



DELIVERY OF COSMETIC INGREDIENTS TO THE SKIN

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Why are some skincare preparations effective and others are not? Only some cosmetics are able to make a visible difference in the skin. To the consumer, this is a critically important issue. Recent advances in skincare have led to the development of products that improve skin appearance and quality in weeks, days, or even hours.

Falling victim to enticing ads and trying products that fall short of their claims, consumers have become disillusioned with cosmetic ads and often dismiss these as false advertising. However, what used to be the science fiction future of the cosmetics industry has now become the present. We have entered a new age in skincare—the age of cosmeceuticals.

The term “cosmeceutical” refers to the blending of knowledge from the cosmetics industry and the pharmaceutical industry. Cosmeceuticals are skincare products combining ingredients and technology from both disciplines. For the consumer this brings the availability of amazingly effective products.

Any product is likely to be more effective if only the best ingredients are used. Very few cosmetics are formulated with medical-quality ingredients. However, to earn this “pharmaceutical grade” designation, these ingredients are tested to verify purity and effectiveness. Other types of ingredients, such as short chain proteins, are usually made in the lab where they are synthesized reliably. Examples of protein technology include growth factors and other cell signaling molecules. Both pharmaceutical grade botanicals and the best protein technologies are quite expensive. Good cosmeceutical companies must be willing to pay for this level of quality. Otherwise, the consumer buys a less effective product, while the company may collect more money per unit sold.

Product development is also a significant cost. The information explosion extends to all fields of knowledge and many advances have occurred in the cosmeceutical industry. The most innovative science is expensive, although the consumer is then able to purchase very effective products.

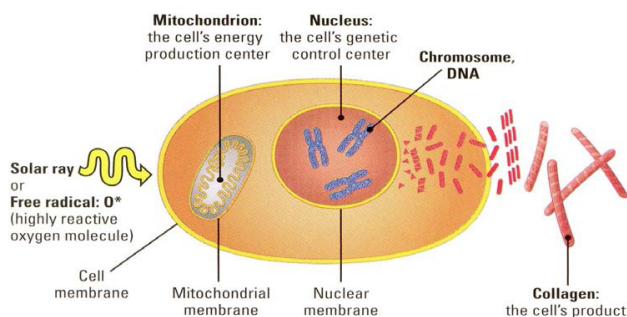
To understand cosmeceutical delivery and the techniques of placing actives within the skin structures, some understanding of skin physiology is required. The skin is a complex organ, designed to serve as a barrier between the inner biologic environment and the outer environment. Without this protection against the outside, the inner organism would be subject to outside temperature variations, solar radiation, and a myriad of toxins and pollutants. In order to deliver beneficial ingredients inside the skin cells, this barrier function of the skin must be overcome selectively; however, it must not be so altered as to fail in protecting the inner organism nor functioning as a barrier.

The outermost layer of the skin, the stratum corneum, has layers of keratin derived from flattened keratinocytes and is designed to be particularly difficult to penetrate. In skincare, however, selective penetration of active ingredients to various skin depths is desired. There are three main entry sites into the skin: pores, hair follicles, and spaces between cells that contain an oil/water fluid matrix. An effective cosmetic must be designed for its beneficial substances to penetrate inside skin cells, yet not damage overall skin integrity. Designing such a product requires considerable biochemical skill and involves much more than simply mixing ingredients together. There must be an orchestration of ingredients, all working together in a very complex way. Some may also interact with each other in desired ways. They will be prepared at specific temperatures and in a special order so that they form the proper end-product. Great knowledge, skill and training are required to design such a cosmetic.



The skin is a complex organ and, as such, must be gently persuaded to allow beneficial substances to pass while still continuing to function properly. The chemical form chosen for the active ingredient can dramatically alter its availability to skin cells. For example, vitamin C is an important skin nutrient that is difficult to deliver inside skin cells where it is metabolically beneficial. Not until INNOVATIVE SKINCARE[®]'s ADVANCE⁺ technology were the prior limitations of pH and concentration requirements for vitamin C overcome, yielding more effective products that were also much more compatible with skin.

If a cosmetic ingredient is to arrive at its proper location in the skin, it must be soluble (dissolvable) in the type of tissue where it will reside. Looking at the picture of a skin cell below, we see skin cells whose borders are composed of lipid soluble (fat dissolvable) membranes. The interior of these skin cells is mostly water and to remain there, a substance must be dissolvable in water (water soluble). This makes delivery of cosmetic ingredients quite complex because water soluble substances will not pass through the border of the cell to the inside where they exert their desired activity. The cosmetic product must therefore be configured with the proper amount of oily substances and watery substances to pass through cell membranes to the interior of the cell. Furthermore, only certain types of fats with specific chemical designs will pass through the borders of skin cells and/or other skin structures. This further illustrates the complexity of effective cosmeceutical design.



Much cosmetic advice is not based on good knowledge of biochemistry and skin physiology. For example, it is

common to be advised never to put alcohol on skin. While it is true that excessive use of highly volatile, quickly evaporating alcohols can cause skin dryness, a variety of special alcohols act as penetration enhancers and antimicrobials in cosmetics. Panthenol is, chemically speaking, also an alcohol; yet panthenol is a form of vitamin B5 and is an essential nutrient for skin cell metabolism of fats, proteins and carbohydrates. Cetyl alcohol is also an alcohol, yet is a waxy substance that is very safe topically and is very useful as a counter-irritant. Tiny skin sections viewed under a microscope show that topical cetyl alcohol causes no microscopic skin changes, dryness, or inflammation.

