[PE1-5] [04/19/2001 (Thr) 15:30 - 16:30 / Hall 4]

Transdermal Controlled Delivery of Tenoxicam: 1. Effects of Vehicles and Enhancers

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Purpose: To evaluate the effect of various vehicles and penetration enhancers on the percutaneous absorption of tenoxicam, a non-steroidal anti-inflammatory drug of oxicam type.
Methods: Permeation studies were conducted using a side-by-side permeation system. Receptor compartments of cells were filled with 40% polyethylene glycol 400 (PEG 400) in normal saline and donor compartments were dosed with saturated solutions of tenoxicam in various vehicles. Vehicles used were water, ethanol, PEG 400, propylene glycol (PG), propylene glycol laurate, diethylene glycol monoethyl ether (DGME), propylene glycol monocaprylate (PGMC), propylene glycol monolaurate (PGML), oleyl alcohol (OAl), isopropyl myristate and propylene glycol dicaprylate/caprate. Cosolvents used were mixtures of DGME/PGMC, DGME/PGML and PG/OAl. As permeation enhancers, various fatty acids including oleic acid (OAc), linoleic acid (LOAc), capric acid, caprylic acid and lauric acid were added to some vehicles. Triethanolamine (TEA) or tromethamine was also added at 1 % concentration as a solubilizer. Samples (100 μl) were taken over 24 hours and drug concentrations were quantitated using HPLC. Flux, lag time and amount permeated were calculated.
Results: Fluxes were low with neat vehicles (0.1-1.1 μg/cm2/hr). In the effects of cosolvents, both of DGME/PGML and DGME/PGMC showed the highest flux of 20.3±8.0 and 13.5±8.0 μg/cm2/hr at a 4:6 ratio, respectively. The cosolvents of PG/OAl increased the flux up to 100 times and 70 times at the ratios of 8:2 and 5:5, respectively, compared to OAl alone (0.3±0.1 μg/cm2/hr). The addition of OAc and LOAc at 3% concentration to PG markedly increased the fluxes which were 41.8±4.0 and 28.5± 5.0 μg /cm2/hr, respectively, while the other fatty acids did not show any enhancing effects. Also, the addition of TEA or tromethamine, rather, decreased the flux when added to PG with OAc or LOAc in spite of improving the solubility of tenoxicam.
Conclusions: It was suggested that these results would be applied to the fabrication of tenoxicam transdermal delivery system.

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Development of novel thermosensitive and mucoadhesive diclofenac liquid suppository using sodium chloride

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Liquid suppository system composed of poloxamers and bioadhesive polymers such as carbopol, polycarbophil and sodium alginate was easy to administer to the anus and mucoadhesive to the rectal tissues without leakage after the dose. However, a liquid suppository containing diclofenac sodium could not be developed using the bioadhesive polymers, since the drug was precipitated in this preparation. To solve this problem, it has been attempted to develop a novel thermosensitive and mucoadhesive liquid suppository system using sodium chloride instead of bioadhesive polymers. Poloxamer P 407 or/and P 188 were used to confer the thermosensitive gelation property. The mixtures of P 407 (15%) and P 188 (15-20%) existed as liquid at room temperature, but gelled at physiological temperatures. Diclofenac sodium significantly increased the gelation temperature and weakened the gel strength and bioadhesive force, while sodium chloride did the opposite. Furthermore, the diclofenac sodium liquid suppository with less than 1.0% of sodium chloride, in which the drug was not precipitated, was inserted into the rectum without difficulty and leakage and retained in the rectum for at least 6 h. These results suggested that the novel thermosensitive and