred to as the hemp type, contains little active principle (cannabidiol is the predominant cannabinoid) but has the elongated bast fibers desired in the manufacture of rope.

The amount of resin found in the pistillate flowering tops of *C. sativa* markedly decreases when the plants are grown in the more temperate climates (Fig. 6–3). Thus, Indian cannabis yields 20% or more of resin; Mexican cannabis 15% or less; Kentucky hemp 8% or less; Wisconsin hemp 6% or less. The active principles are found in the resin in about the same or in even smaller ratios than those just indicated. The hemp leaves contain a small amount of the resin.

Indian cannabis is prepared rather carefully from the pistillate flower heads only and contains relatively few leaves. Mexican and American cannabis consist of the whole upper portion of the stalk of the pistillate plant. Indian cannabis may have an activity many times greater than that of a poor quality of American cannabis. (Figure 6–4 shows the American cannabis plant; Figure 6–5 shows the structural elements in powdered cannabis.)

The unusual sensations induced in humans by the uncontrolled use of cannabis are obtained more promptly and with less drug by inhaling the smoke of burning cannabis than by oral dosage. The importation into the United States of rather crude **Mexican cannabis (marihuana)** cigarettes began several decades ago. As the demand for these cigarettes **(reefers)** increased and the habit of smoking them spread to school children, federal and state narcotic agents started a campaign to stamp out their sale. The importation of Indian cannabis was prohibited, and even large areas of naturally growing American hemp were destroyed. This campaign continues. The substitution of a poor quality drug for the high quality Indian cannabis and the marihuana campaign resulted in discontinued medicinal use of cannabis in the United States.

Indian cannabis yields 15 to 20% of a resin that contains the major active euphoric principle (−)-Δ^9-*trans*-tetrahydrocannabinol, commonly referred to as Δ^9-THC. This compound was isolated almost simultaneously by 2 teams of investigators. One team viewed the compound as a dibenzopyran derivative and assigned the aforementioned name. The other group applied a monoterpene nomenclature, resulting in the designation Δ^1-*trans*-tetrahydrocannabinol. Both names are commonly found in the literature, but the

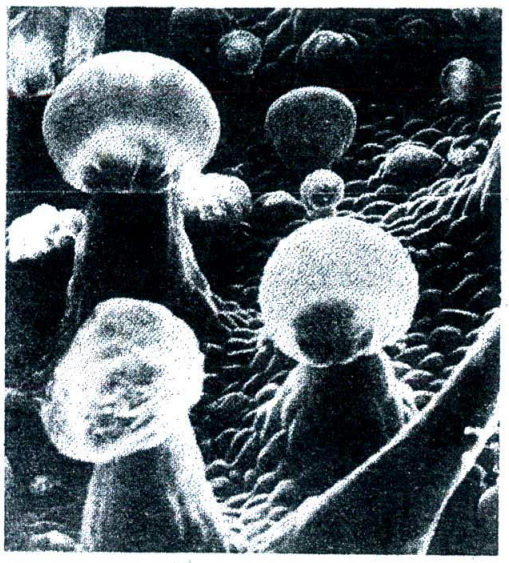


Fig. 6–3. Scanning electron micrograph of stalked and sessile glandular trichomes on the bract of a female plant of *Cannabis sativa*. The glands contain resin. Magnification 390 ×. (Photo, courtesy of Dr. Charles T. Hammond, Department of Biology, Wabash College.)

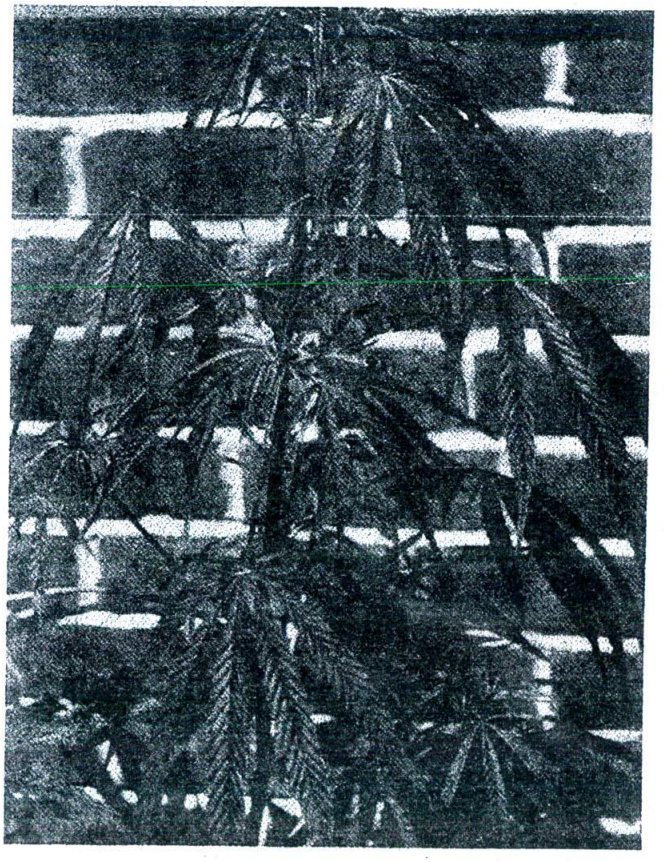


Fig. 6–4. American cannabis.

