

CHAPTER VI

CONCLUSIONS

The particle size of BDM decreased to smaller size of BD after thermal dehydration due to the prominent disruption of BDM during dehydration. The mechanism of dehydration of BDM composed of two major steps of size reduction and dehydration synchronously. The early stage of dehydration dealt with the particle size reduction with partial water removal and the later stage of dehydration mainly controlled the complete dehydration. The solid state interconversion during dehydration of BDM indicated the development of BD and BDM mixture at the early stage of dehydration and only BD after complete dehydration. Therefore, required energy for particle size reduction was practically lower than the energy needed for complete dehydration. The molecular packing and bonding between BD and crystalline water in crystal lattice unit played a major role on dehydration of BDM which eventually lead to particle size reduction. The lower coefficient of packing (K_{chan}) suggested an ease of dehydration and weakness of dehydrated structure after the crystalline water was removed. The hydrogen bonds of BDM were a moderate to weak type that needed only small amount of energy to potentiate dehydration and generated a perturbation of an internal structure. The weakness of the crystal structure after dehydration would lead to structural collapse of BD. The apparent particle size reduction energy was found to depend on the dehydration temperature while the total energy for complete dehydration was temperature independent. The E_a of dehydration of BDM obtained by solid state kinetic methods showed positive values and suggested the "rate" of dehydration was temperature dependent.

Model hydrate, NF hydrates, was obtained from different methods. Different stoichiometry NF hydrates (dihydrate NF, hemipentahydrate NF, trihydrate NF and pentahydrate NF) were generated. Dehydration with desiccant of the pentahydrate NF resulted in the disordered NF, a new hydrated phase which has not been reported elsewhere. The levels of environmental moisture and temperature greatly affected the transformation of not only the anhydrous NF Form A but also the other stoichiometric hydrates. However, the reduction of moisture in an environment was less effective in removing crystalline water of NF hydrates.

The thermal dehydration behavior of hemipentahydrate NF, trihydrate NF and pentahydrate NF found to be complex and composed of at least two steps of dehydration. Unclear dehydration stages were found in the dehydration of hemipentahydrate NF whereas clear steps of dehydration were detected after thermal dehydration of trihydrate NF and pentahydrate NF. An incomplete dehydration of hemipentahydrate NF, trihydrate NF and pentahydrate NF generated the mixture of hydrated transitional phase and the anhydrous NF form A. However, the pure anhydrous NF Form A was found after the complete dehydration of the above three NF hydrates. Thermal dehydration induced only minor particle size reduction of hemipentahydrate NF, trihydrate NF and pentahydrate NF when statistically determined. However, when observed visually by SEM, thermal dehydration did not induce particle size reduction to the extent seen with BDM. Dehydration energy of different stoichiometry of NF hydrates obtained by regular NIDSC correlated well with the general conclusion that less energy of dehydration was required for the lower stoichiometric hydrates. However, the dehydration energy of trihydrate NF and pentahydrate NF were within the same range. It may be due to the location of water molecules and the strength of hydrogen bonding within the crystal lattice. The E_a of every NF hydrates obtained from solid state kinetic were positive and signified the temperature dependency of the rate of dehydration.

The total dehydration energy of NF hydrates were higher than the energy required for BDM. It was due to the higher bonding energy between crystalline water and NF molecules and the more compact structures with minimal void volume. Thus, the NF hydrates retained their structures after dehydration and resulted in an unchanged particle size. Conclusively, dehydration energy and crystal structure void volume after dehydration are two of the factors which may be used and compared to the reference materials (risedronate sodium hemipentahydrate and BDM) to preliminary determine the possibility of particle size reduction of hydrated structures.

The preliminary guideline for choosing organic hydrates for the particle size reduction via thermal dehydration was proposed. The most important factor was the compactness of crystal structure of hydrates. The hydrates with low K_{chan} should provide a high feasibility on structural collapse after dehydration due to more fragile anhydrous crystal structures. In addition, the directions of water channel or tunnel also played a key role on dehydration. The more directions of open-end water channel the

higher dehydration rate. In term of binding forces between active moiety and crystalline water, hydrogen bonding is the fundamental attachment force in lattice structure of most hydrates. The number and strength of hydrogen bond indicates the dehydration possibility. After suitable hydrate model was selected, the recommended experiment for the particle size reduction via thermal dehydration should be performed. Isothermally dehydrated samples are evaluated for the particle size including solid state chemistry. Finally, one should be able to calculate is the apparent particle size reduction energy and the total dehydration energy which are useful as reference values for future dehydration studies.