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New generation of personal care products has industry observers asking themselves, "Is it a cosmetic or a drug?"

The definition seems clear enough: "A cosmetic is a product, except soap, intended to be applied to the human body for cleansing, beautifying, promoting attractiveness or altering the appearance." This is as per Sec. 201(i) FD&C Act. According to Senate Report No. 493 and court decisions, the term "intended" in the legal definition of the term "cosmetic" or in other definitions means, with respect to the use of a product, its directed or prescribed use as determined from the statements made on a product's label or labeling. A cosmetic is also a drug when it is intended to cleanse, beautify or promote attractiveness as well as treat or prevent disease or otherwise affect the structure or any function of the human body (Sec. 201(g) and (i), FD&C Act; Sec. 509, FD&C Act).

In short, one may say that a cosmetic is a product intended to exert a physical, and not a physiological, effect on the human body. A cosmetic is legally also a drug if it is intended to exert a physical as well as a physiological effect because the FD&C Act defines in section 201(g) the term "drug" to mean, among other things, "articles intended for use in the...cure, mitigation, treatment or prevention of disease...and...articles...intended to affect the structure or any function of the body..."

The term "cosmeceuticals" describes cosmetics containing ingredients that are bioactive, exerting effects on people. These are cosmetics with therapeutic, disease-fighting or healing properties. Serving as a bridge between personal care products and pharmaceuticals, these formulations have been developed specifically for their medicinal benefits. "A product can actually be a cosmetic and a drug at the same time, but there is no provision for cosmeceuticals," noted John Bailey, director of FDA's office of cosmetics and colors.

Cosmeceuticals are considered a "non-category" by the FDA. The courts, in deciding whether a product is a "cosmetic," a "drug" or both a "drug" and a "cosmetic," have relied principally on the consumer's perception of the meaning of a label statement and less so on the interpretation of the meaning of a label statement by the labeler or a regulatory agency. For cosmetic labels, no division between active ingredients and other ingredients is required; they are all listed together.

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A Demand for Efficacy

The skin care industry needs a facelift since the sales of facial moisturizers and sun care were flat and the hand and body lotion category declined.¹ The R&D challenge is to develop the know-how to deliver active ingredients to skin while maintaining their maximum therapeutic effect. Technological advances utilizing drug discovery approaches such as high-throughput screening, animal model systems, nanotechnology and biochemical assays has helped create a new generation of scientifically-advanced skin care and cosmetic products. Novel cosmeceutical ingredients are enjoying the "hot new and unique ingredients" status in a fairly mature U.S. cosmetics industry. They are added in topical formulations before there is a solid body of scientific evidence to support their therapeutic performance. These new consumer-friendly ingredients are in products that mimic the effects of more drastic methods, such as dermabrasion and Botox.

So far, only a handful of products on the market have successfully straddled the divide between drugs and cosmetics. These products promise to smooth wrinkles, strengthen skin, inhibit enzymes, trigger growth in elastin and collagen, manipulate skin color or prevent baldness.

Most experts agree that alpha hydroxy acids ushered in the era of cosmeceuticals in a big way. A new generation of acids is creating excitement in the personal care industry. One of them is a poly hydroxy acid from Neostrata, which contains gluconolactone and lactobionic acid. Gluconolactone, an antioxidant polyhydroxy acid, is suitable for all skin types, even sensitive skin. This PHA is composed of multiple water-attracting hydroxyl groups, which hydrate the skin, resulting in enhanced degrees of moisturization. It provides all the smoothing and anti-wrinkle benefits of other AHAs without the irritation. Poly hydroxy acids also contain antioxidant benefits, a property not found in glycolic acid. Lactobionic acid acts as a powerful antioxidant and chelates excess iron in the skin, thereby reducing potential oxidative damage. It is derived from naturally occurring lactose (milk sugar), and can be classified as a complex PHA with potent antioxidant and humectant properties. Lactobionic acid strongly attracts and binds water to produce a natural gel matrix. Its unique film-forming property provides desirable softness and a velvety smoothness to skin. Lactobionic acid is safe and non-irritating, and provides AHA anti-aging and cell turnover benefits to skin.

The use level of gluconolactone is 4-15% and lactobionic acid 3-10% in Neostrata's PHA products. Nu Skin's Tru Face Revealing gel contains lactobionic and gluconolactone acids. NeoStrata has licensed to PHA technology to Lubriderm for exclusive rights in the food, drug, mass merchandise and convenience retail outlets.²

Hordeum vulgare (Stimu-Tex) is available from Pentapharm. It is Spent Grain Wax which is a natural lipid fraction produced from barley via supercritical extraction. The high gamma linoleic acid component of Stimu-Tex enhances the natural structure of and maintainance of the epidermal lipid barrier minimizing water loss and helping skin metabolism. The product has been shown to have anti-histamine-like, anti-pruritic and anti-inflammatory activity, which soothes irritated skin and reduces stinging.

