mucoadhesive liquid suppository system using sodium chloride could be further developed as a more convenient and effective rectal dosage form for diclofenac sodium.

[PE1-7] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Synthesis and In vitro Evaluation of Diclofenac Prodrugs for Improved Dermal Delivery

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Synthesis and In vitro Evaluation of Diclofenac Prodrugs for Improved Dermal Delivery
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Purpose. To synthesize and evaluate alkyl esters of diclofenac as potential dermal prodrugs of diclofenac.
Methods. The prodrugs of diclofenac were synthesized, and their physicochemical properties such as solubilities, pKa's and stabilities in buffered solution and in hairless skin and liver were investigated. The permeation study of prodrugs across hairless mouse skin was carried out employing flow-through diffusion cell.
Results. The methyl- and ethyl ester prodrugs showed higher lipid solubilities in terms of octanol-buffer partition coefficients(log Papparent) of 5.5 and 5.1 at pH7.0, respectively, when compared with diclofenac. They possessed moderate chemical stability in aqueous solutions of various pH's except strong acidic and basic conditions and were readily converted to diclofenac in hairless mouse skin and liver. The prodrugs showed a higher flux across the hairless mouse skin than diclofenac, with a maximum enhancement of 2.6-fold compared to diclofenac. They, however, showed shorter lag time than diclofenac did, and poor aqueous solubilities. They were ca. 1000 times more soluble in propylene glycol than in aqueous solution. Methyl- and ethyl ester prodrugs had the pKa of 6.9 and 7.2, respectively.
Conclusion. Alkyl ester prodrugs of diclofenac could be a potential candidate for improved dermal delivery of diclofenac.

[PE1-8] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

In Vivo Absorption of Poorly Soluble Drug According to Use of pH-Dependently Soluble Polymer as Carrier

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It has been examined the possibility of water insoluble drug into more soluble form using various polymers, which show pH-dependent solubility, i.e., entero-soluble or gastro-soluble polymers.
The final compositions manufactured using both kinds of polymers revealed very different dissolution profiles according to the pH of media as expected. In the case of using Eudragit L100 as an enteric polymer, the model drug was released in nearly intermediate pH much faster and more than the case of using gastro-soluble one, Eudragit E100. This was vice versa in the acidic pH, i.e., faster and more dissolution of latter composition.
According to the followed in vivo absorption experiment with rat, both compositions showed greatly different absorption behavior. Unlikely as expected, the composition containing gastro-soluble polymer revealed to show very reduced absorption, which was lower than that of extract itself. On the other hand, enteric polymer-containing composition had a good absorption behavior, much higher