4.58). Methods. Topical gels containing PGE1 (0.5 %) and PGE1-EE (0.1 %) were formulated with ethanol and propylene glycol as a vehicle, selective terpenes as a penetration enhancer, and HPC-H as a thickening agent. In vitro skin penetration profiles of the drug through the rat's dorsal skin using modified Franz diffusion cell were observed by the simultaneous HPLC assay of [PGE1] and [PGE1-EE] in the receptor compartment. Results. In the skin penetration study for 6 hr, combination of ethanol and propylene glycol in 1:3 v/v ratio as a vehicle increased the flux of PGE1 and its ethyl ester up to 15- and 3-fold, respectively, showing the result of an order of magnitude difference compared to the control formulation (ethanol only). In addition, employment of terpene enhancers to the above gel system further increased the flux of both drugs in decreasing order as follows: limonene > cineole > menthone≥carvone > thymol, which was consistent with the degree of lipophilicity. Limonene which possessed the highest lipophilicity (log P of 4.58±0.23) provided the greatest enhancement for PGE1 and its ethyl ester, revealing increased flux about 6- and 7-fold, respectively. Conclusions. Terpene enhancers in combination with the selective cosolvent mixture in gels exhibited pronounced enhancement for skin penetration of the tested drugs. And the lipophilicity of the enhancer showed a key role in the penetration enhancement.

[PE1-2] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Pharmacokinetic behavior of lipid nanodispersion system for parenteral delivery of paclitaxel in rats

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Purpose. Paclitaxel has demonstrated significant activity in clinical trials against a wide variety of tumors. The clinical application of Taxol®, a commercial product of solubilized paclitaxel with cosolvents of ethanol and Cremophor, however, has been limited largely by hypersensitivity of the excipient. The aim of this study was to formulate paclitaxel-loaded lipid nanodispersions (Px-LN) for i.v. administration without toxic excipients, and to evaluate in vitro characteristics and in vivo pharmacokinetic behaviors. Methods. Hot homogenization method was adopted to prepare Px-LN using a Microfluidizer. The mean diameter and polydispersity index (PI) of LN were determined by PCS. Zetapotential was measured by Zetasizer. The content of paclitaxel in the LN was analyzed by HPLC after dilution with 60% acetonitrile. Px-LN or the reference formulation (Taxol®) at a dose of 5 mg/kg as paclitaxel was given to male Sprague-Dawley rats through the femoral vein for 30 sec. Blood samples were deproteinated with acetonitrile and assayed for paclitaxel by the validated HTLC/MS/MS method. Results. Paclitaxel was successfully incorporated into the lipid nanoparticles with mean particle size of 50 nm (PI<0.3) and the zetapotential of -40mV, which considered to be acceptable for intravenous administration. The content of paclitaxel in the LN was ca. 1.5 mg/ml. The formulation of Px-LN was stable for over 8 months under refrigerated condition. The AUC of Px-LN was 1.7-fold higher than that of Taxol®. The elimination half-life of paclitaxel in terminal phase for the Px-LN was increased more than two times compared to Taxol®. Conclusion. The incorporation of paclitaxel in lipid nanodispersion could increase the bioavailability resulted in extended blood level of the drug with reduced elimination. The LN might be a prospective carrier for the parenteral delivery of water-insoluble lipophilic drugs.

[PE1-3] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Improvement of bioavailability of poorly water□soluble drugs by size reduction technique.

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The prolonged mechanical grinding process may enhance the bioavailability of the drugs due to the change of solid state such as micronization and decrease of crystallinity. A series of attempts to enhance the bioavailability of insoluble drugs have been made by the fine grinding technique using a planetary mill. The objective of the present study is to investigate the possibility of improving the dissolution properties of poorly water- soluble drugs