NANOVECTORS FOR BREACHING THE SKIN BARRIER

Silvia Franzè

Department of Pharmaceutical Sciences, via G. Colombo 71, 20133, Milan

The skin is the largest organ in human body, accounting for more than 10% of the body weight. Although it is an exposed tissue, the delivery of therapeutic compounds through the skin, although attractive, is probably one of the most challenging examples of drug delivery. In fact, on one hand the cutaneous administration of drugs allows to increase the patient compliance with respect to the parenteral routes and to improve the biopharmaceutical properties of compounds given orally. On the other hand, the skin is a very complex and tight membrane, which born to avoid the absorption of exogenous molecules. In particular, the outermost layer of the skin, namely the stratum corneum, represents the main barrier unit. Observed in longitudinal section, the stratum corneum is composed of several columns of elongated, flat and highly keratinized cells, the corneocytes, which are organized in clusters of overlapped cells, sustained by a protein scaffold of keratin filaments. The extracellular spaces instead are filled with a highly dense and crystalline lipid matrix, organized in periodic lamellae. However, the architecture of the stratum corneum presents some discontinuities since, at the lateral junctions of corneocytes, the incomplete overlapping of the cell membranes leads to the formation of some hydrophilic furrows. Moreover, hydrophilic channels with a diameter ranging from 0.4 to 36 nm are also present. The existence of such "nanopores" raised the interest in exploiting the nanotechnology to improve the therapeutic performances of the drugs applied on the skin. In the era of the "*nano*", several nanocarriers (polymeric and metallic nanoparticles, solid-lipid nanoparticles, nanogels, lipid and surfactant based vesicles) have been investigated as a means to deliver therapeutic molecules up to the deepest skin layers. Besides the different attempts made, a huge number of contrasting results about the efficiency of these nanosystems are reported and most of them derive from the use of different animal species and experimental conditions. Up to now, the most promising results have been obtained only using highly fluid and deformable carriers, such as transferosomes, ethosomes and transethosomes or nanoparticles having a loose structure, such as nanogels. In particular, the deformable lipid vesicles have been largely studied and exploited to deliver in and through the skin both small molecules and biological drugs. The great advantage of these lipid vesicles is their supposed ability to assure the drug release only at the epidermis/dermis level. However, many mechanistic aspects about the penetration of lipid vesicles through the skin remain unclear and only few nanocarriers for cutaneous administration are currently in clinical studies. In conclusion, despite the great efforts made in the field in the last 30 years, we are still fighting for the development of a nanocarrier to be applied on the skin for the treatment of severe pathologies.