Alda Karic

<u>Beauty and Chemistry</u>

Beauty may be in the eye of the beholder, but many individuals are obsessed by beauty treatments and cosmetic products promising solutions for all of the skin's needs. Therefore, the cosmetic industry is one of the nation's largest and most profitable enterprises, worth over 50 billion dollars. However, the cosmetic industry's quest to provide eternal youth and beauty to its consumers would not be possible without the chemical sciences. Cosmetics are a direct product of chemical technology and a testament to the importance of that technology in our everyday lives.

The cosmetic industry requires all types of chemists and chemical engineers, from analytical to synthetic chemists, from process designers to production supervisors. The work of these scientists must transparent to ensure the safety of all cosmetic products. The goal to protect the health of consumers by requiring the health and beauty industries to phase out the use of chemicals linked to cancer, birth defects and other health problems, and to replace them with safer alternatives.

History

The word "cosmetic" is derived from the Greek *Kosm tikos*, meaning "having the power to arrange, skilled in decorating giving *kosmein*, 'to adorn,' and *kosmos*, 'order, harmony'." The relationship between chemistry and cosmetics dates back at least to 4000 B.C., when women in Egypt applied a dark powder around their eyes called kohl, made of burnt almonds, copper ores, lead, and ash. Citizens of 1000 B.C. Greece applied chalk or white lead face powder to create a white visage while in Rome, people put barley flour and butter to cover their pimples. In the 19th century, France developed chemical processes that eliminated the use of poisonous substances such as lead and copper on the skin and introduced the use of zinc oxide in facial powders. In the 1920s, cosmetics and fragrances began to be manufactured and mass marketed in the United States leading to the modern era of cosmetics that exists today.

Legislation and Regulation

Cosmetics marketed in the United States must be in compliance with the Federal Food, Drug, and Cosmetic (FD&C) Act and the Fair Packaging and Labeling (FP&L) Act. The FD&C Act is a set of laws passed by Congress in 1938, providing the Food and Drug Administration the authority to oversee the safety of cosmetics. Under the FD&C Act, cosmetics are defined as articles intended for application to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance without affecting the body's structure or functions. Products such as skin creams, lotions, perfumes, lipsticks, fingernail polishes, eye and facial make-up preparations, shampoos, permanent waves, hair colors, toothpastes, deodorants all apply to this definition. Both Acts apply to all cosmetics manufactured in the United States or imported from abroad. The FDA does not require firms to make available safety data or other information of a cosmetic ingredient before marketing, as is required of prescription or over-the-counter drugs. Cosmetics do not require approval because they are topical products that do not alter the structure or function of the skin. Manufacturers or distributors may submit information about the ingredients of the cosmetic product to the agency voluntarily, via the Voluntary Cosmetic Registration Program. Ultimately, however, cosmetic firms are responsible for marketing safe products.

In addition to government agencies, the safety of cosmetic ingredients is evaluated by an independent group of scientific experts called the Cosmetic Ingredient Review (CIR), responsible for assessing the safety of ingredients used in cosmetics.

There also exist cosmetic products that are drugs, meaning they are intended to treat disease or affect the structure or functions of the human body. Examples of products which are drugs as well as cosmetics are anticaries toothpastes such as fluoride toothpastes, sunscreen lotions meant to protect against sunburn, and antidandruff shampoos.

Purpose of Cosmetics

There is unstoppable growth in the use of cosmetics; worldwide annual sales for cosmetics are near 18 billion dollars. The cosmetic industry uses over 5,000 ingredients to make products for purposes such as a) facial treatment and body care, b) personal hygiene (deodorant, shaving creams), c) sunscreen and related products. These products vary in composition according to skin type (normal, oily, dry, mixed, sensitive), age (baby, child, young, adult, elderly) and ethnic group. Recently, consumers have witnessed a proliferation of active cosmetics, also known as cosmoceuticals. Cosmeuticals do not merely affect the appearance or odor of the consumer, but seek to improve the target cells, such as skin, hair, or teeth. As a result, one sees the competitive and diversified cosmetic market that exists in the United States today.

In the morning, we wash our face with a cleanser, soothe our face with a moisturizer, and for some, put on makeup to get ready for the day. The basis of most cosmetics is an emulsion of an oil-in-water, or water-in-oil, where one is dispersed as small droplets in the other. Other ingredients are added to stabilize the mixture, such as surfactants to prevent separation, and thickening agents that control viscosity. Thickening agents consist of electrolytes such as sodium chloride that act by increasing the size of surfactant molecules thereby thickening the product. Polymeric thickeners such as polyamides and inorganic compounds such as silicates and clays are also widely used as thickeners.