Menthol is another alcohol occurring in nature, derived from the species *Mentha*, that gives the mint family a typical taste and smell. Menthol functions as a transdermal delivery agent, taking desirable molecules across the skin barrier to where they are used. It is highly lipid soluble (dissolves in oil) and therefore crosses the skin barrier. It has been proven to assist the movement of many molecules, including medicines, from the surface of the stratum corneum (outer skin layer) to the internal layers of the skin. A unique benefit of menthol is that it enhances absorption of desirable molecules without irritating the skin. In fact, menthol affects the sensory nerve terminal in the skin in a very desirable way that calms and soothes the nerve. The nerve is still able to function because it is not completely numb or anesthetized. Menthol is such an effective counter-irritant that it controls skin irritation from capsaicin, which is found in cayenne pepper. Capsaicin is a profound skin irritant, but when applied with menthol in scientific studies, sensory irritation is reduced.

In particular individuals, skin sensitivity can occur with some ingredients in topical products. Although contact allergy or sensitivity can occur, this is extremely rare in INNOVATIVE SKINCARE[®] products due to meticulous ingredient selection, use of only the purest actives, and sophisticated chemical technology. Persons with frequent allergic or sensitivity reactions are advised to patch test all products prior to use.



Size of the particle in the cosmetic preparation relates dramatically to its ability to penetrate skin and cause an effect. Some cosmetics containing collagen claim that they increase the collagen content of skin. Collagen, being a very large molecule, is unable to penetrate skin even when combined with penetration enhancers, although it can be used as a moisturizing agent. Elastin, on the other hand, is a much smaller molecule and, when placed on the skin, can penetrate the skin and has been found later to be incorporated into connective tissue bundles.

The induction of collagen synthesis within the skin requires a much more complex approach than simply placing collagen on the skin. Collagen is the main protein that supports skin architecture. Damage to collagen by crosslinking will cause wrinkling. Young, healthy collagen has not been damaged by crosslinking, and this skin has good tone and a youthful appearance. Increasing the skin's collagen production is critical in helping to improve aging skin. With aging, the synthesis of collagen declines along with all other body proteins. Collagen production falls about one percent each year of life. Increasing collagen production can restore a more youthful appearance.

Application of alpha hydroxy acids, such as glycolic acid and lactic acid, can increase skin turnover and increase collagen production. Some growth factors can more directly increase collagen synthesis. These substances encourage the skin itself to make more collagen.

Sometimes, combining ingredients in a certain way improves the desired result or otherwise changes their individual action. When kojic acid is used in combination with arbutin glycoside or glycolic acid, the improvement in hyperpigmentation increases by as much as 60% compared to using either ingredient alone. The chemical activity of the preparation to inhibit tyrosinase, an enzyme used in producing melanin, increases as much as 13% by combining these ingredients in the proper way.

Applying a cosmetic in a certain way may also change its activity. For example, increased time of application

usually leads to higher activity. Occlusion (covering the product with plastic or a medical hydrogel) usually increases activity. But a word of caution should be given here: DO NOT try to increase product activity without consulting the manufacturer. In medicine, photoexposure (light exposure) may activate a medicine to achieve its result. Similarly, applying a cosmeceutical in the morning (with light exposure during the day) rather than at night may make a difference in activity. For example, applying iS CLINICAL® ACTIVE SERUM™ in the morning rather than at night causes more noticeable improvement in uneven pigment. Micro-needling, dermal rollers and even use of some home cleansing devices may be designed to increase skin penetration of cosmetic ingredients and activity of products. Increased activity, although perhaps thought to be desirable in certain situations, can also result in an increased likelihood of a sensitizing reaction as well as other possible issues – including systemic penetration beyond the skin surface and into the blood vessels and other parts of the body. Consultation with a knowledgeable and trusted skin professional is advised in these situations.

Topical delivery is not only an important topic in cosmeceuticals; it is also very important in pharmaceutical medicine. New methods of drug delivery that supply medicines to their proper site with less toxicity and more efficient clinical results have made huge strides in recent years. Many more medicines are now given via skin patches, nasal inhalation, and the eye. Many more of these are in development. Truly unique drug delivery methods like medicated disposable diapers and collagen contact lenses which slowly release medicine to the cornea have been used. In the future, liposomes (tiny spherules containing special fat, medicines, and other substances) may be used to deliver DNA gene therapy to skin cells. This could be used to modify the skin changes of aging, other changes in the body related to aging (as decreased hormone production), or to treat other medical problems such as heart disease. This may sound like science fiction, but all of these ideas are already in development and are being discussed in the medical literature. For example, a



vaccine could be delivered to cellular DNA via a liposomal vehicle placed on the skin to immunize a child. Even more exotic would be placement of an inactive drug on the skin that, at the time it was needed for treatment of cancer, could be “turned on” by giving another medicine orally or by skin application.

The recent advances in medicine and chemistry are changing the face of cosmetics. Future developments promise to be even more exciting.