Chapter IV

Discussion and Conclusion

Certain physical properties of Scaphium powders were determined for the purpose of differentiate their relative efficiency as tablet disintegrants. This investigation was also evaluate in comparison with the properties of various commercial disintegrants in tablet made by direct compression using dibasic calcium phosphate and ∝-lactose monohydrate as diluents.

The chemical components of Scaphium powders were polysaccharide, tannin and nitrogenous compounds, The heavy metals, lead and arsenic, are very low. The mercury content of S_2 was higher than of S_1. This may be due to washing the fruit pulp several times with alcohol and the container would have mercury components so liberating to the alcohol medium. This amount was lower than the heavy metals content with allowance in acacia powder according to BP requirement (75).

The photomicrographs (Figures 6,7) provided a better understanding both size and shape of Scaphium powders. The shapes of Scaphium powders were irregular. The particle size of S_1 and S_2 were smaller than of Ac-Di-Sol$^{(R)}$, corn starch. Explotab$^{(R)}$, Kollidon CL$^{(R)}$, Nymcel$^{(R)}$and Starch 1500$^{(R)}$(77). Consequently, the specific surface area of S_1 and S_2 were therefore, larger than of the other disintegrants.

The percent compressibility of Scaphium powders were calculated from bulk and tapped density. This value of S_1 was more than of S_2 but the true density of S_1 and S_2 were the same. However, these properties would not have much effect to the tablets prepared because it was used at rather low concentration in formulations. The determination of bulk swelling rate of S_1 and S_2 could not be achieved because S_1 and S_2 formed gel barrier and prevented water penetration into the particles. The hydration capacity of Scaphium powders were much more than of Ac-Di-Sol$^{(R)}$, corn starch, Explotab$^{(R)}$, Kollidon CL$^{(R)}$, Nymcel$^{(R)}$ and Starch 1500$^{(R)}$ (77).

The concentrations of disintegrants from 0.5 to 5% did not have any effects on weight variation of tablets and also had no interference in the flow rate of granules because of the low concentration employed. The present of Scaphium powders does not seem to have any significant influence on tablet hardness even at concentration of 5% level. Corn starch and Kollidon CL$^{(R)}$ have a soften effect on both diluents because they possessed comparatively poor compression characteristics (5,24).

Ac-Di-Sol$^{(R)}$ and ECG 505$^{(R)}$ when incorporated in dibasic calcium phosphate dihydrate system gave disintegration time less than 60 seconds at all concentrations and compressional forces. It can be seen that Ac-Di-Sol$^{(R)}$ and ECG 505$^{(R)}$ reached their equilibium of water uptake faster than those of the other disintegrants,

especially Ac-Di-Sol(R) was the most efficient material in water uptake capacity (Figures 27-30). The high rate of saturation entailed very short disintegration time for tablets containing Ac-Di-Sol(R) and showed its efficiency at very low concentration (27).

α-Lactose monohydrate tablets containing 0.5 and 1% of Ac-Di-Sol(R) compressed at 3000 pounds exhibited the fastest rate of water absorption in comparison with those tablets making at the other compressional forces. This might be due to the more contact of disintegrant particles at higher compression force to enhance water penetration. The rates of water uptake of tablets at the concentrations of Ac-Di-Sol(R) 3-5% were not different and did not reach their equilibrium of water uptake within 180 seconds. This indicated that Ac-Di-Sol(R) could absorb larger amount of water and lactose also rapidly dissolved in the medium.

Tablets made from α-lactose monohydrate and ECG 505(R) exhibited slightly increase in water uptake when compressional force was increased, except at the concentration of 0.5%. The lag time of water uptake curves in α-lactose monohydrate system were less than in dibasic calcium phosphate dihydrate system. The possible explanation was the dissolution of lactose led to widen the pore in tablet surface so that water could penetrate rapidly into the tablets. The volume of water uptake was also increased when the amount of disintegrant was increased. High compression force produced high affinity to take up

water into the tablet because of continuous contact of ECG 505(R) particles as a result of compaction.

