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A NEW DIFFUSION SYSTEM THROUGH THE MUCOUS MEMBRANES, SKIN AND HAIR

P. Morganti*, A. Lanzone, L. Tiberi*****

* President/Director, R&D - Mavi Sud S.r.l., Aprilia (LT), Italy

** Department of Gynaecology, Catholic University "Sacro Cuore", Rome, Italy

*** R&D, Mavi Sud S.r.l., Aprilia (LT), Italy

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Synopsis

Although mucosae, skin and hair are complex systems that have a common origin, they are different thanks to the presence of mucous, of surface lipidic film and a greater or lesser quantity of keratin.
In order to obtain an optimal cosmetic penetration through this kind of tissues, it is fundamental the substantial modification of the vehycles employed.
To achieve this goal a particular DIFFUSION SYSTEM (MDS®) was developed. This MDS® can be considered the starting point of differentiated vehycles.

Riassunto

Sia le mucose che la cute o i capelli rappresentano sistemi complessi, che pur essendo di origine comune sono dissimili tra di loro per la presenza rispettivamente del muco, del film lipidico di superficie e di una maggiore quantità di cheratina.
Naturalmente per ottenere una penetrazione attraverso tali tessuti, che sia ottimale con l'uso cosmetico, è necessario modificare sostanzialmente i veicoli utilizzati. È stato perciò messo a punto un particolare DIFFUSION SYSTEM (MDS®) in grado di rappresentare la base di partenza di veicoli differenziati.

Mucous membranes are highly specialized ephitelial tissues, totally different from the skin that shares the interest of gynaecologists, dermatologists, cytologists and genito-urinary surgeons.

There are three main differences between mucous membranes and body skin.

The first is the fact that the former is generally covered by a protective and lubrificant mucus over its surface whilst the skin produces continuous and impermeable lipid-filled keratin layers which vary from site to site, and are not modifiable by the presence of the surface lipids film (1).

The second major difference is the sensivity of mucous membranes to circulating hormones, whereas human skin is virtually unaffected by androgenic or aestrogenic hormones until old age is reached.

The third difference of mucous membranes is their turnover rate which is much greater than that of the skin epidermis.

Because of the continous presence and activity of mucus even the keratinized zones of mucous epithelia are maximally hydrated and therefore would be expected to show an incresead permeability to water compared with body skin.

Thus it was recognized that the lipid-filled, intercellular domains is crucially important to barrier function of the skin, such as mucus performs the barrier function of mucous membranes.

For these reasons, cosmetic raw materials and active ingredients used can move through epithelia by simple diffusion, endocytosis or by active transport across membranes to obtain a real cosmetic diffusion system.

It is of most importance the chemical and physical nature of the penetrating selected active ingredient in relation to its movement through the vaginal mucous membranes.

In general, ions have more difficulty in penetrating than molecules, but small molecules, such as glycine or vitamin A, penetrate more easily than larger molecules (2).

Thus, the degree of ionization of an active substance will affect the rate at which is often dependent upon the pH. Moreover generally speaking, the permeability of mucous membrans is similar to that of fully hydrated body skin.

After the evaluation of all these parameters new vehicles have been developed, called Diffusion System® (MDS®), for mucous membranes, skin or hair.

What is the difference between skin and mucous membranes? The skin is covered by a dead durable, highly linked and lipid-filled protein keratin which forms a protective layer against the external environment, the Stratum Corneum (SC).

This "bricks and mortar" structure where the major lipids are between the cells forming the mortar, acts as a barrier against the penetration of organisms and other unwanted materials (3).

Moreover topically applied physiologic lipids cross the SC and enter the nucleated cell layers, followed by an incorporation into lamellar body secretory system.

Because metabolic processing is required, the impact of these lipids on barrier recovering is delayed of about two hours. The ability of these lipids to either worsen, normalize or accelerate barrier recovery rates in human epidermis is dependent on the ratios of the key lipids applied, ceramides, free fatty acids and cholesterol and, of course, on the age of the treated people (4).

Variation in the composition and proportion of these three lipid families can lead to either deterioration, normalization or acceleration of barrier repair.

A ceramide-dominant system, for example, would accelerate barrier recovery in chronologically aged skin, as it does in young skin, whether meanwhile cholesterol alone delays in chronologically aged skin, consistent with the marked abnormality in cholesterol synthesis in aged epidermis (5,6).