There are various chemical ingredients in cosmetics. Moisturizers function as moisture barriers and contain cetyl alcohol ($CH_3(CH_2)_{15}OH$) which prevents oil and water from separating; dimethicone silicone $(C_2H_6OSi)_n$, a silicon-based organic polymer which lubricates the skin; lanolin alcohols, organic compounds used as softeners and found in skin and hair conditioners. Antimicrobials can be found in a variety of face cleansers; they are composed primarily of butyl, propyl, methyl and ethyl parabens, which are preservatives intended to prevent microbial growth and thus ensure consumer safety and product integrity. Thickeners and waxes are substances that increase the viscosity of an aqueous mixture and provide stability; thickeners consist of candelilla[1] waxes and carbomer[2] thickeners and are used in products such as lipsticks or blushes;

Color Cosmetics

Perhaps most popular today are color cosmetics, or “make-up.” There is a lucrative market for color cosmetics ranging from budget products to premium ranges offered by glamorous firms. L'Oréal is currently the largest firm, with revenues of $14.5 billion reported in 2005.

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[1] Candelilla wax is derived from the leaves of Candellila shrub native to southwestern United States. The wax is made by boiling the leaves and stems in sulfuric acid and is collected at the surface whereupon it is further processed.

[2] Carbomer is a thickener used as a gelling agent. It is an expanded molecule obtained via the insertion of a C_2 unit in a given molecule.

Modern lipsticks contain pigments and waxes such as beeswax or carnauba[3] wax, derived from the carnauba palm. The waxes provide the solid structure and a glossy finish to lip products. Fats like cocoa butter are responsible for making the lipstick glide easily on the lips.

Powdered color cosmetics such as eye shadow and blush are based on talc (magnesium silicate). Zinc Oxide (ZnO) absorbs UVA and UVB rays and is a critical component for skin protection. Ultraviolet electromagnetic radiation is received from the Sun. The Sun emits Ultraviolet A, B, and C (UVA, UVB, UVC) bands, but over 98.7% of the UV radiation that reaches the Earth is UVA bands; the rest is absorbed by the earth's ozone layer. UVA radiation is of lower energy than UVB and UVC and does not cause sunburn; however, it leads to indirect DNA damage by generating free radicals, atomic species with unpaired electrons that can lead to disruption of cell cycle and thus cancer. UVA rays also destroy collagen fibers in the skin, important for cell structure. UVB rays are of higher energy and are responsible for direct DNA damage that leads to skin cancers. Zinc Oxide is the broadest spectrum UVA and UVB absorber approved by the FDA.

Sunscreen

Protection from the sun's harmful rays has become a crucial factor for consumers purchasing cosmetic products. Sunscreen is a topical product intended to protect skin from UV radiation. Sunscreen products are regulated in the United States by the FDA, and are categorized as over-the-counter drugs. Sunscreen was first marketed for the body to be used in beach environments; then sunscreens suited for athletes were developed,

[3] Carnauba wax is composed mainly of fatty acids and hydrocarbons. Carnauba wax also contains cinnamic acid, an antioxidant.

meant to protect sweat from removing the sunscreen from the skin. Sunscreen today is a vital component in many face creams, color cosmetics, and even hair products.

The presence of UV filters in cosmetic products provides remarkable benefits for the consumer. In the United States, the incidence of nonmelanoma skin cancer exceeds more than 1 million cases per year; UV-aging is responsible for 80-90% of visible skin aging. Sunscreens prevent the development of squamous cell carcinomas which arise in the squamous cells composing the upper layer of the skin. Sunscreens may also actinic kerastosis, a premalignant condition characterized by thick, crusty skin.

UV filters can be classified as chemical absorbers or mineral reflectors. Chemical sunscreens are aromatic compounds conjugated with a carbonyl group. These chemicals absorb high-intensity UV rays and are subsequently excited to a higher energy state. The energy lost is then converted into longer lower-energy wavelengths, with a return to the ground state. Mineral reflectors such as zinc oxide and titanium dioxide act as physical blocks that reflect light from the skin.

Anti-wrinkle Treatment

Modern society has become obsessed with products promising youthful skin. The plethora of treatments existing today that target skin aging furnishes the competitive cosmetic market. Anti-wrinkle treatments have become a part of the consumer's daily routine in an effort to prevent and correct aging. These treatments can consist of vitamins and antioxidants, topical or oral cosmetic preparations, and even surgery.

