CHAPTER III

RESULTS

3.1 Evaluation of blank tablet properties

3.1.1 Weight variation

Table 3.1 showed the 20 tablets weight of DC and WG blank tablet of 1000, 1400 and 1800 kg CF. The value of mean or average weight, standard deviation (SD) and percent relative standard deviation (%RSD) of both kind of blank tablets at various CF compressed were calculated and also shown in Table 3.1. It was found that weight variation of blank tablet conformed to the weight tolerances of USP for uncoated tablet given in Table 3.2. The weight of both DC and WG blank tablet were in the range more than 324 mg which not more than 2 of the tablets differed from the average weight by more than 5% and no tablet differed by more than 10% of average weight. The result showed that no tablet of DC blank tablet of 1000, 1400 and 1800 kg CF vary from range of 499.4 mg $\pm$ 5%, 500.3 mg $\pm$ 5% and 504.8 mg $\pm$ 5% respectively and as the same result in WG blank tablet of 1000, 1400 and 1800 kg CF, no tablet vary from range of 350.1 mg $\pm$ 5%, 368.1 mg $\pm$ 5% and 366.1 mg $\pm$ 5% respectively. Additionally, percent of relative standard deviation (%RSD) of the weight of both DC and WG blank tablet were very low in the range not more than 1%. In comparison between DC blank tablet and WG blank tablet showed %RSD of the weight of DC blank tablet was less than WG blank tablet.

Table 3.1 Weight variation of DC and WG blank tablet of all tested CF

	Weight of DC blank tablet (mg)			**Weight of WG blank tablet (g)**		
	Compression force			**Compression force**		
Item	**1000 kg**	**1400 kg**	**1800 kg**	**1000 kg**	**1400 kg**	**1800 kg**
1	501.0	499.7	505.5	343.4	367.2	366.4
2	495.6	498.7	503.2	354.8	369.1	365.1
3	499.3	499.5	504.0	351.7	370.0	367.0
4	499.7	499.5	503.7	352.0	370.4	363.2
5	506.7	502.9	503.6	347.3	372.1	362.4
6	497.8	501.1	505.6	353.5	366.9	362.1
7	498.5	502.1	505.8	353.7	366.9	366.4
8	496.7	498.3	505.1	348.0	369.4	365.1
9	500.4	498.6	505.7	354.3	373.0	367.0
10	498.7	502.6	506.2	346.4	373.1	363.2
11	498.7	498.6	504.2	354.3	373.0	362.4
12	502.0	501.2	505.7	348.8	362.6	362.1
13	500.8	498.8	504.6	345.8	372.6	366.6
14	497.6	499.3	505.1	341.9	362.7	369.9
15	500.6	501.2	504.9	358.4	368.3	373.0
16	497.5	502.9	504.1	347.1	369.6	362.3
17	497.3	498.7	503.3	344.9	361.4	370.9
18	497.9	499.4	504.9	352.8	364.0	369.4
19	501.6	500.5	505.8	352.3	363.0	366.3
20	499.1	501.9	504.8	349.8	366.4	370.4
Mean	499.4	500.3	504.8	350.1	368.1	366.1
SD	0.0024	0.0016	0.0009	0.0044	0.0038	0.0033
%RSD	0.49	0.32	0.18	1.25	1.04	0.91

Table 3.2 Weight Variation Tolerances for Uncoated Tablets (Rochville, 2007)

Average Weight of Tablet, mg	Percentage Difference
130 or less	10
From 130 through 324	7.5
More than 324	5

3.1.2 Hardness testing

Table 3.3 showed the hardness of the blank tablet prepared by direct compression and wet granulation of three compression forces. The mean of hardness, standard deviation (SD) and percent relative standard deviation (%RSD) of each kind of blank tablets of trial CF were shown. The hardness of both DC and WG blank tablets were higher when the compression force was increased. The hardness comparison of DC and WG blank tablet of same CF was revealed that the hardness of DC blank tablet of higher CF increased more than of WG blank tablet but the hardness of WG blank tablet of lower CF was higher than DC blank tablet.

Table 3.3 Hardness of DC and WG blank tablet of all tested CF

Tablet number	Hardness of DC blank tablet (Newton)			Hardness of WG blank tablet (Newton)		
	1000 kg	1400 kg	1800 kg	1000 kg	1400 kg	1800 kg
1	25.4	39.6	54.1	29.1	41.3	50.7
2	28.4	41.9	57.5	32.8	38.9	50.4
3	28.7	41.6	58.5	33.1	38.2	53.1
4	25.7	39.6	54.1	33.1	41.9	51.1
5	27.4	38.9	58.8	32.1	37.9	49.4
6	25.7	42.9	54.1	32.5	44.3	49.7
7	26.7	38.9	52.4	36.5	40.2	46.7
8	21.6	40.6	53.4	35.5	42.3	47.3
9	28.1	41.3	54.8	30.1	38.9	49.7
10	30.8	40.9	54.1	33.5	41.6	47.3
Mean	26.9	40.6	55.2	32.8	40.6	49.5
SD	2.49	1.35	2.24	2.19	2.07	1.98
% RSD	9.26	3.32	4.06	6.67	5.12	4.00

3.1.3 Tablet friability

Table 3.4 showed the percent friability of DC blank tablets which were lower than WG blank tablet of all tested CF. Percent friability of both blank tablets decreased when the compression increased.

Table 3.4 Friability of DC and WG blank tablet of all tested CF

Blank tablet	Compression force (kg)	Friability (%)
DC blank tablet	1000	0.97
	1400	0.71
	1800	0.44
WG blank tablet	1000	1.13
	1400	0.83
	1800	0.75

3.1.4 Tablet porosity

Figure 3.1 showed the porosity of DC and WG blank tablet that decreased when the compression force increased. The porosity of DC blank tablet was higher than of WG blank tablet of all trial CF. The data was shown in Table A1, APPENDIX A.

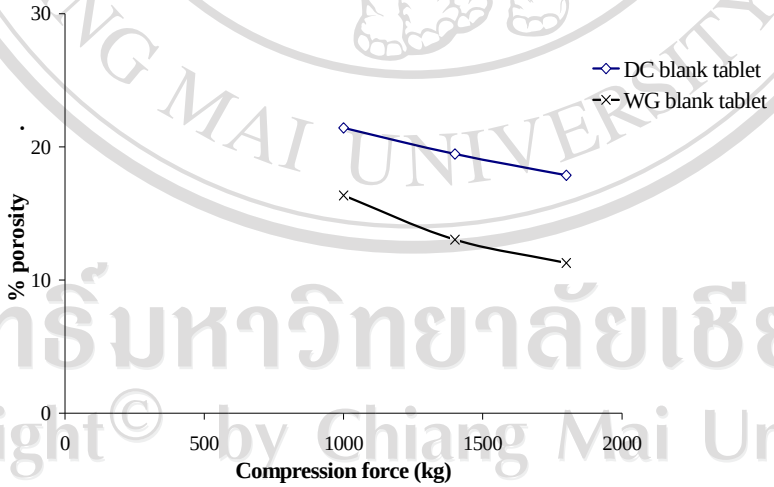


Figure 3.1 Effect of compression force on the porosity of DC and WG blank tablet

3.1.5 Disintegration test

Figure 3.2 showed the disintegration time of DC blank tablet which less than 10 seconds and was faster than of WG blank tablet of the same CF. The result of disintegration time of both DC and WG blank tablet comply with requirement of not more than 30 minutes (1800 seconds) for disintegration. The DC blank tablet of all CF disintegrated under the same range. But for WG blank tablet, the disintegration time depend on CF, more CF longer time of disintegration. The data was shown in Table B1, APPENDIX B.

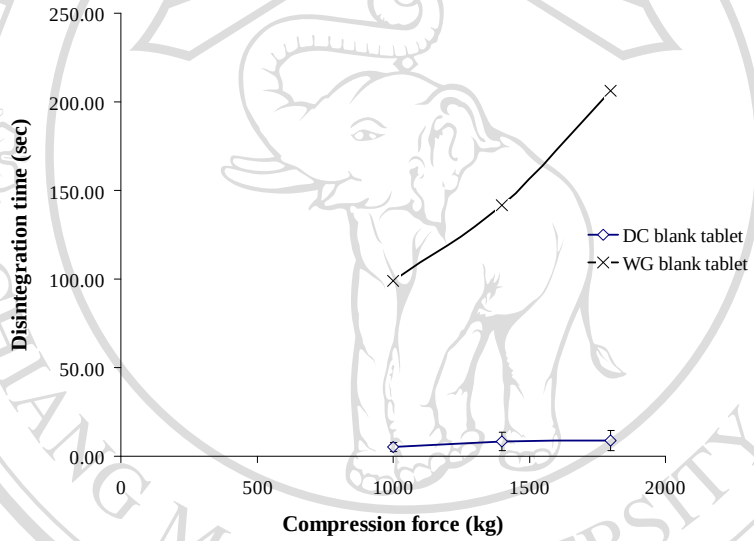


Figure 3.2 Effect of compression force on disintegration time of DC and WG blank tablet

3.2 Study of the penetration of solution after dropping on blank tablet

The distribution and penetration of 0.1% fast green FCF in alcohol on or through the surface of DC blank tablet of 1000 kg CF were inspected by using digital camera. The color solution could distribute well on the surface but penetrate into tablet in short depth. The tablet surface with dropping color solution and the side view of the same tablet are shown in Figure 3.3 (a) and (b) respectively. In Figure 3.3 (c), it showed no trace of the color on the opposite side of dropping.

(a) Dropped side

(b) Lateral side view

(c) Opposite side

Figure 3.3 The DC blank tablet of 1000 kg CF after dropping 0.1% fast green FCF in alcohol

3.3 Tablet characterization studies

The characterization of the tablets after dropping the model drug (CPM, DZP) solution was examined by the following methods. Some method used to characterize and compare with their blank tablet and intact excipients. Dissolution profiles of

DSDT prepared from DC and WG blank tablet were studied and compared with the conventional tablets prepared by DC and WG method and also with the commercial tablet.

3.3.1 Morphology studies by digital camera

The surface of the blank tablet and DSDT were captured by digital camera with high performance. Figure 3.4 showed the surface of the side of DC blank tablet including no dropped and dropped side of all trial CF after dropping a solvent mixture of absolute alcohol and dichloromethane without drug. It was no effect of the solvent on the tablet appearance of all trial CF.

The CPM solution using the mixture of absolute alcohol and dichloromethane as a solvent could not spreading distribute and then non homogeneous pattern on the surface of WG blank tablet of all trial CF as shown in Figure 3.5. Therefore dichloromethane was used as a single solvent for drug solution dropping on the WG blank tablet. Figure 3.6 – 3.8 showed the morphology of the surfaces of DSDT, CPM and DZP, prepared from DC blank tablets comparing with their blank tablets. It was found that the surface was smoother with a reduction of a groove or a crack of tablet surface especially the dropped side of CPM-solution dropping tablet prepared from DC blank tablet. For the surface of WG blank tablet looked smoother than DC blank tablet which the rough surface was not different of higher CF as shown in Figure 3.6 - 3.11. And Figure 3.9 - 3.11 showed the surface of DSDT prepared from WG blank tablet comparing with their blank tablets. It was found the layer of dried drug cover the surface of CPM-solution-dropping tablet and was clearly observed of higher CF such as 1800 kg as shown in Figure 3.12. Furthermore there are small crystals of diazepam on the dropped side of the surface of DZP-solution-dropping tablet and showing a bigger size at higher CF at 1800 kg CF as shown in Figure 3.13.

