CHAPTER 70

Cosmetic Products

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Key Points

- There has been over $1 billion in general business growth for ethnic hair care, beauty, and cosmetics.
- The term *cosmeceuticals* describes a product category that is intermediate between cosmetics and pharmaceuticals.
- The cosmeceutical market is driven by the antiaging market. Baby boomers comprise the largest market share.
- The cosmetic industry is governed by the Food, Drug, and Cosmetic Act and voluntary regulatory programs such as the Cosmetic, Toiletry and Fragrance Association (CTFA) and the Cosmetic Ingredient Review (CIR).
- The process of cosmeceutical product develop involves formulation, vehicle, active ingredient, and preservative considerations.

ABBREVIATIONS

AHA	α-hydroxy acid
CoQ10	coenzyme Q10
CIR	Cosmetic Ingredient Review
CTFA	Cosmetic, Toiletry, and Fragrance Association
FDA	Food and Drug Administration
FDCA	1938 Food, Drug, and Cosmetic Act
OPC	oligomeric proanthocyanidins
OTC	over the counter
SC	stratum corneum
TEWL	transepidermal water loss

OVERVIEW

For the past 50 years, the cosmetics industry has surpassed revenue expectations as one of the fastest-growing and most profitable market sectors in the United States. By all accounts, it appears that the new millennium will continue this record-breaking trend, and today, the growth continues as many companies expand into overseas markets and capitalize on new market segments, such as the fast-growing cosmeceuticals market.[1]

This chapter discusses several aspects of cosmetics use, beginning with an overview of the industry. The discussion includes the impact of cosmeceuticals, significant changes in the marketing of cosmetics, historical milestones in the development and use of cosmetics, the development of federal regulations, the formation of trade associations, and the chemical formulation of cosmetics. After discussing the industry, the chapter reviews various cosmetics products and ingredients, including antioxidants, growth factors, sunscreens, botanicals, and Cosmoleculars.

Impact of Cosmeceuticals

Almost 30 years ago, Albert Kligman introduced the term *cosmeceuticals* to describe a burgeoning product category that was intermediate between cosmetics and pharmaceuticals.[2] Loosely defined, *cosmeceuticals* are any cosmetic, skin care, hair care, body care, foot care, or other products that treat or prevent a medical condition even as they beautify.[3] The market impact of cosmeceuticals is staggering: While the United States saw a 1% annual increase in the sales of skin care products in 2003, sales of cosmeceutical brands had an incredible 83% increase.[4] According to the Fredonia Group, cosmeceutical revenues in the United States are projected to top $5.1 billion by 2007.[5] Today, hundreds of products include vitamin supplements, antioxidants, and growth factors.

Marketing of Cosmetics

The marketing of today's cosmetics is no longer restricted to the pharmacy and department store. In fact, sales in the traditional big retailers have been in a decline. In contrast, cosmeceutical products are now widely available from diverse marketers, including mass, prestige, and alternative distribution channels[5] (Table 70-1).

TABLE 70-1
Places to Purchase Cosmetics[5]

Mass-market retailers
Direct-market retailers
Prestige retailers
Specialty stores
Health spas
Beauty salons
Health clubs and gyms
Physician's offices (including plastic surgeons, dermatologists, ophthalmologists, internists, dentists)
Internet boutiques
Infomercials

VERTICAL STRUCTURE The cosmetics industry is composed of large conglomerates that use *forward vertical integration* to manufacture and market products. According to this structure, large companies set up subsidiaries that distribute or market cosmetics to a variety of markets. What appears to the consumer as a host of different product lines is, in reality, a collection of products distributed from a single research and development source. Most cosmetics manufacturers do not use the practice of outsourcing development and production. In order to respond to quickly changing demands of consumers, production facilities must continually adjust the production processes. Outsourcing the production process would increase the time to bring a new product to market.[6]

THE CONSUMER Marketing strategies are also changing in response to changing consumer demographics and consumer demands. America's aging baby boomers, numbering 78 million, traditionally have driven the market for antiaging or other cosmeceutical products. However, today's market is driven by a new segment of nontraditional consumers as well. For example, increased discretionary spending by growing middle-class populations in Russia and Asia is also driving sales. In addition, the children of baby boomers, generations X, Y, Z, etc., are also fueling the sale of cosmeceuticals, and males 18–30 years of age are now targeted as another key growth segment.[5]

As today's consumers grow more knowledgeable about the physiology of their own skin, these consumers seek more science in personal care products and demand scientific data to back up marketing claims. As a result, clinical studies are often cited, regardless of the quality of scientific data, and doctors are increasingly becoming the spokespersons for skin care brands, adding to the credibility of these brands in the marketplace. Mass marketers are not only aligning with physicians to compete with doctor-owned brands, but the industry is also experiencing buyouts of smaller, doctor-driven brands by the larger companies. In addition to wanting sophisticated products with stable, efficacious active ingredients, consumers are asking for nonsurgical, noninvasive treatments that can be accomplished without visiting a clinic. To this end, several products have been positioned

as a less drastic approach and an alternative to the dermatologist's office.[5]

ETHNIC MARKETS Another growth area in cosmetics is specialized ethnic populations, evidenced by the large success of products targeting the African-American, Hispanic, and Asian-American markets. According to market predictions, general business growth for the ethnic hair care, beauty, and cosmetics market will reach $40 billion by 2011. Products expected to grow in the ethnic markets include fade creams and gels, cleansers, toners, astringents, soaps, emollients, moisturizers, and antiwrinkle products. In the ethnic market, products that target skin discoloration are experiencing the best consumer response.[7]

For African-American consumers, uneven skin tone, sensitive skin, and acne-prone skin are the most problematic areas. Products targeting the African-American market have been most successful when sold at the mass-market and drugstore levels, as demonstrated by the success of certain ethnic products sold in Walgreen's and Wal-Mart stores. Ethnic skin care lines are handled more often through distributors compared with general-market products. This is so because successful marketing of ethnic products requires careful use of finely tuned distribution channels. Cofounder Dr. Cheryl Burgess and representatives of U.S. Black Opal note the success of distributors with operations in the United Kingdom, including destinations in the Caribbean, Botswana, Brazil, and Zaire.[7]

Certain ingredients are extremely popular among African Americans, including α-hydroxy acid (AHA) and cocoa butter—AHA reduces the ashy appearance of skin in some African Americans by speeding up the natural process of sloughing off dead skin cells, and cocoa butter has helpful emollient properties.[7]

Another indicator of the success of products targeting ethnic populations is the acquisition of cosmetics companies in non-Western countries, for example, L'Oreal's purchase of Yue Sai Kan Cosmetics and Carson, Inc.[7]