Wrinkles are fine or coarse lines on the skin of the face associated with alterations of collagen and elastin in skin. It is difficult to attribute a single cause to wrinkles, but all scientific evidence attributes wrinkles to UV radiation.

Moisturizers are the most fundamental way to delay skin aging. The use of moisturizers on the face leads to improvement in structure of the stratum-corneum (the outermost layer of the skin), to hydration, and to prevention of water loss. Alpha- and Beta-hydroxy acids, now a popular component in many creams, can also reduce wrinkles. The hydroxyl acids are a class of compounds consisting of a carboxylic acid with a hydroxyl group on either the alpha or beta carbon. Glycolic acid is the most well known of the alpha-hydroxy acids.

Numerous clinical trials have proved retinoids to be effective in wrinkle effacement. Retinoids are chemical compounds related to Vitamin A, and play an important function in regulating epithelial growth. Retinol is used as an anti-aging tool; vitamin A is absorbed into the skin, promoting skin cell turnover and collagen synthesis. Topical administration of hormones such as estradiol has also shown increased skin thickness.

The concern of many consumers who resort to topical creams as anti-wrinkle tools is the considerable time necessary to see effective results of the treatment. Thus, many are lured by the quick-fix of wrinkles provided by Botox. The Botox phenomenon has swept the country, with Botox manufacturer Allergan reporting sales of $1.2 billion in 2007 alone. Botox, or botulinum toxin, is a neurotoxin produced by the bacterium Clostridium botunilum. Botox is a highly poisonous substance, but when used cosmetically, it is injected only in small doses. Botox was approved for use by the FDA in 1989 for treatment of hemifacial spasms; only in 2002 did the FDA announce approval of the toxin for the purpose of minimizing the appearance of frown lines between the eyebrows. The toxin is a polypeptide that performs its action by blocking the release of acetylcholine from vesicles in the pre-synaptic neuron. Acetylcholine does not pass into the neuromuscular junction and the toxin thereby affects nerve impulses and causes sagging paralysis of muscles.

Surfactants

Surfactants are the most versatile ingredients of cosmetic products. Surfactants provide stable and homogeneous formations; they are responsible for the cleansing, foaming, and antimicrobial properties of cosmetics. Surfactants are organic compounds synthesized to provide a molecular composition where a hydrophobic alkyl chain is bonded to a hydrophilic ion or polar group. Four types of surfactants exist, depending on the charge of the ionic group: anionic (negative charge), cationic (positive charge), nonionic (hydrophilic group), and amphoteric (positive and negative charge on the same molecule). The type of surfactant used depends on the function of the cosmetic product. Cosmetics like shower gels and shampoos use anionic surfactants. Cationic surfactants with antimicrobial properties are used in mouthwash products. Nonionic surfactants such as ethylene oxide solubilize and emulsify cosmetic formulations such as creams and lotions.

Encapsulation Systems

In developing cosmetic products, the producer must determine whether the ingredients are properly transported to their necessary target sites, such as the skin or hair, and not degrade upon application. Encapsulants, which separate ingredients that otherwise do not mix well, provide a sophisticated as well as a safe and effective delivery system of beneficial ingredients present in many cosmetic products. Recent extensive research has resulted in the development of encapsulants for use as controlled delivery systems. Encapsulation systems are based on emulsion technology and polymer chemistry; they require a phase-separation process that encapsulates hydrophobic materials such as oils, dyes, and fragrances. Early encapsulants were not efficient, as they broke down before reaching their target. Today, encapsulants are used to preserve the activity of a given ingredient in a variety of skin-care products, antiperspirants, color cosmetics, and shampoos. The demand for these carrier systems is growing at 5-10% a year, with sales reaching $90 million in 2006.

Recent years have seen extensive dermatological and cosmetic use of encapsulation. Encapsulants are used in topical formulations as drug-carrier vehicles that control drug release. Microparticles are widely used as drug reservoirs in skin products. Microencapsulation is a process by which thin coatings of inert natural or synthetic polymer materials are deposited around microsized particles of solids or droplets of liquids. Microparticles consist of two major parts: the inner part is the core material that contains the active ingredient(s) that are solids, liquids, or gases; the outer part is the coating material composed of a high-molecular weight polymer that is nontoxic and does not react with the core material. The size of microparticles initially varied from 5 micrometers to 2 milimeters; in 1980, products with smaller dimensions were developed, such as nanoparticles (10-1000 nanometers in diameters) and microspheres (1-10 micrometers).

