

pharmacokinetic parameters and the bioavailability of paclitaxel(50mg/kg) orally in rats. The plasma concentration of paclitaxel pretreated with quercetin(pretreated group) were increased significantly ($p<0.01$) compared to that of control, but those of paclitaxel combined with quercetin(combined group) were not affected. Area under the plasma concentration-time curve (AUC) of paclitaxel pretreated with quercetin was significantly ($p<0.01$) higher than that of control. Peak concentration (C_{max}) of paclitaxel pretreated with quercetin were significantly increased ($p<0.01$) compared to that of control. Time to peak concentration (T_{max}) of paclitaxel pretreated with quercetin decreased significantly ($p<0.05$) than that of control. Half-life ($t_{1/2}$) of paclitaxel pretreated with quercetin was significantly prolonged ($p<0.05$) compared to that of control. Based on these results, it might be concluded that quercetin may enhance bioavailability of paclitaxel due to the inhibition of cytochrome P450 and P-glycoprotein, which are engaged in paclitaxel absorption and metabolism in liver and gastrointestinal mucosa, respectively.

[PE2-21] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Bioequivalence of Two Enalapril Maleate Tablets (Enalapril maleate 20 mg)

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Bioequivalence of two enalapril maleate tablets, formulation A and B, was evaluated according to the Korean Guidelines for Bioequivalence Test (KGBT 2001). Twenty healthy male volunteers (19–27 years old) were randomly divided into two groups and a randomized 2x2 cross-over study was performed. Following oral administration of enalapril maleate tablets (20 mg dose), blood sample was taken at pre-determined time intervals and the concentrations of enalapril in plasma were determined using LC-MS. A statistical difference of bioavailability parameters (AUClast, C_{max} , and T_{max}) between the two formulations was tested by ANOVA(EquivTest ver 2.0, Statistical Solutions Ltd.). The result showed that the differences in AUClast, C_{max} , and T_{max} between the two formulations were 3.36%, 0.44%, and -1.11%, respectively. Ninety percent confidence intervals of Log(AUClast) and Log(C_{max}) were 0.9829~1.2002 and 0.9491~1.1237, respectively.

[PE2-22] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Plasma Pharmacokinetics and Urinary Excretion of Isoflavones After Ingestion of Soy Products with Different Ratio of Aglycone/Glucoside in Korean women

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Lately, soybeans have received considerable public attention for their potential roles in the prevention of the chronic diseases. Epidemiologic study showed that Asian countries have significant health benefits because of the high contents of the isoflavones in their traditional diets(soybean-rich diet). This study was carried out to determine pharmacokinetic parameters of isoflavone in Korean woman. Pharmacokinetic study of three soy products(isogen, soymilk, and fermented soybean) with different ratio of aglycone/glucoside in 26 healthy female volunteers(20-30 years of age) was performed. After ingestion of three soy products, the plasma and urine concentrations of isoflavones were measured by HPLC. The pharmacokinetic parameters were estimated using the WinNonlin program. The plasma AUC of daidzein in soymilk($2101\pm352 \mu\text{g hr/L}$) ingested group was significantly lower than those of isogen($2628\pm573 \mu\text{g hr/L}$) and fermented soybean($2593\pm465 \mu\text{g hr/L}$) ingested group. The plasma C_{max} of daidzein in soymilk($231\pm44\text{ng/ml}$) ingested group was significantly higher than those of isogen($160\pm32\text{ng/ml}$) and fermented soybean($195\pm35\text{ng/ml}$) ingested group. The half-life of daidzein and genistein in soymilk ingested group(5.9h and 5.6h respectively) was significantly shorter than those of in isogen(9.6h and 8.5h respectively) and fermented soybean(9.5h and 8.2h respectively) ingested group. The urinary recovery of daidzein and genistein were 42% and 17% in isogen ingested group, 46% and 23% in fermented soybean ingested group, and 33% and 22% in soymilk ingested group. In conclusion, soy products containing high aglycone forms of isoflavone are more effective than soy products containing low isoflavone

aglycone to maintain the desirable level of isoflavones in plasma. Further works that dose response, durational, and interventional studies will be required to contribute to efficiency of soyfoods ingestion for the increase bioavailability of isoflavone that influence the human health.

[PE3-1] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Iron succinyl casein encapsulated alginate beads for the treatment of iron deficiency anemia

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Iron deficiency is the most common nutritional problem worldwide. Oral iron supplementation programs have failed because of noncompliance and gastrointestinal toxicity. The purpose of this study was to explore the possibility of alginate gel bead as an oral controlled release system of iron supplements and increase the stability of iron succinyl casein (ISC). Alginate beads containing ISC were prepared by the gelation of sodium alginate with calcium cations. The release profiles of ISC were investigated according to the concentration of polymer, the drug/sodium alginate ratio, the concentration and type of cation, curing time and pH of calcium chloride solution. Calcium content according to the curing time and weight distribution of alginate gel beads were observed. An interaction between alginate and drug was also observed. Stability test was continued for 3 months. Alginate beads were stored inside the media such as calcium gluconate solution. The drug release from alginate gel beads at pH 6.8 showed nearly zero order release rate which was more rapid than that at pH 1.2. Encapsulation efficiencies for ISC were more than 96%. Scanning electron microscopy revealed differences among the types of cation. Alginate beads were moderately stable inside the media. Since alginate gel beads of iron supplements were stable and the release of iron supplements could be controlled by the regulation of the preparation of alginate beads, the alginate beads may be used for a potential oral controlled release system of iron supplement such as ISC.

[PE3-2] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Transdermal and topical LMWH delivery from ultradeformable and other vesicles: Characterization and in vitro and vivo permeation studies

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To increase skin permeability of LMWH (Low Molecular Weight Heparin), ultradeformable liposomes were developed. Ultradeformable liposomes were developed by Egg phosphatidylcholine (Egg-PC) and edge activator. Entrapment efficiency, vesicle size and zeta potential of vesicles were determined and characterized for deformability and stability. Transepidermal permeation of LMWH was compared to saturated aqueous control in vitro. The steady-state flux and its maximum time were calculated from the flux curves. Skin deposition was also assessed. The effect of various formulations on the transport of LMWH in hairless mouse skin was investigated. Biologic activity of transdermally delivered LMWH was measured by anti-Xa activity. Entrapment efficiency depended on the concentration of Egg-PC. Vesicle size of ultradeformable, conventional liposomes and ethosome were ranged from 82-85nm, 180-188nm, 83-87nm, respectively. Permeation into epidermal membrane of LMWH-loaded ultradeformable vesicle was greater than those of liposome, ethosome and standard solution. A steady-state flux of LMWH in ultradeformable liposome was 0.252 IU/hr.cm². It was a 4.5-fold increase compared to other vesicles. Maximum concentrations of LMWH were 5.72, 1.23 and 2.13 IU/ml, respectively. Skin deposition was increased by 10-fold compared to control. After transdermal administration of LMWH-loaded vesicle in hairless mouse (25 IU/g), the extent of LMWH permeation was dependent of vesicles. Anti-Xa activity increased in ultradeformable liposome. Moreover, transdermal delivery of LMWH resulted in sustained anti-Xa levels in the blood. A peak concentration of 1.2 IU/ml was obtained of 8 hr after transdermal dosing of ultradeformable liposome containing LMWH, exhibiting an absolute bioavailability of 28.7 %. These results suggest that transdermal delivery of LMWH in ultradeformable liposome has the potential to replace injection in humans and also applicable for the topical LMWH formulations.