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## Enhancing Effect of Chiral Enhancer Linalool on Skin Permeation of Naproxen

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### Abstract

**Objective:** To investigate the permeation-enhancing effect of dl-linalool, d-linalool, and l-linalool on model drugs across excised rat skin and the effect of linalool on the ceramides in stratum corneum lipids.

**Methods:** In vitro skin permeation studies were performed with Valia-Chien diffusion cells, and the permeation samples were analyzed by high performance liquid chromatography with chiral stationary phase. Infrared spectroscopy was used to investigate the effect of linalool on stratum corneum lipids.

**Results:** When the donor vehicles added with 1% dl-linalool, 1% d-linalool, or 1% l-linalool, the steady-state skin permeation rate of naproxen was  $(2.47 \pm 0.63)$ ,  $(1.53 \pm 0.54)$ ,  $(1.73 \pm 0.48)$   $\mu\text{g}\cdot\text{cm}(-2)\cdot\text{h}(-1)$ , respectively, which is 2.49, 1.55, and 1.75 times (all  $P < 0.05$ ) compared with control group  $[(0.99 \pm 0.42)\mu\text{g}\cdot\text{cm}(-2)\cdot\text{h}(-1)]$ , and the differences were statistically significant (all  $P < 0.05$ ). The permeation-enhancing effect of dl-linalool on naproxen was found significantly greater than that of d-linalool and l-linalool (both  $P < 0.05$ ). Compared with the control group, the stratum corneum treated with dl-linalool shifted to higher wave number on  $2.09\text{ cm}(-1)$  of asymmetric CH<sub>2</sub> stretching vibrations in attenuated total reflection-fourier transform infrared spectroscopy analysis. However, stratum corneum treated with d-linalool and l-linalool did not display this phenomenon.

**Conclusion:** The disturbing degree of dl-linalool on stratum corneum lipids (ceramides) is different from that of linalool enantiomers, suggesting their different enhancing effect on the same drug.

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