PERVASIVE MARKETING VERSUS HEALTHY COSMESIS The continued growth of the cosmetics industry is not terribly difficult to understand given America's obsession with perfect physicality and perfect beauty. Whether from Hollywood, the cosmetics industry, or even the medical health profession, Americans receive a steady dose of media images and messages *instructing* consumers to obtain physical perfection. Richard Fried writes, "Healthy cosmesis lies midway between total self-neglect and extreme makeover."[8] He notes that the dermatologist can play an integral role in the patient's decision-making process, providing clarity in a market that is permeated with unsubstantiated claims.[8]

Marketing claims tout the miracle-like effects of cleansers, moisturizers, skin supplements, and antiaging products. However, clinical studies that support these claims of miracle-like efficacy are often absent, flawed, or based on very small study populations, and many times the only clinical data are available from the product's manufacturer.[4]

HISTORY OF SKIN CARE PRODUCTS

Development of the Cosmetics Industry

Cosmetics were used for religious, medical, and personal care purposes by ancient societies that included the Egyptians, Chinese, and Indians. Based in part on ancient Egyptian pharmacopeia, the growth of cosmetics continued to develop in Rome and Greece. For several centuries, Rome remained a center of important cosmetic development, evidenced by the formulation of the first cold cream by Galen (AD 130–200). The Islamic culture encouraged the development of the beauty culture and contributed great advances in the use of botanical treatments for cosmetology. The thirteenth century marked the beginning of a divergence between formalized medicine and the science of cosmetology.[9] Moving forward, the cosmetics industry increasingly focused on the science of beauty, leaving behind medicine. Cosmetic products would not share medical status again until the flourishing of cosmeceuticals in the 1980s. Indeed, the debut in 1983 of these hybrid products—merging the research interests of science, medicine, and beauty—marked the birth of the modern cosmeceuticals industry.[10]

By the eighteenth century, most cosmetics were formulated in private homes from ingredients purchased at pharmacies. By the nineteenth and twentieth centuries, several important developments in the formal regulation of the industry helped to shape the modern-day cosmetics industry.[5] With the advent of formal regulation, the industry began gaining consumer confidence through improved safety, efficacy, and product stability. Today, many companies conduct cosmetics research with the same safety and testing methods used by pharmaceutical research and development.[5]

Development of Cleansers and Moisturizers

Some of the earliest cosmetic therapies were introduced by Galen, a Roman physician/cosmetician who invented cold cream, an emulsion of olive oil and beeswax. Much later, in the early 1900s, Paul Gersen Unna introduced Unna's boot, essentially a zinc oxide paste that is still the therapy of choice for stasis ulcers. Petrolatum was introduced in 1872 and has been hailed as the moisturizer *par excellence* without a serious rival in more than 100 years.[2]

REGULATORY AGENCIES

History of Regulation

Unlike the long history behind the development of the cosmetics industry, the passage of government regulations to establish the safety of cosmetics is a fairly recent historical development. The passage of the Food, Drug, and Cosmetic Act (FDCA) in 1938 marked the beginning of legislation to protect the consumer from unsafe cosmetic formulations.[1]

Beginning in the 1800s, a growing problem with tainted medications and food preservatives led to grass roots groups such as the Pure Food Movement, which helped to generate support for regulatory reforms that were made law by the Pure Food and Drug Act of 1906 (PFDA). However, the far-reaching legislation was stripped of its main powers of enforcement prior to becoming law.[9]

Concerns for consumer protection continued to fulminate in the 1900s, mainly at the state level. Politicians, recognizing a populist cause, exploited the horror stories (partly true, partly tall tale) illustrating the terrible harms caused by unregulated medications and cosmetics. The reform movement also was aided by a series of highly publicized books that demonized the practices of the food, drug, and cosmetics industry. These events eventually culminated in formulation of the 1938 Food, Drug, and Cosmetic Act.[1]

Provisions of the act addressed both adulteration and misbranding controversies. For example, the act states that a cosmetic is considered adulterated if it "contains any poisonous or deleterious substance that may render it injurious to

users under customary conditions of use." In addition, the misbranding provisions prohibit labeling that is "false or misleading in any particular way."[11] Labeling provisions required by the FDA for the cosmetics industry include (1) proper cosmetic labeling, (2) declaration of ingredients, (3) label warnings, (4) tamper-resistant packaging, (5) contents quantity, and (5) the name and address of the manufacturer, packer, and distributor. The FDA defines *cosmetics* as 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" while maintaining the structure and function.[11]

Throughout the 1900s, regulation of cosmetics was further defined, amid a continuing battle between consumers, manufactures, trade organizations, politicians, and the government—culminating in establishment of a voluntary regulatory program (discussed below).

COSMECEUTICALS: REGULATORY DILEMMA The dual nature of cosmeceuticals presents new challenges to lawmakers for classifying and regulating these products. The challenges range from fundamental questions to practical concerns. For example, should regulators reclassify drugs as cosmetics when manufacturers remarket products—not for their original therapeutic effect—but for newly discovered cosmetic side effects? Could drug vehicles themselves—absent any active ingredients—be given drug status based on their therapeutic effects as occlusive agents? In some cases, regulators have attempted to distinguish drugs from cosmetics based on the concentration of an active ingredient. However, no scheme is without drawbacks. Consider that the efficacy of AHA is more dependent on the design of the vehicle than on the concentration of AHA. As the cosmeceutical market grows, the regulatory difficulties are certain to be compounded.[12]

Cosmetic, Toiletry, and Fragrance Association (CTFA)

The CTFA was founded in 1894 as the Manufacturing Perfumes Association. The first decade of the association's existence was devoted primarily to furthering the industry's interests by helping to repeal several major tariffs and taxes. The association was very active in the 1920s as the cosmetics industry, boosted by the emerging flapper look in place of the more reserved Victorian style, experienced an explosion of growth. In 1937, the organization—renamed the American Manufacturers of Toilet Articles—gave support to the basic tenets of the legislation that would lead to the 1938 Food, Drug, and Cosmetic Act and lobbied for federally standardized regulations in place of a patchwork of state laws.[1]

In the 1970s, the CTFA worked closely with the FDA to establish a system of voluntary regulation, in which the industry provided regular registration of manufacturing establishments, submission of data on finished products, and reporting of consumer complaints. In the 1970s era of consumer and environmental concerns, the CTFA's program of voluntary regulation demonstrated the industry's willingness to supply information to the FDA while discouraging congressional legislation at the same time.[1] Today, about 40% of manufacturers voluntarily register their products with the FDA.[13]

In 1973, the first edition of the *Cosmetic Ingredient Dictionary* was published. The publication eventually gained international acceptance and would later provide an instrument for proper cosmetic ingredients labeling.[1]

The 1970s saw continued pushes for increased regulation of cosmetic ingredients labeling. Although the CTFA opposed the attempts to remove the voluntary regulation program, the CTFA eventually found itself working with the FDA to establish legislation, and in 1976, it supported further regulations on ingredient labeling. Manufacturers were required to substantiate the safety of their products or include a warning statement that the safety of the product had not been determined.[1]

