

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**

CHOI Sung-Up<sup>o</sup>, Lee Jung-Min, Lee Byoung-Moo, CHOI Young Wook  
*College of Pharmacy, Chung-Ang University, SEOUL 156-756, KOREA*

Purpose. Paclitaxel has demonstrated significant activity in clinical trials against a wide variety of tumors. The clinical application of Taxol<sup>2</sup>, 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<sup>3</sup>) 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<sup>2</sup>. The elimination half-life of paclitaxel in terminal phase for the Px-LN was increased more than two times compared to Taxol<sup>2</sup>. 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.**

Choi Wookik<sup>o</sup>, Kim Hyun Il, Kwak Seong Shin, Choi Hee Kyu, Ha Jong Hak, Hwang Sun Hwan, Lee Dong Beom  
*Pusan National University*

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

such as diphenyl hydrantoin (phenytoin) and diphenyl dimethyl dicarboxylate (DDB) based on the molecular interaction between drug and additives during pharmaceutical processing to be related with the bioavailability behavior. Here, the characterization on molecular interaction present drug and additives occurred during grinding pharmaceutical process was mainly measured using particle size analyzer. It was confirmed based on The data from in vitro test for bioavailability of solubility and dissolution rate is that the solubility data of ground samples could be improved by decreasing the particle size of ground samples and the solubility of nano-sized particle by a nanomizer was significantly enhanced higher than intact DDB.

**[PE1-4] [ 2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function ]**

### **The Study of Stability of Oral Pharmaceutical Liquid Preparation II**

**Kang Min Kyung**<sup>o</sup>, Park So Min, Choi So Young, Kim Kil Soo

*College of Pharmacy , Ewha Womans University*

The available period of oral pharmaceutical liquid preparations was decided according to the study of the stability of unopened preparations. But if one reuses the drug after opening the sealed cap , the major components of the drug could change in quality. In addition, there isn't any accurate information about the available period of opened oral pharmaceutical liquid preparations. In this study, a long term test, an accelerated test and a microbial limit test are run with C ( pseudoephedrine and triprolidine ), D ( ibuprofen ) that are marketed and used frequently . Sample products are stored as the state of CLOSE ( store it as initial marketed form, unopened ) and the state of C/O ( open and close cap regularly after opening it ) .The results from above two states are analyzed comparing with each other. The active substances of each product are assayed by HPLC method described in compendial monographs. In the long term test, there wasn't any significant change of active substances until 4 months. Syrups stored in each condition in the long term test didn't show any significant change in physical testing of pH, color, and odor. But in accelerated test, the change of active substances is greater than that in the long term test and is proportional to temperature. In the microbial limit test , any bacteria and fungi have not been observed until 3 months.

**[PE1-5] [ 2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function ]**

### **Poly(l-lactide) membranes with biomimetic nanolayer for bone induction for tissue regeneration**

**Chung Jieun**<sup>o</sup>, Lee Jue-Yeon, Kim Kyung Hwa, Baek Hyun Jin, Ku Young, Chung Chong Pyung, Lee Seung Jin  
*Department of Pharmacy, College of Pharmacy, Ewha womans University, Seoul, Korea, Department of Periodontology, College of Dentistry, Seoul National University, Seoul, Korea*

The healing of a bone defect is complex, and involves a wide range of cellular, molecular, physiological, and biological processes. The main effect of bone substitute is to promote wound healing by induce cell proliferation. Bone defect sites usually are localized below the original bone surface; therefore, space production and maintenance between the membrane and the original bone surface is essential. As a result, membranes must have proper mechanical strength to prevent the collapse of the soft tissue and maintain wound space that permits bone growth. In addition, biodegradability is further required to avoid second retrieval surgery. In our study, porous membranes of poly (L-lactide) (PLLA) were fabricated to provide and maintain sufficient space for bone growth. Collagen, gelatin, chitosan have been widely used as biomaterials, and these may be attractants for osteoblasts wound repair. In this work, the focus was on the nanofibers or nanoparticles of collagen, gelatin and chitosan modified PLLA membranes by electrospinning method, and to investigate their effects on the physico-chemical and biological property of the materials.

**[PE1-6] [ 2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function ]**

### **Intravenous and Intra-arterial Delivery of Plasmid DNA/Cationic Lipiodol Emulsion**