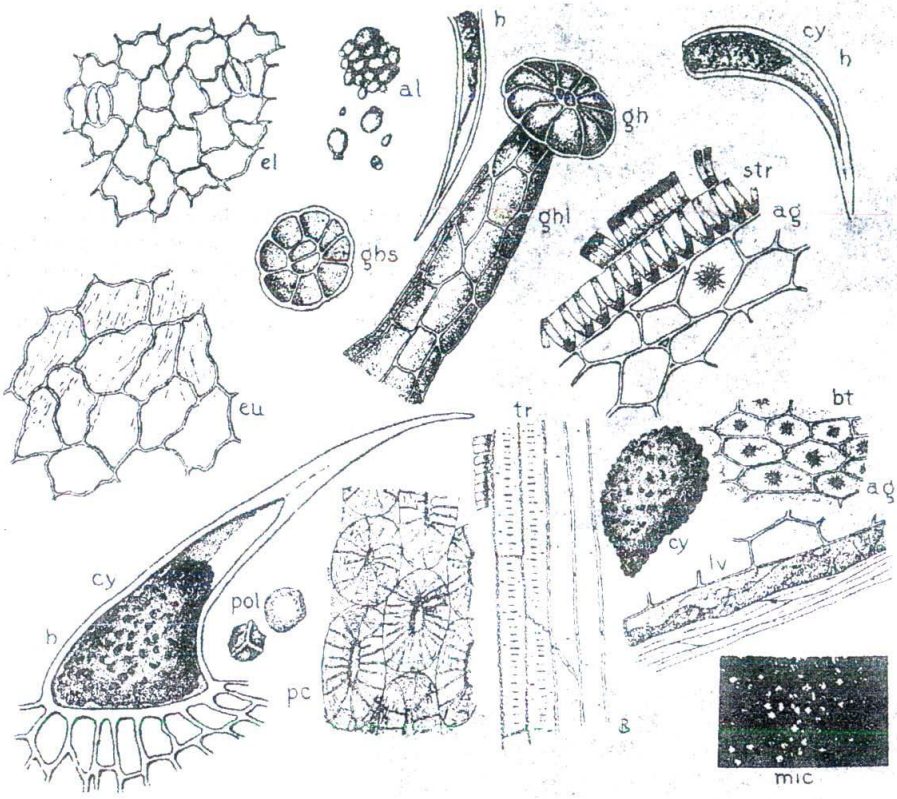
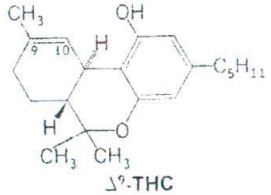


Fig. 6–5. Powdered cannabis. *el*, Epidermis from lower surface of leaves with sinuate vertical walls and numerous oval stomata, and *eu*, from upper surface, with straight walls and no stomata; *h*, nonglandular hairs, numerous, unicellular, rigid, curved, with a slender pointed apex and an enlarged base, usually containing a cystolith *(cy)*, but frequently broken, and the cystolith freed; glandular hairs of 2 kinds, 1 with a short 1-celled stalk *(ghs)* and the other with a long multicellular stalk *(ghl)*, the head *(gh)* in both kinds being globular and consisting of 8 to 16 cells; *bt*, fragments of bracts and leaves showing yellowish brown laticiferous vessels *(lv)*, numerous rosette aggregates *(ag)* of calcium oxalate, 5 to 30 μ in diameter, strands of spiral *(str)* or reticulate *(tr)* vessels, and phloem; *(pc)*, fragments of fruits with palisadelike, nonlignified cells with yellowish brown, finely porous walls; tissues of embryo and endosperm with numerous oil globules and aleurone grains *(al)*, the latter 5 to 10 μ in diameter and displaying crystalloids and globoids; *pol*, pollen grains; *mic*, photomicrograph of leaf fragment showing a rosette aggregate of calcium oxalate crystals in nearly every cell. (Drawings by Paul D. Carpenter.)

dibenzopyran nomenclature is now more widely used in this country.