On the other hand, the unkeratinized mucus epithelia have living cells on their surface which would be very vulnerable to attack by micro-organisms and to the effects of toxic molecules where it not for the presence of mucus (7).

Moreover, the hair is modified epidermal cells composed of keratin, the main component of the horny layer in the skin. In biochemical terms keratin is a proteinaceous material where numerous s-s bonds create a framework between peptide chains resulting in very low solubility.

In histological terms, it is composed in three parts: keratin fibres, interfibrous materials and horny intermembrane materials.
However, in the keratinization process of forming hair, the cells are not all alike; the medulla, the cortex, the cuticle and the inner root sheath differentiate into cells with characteristic morphology and they each have characteristic forms of keratin.
The cells forming the outer root sheath are very similar in the form to the basal cell layer and spinous cells of the epidermis.
Cuticle has a rough surface composed of hard keratin protein; it is easily worn off by excessive brushing or strong shampoo and it is subject to the greatest environmental stresses including dry atmospheres, UV-light, sea water, swimming-pool chlorine, etc.
In particular, the cuticle of the hair shaft is directly affected by these stresses resulting in several cumulative types of damage.
For this reason hair splits and breaks easily. The penetration through all the tissues, the skin and the mucous membranes or the hair, is enhanced by the phenomenon of hydration.
What is interesting to remember is the protective action of mucus depending on its physio-chemical characteristics and on the specific, highly active macromolecular system such as immunoglobulins and other substances which it contains (8,9).
In fact mucus is a solution of a number of polymers which behaves quite differently from a solution of small molecules, when two unlike polymers in solution are mixed they tend to remain as two distint solutions, whereas solutions of two macromolecular systems intermingle.
Thus, in the first case, it may be said that the one polymer is insoluble in the other, and in the second case, each is *soluble* in the other's solution.
This phenomenon seems to be well connected to the normal forces existing between molecules, such as hydrogen bonding, Van der Waal's forces, and hydrophobic interactions, which are usually stronger between like molecules than between unlike molecules.
A special Diffusion System® (MDS®) (Fig. 1) was studied to improve and to facilitate the absorption

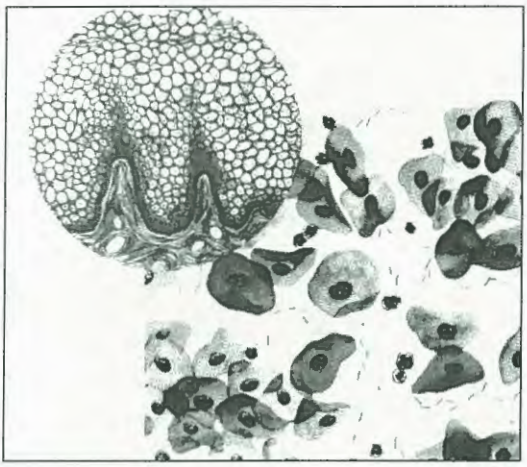

Fig. 1.

of active raw materials through the skin and the mucous membranes for the vehicle formulation of gynecological and/or dermatological products.
Have been selected specific macromolecules which have a structure compatible with the molecules of the mucus glycoprotein, thus enabling them to enter the environment of the mucus layer (10).
Moreover the vehicle used allows also smaller active molecules to interchange between the living epithelial cells and their surroundings, depending on their molecular size and ionic charge (11, 12).
This is the reason of the patented use of gelatin-glycine and/or gelatin-arginine, or gelatin-cystine necessary for enhancing both the hydration of mucus membranes and penetration rate of the active compounds (13-15).
Because of this all the components of MDS® are miscible with mucus and migrate to the outer surface of the mucus where they form a monolayer with the mucus-like portion of their molecules in the mucus phase and the other portion protruding into the surrounding medium.
These may be the reasons of the demonstrated clinical activity of some gynaecological cosmetics such as Elageno® A Monodose or Elageno® A Gel (15-18). They form an organized defensive barrier at the interface between the epithelia surface and its environment and mantain the normal pH values,