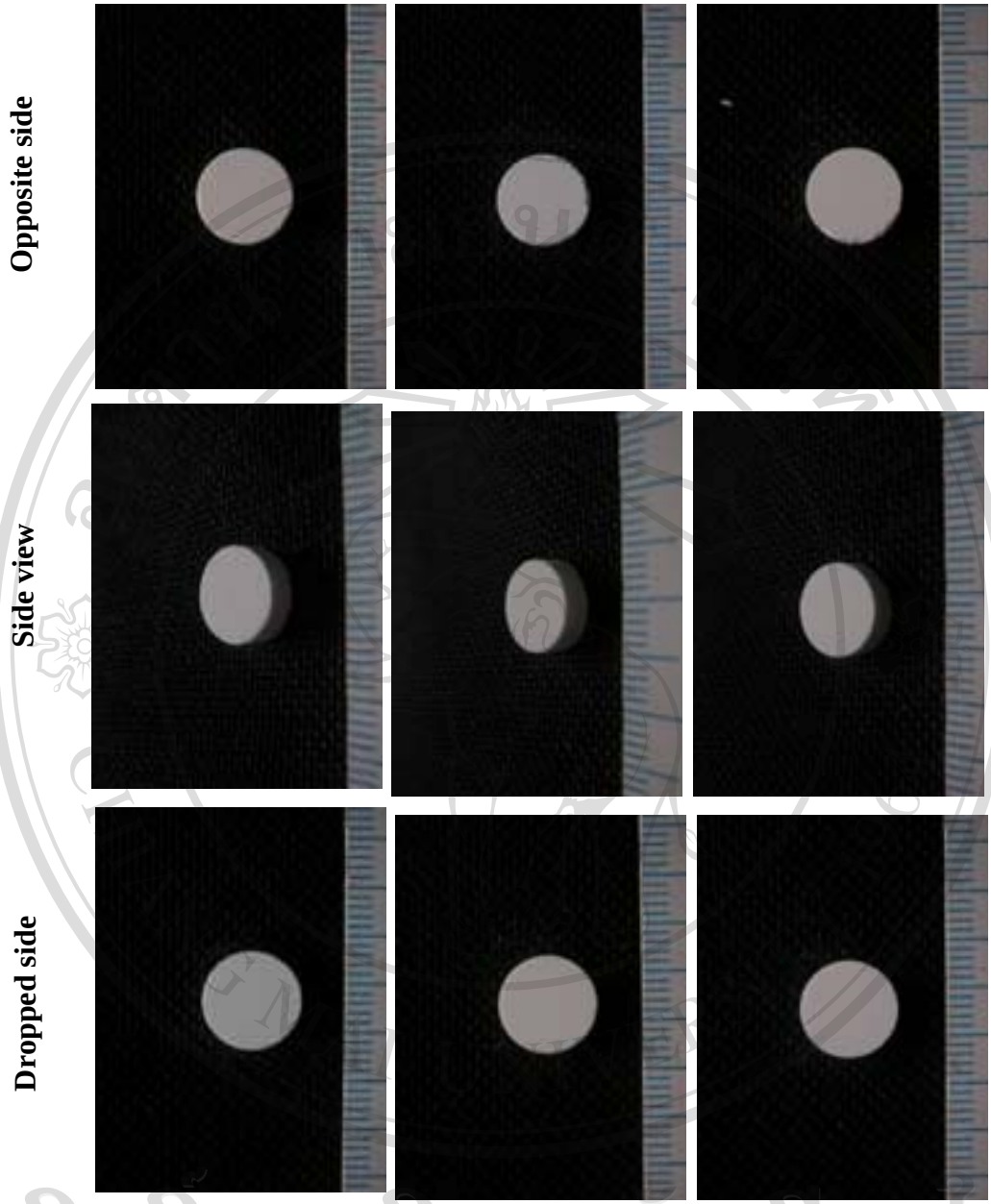


Figure 3.4 The aspect of the surface of DC blank tablet of all tested CF after dropping the solvent without drug

(a) 1000 kg CF

(b) 1400 kg CF

(c) 1800 kg CF

Figure 3.5 The surface of WG blank tablet of all tested CF after dropping CPM solution using a mixture of absolute alcohol and dichloromethane (1:3 by volume) as the solvent