Δ⁹-THC

Other constituents isolated from cannabis resin include cannabinol, cannabidiol, cannabidiolic acid, cannabichromene, cannabigerol, and Δ⁸-*trans*-tetrahydrocannabinol. Tetrahydrocannabinols (Δ⁸- and Δ⁹-THC) possess euphoric activity, cannabinol is weakly active, and cannabichromene and cannabidiolic acid are sedative principles. Δ⁹-THC has been synthesized and the pure compound utilized for physiologic studies in human beings. It was found to be more potent when smoked than when taken orally. Δ⁹-THC is available under the name of dronabinol (Marinol®) for the control of nausea in cancer chemotherapy.

Cannabis is cultivated to a considerable

extent for its bast fibers, **hemp**, and for its fruits, **hempseed;** the latter contain about 20% of a fixed oil that is expressed and used in the manufacture of paints and soap; the cake meal is used as cattle food.

OLEORESINS

Oleoresins are homogeneous mixtures of resins and volatile oils.

There is no sharp line of demarcation between these various types of resinous substances, and classification is sometimes difficult. Small proportions of volatile oils are present in many resins. Depending on the relative amount of volatile oil in the mixture, oleoresins may be liquid, semisolid, or solid. Usually, there is a small amount of "natural" exudate from oleoresin-containing trees owing to insect stings, broken branches, and other injuries, but the commercial supplies are generally obtained by artificial incision through the bark and even into the wood.

Turpentine

Turpentine, gum turpentine, or gum thus is the concrete oleoresin obtained from *Pinus palustris* Miller and from other species of *Pinus* (Fam. Pinaceae).

"Gum" turpentine or "gum" is a common name among the collectors and dealers of turpentine but is a misnomer from the scientific standpoint. Turpentine is not related to the true gums and mucilages of carbohydrate origin.

Turpentine is collected from the longleaf pine (*P. palustris* Miller) and from the slash pine (*P. elliottii* Engelmann var. *elliottii*) that grow in North and South Carolina, Georgia, and northern Florida. The trees form vast forests and present a characteristic appearance owing to the "face" of the cut surface (Fig. 6–6). Turpentine yields depend on the treatment and the size of the tree. Large trees measuring 45 to 50 cm in diameter are preferred, although smaller trees may be turpentined also. If skillfully worked, trees yield for 15 to 20 years.

The oleoresin is secreted in ducts located directly beneath the cambium in the sapwood. During the spring of the year, bark is chipped from the tree by using a "bark hack," a long-handled cutting blade. Following removal of the rounded chip, a spray of 50% solution of sulfuric acid is applied to the freshly cut surface. As the sap (oleoresin) flows, it is guided by metal gutters into containers attached directly to the tree trunk; the thick liquid that collects is removed periodically and taken to the turpentine still.

The older method of chipping "deep and often" into the wood does not produce as much flow, requires more man-hours of labor per tree, and, because of the flat surface of the face, deteriorates the value of the butt log for lumbering purposes. Another method of collecting, i.e., making a "box" in the trunk to collect the sap, is no longer used.

The acid treatment collapses the thin-walled parenchymal cells that line the resin ducts. This allows the duct channels to become larger, providing a more rapid flow of oleoresin and reducing the chances of hardened secretions blocking the outlets. The acid does not stimulate greater production of oleoresin by the tree, but it enables more oleoresin from the ducts to escape, thus prolonging the flow. If applied properly, acid treatment does not injure the tree. This method has been much more successful than the fungous culture method used several years ago.

The usual turpentining season lasts about 32 weeks. The product of the first year's cutting is superior and is known as "virgin" turpentine. On steam distillation, it yields from 15 to 30% of volatile oil (turpentine oil, see page 111), whereas the product of the second or third year may yield not more than 10% of oil. The hot filtered residue left after distillation constitutes rosin (see page 140).

The United States is the world's largest producer of rosin and turpentine, accounting for about 70% of the supply. This in-

Fig. 6–6. Stand of turpentine pine trees near Gainesville, Florida.

dustry is often referred to as "naval stores" trade because the wooden sailing vessels of the 17th century used enormous quantities of tar and pitch obtained from the coniferous forests of Europe. Since then, the trade has followed the location of the pine forests, moving from New England southward as the trees were depleted or became inaccessible.

Living pine trees are just one source of turpentine oleoresin. In addition, the product is obtained by steam distilling pine stumps and also by working up the black liquor soap produced in the Kraft pulping process. Total production in the United States has remained nearly constant for almost a century. About 30 million gallons of turpentine oil, prepared by distillation of the oleoresin, and 1 billion lb of rosin are produced annually from all sources.

