KIRK-OTHMER CHEMICAL TECHNOLOGY OF COSMETICS

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PREFACE

Cosmetic preparations and usage are rooted in antiquity, when suspensions of natural pigments in lipids were used to enhance appearance, and fragrant plant concoctions were widely traded.

Cosmetics represent a large group of consumer products designed to improve the health, cleanliness, and physical appearance of the human exterior and to protect a body part against damage from the environment. Cosmetic products are promoted to the public and are available without prescription.

A large number of raw materials—ingredients—are used to prepare cosmetics. Some of these ingredients are active component, for example, have moisturizing or conditioning effects, and are typically used in limited quantities, whereas other ingredients are used to formulate the products and are used in relatively larger amounts. The combination of various substances determines the nature of the finished cosmetic. Several specialized technologies have been perfected for cosmetic products. Among these, emulsification, stick technology, and powder blending are prominent.

Different laws and regulations apply to prescription drugs, over-the-counter drugs and cosmetics. The use of ingredients in cosmetics is essentially unrestricted and may include new or not well-known substances.

This volume contains carefully selected articles from Wiley's renowned ***Kirk-Othmer Encyclopedia of Chemical Technology,*** which have been updated and revised for this volume***,*** as well as new contributions. The articles cover key topics related to product groups, ingredients, formulation technology and related regulatory aspects. This book will be of interest to chemists, perfumers, R&D, and other professionals in the cosmetic and personal care industry, as well as advanced students who intend to enter this multi-billion dollar global industry.

PART I

PRODUCTS

1

COSMETICS

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1.1. INTRODUCTION

Cosmetics are products created by the cosmetic industry and marketed directly to consumers. The cosmetic industry is dominated by manufacturers of finished products, but also includes manufacturers who sell products to distributors as well as suppliers of raw and packaging materials. Cosmetics represent a large group of consumer products designed to improve the health, cleanliness, and physical appearance of the human exterior and to protect a body part against damage from the environment. Cosmetics are promoted to the public and are available without prescription.

The difference between a cosmetic and a drug is often confusing. In the United States, the inclusion of a drug constituent, as defined by the Food and Drug Administration (FDA), in a cosmetic product may make the product a drug; whenever there is a claim for pharmacological activity of one of a product's constituents, the product is a drug. Some products are identified as quasi or over-the-counter (OTC) drugs according to each country's regulations. The composition, claim structure, and distribution of OTC products may be more tightly regulated than those of pharmacologically inactive cosmetics. The difference between an ordinary cosmetic and a quasi or OTC drug may not be readily apparent; it is based on statutory regulations. Certain types of products, such as hair-growth products and skin rejuvenators, are not cosmetics, and OTC claims for hair growth or skin rejuvenation are not allowed in the United States. These products have been referred to as cosmeceuticals.

Cosmetics, regardless of form, can be grouped by product use into the following seven categories: (*1*) skin care and maintenance, including products that soften (emollients and lubricants), hydrate (moisturizers), tone (astringents), protect (sunscreens), etc., and repair (antichapping, antiwrinkling, antiacne agents); (*2*) cleansing, including soap, bath preparations, shampoos, and dentrifices; (*3*) odor improvement by use of fragrance,

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deodorants, and antiperspirants; (*4*) hair removal, aided by shaving preparations, and depilatories; (*5*) hair care and maintenance, including waving, straightening, antidandruff, styling and setting, conditioning, and coloring products; (*6*) care and maintenance of mucous membranes by use of mouthwashes, intimate care products, and lip antichapping products; and (*7*) decorative cosmetics, used to beautify eyes, lips, skin, and nails.

Reference 1 gives formulations for products in all of the categories listed above.

1.2. HISTORY

Cosmetic preparations and usage are rooted in antiquity, when suspensions of natural pigments in lipids were evidently used to enhance appearance, and fragrant plant concoctions were widely traded. The use of cosmetics for adornment is recorded in biblical writings, and the use of soap, probably a hydrolysate of animal lipids by wood ashes, was encouraged for cleanliness. The benefits of bathing were fully known to the ancients, who built elaborate bathhouses. Bathing became less popular in Western cultures during the Middle Ages but again became accepted during the eighteenth and nineteenth centuries.

The use of fragrant substances has been continuous, and the use of lipids or emollients for anointing is fully documented in historical writings. However, it is probably not justifiable to identify the recipes passed on from antiquity as cosmetics. The compositions based on folklore and mysticism were replaced by more scientifically acceptable products beginning about 1875. The first edition of a handbook of cosmetic chemistry published in 1920 included a foreword noting that scientific cosmetic chemistry did not exist prior to that publication (2). A few years later, texts on cosmetic chemistry and other formularies became available (3, 4).

The Society of Cosmetic Chemists, with individual memberships, was founded in the United States after World War II, based on the belief that scientific expertise and exchange were the foundations for future expansion of the cosmetic industry. Prior to that time, knowledge of cosmetic formulation was jealously guarded. Related scientific societies emerged in other countries and have since joined to form the International Federation of Societies of Cosmetic Chemists.

1.3. REGULATION OF THE COSMETIC INDUSTRY

In the United States, the 1938 revision of the Federal Food and Drug Act regulates cosmetic products and identifies these materials as:

> (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles, except that such term shall not include soap.

This definition establishes the legal difference between a drug and a cosmetic. It is clearly the purpose of, or the claims for, the product, not necessarily its performance, that legally classifies it as a drug or a cosmetic in the United States. For example, a skin-care product intended to beautify by removing wrinkles may be viewed as a cosmetic because it alters the appearance and a drug because it affects a body structure. Different laws and regulations apply to each type of product. Firms sometimes violate the law by marketing a

cosmetic with a drug claim or by marketing a drug as a cosmetic without adhering to requirement for drug. The term cosmeceutical used to mean a product that has two functions has no meaning under the law (5).