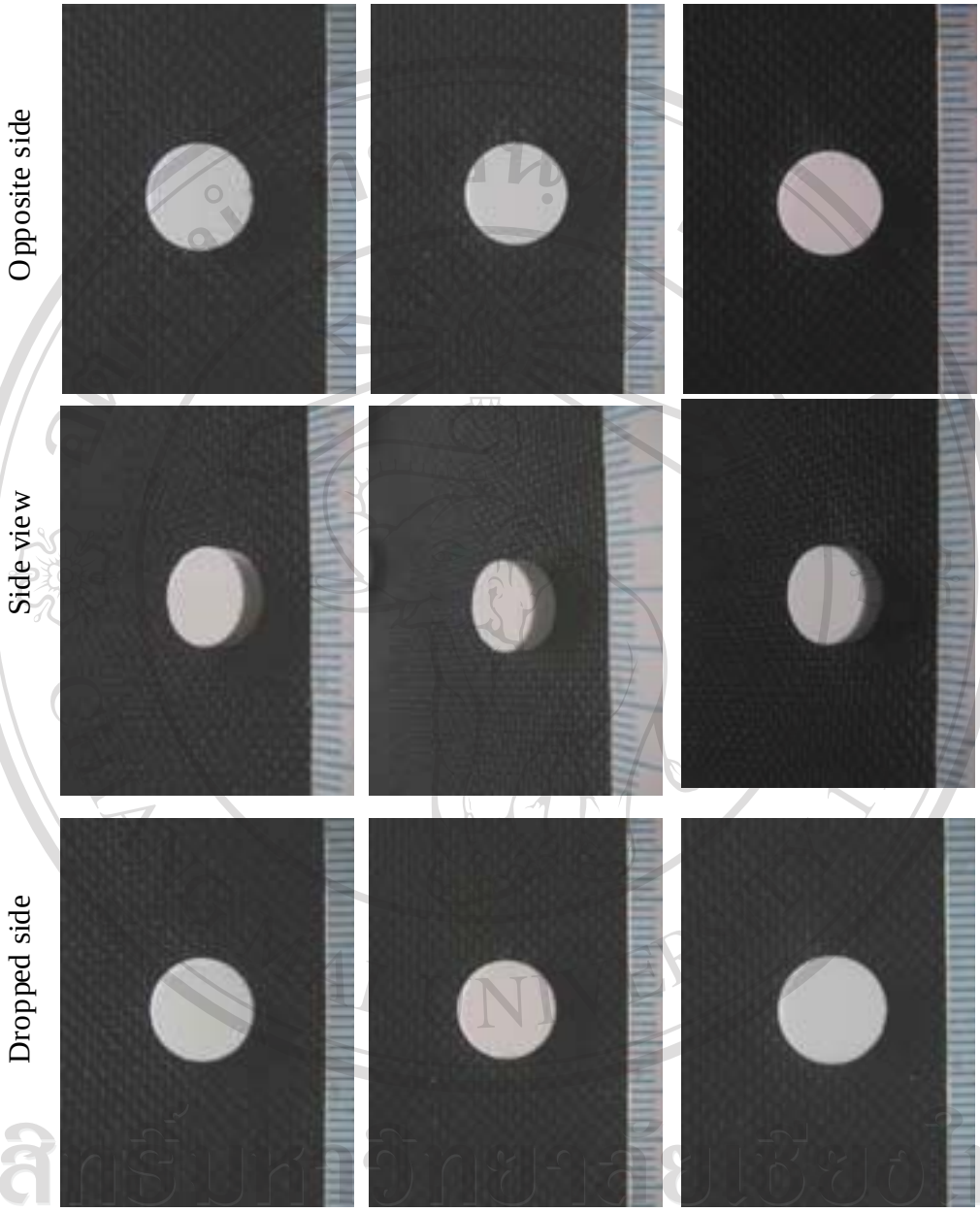


Figure 3.6 The surface of DSDT compared with DC blank tablet of 1000 kg CF

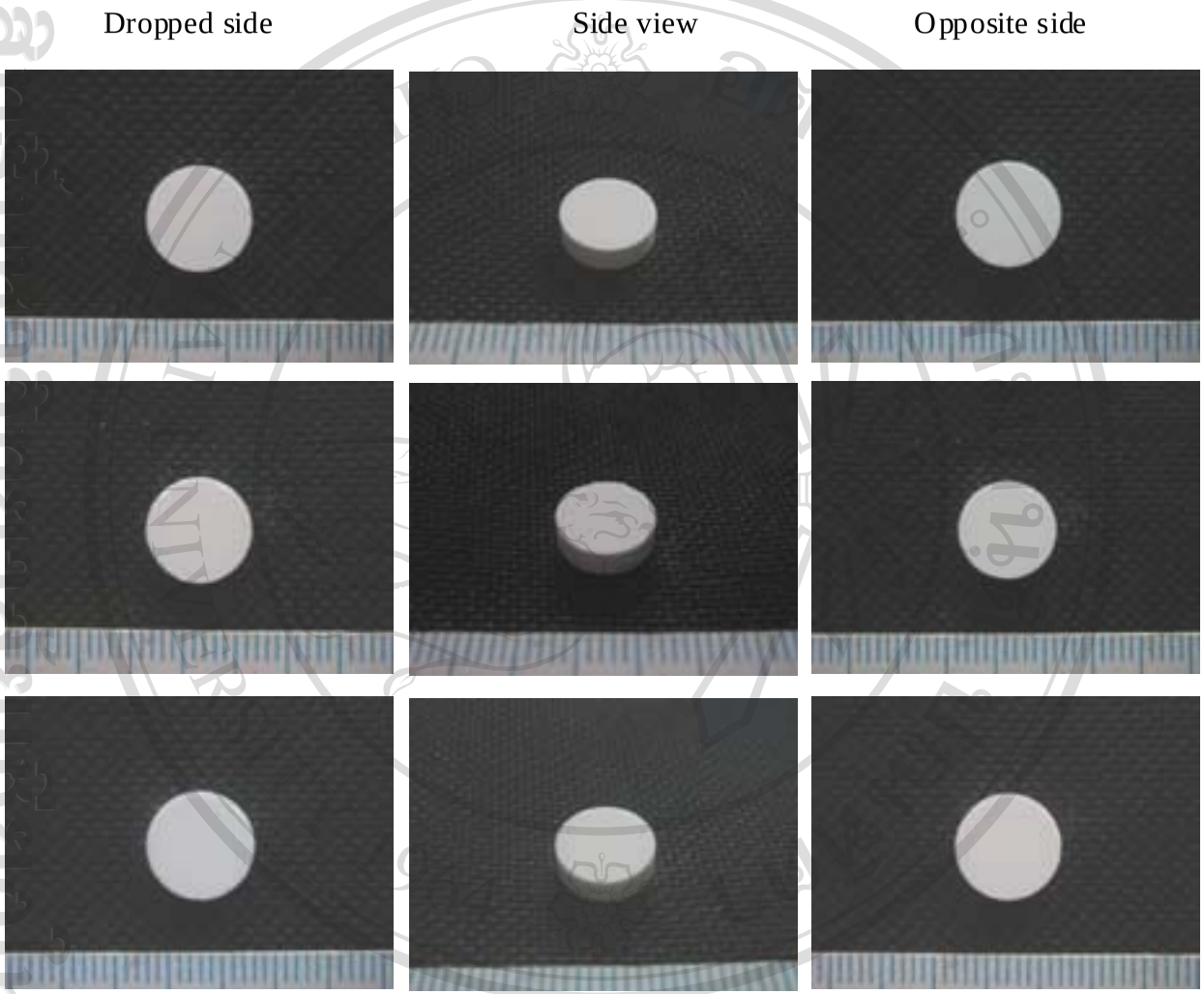


Figure 3.7 The surface of DSDT compared with DC blank tablet of 1400 kg CF

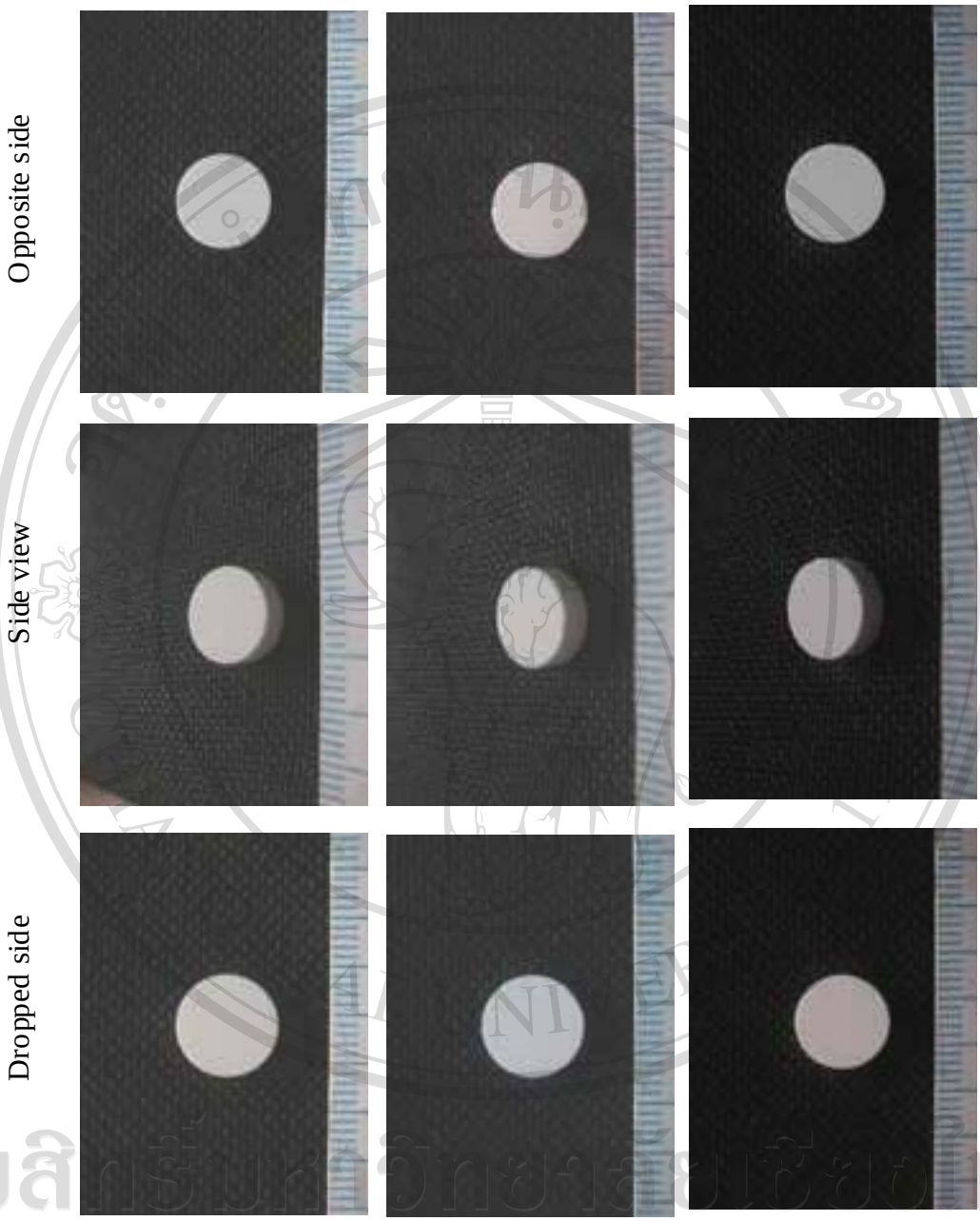


Figure 3.8 The surface of DSDT compared with DC blank tablet of 1800 kg CF

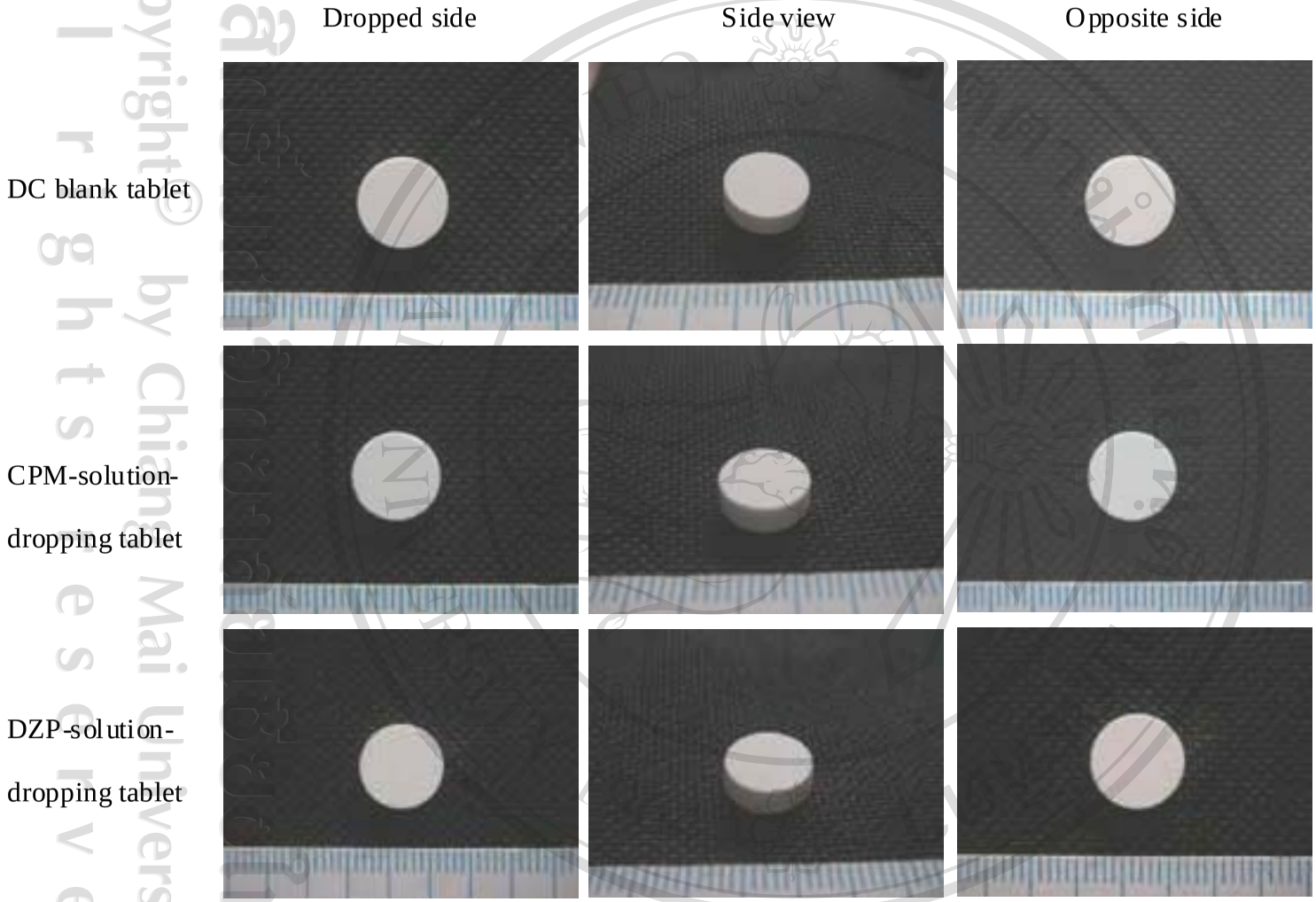


Figure 3.9 The surface of DSDT compared with WG blank tablet of 1000 kg CF

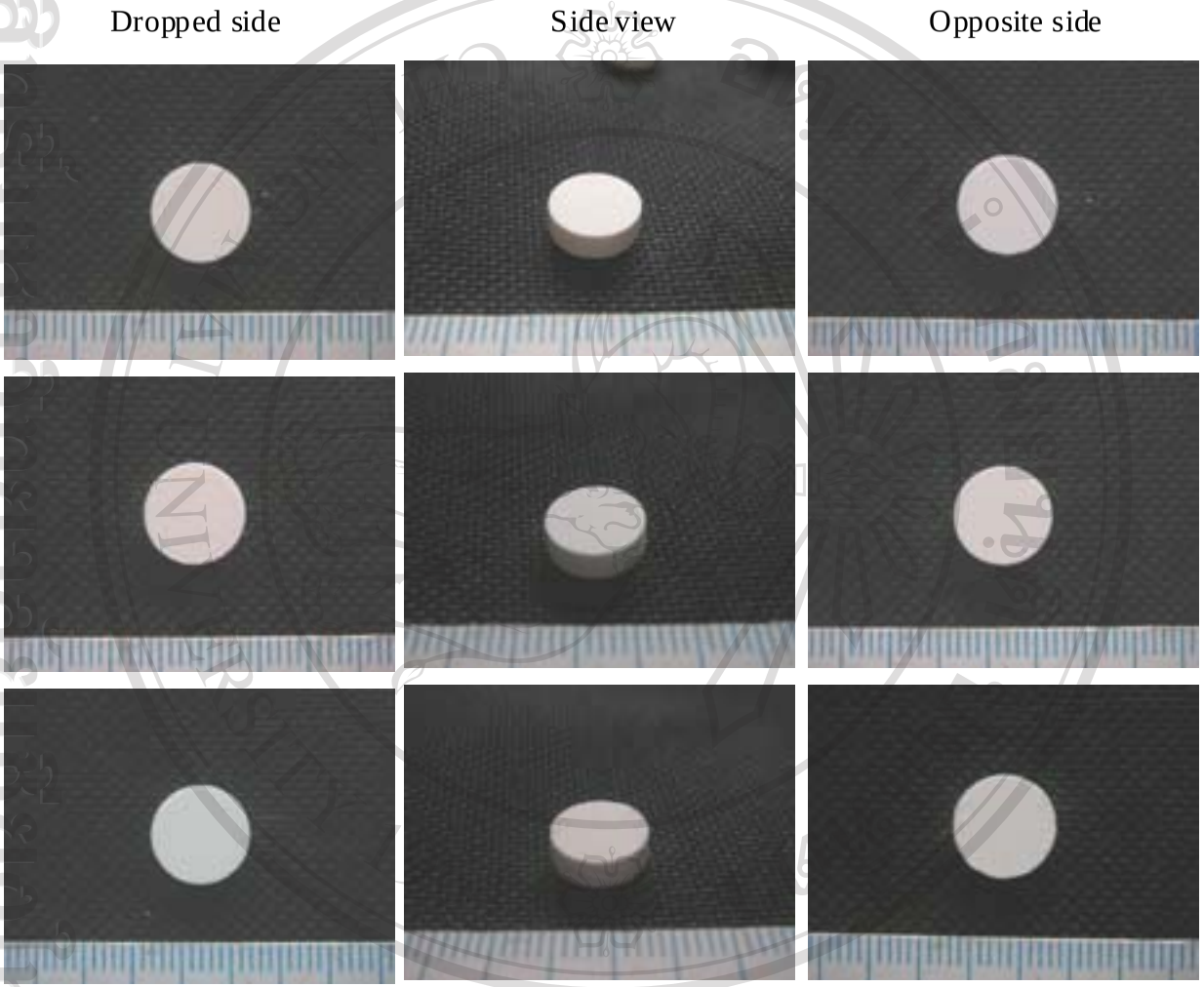


Figure 3.10 The surface of DSDT compared with WG blank tablet of 1400 kg CF

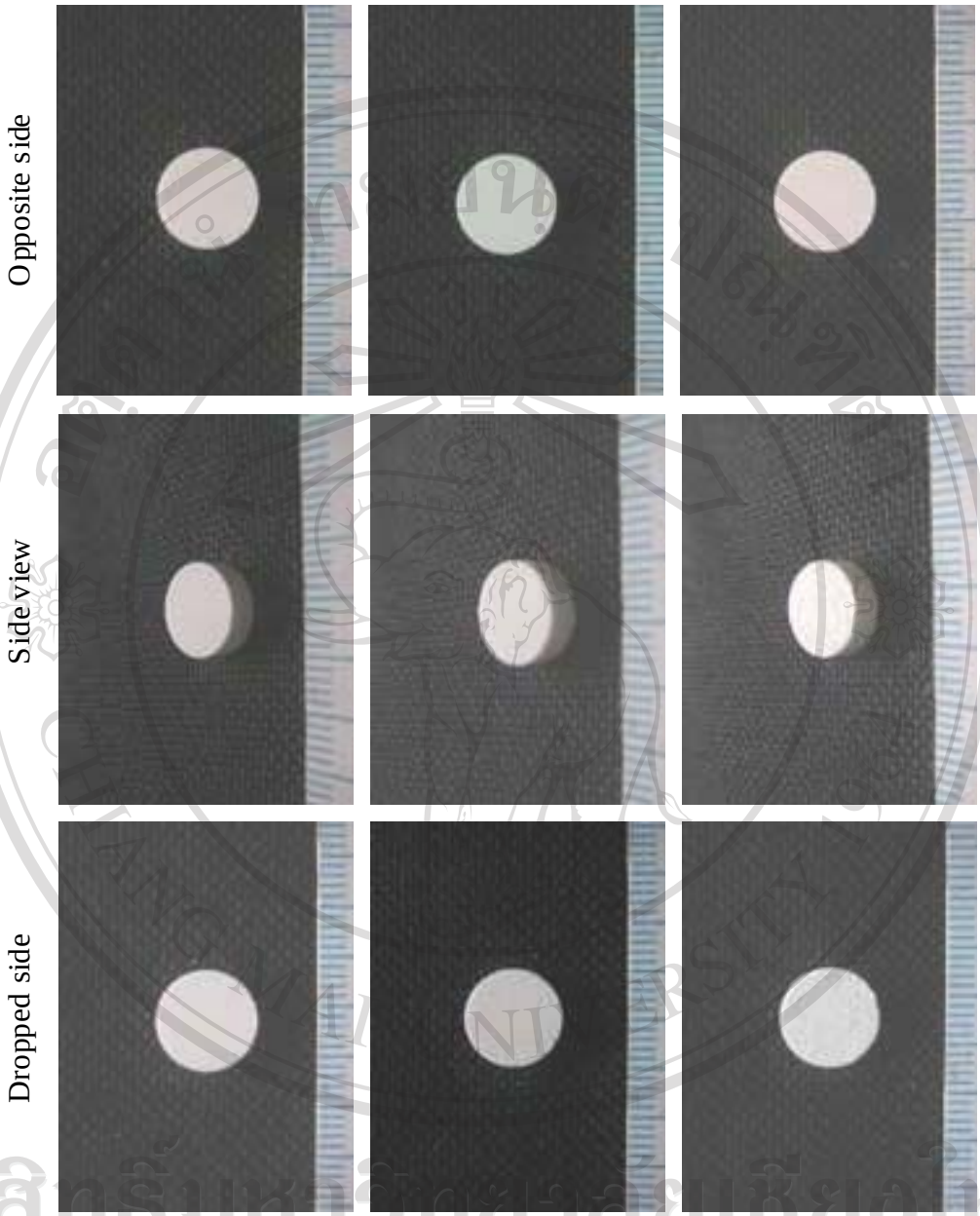


Figure 3.11 The surface of DSDT compared with WG blank tablet of 1800 kg CF

Figure 3.12 Layer cover of the surface of CPM-solution-dropping tablet prepared from WG blank tablet of 1800 kg CF

Figure 3.13 Small crystals of diazepam on the surface of DZP-solution-dropping tablet prepared from WG blank tablet of 1800 kg CF

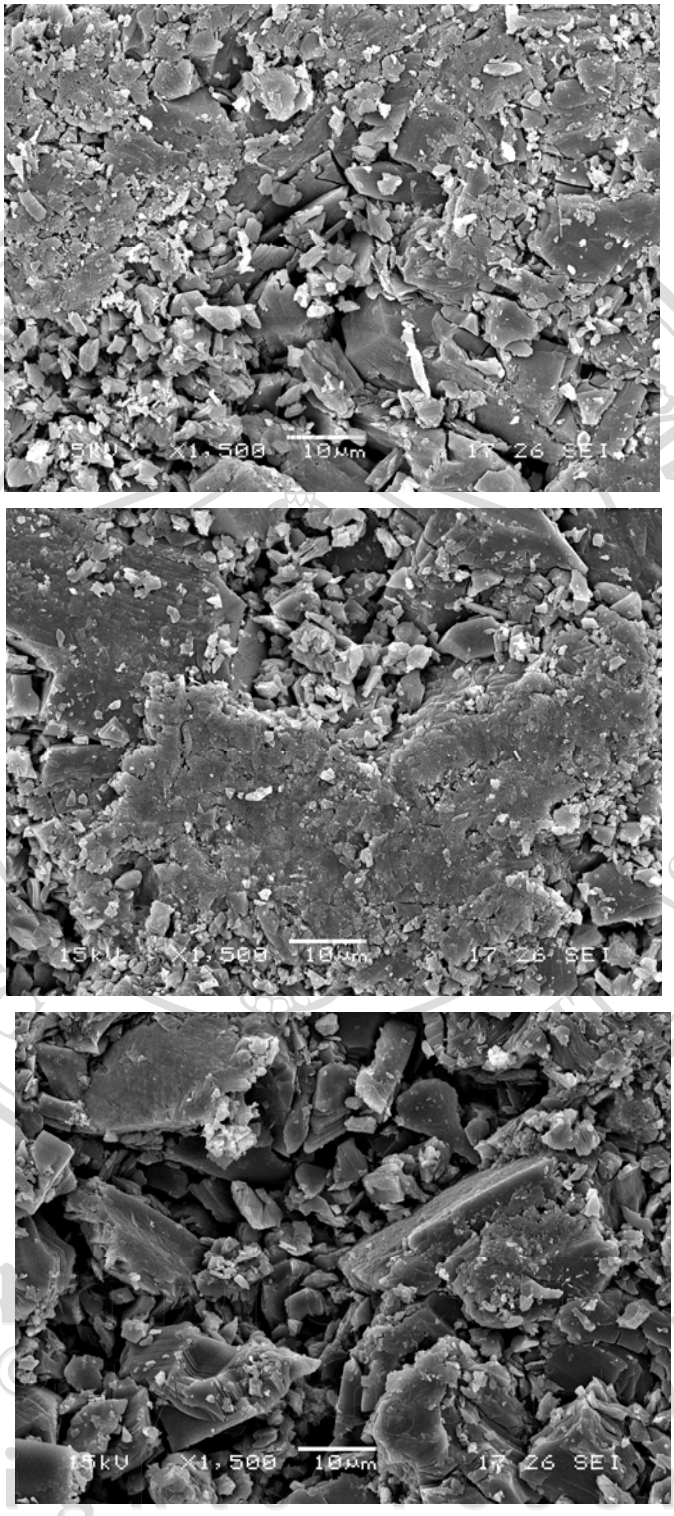
3.3.2 Morphology studies by scanning electron microscope

The DSDT was coated with gold before examined by SEM with magnification of 1500X except for the DZP-solution-dropping tablet prepared from DC blank tablet of 1400 kg CF which using magnification of 1000X. Figure 3.14 – 3.16 showed the SEM morphology of dropped side of tablet surface of DSDT prepared from DC blank tablet in comparison with DC blank tablet surface compressed at 1000, 1400 and 1800 kg CF respectively. In similar process, Figure 3.17 – 3.19 showed the SEM morphology of dropped side of tablet surface of CPM-solution and DZP-solution dropping tablet prepared from WG blank tablet in comparison with WG blank tablet surface compressed at 1000, 1400 and 1800 kg CF respectively.

