

Biol. Pharm. Bull., 24, 78-83 (2001).

A protective effect against undesirable increase of dihydroetorphine permeation through damaged skin by using pressure-sensitive adhesive tape with an ethylene-vinyl acetate co-polymer membrane

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The release kinetics of dihydroetorphine (DHE) from pressure-sensitive adhesive (PSA) tape with an ethylene-vinyl acetate co-polymer (EVA) membrane as a diffusion-controlling membrane and its protective effect from an unpredictable increase in skin permeation of DHE caused by stratum corneum damage were investigated. The DHE flux through the EVA membrane was enhanced with the increase of vinyl acetate content. Although the DHE release from the PSA tape was proportional to the square root of the time, the release from the PSA tape covered with the EVA membrane was dominated by zero-order rate. The release rate increased by the addition of isopropyl myristate to the PSA layer, due to the increase of solubility and diffusivity of DHE in the PSA layer, and not a decrease of permeation resistance in the EVA membrane. When using the PSA tape with the EVA membrane, the steady-state flux of DHE through hairless rat skin with stratum corneum damage was not 2-fold more than that through non-damaged skin. Plasma DHE concentration rose promptly above 5 ng/ml after the application of the PSA tape onto the damaged skin in hairless rat. In contrast, when the PSA tape with the EVA membrane was applied onto the damaged or non-damaged skin, plasma concentrations in the both cases were maintained in the therapeutic range (0.2-1.2 ng/ml). These results suggest that the PSA tape with the EVA membrane can be used to protect from the unpredictable increase in skin permeation of DHE due to stratum corneum damage.