CHAPTER V

CONCLUSIONS

The planetary mixer was found to be suitable for melt pelletization. The use of molten form of binder gave less deposition of wet mass onto the mixing bowl. The mixing speed, mixing temperature and mixing time affected the formulation and physical properties of diclofenac sodium pellets.

The amounts of binder required to form blank pellets were different and depended on types of binder and filler. For lactose, the amounts of Compritol 888 ATO® and Tristearin® required to form pellets were generally higher than those of glyceryl monostearate, Precirol® ATO5 and Gelucire 50/02. For dbcp, the amounts of Compritol 888 ATO® required to form pellets were generally less than those of glyceryl monostearate, Precirol® ATO5 and Gelucire 50/02. However, the amounts of Tristearin® required to form pellets was not affected by the types of filler.

The amount of the binder required was also dependent on drug incorporation. When diclofenac sodium was incorporated into the formulation, the amounts of binder required to form pellets were less.

In this study, the important variables affecting the properties of DS-GMS pellets were mixing speed and types of filler, whereas mixing temperature and time were less important. There was also interaction effects from mixing speed, temperature, time and types of filler.

An increased mixing speed resulted in a narrow size distribution and larger granules. An increased mixing temperature did not result in clear effect on particle size and size distribution of DS-lactose-GMS pellets, but reduced particle size and size distribution of DS-dbcp-GMS pellets. It was likely that increasing mixing time yielded more lump > 2.8 mm for both DS-lactose-GMS and DS-dbcp-GMS pellets.

The DS-dbcp-GMS pellets were denser at high mixing speed, 200 rpm but DS-lactose-GMS pellets were of opposite result. Pellets also became densified when using high mixing temperature, 25°above melting point of GMS. However, the effect of mixing time was not clear. In general, the DS-dbcp-GMS pellets were smoother and rounder than DS-lactose-GMS pellets. The DS-dbcb-GMS pellets were also denser than DS-lactose pellets.

The lower melting point of binder gave rise to rounder. Lower viscosity produced narrow size distribution of pellets.

All pellets possessed good flowability in terms of angle of repose, flow rate and % compressibility.

The drug content of DS-lactose pellets complied to pharmacopoeia, USP 27, whereas the drug content of DS-dbcp pellets were out of pharmacopoeia standard. The uniformity of drug content of a DS-lactose-GMS pellet formulation prepared by mixing speed of 100 was of % RSD more than 2.00, implying that mixing speed of 100 was not suitable.

X-ray diffraction, IR spectroscopy, differential scanning calorimetry and HPLC analysis confirmed that degradation product of diclofenac, diclofenac related compound A, did not occur.

The dissolution test of DS pellets was not clear. There may be many effects on drug release but mixing time was not significant factor.

The accelerated stability results of DS-lactose pellets stored at 45°C and 75% RH for 4 mouths signified that the drug content of DS-lactose pellets were stable.

The formulation with dbcp and GMS was not suitable for preparation of DS pellets because of drug degradation, although smooth and rounded products could be obtained.