It was found that the surface of DC blank tablet compressed at 1800 kg CF was smoother, less porous and intact DCP dihydrate particle not found on the surface when comparing with tablet of 1400 kg and 1000 kg CF as shown in Figure 3.16 (a), 3.15 (a) and 3.14 (a) respectively. In some area of tablet surface, the continuous surface was found. From the SEM, The pore size was less than 10 microns. The shape and size of DCP dihydrate were different from the intact DCP dihydrate which shown in Figure 3.20. The morphology surface of CPM-solution-dropping tablets prepared from DC blank tablets compressed at 1000, 1400 and 1800 kg CF in Figure 3.14 (b), 3.15 (b) and 3.16 (b) respectively were similar to the surface of DC blank tablets of the same CF. Except for 1400 kg CF tablet surface it could be found possibly CPM on the surface which the SEM of CPM was shown in Figure 3.23. Of DZP-solution-dropping tablet prepared from DC blank tablet of 1000 kg CF in Figure 3.14 (c), the surface was found having higher porosity than DC blank tablet of the same CF. But for the prepared tablet of 1800 kg CF, its surface, Figure 3.16 (c), was smoother than of tablet of 1400 kg CF which was shown in Figure 3.15 (c) and however the same appearance of the surface was shown as DC blank tablets of the same CF.

Figure 3.17 (a), 3.18 (a) and 3.19 (a) showed the surface of WG blank tablet smoother than of DC blank tablet which corresponded to the tablet porosity as shown in Figure 3.1. It was found that the surface of WG blank tablet was partly smooth and no intact lactose particle was found which SEM of lactose was shown in

Figure 3.22. When more CF was used, smoother surface was appeared as shown in Figure 3.19 (a), 3.18 (a) and 3.17 (a) of 1000, 1800 and 1800 kg CF. The surface of CPM-solution-dropping tablets which were shown in Figure 3.17 (b), 3.18 (b) and 3.19 (b) of all CF used looked similar to their blank tablets compressed at the same CF. For all DZP-solution-dropping tablets, surface looked smoother than the WG blank tablet of the same CF as shown in Figure 3.17 (c), 3.18 (c) and 3.19 (c). Apparently in Figure 3.19 (c) of 1800 kg CF, the surface of DZP-solution-dropping tablet revealed the multiple layer and diazepam particles which shown in Figure 3.26 had not been found.

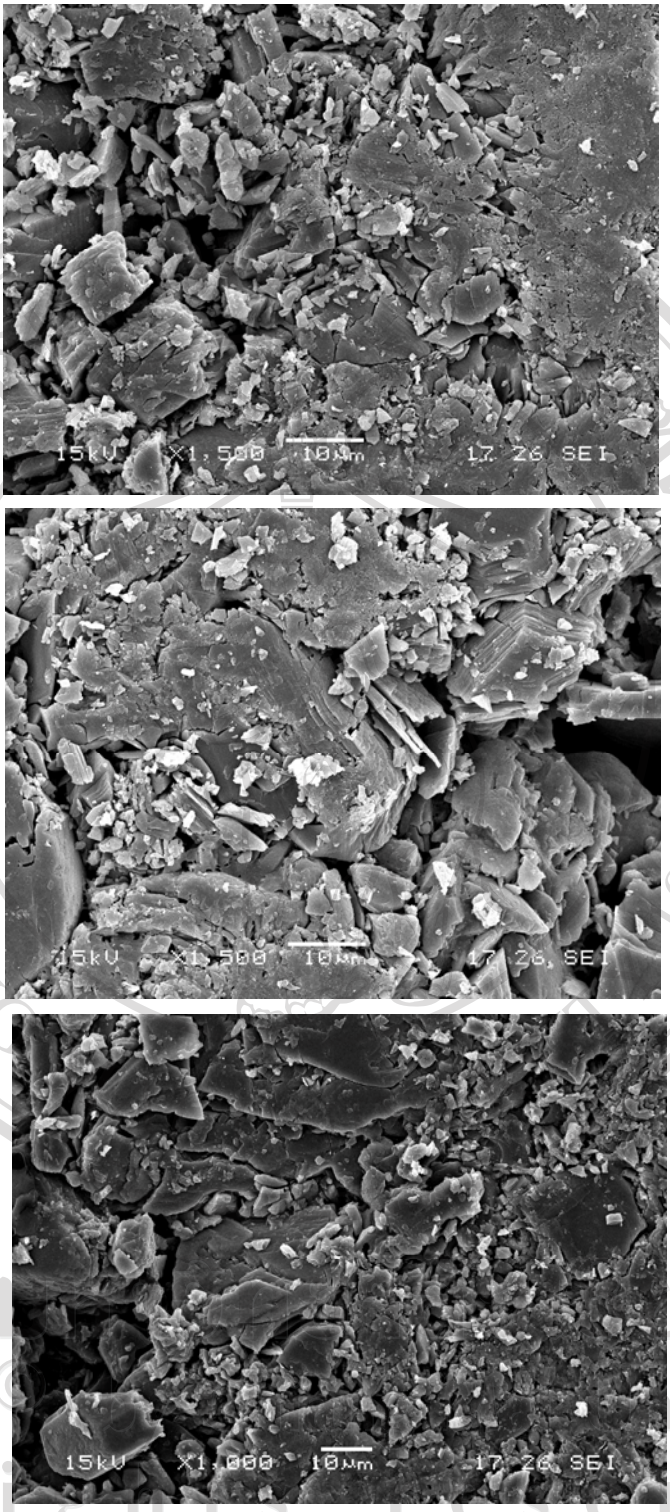


(a)

(b)

(c)