Phenethyl benzoate (X-Tend 226) from ISP Corp. is a new, proprietary polar ester with high solubilizing capacity for oxybenzone and avobenzone. This ester of 2-phenylethyl alcohol and benzoic acid offers increased performance benefits in sun protection products by boosting the critical wavelength and the UVA/UVB ratio of avobenzone.

Boswellic acids were found to inhibit two pro-inflammatory enzymes, 5-lipoxygenase (which generates inflammatory leukotrienes) and human leukocyte elastase (HLE). HLE is a serine protease which initiates injury to the tissues, which in turn triggers the inflammatory process.⁵ Boswellin from Sabinsa is a standardized extract from Boswellia Serrata which contains boswellic acids. L'Oréal's Wrinkle De-Crease contains Boswelox, a phyto-complex combining boswellic acid and manganese. The product is claims reduction of the appearance of expression lines and wrinkles within three weeks

of use.

Vitamin E Alternatives

Dimethylmethoxy chromanol is a synthetic vitamin E analog called lipochroman-6. According to Lipotec SA, it is a synthetic tocopherol analogue with great potential as a free radical scavenger and antioxidant. At 0.05%, lipochroman-6 is said to be 20 times more potent than its parent compound, α -tocopherol, and 1000 times more efficient than α -tocopherol in inhibiting lipid peroxidation. It can therefore be used at very low concentrations from 0.1-0.5 parts per thousand. The active has proven its efficacy as a protection against lipoperoxidation, especially by dangerously reactive nitrogen species (RNS). It may be a more potent chemopreventive form of vitamin E compared to the more-studied α -tocopherol. It differs structurally from vitamin E only in the methyl group substitution at the 5-position.

Astaxanthin is a naturally-occurring carotenoid pigment found in aquatic animals and micro-algae. This powerful biological antioxidant is based on patented technology from Mera Pharmaceuticals, a marine biology company based in Hawaii. Astaxanthin exhibits strong free radical scavenging activity and protects against lipid peroxidation and oxidative damage of cell membranes and tissues. Studies suggest that astaxanthin can be more than 1000 times more effective as antioxidant than vitamin E.³ Astaxanthin has been shown to be a powerful quencher of singlet oxygen activity in in vitro studies and is a strong scavenger of oxygen free radicals, at least 10 times stronger than beta-carotene. Astaxanthin has been the focus of a large and growing number of peer-reviewed scientific publications. The astaxanthin molecule is similar to that of the familiar carotenoid beta-carotene, but the small differences in structure confer large differences in the chemical and biological properties of the two molecules. In particular, astaxanthin exhibits superior antioxidant properties to beta-carotene in a number of in vitro studies. Astaxanthin-containing preparations for prevention of light aging of skin have been developed.⁴ The molecule shows great promise but has yet to be fully exploited in topical products.

Disodium lauriminodipropionate tocopheryl phosphate (Vital ETTM) is a new unique bio-functional vitamin E phosphate complex which delivers proven anti-erythema and anti-inflammatory benefits in sun care, skin treatment and color cosmetics. The technology relies on a process known as phosphorylation, which increases the biological effectiveness of compounds by keeping them stable until needed by the body. The complexation of the phosphorylated compound allows more efficient delivery of the compound to the body either topically or orally. U.S. clinical trials, have shown much greater efficacy in both the prevention and amelioration of redness from UV exposure when topically applied to the skin at a level of 1% in an emulsion compared to vitamin E acetate. International Specialty Products Inc. distributes the material in the personal care industry for Vital Health Sciences.

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Botox Alternatives

After Botox hit the market, the cosmetic industry rolled out an array of active ingredients that are said to mimic the action of Botox. The three most popular products sold online are: Avotox which

contains 10% acetyl hexapeptide-3, Bioque Serum XL contains 15% acetyl hexapeptide-3 and Strivectin SD which contains Striadril Complex consisting of palmitoyl pentapeptide 3, palmitoyl oligo-peptide and numerous botanical extracts.

