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•	(III)
•	Construction of Quantitative Structure Permeability Relationship (QSPR) with Skin Permeability Normalized to Biological Parameters/Genetic Polymorphism of Individual Skin (III)
•	• NSC95-2320-B038-002
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•	9508 ~ 9607
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•	Permeability; QSPR; TEWL
•	(permeability) (QSPR) (Ko w) aspirin diclofenacsodium diflunisal flufenamicacid ibuprofensodium ketoprofen nabumetone naproxen piroxicam tenoxicam BALB nu ( ) QSPR (clogP 2 clogP 2) QSPR kp kp

clogP>2 clogP<2 3
(transcellular) (intercellular) (transappendageal)
(clogP<2) (clogP>2)
intercellular transcellular
intercellular ( )
QSPR

- Skin permeability is used as a key parameter for describing the percutaneous transport of solutes, and as such, it is essential for designing and evaluating the efficacy of drug delivery system through the skin. Historically, quantitative structure-permeability relationships (QSPR) have been constructed between the average permeability coefficient (kp) of solutes through the skin and their molecular weight (MW) and octanol water partition coefficient, Ko w. However, it was recognized that QSPR model evaluation should take into consideration of the possible impact of biological parameters of skin (transepidermal water loss (TWEL), hydration content, lipid content, resonance running time, and elasticity) on drug permeation and the permeation through different penetration routes in the skin for those drugs with different lipophilicity (calculated octanol-water partition coefficient, clog P) was influenced by various physicochemical factors of drug at different extent. In this study, the in vitro permeation study of ten model drugs divided into two groups (clog P < 2, ibuprofen sodium, diclofenac sodium, flufenamic aicd, aspirin and tenoxicam; and clog P > 2, ketoprofen, naproxen, piroxicam, nabumetone and diflunisal) through individual nude mice skin was examined to determine individual kp and the biological parameters for each individual skin were measured as well. The MW and clog P of model drugs and the biological parameters of skin all were then taken into consideration in the construction of QSPR model for individual kp. The preliminary results show that a simple relationship between the kp and the MW and clogP of ten model drugs was obtainable: 0.61). TEWL MW Both relationships demonstrate that except MW and clog P, TEWL was the only biological parameters of the skin was statistically examined to be positively influential at the similar extent on kp for both groups of model drug. The MW and clog P of drugs have the same negative and positive effects, respectively, on kp for two groups of drugs with clog P > 2 and clog P < 2, but the influential extent for the former greater than that for the latter. In terms of three main routes for drugs penetration through the stratum corneum: transcellular, intercellular and transappendageal route, hydrophilic drugs (clog P < 2) might be mainly transported through the transcellular pathway while lipophilic drugs (clog P > 2) through the intercellular pathway. It was reasoned that lipid compositions and integrity in the intercellular route might have greater influence on drug permeation in term of molecular size (MW) and lipophilicity than that for the transcellular route that was filled with hydrophilic and fibrous keratin. In conclusion, QSPR model evaluation for kp based on the lipophilicity of model drugs could be statistically improved with taking into consideration of the biological parameters of the skin.