Also evolving in the 1970s was the creation of another landmark volunteer regulatory program, the Cosmetic Ingredient Review (CIR). The CIR was established as a voluntary program to evaluate published and unpublished data on cosmetic ingredient safety. Today, the Expert Panel of the CIR is composed of scientists from the disciplines of dermatology, pharmacology, chemistry, and toxicology who have been publicly nominated by consumer, scientific, industry, and government agencies. The CIR program provides an open forum to present safety information and encourages congressional and public discourse.[1]

The CTFA is also responsible for *Cosmetic Industry ON CALL,* a publication created for industry members, government officials, medical professionals, and consumers to provide timely alerts regarding important ingredient safety information.[1]

Throughout the last quarter-century, the CTFA has helped industry, government, and consumers steer through many difficult social and legal challenges in cosmetics; for example, efforts to work with animal rights groups, safety testing of color additives, and regulation of volatile organic compounds, to name a few.[1]

The CTFA founded Look Good Feel Better—an initiative to advance the awareness and special use of cosmetics by cancer patients—and launched several initiatives to create funding for the program. Look Good Feel Better is funded by the cosmetics industry through the CTFA foundation to help female cancer patients overcome the appearance-related side effects and help to improve patients' self-esteem.

INTERNATIONAL COSMETIC INGREDIENT DICTIONARY The desire to normalize the process of describing botanical ingredients began in the United States. In the 1990s, an explosion of interest in botanicals drove the earliest rules for identifying and labeling botanical ingredients. At first, ingredients were labeled intuitively, for example, from a common name, such as apple or orange. However, as ingredients became increasingly more specialized, it became apparent that new rules for assigning names would be required. In addition, the intuitive terms developed in the United States were of little use internationally. With the help of the CTFA International Nomenclature Committee, several meetings were held in the United States and internationally. As a result of the meetings, the CTFA recommended that new rules recognize scientific terminology, using Latin genus and species names, as the basis for botanical-derived ingredients in nomenclature. In 1995, the sixth edition of CTFA's *International Cosmetic Ingredient Dictionary* introduced the labeling of botanical ingredients, showing both Latin and common botanical names.[1]

GENERAL BACKGROUND

Product Development

FORMULATIONS The formulation of a dermatologic product must satisfy certain requirements that include bioavailability of an agent, chemical and physical stability, freedom from contamination,

and patient acceptability. Satisfaction of these requirements becomes a complex challenge when designing a delivery vehicle in conjunction with a specific target site for products applied to the skin. Cosmetic products may target the skin surface, the horny layer, sweat ducts, or living skin cells. To reach one of these targets, a vehicle must be individually designed to accommodate the specific needs of a therapeutic agent and a specific therapeutic target. Therefore, product formulation and vehicle design are almost synonymous.[14]

DERMATOLOGIC VEHICLE Dermatologic vehicles include topical liquids (lotions or liquid emulsions), anhydrous and hydrous semisolids, patches and tapes, liposomes, and microparticles. Some basic questions in the development of a delivery system may be answered early on. For example, what degree of occlusion will be needed, or will a penetration enhancer be required‡ Occlusion affects the percutaneous absorption of a product by changing the hydration of the SC and raising skin temperature. Penetration enhancers change the normal resistance of the SC.[14]

PRESERVATIVES Cosmetics can suffer degradation through oxidation and hydrolysis. Microbial growth can produce enzymes that cause degradation of active ingredients and change pH. Preservatives are generally required for any topical product containing water. Preservatives prevent or limit fungal and bacterial growth and contamination—after the product is manufactured, during storage, and in the hands of the consumer.[14]
Au1] Vitamin E (tocopherol) and EDTA are common preservatives in cosmetics.[1]

ACTIVE INGREDIENTS The use of generic drugs has helped the health care and health insurance systems to extend therapies to many patients who, without generic pricing, would not be able to sustain prescription drug costs. However, these benefits are not afforded without a tradeoff. In several cases, the interchangeability of products leads to therapy failure. This can be the result of (1) failure of a vehicle to deliver enough active ingredient or (2) patient noncompliance that results when inert ingredients in the vehicle cause adverse effects. Most disturbing is the misinterpretation by a clinician that an active ingredient has failed when the culprit actually may be the generic's vehicle.[15]

Generic Evaluation The interchangeability of two formulations is evaluated by three measures: (1) pharmaceutical or chemical equivalence, (2) bioequivalence of the active ingredient, and (3) therapeutic equivalence. For topical formulations, measuring bioavailability is more involved because active ingredients are present in very low concentrations in these formulations. The low concentrations are problematic because they lead to difficulties in accurately measuring the concentration of active ingredient in blood, and blood levels are often not representative of the concentration at the target site—the skin. As shown in Table 70-2, generics are allowed significant variation from brand-name drugs. Even small modifications to a product vehicle cause significant changes in therapeutic efficacy. This may call into question any assumptions of true equivalence.[15]

LABEL TERMS THAT MISLEAD The marketing of cosmetics often relies on the use of promotional terms such as *fragrance-free* and *hypoallergenic* to suggest that a product has special characteristics. These product claims often cause consumers to form grand assumptions about product ingredients. Unfortunately, these promotional terms have very imprecise meanings and may mislead consumers about the actual qualities and ingredients of a cosmetic. In many cases, consumers simply jump to conclusions, such as the assumption that "natural" products are superior. In other cases, federal standards or definitions are entirely absent, leaving claims about ingredients unchallenged, with regard to actual ingredients or scientific basis. A few of these terms are presented below.

Alcohol-Free Cosmetics that are labeled "alcohol-free" are sometimes chosen by consumers because they believe that alcohol will dry out their skin or hair. However, alcohol-free only pertains to the absence of ethyl alcohol. Cosmetic products, including those labeled "alcohol-free," still contain other alcohols, such as cetyl, stearyl, or lanolin alcohol. These alcohols, known as *fatty alcohols,* have a variety of effects quite different from those of ethyl alcohol.[16]

Hypoallergenic When cosmetics are labeled "hypoallergenic" or "allergy tested," many consumers assume that ingredients contained in the product are gentler to the skin or safer than nonhypoallergenic cosmetics. However, both dermatologists and the FDA say the term has very little meaning. Indeed, the FDA states that "almost all cosmetics can cause allergic reactions in certain individuals."[17] The FDA provides no federal standards or definitions to govern the use of the term, and manufacturers of cosmetics labeled "hypoallergenic" are not required to substantiate their claims. Not surprisingly, the FDA found that a majority of cosmetics labeled "hypoallergenic" contained the same ingredients as nonhypoallergenic cosmetics.[17]

