

The Art and Science of New Advances in Cosmeceuticals

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KEYWORDS

- Cosmeceuticals • Antiaging preparations • Antioxidants
- Acne • Skin pigmentation

The cosmeceutical category is an undefined, unclassified, and unregulated area of skin treatment that is yet in its infancy. Traditional cosmeceuticals involve the topical application of biologically active ingredients, which affect the skin barrier and overall skin health. The ability of these ingredients to enhance skin functioning depends on how they are formulated into creams, lotions, and so forth, which can maintain the integrity of the active ingredients, deliver these ingredients in a biologically active form to the skin, reach the target site in sufficient quantity to exert an effect, and properly release the ingredients from the carrier vehicle.

In the United States and Europe, cosmeceuticals are sold as cosmetics, making marketing, packaging, and aesthetic appeal important considerations.¹ However, in Japan, a novel category of quasi-drugs exists that encompasses these biologically active formulations sold directly to consumers. Because cosmeceuticals intend to deliver on a higher level than cosmetics that simply color and scent the skin, cosmeceuticals should be clinically tested for efficacy not only to insure a proven skin benefit but also to substantiate marketing claims.²

Cosmeceuticals are viewed as cosmetics in the United States and must be careful to make only appearance claims. For example, they can claim to improve the appearance of wrinkles, but not get rid of wrinkles. Improving appearance is a cosmetic claim, whereas getting rid of wrinkles is a functional drug claim. Cosmeceuticals can also brighten skin and improve radiance, but they

cannot treat abnormal pigmentation. Treating abnormal pigmentation is a drug claim. The recognition that there are governmental limitations on efficacy claims restricts cosmeceutical development because products can only be assessed in terms of their ability to improve skin appearance but not function. Improving function would remove the cosmeceutical from the cosmetic category and place it in the drug category.

COSMECEUTICAL DEVELOPMENT

Basically, cosmeceuticals are functional cosmetics, which means that the ingredients that are included in formulations must come from a list of raw materials that are generally recognized as safe, else the cosmeceutical would be classified as a drug. The easiest source of new cosmeceutical ingredients is the plant kingdom. Plants are rich in endogenous antioxidants because they must survive in an environment rich in UV radiation insults. Plant extracts are also thought to be safe and meet the Food and Drug Administration criteria for substances that can be put in over-the-counter (OTC) formulations. It is generally thought that substances that are safe for oral consumption can be assumed safe when applied topically. This thinking has led to a renewed interest in herbal preparations, which form the basis for functionality in many cosmeceuticals.

The search for novel herbs has led to the gathering of flowers, seeds, roots, leaves, twigs, and berries from plants all over the world. This gathering can be a complex process because the

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constituents of a plant extract are influenced by the season in which the plant material was picked, the growing conditions, and the processing of the botanic. Once a possible functional cosmeceutical active ingredient has been identified and synthesized, it is typically applied to a fibroblast cell culture and the supernatant is placed on a gene chip to look for upregulation or downregulation of key skin mediators. For example, the ingredient may downregulate matrix metalloproteinases (MMPs), leading to a decrease in collagen degradation, providing the data for an antiaging claim. Sometimes the ingredient is further tested in a rodent model for confirmation of the desired skin benefits. The active ingredient is then placed in a vehicle suitable for human application, and clinical studies are undertaken. Successful human clinical studies pave the way for successful introduction into the marketplace via ingredient licensing arrangements.

COSMECEUTICAL CONCERNS

Although cosmeceuticals represent the future of skin care, there are also some concerns that should be considered. Not all plant extracts are beneficial to the skin. Many plants contain toxic metabolites, irritants, or allergens in addition to beneficial antiinflammatory agents. For example, feverfew, botanically known as *Tanacetum parthenium*, is a perennial flowering plant that contains antiinflammatory ingredients in its leaves. The leaves contain oils, such as terpenes and linalool; flavonoid antioxidants; and parthenolides that are sesquiterpene lactones.³ Parthenolide is a skin irritant that must be removed before feverfew extra can be incorporated into cosmetic preparations. Parthenolide is a distant relative of poison ivy, which is also a natural botanic extract inappropriate for skin application.

Other considerations include the growing habits of the plant. Some plants can only be seasonally harvested, unable to provide raw materials for year-round product manufacture. Other plants grow so slowly that overharvesting of the plant is possible, creating endangered plants. Many plants that grow in the Brazilian rain forest are being overharvested for cosmetic use, giving rise to a new concern in skin care manufacture known as sustainability. Sustainability is focused on ensuring the safe and continuing propagation of all plant materials. Even though many consumers want “natural” plant-derived ingredients because they are concerned about health issues, the use of highly specific synthetic plant isolates may be more environmentally friendly and may lower the incidence of allergic or irritant contact dermatitis.

Another solution is to develop plant cell cultures known as bioreactors.⁴ Care must be taken to protect plant materials from extinction.

COSMECEUTICAL CLASSIFICATION

The number of ingredients that can be formulated into cosmeceuticals is limited only by the imagination of the cosmetic chemist. Because cosmeceuticals are unregulated, the potential uses of cosmeceuticals are also unlimited. Cosmeceuticals could be developed to improve skin radiance, minimize acne, create the appearance of plump lips, optimize skin texture, shine hair, decrease nail brittleness, shrink facial pore appearance, create skin luminosity, improve the appearance of stretch marks, encourage pigmentation evenness, and so forth. If it would sell, it would be created. This article focuses on the more traditional use of cosmeceuticals relevant to skin care, including acne and antiaging uses.

COSMECEUTICALS FOR ACNE

A variety of preparations have been introduced for skin care that fall outside the prescription and the OTC drug realm. Oral and topical antibiotics and engineered retinoids form the basis for prescription-only therapies. Benzoyl peroxide, salicylic acid, and sulfur are the major ingredients from the acne monograph that are found as sole active ingredients in the concentration specified in most OTC acne drugs. The unregulated cosmeceutical acne category is based on natural acne-inhibiting substances of salicylic acid from willow bark, elemental sulfur, and tea tree oil.

Willow Bark (Salicin)

The white willow, known as *Salix*, contains a chemical known as salicin in its bark, which is a rich source of tannins and flavonoids. Salicin is the precursor of salicylic acid, comprising about 1% of the white willow bark extract, whereas other glycosides comprise about 12%. Salicylic acid is a colorless crystalline oil-soluble phenolic compound incorrectly classified as a β -hydroxy acid in which the OH group is adjacent to the carboxyl group. Synthesis of salicylic acid involves the treating of sodium phenolate, the sodium salt of phenol, with carbon dioxide at 100 atm pressure and 390 K temperature followed by acidification with sulfuric acid.

Salicylic acid, also known as 2-hydroxybenzoic acid, has a rich history in medicine. Salicylic acid is used as an antiinflammatory inhibiting arachidonic acid (because it is chemically related to

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