ジクロフェナックナトリウムの in vitro ラット腹部皮フ透過：油脂の選択とアルコール添加の影響

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In Vitro Transport of Sodium Diclofenac across Rat Abdominal Skin: Effect of Selection of Oleaginous Component and the Addition of Alcohols to the Vehicie

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ABSTRACT The *in vitro* percutaneius transport of sodium diclofenac from various oil vehicles was examined using rat abdominal skin as a modeel skin membrane. The overall transport of diclofenac through the skin from the oleaginous vehicles was very poor because of a poor solubility of sodium diclofenac in nonpolar oils. To increase the solubility and the permeability of sodium diclofenac, ethanol and n-octanol were added to each oil (designated as the formulated vehicles). The addition of ethanol and n-octanol to the nonpolar vehicles resulted in an extreme increase in drig solubility in each vehicle, with a remarkable increase in the permeation of diclofenac. The effects of oil components in the formulated vehicle on the permeation of diclofenac across the skin were in the following order: squalane≧squalene>liquid paraffin>middle chain triglyceride>olive oil>castor oil.

In order to clarify the reason for the differences in permeation of diclofenac from these formulated vehicles, the release of diclofenac and *n*-octanol from these vehicies *in vitro* was studied. The release rates of *n*-octanol from the formulated vehicles were in the following order: liquid paraffin>squalene≧squalane>middle chain triglyceride≧olive oil>castor oil, On the other hand, a linear correlation was odserved between the initial release rate of diclofenac from ths formulated vehicle

and the *in vitro* permeation of diclofenac through the rat skin. Thus, the oil component in the formulated vehicie affects the release of the drug and the enhancer from the vehiclc to the skin. The transport rate of diclofenac from the formulated vehicle of squalane at the steady state proportionally increased with an increase of drug concentration, and the lag times were not influenced by a change of the drug concentration in the formulated vehiciec. Therefore, it may be suggested that the intrinsic permeation of diclofenac through the skin is not influenced by the concentration of sodium diclofenac in the vehicle. From these results, it is considered that the important factors in increasing the skin permeation of a drug from an oil vehicle are to select oils which have a low affinity for the drug and enhancer, and to increase the drug concentration in the oil.

抄録　ジクロフェナックナトリウム（D.Na)の皮フ透過を，ラット腹部皮フを用いて，in vitroで検討した。DNaを油脂に加えただけでは，皮フ透過は認められらいが，アルコール類の添加により，透過量は増加した。その増加程度は，基剤としての油脂の種類により異る。

油性基剤からの皮フ透過性向上の為には，使用油脂の選択が重要であり，油脂中の薬物の溶解度を増加させる工夫が必要である。

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