The FDA is responsible for enforcing the 1939 act as well as the Fair Packaging and Labeling Act. In light of the difficulty of differentiating between cosmetics and drugs, the FDA has in recent years implemented its regulatory power by concluding that certain topically applied products should be identified as OTC drugs. As a group, these OTC drugs were originally considered cosmetics and remain among the products distributed by cosmetic companies. They include acne, antidandruff, antiperspirant, astringent, oral-care, skin-protectant, and sunscreen products.

The use or presence of poisonous or deleterious substances in cosmetics and drugs is prohibited. The presence of such materials makes the product "adulterated" or "misbranded" and in violation of good manufacturing practices (GMP), which are applicable to drugs and, with minor changes, to cosmetics (6).

In contrast to prescription drugs, OTC drugs and cosmetics are not subject to preclearance in the United States. However, the rules covering OTC drugs preclude introduction of untested drugs or new combinations. A "new chemical entity" that appears suitable for OTC drug use requires work-up via the new drug application (NDA) process. In contrast, the use of ingredients in cosmetics is essentially unrestricted and may include less well-known substances.

1.3.1. Color Additives

The FDA has created a unique classification and strict limitations on color additives. Certified color additives are synthetic organic dyes that are described in an approved color additive petition. Each manufactured lot of a certified dye must be analyzed and certified by the FDA prior to usage. This regulation is covered by the Federal Food Drug and Cosmetic Act. Color lakes are pigments that consist of an insoluble metallic salt of a certified color additive deposited on an inert substrate. Lakes are subject to the color additive regulations of the FDA and must be certified by FDA prior to use. Noncertified color additives require an approved color additive petition, but individual batches need not be FDA certified prior to use.

Hair colorants, the fourth class of color additives, may be used only to color scalp hair and may not be used in the area of the eye. Use of these colorants is exempt, that is, coal-tar hair dyes may be sold with cautionary labeling, directions for preliminary (patch) testing, and restrictions against use in or near the eye. The FDA diligently enforces the rules governing color additives and limits the use of, or even delists colorants deemed unsafe. The list of substances specifically prohibited for use in cosmetics is short.

Under the Fair Packaging and Labeling Act, the FDA has instituted regulations for identifying components of cosmetics on product labels. To avoid confusion, the Personal Care Products Council (PCPC)(formerly CTFA) has established standardized names for about 6000 cosmetic ingredients (1). Rigid U.S. labeling requirements mandate that ingredients be listed in order of descending concentration.

1.3.2. European Regulations

Regulations for cosmetics differ from country to country but, in general, are similar to or patterned after U.S. regulation. Thus, the identification of a cosmetic in the

European Community differs only marginally from that in the United States. A 1991 European Economic Community (EEC) [now the European Union (EU)] directive defines a cosmetic as:

> any substance or preparation intended for placing in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view to cleaning them, perfuming them, protecting them, keeping them in good condition, changing their appearance and/or correcting body odours.

The EU Directive asserts that cosmetic products must not damage human health when applied under normal or reasonably foreseeable conditions of use. Also, the Directive states that the label of a cosmetic should include a list of ingredients in descending order of weight at the time of manufacture.

The 27 EU members have transposed the European Union Directive enacted in 1976 into law. Each member state has health authorities that can regulate cosmetics within the state's boundaries. The EU Scientific Committee on Consumer Products (SCCP) is responsible for reviewing all special and active ingredients and assessing conditions for safe use. The results are published on the SCCP website. Today Annex II of the Directive lists 1300 banned ingredients, although some would never be used in cosmetics, e.g., jet fuel. The EU allows the marketing of cosmetic products with certain medicinal properties. In the United States, these products would be regulated as over-the-counter drugs (7).

1.3.3. Japanese Regulation

Cosmetics in Japan are defined as externally used articles for cleaning, beautifying, promoting attractiveness, and altering the appearance of the human body and for keeping the skin and hair healthy, provided that the action of the article on the human body is mild. Articles intended for use in diagnosis, treatment of disease, and those intended to affect the structure or any function of the body are identified as quasi drugs and are excluded. Japanese law identifies the following as quasi drugs: products for the prevention of foul breath or body odor; products for the prevention of prickly heat; products for the prevention of hair loss, promotion of hair growth, or removal of hair; hair dyes; agents for permanent waving of hair; and agents combining cosmetic effects with the purpose of preventing acne, chapping, itchy skin rashes, chilblains, or disinfection of the skin or mouth.

The Japanese government regulates the cosmetic industry through its Ministry of Health Labor and Welfare according to the Pharmaceutical Affairs law (Law 145) established August 10, 1960. Japan has adopted a list of prohibited ingredients, a list of restricted ingredients, a positive list of UV filters, and a positive list of preservatives (8). Other than these restrictions, the burden ensuring product safety has been shifted to the cosmetic manufacturers. Any product shown to be safe can be used. Until recently, a manufacturer or importer of cosmetics was required to obtain pre-market approval. Since 2001, Japan cosmetic companies are required to produce notification of product brand prior to manufacturing or importing.

Japan is an example of a country replacing costly pre-market registration with manufacturer responsibility for product safety and post-market surveillance without compromising consumer safety.

Regulatory changes and discussions of the impact of regulations on the manufacture and import of cosmetic products are available in manuals published by the PCPC (9, 10).

1.3.4. Canadian Regulations

The Canadian government regulates cosmetics through Health Canada's Cosmetic Program. The basis for regulation comes through the Food and Drug Act and Cosmetic Regulations. The program has the mandate of protecting the Canadian people by minimizing the risk associated with cosmetics. The program defines requirements for manufacturing, labeling, distribution, and sales of cosmetics. Manufacturers are responsible for demonstrating the product is safe for its intended use. Regulations are enforced by Health Canada and its officers who manage all aspects of product safety (7).

