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PGE1 has been paid attention as a remedy of impotence by the improvement of blood flow. For the transdermal delivery, we investigated terpenes as penetration enhancer in comparison to oleic acid and lauryl alcohol and their mechanism in the transdermal delivery of PGE1. The terpenes included (S)-(+)-carvone, cineol, eugenol, (R)-(+)-limonene, L-(-)-menthol, menthone, nerolidol at 5%w/v concentrations in 50% ethanol. The penetration rate of PGE1 across excised hairless mouse skin was experimented using Keshary-Chien diffusion cell at 37℃. Fourier transform infrared (FT-IR) spectroscopy, differential scanning calorimetry (DSC) and cholesterol solubility test studies were undertaken to investigate the effect of enhancers on the biophysical properties of the stratum corneum in order to understand the mechanism of percutaneous absorption enhancement of PGE1 by terpenes. The results of permeation studies suggest the eugenol should be the effective penetration enhancer in the delivery of PGE1. In addition, FT-IR results indicate that most terpenes, especially limonene and menthol caused the lipid extraction and DSC data show eugenol and oleic acid clearly increased the average lipid acyl chain disorder of treated sample. The cineol among terpenes has the best cholesterol solubility. The eugenol is found to have an influence on the lipid matrix of the stratum corneum the most significantly.

[PE1-2] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Controlled release of mefenamic acid(MFA) from MFA-soid dispersion system-hollow type suppository inserted polyvinyl alcohol hydrogel capsule

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Solid dispersion system of mefenamic acid, a model poorly water-soluble drug with povidone(K-30) was prepared by the solvent method to improve its solubility. A marked increase in the dissolution rate of mefenamic acid was attained by solid dispersion system. Hollow type suppositories inserted polyvinyl alcohol(PVA) hydrogel capsule were prepared using Witepsol H-15 as a base to improve the controlled release of drug. Mefenamic acid was loaded in both hydrogel capsule and suppository base. The hollow type suppositories with capsule significantly retarded release rate of drug as compared with hollow type suppositories without capsule and conventional suppositories. When the suppositories loaded with mefenamic acid in both hydrogel capsule and base were administered to rats, controlled release of drug was observed from the plasma concentration-time profile. These suppositories showed the enhancement of both AUC and MRT of drug compared with those of control suppositories. The application of the hollow type suppositories inserted PVA hydrogel capsule might be beneficial to not only water-soluble drug but poorly water-soluble drug in the controlled rectal delivery of drug.

[PE1-3] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

in vivo Evaluation of Ketoprofen-Monostearin Pharmacosome

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Ketoprofen, a potent analgesic non-steroidal anti-inflammatory drug, is effective in the treatment

of osteoarthritis, rheumatoid arthritis and the associated arthritic disorders. However, it exhibits gastrointestinal side effect associated with all NSAIDs.
Pharmacosome, which facilitates membrane transfer and improves bioavailability. can be defined as a colloidal dispersion of drugs covalently bound to lipids.
KT-pharmacosome(ketoprofen-monostearin pharmacosome) was synthesized from ketoprofen and monostearin.
This thesis evaluates the bioavailability and the ulcerogenic activity of KT-pharmacosome.
KT-pharmacosome was administrated intravenously, orally and intramuscularly to rat and the pharmacokinetic parameters were compared. In addition, ulcerogenic activity was observed.
Compared with the application of ketoprofen, KT-pharmacosome significantly increased the Cmax AUC and bioavailability of oral administration. After oral administration of ketoprofen and KT-pharmacosome, the average number of ulcer index was investigated. KT-pharmacosome was 0.6 times less irritating to the gastric mucosa than ketoprofen.
This thesis confirms ketoprofen-monostearin pharmacosome formulation improves the bioavailability and reduces the gastrointestinal side effect.

[PE1-4] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

ME-based Hydrogel Containing Lidocaine for Premature Ejaculation

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Several topical preparations containing lidocaine, a widely used local anesthetic agent, have been developed and marketed recently for the treatment of premature ejaculation. In this study, microemulsion(ME)-based hydrogels containing lidocaine were prepared by dispersing ME to hydrogel bases such as carbomer gel, sodium alginate gel, and sodium carboxymethylcellulose gel. Lidocaine-containing ME was thermodynamically stable and has a diameter ranging from 10 to 100nm. In vitro skin permeation of lidocaine from ME-based hydrogels followed apparent zero-order kinetics. ME-based hydrogel showed higher drug permeation during fifteen minutes compared with alcoholic hydrogel, reference preparation. On the other hand, tail flick test in rats was introduced to compare in vivo local anesthetic effects of different hydrogels, showing the superior results with ME-based hydrogel. In optical microscopy observation, recrystallization of lidocaine was observed within 5min after application of reference hydrogel, but there was no change in ME-based hydrogels even after 30min. This result indicated that ME-based hydrogels had some advantages of the increased skin penetration, controlled release and physical stability compared with alcoholic hydrogels. Finally it is possible to conclude that ME-based hydrogels containing lidocaine could be a good topical delivery system for the treatment of premature ejaculation.

[PE1-5] [10/19/2000 (Thr) 15:00 - 16:00 / [Hall B]]

Synthesis and in vitro Evaluation of Ketoprofen -Monostearin Pharmacosome

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Pharmacosome can be defined as a colloidal dispersion of drugs covalently bound to lipids and may exist as ultrafine vesicular, micellar or hexagonal aggregates of the drug-lipid complex. Such compound can be a strongly amphiphilic molecule, which facilitates membrane transfer and improves bioavailability. The approach of the pharmacosome can make avoid the problems of the drug incorporation into the liposome, the drug leakage from the carrier and the insufficient shelf stability.