Dermal pharmacokinetics of ketoprofen and its photoproducts in the guinea pig

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Purpose: Transdermal therapeutic systems (TTSs) are widely used in clinical medication because of their advantages over the oral formulations. However, photoallergic reactions induced by UV exposure have been reported in TTS containing ketoprofen (KP). These adverse drug reactions are caused by photoproducts of KP (KP-PPs), but their characteristics in the skin in vivo are not clarified. We evaluate dermal pharmacokinetics of KP and KP-PPs in the skin.

Methods: Mohrus™ tape was applied to the skin of female Hertley guinea pig after the hair shaving. Unbound KP concentration in the skin was monitored by the dermal microdialysis (MD) under the UV-irradiation or non-irradiation condition. The amounts of KP and 3 major KP-PPs, i.e., KP-OH, Ac-KP and Et-KP, in the skin were determined by the extraction method. Binding properties of these compounds to the homogenate of the skin tissue were examined.

Result: Neither of the KP-PPs was detected in MD studies because of their low recoveries to the dialysate. The total mass (KP and KP-PPs) extracted from the UV-irradiated skin is significantly lower than that from the UV non-irradiated skin. Binding ratio of KP-PPs to the skin homogenate was much higher than that of KP.

Conclusion: The higher binding characteristics of KP-PPs than KP suggest that the decrease of the total mass (KP and KP-PPs) extracted from the UV-irradiated skin would be caused not by the changes in tissue binding but by some other physiological factors; such as increase in dermal blood flow by the UV irradiation, photobinding to the skin, and so on.