1.4. PRODUCT REQUIREMENTS

1.4.1. Safety

Cosmetic products must meet acceptable standards of safety during use, must be produced under sanitary conditions, and must exhibit stability during storage, shipment, and use. Cosmetics are not lifesaving or life-prolonging drugs, and the requirements for innocuousness are absolute. In the United States, the manufacturer bears the responsibility for not using injurious or questionable ingredients. The safety of each ingredient used in each finished cosmetic product must be adequately substantiated prior to marketing. In countries that have positive lists of ingredients that may be used in cosmetics, the burden for testing each finished cosmetic products is reduced. Positive listing assumes, without requiring evidence, that no adverse effects result from the use of a mixture of safe ingredients.

For many years the safety of cosmetic ingredients has been established using a variety of animal safety tests. The use of animal testing has declined dramatically in recent years. Animal welfare organizations have urged that this type of safety testing be abandoned. Despite widespread use of cosmetics without professional supervision, the incidence of injury from cosmetic products is rare. In part, this is the result of extensive animal safety testing of components as well as of finished products. Such animal testing was considered mandatory from about 1945 to about 1985. Since the mid-1980s animal testing has been significantly reduced. The cosmetic industry has invested in the search for valid alternative tests. Today the PCPC supports limited and ethical use of animal and *in vitro* tests for new or novel ingredients (11).

In vitro safety testing technology is becoming more common. Validation of these methods is based on comparisons with early animal safety data. In the United States, the PCPC created the Cosmetic Ingredient Review (CIR) for the purpose of evaluating existing *in vitro* and *in vivo* data and reviewing the safety of the ingredients used in cosmetics. The CIR is an independent nonprofit body. The review of ingredients is prioritized based on frequency of use, concentration used, the area of use, and consumer complaints. The CIR conclusions are available from the PCPC.

California law prohibits animal testing when alternatives have been scientifically validated and adopted by appropriate agencies. To date, validated and alternative test methods are not available to replace all types of safety testing. The industry supports various groups that are involved in evaluating alternative methods of testing. Among them are

The Scientific Advisory Committee on Alternative Toxicological Methods, Interagency Coordinating Committee on the Validation of Alternative Toxicological Methods (http://ccyam.nieh.nih.gov), and the National Toxicology Program Interagency for the Evaluation of Alternative Toxicological Methods.

Many cosmetic companies have made efforts to find new testing methods. In addition to the CIR process, the cosmetic industry has instituted a second, important, self-regulatory procedure: the voluntary reporting of adverse reactions, which is intended to provide data on the type and incidence of adverse reactions noted by consumers or by their medical advisors. This reporting procedure creates early awareness of problems handled outside hospital emergency facilities or centers for acute poisoning.

Many consumers now look for the "no animal testing" label as part of their decision to purchase a product. The PCPC advises that individual companies be contacted for information on their testing techniques.

Safety testing of a finished cosmetic product should be sufficient to ensure that the product does not cause irritation when used in accordance with direction, neither elicits sensitization nor includes a sensitizer, and does not cause photoallergic responses.

A particularly critical test for establishing the safety of cosmetics is the exaggerated-use test, in which panelists, often under medical supervision, use a product at frequencies that exceed the normally expected usage. Any adverse reactions, including subjective reports of burning or itching without clinical symptoms, suggest that the product should be examined further. This test also can be used to elicit comments concerning product acceptability.

Repeated usage of certain common cosmetic ingredients can elicit a response within the sebaceous gland apparatus that generates comedos. The cause of this phenomenon is not entirely clear, but an animal (rabbit ear) test purportedly measures the comedogenic potential of cosmetic ingredients or finished products (12). Controversy surrounds the identity of comedogenic substances and the concentration required to elicit the response. Thus use of cosmetic ingredients that have been suspected of causing comedogenicity are generally avoided.

The FDA reports that there is no federal regulation regarding hypoallergenic products. Cosmetic manufacturers claim fewer allergic reactions, but can have little meaning for dermatologists. The FDA suggests that the consumer can use a product with hypoallergenic claims and compare against another product that does not report such claims (13).

1.4.2. Production Facilities

The manufacture of acceptable cosmetic products requires not only safe ingredients but also facilities that maintain high standards of quality and cleanliness. Most countries have established regulations intended to assure that no substandard product or batch is distributed to consumers. Good Manufacturing Practices (GMP) represent workable standards that cover every aspect of drug manufacture, from building construction to distribution of finished products. GMPs in the United States that have been established for drug manufacture are commonly used in cosmetic production (6).

1.4.3. Contamination

Manufacturers of cosmetics must be careful to guard against chemical and microbial contamination. Chemical contamination, which may result from the presence of undesirable

impurities in raw materials, is avoidable by adhering to rigid specifications for raw materials. Compendial specifications and publications by the PCPC and other professional societies form the basis of most intracompany raw material specifications. Moreover, all packaging components must meet not only physical and design specifications but also such chemical requirements as extractables and absence of dust and similar contaminants.

Chemical contamination arising from overheating or other decomposition reactions during processing or from improper storage of incoming supplies must also be avoided. For these reasons, adherence to documented production processes and periodic reassays of stored supplies are required. Additionally, final chemical or physical examinations of the finished and filled products are required to ascertain that no inadvertent chemical contamination has occurred during manufacture and that no undesirable ingredients are present.

An entirely different type of contamination arises from the presence of microbiota in a product. As in the case of chemical contamination, compendial requirements for microbiological purity exists. Pharmacopoeial standards vary from country to country, and manufacturers must use the specifications and kill times that meet local requirements.

