〔Drug Develop. Ind. Pharm., **18**, 919-937 (1992)〕 [Lab. of Pharm. Engineering]

Design of Redispersible Dry Emulsion as an Advanced Dosage Form of Oily Drug (Vitamin E Nicotinate) by Spray-Drying Technique.

HIROFUMI TAKEUCHI, HIDETO SASAKI, TOSHIYUKI NIWA, TOMOAKI HINO, YOSHIAKI KAWASHIMA*, KEIZOU UESUGI, HIROSHI OZAWA

An oily drug, dl-α-tocopherol nicotinate (VEN) was transformed to the newly developed powder form, termed dry emulsion, by spray-drying the emulsified VEN or oily solutions of VEN with additives. The drug releasing property from the resultant particles was dependent on various factors such as the emulsifying method and the type and amount of the oily carrier and surfactant formulated. The desired releasing property was offered by use of medium chain triglyceride (MCT) as the oily carrier and polyoxyethylene-polyoxypropylene-blockcopolymer (Pluronic F-68) or polyoxyethylenesorbitan monolaulate (Tween 80) as the emulsifying agent. The difference in drug releasing property with various formulations was found to be mainly attributed to the differencce in physical state of VEN and surfactant in the dry emusion particle, which was detected by differential scanning calorimetry.

〔Chem. Pharm. Bull., **40**, 1573-1581 (1992)〕 [Lab. of Pharm. Engineering]

Particle Design for Antidiabetic Drug by the Spherical Crystallization Technique. IV. Assessment of Compressibility of Agglomerated Tolbutamide Crystals Prepared by Crystallization Technique.

AKIMITSU SANO, TAKEO KURIKI, YOSHIAKI KAWASHIMA*, HIROFUMI TAKEUCHI, TOMOAKI HINO, TOSHIYUKI NIWA

Three different crystallization methods, *i.e.*, the solvent change (SC) method, neutralization (NT) method and quasi-emulsion solvent diffusion (QESD) method, were employed to prepare agglomerated tolbutamide crystals (referred to as SC-A, SC-B, NT and QESD). Each of the agglomerated crystals or unagglomerated tolbutamide crystals (abbreviated as bulk) alone (single formulation), magnesium stearate (MgSt ; a lubricant)-added single formulation sample (formulation A), and Kollidon CL (a disintegrating agent)-added formulation A samples (formulation B) were compacted into tablets by the direct tableting method. With the objective of elucidating the compressibility of these samples, the following parameters were analyzed : (1) the course of change in the powder bed volume as a function of the applied compression pressure, (2) the pressure-transmission ratio from the upper punch to the lower punch, (3) the course of decompression (ejection force) and (4) the tensile strength of the tablets determined by the diametric compression method. The results of each sample were compared.

〔Chem. Pharm. Bull., **40**, 1911-1916 (1992)〕 [Lab. of Pharm. Engineering]

Preparation of Powdered Phospholipid Nanospheres by Spray Drying in an Aqueous System with Sugars.

YOSHIAKI KAWASHIMA*, TOMOAKI HINO, HIROFUMI TAKEUCHI, TOSHIYUKI NIWA, EIJI KAWAKATSU, MASANORI KAYANO, KATSUMI IDA, HIROSHI OZAWA

Phospholipid nanosphere dispersion was prepared from phosphatidylcholine with or without vitamin E by the heating method. The dispersed particles had diameters of 8.6-150 nm. These nanosphere dispersions were powdered with sugars such as sucrose, lactose and mannitol by spray drying in an aqueous system. The resultant powders, except coformulation with mannitol, consisted of spherical, homogeneous and freely flowing particles, in which the sugar was amorphous. The powder yielded a nanosphere dispersion having almost the same particle size and optical density as the original dispersion when rehydrated with water. The particle size of rehydrated nanospheres with vitamin E increased with the increasing amount of vitamin E coformulated. A water-soluble drug, 5-fluorouracil, could be entrapped in the nanospheres by rehydrating the powdered nanospheres with an aqueous solution of the drug. All the steps from the preparation of the original nanosphere dispersion to spray drying were performed in an aqueous system without using any organic solvent.