Natural or All Natural Many consumers also believe that "natural" or "all natural"

TABLE 70-2
Terminology of Generic Drug Evaluation[15]

TERM	COMMENT	
Therapeutic equivalence	A comparison of the therapeutic efficacy and toxicity profile of two different drugs given by the same dosage regimen to patients being treated.	
Bioavailability	The rate at and the extent to which an active ingredient is absorbed from the site of administration and reaches the systemic circulation.	
Bioequivalence	A comparison of the relative bioavailability of two different drug products in the same test population.	
Pharmaceutical equivalence	***Constant***	***Variable***
	Active ingredient	Inert ingredients (binders, fillers, excipients)
	Strength	Color
	Route of administration	Flavor
	Dosage form (tablet vs capsule)	Shape
		Scoring
		Configuration
		Packaging
		Shelf life
		Manufacturing process

ingredients are better for the skin. However, the FDA warns that the implied superiority of natural ingredients is based neither in fact nor in scientific legitimacy. Moreover, there is no official government definition for *natural* or *all natural*.[18] "All natural" products contain plant-derived substances that are conducive to microbial growth, causing them to have an unusually short shelf life. Consumers and manufacturers should carefully consider the risk of contamination in products that contain nontraditional preservatives or no preservatives at all.[13]

Fragrance-Free and Unscented Cosmetics labeled "fragrance free" or "unscented" suggest that a product contains no fragrance or that no fragrance has been added. However, fragrance-free products may contain fragrance ingredients in small quantities to mask offensive odors caused by various ingredients, for example, the fatty odor of soap. Most manufacturers list these small quantities of fragrance among their ingredients, even though the FDA requires no such labeling.[19]

Preservative-Free Consumers also believe a product is superior, natural, or less harmful to skin if labeled "preservative free." However, most cosmetic preparations require preservation to prevent spoilage owing to microbial action or to retard oxidative deterioration, particularly that of fats and oils. Many of the components of cosmetics can serve as substrates for microbes, and contamination of a cosmetic, usually from airborne bacteria or fungi, can cause partial or total deterioration of the product.[20] There are no regulations requiring cosmetic manufactures to indicate the shelf life on the labels of their products. However, voluntary shelf-life guidelines have been developed by the cosmetics industry. For example, products used in the area of the eye have a shorter recommended shelf life. Accordingly, industry experts recommend replacing mascara 3 months after purchase.[13]

Some products labeled as "preservative free" actually may contain preservatives. This is so because manufactures can exploit loopholes in the regulations to make preservative-free claims. Manufactures can exclude preservatives from the ingredients label if raw material used in the product was preserved unnecessarily or if a raw material is overpreserved using any preservative, whether synthetic or natural.[21]

In 2004, concerns about the possible connection between parabens and breast cancer caused significant ramifications in the preservative industry and led some manufacturers to seek preservative-free systems to control microbial growth and prevent product deterioration. However, industry efforts have not yielded a satisfactory solution that is readily adaptable to current manufacturing requirements.[21]

In Japan, a different approach has been taken by the Fancl Corp. In 1999, Fancl built a $45 million manufacturing facility to execute the company's 25-year-long preservative-free philosophy. The new facility adopted a novel manufacturing process that eliminated the need for adding preservatives to cosmetics. Much of this is accomplished through automated processes that take place in bacteria-free environments. The company uses clean rooms, air filtration, and vigilant quality control to keep products from becoming contaminated with bacteria. Many of the processes meet medical and pharmaceutical manufacturing standards.[22]

COSMETIC PRODUCTS

Cleansers

Cleansers generally fall into two categories: soap and synthetic detergents. Soap, the most common known cleanser, damages skin because it fails to distinguish between unwanted dirt and important intercellular lipids. Certain lipids in the SC contribute to the water-holding function of the SC.[23–25] The water content in the SC is largely responsible for the flexibility and amount of shedding in this layer. The uptake of water and water-holding capacity, in turn, depends primarily on the quantity of natural moisturizing factor (NMF)—the water-soluble hydroscopic and surface-active materials present in the SC.[26,27] When soap disrupts the NMF, it reduces the skin's capacity to retain water, and transepidermal water loss (TEWL) leads to dry skin.

Soap causes the pH of skin to change and strips away valuable humectant agents, resulting in irritant contact dermatitis.[28] An alternative to soap is *syndets* (synthetic detergents). Although syndets remove less unwanted dirt, syndets spare more intercellular lipids, and the pH remains adjusted.[28] The use of syndets leaves the skin more capable of retaining moisture and thus avoids drying the skin out.

It is important to avoid certain additives in cleansers, especially if there is a history of sensitive skin. Examples include detergents such as sodium lauryl sulfate, parabens, and fragrances.[28] Table 70-3 lists several types of cleansers and their main attributes.

TABLE 70-3
Cleansers[28]

Type of Cleanser	Formulation Comments
Soap	Composed of anionic surfactants Drying and irritating to skin Raises pH of skin (neutral to alkaline)
Superfatted soap and beauty bars	Composed of anionic surfactants Drying and irritating to skin Causes follicular plugging Raises pH of skin (neutral to alkaline) Emollient may be added to reduced dryness
Dermatologic bars/cakes	Composed of amphoteric, anionic, and nonionic surfactants May raise pH of skin Emollient added to reduced dryness and irritation
Cosmetic liquid cleansers	Composed of amphoteric, anionic, and nonionic and silicone surfactants Can be mild and less irritating to skin Generally have pH similar to skin Generally have emollients and humectants added
Antiseptic and antibacterial washes	Composed of amphoteric, anionic, and nonionic surfactants May raise pH of skin Emollients added to reduced dryness and irritation Adjunct to acne treatment May help control bacteria, not believed to penetrate follicle Potentially less irritating and drying than topical bactericide.

TABLE 70-4
Moisturizer Ingredients[28]

Type of Ingredient (Function)	Examples	Side Effects and Problems
Occlusive agents (block water loss in the stratum corneum)	Lanolin, mineral oil, petrolatum	Messy Some can cause folliculitis May clog pores May cause contact dermatitis (lanolin) Can block hair follicles and cause pustules (folliculitis) or boils Can aggravate acne or cause an unsightly facial rash, perioral dermatitis
Humectants (hydroscopic substances that attract moisture)	α-Hydroxy acids, amino acids, collagen, elastin, glycerin, glycogen, glycosphingolipids, glycosaminoglycans, hyaluronic acid, lecithin, phospholipids, polysaccharides, proteins, pyrrolidone carboxylate (NaPCA), sodium hyaluronate, sorbitol, sugars, and urea	Some may cause irritation (urea, lactic acid)
Emollients (smooth and soften skin by failing the spaces between skin flakes)	Cholesterol, fatty acids, myristates, palmitates, squalene, stearates, and triglycerides	Not always effective May cause allergic reaction
Anti-irritants (reduce itching and irritation)	Allantoin, bisabolol, glycyrrhetinic acid, and vitamin C	Not always effective May cause allergic reaction
Antioxidants (may aid in cell turnover and healing and may reduce dehydration)	Selenium, superoxide dismutase, vitamin A (retinyl palmitate and retinol), vitamin C, ascorbyl palmitate and magnesium ascorbyl palmitate, β-glucan, vitamin E (α-tocopherol, tocotrienol), curcumin, coenzyme Q10, and α-lipoic acid	Not always effective May be irritating

Moisturizers

Moisturizers assist in skin repair by creating a suitable environment for healing. Moisturizers accomplish this by reducing the loss of water and creating a barrier on the skin. Moisturizer ingredients can be broken into three basic categories: (1) occlusive agents, (2) humectants, and (3) emollients[28] (Table 70-4).

