

Role of stratum corneum lipid in partitioning of water soluble drug: ^{31}P -NMR as probe

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Objectives of this study were (a) to determine the structure (or arrangements of bilayers in Stratum Corneum, SC) by NMR, (b) and to study the role of these lipid bilayers in partitioning of water soluble drug (Amitriptyline HCl, AMH). The apparent partition coefficient of AMH in different systems [n-octanol/buffer(pH 7.4), iso-propylmyristate/buffer(pH 7.4), mineral oil/water] was determined (Cordero et al., 1997). Apparent partition coefficient (K_{app}) for AMH between SC (untreated and treated) and buffer (pH 7.4) were determined by the depletion method. As can be seen from Table 1, the apparent partition coefficient values of AMH in all the solvent systems is a good indication that AMH partition well into the skin. In all these systems physicochemical properties of solvent is correlating with behavior of drugs in the skin especially in SC. These solvent systems are same as SC from physicochemical point of view [like solubility parameter (δ) of n-octanol is equal to SC ($\delta=10$) and polarity-nonpolarity balance in IPM mimic the SC environment] but still these are not able to predict the drug permeation or partitioning behavior in SC exactly because each solvent system is simulating only a part of SC environment, not a single solvent system simulating whole environment as in SC. Hence, partition coefficient of the drug was determined in SC/buffer system.

The results of ^{31}P -NMR (Bruker, 300 MHz) showed that the lipids were organized in the form of bilayers and these bilayers are arranged in hexagonal shape [Fig-1(a)]. Thus in case of intact SC hydrophilic region of lipids act as probe to retain the water on the surface of SC. Hence the partition coefficient of drug in intact SC was higher than that of in a delipidized

SC. The reason for lower partition coefficient value in delipidized SC is destruction of all ordered structure (hexagonally arranged lipid bilayer) by extraction of lipids from the SC [Fig-1(b)] and thereby resulting in decreased water retaining capacity of SC.

Table 1: Partition Coefficient in different systems

System (n=3)	Mean (\pm S. D.)
n-Octanol/ Buffer (pH 7.4)	36.57 (2.05)
IPM/Buffer (pH 7.4)	9.85 (0.62)
MO/Water	14.34 (0.95)
SC (untreated)	0.83 (n=2)
SC (treated)	0.116 (0.021)

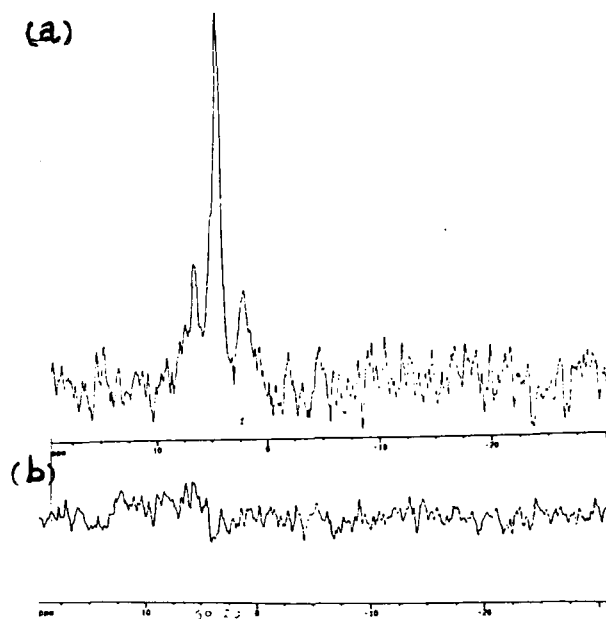


Figure 1: ^{31}P -NMR of (a) untreated SC, and (b) hexane treated SC.

Cordero JA, Alarcon L, Escribano E, Obach R, Domenech J., (1997) J. Pharm. Sci., 86: 503-507.