There are numerous corporations focused on specialty encapsulation chemistry, such as Ciba, Teguba, and Wacker Chemie, each perfecting its own version of the encapsulant. For example, Ciba formulated an encapsulation particle about 20-40 nanometers in diameter with a phospholipid outer layer and an inner lipid cavity that contains the active ingredient.

Evonik Industries (formerly known as Degussa) has its version of encapsulants, known as *Tegospheres*. Tegospheres are stable in skin environments of pH 6.5 or higher and the first version encapsulated the anti-wrinkle ingredient retinol. Tegospheres contain the methacrylate polymer, the skin active ingredient, and an anti-clumping silica ingredient which are mixed and dried. Tegospheres are about 20 micrometers in diameter.

Moisture triggers the release of active ingredients from cyclodextrins, carrier systems for the firm Wacker Chemie. The cylindrical molecules of cyclodextrin are hydrophilic on the outside and lipophilic on the inside. The interior cavities sustain lipophilic ingredients and protect them against light, heat, and air until the moisture on the skin triggers their release.[1]

Encapsulants have been widely used for delivering vitamins and botanicals to the skin; the capsules break upon friction and release ingredients. Chemists are relying now on encapsulants to deliver active ingredients to the skin. The capsules can be triggered to break due to exposure to moisture on the skin or the change from basic pH in the bottle to the acidic environment of the skin. Bacteria present on the skin may also play a role in releasing the microcapsules. The technique has been applied to suntan lotions, which transmit color carrying particles once rubbed into the skin to develop a tan, and in toothpastes that release flavors or antibacterials upon brushing.

The technology has certainly piqued the interest of chemical firms. Many small firms such as Israeli- based Tagra Biotechnologies and California's Aquea-Scientific are researching new methods for encapsulation. Larger firms such as Dow Chemical are developing their own encapsulation technologies. Dow intends to take a different approach, offering the encapsulation technology to customers, who can then incorporate their own ingredients. Dow's technology is based on vesicles that form when copolymers of ethylene oxide and butylene oxide surround active ingredients. The diameter of the liquid-crystalline structure is about 5 μm.[2] The vesicles slowly disperse their contents as they dry on the skin, which can provide sustained delivery of ingredients such as vitamins to the skin.

Alternatives to Animal Testing

All responsible cosmetic firms have the goal of protecting their consumers first and foremost; however, ensuring product safety has prompted the use of animals for cosmetic testing, with severe ethical and economic implications. Scientist today need to reconcile these problems and ensure product integrity while replacing or reducing the use of animals. Worldwide, more than 50 million animals are used in biomedical research each year; for toxicological research, the most largely used species are mice and rats. Traditionally, animal testing was used to measure severe forms of skin toxicity, and various regulatory authorities have previously required animal-test data for a chemical or cosmetic product before allowing it to be manufactured or marketed.

Animal testing has come under harsh scrutiny and is now deemed inhumane and unnecessary. The criticism of animal testing has led to legislative consequences. The seventh amendment to the European Union's Cosmetic Directive bans animal testing after March 2009 and the sale of products tested on animals or containing ingredients tested on animals.

In the United States, there is no ban on animal testing. Under the provisions of the Animal Welfare Act and the National Institute of Health's *Guide for the Care and Use of Laboratory Animals*, a procedure can be performed on an animal only if its purposes can be scientifically justified. Regulation also requires researchers to consult with their Institutional Animal Care and Use Committee (IACUC) that insures alternatives to animal testing have been considered, tests are not duplicative, and proper pain relief is provided to the animal unless the relief administration would hinder the experiment.

It is clear that better experimental design will lead to reduced use of animals and create new alternatives, such as tissue culture models or computer simulation. Advanced materials are now proposed as substitutes for animals, such as reconstructed eye tissue and skin models derived from donor cells obtained from cosmetic surgery. With the EU ban looming, cosmetic titans such as L'Oreal and Procter and Gamble are investing in alternatives to animal testing; L'Oreal has spent over $800 million in the last 20 years, and Procter and Gamble has spent $225 million in an effort to find substitutes for animal testing.

