[*Chem. Pharm. Bull.*, **48**, 585-588 (2000)] [Lab. of Pharm. Engineering]

Temperature-Induced Crystallization and Compactibility of Spray Dried Composite Particles Composed of Amorphous Lactose and Various Types of Water-Soluble Polymer.

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The purpose of this study was to investigate the temperature-induced crystallization and the compactibility of the composite particles containing amorphous lactose and various types of polymers. The composite particles were prepared by spray-drying an aqueous solution of lactose and various types of gel forming water-soluble polymers. The stabilizing effect of hydroxypropylcellulose and polyvinyl pyrrolidone on amorphous lactose in the composite particles was smaller than that of sodium alginate in comparing at the same formulating ratios. The difference in the stability of amorphous lactose in the composite particles was attributed to the difference in the glass transition temperature (Tg) of the composite particles caused by the polymers formulated. The tensile strength of the composite particles was increased with an increase in water content in the particles. The difference in compactibility of the composite particles containing the different amount of polymer and water could be explained by the difference in Tg of the particles.

[*Advanved powder Technol.*, **11**, 323-332 (2000)] [Lab. of Pharm. Engineering]

In Vitro Inhalation Behavior of Spherically Agglomerated Steroid Particles with Carrier Lactose.

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In order to prepare a dry powder inhalation (DPI) formulation for steroid KSR-592, we designed agglomerates consisting of fine primary drug particles suitable for inhalation by the spherical agglomeration method. The agglomerates easily disintegrated into the primary particles and were deposited on carrier lactose particles by use of a conventional agitation mixer in a short period, e.g., 2-10 min. The inhalation behavior of the DPI formulation evaluated with a twin impinger and a cascade impactor in vitro was determined by the mixing time of the agglomerated crystals with the carrier lactose particles. The DPI formulation prepared by mixing for 2 min showed the highest respirable fraction value compared with the formulations mixed for other length of time.

[*Biol. Pharm. Bull.*, **23**, 274-278 (2000)] [Lab. of Pharmaceutics]

Selection of Mobile Phase in High-Performance Liquid Chromatographic Determination for Medicines.

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A convenient method was developed to select mobile phase to separate drugs commonly used in clinical therapy, using high-performance liquid chromatography (HPLC). The separation conditions determined by this method were similar for each compound. Two kinds of mobile phase, a mixture of acetonitrile-phosphate buffers, pH 4.2 and 2.5, was used and the composition of mobile phase used for a drug in HPLC analysis was systematically determined. According to the proposed method, the composition of mobile phase, with which retention time value was between 4 to 8 min in the isocratic condition, was examined for 75 drugs clinically used. Seventy-two of the 75 drugs were analyzed well in the mobile phase. Using this method, the time required for not only the setting of HPLC conditions but also the analysis will be shortened.

[*J. Biochem.*, **128**, 933-939 (2000)] [Lab. of Pharmaceutics]

Zinc Induces Mixed Types of Cell Death, Necrosis, and Apoptosis, in Molt-4 Cells.

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To investigate the mode of zinc-induced cell death, the associated morphological changes, and biological events were examined in zinc-treated Molt-4 cells. Fluorescence microscope observations of zinc-treated cells indicate that the metal induces both necrosis and apoptosis. The results from flow cytometric analysis confirm that zinc induces mixed types of cell death, necrosis and apoptosis, and that the former induction occurs earlier and at a greater frequency. Although hallmarks of apoptosis such as abnormal chromosome condensation and release of cytochrome c appeared, zinc did not induce increases in caspase-3 like protease and caspase-8 activities, and caused slightly hypodiploid cells. Furthermore, the induction of cell death and annexin-positive cells was not blocked by the caspase inhibitors. These results indicate that zinc induces both necrosis and apoptosis, without caspase-3 activation.