In dibasic calcium phosphate dihydrate with concentrations of Explotab(R) at 0.5 and 1%, tablets compressed with low compressional force had higher rate of water uptake than those compressed with high compressional force because of the larger pore size they possessed. It was noticed that high compression force resulted in decrease the porosity of tablets and also decrease the rate of water penetration. From this reason, the longer lag time took place according to the smaller porosity of tablets. When the concentrations of Explotab(R) 3-5%, the rates of water uptake of tablets at high compressional force were more than those at low compressional force due to the continuous contact of disintegrant particles leading water to penetrate rapidly into tablets.

A fast disintegration time would be obtained when the tablets made from α-lactose monohydrate and Explotab(R) Moreover, the disintegration time of tablets were not affected by the concentration of Explotab(R) or the compressional force. It can be seen that the rate and volume of water uptake of tablets with Explotab(R) were the highest in comparison with those with the other disintegrants. This might be due to water continuously penetrated into tablets caused by rapid dissolution of lactose and high volume of water uptake of Explotab(R).

For dibasic calcium phosphate dihydrate system, tablets containing corn starch at 0.5 and 1% levels disintegrated longer than 30 minutes at all compressional forces because they exhibited very little water uptake. However, when the concentration of corn starch was higher than 3%, the more water uptake occurred and disintegration time of tablets became shorter. An improvement of water uptake was observed when the compressional force increased, this may be caused by the continuous contact between starch grains. It was realized that the rate and volume of water uptake of tablets with corn starch were very small. The results indicated that corn starch at low concentration was the least effective to improve water penetration in comparison with the other disintegrants.

The increase of compressional force affected the water uptake of α-lactose monohydrate tablets containing corn starch in the range of 0.5 to 1%. This might be the reduction of the pore size inhibiting water to penetrate into tablets so that disintegration time became longer. However, at high concentrations of 3 to 5%, the continuous contact of disintegrant particles may occur, thus the water uptake rate increased with increase in compressional force even if the pore size within tablets might be reduced. The disintegration time of tablets compressed at high compressional force were shorter than those of tablets compressed at low compressional force according to the more rapid of water uptake.

In case of dibasic calcium phosphate dihydrate tablets composed of Kollidon CL$^{(R)}$, both increasing compressional force and concentration of Kollidon CL$^{(R)}$ caused an increase of water penetration. As might be expected, Kollidon CL$^{(R)}$ at higher compression pressure had affinity to take up water because of continuous contact between particles of disintegrant. The volume of water uptake was slightly increased with increasing concentration of Kollidon CL$^{(R)}$, the lag time was also shorter. This indicated that the volume of water uptake was not the main effect on rapid disintegration time of tablets, but the rapid rate of water uptake was also important.

For α-lactose monohydrate system, both increasing compressional force and concentration of Kollidon CL$^{(R)}$ caused an increase of water uptake rate. Disintegration time of tablets at all disintegrant concentrations and compressional forces were slightly different and could not be related to water uptake. The results of short disintegration time of water soluble system would depend upon the combine effect between dissolution of water soluble diluent and rapid water sorption of disintegrant.

The rate of water uptake tended to play an important role on disintegration time of dibasic calcium phosphate dihydrate tablets containing L-HPC. At the concentrations of 0.5 and 1.0%, the rates of water uptake increased with decrease in compressional force owing to larger pore size at low compression. Increasing compressional force exerted

influence on water penetration of tablets by reducing pore size and prolonging disintegration time. However, at high concentrations of L-HPC (3 and 5%), the continuous contact of L-HPC particles would be predominant factor causing the teblets disintegrated in shorter time when the compressional forces were increased.

In the case of tablets made from α-lactose monohydrate and L-HPC, both compressional force and concentration of L-HPC appeared to have no effect on disintegration time. Disintegration time of all tablets had no correlation with water uptake. The results of short disintegration time of water soluble system would depend upon the combine effect between dissolution of water soluble diluent and water penetration of L-HPC.