Turpentine occurs as yellowish, opaque masses that are lighter internally, more or less glossy, sticky when warm, and brittle in the cold. Its odor and taste are characteristic. It is freely soluble in alcohol, ether, chloroform, and glacial acetic acid.

The drug constituents are volatile oil and resin. It contains not more than 2% of foreign organic matter.

USE. It is employed externally as a counterirritant.

Capsicum

Capsicum or cayenne pepper is the dried, ripe fruit of *Capsicum frutescens* Linné, known in commerce as African chillies, of *C. annuum* Linné var. *conoides* Irish, known in commerce as Tabasco pepper, or *C. annuum* var. *longum* Sendt, known in commerce as Louisiana long pepper, or of

a hybrid between the Honka variety of Japanese capsicum and the old Louisiana short capsicum, known in commerce as Louisiana short pepper (Fam. Solanaceae). Capsicum must be labeled to indicate which variety is contained in the package.

Capsicum is from the Latin *capsa*, meaning a box, and refers to the partially hollow, boxlike fruit; *frutescens* is Latin and refers to the shrubby character of the plant; and *annuum* is Latin and refers to the annual character of the plant.

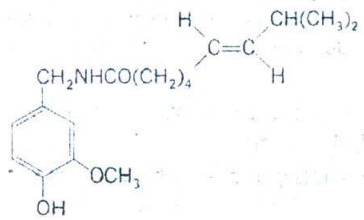
C. frutescens is a small spreading shrub reaching 1 meter in height and is indigenous to tropical America and cultivated in tropical localities in Africa, India, America, and Japan. Apparently, the more tropical the climate, the more pungent the fruit. *C. annuum* is an herbaceous, annual form cultivated in mildly temperate to semitropical localities in central and southern Europe, Mexico, the United States, and other countries. It is cultivated under the names of garden pepper, paprika, pimiento, Mexican chillies, Tabasco pepper, and others. All of these are less pungent than African chillies but are desirable as condiments. The medicinal value of capsicum as a rubefacient depends on its pungency.

African cayenne comes chiefly from Kenya and Tanzania in East Africa and Sierra Leone in West Africa and is usually designated in the trade by the port from which it is shipped. Japanese chillies, usually exported from Kobe, are somewhat less pungent than African capsicum but more pungent than Madras or Bombay chillies from India. Of the millions of pounds annually imported into the United States, about one half comes from India, one third from Japan, and one sixth from Africa.

Capsicum was first mentioned in 1494 by Chauca, a physician who accompanied Columbus on his second voyage to the West Indies. Plants were introduced into India by the Portuguese at an early date and later into Africa.

Tabasco peppers are about twice the size and Louisiana peppers up to 10 times the size of African capsicum. The outer epidermis of the pericarp of these peppers consists of irregular (not quadrangular) cells with thickened and strongly beaded, lignified, radial walls. They also possess a hypodermis of elongated cells with thickened, strongly beaded radial walls of cellulose or cuticularized cellulose. These features readily distinguish these peppers, in whole or powdered form, from genuine African capsicum.

Capsicum contains capsaicin (about 0.02%), an extremely pungent principle, in the dissepiments of the fruit. Capsaicin is a phenol having the formula:



Capsaicin

It imparts a distinctly pungent taste to water, even when diluted to 1 part in 11 million parts of water. Capsicum also contains about 1.5% of a volatile oil, a fixed oil, carotenoids, and up to 0.2% of ascorbic acid (vitamin C).

USES AND DOSE. Capsicum is an irritant and a carminative; it is used as a rubefacient and also as a stimulant and a condiment. The usual dose is 60 mg. **Capsicum oleoresin** has the same properties. The usual dose is 15 mg.

PROPRIETARY PRODUCTS. Capsicum is an ingredient in a number of external analgesic preparations, including Absorbent Rub®, Heet®, Infra-Rub®, Omega Oil®, and Sloan's®.

ALLIED DRUGS. Paprika, Hungarian paprika, or Turkish paprika is a large-fruited pepper obtained from varieties of *C. annuum*. It apparently is indigenous to America and was first introduced to Spain and then to Greece, Turkey, and Hungary. The fruits, when fresh, are 5 to 10 cm in length,

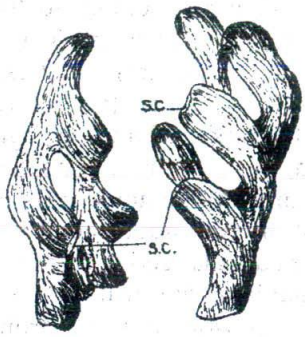


Fig. 6–7. Jamaica ginger: Irregularly branched rhizomes (4 to 16 cm long and 4 to 20 mm thick) from which the cork has been removed, showing depressed stem scars *(sc)* at the ends of the branches; the rhizomes are longitudinally striate, somewhat yellowish to light brown in color, break with a short-fibrous, starch-resinous fracture, and have an aromatic odor and a pungent, aromatic taste.

