Analysis of Solid State Molecular Interaction and the Application to Molecular Pharmaceutics

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We have been investigating the effects of molecular states of drugs on quality of dosage forms, dissolution property, stability and bioavailability. Important fundamental physico-chemical studies have been performed from the stand point of molecular pharmaceutics.

When a crystalline drug was ground with a pharmaceutical additive such as crystalline cellulose, the drug crystals were changed into an amorphous state through mechanochemical effects. When cyclodextrins, cholic acids, or urea derivatives was used as an additive, the inclusion complex with some organic compounds was interestingly formed by co-grinding. In some cases, co-crystal formation was observed by mechanochemical treatment.

The formation of stable suspension consisting of uniform sub-micron particles was observed when a ground mixture of water insoluble drug and cyclodextrin hydrate crystals was dispersed into water. When three-components grinding with polymer, surfactant and drug was carried out, a nano suspension with excellent dispersibility was also obtained. Improvement of bioavailability was observed by the oral administration of nano suspension.

We have proposed the sealed heating method as a new method for preparing cyclodextrin inclusion compounds. We investigated the mechanism of inclusion formation during the heating process using powder X-ray diffraction, thermal analysis, IR and NMR. Using linear amylose and cholic acids as host compounds, we are attempting to investigate the complexation mechanism as well.

The drug molecules adsorbed into mesoporous materials via gaseous phase exhibited characteristic properties that are different from the intact crystals. Recently, FSM-16 was developed as well controlled porous silica. The peculiar properties were studied using solid state fluorescent spectroscopy and NMR.