Dibasic calcium phosphate tablets with Scaphium powders exhibited higher rate of water uptake than those with corn starch. The Scaphium powders tended to have superior efficiency to corn starch in improvement of disintegration time. Increasing compressional force exerted influence on reduction of pore size of tablets and led to reduce in water penetration thus prolonged disintegration time. For dibasic calcium phosphate dihydrate tablets containing 3% of Scaphium powders showed the fastest disintegration time in corresponding with the highest amount of water uptake. This can be explained that the concentration of Scaphium powders at 3% seemed to be optimum concentration. The gel formation would be occurred

when incorporated Scaphium powders higher than 3%. The water penetration curves of tablets with 3% Scaphium powders exhibited slight increase in water uptake in comparison with those of 0.5 and 1%. Slow rate of water uptake at 5% level of Scaphium powders may be due to the gel formation of Scaphium powders built up the barrier preventing the water to penetrate into the tablet matrices.

The compressional force had a little influence on disintegration time of α-lactose monohydrate tablets containing S_1 and S_2. The fastest disintegration time was found when the concentrations of S_1 and S_2 were used at 0.5% level. It was noticed that increasing concentrations of S_1 and S_2 were not much increased in water uptake. The more concentrations of S_1 and S_2 were added, the lower rates of water uptake were observed. The disintegration time of the tablets with higher concentrations of S_1 and S_2 were much increased whereas the rates of water uptake were decreased. As previously mentioned, it may be due to gel formation of S_1 or S_2 and rapid dissolution of lactose caused an increase in viscosity of liquid around the tablets.

The mechanism of action of disintegrants is very complex and connot be readily simplified into one or more categories. While it seems appararent that water uptake played a dominant role to be the step limiting the rate of disintegration for the tablet systems use in this study. The lag time of water uptake occurred according to the surface phenomena such as surface tension of water and

contact angle between liquid and solid had an effect on disintegration time. The shorter lag time of water uptake resulted in more rapid disintegration. But a certain amount of water must be available for disintegrant to swell before it can act effectively. It was found that the lag time of various disintegrants in α-lactose monohydrate system were less than in dibasic calcium phosphate dihydrate system. The reason was that the dissolution of diluent led to widen the pore in tablet surface. In spite of the initial rates of α-lactose monohydrate system seemed to be higher than those in dibasic calcium phosphate dihydrate system, but after that the rate of α-lactose monohydrate system became slower owing to the viscous solvent produced by dissolution of diluent and disintegrant. Moreover, disintegration time of α-lactose monohydrate tablets were not much different among various disintegrants utilized as found in dibasic calcium phosphate dihydrate system. In addition, dibasic calcium phosphate dihydrate diluent was prefered to α-lactose monohydrate in evaluating comparative efficiency among disintegrants. The dominant properties of dibasic calcium phosphate dihydrate are water insoluble and has practically no instrinsic disintegrant property so that the result of disintegration would occur according to the efficacy of disintegrant itself (80,81).

The results of disintegration tests completely support observation obtained in the tests of water penetration. Thus water penetration seems to be the step

that limits the rate of disintegration for the tablets studied (7). In this present study, the fastest disintegration time of tablets were found when incorporated S_2 at 3% and 0.5% levels in dibasic calcium phosphate dihydrate and α-lactose monohydrate systems, respectively. Thus these concentrations were chosen to incorporate with active substance. Hydrochlorothiazide was employed as a model drug owing to its slightly water soluble (20). The tablet should disintegrate into fine particles in order to obtain good dissolution. Therefore, good disintegrants would reflect the efficacy of hydrochlorothiazide tablets.

The physical properties of hydrochlorothiazide tablets with S_2 in both diluents such as weight variation, percent labeled amount, content uniformity were well within USP requirements. The friability of tablets for all formulations were within acceptable limited (less than 1%) when the hardness of tablets was controlled in the range of 5 to 7 kilopounds. It has been stated that the presence of S_2 does not seem to have any significant effect on the physical properties of hydrochlorothiazide tablets in both diluents due.to low concentration use.

