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

than former gastro-soluble polymer-containing one and extract itself.
Consequently, the use of enteric polymer as the carrier for improving the absorption is more possible than gastro-soluble one in spite of its nearly complete dissolution in gastric circumstance.

[PE1-9] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Controlled Release of Triprolidine from EVA membrane

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Oral administration of triprolidine, antihistamines, may cause many adverse effects such as dry mouth, sedation, dizziness, and transdermal drug delivery was considered. EVA (ethylene vinyl acatate) membrane which is heat-processible, flexible, inexpensive material was used for transdermal drug delivery. The permeability of triprolidine through EVA membrane was studied. The EVA matrix containing triprolidine were fabricated and the release patterns were observed. The effects of polyethylene glycol 400, membrane thickness, drug concentration, temperature, and vinyl acetate content of EVA were studied. The solubility of triprolidine increased exponentially as the increased volume fraction of PEG 400 in saline. The release rate of drug from EVA matrix increased with increased temperature, loading dose, and vinyl acatate content of EVA. The EVA membrane might be useful for the development of transdermal drug delivery system.

[PE1-10] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Solubilized formulations of ibuprofen in soft capsule employing SMEDDS

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Ibuprofen, a poorly water soluble nonsteroidal antiinflammatory drug was incorporated in self-microemulsifying drug delivery system(SMEDDS) to improve oral absorption and bioavailability. First of all, solubility of ibuprofen in various ingredients was determined to optimize SMEDDS formulations, revealing the results of several hundred times higher solubility in oils and surfactants than that of water. Phase diagram with various regions including microemulsion area was depicted. Secondly, comparative dissolution tests were carried out under the various conditions of different media with two generic tablets from different company as control preparation. Soft capsules of SMEDDS formulation showed the better dissolution profiles, especially in acidic condition, than the other controls. For the period of 2 hr dissolution in pH 1.2 medium, it reached over 70% dissolution from soft capsules, compared to less than 40% dissolution from control tablets. Finally, in vivo pharmacokinetic parameters were obtained after an oral administration of ibuprofen preparations to Sprague-Dawley rats. SMEDDS formulations of ibuprofen showed higher Cmax with greater AUC(0-12hr) than the suspension of control tablets or ibuprofen powder. Therefore, it is possible to conclude that a newly developed soft capsules containing SMEDDS-formulated ibuprofen might provide an alternative preparation to improve oral bioavailability of water-insoluble ibuprofen.

[PE1-11] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Development of Targeted Gene Delivery Systems

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