Figure 3.14 The SEM morphology of upper surface of the tablet compressed at 1000 kg CF:- (a) DC blank tablet, (b) CPM-solution-dropping tablet and (c) DZP-solution-dropping tablet prepared from DC blank tablet

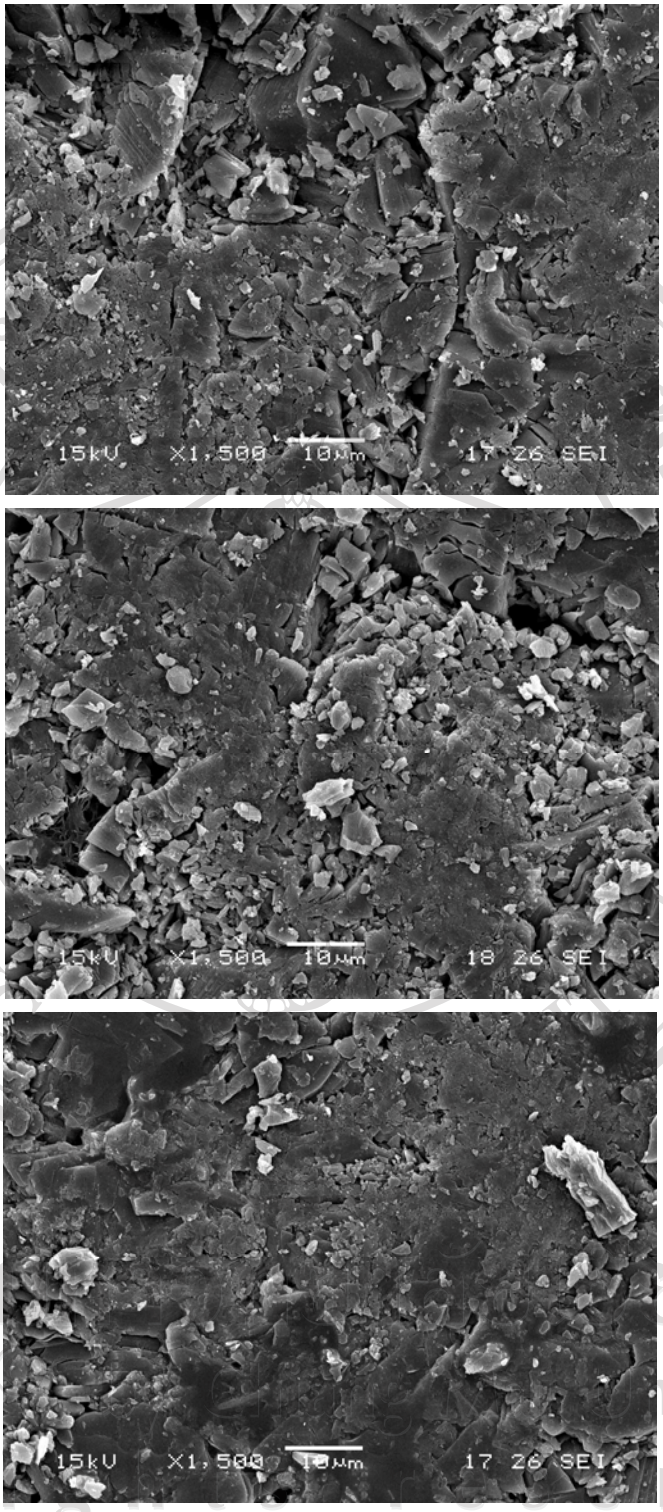


(a)

(b)

(c)

Figure 3.15 The SEM morphology of the surface of the tablet compressed at 1400 kg CF:- (a) DC blank tablet, (b) CPM-solution-dropping tablet and (c) DZP-solution-dropping tablet prepared from DC blank tablet

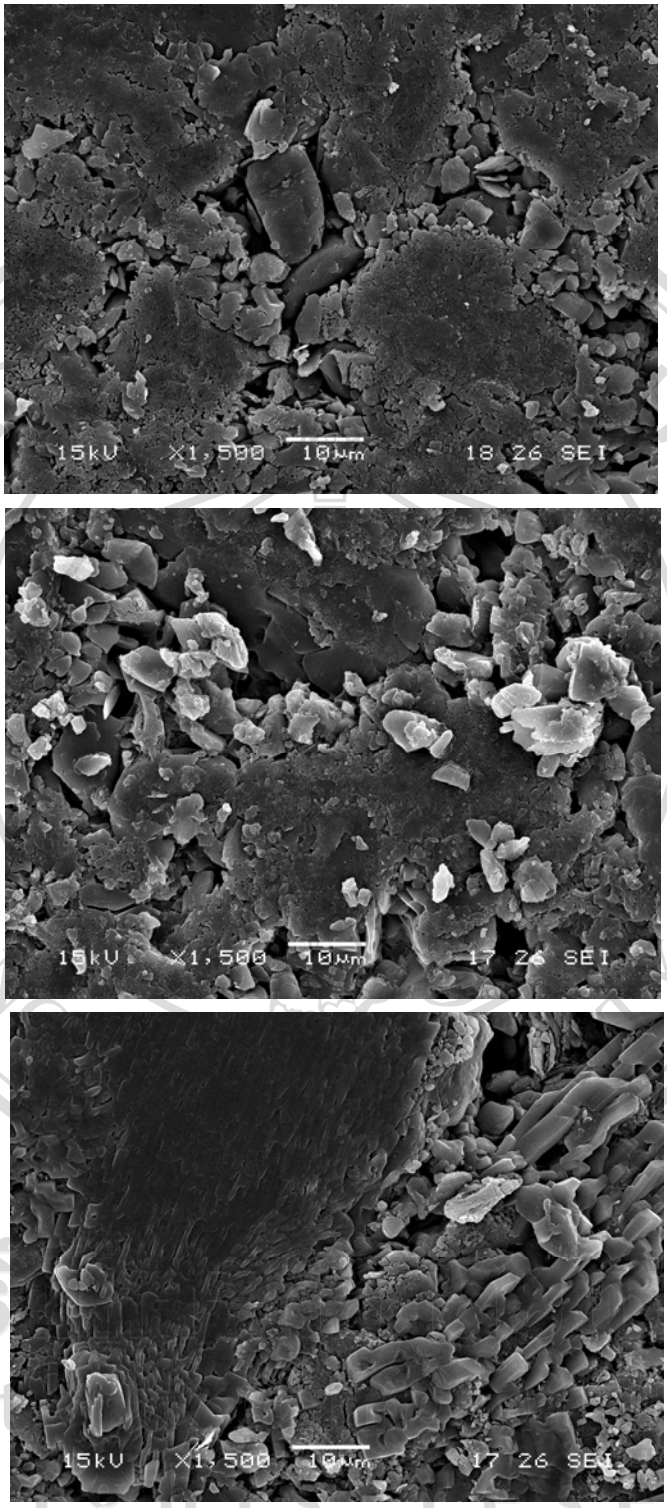


(a)

(b)

(c)

Figure 3.16 The SEM morphology of the surface of the tablet compressed at 1800 kg CF:- (a) DC blank tablet, (b) CPM-solution-dropping tablet and (c) DZP-solution-dropping tablet prepared from DC blank tablet

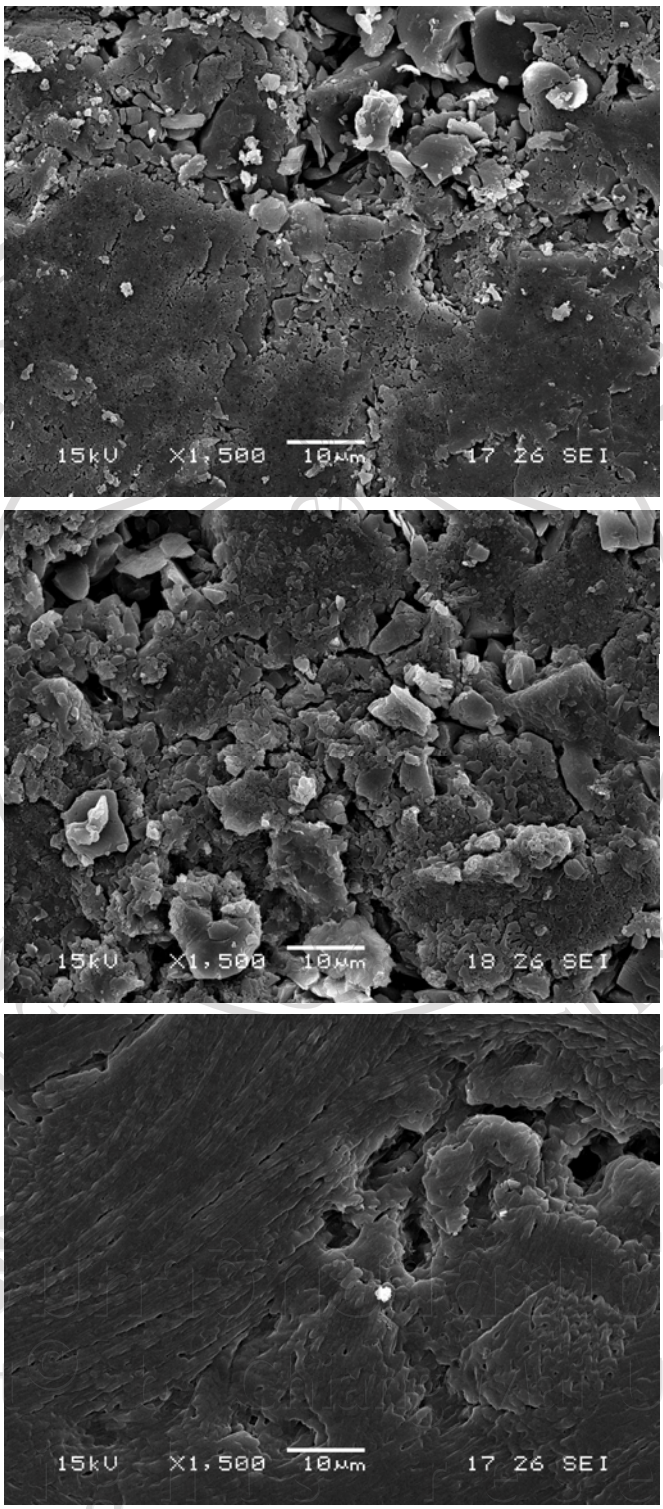


(a)

(b)

(c)

Figure 3.17 The SEM morphology of the surface of the tablet compressed at 1000 kg CF:- (a) WG blank tablet, (b) CPM-solution-dropping tablet and (c) DZP-solution-dropping tablet prepared from WG blank tablet

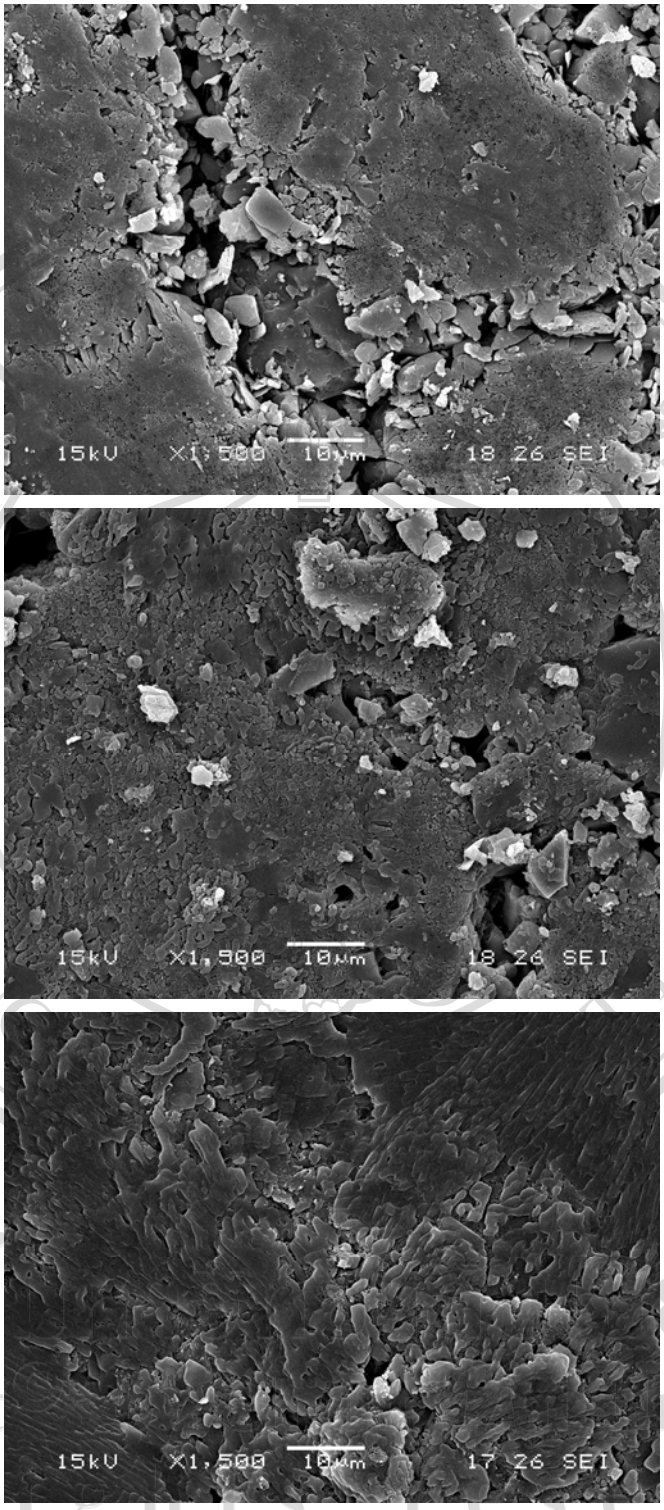


(a)

