Fundamentals of Skin Penetration

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Do you know why skin care products work differently for each of us? It is due to the topical delivery system and penetration properties of our skin which help them work effectively.

What is a topical delivery system?

We apply various skin care products to protect and maintain healthy skin. The active ingredients we apply externally reach the inner layer of skin by penetration. It is important for the actives to reach directly into the surface layers to give us the desirable results. The performance ingredients are designed in a certain way to

reach the stratum corneum in the epidermis (*Do you remember reading about the stratum corneum in our previous article? If not, check out the Fundamentals of Skin biology article*). This is because as all the crucial actions like cell regeneration, collagen production etc., happen in the epidermis. Therefore, the ingredients reaching surface level to penetrate is a keen step in the process of delivery.

Let us now understand the importance of topical delivery systems and skin penetration. There are two relevant studies that come to play in this process. The first is formulation development where formulating chemists are interested in enhancing the delivery of materials. Secondly, toxicologists are concerned with penetration and absorption of materials for safety assurance. Therefore, formulation chemists and toxicologists play a keen role in the development of effective skin care products by understanding topical delivery systems and skin penetration properties.

Why is topical delivery system a point of focus in cosmetics?

Today, there are several skin care products which are not just a blend of oil, water, and emulsifiers, but also some active ingredients which accelerate the performance of the mixture for the betterment of our skin conditions. Hence, a clear understanding of topical delivery systems is the key in skin care formulations. It is observed that most of the active ingredients like exfoliators, moisturizers, and film formers can deploy their effectiveness on skin's surface. Nonetheless, to target the biological processes such as collagen production, active ingredients tend to show greater efficacy if they penetrate the stratum corneum in the epidermis.

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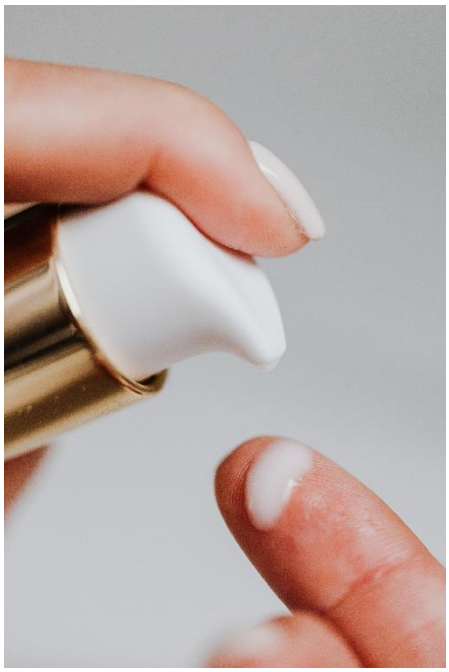
The three routes of penetration

Now that we have a brief understanding of the stratum corneum, let us discuss the three routes of cosmetic penetration: intercellular route, transcellular route, and trans appendageal route.

To have a clear picture of this, let us imagine the stratum Corneum as a "brick and mortar" structure, where keratinocytes are the "bricks" and the lipid matrix is the "mortar." Ingredients that penetrate using the intercellular route travel around bricks (i.e., keratinocytes) and through the mortar (i.e., lipid matrix). The lipid matrix being oil-soluble makes it favourable for lipophilic molecules to sink in, which is the reason behind the intercellular route being the predominant route of penetration through stratum corneum.

Next is the transcellular route, which is considered to be a difficult path for penetration. Ingredients that pass through this route pass directly through keratinocytes, making it a layered penetration process. The molecules in ingredients first pass through the dead keratinocytes' outer layer. After the passage through keratinocytes, ingredients then go through the hydrophilic center, which attracts water molecules and nanoparticles, and then through the lipophilic layer as well to reach the stratum corneum. Regardless of being a difficult path, the transcellular route acts favourable to those ingredients which have both hydrophilic and lipophilic properties.



The final route is the trans appendageal route, which is also known as the "pore pathway" and has ingredients passing through hair follicles and their sebaceous glands. Despite being one of the easiest routes of all, hair follicles and sweat glands cover only 0.1% of the total skin's surface which makes the trans appendageal route a less likely to be used for topical delivery.

Factors dictating an active's route of penetration.