Remarkable progress is being made at UC Berkeley, in conjunction with researchers from Rensselaer Polytechnic Institute and Solidus Biosciences Inc in creating efficient and more accurate methods to test drug compounds and cosmetics without the use of animals. Researchers have invented biochips that mimic the body and can reveal the toxicity of compounds. The two biochips, the DataChip and the MetaChip together reveal the toxicity of chemicals on various organs in the body and whether the compounds become toxic once metabolized in the body. As Douglas Clark, co-lead author and co-founder of Solidus Biosciences and professor of chemical engineering at

UC Berkeley, states, "obviously cosmetics need to be safe, and ensuring the safety of new compounds without testing them on animals presents a new challenge to the industry, especially as the number of compounds increases. These chips can meet this challenge by providing comprehensive toxicity data very quickly and cheaply."

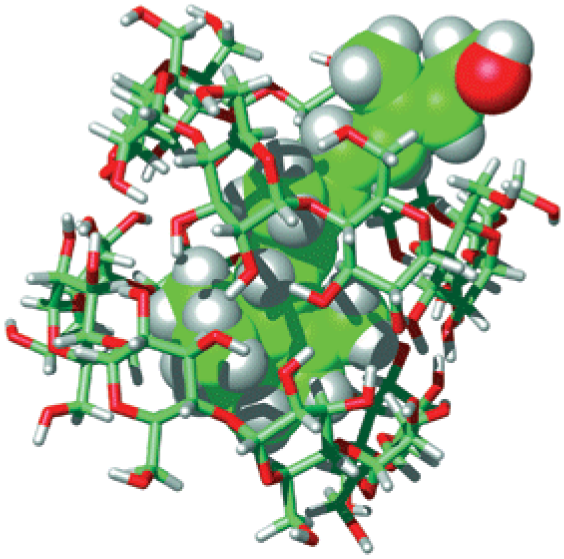
The DataChip consists of 1,080 three-dimensional human cell cultures and acts as a fast screen for toxicity of chemicals on different types of cells. In 2005, the MetaChip was introduced; it mimics the metabolic actions of the liver and thus can be used to determine how different people can react to a certain drug.

Safety Evaluation and Skin Corrosion

Our skin is frequently exposed to cosmetic products; therefore, a particular product or ingredient can potentially cause skin irritation or skin damage, defined as the production of irreversible tissue damage to the skin that can occur as a result of a manufacturing error or misuse by the consumer. In the past, skin damage was assessed using animal studies but recently in-vitro tests have been used. The rat skin resistance transcutaneous electrical (TER) assay assesses skin sensitivity for damage by applying the test material to the epidermal surface of a rat skin disc for 2 and 24 hours, followed by measurement of the transcutaneous electrical resistance of the skin disc. These resistances are then used to evaluate the integrity of the stratum corneum, the outermost layer of the epidermis, and barrier function. The human skin model assay uses three-dimensional models to mimic human skin. The models are generated by growing keratinocyte cultures, the cell type that accounts for 90% of the epidermis. The test material is applied topically for up to 4 hours to a three-dimensional human skin model. Corrosive materials are indicated by producing a decrease in cell viability; corrosive chemicals are able to penetrate the stratum corneum via diffusion or erosion to cause cell death.

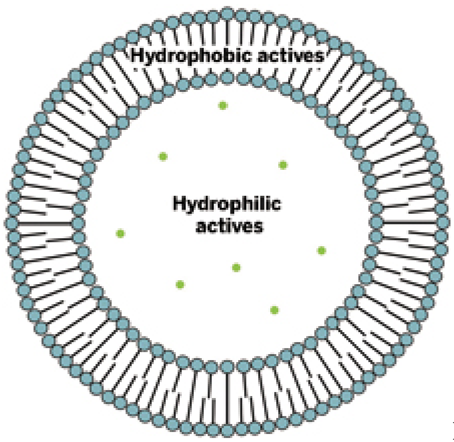
Conclusion

Cosmetics and other personal-care products are the most widely used chemical products in our everyday lives. The ready availability of these products highlights the importance of the chemical sciences in providing safe and effective cleaning agents and cosmetics for the consumer. After all, most of us turn to synthetic makeup to improve our genetic makeup. However, chemical scientists have a responsibility to encourage all powerful corporations in this multi-billion dollar industry to disclose information and use quality ingredients to ensure safety for consumers. Chemical technology, directed at humane ends, can ensure profitability as well as compatibility of cosmetics with the human body. Ultimately, cosmetic products, invented, developed and manufactured by chemists and chemical engineers, contribute to our high standard of living.

[1] 

Wacker

Cyclodextrins release their ingredients as moisture on the skin dissolves the starch-based protectant shell.

[2] 

Dow Chemical

Dow Chemical's not-yet-released ethylene oxide/butylene oxide block copolymer vesicle technology.