"The role of the conformational profile of polysaccharides on skin penetration: the case of hyaluronan and sulfates thereof"

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Purpose. To provide a relationship between diffusion processes of hyaluronans (HA) through the human epidermis and their physico-chemical properties. In particular, the present work focused attention on the impact of molecular weight, conformation and polarity on the skin penetration ability of these polysaccharides.
Methods. Low- and medium-molecular weight HA and the corresponding derivatives at two degrees of sulfation (HAS) were tested. The transdermal penetration of HA polymers was experimentally determined by the Franz diffusion cell method using human epidermis as membrane The localization and the diffusion pathway of HA through human epidermis were followed by confocal laser scanner microscopy using a FITC-labeled HA. The possible relationship between the HA conformation and the ability to permeate the human epidermis was studied by in silico molecular dynamics (MD) simulations.
Results. The in vitro experiments evidenced that HAs cross the epidermis mainly through a transcellular route, the higher the molecular weight, the higher the permeated amount. The epidermis resulted more permeable to the HAS than HA and the permeated amount increases with the degree of sulfation. The molecular dynamics study evidenced how the observed permeation behaviour can find compelling explanations in the conformational profiles since the permeation increases with the capacity to assume extended and flexible structures, as encoded by the values of radius of gyration: the highest the value of radius of gyration, the highest the permeated amount.
Conclusions. This work demonstrated that the main parameters that rule the diffusion of small molecules through the skin are not limiting factors for the skin permeation of hyaluronans. These molecules have a great affinity for corneocytes and likely cross human epidermis mainly through a transcellular route, rather than the intercellular one. Moreover, the molecular dynamics study revealed that a simple parameter such as the radius of gyration, which is an expression of the polymer folding, could be used in predicting the extent of the permeation of a homogeneous family of polysaccharides through human skin.