1.4.4. Stability

An additional mandatory requirement for cosmetic products is chemical and physical stability. Interactions between ingredients that lead to new chemical entities or decomposition products are unacceptable. Stability testing becomes particularly critical if the product includes an active or drug constituent for which a specific performance claim is made. In the absence of an expiration date, a cosmetic product or an OTC drug should be stable for 60 months at ambient temperature. This temperature is a function of climatic zones. Therefore, controlled temperature storage, sometimes at controlled relative humidity, is universally recognized as ideal despite its attendant cost. In order to demonstrate long-term chemical stability on the basis of short- or intermediate-term studies, formulations are stored routinely at elevated temperatures, normally 37, 45, or 50°C. Changes are extrapolated to ambient temperatures using the Arrhenius equation for reaction rates.

Another type of chemical change is initiated by light, which may trigger autolytic, that is, free radical (Type I) or singlet oxygen (Type II) reactions. These changes are routinely classified as oxidation. Rancidity in cosmetics, especially those containing unsaturated lipids, is commonly prevented by use of antioxidants.

Requirements for physical stability in cosmetics are not as rigid as those for chemical stability. As a rule, minor changes in viscosity or appearance are acceptable to users. More drastic changes, resulting from separation of an emulsion because of creaming or oiling, are not acceptable. Short-term physical, or viscosity, changes cannot be extrapolated to long-term performance. Changes observed during static viscosity tests have little predictive value for long-term viscosity or emulsion stability. Short-term dynamic viscosity tests also do not allow prediction of long-term viscosity changes, but these can sometimes be used to predict changes in the nature of emulsions. Zeta potential and particle size determination can provide predictive information on emulsion behavior.

1.4.5. Performance

Consumer acceptance is a criterion on which cosmetic marketers cannot compromise. Whereas the likes and dislikes of consumers are in a state of constant flux, some

product features are critical. A deodorant that does not deodorize or a hair coloring that fades in sunlight is unacceptable. Performance is tested by *in vitro* techniques during formulation, but the ultimate test of a product's performance requires in-use experience with consumers and critical assessment by trained observers. Performance tests can sometimes be combined with in-use safety tests, and protocols for such programs have been developed.

1.5. INGREDIENTS

Manufacturers of cosmetics employ a surprisingly large number of raw materials. Some of these ingredients are active constituents that have purported beneficial effects on the skin, hair, or nails, for example, acting as moisturizers or conditioners. These substances are generally used in limited quantities. Other ingredients are used to formulate or create the vehicle. These are bulk chemicals used in comparatively large amounts. The resulting combination of various substances affects the nature (viscosity, oiliness, etc.) of the finished cosmetic. As a rule, numerous combinations and permutations are tested to optimize textural characteristics and to match these to consumers' preferences. Finally, cosmetics may include substances added primarily to appeal to consumers. These ingredients need not contribute appreciably to product performance.

About 6000 different cosmetic ingredients have been identified (1). These can be divided into smaller groups according to chemical similarity or functionality. Table 1.1 represents a breakdown by functionality on the skin or in the product. The chemical identity of only one ingredient that performs the desired function is given. In most cases, other equally effective substances exist. The diversity of functions required in cosmetics is evident, and cosmetic ingredients may perform more than one function or belong to more than one chemical class. A typical example is sodium DL-2-pyrrolidinone-5-carboxylate (sodium PCA) [28874-51-3], $NaC_5H_7NO_3$. Chemically, this compound may be viewed as an amide, a heterocyclic compound, or an organic salt; functionally, it is a humectant and skin-conditioning agent.

Ingredients exhibiting certain functions are required in many types of cosmetic products. Antioxidants and preservatives are especially critical for product shelf life and quality during usage. Shelf life is defined herein as that period of time during which a product in an unopened package maintains its quality and performance and shows no physical or chemical instability. Antioxidants and preservatives do not contribute to physical stability but are included in cosmetic products to ensure oxidative stability and to control microbial contamination. Once a package has been opened, oxidative processes may cause the product to deteriorate, and microbial species may gain access to the product. These additives are expected to impart some protection even under these circumstances.

1.5.1. Antioxidants

Some antioxidants useful in cosmetics are listed in Table 1.2. The operant mechanisms are interference with radical propagation reactions, reaction with oxygen, or reduction of active oxygen species. Antioxidants are intended to protect the product but not the skin against oxidative damage resulting from ultraviolet radiation or singlet oxygen formation.

TABLE 1.1. Cosmetic Functions and Representative Ingredients[a]

Function	Ingredient[b]	Molecular Formula	CAS Registry Number
	Biologically active agents		
Antiacne	Salicylic acid	$C_7H_6O_3$	[69-72-7]
Anticaries	Monosodium fluorophosphate	Na_2HPO_3F	[10163-15-2]
Antidandruff	Zinc pyrithione	$C_{10}H_8N_2O_2S_2Zn$	[13463-41-7]
Antimicrobial	Benzalkonium chloride		[8001-54-5]
Antiperspirant	Aluminum chlorohydrate	$Al_2ClH_5O_5$	[12042-91-0]
Biocides	Triclosan	$C_{12}H_7Cl_3O_2$	[3380-34-5]
Sunscreen	Octyl methoxycinnamate	$C_{18}H_{26}O_3$	[5466-77-3]
Skin protectant	Dimethicone	$(C_2H_6OSi)_nC_4H_{12}Si$	[9006-65-9] [63148-62-9]
		$(C_2H_6OSi)_n$	[9016-00-6]
External analgesic	Methyl salicylate	$C_8H_8O_3$	[119-36-8]
	Nonbiologically active agents		
Abrasive			
Skin	Oatmeal		
Teeth	Dicalcium phosphate	$Ca_2(HPO_4)_2$	[7757-93-9]
Antifoam	Simethicone		[8050-81-5]
Antioxidant	Ascorbic acid	$C_6H_8O_6$	[50-81-7]
Antistatic agent	Dimethylditallow alkylammonium chlorides		[68783-78-8]
Binder	Hydroxypropylcellulose		[9004-64-2]
Chelator	Hydroxyethyl ethylenediamine triacetic acid (HEDTA)	$C_{10}H_{18}N_2O_7$	[150-39-0]
Colorant			
Pigment	Ultramarine	$Na_7Al_6Si_6O_{24}S_2$	[1317-97-11]; [1345-00-2]; [12769-96-9]
Dye	FD&C Red No. 4	$C_{18}H_{16}N_2O_7S_2{\cdot}2Na$	[4548-53-2]
Emulsion stabilizer	Xanthan gum		[11138-66-2]
Film former	PVP	$(C_6H_9NO)_x$	[9003-39-8]
Hair colorant	*p*-Phenylenediamine	$C_6H_8N_2$	[106-50-3]
Hair conditioner	Sodium lauroamphoacetate	$Na_2C_{18}H_{35}N_2O_3{\cdot}HO$	[14350-96-0]