5 to 7 cm in diameter, more or less inflated, and bright red.

Spanish paprika or pimiento is paprika grown in Spain. The succulent pericarp is used for stuffing olives, and the dry pod is ground as a spice.

Ginger

Ginger or zingiber is the dried rhizome of *Zingiber officinale* Roscoe (Fam. Zingiberaceae), known in commerce as Jamaica ginger, African ginger, and Cochin ginger (Fig. 6–7). The outer cortical layers are often either partially or completely removed. *Zingiber* is from the Arabic *Zindschebil*, meaning root of Zindschi (India). The specific name refers to its use as an ingredient of preparations made in drug shops.

The ginger plant is propagated in Jamaica by rhizome cuttings that are planted in March and April. The rhizomes are dug and peeled in December and January. As soon as they are peeled, the rhizomes are washed in water for hours, then dried in the sun for 5 to 6 days. They are covered at night and during rainy weather.

Ginger was known in China as early as the 4th century B.C. It was used as a spice by the Greeks and Romans. From the 11th to the 13th centuries, ginger was a common import from the East. Marco Polo observed it in China and India from 1280 to 1290. Ginger was introduced into Jamaica and other islands of the West Indies by the Spaniards, and drug exports from the West Indies to Spain were made in considerable quantities as early as 1547. Exports from Jamaica to all parts of the world amount to more than 2 million lb annually.

Ginger owes its characteristic aroma to about 1 to 3% of a volatile oil, the principal constituents of which are 3 sesquiterpenes: bisabolene, zingiberene, and zingiberol. The characteristic pungency of the drug is attributed to ginger oleoresin, from which 2 aromatic ketones, zingerone and shogaol, have been isolated. In addition, ginger contains more than 50% of starch.

USES AND DOSE. Ginger is classed as a flavor; it is used as a condiment, an aromatic stimulant, and a carminative. The dose is 0.6 g. **Ginger oleoresin** has the same properties. Much of the ginger consumed in the present-day market is used in the manufacture of ginger ale.

White Pine

White pine or white pine bark is the dried inner bark of *Pinus strobus* Linné (Fam. Pinaceae). The white or Weymouth Pine is the principal timber pine of the northern United States and Canada. The outer corky layer of the bark is removed before the inner portion is dried.

Pinus is the ancient Latin name, probably akin to *pinna*, and means a feather, referring to the somewhat featherlike foliage of many of the species. The specific name, *strobus*, pertains to the cones or strobiles.

The alcoholic extract forms about 30% of the drug and contains tannic acid and an oleoresin. The bark contains considerable mucilage and a small quantity of coniferin; the latter is usually present in the cambial layer of all of the species of *Pinus* as well as in other genera of the Pinaceae.

USE AND DOSE. White pine has expectorant properties. The usual dose is 2 g.

PROPRIETARY PRODUCTS. Creomulsion® and Prunicodeine®.

Copaiba

Copaiba or balsam copaiba is an oleoresin derived from South American species of *Copaifera (Copaiba)* (Fam. Leguminosae). The oleoresin is formed in schizolysigenous cavities in the wood and seems to be a metamorphosed product of the cell walls; these cavities sometimes contain several liters of the oleoresin. The trees are tapped or boxed (see turpentine, page 147) to the center of the tree and the oleoresin conducted directly to containers. A tree frequently yields 20 to 24 liters.

It should be noted that the term "balsam" is erroneously applied. Copaiba is an oleoresin and contains neither benzoic nor cinnamic acid. It consists of a volatile oil, resin acids, and a small quantity of a bitter principle.

USES AND DOSE. Copaiba was used as a genitourinary disinfectant. It has diuretic, stimulant, expectorant, and laxative properties. The dose is 1 ml.

OLEO-GUM-RESINS

Oleo-gum-resins are mixtures of resin, gum, volatile oil, and, frequently, small quantities of other substances. The principal oleo-gum-resins are myrrh and asafetida.

Myrrh

Myrrh or gum myrrh is an oleo-gum-resin obtained from *Commiphora molmol* Engler, from *C. abyssinica* (Berg) Engler, or from other species of *Commiphora* Jacquin (Fam. Burseraceae). The name myrrh is from the Arabic *murr*, meaning bitter; *Commiphora* is Greek and means gum bearing; *molmol* is the native Somali name; and *abyssinica* refers to the habitat of the plants. The plants are small trees that sometimes attain a height of 10 meters and are found growing on the Arabian peninsula and in Ethiopia and Somalia.