There are several physiochemical characteristics in active ingredients that can trigger the molecules to choose an optimal route of delivery. It could be one route at a time or all three at once. In addition to physiochemical characteristics, there are many factors that play a role in determining the right route of penetration. It could be molecules themselves, their concentration, weight, solubility, and ionic charge. As for molecular weight, if the molecules weigh smaller than about 500 Daltons, then they can typically penetrate the stratum corneum. For solubility, as the stratum corneum is rich in lipids, oil-soluble ingredients can penetrate more easily than water-soluble ingredients. As for ionic charges, neutral molecules find it more effective to penetrate the skin barrier rather than cationic or anionic molecules.

Here, there is a partition coefficient that describes the solubility ratio between two immiscible solutions at equilibrium. Let us break this down by imagining a funnel containing two liquids X and Y which are not mixed with a solute Z until later. The partition coefficient is the level at which the Z solute can dissolve in each unmixed layer that is typically compared in a ratio where one solvent is water and the other is a hydrophobic solvent (i.e., the water-repellent or water insoluble).

The factor of hydration is another factor of penetration, so let us dig deep into it.

Water acts as both a vehicle and plasticizer. The stratum corneum is always partially hydrated but also can absorb additional water. Fully hydrated tissue can cause the stratum corneum to increase absorption five to six times its weight, making it thicker. Thicker skin tissue can act as a non-permeable wrap or have higher water content, which can increase the temperature and accelerate transport rate.

One final factor that affects transdermal support is delipidization. This is the process of removing lipids or lipid groups, often from a protein. The hydrophobic nature of skin's surface is revealed when it is exposed to organic solvents. In the process of de-lipidization, skin lipogenesis is continuous, where sebaceous secretion forms an irregular film of 0.4-4um thick on the surface. These variations in composition of surface lipids have been studied by Wilkinson in 1969. This research study was about squalene, free fatty acids, free sterols, and sterol esters. Wilkinson proved that this layer of lipids is not only waterproof, but also prevents water-soluble cosmetic ingredients from penetrating the stratum corneum.

Technological availabilities for the topical delivery

Active bioavailability is the key to improve efficacy of skin care formulations. Bioavailability is the penetration rate at which the active ingredients travel to reach its site of action. This happens with Fick's law of diffusion where the rate of penetration of an active from a topical formulation depends on passive diffusion into the skin. Passive diffusion can depend on the concentration of an active ingredient, the diffusion constant of an active ingredient molecule, and the interaction between the ingredients with the skin.

Let us now discuss the technologies used by cosmetic formulators.

First, solid core microvectors are a type of anhydrous delivery system which relies on absorption of active ingredients into a silica microsphere. This helps in the delivery of loaded actives into the skin. Microvectors are composed of dehydrated compounds of the extracellular matrix with silica particles in an anhydrous carrier.

When this dehydrated microvector gets in touch with water on skin, it then "comes to life." The hydrated microvector then penetrates the skin and delivers the active ingredients.

Second, liposomes are an encapsulation technology used to enhance topical delivery of cosmetic actives. They are a microscopic spherical vesicle with a structure that closely mimics cell membranes. Cosmetic ingredients typically have better stability, penetration properties and efficacy when in its liposomal form. Hence, liposomes can serve as an effective delivery system for both water and oil-soluble cosmetics. This technology allows hydrophilic actives to be loaded in an aqueous inner core, while lipophilic actives can be separately loaded in a lipid bilayer. Cosmetic liposomes are designed to break on the skin and fuse with epidermal lipids which then create pores to allow delivery of loaded actives. A higher penetration occurs when it is delivered through the stratum corneum with penetration stopping at living epidermal cells.

Third, biochelation technology is used to enhance the bioavailability of cosmetic actives and is a vegetal peptide technology focused on sustainability properties. Biochelates are used in a variety of personal care formulations as they are completely biodegradable. Later, fermentation of yeast with minerals and vitamins creates yeast-glycopeptide minerals. Since alcohol is replaced with vegetable glycerine, it binds plant phytochemicals effectively and is more bioavailable. Hence, this is a great way to incorporate important elements into cosmetic formulations as they pass more readily through cell membranes.

This might sound like extensive research, but it is important to *know your skin to glow your skin!*

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