Novel Cosmeceutical Delivery Methods

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Getting active ingredients into the skin is the difference between cosmetic fluff and efficacy. Technically, cosmeceuticals are cosmetics and do not enter the skin; if they entered the skin, they would be classified as drugs, which would limit the tremendous ingenuity possible in cosmeceutical development. Not all cosmeceutical ingredients should penetrate the skin because some are intended to function on the skin's surface while others theoretically must reach the dermis to actually achieve the optimal effect. For example, sunscreens should remain on the stratum corneum to either absorb UV radiation and convert it to heat or reflect UV radiation. A penetrating sunscreen formulation would be suboptimal, as UV entry into the skin could create reactive oxygen species before the sunscreen could act. In contrast, other ingredients such as antioxidants do not function optimally on the stratum corneum and should reside in the viable compartments of the skin where oxidative damage affects DNA.

New developments in delivery technology have changed the way cosmeceuticals interact with the skin. Many of these techniques have been used to optimize topical drug delivery, which has further blurred the distinction between pharmaceuticals and cosmeceuticals. This article examines some of the novel cosmeceutical delivery methods currently available in the marketplace.

Cyclodextrin Complexes

Cyclodextrin complexes are used in currently marketed topical formulations of metronidazole 1%. Metronidazole is an interesting molecule that is not readily soluble in either water or oil. The older topical metronidazole 0.75% formulations represented the highest concentration of metronidazole that could be dissolved in a cream, gel, or lotion. Cyclodextrin complex technology made it possible to dissolve metronidazole 1%. Minoxidil is another drug that can be solubilized better using cyclodextrin complex technology, which can be further adapted to cosmeceutical ingredients.

Cyclodextrins are cyclic oligosaccharides that are formed into a ring to create an internal cavity where other substances can be placed. The 3 natural cyclodextrins—α-, β-, and γ-cyclodextrins—differ in ring size and solubility. For example, γ-cyclodextrins can be used for topical delivery of vitamin D. The value of cyclodextrins lies in their ability to protect their internal contents from oxidative, photolytic, and thermal damage, while increasing solubility. Vitamins C and E are light-sensitive vitamins that can be protected from photolytic damage in a cyclodextrin ring. Molecules that are incompatible and might interact also can be isolated and protected using cyclodextrins, and foul-smelling molecules can be isolated to prevent product odor.

Microsponges

Microsponge technology was introduced to the dermatology field in topical pharmaceutical formulations containing tretinoin and benzoyl peroxide, but it also is a valuable means of delivery in cosmeceuticals. Microsponges are porous polymer systems that can entrap a variety of substances for timed release onto the skin's surface. For highly irritating substances or those that need a long time to take effect, this technology is a major advancement. Microsponges also can change the feel of a cosmeceutical product, making the product less greasy, sticky, or tacky when substances with undesirable aesthetics are added to the microsponges.

There are 2 types of microsponge systems available for formulation: small microsponges (particle size <50 µm) and larger microsponges (particle size 100–200 µm). Ingredients can be loaded onto the microsponge using 2 methods, both yielding different delivery possibilities. The first technique is to soak the microsponge in a solvent solution containing the active ingredient. The solvent then is evaporated, leaving the active ingredient on the outside of the microsponge. The second technique is to mix the active ingredient with the microsponge

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polymer when it is being formed. Because the microsponge can be crushed when it is rubbed into the skin, the second method insures better time-released delivery.

Microsponges are used in dandruff shampoos, which are classified as over-the-counter drugs. Zinc pyrithione and selenium sulfide are antifungals/anti-inflammatories that commonly are used for the treatment of dandruff and possess a foul smell. The odor can be reduced by utilizing microsponge technology. Microsponges also are gaining traction for use in higher-priced cosmeceuticals.

Nanoemulsions

Another method for enhancing cosmeceutical delivery is a variation on traditional emulsions that are based on oil-in-water or water-in-oil formulations containing large droplets that do not penetrate the stratum corneum readily. Nanoemulsions possess the same formulation, except the droplets are on the nanoscale of 20 to 100 nm.[1,2] When the nanodroplets are larger than 100 nm, the emulsion appears white, while nanoemulsions with nanodroplets of 70 nm are transparent. Nanoemulsions offer the ability to deliver highly hydrophobic or lipophilic substances to the skin, which otherwise could not penetrate the stratum corneum.[3] This method provides unique nanocarrier opportunities because the stratum corneum is an excellent barrier to lipophilic cosmeceuticals.

Cosmeceutical nanoemulsions of ubiquinone, also known as coenzyme Q10, have been developed. It is an important antioxidant manufactured by the body and found in all skin cells. Topical penetration had been challenging; however, Hoppe et al[4] was able to demonstrate penetration of coenzyme Q10 into the viable epidermis and a reduction in oxidation with weak photon emission. Theoretically, higher concentrations of ubiquinone in the skin would enhance endogenous antioxidant capabilities, thereby preventing oxidative damage to cellular structures.[5]

Another use for nanoemulsions in cosmeceuticals is in the delivery of hyaluronic acid (HA), a natural glycosaminoglycan found in the dermis that functions as a humectant. Hyaluronic acid nanoparticles can create an imperceptible film on and within the stratum corneum to attract water and create the illusion of smoothness by filling in fine lines and increasing the skin's water content. These examples highlight the utility of nanoemulsions as cosmeceutical penetration enhancers.