(*continued*)

TABLE 1.1. (*Continued*)

Function	Ingredient[b]	Molecular Formula	CAS Registry Number
Humectant	Glycerol	$C_3H_8O_3$	[56-81-5]
Deodorant			
Mouth	Zinc chloride	$ZnCl_2$	[7646-85-7]
External	Cetylpyridinium chloride	$C_{21}H_{38}ClN$	[123-03-5]
Preservative	Propylparaben	$C_{10}H_{12}O_3$	[94-13-3]
Emollient	Octyl stearate	$C_{26}H_{52}O_2$	[22047-49-0]
Skin-conditioning agent			
General	Pyrrolidinone carboxylic acid (PCA)	$C_5H_7NO_3$	[98-79-3]
Occlusive	Petrolatum	C_nH_{2n+2}	[8009-03-8]
Film forming	Hyaluronic acid		[9004-61-9]
Solvent	Ethanol	C_2H_6O	[64-17-5]
Cleansing agent	Sodium lauryl sulfate	$C_{12}H_{25}NaO_4S$	[151-21-3]
Emulsifying agent	Polysorbate 65		[9005-71-4]
Foam booster	Cocamide DEA		[68140-00-1]
Suspending agent	Sodium lignosulfonate		[8061-51-6]
Hydrotrope	Sodium toluenesulfonate		[12068-03-0]
Viscosity-controlling agent			
Decrease	Propylene glycol	$C_3H_8O_2$	[57-55-6]
Increase	Hydroxypropylmethyl-cellulose		[9004-65-3]

[a]Additional functions may be found in Ref. 1.
[b]PCPC adopted names are used; this notation is used for cosmetic labeling.

TABLE 1.2. Free-Radical-Inhibiting Antioxidants or Reductants Useful in Cosmetics[a,b]

Antioxidant	CAS Registry Number	Molecular Formula
Ascorbic acid	[50-81-7]	$C_6H_8O_6$
Ascorbyl palmitate	[137-66-6]	$C_{22}H_{38}O_7$
Butylated hydroxyanisole (BHA)	[25013-16-5]	$C_{11}H_{16}O_2$
Butylated hydroxytoluene (BHT)	[128-37-0]	$C_{15}H_{24}O$
t-Butyl hydroquinone	[1948-33-0]	$C_{10}H_{14}O_2$
Cysteine	[52-90-4]	$C_3H_7NO_2S$
Dilauryl thiodipropionate	[123-28-4]	$C_{30}H_{58}O_4S$
Dodecyl gallate	[1166-52-5]	$C_{19}H_{30}O_5$
Ellagic acid	[476-66-4]	$C_{14}H_6O_8$
Erythorbic acid	[98-65-6]	$C_6H_8O_6$
Kaempferol	[520-18-3]	$C_{15}H_{10}O_6$
Nordihydroguaiaretic acid	[500-38-9]	$C_{18}H_{22}O_4$
Propyl gallate	[121-79-9]	$C_{10}H_{12}O_5$
Quercetin	[117-39-5]	$C_{15}H_{10}O_7$
Sodium ascorbate	[134-03-2]	$C_6H_7NaO_6$
Sodium sulfite	[7757-83-7]	Na_2SO_3
Thioglycolic acid	[68-11-1]	$C_2H_4O_2S$
Tocopherol	[59-02-9]; [1406-18-4]	$C_{28}H_{48}O_2$

[a]Ref. 1 includes a more comprehensive listing.
[b]Use levels are normally about 0.1% and rarely exceed 0.2%.

1.5.2. Preservatives

Several micro-organisms can survive and propagate on unpreserved cosmetic products. Preservatives are routinely added to all preparations that can support microbial growth. The choice of a preservative for a given product is difficult. Anhydrous preparations and products containing high levels of ethanol or *i*-propanol may not require the addition of preservatives.

Contamination during manufacture is common, even when microbially clean ingredients are used. Water, which is almost ubiquitous in cosmetic products, is especially troublesome and must be free from contaminating micro-organisms. All other ingredients should be screened for the presence of microbial species and batches of raw materials of dubious purity may have to be rejected. Cleanliness during manufacture, processing, and filling must be strictly maintained. Despite these precautions, microbial integrity of products may require the presence of one or more preservatives that are compatible with the product's ingredients. Products should not support the growth or viability of any microbial species that may have been accidentally introduced. Preservatives are also required to reduce contamination by consumers during normal use. Powerful preservative action to create self-sterilizing products is required. Whereas production of sterile cosmetics may be practicable, maintenance of sterility during use is problematical, because fingers and cosmetic applicators are not sterile.