(b)

(c)

Figure 3.18 The SEM morphology of the surface of the tablet compressed at 1400 kg CF:- (a) WG blank tablet, (b) CPM-solution-dropping tablet and (c) DZP-solution-dropping tablet prepared from WG blank tablet



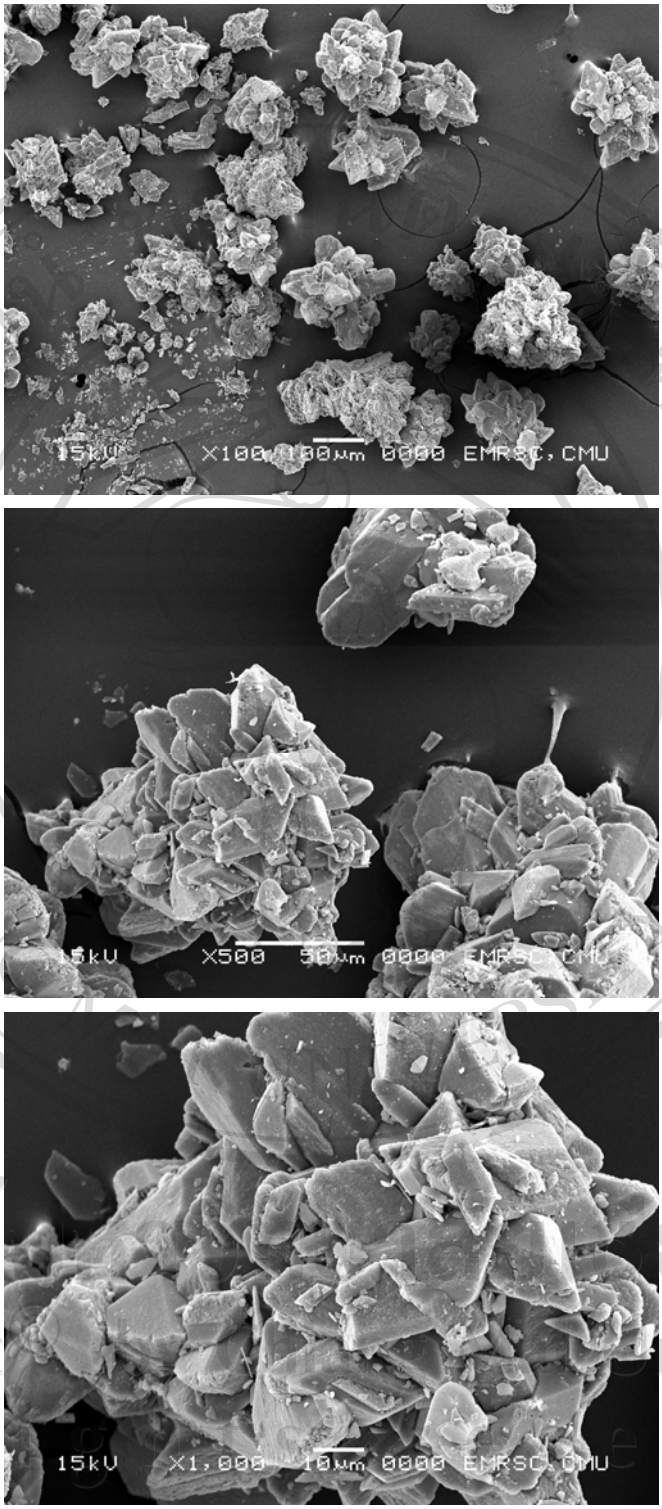
(a)

(b)

(c)

Figure 3.19 The SEM morphology of the surface of the tablet compressed at 1800 kg CF:- (a) WG blank tablet, (b) CPM-solution-dropping tablet and (c) DZP-solution-dropping tablet prepared from WG blank tablet

The CPM and diazepam particles could not be found on the surface of DSDT by SEM. Additionally the SEM was used to characterize powder scratched from near surface and deeper area of tablet surface. The SEM morphology show the appearance of the size and shape of particles in CPM–solution-dropping tablets from DC blank tablets of all tested CF and from WG blank tablets of 1000 and 1400 kg of CF with magnification 100X, 500X and 1000X as shown in Figure 3.27 – 3.29 and 3.30 – 3.31 respectively. Figure 3.32 and 3.33 showed the SEM morphology of powder scratched from near surface area of DZP-solution-dropping tablet surface from DC and WG blank tablets, respectively, of all tested CF, with magnification 1000X. They were compared with SEM morphology of each excipient used in DC and WG tablets before tablet compaction such as dibasic calcium phosphate dihydrate (DCP dihydrate), Ac-Di-Sol®, Pharmatose® (lactose monohydrate), magnesium stearate and talcum as shown in Figure 3.22 - 3.24 respectively as well as CPM and diazepam powder in Figure 3.25 and 3.26 with the same magnification. The SEM images of such excipients powder corresponded to the information stated in the literature (Raymond et al., 2006). The morphology of CPM powder shows the angular shape and smooth surface with over 50 micron-size range. The size and shape of diazepam powder as shown in Figure 3.26 look like lactose in Figure 3.22 but they have smoother surface.

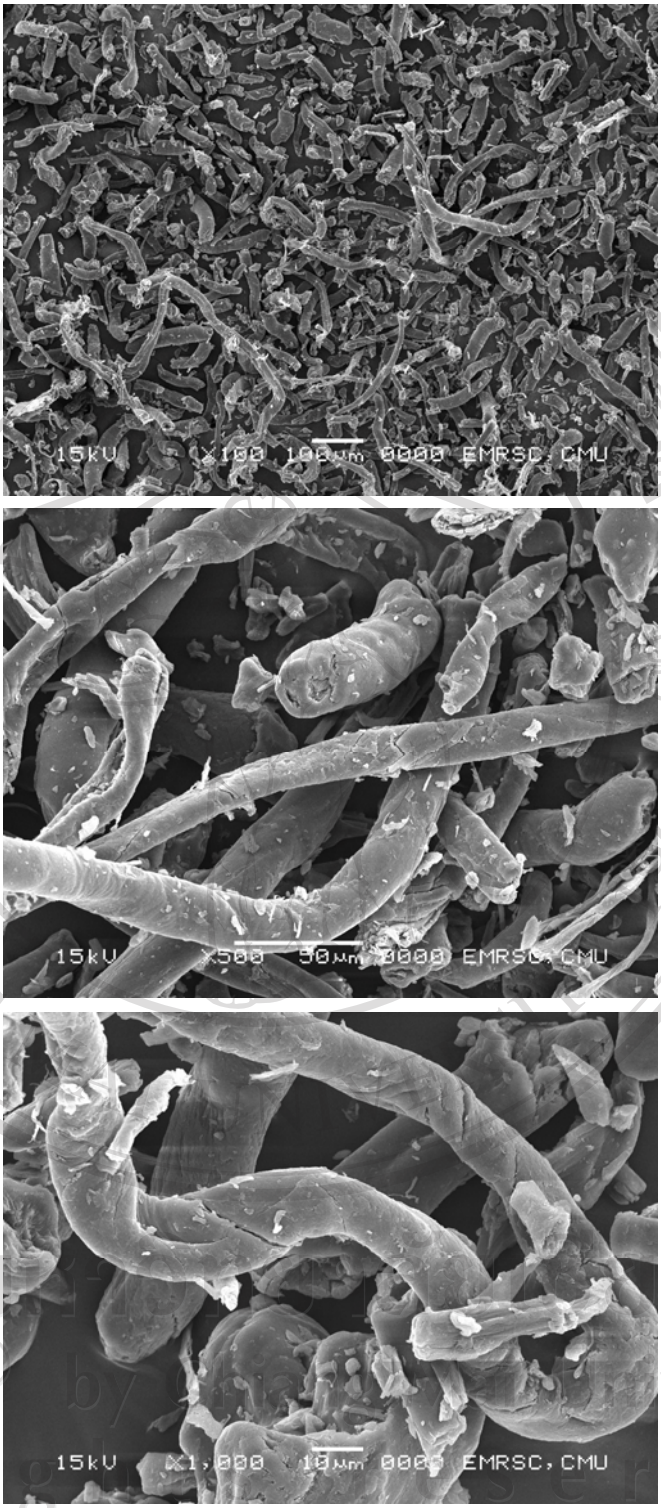


(a)

(b)

(c)

Figure 3.20 SEM morphology of DCP dihydrate with magnification
(a) 100 X (b) 500 X (c) 1000 X

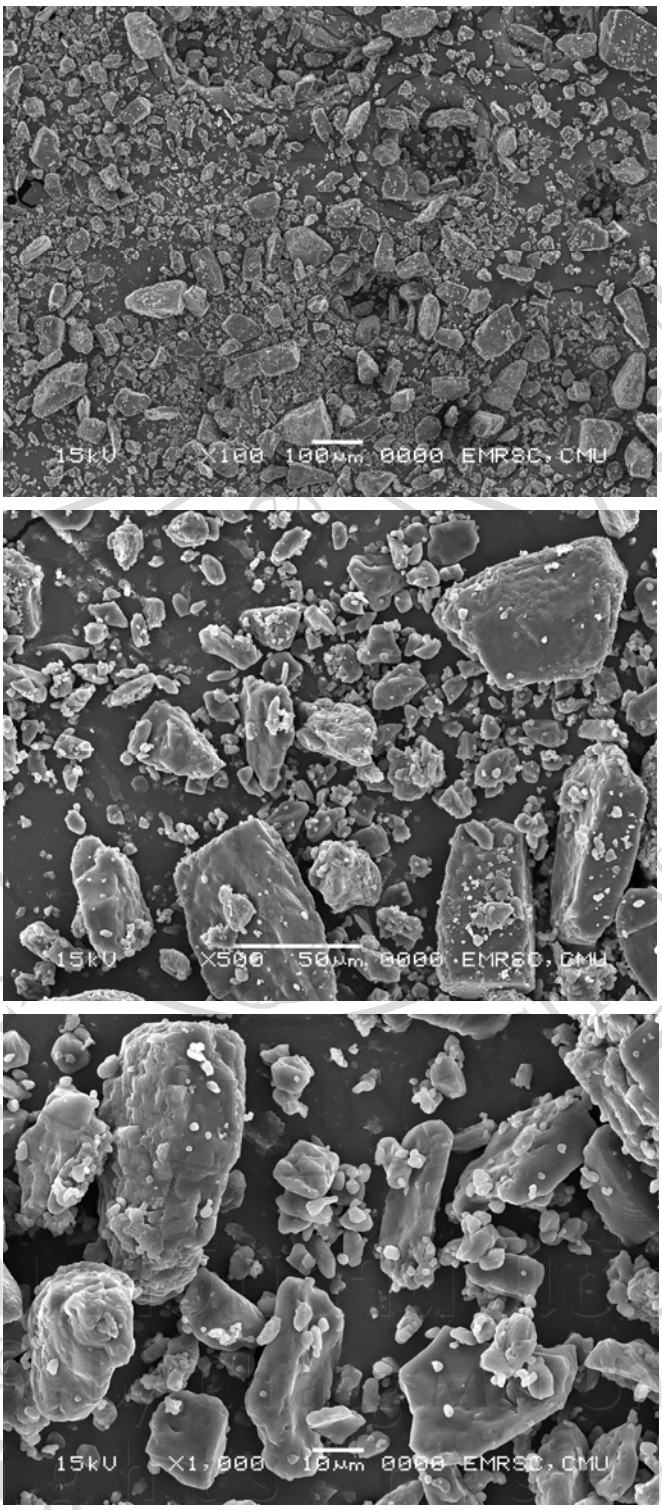


(a)

