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Title: A comparison of skin delivery of ferulic acid and its derivatives: evaluation of their efficacy and safety.

Authors: Zhang LW; Al-Suwayeh SA; Hsieh PW; Fang JY

Author's Address: Pharmaceuticals Laboratory, Graduate Institute of Natural Products, Chang Gung University, Kweishan, Taoyuan, Taiwan.

Source: International Journal Of Pharmaceutics [Int J Pharm] 2010 Oct 31; Vol. 399 (1-2), pp. 44-51. *Date of Electronic Publication:* 2010 Aug 06.

Publication Type: Journal Article

Language: English

Journal Information: *Country of Publication:* Netherlands *NLM ID:* 7804127 *Publication Model:* Print-Electronic *Cited Medium:* Internet *ISSN:* 1873-3476 (Electronic) *Linking ISSN:* 03785173 *NLM ISO Abbreviation:* Int J Pharm *Subsets:* In Process; MEDLINE

Abstract: Ferulic acid (FA) can be used as an antioxidant to prevent damage from ultraviolet (UV) radiation and skin carcinogenesis. To this end, the feasibility of the skin absorption of FA and its derivatives was evaluated in the present study. The percutaneous absorption of five compounds into/across porcine skin was measured and compared using Franz diffusion cells. The skin delivery from pH 6 and 9.9 buffers was the highest for ferulic acid ethyl ether (FAEE), followed by coniferyl aldehyde (CD), coniferyl alcohol (CA), FA, and 3-hydroxy-4-methoxycinnamic acid (HMA). The skin deposition and flux of FAEE with a pH 6 buffer were 136 nmol/g and 26 nmol/cm(2)/h, respectively. No significant difference in permeation profiles was observed between the two pH buffers. According to permeation via the skin with different treatments (delipidization, ethanol, and oleic acid treatments), it was determined that the lipid bilayers in the stratum corneum (SC) comprised the predominant barrier for FA permeation. On the other hand, FAEE could easily partition into and penetrate across the skin through intercellular pathways. Nude mouse was used as an in vivo animal model to examine the amount of permeants remaining in the skin. The in vivo skin deposition was generally correlated with the in vitro results. The in vivo skin deposition of FAEE (145 nmol/g) was comparable to that of CD (150 nmol/g). The safety study which examined transepidermal water loss (TEWL), erythema, and the skin pH value demonstrated that the topical application of FA and related compounds for up to 24h did not cause skin irritation. It can be concluded that topical delivery may serve as an efficient and safe route for FA and its derivatives against photodamage.
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Entry Dates: *Date Created:* 20100921

Update Code: 20101210

PMID: 20692328

Database: MEDLINE