Fig. 2. Before treatment with a cationic-conditioner

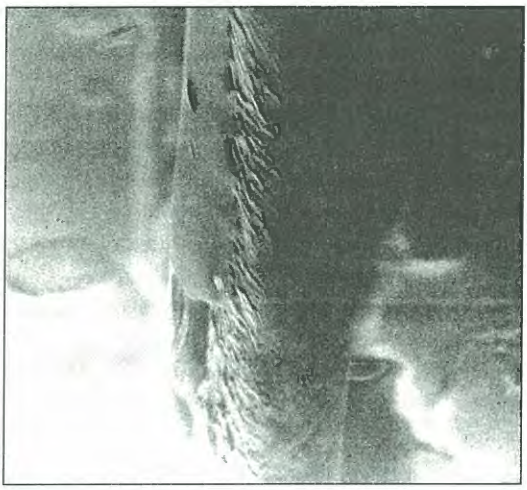

Fig. 3. After treatment with a cationic-conditioner

protecting the underlying cells against bacterial and viral infections. Contemporary throughout the activity of the vitamin A and PCA, Elageno® A seems to stimulate or induce also the formation of mucoproteins and other mucus substances.

Moreover, to reduce the damages of the hair it is useful to use, for example, cationic surfactant molecules to be absorbed on the hair surface. The hydrophilic group of the cationic surfactant faces towards the hair and is absorbed on to it electrostatically, while the lipophilic group is oriented outward. As a conseguence, the hair surface is covered by lipophylic groups making it smooth and protected (Fig. 2 ,3).

This is one of the principles the MDS® is based on. The system has been developed also for the formulation of hair products, such as shampoos, hair conditioners and lotions (19-20).

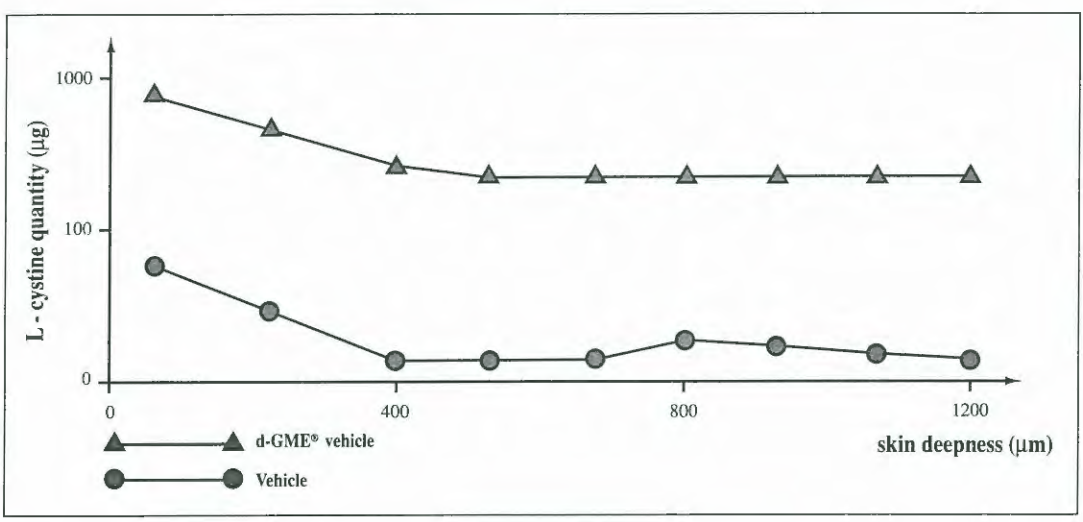

Fig. 4. Average L-cystine distribution in the scalp in function of cutaneous deepness. After one topical application (20 stripping)

Through the use of special oils, quaternized compounds and molecules that enhance the penetration (Fig. 4) became possible the formulation of new shampoos suitable to remove dirt, without damaging the protective lipidic film that covers both the scalp and the hair and capable to protect the hair from environmental damages while improving hair turnover by extending their anagenic cycle.
Thanks to a simple phenomenon of molecular chemistry active ingredients are made through the MDS® perfectly similar to hair keratins.
Thus they immediately fix to hair locks and leave on the hair an even film of substances that keep nourishing and protecting it until next washing.
What is of most interest is that this new DIFFUSION SYSTEM developed by our Research Team proved to be extremely adaptable and consistent with any cosmetic formulation requirements nowadays.

Author Address:
Pierfrancesco Morganti, Ph. D.
Mavi sud Srl
Viale dell'Industria, 1
04011 Aprilia (LT)
Tel: +39.6.92.86.261
Fax: +39.6.92.85.321

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