[*J. Controlled Release*, **67**, 29-36 (2000)] [Lab. of Pharm. Engineering]

Utilization of Poly (DL-lactide-co-glycolide) nanoparticles for Preparation of Mini-depot Tablets by Direct Compression.

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The objectives of this study were to prepare the long-acting matrix tablets by direct compression of the mixture of drug and poly (DL-lactide-co-glycolide) (PLGA) nanoparticles and to clarify the effects of such factors as polymer species, mixing ratio of nanoparticles with different molecular weights, and the tablet weight on the drug release and to discuss the mechanism of drug release from matrix tablets. Mini-matrix tablets were prepared to investigate the possibility of application as an implantable dosage form. Matrix tablets with various biphasic release patterns could be prepared by altering the molecular weight or copolymer ratio of PLGA. The addition of nanoparticles of low molecular weight PLGA to those of high molecular weight reduced the release rate at the initial release phase, but that at the second release phase was almost entirely unaffected by mixing ratio. Hydration analysis suggested that the initial release rates were correlated well with the swelling properties of tablets.

[*Pharm. Develop. Technol.*, **5**, 355-363 (2000)] [Lab. of Pharm. Engineering]

Temperature- and Moisture-Induced Crystallization of Amorphous Lactose in Composite Particles with Sodium Alginate Prepared by Spray-Drying.

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The purpose of this study was to investigate the temperature- and moisture-induced crystallization of amorphous lactose in the composite particles prepared by spray-drying an aqueous solution of crystalline lactose and sodium alginate. The temperature-induced crystallization of amorphous lactose in the composite particles was suppressed by increasing the amount of sodium alginate in the particles. The stabilizing effect of sodium alginate on amorphous lactose in the composite particles was greater than that in physical mixtures having the same formulating ratios. The improved stability of amorphous lactose in the composite particles was attributed to an increase in the glass transition temperature (Tg) of the mixture. The Tg values of the composite particles containing sodium alginate were higher than the theoretical line predicted by two components of the Gordon-Taylor equation. These results suggested that there was a specific interaction between the sodium alginate and lactose molecules.

[*Pharm. research*, **17**, 94-99 (2000)] [Lab. of Pharm. Engineering]

Spray-Dried Lactose Composite Particles Containing an Ion Complex of Alginate-Chitosan for Designing a Dry-Coated Tablet Having a Time-Controlled Releasing Function.

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The properties of novel spray-dried lactose composite particles suitable for the coating filler of a dry-coated (DC) tablet having a long induction period in drug release were investigated. The micromeritic properties of SD(L/AL-CS) were compared to those of the SD composite particles of L/AL. The drug release profiles of DC tablet with SD(L/AL-CS) contained a long induction period followed by a rapid drug release phase. The induction period for drug release to occur was increased with an increase in the degree of deacetylation of chitosan and in the amount of chitosan in the formulation. The prolongation of induction period was attributed to the formation of an insoluble ion complex between sodium alginate and chitosan in the composite particles, which could form a rigid gel structure on the tablet surface. Conclusions. A time-controlled release tablet was designed with the composite particles of lactose containing the AL-CS ion complex. The induction period of the DC tablet could be prolonged in order to deliver the drug to the colon by controlling the type and amount of SC formulated in the composite particles.

[*S.T.P. Pharm. Sci.*, **10**, 213-219 (2000)] [Lab. of Pharm. Engineering]

In Vitro and In Vivo Evaluation of Mini-depot Tablet Prepared Using Poly (DL-lactide-co-glycolide) nanoparticles as Retardant Material.

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The objectives of this study were to prepare mini-tablets by the direct compression of poly (DL-lactide-co-glycolide) (PLGA) nanoparticles were prepared using a modified spontaneous emulsification solvent diffusion method, and a drug (theophylline) and to clarify the effects of factors on the in vitro release rate. In vivo release was then assessed in rats and compared with the in vitro release properties of PLGA or end-capping the terminal carboxylic acid in PLGA (EC-PLGA) nanoparticles. Both PLGA and EC-PLGA mini-tablet showed biphasic release profiles. The critical pH value at which release rates increased markedly was higher for EC-PLGA mini-tablets than for PLGA tablets. It appeared that the in vivo release rate correlated well with the in vitro rate determined at pH 7. EC-PLGA nanoparticles could be used as an effective in vivo retardant material for depot use by direct compression.