[*Int. J. Pharm.*, **172**, 179-188 (1998)] [Lab. of Pharm. Engineering]

Effect of Surface Morphology of Carrier Lactose on Dry Powder Inhalation Property of Pranlukast Hydrate.

Yoshiaki KAWASHIMA,* Takanori SERIGANO, Tomoaki HINO, Hiromitsu YAMAMOTO and Hirofumi TAKEUCHI

The effects of surface morphology of carrier lactose on dry powder inhalation (DPI) property of pranlukast hydrate (PH) were investigated. The PH was mixed with 9-fold weights of carrier lactose, *i.e.* pharmatose 325M, 200M, DCL-11, DCL-21, spray dried amorphous (SDGa), -crystallized (SDGc) lactoses and fluidized bed granulated lactose (FBG) with various surface morphologies. Carrier lactose with higher specific surface area like FBG emitted effectively PH particles, whereas they reduced the respirable fraction, resulting in lower inhalation efficiency. The SDGc having lots of microscopical projection on the surface improving the inhalation efficiency. The SDGa, smoothed sphere particle, did not improve the inhalation efficiency, owing to fairly strong adhesion between PH and lactose particles. Those finding indicated that the separation of drug particles from carrier lactose was a determining step to improve inhalation process for DPIs, as far as lactose particles emitted satisfactorily PH particles from the inhalation device.

[*Int. J. Pharm.*, **173**, 243-251 (1998)] [Lab. of Pharm. Engineering]

Design of Inhalation Dry Powder of Pranlukast Hydrate to Improve Dispersibility by the Surface Modification with Light Anhydrous Silicic Acid (AEROSIL 200)

Yoshiaki KAWASHIMA,* Takanori Serigano, Tomoaki HINO, Hiromitsu YAMAMOTO and Hirofumi TAKEUCHI

A new particle design method was proposed for dry powder inhalation of hydrophobic cohesive drug particles (pranlukast hydrate, D50=2.1μm) by the surface modification with hydrophilic colloidal silica (AEROSIL D50=16nm). The surface of drug particle was modified by compounding AEROSIL (2-10%) under shear with a manually operating mortar (PM method) or a high-speed elliptical-rotor-type mixer (TC method). The surface modifications were also conducted by lyophilizing (FD method) or spray drying (SD method) the aqueous dispersions of the drug and AEROSIL. The inhalation efficiency (EI) of modified particles with TC, FD and SD methods were dramatically increased up to 66.9, 52.7 and 47.7%, respectively, with increasing AEROSIL content. The surface modification to hydrophilic with AEROSIL reduced the cohesive force between the drug particles, owing to the decrease in van der Waals and electrostatic forces, improving the dispersibilities of emitted particles from the Spinhaler.

[*Int. J. Pharm.*, **174**, 91-100 (1998)] [Lab. of Pharm. Engineering]

Spray-dried Composite Particles of Lactose and Sodium Alginate for Direct Tabletting and Controlled Releasing.

Hirofumi TAKEUCHI, Takehiko YASUJI, Tomoaki HINO, Hiromitsu YAMAMOTO and Yoshiaki KAWASHIMA*

A novel composite particle suitable for the filler of controlled-release matrix tablets was prepared by spray-drying an aqueous solution of α-lactose monohydrate and sodium alginate. The spray-dried (SD) particles had an excellent flowing property due to their spherical shape and sharp particle size distribution. When the SD particles were compressed into a tablet (100 -- 400 MPa), the tensile strength of compacts was much higher than that of a commercial lactose for direct tabletting and a physical mixture of lactose and sodium alginate particles. The improvement in compressibility of the SD particles was attributed to an increased deformability of particles with a decrease in crystallinity of lactose. The drug release from the matrix tablet prepared with the SD particles and acetaminophen in JPXIII No. I medium (pH 1.2) was more prolonged than that of a physically mixed tablet of lactose, sodium alginate and the drug, because of the improved gel forming property of sodium alginate formulated in the SD particles.

[*J. Pharm. Sci. Technol., Jpn.*, **58**, 125-135 (1998)] [Lab. of Pharm. Engineering]

A Study of Microwave Sterilizer for Injection Ampules (No. 4): Application to Sterilization of Thermally Labile Drug Solutions.

Koichi SASAKI, Washiro HONDA, Shigemitu OHSAWA, Yasuo MIYAKE and Yoshiaki KAWASHIMA*

A continuous microwave sterilizer (MWS) was developed. The MWS is a new sterilization system using microwave dielectric heating. Here we report the application of the MWS to thermally labile drug solutions whose sterilization was not possible with conventional autoclaving. We selected nine strains of microorganisms with heat resistance close to that of microorganisms found in a bioburden. Each microbial suspension was heated for 12 sec with the MWS at 81–128°C. Microorganisms detected in a bioburden can be reliably sterilized with the MWS at 81–125°C. The deterioration in quality of thermally labile drug preparations (ascorbic acid and pyridoxamine phosphate) following sterilization with the MWS or an autoclave was evaluated. The MWS allows reliable sterilization of thermally labile drug preparations without quality deterioration. When decompositions of the active ingredient following sterilization were compared, no differences were observed in decompositions induced by the two methods of sterilization.