ABSTRACT BOOK ABSTRACTS



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MEDICAL THERAPIES AND PHARMACOLOGY

## RAMAN SPECTROMETRY CHARACTERIZATION OF INGENOL MEBUTATE PENETRATION IN HUMAN EPIDERMIS

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Introduction: Ingenol mebutate (IM) is a recent treatment for actinic keratoses (AK). Its biological effect has been evaluated in some reflectance confocal microscopy (RCM) and histopathological studies. However, its penetration and transformation in the skin has not been studied.

Objective: We evaluated the biological effects and the penetration of IM in the skin by using RCM and Raman spectrometry (RS), respectively.

Materials and Methods: We first identified IM signature by RS. Then we applied 500µg of IM contained in 1 g of commercially available gel on the skin derived from a breast reduction of a man, and we examined by RCM, RS and histological examination the treated and untreated area (at 3 cm distance) at time 0 and 1,2,3,4,5,18, 24 and 48 hours.

Results: IM was characterized by a peak at 2922cm-1 that corresponded to DL-2-methylbuyricacid. However, it was not possible to identify this peak within the treated epidermis.

RCM and histopathological examinations of the treated area showed keratinocyte necrosis (2hrs), lymphocyte exocytosis (3hrs), epidermal disorganization (4hrs), acantholysis (18hrs), pericapillary inflammatory infiltrate (24hrs) and loss of the dermo-epidermal junction (48hrs). Control area showed inflammatory pericapillary infiltrate (1hr) and lymphocyte exocytosis (18hrs).

Conclusions: It was not possible to characterize IM within the epidermis by RS either











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because of its dilution or, more probably, due to its transformation. Since epidermal changes were early and well visible at histology and RCM, IM seems to have a direct action. IM is extracted from a plant Euphorbia peplus and it is very likely that this active ingredient is the result of a natural selection to discourage predators to consume this plant. It is plausible that IM immediately interacts with the animal to cause irritation with a rapid change of its chemical structure, which could explain why we could not find the peak at 2922 cm-1.



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