OCCLUSIVE AGENTS Occlusive agents are defined by their ability to stop or retard water loss. Petrolatum is the superior choice of occlusive agents.[29] Other choices include lanolin, silicones, and mineral oils. It is highly recommended to apply occlusive agents right after cleansing to trap the maximum quantity of water in the skin[28] (see Table 70-4).

HUMECTANTS Humectants can improve the overall hydration of the skin by attracting moisture. However, when using high levels of humectants, an occlusive agent also should be used to help prevent water loss from surrounding cells. Without an occlusive agent to trap moisture, the skin actually could dry out even further.[28,29] Examples of common humectants include AHAs, amino acids, collagen, elastin, glycerin, glycogen, glycosphingolipids, glycosaminoglycans, hyaluronic acid, lecithin, phospholipids, polysaccharides, proteins, pyrrolidonecarboxylate, sodium hyaluronate, sorbitol, sodium PCA, sugars, and urea. Some of these may cause irritation (e.g., urea and lactic acid)[28] (see Table 70-4). [Au2]

EMOLLIENTS Emollients provide a soft, smooth feeling that consumers desire. The smooth feeling is actually achieved by filling in spaces between skin flakes. Emollients are classified according to their composition. Hydrogel emollients are either surface-active, providing a thin layer at the surface, or they are carbomer gels, which penetrate deeper into the skin. Oil-in-water emollients come in the form of lotions or creams. These emollients posses a hydrophilic external phase with superb absorption rates. Emollients can be incorporated easily into products.[28,30] On the other hand, water-in-oil emollients have a lipophilic external phase. Since these emollients mainly include petrolatum and/or paraffin oil, they are aesthetically less pleasing and usually are used in more chronic disease situations[30] (see Table 70-4).

Examples of common emollients found in moisturizers include cholesterol, fatty acids, myristates, palmitates, squalene, and triglycerides[28] (see Table 70-4). The most effective moisturizers are anhydrous lanolin and petrolatum, which have very little water and probably act by retarding loss of water.[29]

To replace diminished moisturizing and barrier properties in cases of deficit sebum production, future moisturizers will contain optimal molar ratio of skin surface lipids that mimic synthetic molecules, such as pseudoceramides. Other products under development include the acrylate polymer, a spherical microparticle that absorbs and binds sebum.[31]

Sun Protection

Terrestrial sunlight consists of ultraviolet B radiation (UVB, 280–320 nm), UVA radiation (320–400 nm), visible light (400–800 nm), and infrared (IR) radiation (800 nm and above). To protect human skin from free-radical generation, skin has a sophisticated antioxidant system that includes superoxide dismutase, glutathione reductase, and glutathione peroxidase. However, UV light damages skin throughout life because the cutaneous antioxidant system is less than 100% effective. In addition, these cutaneous antioxidant

TABLE 70-5
FDA Sunscreen Final Monograph Ingredients[33]

Drug Name	Concentration %	Absorbance
Aminobenzoic acid	≤15	UVB
Avobenzone	2–3	UVA
Cinoxate	≤3	UVB
Dioxybenzone II	≤3	UVB, UVA
Homosalate	≤15	UVB
Menthyl anthranilate	≤5	UVA
Mexoryl	≤8	UVA
Octyl methoxycinnamate	≤7.5	UVB
Octisalate	≤5	UVB
Oxybenzone	≤5	UVB
Padimate O	≤8	UVB
Phenylbenzimidazole sulfonic acid	≤4	UVB
Sulisobenzone	≤10	UVB, UVA
Titanium dioxide	2–25	Physical
Trolamine salicylate	≤12	UVB

systems themselves experience continuous damage from the sun, compromising their effectiveness.[32] For many years, scientists have known that UVB causes sunburn and serves as a surrogate for more serious skin disorders, including cancer. However, scientists have come to believe that UVA also may contribute to skin disorders, including photoaging and skin cancers.[32]

Sunscreens traditionally have been categorized as chemical absorbers, physical blockers, or both. Chemical sunscreens generally have aromatic compounds that absorb high-density UV rays, causing excitation to a higher energy state (Table 70-5). When the molecules return to the ground state, the energy absorbed in the photochemical process causes the emission of longer, safer wavelength radiation. Physical blockers are opaque compounds that reflect the sun's light. Recent research indicates that the newer micronized forms of physical blockers also may function in part by absorption.[33]

UVA SUNSCREENS Although benzophenones are primarily UVB absorbers, oxybenzone absorbs through UVA, making it a broad-spectrum absorber. It significantly augments UVB protection when used in a given formula. The anthranilates are weak UVB filters that absorb mainly in the near-UVA portion of the spectrum, making them less effective than benzophenones. Butyl methoxydibenzoylmethane provides superior protection through a greater portion of the UVA range. Although it is a significant addition to true broad-spectrum UV protection, concerns have been raised regarding its photostability and potential to degrade other sunscreen ingredients.[33]

It is recommended that all skin types and ethnic groups be advised and encouraged to use daily sun protection. The level of protection from sunscreen is indicated using the sun protection factor (SPF). Although consumers readily understand the meaning of the number—the higher the number, the greater the protection—studies show that people often mistake the higher SPF number as meaning that they can stay in the sun longer. Indeed, studies have shown that using higher SPF sunscreens has led to increased sun exposure by consumers. In addition to consumers misusing the SPF information, other problems exist. Consumers fail to correctly apply sunscreens—applying too little, too infrequently—perhaps as a result of labeling confusion. Descriptors such as "sun block," "all-day protection," "broad spectrum," "waterproof," and "water resistant" are misleading, especially since all sunscreens allow some portion of damaging UV radiation to penetrate the skin.[33]

Many of the organic chemicals commonly used in sunscreen products have not been tested for long-term safety. For example, titanium dioxide– and zinc oxide–based sunscreens have been promoted on the assumption that they are less harmful than organic sunscreen absorbers. However, the use of titanium dioxide as a sunscreen also has no long-term safety data.[33]

There is a growing interest in botanicals for sun protection, and research has found that some plant oils contain natural sunscreens. For example, sesame oil resists 30% of UV rays, whereas coconut, peanut, olive, and cottonseed oils block out about 20%. Although mineral oil does not resist any UV rays, it helps to protect skin by dissolving the sebum secreted from oil glands, thus assisting evaporation from the skin. Tea tree oil is a popular component of sunscreen formulations that relieves sunburn by increasing blood flow in capillaries and bringing nutrients to damaged skin.[33]

Evidence is growing that the addition of antioxidants to sunscreen formulations can protect human skin against UVB, UVA, and IR irradiation. In a study of 30 patients, Muizzuddin and colleagues[32] demonstrated significant protection from a cocktail of antioxidants. Results indicated protection from UVB, UVA, and IR irradiation.