Pharmacopoeias and PCPC publications provide guidelines for challenge test procedures and limits on microbial counts (1). The compendial requirements for kill of micro-organisms vary significantly, and alternative test methods may be required (14). As a general rule, pathogenic organisms should be absent (15). Table 1.3 lists a number of antimicrobial preservatives used in cosmetic products. Experience has shown that some

TABLE 1.3. Antimicrobial Preservatives Useful in Cosmetics[a,b]

Name	CAS Registry Number	Molecular Formula
Benzoic acid[c]	[65-85-0]	$C_7H_6O_2$
Benzyl alcohol	[100-51-6]	C_7H_8O
5-Bromo-5-nitro-1,3-dioxane	[30007-47-7]	$C_4H_6BrNO_4$
2-Bromo-2-nitropropane-1,3-diol	[52-51-7]	$C_3H_6BrNO_4$
Butylparaben	[94-26-8]	$C_{11}H_{14}O_3$
Calcium propionate	[4075-81-4]	$CaC_6H_{10}O_4$
Chlorobutanol	[57-15-8]	$C_4H_7Cl_3O$
m-Cresol	[108-39-4]	C_7H_8O
o-Cresol	[95-48-7]	C_7H_8O
p-Cresol	[106-44-5]	C_7H_8O
DEDM hydantoin	[26850-24-8]	$C_9H_{16}N_2O_4$
Dehydroacetic acid	[520-45-6]	$C_8H_8O_4$
Diazolidinyl urea	[278-92-2]	$C_{11}H_8O_2$
Dimethyl oxazolidine	[51200-87-4]	$C_5H_{11}NO$
DMDM hydantoin	[6440-58-0]	$C_7H_{12}N_2O_4$
7-Ethylbicyclooxazolidine	[7747-35-5]	$C_7H_{13}NO_2$
Ethylparaben	[120-47-8]	$C_9H_{10}O_3$
Formaldehyde	[50-00-0]	CH_2O
Glutaral	[111-30-8]	$C_5H_8O_2$
Glyoxal	[107-22-2]	$C_2H_2O_2$
Imidazolidinyl urea	[39236-46-9]	$C_{11}H_{16}N_8O_8$
Iodopropynyl butylcarbamate	[55406-53-6]	$C_8H_{12}INO_2$
Isobutylparaben	[4247-02-3]	$C_{11}H_{14}O_3$
Isopropylparaben	[4191-73-5]	$C_{10}H_{12}O_3$
MDM hydantoin	[116-25-6]	$C_6H_{10}N_2O_3$
Methylchloroisothiazolinone	[26172-55-4]	C_4H_4ClNOS
Methyldibromoglutaronitrile	[35691-65-7]	$C_6H_6Br_2N_2$
Methylisothiazolinone	[2682-20-4]	C_4H_5NOS
Methylparaben	[99-76-3]	$C_8H_8O_3$
Phenethyl alcohol	[200-456-2]	$C_8H_{10}O$
Phenol	[108-95-2]	C_6H_6O
Phenoxyethanol	[122-99-6]	$C_8H_{10}O_2$
Phenylmercuric acetate	[62-38-4]	$HgC_8H_8O_2$
Phenylmercuric benzoate	[94-43-9]	$HgC_{13}H_{10}O_2$
Phenylmercuric borate	[102-98-7]	$HgC_6H_7BO_3$
o-Phenylphenol	[90-43-7]	$C_{12}H_{10}O$
Propylparaben	[94-13-3]	$C_{10}H_{12}O_3$
Quaternium-14	[27479-28-3]	$C_{23}H_{42}N{\cdot}Cl$
Quaternium-15	[51229-78-8]	$C_9H_{16}ClN_4{\cdot}Cl$
Sodium dehydroacetate	[4418-26-2]	$NaC_8H_7O_4$
Sodium phenolsulfonate	[1300-51-2]	$NaC_6H_5O_4S$
Sodium phenoxide	[139-02-6]	NaC_6H_5O
Sodium pyrithione	[3811-73-2]	NaC_5H_5NOS
Sorbic acid[c]	[110-44-1]	$C_6H_8O_2$
Thimerosal	[54-64-8]	$NaHgC_9H_9O_3S$
Triclocarban	[101-20-2]	$C_{13}H_9Cl_3N_2O$
Triclosan	[3380-34-5]	$C_{12}H_7Cl_3O_2$
Zinc pyrithione	[13463-41-7]	$ZnC_{10}H_8N_2O_2S_2$

[a]Ref. 1 includes a more comprehensive listing.
[b]Use levels are product dependent but generally do not exceed 0.25%.
[c]The acid salts are also used.

of the most commonly used preservatives are inactivated by a variety of surfactants. For example, the parabens (esters of *p*-hydroxybenzoic acid) are exceptionally sensitive to the presence of nonionic surfactants, presumably as a result of micellization of the antimicrobial by the surfactant. Over the years, preservation problems have resulted in the introduction into cosmetics of unusual substances that exhibit suitable antimicrobial spectra. However, some of these ingredients reportedly are irritants or sensitizers. Controversies in the scientific literature over the use of these substances are aggravated by regulatory acceptance or prohibition, which may differ from country to country. Table 1.3 includes preservatives that may be barred in certain countries.

Local restrictions concerning the inclusion of preservatives and other constituents are dependent on the cosmetic product's method of use. Products that are allowed to remain on the skin are differentiated from those that are meant to be rinsed off. Components of products left on the skin can be expected to penetrate the viable epidermis and to be systematically absorbed. Products that are rinsed off shortly after skin contact, such as shampoos, can, if properly labeled, contain preservatives that might elicit adverse reactions if left on the skin. Typical examples of such preservatives are formaldehyde, formaldehyde releasers such as Quaternium 15 or MDM hydantoin, and the blend of methylchloroisothiazolinone and methylisothiazolinone.

Decorative eye cosmetic products have been reported to be subject to pathogenic microbial contamination. Regulatory agencies in several countries, therefore, permit the use of mercury-containing preservatives in eye makeups. The infections reported were to a large extent caused by contamination during use, and the introduction of self-sterilizing preparations seems warranted.

