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ACCEPTED MANUSCRIPT

Low systemic exposure and calcemic effect of calcipotriol/betamethasone ointment in

rats with imiquimod-induced psoriasis-like dermatitis

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0. Abstract

Vitamin D₃ (VD₃) analogues-containing ointments are known to occasionally cause

hypercalcemia in psoriasis patients, and the frequency of hypercalcemia is suggested to vary

based on the VD₃ analogue used. In this study, to address the differences in calcemic effects

of VD₃-containing ointments, the calcemic effects of marketed VD₃-containing ointments,

including calcipotriol (Cal), maxacalcitol (Max), tacalcitol (Tac), calcipotriol/betamethasone

dipropionate (Cal/BDP) and maxacalcitol/betamethasone butyrate propionate (Max/BBP)

ointments, were evaluated in a rat model of imiguimod-induced dermatitis. The topical

application of Tac, Max and Max/BBP ointments, but not Cal and Cal/BDP ointments, to the

imiquimod-induced skin lesions significantly induced an increase in the serum calcium level

compared with the vaseline-treated group. Calcemic effect of VD₃ analogues in rats treated

with VD₃-containing ointments was analyzed by evaluating the expression of vitamin D

receptor target genes, such as Cyp24a1, Trpv5 and CalbindinD28k, in the intestine and kidney.

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