Acetyl hexapeptide-3 (Argireline) is an anti-wrinkle peptide, which works through a unique mechanism that relaxes facial tension leading to a reduction in superficial facial lines and wrinkles with regular use. Active argireline levels in the final product ranges from 0.0015 to 0.005%. A study published in the International Journal of Cosmetic Science used a 10% concentration in an oil/water emulsion. The results showed reduced wrinkle depth up to 30% after a 30-day treatment.^{6,7}



Palmitoyl oligo-peptide is a lipophilic modified peptide developed by Sederma SA and owned by Croda and is marketed as Matrixyl.

New cosmetic ingredients enable consumers to get all the benefits of botox injections without having to resort to needles.

Pentapeptides are composed of the amino acids lysine, threonine and serine, which are made lipophilic by the attachment of palmitic acid. This leads to the sequence Pal-Lys-Thr-Thr-Lys-Ser (five amino acids), a combination that mimics nature's tissue-regenerating processes by signaling the cells of the dermis to synthesize proteins (collagen I, III, IV) and polysaccharides (glycoaminoglycans, hyaluronic acid) which make up the connective tissue necessary for padding the skin. Two teams of investigators say palmitoyl pentapeptide is as effective as retinol in improving the effects of photo-aging but without the side effects often associated with retinol. These were two separate trials supported by Sederma SA. The first study examined the effects of palmitoyl pentapeptide 3 ppm versus retinol 700 ppm to crow's feet area on photo-aged skin. The second study examined the effects of palmitoyl pentapeptide 5 ppm on the structure of elastin and collagen IV in women with photo-aged skin. Palmitoyl pentapeptide triggered growth in elastin and collagen IV and enhanced the structure of elastin and collagen IV. The peptide was not associated with any side effects and was "a safe and potent alternative to retinoids in wrinkle repair."

Oligopeptides obtained by the biotransformation of native proteins from the seeds of *Hibiscus esculents* L. (okra) is a patented complex in Myoxinol LS 9736 (Cognis). It is primarily composed of low molecular weight oligopeptides, allowing good bioavailability. These botanical peptides combat wrinkles in a similar way to botulinic toxin, by inhibiting the mechanical factors responsible for the appearance of expression lines on the face. This novel active ingredient has a dual action, working biologically to retard the aging of cells (anti-free radical activity), and mechanically to inhibit facial muscle contraction. It prevents the formation of dynamic wrinkles such as horizontal and vertical frown lines across the forehead, crow's feet around the eyes and naso-labial lines around the mouth. The ingredient's potential as an anti-wrinkle agent was proven using an in-vitro test on contraction of innervated muscle cells. The ingredient's ability to inhibit the spontaneous contraction of muscle cells was evaluated by measuring the frequency of contractions over 24 hours using Carisoprodol, a known muscle relaxant, as a positive control. Cognis claims that a cream containing 1% Myoxinol LS 9736 applied to the crow's feet area over a three-week period, suggested considerable anti-aging properties: skin was smoother and wrinkles were 26% less noticeable due to significant reduction in muscle cell contractions, the primary mechanical factor responsible for the appearance of dynamic facial wrinkles. The contraction-inhibiting effect stops 24 hours after application.

Phytoestrogens and Steroid Precursors

Estrogen Replacement Therapy is the established treatment for menopause; it also improves skin dryness and reduces wrinkling. Yet, if estrogen is added to skin creams or lotions, these products are considered drugs according to the FDA. Phytoestrogens, on the other hand, are not considered drugs at this time, because they are not animal estrogens and do not pose the same health risks. Most of what is known about phytoestrogenic plants and their effectiveness is based on their historic use, especially in Chinese medicine. Biobalance natural progesterone cream is being marketed over the internet for treatment of symptoms of hormone imbalance due to loss of progesterone and estrogen as in peri-menopause. The CID lists USP Natural Progesterone as one of the ingredients along with vitamin E, retinyl palmitate, L-lactic acid and other extracts.

DHEA (dehydroepiandro-sterone) is a secretive product of the human adrenals whose serum concentration declines with aging. DHEA has indirect endocrine and intracrine actions due to conversion to androgens and estrogens. The administration of the steroid hormone precursors pregnenolone DHEA, as well as the natural hormone progesterone, via the transdermal route has some important advantages over the oral delivery of these substances where there is significantly less delivery of the actives to the body. In recent years, a vast number of products have been sold over the internet that contain these active ingredients. An excellent composition for transporting PREG, DHEA and progesterone through the skin is an oil-in-water emulsion that contains components of the fatty tissue of the skin along with suitable permeation enhancers and use of liposomes and nanospheres.