Today, the addition of antioxidants is common among cosmeceuticals, especially for the purpose of treating photodamaged skin. However, the investigations of antioxidant use for preventing damage are in the very early stages of research and development.[4]

Clothing should not be overlooked as an integral part of sun protection. Wide-brimmed hats should be worn, and clothes should be chosen carefully with an appropriate fabric. Loosely woven fabrics may still transmit UV, up to 30% of UV with wet fabrics such as swimsuits. In addition, a white T-shirt has an SPF of 5–9, and UV-protective fabrics raise the SPF to 30.[33]

Antiaging Formulations: Overview

Just as antiaging products overtook the vitamin and supplements industry in the 1990s, antiaging products, referred to as *cosmeceuticals* are flooding the cosmetics marketplace. However, because the therapies are not classified or marketed as drugs, cosmeceuticals lack FDA oversight, and many claims go unsubstantiated. Before recommending antiaging therapies, dermatologists should seek clinical data on the efficacy of a product in a scientific, peer-reviewed journal independent of the manufacture's data. At a minimum, dermatologists should determine whether an ingredient has been shown to penetrate the skin and whether the proposed effects have been documented histologically, biochemically, or at the molecular level. In particular, dermatologists should warn patients that encouraging data from in vitro studies might prove irrelevant if an agent fails to penetrate human skin.[35] The first generation of antiaging cosmetics, mostly antioxidants, has been followed by a second generation of antiaging cosmetics comprised mainly of

TABLE 70-6
Partial List of Cosmeceutical Agents[4]

First-Generation Cosmeceuticals
Vitamin A (retinoids, retinoic acid, retinol)
Vitamins C, B, E
Coenzyme Q10
Idebenone
α-Lipoic acid
Grape seed extract
Green tea
Superoxide dismutase

Second-Generation Cosmeceuticals
Copper peptides (Cu + glycyl-L-histidyl-L-lysine)
Growth factor-containing preparations:
- TNS Recovery Complex
- 4% Skin Growth Factor from placental extract
- Recombinant EGF
- Recombinant TGF-β1

Pal-KTTKS (palmitoyl pentapeptide)

growth factors[4] (Table 70-6). Experts are now evaluating the use of hormone therapy in skin care products,[35] for example, synethetic peptides such as Argireline to relax muscle and dimethylaminoethanol (DMAE) to reduce fine lines and wrinkles.

Exfoliants

AHAs are naturally occurring organic carbolic acids found in numerous cosmetics. AHAs are found in food sources, including fruit, sour milk, molasses, honey, and sugar cane, and can be synthesized as well.[36] Glycolic acid and lactic acid are the two most common AHAs used in cosmetics, although many others are used in combination.[37] AHAs diminish skin scales (exfoliate), remove excess skin oil, and moisturize the skin. In addition, studies suggest that AHAs and β-hydroxy acids (BHAs) also may assist in the rejuvenation of photodamaged skin.[36–38] These compounds reduce corneocyte cohesion by modulating the secretion of cytokine- and keratinocyte-derived growth factors, possibly leading to the disruption of ionic bonds between corneocytes. AHAs reduce skin thickness, resulting in greater flexibility of the skin and reduced cracking and fissuring at the skin surface.[36,39]

Although AHAs initially gained interest in skin therapy because of the capacity to treat ichthyosis, the use of AHAs dates back to ancient times, when wine and sour milk were sometimes used to rejuvenate skin.[36] At the proper concentration, AHAs can be used as peeling agents.[37] Elsewhere, glycolic acid was demonstrated to be effective for treating pseudofolliculitis barbae,[39] and salicylic acid has been successful in treating hyperkeratosis.[36,39–42]

Unlike true keratolytics, AHAs exert influence at lower, newly forming levels of the SC.[36] Many patients experience irritation from using products containing AHAs. While prescription and OTC products differ only in pH and concentration, studies have shown that efficacy depends more on pH than on concentration.[38] Chemical peels have nearly all been replaced with AHA-containing products.[37]

Skin Supplements and Nutrients

VITAMIN C Since skin uses endogenous antioxidants to protect itself from photodamage, the potential to use cosmetics containing antioxidants for additional protection is not unexpected.[43] Antioxidants applied topically have been shown to be effective in stabilizing free radicals on the skin, but absolute proof as to the clinical value has not yet been provided.[44] Because proof is still lacking, the FDA limits the labeling of cosmetics to only the chemical name—for instance, ascorbic acid instead of vitamin C—so that consumers do not automatically assume that a cosmetic will provide the commonly understood benefits of vitamin C taken orally.[45]

Vitamin C is a free-radical scavenger and a cofactor for the hydroxylation of procollagen. In addition, pretreatment with vitamin C has been shown to reduce sunburn cells in porcine and human skin exposed to UV light. As an ascorbic acid, vitamin C is very unstable, causing manufacturers often to replace it with ascorbyl palmitate. However, only L-ascorbic acid significantly increases vitamin C levels in the skin. Very few human studies have demonstrated the potential photoprotective properties of vitamin C.[46] However, a few studies are worth noting. Vitamin C was shown to reduce wrinkling in a double-blind, vehicle-controlled clinical investigation with 19 participants.[35] In addition, a recent 6-month double-blinded, randomized trial showed a highly significant increase in the density of skin microrelief and a decrease in furrows.[47]

VITAMIN E Vitamin E is a well-known antioxidant that contains mixed tocopherols, a class of very strong antioxidants.[48] Many studies have shown that vitamin E can help to decrease the effects of psoriasis and erythema and may help in reducing the risk of skin cancer. Vitamin E also has been shown to help in the reduction of scarring from wounds and to help reduce the appearance of stretch marks.[35]

Vitamin E *acetate* is often used instead of vitamin E in skin care products because it lacks the free phenolic hydroxyl group. However, vitamin E acetate is biologically inactive. Despite this, the addition of vitamin E acetate to skin care products appears to protect skin against the harmful affects of sunlight after topical application. This is so because vitamin E acetate is a provitamin that is converted to the active vitamin by hydrolysis in the skin.[49]