Poration

One method of changing the barrier capabilities of the stratum corneum is to literally poke holes in the barrier.[6] Devices manufactured for this purpose are adapted from acupuncture equipment that uses tiny sterilized, tapered, stainless-steel, solid-core needles that are placed on a roller. The roller is moved over the skin with pressure applied to push the needles into the skin, creating tiny pores. The needles are spaced to minimize pain and are exquisitely sharpened to decrease crush injuries to the skin. The number of times the poration roller is moved over the skin directly correlates with the number of pores created and the extent of the barrier damage.

There are 2 ways to physically increase the degree of penetration in cosmeceuticals using poration, which also is known as microneedling: the cream can be applied prior to the use of the roller or after the pores have been created. Most commonly, the cream is applied first and pushed into the skin with the porator needles. This strategy requires that the cosmeceutical is carefully formulated and does not contain irritants or toxic substances because the ability of the stratum corneum to block penetration is bypassed. Stinging and/or burning may occur if low-pH substances, such as lactic, glycolic, or ascorbic acids, are pushed into the skin. Preservatives designed to maintain cosmeceutical stability also may not be the best ingredients to introduce into the dermis. Patients should be discouraged from using standard skin care products when undergoing poration; rather, they should utilize cosmeceuticals that are designed for this application.

Poration also is intended to wound the skin in columns, similar to fractionated CO_2 lasers, to encourage tissue regeneration. It is theorized that this controlled wounding increases collagen and glycosaminoglycan production without producing visible scarring. Much of the success achieved using poration depends on the expertise of the user and the design of the device. Many dermatologists in Europe are using poration immediately following dermal HA injections to attempt to improve the result and longevity of the filler; however, no controlled studies on this technique have been published to date.

A variation on poration has been introduced to the professional dermatology market. A device that looks similar to a hinged plastic spoon with pyramidal plastic spines on the back can be pressed into the skin. The spines are so small that they theoretically can fit between nerve fibers, allowing for painless poration of the skin. I have studied this application technique for the administration of botulinum toxin and HA with little success. The major problem was the single-use needles, which bent easily, thereby creating concern that the needles might break off in the skin and cause a foreign-body reaction. New material technology that does not bend or break in the skin may solve this problem, but further research is required.

Electroporation

The effects of poration can be augmented in combination with electricity. The same solid needles placed on a metal roller can be electrified with high-strength pulsed electric fields. If the field strength is low (transdermal voltage <100 V), charged molecules can transport through the skin. If the field strength is high (>100 V), the lipid bilayers of the skin are disrupted and transbilayer transport occurs through the electropores within the lipid layers.[7] A study by Vanbever et al[8] demonstrated a 2-fold increase in transdermal delivery of mannitol using electroporation.

Iontophoresis

Another electrical delivery technique for penetration enhancement is iontophoresis, which also utilizes an electric current to allow substances to penetrate the skin.[9] Iontophoresis applies a small voltage of 10 V or less to the skin with a continuous constant current of 0.5 mA/cm^2 or less. This voltage is much lower than electroporation and is constant instead of pulsed.[10] Iontophoresis currently is under investigation for use with transdermal patches, whereby a device that generates a constant electric current is affixed to the passive transdermal patch to facilitate cutaneous penetration. The advantage of this technique is that peptides and proteins, which currently are applied topically as cosmeceuticals, can be pushed across the stratum corneum by electromotive force. In addition, large and charged molecules can be delivered, which is not possible through passive delivery across the skin.[11]

Galvanic Current

Galvanic current is different from electroporation in that it utilizes a constant, low-voltage direct current. The principle of this method is that the skin can be enhanced through an electrochemical process that either attracts or repels charged ions. The current is administered through electrodes that touch the skin. Galvanic devices have been used to cleanse the face in an aesthetic procedure (known as desincrustation) and to treat cellulite in the body. It is thought that galvanism works on cellulite by increasing vascular and lymphatic drainage by improving the functioning of the cellular membrane and allowing trapped fluid and lipids to be dispersed and eliminated. The galvanic current is used in conjunction with topical cosmeceuticals to enhance the effect. Some physicians believe that the treatment alters electrical channels in the skin to enhance penetration of the topical agent; however, there are limited data in the medical literature regarding this technique.

Summary

Delivery methods for cosmeceuticals are key in targeting ingredients to reach the proper locations to exhibit the desired effects. Although many of these delivery systems are used in pharmaceutical formulations, claims from manufacturers can only relate to improved appearance; the manufacturers may not make functional claims when discussing cosmeceuticals, which limits the ability to advertise the use of novel delivery methods. Consumers may note better aesthetics and improved odor due to these novel delivery methods.

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