1.5.3. Lipids

Natural and synthetic lipids are used in almost all cosmetic products. Lipids serve as emollients or occlusive agents, lubricants, binders for creating compressed powders, adhesives to hold makeup in place, and hardeners in such products as lipsticks. In addition, lipids are used as gloss-imparting agents in hair-care products. The primary requirements for lipids in cosmetics are absence of excessive greasiness and ease of spreading on skin. Oily lipids, principal constituents of emulsions (creams and lotions), are well suited for inclusion in massage products, oils used to treat the skin (bath oils), ointments, suntan oils, and the like. Selection for a specific application is made on the basis of chemical inertness and physical properties. Petrolatum, mineral oils, polymeric silicones, polybutenes, and related substances are ingredients used for skin and hair conditioning. Conditioning is cosmetic jargon for describing a substance's beneficial effect on the substrate. For example, quaternary compounds are substantive to skin and hair proteins and thus can produce conditioning effects. Similarly, lipidic compounds without substantive functional groups, for example, tricaprin, condition skin merely by their presence on the surface. A selected listing of cosmetically useful lipids is provided in Table 1.4.

1.5.4. Solvents

Solvents can be added to cosmetics to help dissolve components used in cosmetic preparations. Water is the most common solvent and is the continuous phase in most suspensions and water/oil (w/o) emulsions. Organic solvents are required in the preparation of colognes, hair fixatives, and nail lacquers. Selected solvents are used to remove soil,

TABLE 1.4. Cosmetically Useful Lipids[a]

Material	CAS Registry Number	Molecular Formula
	Emollients	
Butyl oleate	[142-77-8]	$C_{22}H_{42}O_2$
Caprylic/capric glycerides	[65381-09-1]	
Cetyl lactate	[35274-05-6]	$C_{19}H_{38}O_3$
Dibutyl sebacate	[109-43-3]	$C_{18}H_{34}O_4$
Diisobutyl adipate	[141-04-8]	$C_{14}H_{26}O_4$
Ethyl linoleate	[544-35-4]	$C_{20}H_{26}O_2$
Glyceryl isostearate	[32057-14-0]	$C_{21}H_{42}O_4$
Hydrogenated palm kernel glycerides[b]		
Isodecyl myristate	[17670-91-6]	$C_{24}H_{48}O_2$
Isopropyl stearate	[112-10-7]	$C_{21}H_{42}O_2$
Lauryl lactate	[6283-92-7]	$C_{15}H_{30}O_3$
Mineral oil	[8012-95-1]	C_nH_{2n}
Myristyl myristate	[3234-85-3]	$C_{24}H_{56}O_2$
Oleyl oleate	[3687-45-4]	$C_{36}H_{68}O_2$
PPG-10 cetyl ether	[9035-85-2]	$(C_3H_3O)_2C_{16}H_{34}O$
Propylene glycol dicaprylate	[7384-97-6]	$C_{15}H_{19}NOS{\cdot}HCl$
Squalene	[111-02-4]	$C_{30}H_{50}$
Wheat germ glycerides	[58990-07-8]	
	Occlusive agents	
Acetylated lanolin	[61788-48-5]	
Butyl stearate	[123-95-5]	$C_{22}H_{44}O_2$
Caprylic/capric triglyceride	[65381-09-1]	
Dimethicone	[9006-65-9]	$(C_2H_6OSi)_nC_4H_{12}Si$
Hydrogenated rice bran wax[c]		
Lauryl stearate	[5303-25-3]	$C_{30}H_{60}O_2$
Paraffin	[8002-74-2]	C_nH_{2n+2}
Pentarerythritol tetrastearate	[115-83-3]	$C_{77}H_{148}O_8$
Petrolatum	[8009-03-8]	C_nH_{2n+2}
Propylene glycol dipelargonate	[225-350-9]	$C_{21}H_{40}O_4$
Stearyl erucate[d]		$C_{40}H_{78}O_2$
Trilinolein	[537-40-6]	$C_{57}H_{98}O_6$
	Natural lipids	
Apricot kernel oil	[72869-69-3]	
Beeswax	[8006-40-4]	
Carnauba	[8015-86-9]	
Castor oil	[8001-79-4]	
Coconut oil	[8001-31-8]	
Japan wax	[8001-39-6]	
Jojoba wax	[66625-78-3]	
Lanolin	[8006-54-0]	
Mink oil[e]		
Olive oil	[8001-25-0]	
Ozokerite	[8021-55-4]	
Rice bran oil	[68553-81-1]; [84696-37-7]	

Sesame oil	[8008-74-0]
Sunflower seed oil	[8001-21-6]
Vegetable oil	[68956-68-3]
Walnut oil	[8024-09-7]

[a]Ref. 1 includes a more comprehensive listing.
[b]This is a hydrogenated mixture of mono-, di-, and triglycerides derived from palm kernel oil.
[c]Prepared by partial hydrogenation of rice bran wax.
[d]Erucic acid, *n*-octadecanol ester.
[e]Oil obtained from subdermal fatty tissue of genus *Mustela.*

sebum, and makeup from skin. Solvents used in cosmetics include acetone, denatured alcohol, butoxyethanol (ethylene glycol monobutylether), diethylene glycol, dimethyl isosorbide, ethyl acetate, heptane, isopropyl alcohol, mineral spirits (boiling range 110–155°C), polyethylene glycol (mol. wt. from 200 up to 15,000), propylene glycol, toluene, and tricaprin (glyceryl tri-*n*-decanoate). A comprehensive listing may be found in Ref. 1. The selection of solvents for use in cosmetics is a complex task because of odor as well as topical and inhalation toxicities.

1.5.5. Surfactants

Substances commonly classified as surfactants or surface active agents are required in a wide variety of cosmetics. These are often categorized on the basis of ionic character but are grouped in Table 1.5, which includes at least one member from each of the various chemical types of surfactants, on the basis of utility in cosmetics. Prolonged contact with anionic surfactants can cause some swelling of the skin. Although this is a temporary phenomenon, skin in this swollen condition allows permeation of externally applied substances. Nonionic surfactants as a group are generally believed to be mild even under exaggerated conditions. The more hydrophobic nonionics, those that are water dispersible (not water-soluble), can enhance transdermal passage. Amphoteric surfactants as a group exhibit a favorable safety profile. Finally, cationic surfactants are commonly rated as more irritating than the anionics, but the evidence for generalized conclusions is insufficient.

