



DELIVERY OF COSMETIC INGREDIENTS TO THE SKIN

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Why are some skincare preparations effective and others are not? Understanding this concept will explain why only some cosmetics are able to make a visible difference in the skin. To the consumer, this is important because although many skincare products do not work, recent advances in skincare have made products available that provide dramatic visible improvements in skin quality and reduction in fine wrinkling after only several weeks...in some cases several days.

For decades, the public has been subjected to the advertising claims of cosmetics companies promising more youthful, vibrant, healthy skin. Unfortunately, in the past most of these claims have been false. Falling victim to enticing ads and trying products that don't live up to their claims, consumers have become jaded to cosmetic ads and tend to dismiss it 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 preparations—the age of cosmeceuticals.

Cosmeceutical refers to the marriage of the cosmetics industry with the pharmaceutical industry. Cosmetics companies make cosmetics. Pharmaceutical companies make medicines. Cosmeceuticals are skincare products that combine cosmetics and medicines. What this means to the consumer is that they actually work.

To understand cosmeceutical delivery, one must have some understanding of skin physiology. The skin is a complex organ, designed to assist in body temperature regulation and to serve as a barrier between the inner biologic environment and the outer environment. Without protection against the outside environment, the inner organism would be subject to outside temperature variations, solar radiation, and a myriad of toxins. In order to deliver necessary ingredients inside skin cells, this barrier function of the skin must be overcome selectively; however, it must not be so altered as to no longer protect the inner organism or continue to function as a barrier in the future.

The outer horny layer of the skin, the stratum corneum, has layers of keratin made by keratinocytes (this term refers to cells that make keratin) and is designed to be particularly difficult to penetrate. We also want different substances to penetrate to different depth levels in the skin for best results. There are four major 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 so that its beneficial substances can somehow get inside skin cells, affecting their metabolism in a way that improves their health, yet not damaging overall skin integrity. Designing such a cosmetic cannot be a naïve project and requires considerable biochemical skill. It involves much more than simply mixing a bunch of ingredients together. There must be an orchestration of ingredients, all working together in a very complex way, interacting with each other in certain ways, prepared at specific temperatures and in a special order so that they work together as desired. Imagine the knowledge, skill and training necessary 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 work as it should. The stratum corneum is designed to be difficult to penetrate. The chemical form chosen for the substance can dramatically alter its availability to skin cells. Vitamin E, however, does penetrate this layer to some degree and enters skin cells at deeper levels to serve as a potent antioxidant, fighting changes of ordinary skin metabolism byproducts, aging, and sun damage. However, Vitamin E Acetate (as found in iS CLINICAL® POLY-VITAMIN™ SERUM) has better antioxidant ability to fight aging and sun damage and can get into skin cells more easily than plain Vitamin E. In general, esthers of substances are more easily transported across the skin surface. Potassium cetyl phosphate (iS CLINICAL® FIRMING COMPLEX) is the esther of cetyl alcohol and

phosphoric acid. Vitamin A palmitate (iS CLINICAL® POLY-VITAMIN™ SERUM, FIRMING COMPLEX, MOISTURIZING COMPLEX, BODY COMPLEX) is the ester of Vitamin A and palmitic acid; as such, it has much better skin penetration to its target site than regular Vitamin A.

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 skin above, we see skin cells that have their borders 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 more complex because water soluble substances will not pass through the border of the cell to the inside but they must get to the inside of the cell to be used in cellular metabolism to achieve a desired result. The emulsion (cosmetic mixture) 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. They must also be layered in a specific way. This is made more difficult because only certain types of fats with specific chemical designs will pass through the borders of skin cells and/or other skin structures. This again illustrates the complexity of effective cosmeceutical design.

Many books give cosmetic advice that is not based on good knowledge of biochemistry and skin physiology. For example, it is common to be advised never to put alcohol on your skin. Certainly, isopropyl alcohol (rubbing alcohol) is a poor choice as it is drying. However, SD Alcohol 40 is ethyl alcohol, which we commonly drink and has useful functions in a cosmetic preparation. A variety of special alcohols act as penetration enhancers and antimicrobials in cosmetics (phenoxyethanol in iS CLINICAL® ACTIVE SERUM™, butylene glycol in iS CLINICAL® MOISTURIZING COMPLEX). Frequently, experts negatively target compounds called alcohols. They may not know, for example, that panthenol is, chemically speaking, an alcohol. Panthenol is a form of vitamin B5 (iS CLINICAL® POLY-VITAMIN™ SERUM, HYDRA-COOL™ SERUM). Vitamin B5 is an essential element for skin cell metabolism of fats, proteins and carbohydrates. It is absolutely essential for cellular function. Cetyl alcohol (iS CLINICAL® FIRMING COMPLEX) is, strictly speaking, also an alcohol. It is called an alcohol but is really more of a waxy substance derived from the sperm whale that is very safe topically and is a wonderful counter-irritant. Tiny skin sections viewed under the microscope show that topical cetyl alcohol causes no microscopic skin changes, thus showing that it causes no skin damage.

