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Polystyrene (i.e., material for Transwell) and acrylic (i.e., material for Ussing chamber) compounds are frequently found in laboratory wares that are typically used in drug transport studies. However, adsorption of cyclosporin A (CsA), a lipophilic polypeptide, has been recognized as a potential problem in the analyzing of data obtained from transport studies involving these materials. Therefore, the objective of this study is to identify agent(s) that prevents CsA adsorption to the plastic laboratory apparatus. Addition of polyehtylene glycol, a compound that is known to prevent drug adsorption, did not block the adsorption of the drug to Transwell. However, addition of serum reduced adsorption of CsA by more than 95% compared with that found in untreated laboratory wares, probably by a preferential binding of the drug to protein in serum. Therefore, the result suggested that this simple modification may be applicable in the prevention of CsA adsorption in quantitive studies involving Transwell.

[PE1-13] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

The Ultra-fine Grinding Mechanism of Inorganic Powders and surface Modification in a Stirred Grinding Media Mill : Discussion for Mechanochemical Effect

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Recently, the grinding accompanying mechanochemical phenomenon has been researched variously. However, it is difficult to evaluate the mechanochemical phenomenon of the relationship between mechanical energy added in grinding accompanying mechanochemical phenomenon and structure change of material in uniform quantity. The mechanochemical change have widely correlation with chemical reactivity such as dissolution, oxidation, reduction, decomposition, polymerization, synthesis, and physical property, so that the fields of application are very wide and important. In this experiment, the mechanochemical phenomenon of talc, changed into talc with hydrophilic surface when hydrophobic talc is ground in stirred media mill, is studied and applied to surface modification. The results show that the hydrophilic talc is produced when hydrophobic talc is ground finely without any additive due to structure change of talc by grinding. Also, the hydrophilic characteristics are examined experimentally in related with species and addition amount of additives and grinding operation conditions. From the this research, the possibility of controlling hydrophilic characteristic according to experimental conditions was confirmed.

[PE1-14] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

A Study on the Test Methods in Korean Pharmacopoeia(II)

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Dissolution test plays an important role both in the quality control process and in predicting release and absorption behaviors of drug using in vitro test methods. We developed simple matrix systems for the controlled delivery of highly soluble drug, Diltiazem·HCl. Hydroxypropylcellulose (HPC) was used as release-regulating materials. The purpose of this study is to compare in vitro dissolution test with in vivo bioavailability test by in vivo-in vitro correlation. Physical properties of tablets such as hardness, thickness, friability, content uniformity and dissolution profiles were evaluated. Release kinetics of diltiazem from matrix tablets were dependent on pH and HPC contents. As HPC content increased, release rate of diltiazem was slower. In water, simulated intestinal fluid TS without

pancreatin (pH 6.8), cumulative release rate of diltiazem was almost 90 % in 24 hr, but in simulated gastric fluid TS without pepsin (pH 1.2), its cumulative release rate was almost 60 %. And stirring rate and dissolution apparatus did not affect release rate of diltiazem. Diltiazem tablets with three different in vitro release profiles were administered to four dogs. The slower dissolution rate of tablets were, the more bioavailability decreased. And Cmax (ng/mL), Tmax (hr), and AUC (ng·hr/mL) decreased. A significant relationship between MDT 70 and AUC was found (R2=0.94). It can be possible to predict in vivo kinetics of drug through dissolution test in certain conditions. And development and application of various dissolution test are required.

[PE1-15] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Formation of nano-particles of slightly soluble medicines by planetary ball milling:(III) Co-grinding effect of Ursodeoxycholic acid and surfactants

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Dry co-grinding of Ursodeoxycholic acid(UDCA) and surfactants(①Sodium lauryl sulfate, ②Polyvinyl alchol, ③Methyl cellulose) was carried out using a planetary ball mill for its nano-particle sized of UDCA. Purpose of this experiment is to improve bioability of poorly water-soluble drugs.
320 g of zirconium oxide balls of 2 mm diameter and 12~13.5 g of UDCA mixed with 1.5~3 g surfactants(①Sodium lauryl sulfate, ②Polyvinyl alchol, ③methyl cellulose) were loaded into a 372 ㎖ zirconium pot and ground at 112 r.p.m.
Mastersizer(Malvern, U.K) and Image-Bora(Bora Software, Korea) to measure the particle size were used. The powder X-ray diffraction patterns were measured at room temperature with a X-ray diffractometer.
These results indicate that the addition of various surfactants to UDCA leads to form finer particles than the powder ground without any additives.

[PE1-16] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Pharmacokinetics of 2, 4-Dihydroxybenzaldehyde and 3, 4-Dihydroxybenzaldehyde, Constituents of Gastrodia elata, in Rats

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The pharmacokinetics of 3, 4-dihydroxybenzaldehyde(3, 4-HBA), 2, 3-dihydroxy- benzaldehyde (2,3-HBA), constituents of Gastrodia elata(GE), were investigated in rats. GE is an oriental medicinal herb which has been used traditionally for the treatment of various brain disease including convulsion and epilepsy. Male S.D. rats were cannulated in the femoral vein and artery, bile duct and ureter. After i.v administration of 3, 4-HBA and 2, 4-HBA to rats, the concentrations of 3, 4-HBA and 2, 4-HBA in plasma, bile and urine were analyzed by a validated HPLC. Pharmacokinetic parameter values of Cmax, Tmax, AUC, t1/2 and clearance were determined. The AUCs of 3, 4-HBA and 2, 4-HBA were 562.1 and 661.9ug min/ml, respectively. Elimination half lives were 5.0 and 37.6min for 3, 4-HBA and 2, 4-HBA, respectively. MRT of 3, 4-HBA and 2, 4-HBA were 6.0 and 7.3min. Urinary and biliary excretion fraction were small. The data suggest that most of 3, 4-HBA and 2, 4-HBA were eliminated through metabolism. To develop better anticonvulsants, derivatives of HBA with longer biological half-lives should be designed.