The oleo-gum-resin exudes naturally or from incisions made in the bark; it is at first a yellowish color, but soon hardens in the intense heat of these countries, becomes darker, and is then collected. There are 2 principal commercial varieties of myrrh: **Africa or Somali myrrh** and **Arabian or Yemen myrrh.** The former is considered the better of the two. Practically all of the commercial supply comes from Somalia.

There are numerous references to myrrh in the Old Testament, but it is highly possible that the product thus designated was bdellium. Myrrh was an ingredient of the embalming material of the Egyptians. Its use in incense and perfumes in ceremonial religious life since the days of remote antiquity is well known. Theophrastus, Pliny, and other early writers mention myrrh, and from early times it has been valued in domestic medicine for its aromatic qualities.

Myrrh contains a yellow or yellowish green, rather thick, volatile oil, 2.5 to 8% that has the characteristic odor of myrrh resin, 25 to 40%, composed of several constituents, among which are resin acids (α-, β-, and γ-commiphoric acids), resenes, and phenolic compounds, one of which yields protocatechuic acid and pyrocatechin; gum, about 60%, consisting of soluble and insoluble portions and forming a mucilage that does not readily ferment (being of the acacia type) and yielding arabinose as one of the products of hydrolysis; and a bitter principle, sparingly soluble in water but soluble in alcohol.

USES. Myrrh is a protective; it has also been employed as a stimulant and a stomachic. It is used in mouthwashes as an astringent.

PROPRIETARY PRODUCTS. Astring-O-Sol® and Odara®.

BALSAMS

Balsams are resinous mixtures that contain large proportions of benzoic acid, cinnamic acid, or both, or esters of these acids.

Benzoin is sometimes referred to as a balsamic resin. The medicinal balsams include Tolu balsam, Peru balsam, styrax (Levant and American), and benzoin (Siam and Sumatra).

Storax

Storax is a balsam obtained from the trunk of *Liquidambar orientalis* Miller, known in commerce as Levant storax, or of *L. styraciflua* Linné, known in commerce as American storax (Fam. Hammamelidaceae). Storax is also known as **liquid storax** or **styrax.**

The term *styrax* is from the Arabian *assitirax*, meaning a sweet-smelling exudation; *Liquidambar* is from the Latin *liquidus*, meaning fluid, and from the Arabian *ambar*, meaning amber; *orientalis* means pertaining to the Orient; and *styraciflua* means to flow storax.

L. orientalis is a tree that attains a height of about 15 meters and grows in Asia Minor. *L. styraciflua* is a tree that attains a height of up to 40 meters and grows in southern North America, Central America, and northern South America. Levant storax is a pathologic product; its formation is induced by bruising or puncturing the bark of the tree in early summer, thereby causing the cambium to produce new wood with balsam-secreting ducts. In autumn, the bark, which is more or less saturated with balsam, is peeled off and the balsam is recovered by pressing. The bark is then boiled in hot water and pressed again. The balsam is poured into casks or cans and is usually exported via Smyrna.

Most of the American storax is produced in Central America where large forests of *L. styraciflua* are found. The balsam exudes into natural pockets between the bark and the wood and may be located by excrescences on the outside of the bark. These pockets, which contain up to 4 kg of the balsam, are tapped with gutters and the balsam is led into containers. The balsam is exported in tin cans. A large quantity is also produced in the United States but is used mostly in the tobacco industry for flavoring cigarettes.

The early Arabian physicians were acquainted with storax, and it is mentioned as early as the 12th century. Most of the styrax used in pharmacy comes from Turkey and Honduras.

Levant storax occurs as a viscid, grayish to grayish brown, more or less opaque, semiliquid mass that deposits a heavier, dark brown, oleoresinous stratum on standing. American storax is a nearly clear, yellowish brown semiliquid that becomes hard, opaque, and darker colored. Storax is transparent in thin layers; its odor is agreeable and its taste is balsamic. Storax is insoluble in water but almost completely soluble in warm alcohol.

Levant storax consists of about 50% of 2 resin alcohols, α-storesin and β-storesin, which are partly free and partly in combination with cinnamic acid. α-Storesin is amorphous but forms a crystalline compound with potassium. β-Storesin occurs as white flakes that do not form a crystalline compound with potassium. Storax also contains storesin cinnamate, 10 to 20%; styracin or cinnamyl cinnamate, 5 to 10%, in needle-crystals that are colorless, odorless, and tasteless; phenylpropyl cinnamate, 10%, a liquid with the odor and taste of styrax; volatile oil, 0.5 to 1%; a trace of vanillin; free cinnamic acid, from 2 to 5%; and small amounts of several other substances. Free cinnamic acid may be obtained from storax by microsublimation with a yield of up to 20%.