(b)

(c)

Figure 3.21 SEM morphology of Ac-Di-Sol® with magnification
(a) 100X (b) 500X (c) 1000X

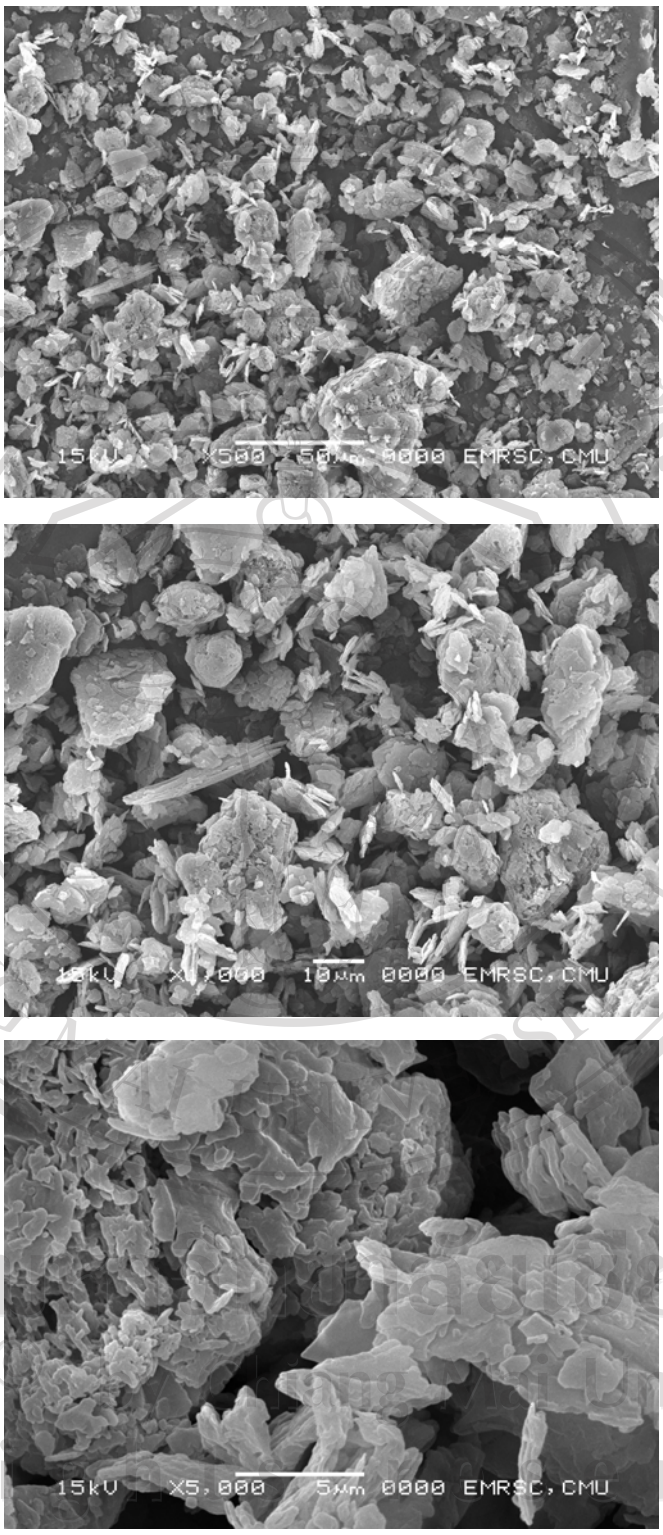


(a)

(b)

(c)

Figure 3.22 SEM morphology of Pharmatose® with magnification
(a) 100X (b) 500X (c) 1000X

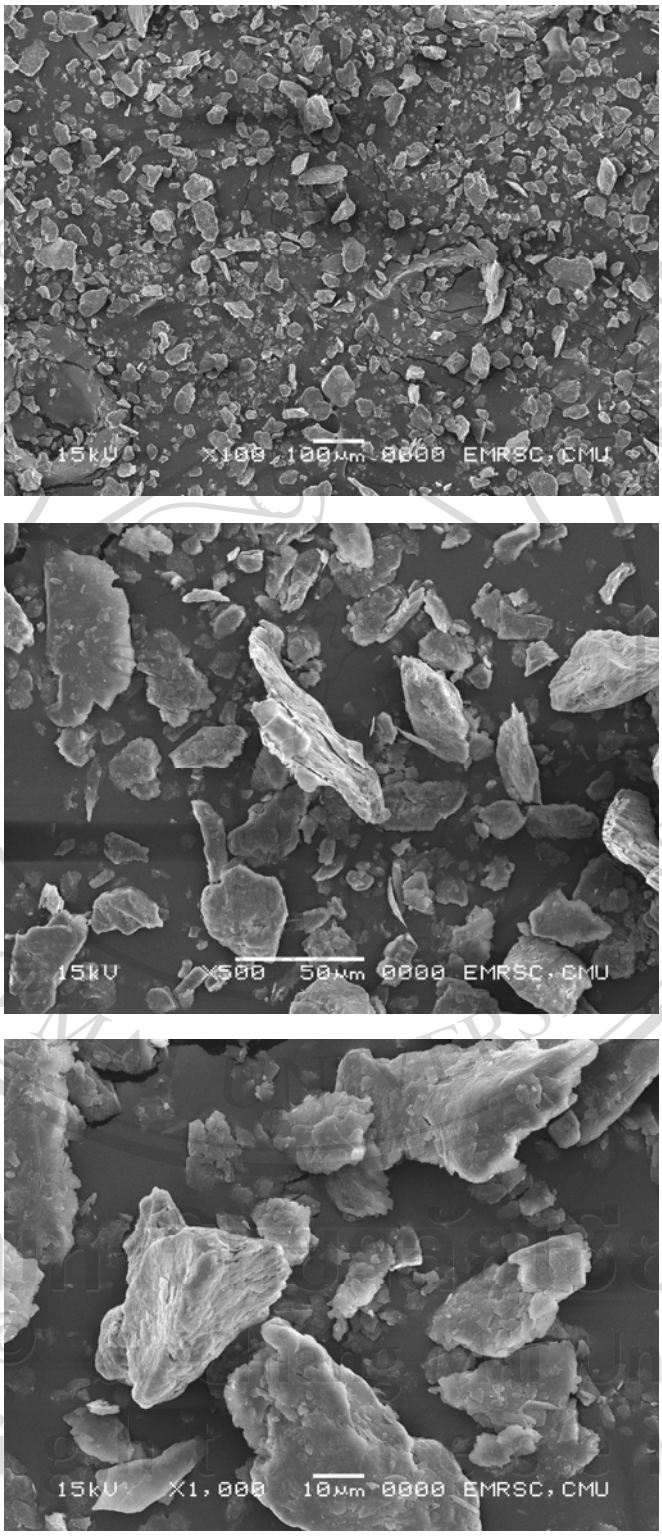


(a)

(b)

(c)

Figure 3.23 SEM morphology of magnesium stearate with magnification (a) 100X (b) 500X (c) 1000X



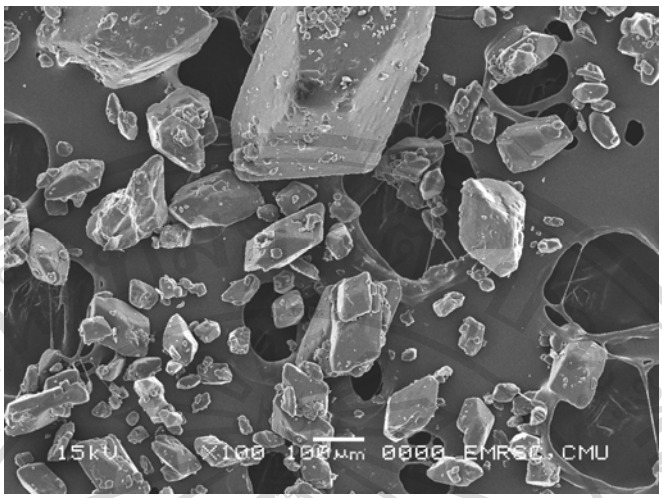
(a)

(b)

(c)

Figure 3.24 SEM morphology of talcum with magnification

(a) 100X (b) 500X (c) 1000X



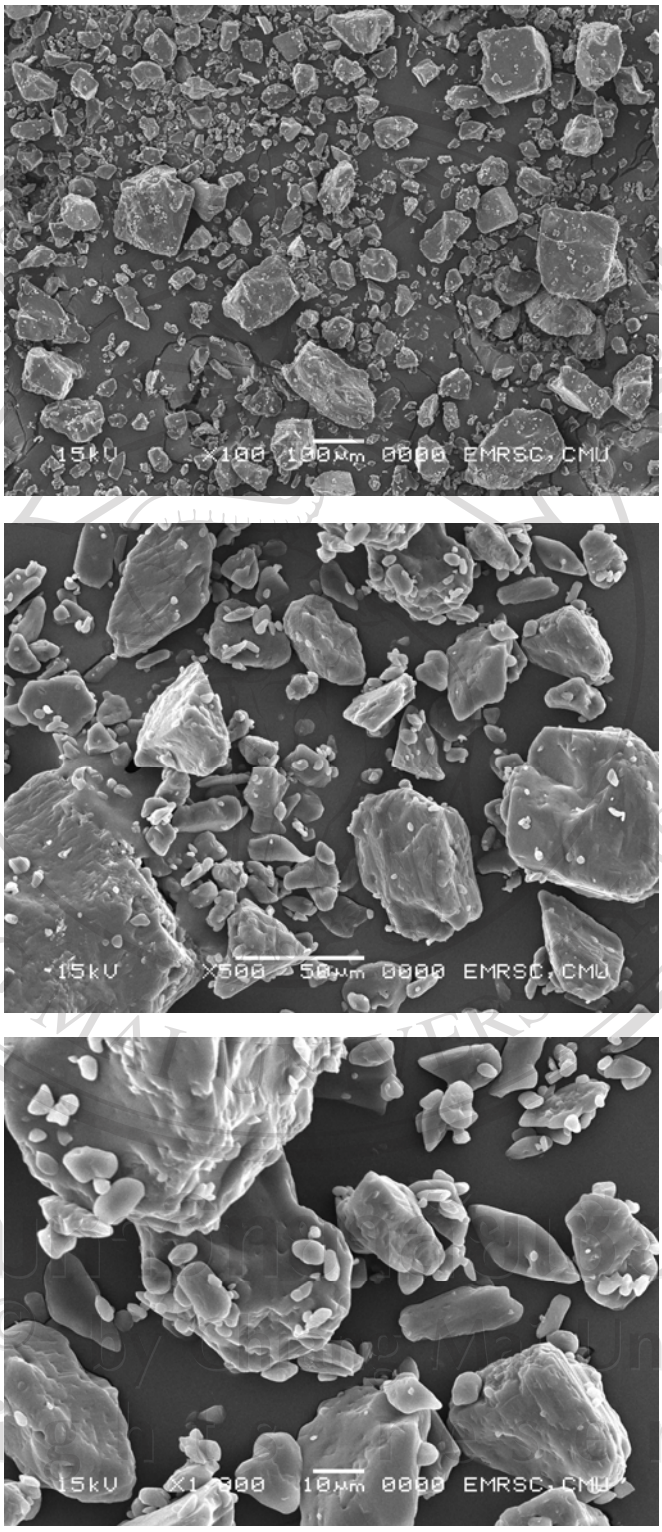
(a)

(b)