Transdermal vs. Oral Delivery

Transdermally-delivered steroidal precursors and hormones are up to 80% more bioavailable than equivalent dosages of orally-administered steroid hormones. In practical terms, an oral dose of 25 mg DHEA might be equivalent to 5 mg that is transdermally-delivered.⁸ Products can be purchased online, such as Born Again's DHEA skin cream, which contains 25 mg of natural DHEA in each half teaspoon. The product claims to combine the anti-aging properties of DHEA with antioxidants and bioflavonoids. DHEA Pro gel for women from Mead Labs contains progesterone and DHEA for massaging into the soft areas of the skin, such as upper chest, inner arms, abdomen, inner thighs or behind the knees. The adverse effects of DHEA, which include increased facial sebum production, acneiform dermatitis and mild hirsutism, have been reported in women taking DHEA orally in dosage ranging from 25-200 mg/day.^{8,9}

Skin Lightening and Brightening

Potassium azeloyl diglycinate (azeloglicina) is an innovative water-soluble ingredient with sebum normalizing and skin lightening properties of azelaic acid with moisturizing and elasticizing properties of glycin. Azeloglicina is the patented ingredient of Sinerga S.p.a. of Milan, Italy. It is recommended for oily, seborrheic skin and as a skin-lightening agent to reduce the color of melanin aggregates or age spots. It represents a valid alternative to kojic acid dipalmitate.

Alpha-arbutin (hydroquinone-D-glucopyranoside), a skin lightening and brightening ingredient¹⁰ is up to 10 times more stable and effective than the ordinary beta-arbutin used by many other skin care companies. It is the epimer of arbutin, which even in very low concentration can inhibit the activity of tyrosinase. Its inhibitory mechanism is different than that of arbutin. Available from Pentapharm for skin de-pigmentation, it protects the skin against damage caused by free radicals. Most cosmetics companies don't use "arbutin" in their products because of patents controlling its use for skin lightening. To get around this problem many companies use plant extracts that contain arbutin, a glycosylated hydroquinone derivative from the leaves of the bearberry,

cranberry and blueberry shrubs, and most types of pears such as bearberry. Unfortunately, there is no research that shows the plant source of arbutin has any impact on skin, especially not in the tiny amounts used in cosmetics. Alpha-arbutin is the most effective, when compared to beta-arbutin, bearberry extract and kojic acid. Also, no literature is available to provide data on the amount of bearberry extract or arbutin that is hydrolyzed to hydroquinone on the skin. Arbutin inhibits the formation of melanin pigment by inhibiting melanosomal tyrosinase activity, rather than the suppression of the synthesis and expression of this enzyme. According to manufacturers arbutin is an effective depigmenting agent at a concentration of 1%. Shiseido's Whitess Intensive Skin Brightener (\$120 for 1.4 oz.) has a rather high concentration of arbutin (about 5%).

Conclusion

Cosmeceuticals have taken on a new meaning. Innovative skin care products are making increasingly bold claims, with breakthrough packaging to give a very strong message. Consumers are now more savvy about product performance and are on the lookout for functional products that promise medicinal or treatment attributes.

References:

1. M. Henson, "Skin Science," Happi, May, p. 102.
2. Website: NeoStrata Company, Inc., 4 Research Way, Princeton, NJ 08540 USA.
3. Jyonouchi, H., L. Zhang, M. Gross, and Y. Tomita. 1994. Immunomodulating actions of carotenoids: Enhancement of in vivo and in vitro antibody production to T-dependent antigens. *Nutr. Cancer* 21: 47-58.
4. Suzuki, K., H. Masaki, and M. Takei. 1996a. External preparation for skin. Japanese Patent No. 08073311, No. #08073312.
5. Majeed, M. Prakash, L. Badmaev, V., Nujoma, Y., Natarajan, S., Norton, T., Sysler, M., Gopinathan, S., and Alegesan, K (1999), "Redefining our standards, Boswellin, the only natural leukotriene and HLE inhibitor". Sabinsa Corporation.
6. V. Kanga, Skin care delivery systems, Happi, 47 (January 2004).
7. International Journal of Cosmetic Science (Vol. 24, No. 5, October 2002).
8. Labrie C., Flamand M, Belanger A, Labrie F. high bioavailability of DHEA administered percutaneously in the rat. *J Endocrin* 1996, 150 (Suppl):S107-S118.
9. Morales AJ, Haubrich RH, Hwang JY et al. The effects of 6 months treatment with 100 mg daily dose of DHEA. *Clin Endocrinol* 1998, 49:421-432.
10. Brochure: Pentapharm Ltd., Basel, Switzerland.

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