American storax contains related storesins and other principles of Levant storax: it yields 7% of volatile oil by steam distillation and contains about 28% of cinnamic acid, 23% of cinnamein, 35% of resin esters, and 2% of resin acids.

USES AND DOSE. Storax is a pharmaceutic aid for compound benzoin tincture. It has been used as a stimulant, an expectorant, and an antiseptic. When used internally, the dose is 1 g.

Peruvian Balsam

Peruvian balsam, Peru balsam, or balsam of Peru is obtained from *Myroxylon pereirae* (Royle) Kłostzsch (Fam. Leguminosae). *Myroxylon* is from the Greek *myron*, meaning ointment, and *xylon*, meaning wood; *pereirae* is in honor of Jonathan Pereira (1804 to 1853), an English pharmacognosist. "Peru" refers to the early importation of the balsam into Spain via Lima, Peru.

The balsam trees attain a height of about 25 meters and are especially abundant along the coast of El Salvador in Central America. The tree has been naturalized in Florida and in Sri Lanka. It was frequently referred to by writers who described the conquest of Guatemala in 1524. In the 17th century, the drug appeared in German pharmacy, after which its use became universal.

The balsam is a pathologic product and is formed by injury to the trees. The tree is beaten on 4 sides and then scorched with a torch to cause the bark to separate from the trunk. Four intermediate strips are left uninjured so as not to kill the tree. Within a week, the bark drops from the trunk and the balsam begins to exude freely from the exposed wood. The areas are then wrapped with rags that are removed from time to time when they become saturated with balsam. The rags are then boiled with water and, as the water cools, the balsam settles out, is recovered, strained, and packed, usually in tin cans. Most of the commercial supply comes from El Salvador, although some is produced in Honduras.

Peruvian balsam occurs as a dark brown, viscid liquid that appears reddish brown and transparent in thin layers. It is free from stringiness or stickiness and has an empyreumatic, aromatic, vanillalike odor and a bitter, acrid, persistent taste.

The drug contains cinnamein, about 60%, which is a volatile oil consisting chiefly of benzyl cinnamate and a lesser amount of benzyl benzoate; resin esters, 30 to 38%, which are composed mostly of peruresinotannol cinnamate and benzoate; vanillin; free cinnamic acid; peruviol; and other substances in small amounts.

USES. Peru balsam is a local protectant and rubefacient; it also is a parasiticide in certain skin diseases. It is an antiseptic and vulnerary and is applied externally either alone, in alcoholic solution, or in the form of an ointment.

PROPRIETARY PRODUCTS. The drug is employed for its astringent properties in various preparations used to treat hemorrhoids. These include Anusol® suppositories and Wyanoid® ointment and suppositories.

Tolu Balsam

Tolu balsam is a balsam obtained from *Myroxylon balsamum* (Linné) Harms (Fam. Leguminosae). Tolu balsam is sometimes called balsam of Tolu.

The balsam trees grow abundantly along the lower Magdalena River in Colombia. Tolu is a district near Cartagena, where the balsam was once extensively produced.

Balsam of Tolu is usually considered to be a pathologic product similar to balsam of Peru or coniferous oleoresins. V-shaped incisions are made through the bark and sap wood, and calabash cups receive the flow of balsam. Similar cuts are made higher on the trees; sometimes as many as 20 incisions are made on a tree. The balsam is collected from the cups and transferred to tin containers in which it is shipped.

Some balsam of Tolu is also produced in Venezuela, and trees are now being cultivated in the West Indies. Tolu balsam was used by the natives in Colombia and Venezuela. Monardes (1574) described its collection, stating that the drug was much esteemed by the Indians and later by the Spanish, who introduced it into Europe.

Much of the balsam of Tolu entering the United States comes from Great Britain, where a certain amount of the volatile oil has been removed. Sufficient oil remains,

however, so that the balsam meets the official requirements.

Tolu balsam occurs as a plastic solid that gradually hardens, becoming brown or yellowish brown. It is transparent in thin layers, brittle when old, dried, or exposed to cold, and shows numerous crystals of cinnamic acid. Its odor is agreeably aromatic, resembling that of vanilla, and its taste is aromatic and slightly pungent.

The drug contains resin esters, 75 to 80%, chiefly toluresinotannol cinnamate with a small quantity of the benzoate; volatile oil, 7 to 8%, chiefly benzyl benzoate; free cinnamic acid, 12 to 15%; free benzoic acid, 2 to 8%; vanillin; and other constituents in small quantities.