According to the results of dissolution of hydrochlorothiazide in dibasic calcium phosphate dihydrate system (Figure 75), S_2 at 3% level gave higher dissolution rate of hydrochlorothiazide than of the tablets with 2% level of S_2. It could be suggested that S_2 at concentration of 2 or 3% could be considerably effective in water

insoluble system. In addition, the dissolution of hydrochlorothiazide tablets containing S_2 at both concentrations were acceptable within USP requirement (74).

For hydrochlorothiazide tablets in α-lactose monohydrate system, the tablets tended to erode or dissolve instead of disintegration. The hydrochlorothiazide tablets without disintegrant slowly dissolved and the disintegration time was 931 seconds while those containing S_2 0.5% compressed the same hardness showed the disintegration time 43 seconds. The reason was owing to S_2 widening the pore size of tablets thus enhanced water to penetrate into the tablets. The disintegration time of the tablets became shorter. In the case of dissolution of hydrochlorothiazide tablets with S_2 at 0.5% were well within USP limit whereas those without disintegrant were lower than the standard limit (Figure 76). It was indicated that the ability of S_2 as tablet disintegrant at low concentration of 0.5% was considerably acceptable in water soluble system.

Conclusion

The results emphasized that Scaphium powders possessed disintegrating properties superior to corn starch and inferior to superdisintegrants such as Ac-Di-Sol$^{(R)}$, ECG 505$^{(R)}$, Explotab$^{(R)}$, Kollidon CL$^{(R)}$ and L-HPC. At the concentrations of disintegrants between 0.5-3%, the comparison of disintegrating properties between Scaphium powders and the other disintegrants could be concluded as follows :

S_1 or S_2 > corn starch

> L-HPC 0.5 %

$\simeq$ L-HPC 1%

< L-HPC 3%

> Explotab$^{(R)}$ 0.5%

< Explotab$^{(R)}$ 1-3%

$\simeq$ Kollidon CL$^{(R)}$ 0.5%

< Kollidon CL$^{(R)}$ 1-3%

< ECG 505$^{(R)}$

< Ac-Di-Sol$^{(R)}$

The disintegrating characteristics of tablets containing S_1 or S_2 behave like other superdisintegrants, they expanded and exploded into primary partciles. There is no doubt that water uptake must be the first step in any process of disintegration. Therefore, the rate of disintegration of tablets can be limited by the rate and extent of liquid absorption by the system. The volumes of water uptake of tablets containing various disintegrants were ranked as follows : Explotab$^{(R)}$> Ac-Di-Sol$^{(R)}$$\geq$ ECG 505$^{(R)}$ $\geq$ L-HPC > S_1 or S_2 > Kollidon CL$^{(R)}$> corn starch > blank. The outstanding of Scaphium powders as tablet disintegrant is ability to bring about rapid disintegration with relatively low concentration. In the case of higher concentration, penetration of water was found to be reduced. This may be due to gelatinization effect when amount of Scaphium powders were increased. This effect caused prolong disintegration time and may retard the dissolution of the active drug.

S_2 also showed slightly superior on physical properties to S_1 such as hydration capacity and moisture sorption. This might be due to low content of fibre substance of S_2. However, the efficiency in improving tablet disintegration time of both fractions were approximately the same. Compressional force played significant effect on water penetration by reducing pore size and producing continuous contact between disintegrant particles in dibasic calcium phosphate dihydrate system and both factors exhibited different effects in relation to compressional force. In the case of α-lactose monohydrate system, the dissolution of lactose occurred by erosion at the surface of tablets and the requirement of disintegrant only assist to take up water into the compact. Therefore, the combining roles between water penetration and dissolution of diluent are important for water soluble system.

In conclusion, Scaphium powder appeared to be the promising candidate to be developed as tablet disintegrant using in direct compression. The Scaphium powder definitely enhanced the dissolution of active drug employed in this study. Bleaching of the pulp is essential to make Scaphium powder become less intense or absolutely white colour. Further studies on the chemical properties of Scaphium powder should be carried out. Chemical modifications such as acetylation, carboxymethylation and crosslinking reactions should be observed in order to alter the physical properties of Scaphium powder especially less gelling formation which could lead to more efficient disintegrating properties.