TABLE 1.5. Cosmetic Surfactants[a]

Material[b]	CAS Registry Number	Molecular Formula
	Cleansing agents	
Ammonium laureth sulfate[c,d]	[32612-48-9]	$(C_2H_4O)_nC_{12}H_{26}O_4S{\cdot}H_3N$
Cetalkonium chloride	[122-18-9]	$C_{25}H_{46}N{\cdot}Cl$
DEA myristate	[53404-39-0]	$C_{14}H_{28}O_2{\cdot}C_4H_{11}NO_2$
Decyl polyglucose[d,e]		
Dioctyl sodium sulfosuccinate[c,d]	[577-11-7]	$C_{20}H_{38}O_7S{\cdot}Na$
Disodium cocoamphodiacetate[d]	[68650-39-5]	
Disodium laurimino dipropionate[d]	[3655-00-3]	$C_{18}H_{35}NO_4{\cdot}2Na$
Lauryl betaine[c,d]	[683-10-3]	$C_{16}H_{33}NO_2$
Lauryl pyrrolidone[d]	[2687-96-9]	$C_{16}H_{31}NO$
Nonoxynol-12	[9016-45-9]	$(C_2H_4O)_nC_{15}H_{24}O$
Myristamine oxide[c,d]	[3332-27-2]	$C_{16}H_{35}NO$
PEG-50 stearate	[9004-99-3]	$(C_2H_4O)_nC_{18}H_{36}O_2$
Potassium dodecylbenzenesulfonate[d]	[27177-77-1]	$KC_{18}H_{30}O_3S$

(*continued*)

TABLE 1.5. (*Continued*)

Material[b]	CAS Registry Number	Molecular Formula
Potassium oleate	[143-18-0]	$KC_{18}H_{34}O_2$
Sodium cocoyl glutamate[d]	[68187-32-6]	
Sodium C_{14-16} olefin sulfonate[d]	[68439-57-6]	
Sodium laureth phosphate[c,d]	[42612-52-2]	
Sodium lauryl sulfate[c,d]	[151-21-3]	$NaC_{12}H_{26}O_4S$
Sodium methyl oleoyl taurate[c,d]	[137-20-2]	$NaC_{21}H_{41}NO_4S$
Sodium nonoxynol-25 sulfate	[9014-90-8]	$(C_2H_4O)_nC_{15}H_{24}O_4S{\cdot}Na$
Sodium oleoyl isethionate[d]	[142-15-4]	$NaC_{20}H_{38}O_5S$
Sodium stearate[c]	[822-16-2]	$NaC_{18}H_{36}O_2$
TEA-abietoyl hydrolyzed collagen[d]	[68918-77-4]	
TEA-lauryl sulfate[d]	[139-96-8]	$C_{12}H_{26}O_4S{\cdot}C_6H_{15}NO_3$
TEA-oleoyl sarcosinate[c]	[17736-08-2]	$C_{21}H_{39}NO_3{\cdot}C_6H_{15}NO_3$
Emulsifying agents		
Ceteareth-10	[68439-49-6]	
Cetrimonium bromide	[57-09-0]	$C_{19}H_{42}N{\cdot}Br$
Laneth-5	[3055-95-6]	$C_{22}H_{46}O_6$
Lecithin	[8002-43-5]	
Nonoxynol-9	[14409-72-4]	$C_{33}H_{60}O_{10}$
PEG-20 dilaurate	[9005-02-1]	$(C_2H_4O)_nC_{24}H_{46}O_3$
PEG-8 oleate	[9004-96-0]	$(C_2H_4O)_nC_{18}H_{34}O_2$
Poloxamer 407	[9003-11-6]	$(C_3H_6O{\cdot}C_2H_4O)_x$
Polyglyceryl-8 oleate	[9007-48-1]	
Polysorbate 60	[9005-67-8]	
Sorbitan sequioleate	[8007-43-0]	
Sucrose stearate	[25168-73-4]	$C_{30}H_{56}O_{12}$
Foam boosters		
Cocamine oxide	[61788-90-7]	
Lauramide DEA	[120-40-1]	$C_{16}H_{33}NO_3$
Myristamide MIPA	[10525-14-1]	$C_{17}H_{35}NO_2$
Myristaminopropionic acid	[14960-08-8]	$C_{17}H_{35}NO_2$
Hydrotropes		
Ammonium xylenesulfonate	[26447-10-9]	$C_8H_{10}O_3S{\cdot}H_3N$
Potassium toluenesulfonate	[16106-44-8]	$C_7H_8O_3S{\cdot}K$
Sodium methyl naphthalene sulfonate	[26264-58-4]	$C_{11}H_{10}O_3S{\cdot}Na$
Solubilizing agents		
Cetareth-40	[68439-49-6]	
Oleth-44	[9004-98-2]	$(C_2H_4O)_nC_{18}H_{36}O$
PEG-40 stearate	[9004-99-3]	$(C_2H_4O)_2C_{18}H_{36}O_2$
Suspending agents		
Behentrimonium chloride	[17301-53-0]	$C_{25}H_{54}N{\cdot}Cl$
Benzethonium chloride	[121-54-0]	$C_{27}H_{42}NO_2{\cdot}Cl$
Sodium lignosulfonate	[8061-51-6]	
Sodium polystyrene sulfonate	[9003-59-2]	$(C_8H_8O_3S{\cdot}Na)_x$

[a] Ref. 1 includes a comprehensive listing.
[b] PCPC names are used.
[c] Belongs to a chemical class especially useful in facial and body washes.
[d] Belongs to a chemical class especially useful in shampoos.
[e] Decyl ether of a glucose oligomer.