USES. Tolu balsam is a pharmaceutic aid for compound benzoin tincture. It is sometimes used as an expectorant and is extensively used as a pleasant flavoring in medicinal syrups, confectionery, chewing gum, and perfumery.

Benzoin

Benzoin is the balsamic resin obtained from *Styrax benzoin* Dryander, *S. parallelo-neurus* Perkins, known in commerce as Sumatra benzoin, *S. tonkinensis* (Pierre) Craib ex Hartwich, or other species of the Section *Anthostyrax* of the genus *Styrax*, known in commerce as Siam benzoin (Fam. Styraceae). *Styrax* is the ancient Greek name of storax applied to a sweet-scented gum and to the tree producing it; *benzoin* is from the Arabic *ben*, meaning fragrant, or the Hebrew *ben*, meaning a branch, and *zoa*, an exudation, meaning the juice of the branch; *tonkinensis* is named after Tonkin, the northern region of Vietnam.

The plants are trees of medium height that grow in southeastern Asia and the East Indies. *S. benzoin* is cultivated throughout Sumatra; *S. tonkinensis* in Thailand, Vietnam and Laos. Benzoin is a pathologic product developed by incising the bark. After about 2 months, the exuding balsamic resin becomes less sticky and firm enough to collect.

The first tapping of *S. benzoin* yields the so-called almond tears. The second tapping yields a more fluid substance. The almond tears and the fluid substance are imported into Singapore and are admixed (possibly with adulterants) to produce block benzoin.

In Thailand, the separate tears are scraped from the trees. New incisions are continually made until the trees die. The tree contains no secretory cells, nor does it contain the constituents of the balsamic resin until it is incised. The bark of the normal tree contains considerable tannin. The resinotannols in benzoin are probably produced from this tannin. Benzoin was unknown to the Greeks and Romans. It was first mentioned by Ibn Batuta, who visited Sumatra in the 14th century. In the 15th century, it still appeared as a precious balsam, but in the 16th century it was an article of Venetian commerce.

The use of Siam benzoin is confined almost entirely to perfumery. The tears of Siam benzoin are graded according to size and color; the smaller tears and siftings are darker in color. In pharmacy, only the Sumatra benzoin is used. Before World War II, Sumatra benzoin was obtained directly from Sumatra; today almost all Sumatra benzoin is imported from Singapore.

Sumatra benzoin occurs as blocks or irregular masses composed of tears of variable size imbedded in a translucent or opaque matrix. It is brittle and internally the tears are milky white, becoming soft when warmed and gritty when chewed. The matrix is reddish or grayish brown; the odor is agreeable, balsamic, and resembles that of styrax; the taste is aromatic and resinous.

Siam benzoin occurs mostly in separate concavo-convex tears that are yellowish brown to rusty brown externally and milky white on the freshly broken surface. The tears are brittle but become soft when warmed and plastic when chewed. Siam benzoin has a vanillalike odor.

Siam benzoin consists principally of

coniferyl benzoate (60 to 70%), plus smaller amounts of free benzoic acid (10%), the triterpene, siaresinol, (6%), and a trace of vanillin.

Sumatra benzoin contains free balsamic acids, chiefly cinnamic (10%) and benzoic (6%), as well as esters derived from them. Triterpene acids, especially 19-hydroxyoleanolic and 6-hydroxyoleanolic, and traces of vanillin, phenylpropyl cinnamate, cinnamyl cinnamate, and phenylethylene are also present.

Sumatra benzoin yields not less than 75% of alcohol-soluble extractive; Siam benzoin yields not less than 90% of alcohol-soluble extractive.

USES. Benzoin possesses antiseptic, stimulant, expectorant, and diuretic properties.

Compound benzoin tincture is employed as a topical protectant and is applied as required. It contains benzoin, aloe, storax, and Tolu balsam and is valuable as an expectorant when vaporized.

PROPRIETARY PRODUCT. VapoSteam®.

Benzoic acid is now a synthetic product but was first obtained by sublimation from Sumatra benzoin.

It occurs as white crystals, usually in the form of scales or needles. It has a slight odor of benzoin and is volatile at moderate temperatures, freely so in steam.

Benzoic acid and its sodium salt are extensively used as preservatives of foods, drinks, fats, pharmaceutic preparations, and other substances. Medicinally, benzoic acid is used primarily as an antifungal agent. It is an ingredient in benzoic and salicylic acids ointment (Whitfield's ointment), which is effective in the treatment of athlete's foot and, to a lesser extent, ringworm.

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