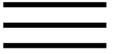


Hydrolysis of a series of parabens by skin microsomes and cytosol from human and minipigs and in whole skin in short-term culture.

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Hydrolysis of a series of parabens by skin microsomes and cytosol from human and minipigs and in whole skin in short-term culture

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Abstract

Parabens are esters of 4-hydroxybenzoic acid and used as anti-microbial agents in a wide variety of toiletries, cosmetics and pharmaceuticals. It is of interest to understand the dermal absorption and hydrolysis of parabens, and to evaluate their disposition after dermal exposure and their potential to illicit localised toxicity. The use of minipig as a surrogate model for human dermal metabolism and toxicity studies, justifies the comparison of paraben metabolism in human and minipig skin. Parabens are hydrolysed by carboxylesterases to 4-hydroxybenzoic acid. The effects of the carboxylesterase inhibitors paraoxon and *bis*-nitrophenylphosphate provided evidence of the involvement

of dermal carboxylesterases in paraben hydrolysis. Loperamide, a specific inhibitor of human carboxylesterase-2 inhibited butyl- and benzylparaben hydrolysis in human skin but not methylparaben or ethylparaben. These results show that butyl- and benzylparaben are more selective substrates for human carboxylesterase-2 in skin than the other parabens examined. Parabens applied to the surface of human or minipig skin were absorbed to a similar amount and metabolised to 4-hydroxybenzoic acid during dermal absorption. These results demonstrate that the minipig is a suitable model for man for assessing dermal absorption and hydrolysis of parabens, although the carboxylesterase profile in skin differs between human and minipig.



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Abbreviations

hCE1, human carboxylesterase-1; hCE2, human carboxylesterase-2; hCE3, human carboxylesterase-3; BNPP, *bis*-nitrophenyl phosphate; MeP, methylparaben; EthP, ethylparaben; ProP, propylparaben; ButP, butylparaben; BzP, benzylparaben; OHBA, 4-hydroxybenzoic acid

Keywords

Parabens; Skin; Carboxylesterases

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