Strictly chemically speaking, menthol is another alcohol. A frequently seen bit of cosmetic advice is to avoid the use of menthol. However, menthol, if combined with certain other ingredients in a mixed cosmetic preparation, can be quite useful in achieving specific desired effects. Menthol occurs widely in nature, derived from the species *Mentha* and gives the mint family their typical taste and smell. Menthol functions as a transdermal delivery agent (takes desirable molecules across the skin barrier to where they are needed). 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. It acts as a soothing agent to the nerve terminal. The nerve is still able to function, i.e. it is not completely numb or anesthetized and can sense pain. 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.

Some of the chemicals mentioned in this article are known to cause skin reactions in some people. Let's discuss this for a minute, as it is very important. Contact allergy or sensitivity has been reported, literally, for every substance found in skincare products. Just search the medical literature and you will find a report of sensitivity for absolutely every ingredient. This does not mean that they are all bad. In fact, if a skin care product really could guarantee that no one on the planet would develop any reaction to it, it would have to be inert. Inert is an exact scientific term that means it has no action whatsoever. In other

words, it would do absolutely nothing. It would have no effects, neither harmful nor beneficial, on the skin. Why buy a product that does nothing? Any product that achieves a desirable result for the skin has activity, or desired action. It does something. Anything that is active may cause a reaction in some individuals, although the incidence of this may be very low—or, as in the case of capsaicin (cayenne pepper) applied to the skin, very high. In fact, the consumer wants an active product to achieve a specific improvement. If you have a history of allergy or sensitivity, though, it is advisable to patch test any and all products prior to use. If you want to be absolutely safe, you should patch test even if you have no history of sensitivity. As you read through this article and see the complexity of reactions initiated by a cosmeceutical ingredient and designed to produce certain beneficial results, it is easy to understand that, as all these complex interactions are occurring, the possibility exists of certain individuals developing reactions to various products.

Size of the particle in the cosmetic preparation relates dramatically to its ability to penetrate skin and cause a biologic effect. Some cosmetics containing collagen claim that they increase the collagen content of skin. This is false. Collagen, being a very large molecule, is unable to penetrate skin even when combined with penetration enhancers or other vehicles. Elastin (iS CLINICAL® MOISTURIZING COMPLEX), 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 collagen bundles. In any of these cosmetic preparations containing collagen, the collagen simply serves as a moisturizing agent. Although it might be useful in this regard (iS CLINICAL® MOISTURIZING COMPLEX), they should not claim it increases collagen.

The induction of collagen synthesis requires a much more complex approach than simply smearing 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. Application of alpha hydroxy acids (glycolic acid, lactic acid in iS CLINICAL® ACTIVE SERUM™) to the skin can affect the deeper layers of the skin, the dermis, and increase collagen production.

Note that these substances induce the skin itself to make more collagen; already-made collagen cannot be put into the skin. (Note that we are referring here to the normal functional activity of collagen in maintaining skin integrity rather than to collagen injections in plastic surgery procedures, which are done for another purpose.) These alpha hydroxy acids can induct functional activity of fibroblasts (cells producing collagen) and increased collagen production. Increasing collagen production in the skin is particularly critical in helping correct aging skin. With aging, the production of all proteins in the body, including collagen, decreases gradually with time until it is down about 50% by the age of 60. Increasing the collagen production in aging skin returns it to a more youthful appearance.

Sometimes combining ingredients in a certain way improves the desired result or changes their individual action in some way. When kojic acid is used in combination with arbutin glycoside or glycolic acid (iS CLINICAL® ACTIVE SERUM™), the improvement in hyperpigmentation (uneven skin color) increases by as much as 60% compared to using the arbutin glycoside or glycolic acid alone. The chemical activity of the preparation in acting as a tyrosinase inhibitor (tyrosinase is the enzyme affected in the production of melanin pigment) increases as much as 13% by combining these ingredients in the proper way.

Applying a cosmetic in a certain way may change its activity. For example, increased time of application usually leads to higher activity. Occlusion (covering the product with something, as plastic or a medical membrane/hydrogel) usually increases activity. A word of caution - 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. (Applying iS CLINICAL® ACTIVE SERUM™ in the morning rather than at night causes more noticeable improvement in uneven pigment.).

Keep in mind that increased activity, although possibly desirable, can lead to a higher chance of a sensitizing reaction, so patch testing is advisable.

Substance delivery to the target organ is not only a hot topic in cosmeceuticals. It is one of the most rapidly developing areas in medicine and pharmaceuticals. New methods of drug delivery that supply medicines to their proper site with less toxicity and more efficient clinical result has made huge strides in recent years. Many more medicines are now given via skin patches, nasal inhalation, the eye, and many more are presently 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 sounds 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.