Recently, Nakayama found that α-tocopherol-6-*O*-phosphate provided protection against UVB-induced damage in cultured mouse skin. In the study, which compared α-tocopherol-6-*O*-phosphate with α-tocopherol acetate, the water-soluble provitamin E provided greater protection that α-tocopherol acetate against sunburn cell formation, DNA degradation, and lipid peroxidation.[50]

α-LIPOIC ACID α-Lipoic acid is a naturally occurring dithiol compound known as an *essential cofactor* for mitochondrial energy production via the citric acid cycle.[51,52] α-Lipoic acid scavenges hydroxyl radicals, singlet oxygen, and nitric oxide and has been afforded "superantioxidant" status because it is both water- and lipid-soluble.[53] To direct antioxidant activity, α-lipoic acid protects vitamins E and C and downregulates the transcription factor NFκB.[53] In addition, the powerful antioxidant prevents lipid peroxidation in the cell membrane by reducing glutathione.[54]

α-Lipoic acid is under investigation as a possible agent to treat pathophysiologies of many chronic diseases. It improves polyneuropathies and glycemic control in association with diabetes and mitigates toxicities of heavy metals.[51] In vitro studies have shown α-lipoic acid to have anti-inflammatory properties. It has recently become a popular additive in cosmetics designed to treat benign photodamage.[54] However, only limited data on efficacy are available. Although α-hydroxy acid has been shown to penetrate into subcutaneous tissues,[55] properly designed clinical trials are still needed to demonstrate the efficacy of manufacturers' claims.[52]

COENZYME Q10 Reactive oxygen species, formed in the mitochondrial respiratory

chain, have been implicated in a number of diseases and in the natural aging process.[56] Coenzyme Q10 (ubiquinone, CoQ10) is a naturally occurring antioxidant that quenches free-radical formation in the mitochondria. Coenzyme Q10 originally gained interest as a potential cancer treatment when investigators discovered that cancer patients experienced reduced levels of the enzyme. Although initial studies of using CoQ10 as a potential cancer treatment were encouraging, well-designed studies with definitive results are still lacking.[57]

Investigation of CoQ10 in treating human skin conditions also has been promising. In vitro studies found that topical CoQ10 reduced UV-induced expression of collagenase in cultured fibroblasts and provided antioxidant activity in human skin. In addition, a small 6-month controlled trial found a modest improvement in periorbital lines following 10 weeks of treatment with twice-daily topical CoQ10.[4]

IDEBENONE Idebenone is a short-chain biosynthetic analogue of CoQ10 containing the antioxidant properties of CoQ10 but with greater capacity to quench free-radical generation.[56] The drug was developed originally for the treatment of cerebral ischemia–induced lesions. However, the results of treating neurologic disease with idebenone have not been encouraging.[58]

The potential for using idebenone to treat skin conditions has been demonstrated in several in vitro and in vivo studies and at least one clinical study. In an assay designed to screen for potential treatments of common neurodegenerative disorders—involving reactive radicals and oxidative stress—idebenone provided protection from endogenous oxidative stress in skin fibroblasts derived from Friedreich ataxia patients.[58] In addition, in vitro studies indicated greater antioxidant capacity, compared with CoQ10, vitamins E and C, kinetin, and α-lipoic acid. Moreover, clinical photographs showed an appreciable improvement in periorbital lines, and immunostaining confirmed downregulation of MMP expression.[4]

[Au3]

FURFURYLADENINE N_6-Furfuryladenine is a plant-derived growth hormone known to have senescence-retarding effects in plants.[59] This cytokinin's antiaging effects—notably, antioxidant properties protecting DNA and protein from oxidative and a glycoxidative damage—have been demonstrated effectively in several in vitro and in vivo studies using plants, cultured human skin cells, and fruit flies.[59,60] Unfortunately, there are only a limited number of studies testing its efficacy in humans. The studies in humans, sponsored by manufacturers of furfuryladenine, have indicated that furfuryladenine may be equivalent or superior in effectiveness to Retin A. Manufacturers also reported that treatment with furfuryladenine produced few side effects.[61]

COPPER PEPTIDES The role of copper in stimulating angiogenesis has been acknowledged for over two decades, and copper peptides have exhibited dermal wound-healing properties in several studies.[62,63] For example, copper sulfate induced expression of vascular endothelial growth factor (VEGF) in primary and transformed human keratinocytes, and topical copper sulfate accelerated wound healing in murine dermal skin.[64] Copper peptides have been shown to (1) stimulate collagen[63] and elastin[4] formation, (2) stimulate the formation of glycosaminoglycans,[65] (3) increase blood vessel formation and oxygenation within the skin,[64] and (4) provide potent antioxidant protection.[4]

Important studies include a well-designed 12-week study that demonstrated increased skin density in 67 patients. Copper peptides also have enhanced healing of postoperative wounds and diabetic foot ulcers.[4]

GROWTH FACTORS Growth factors, important in wound healing, are present in a number of cosmeceuticals. Among the growth factors found in new cosmeceutical products, trandforming growth factor β (TGF-β) is the most important collagen-stimulating growth factor. TNS Recovery Complex by SkinMedica is a tissue-repairing complex containing growth factors derived from cultured fibroblasts of neonatal foreskin. The growth factors contained in TNS Recovery Complex help to repair sun-damaged skin by stimulating the epidermal thickening and deposition of collagen. TNS Recovery Complex also contains antioxidants, matrix proteins, and soluble collagens.[4]

Efficacy of the product has been demonstrated in a single small study conducted by the manufacturer, in which 79% of patients showed clinical improvement, as measured by optimal prophylimetry and investigator grading.[4]

However, significant questions exist about whether these large molecules cross the SC and whether it is even necessary for these molecules to cross the SC to stimulate collagen production. Large clinical studies are still needed.[4]

GREEN TEA Green tea contains polyphenols known to have superior antioxidant activity.[66] In cosmetic science, the term *green tea* does not refer to common herbal tea. Instead, *green tea* refers to the product of a careful process in which the leaves of the plant *Camellia sinensis* are processed, taking care to avoid oxidation and polymerization of the polyphenolic components. In green tea, the most powerful of these polyphenols is (–)-epigallocatechin-3-gallate (EGCG).[66]

Preclinical studies in mouse models have provided evidence that green tea polyphenols provide protection against UVB-induced immunosuppression and the generation of reactive oxygen species. Topical application to mice demonstrated protection against several tumorigenic agents and was associated with the inhibition of several biochemical markers of chemical carcinogenesis. In other studies, topical application to both mice skin and human skin demonstrated that green tea may have the potential to reduce UV-induced oxidative stress-mediated skin diseases in humans.[66]

Recent reports also suggest that EGCG reactivates dying cells. According to Dr. Stephen Hsu, old skin cells found in the upper layer of the skin appear to start dividing after exposure to EGCG. It also was reported that exposure to EGCG accelerates the differentiation process among new cells.[67]

Liao and Hiipakka[68] have shown that green tea polyphenols are potent inhibitors of type 1,5-α-reductase, suggesting the potential use of green tea polyphenols in the treatment of androgen-mediated skin disorders such as androgenetic alopecia.

