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MEETING ABSTRACT

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Bile acids alter clindamycin permeation through the skin: *in vitro* permeability study

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Background: Acne vulgaris affects approximately 9.4 % of the global population, regardless of age, gender, race and skin type. It has been estimated that 11 million prescriptions per year are aimed at treating this dermatosis. Clindamycin-based topical preparations are well tolerated and widely applied in the treatment of mild-to-moderate acne. However, poor bioavailability, restricted drug penetration depth and rising antimicrobial resistance considerably limit their therapeutic efficacy. Penetration enhancement represents a promising and rational strategy to overcome the drawbacks of conventional topical formulations.

Methods: We carried out the skin parallel artificial membrane permeability assay (skin-PAMPA) to examine the skin permeability of clindamycin hydrochloride, alone and in combination with cholic acid (CA) or deoxycholic acid (DCA). Bile acids were used in submicellar concentrations. The measurements were conducted at two relevant pH values (5.5 and 6.5). After the incubation period, clindamycin hydrochloride concentrations in both compartments were determined spectrophotometrically and apparent permeability coefficients (P_{app}) were calculated.

Results: Bile acids altered the skin-PAMPA membrane permeability of clindamycin hydrochloride in a concentration-dependent manner. Both CA and DCA at the highest studied concentration of 100 µM increased the permeability of clindamycin hydrochloride *in vitro*. This effect was more pronounced in the case of CA and at a higher studied pH value of 6.5, which is characteristic of most dermatological indications treated with topical clindamycin preparations.

Discussion: The results of our study suggest that CA is a more promising penetration enhancer for clindamycin hydrochloride in a solution formulation, compared to DCA. Notably, the increase in the drug permeability was more prominent at pH 6.5, typical for inflammatory skin diseases, including acne. This could be explained by clindamycin / cholic acid complex's higher stability than the clindamycin / deoxycholic acid complex, as revealed by molecular mechanics calculations.

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Keywords: clindamycin – bile acids – skin – transdermal application – drug permeability

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