Presently, numerous products are supplemented with green tea, even though the concentration of active polyphenols in these products is unknown, and controlled clinical trials have not been conducted.[66]

GRAPE SEED EXTRACT Grape seed extract contains polyphenols, mainly flavonoids, including oligomeric proanthocyanidins (OPCs), which have antioxidant capabilities 20 times greater than vitamin E and 50 times greater than vitamin C.[69,70] Studies suggest that grape seed extract binds to collagen, where its antioxidant effects promote youthful skin, elasticity, and flexibility.[71] Studies also show that OPCs help to protect the body from several age-related diseases, including cardiovascular disease and cancer.[71,72]

TABLE 70-7
Plant Derivatives for Cosmetic Use[75]

Skin Care Property	Plant Derivative
Astringent	Witch hazel, Hawthorne
Emollient	Allman oil, hazelnut oil, sesame oil, wheat germ oil
Moisturizer	Aloe vera, jojoba, Shea butter
Refreshing	Camphor, hypericum, cypress
Softening	Geranium, licorice
Soothing	Aloe vera, avocado oil, chamomile (bisabolol), Linden flower, lotus, seaweed
Toner	Elder, horsetail, marjoram, sage
Miscellaneous:	
Decreases skin edema	Marigold
Anti-irritant	Allantoin
Strengthens nails	Myrrh

OPC flavonoids have been shown to strengthen and repair connective tissue.[71] Grape seed extract may aid wound healing in two ways. Studies show that grape seed extract helps the body make more VEGF for angiogenesis to regenerate damaged blood vessels, and it also decreases the amount of free radicals in the wound site.[71,73]

PEPTIDES Oligo-, penta- and hexapeptides such as retinoids improve the appearance of photodamaged skin by stimulating collagen production, resulting in thickening of the skin. Palmitoyl pentapeptide (pal-KTTS) is a procollagen pentapeptide fragment showing efficacy in several well-designed studies for improving photoaged skin, including wrinkle appearance, age spots, and skin firmness. Histologic assessments in studies showed positive changes to elastin and collagen IV.[74] In addition, palmitoyl pentapeptide was comparable with significantly higher concentrations of retinol in reducing fine lines and wrinkles and improving hyperpigmentation and dark circles. The pentapeptide was less irritating, did not cause redness or barrier damage, and had no effect on TEWL.[4]

BOTANICALS It is likely that plant-derived ingredients were among the very first cosmetics. Ingredients used since ancient times include colorants, plant juices (for soothing and protection from insects), and fragrant oils. Several plant derivatives are purported to have various skin care properties, as seen in Table 70-7.[75] Caution must be observed because plants can cause serious allergic reactions in certain individuals.[54]

RETINOLS In 2004, retinol was reportedly a component of at least 60 cosmeceutical products.[4] However, the prominence of retinol in consumer skin care products should not be viewed without substantial attention to the differences between prescription-strength retinoids and retinols in consumer skin care products. Topical retinoids are prescription-strength drugs with the ability to help normalize hyperkeratinization and provide anti-inflammatory effects. In contrast, all-*trans*-retinol is a parent form of vitamin A and has limited efficacy.[76] Some experts propose that the benefits of the parent form of retinol are due to the oxidation of all-*trans*-retinol to the active retinoid after absorption into skin cells.[77] Retinol is present in consumer skin care products in widely varying categories. Some retinol products are efficacious,[78] some are present below clinically effective concentrations,[4] and other consumer skin care products contain biologically inactive retinol forms.[79] However, the lower concentrations make these products less irritating than prescription-strength retinoids. Retinol has been combined with other products, including AHAs, to improve results.[4]

Topical all-*trans*-retinoic acid protects the skin against damage from UVA and UVB rays by facilitating the ability to prevent collagen loss and the ability to stimulate new collagen formation within the capillary dermis of sun-exposed skin.[80,81] These protective properties form the basis for its use in minimizing the appearance of fine wrinkle lines.

NEW AND INNOVATIVE APPLICATIONS FOR SOY IN SKIN CARE The soybean, with its broad spectrum of components, including proteins, essential fatty acids, phytosterols, isoflavonoids, lecithins, and saponins, has long been known to have skin care benefits from its use in traditional Chinese medicine. Scientists have identified several possible applications in skin care, and current research is successfully uncovering the mechanisms behind these skin care applications. Potential applications include (1) providing oil control, (2) providing moisturization, (3) delaying hair regrowth, (4) enhancing skin elasticity, and (5) reducing the appearance of pigmentation and UV-induced erythema and pigmentation.[82,83]

Scientists have determined that small soybean proteins [soybean trypsin inhibitor (STI) and Bowman Birk inhibitor (BBI)] can reduce hyperpigmentation through regulation of the protease-activated receptor 2 (PAR-2) pathway.[84] Cosmetic formulations containing these proteins have been shown clinically to help even out skin tone and smooth skin texture.[82,83]

Cosmetic scientists also found that a natural soy formulation could effectively reduce the appearance of unwanted facial hair above the upper lip area while improving the overall skin appearance and skin condition.[85]

The Future of Cosmeceuticals

One of latest technologies in development is the use of spin traps. These are the very newest antioxidants, which catch or trap an aberrant electron as it starts to spin out of control and returns it to its orbit before it can do any damage. Although the use of spin traps in dermatology is in its infancy, these compounds have shown a great deal of promise in the field of dermatology.[86]

Spin traps were used originally as a way to measure free-radical activity both in vivo and in vitro through their ability to form stable complexes. The most well-known spin trap is phenyl butyl nitrone (PBN).[86]

CONCLUSION

The cosmetic industry is an ever-changing, ever-growing market that promises to continue providing novel agents for maintaining healthy skin. The true clinical efficacy of some of these products remains to be proven. However, many products are known to provide clinically relevant results. In time, clinical efficacy and safety data will be supplied.

The development and tremendous growth in cosmeceutical sales are a response to consumer demands for more scientific and sophisticated cosmetic products. The first generation of cosmeceuticals provided supplements and antioxidants. The second generation of cosmeceuticals focused on

growth factors to help stimulate repair of photoaged skin. While the twentieth century brought the development of cosmeceuticals, the twenty-first century will mark the introduction of new skin care technology in the form of Cosmoleculars—designer molecules in cosmetics products.[86]

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