(c)

Figure 3.25 SEM morphology of CPM with magnification

(a) 100X (b) 500X (c) 1000X



(a)

(b)

(c)

Figure 3.26 SEM morphology of diazepam with magnification
(a) 100X (b) 500X (c) 1000X

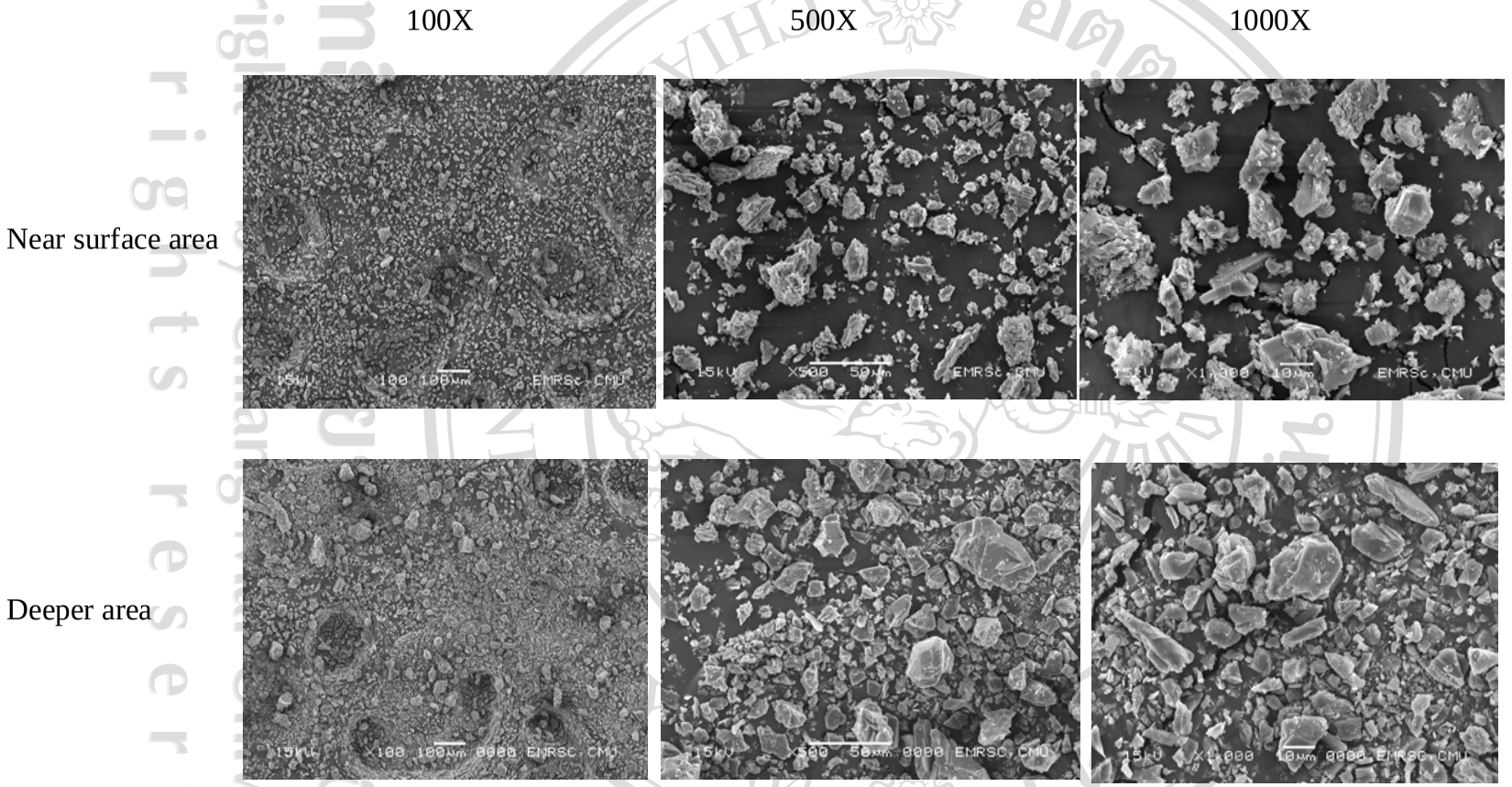


Figure 3.27 SEM morphology of powder scratched from near and deeper surface of CPM-solution-dropping tablet prepared from DC blank tablet compressed at 1000 kg CF

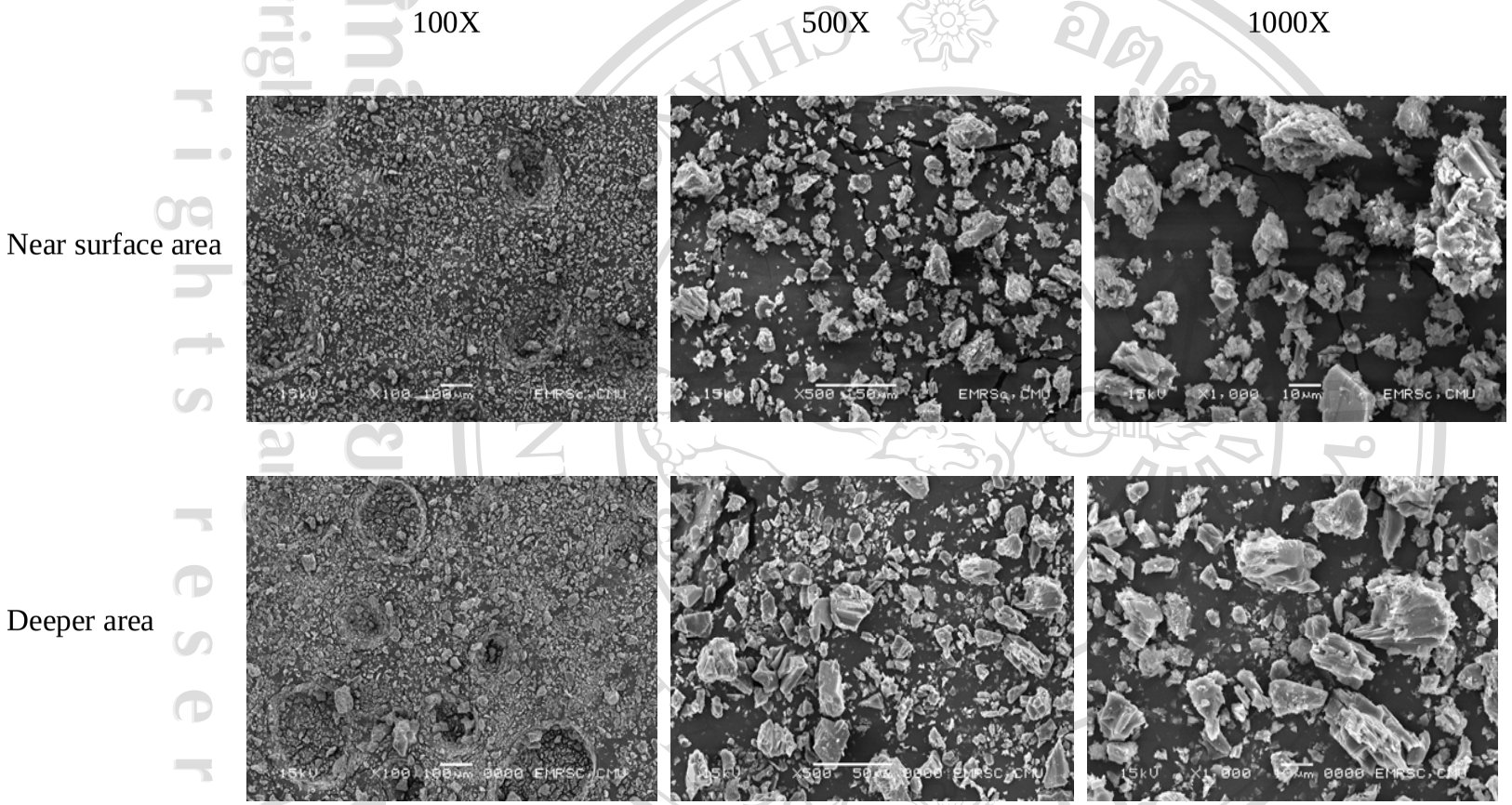


Figure 3.28 SEM morphology of powder scratched from near and deeper surface of CPM-solution-dropping tablet prepared from DC blank tablet compressed at 1400 kg CF

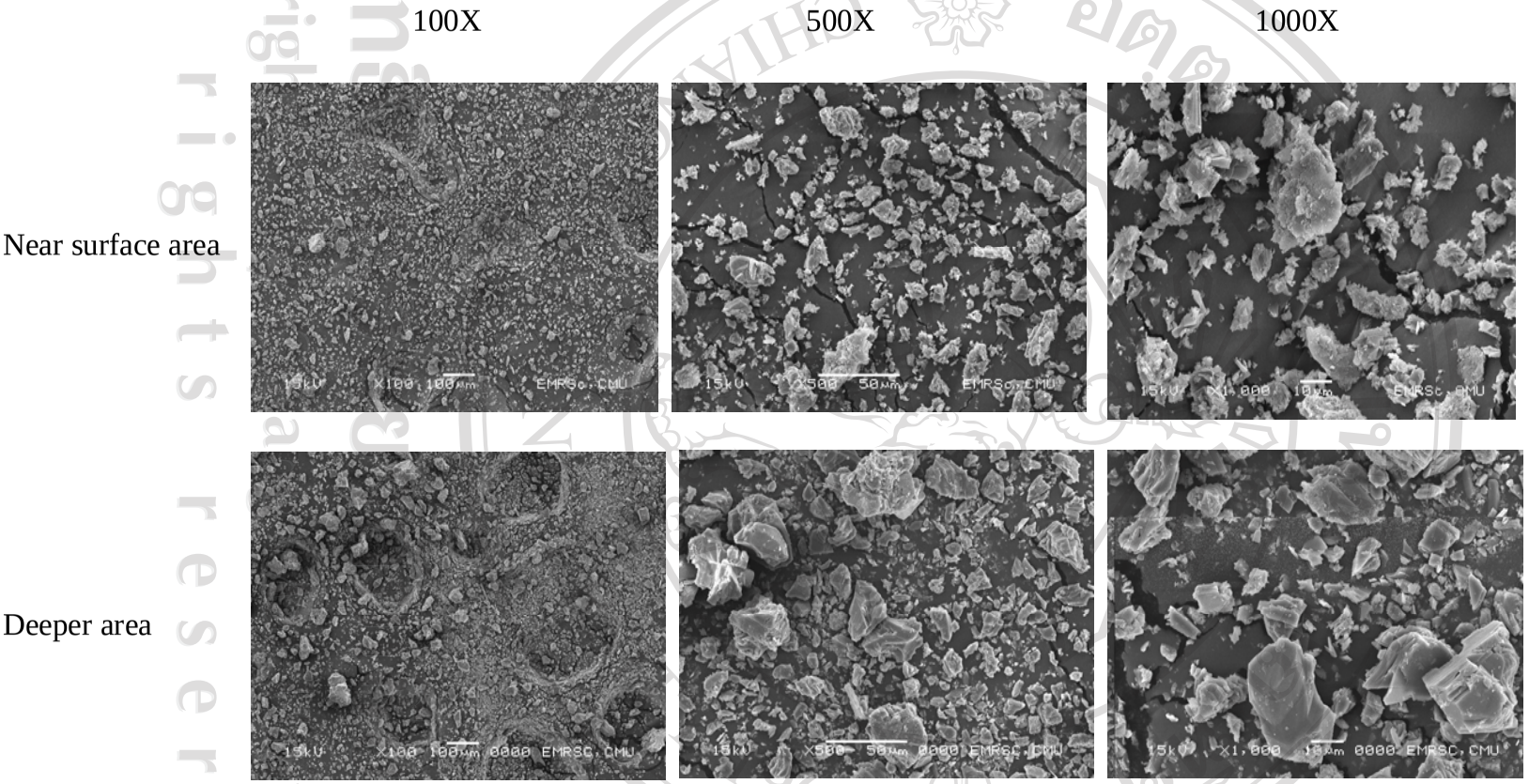


Figure 3.29 SEM morphology of powder scratched from near and deeper surface of CPM-solution-dropping tablet prepared from DC blank tablet compressed at 1800 kg CF

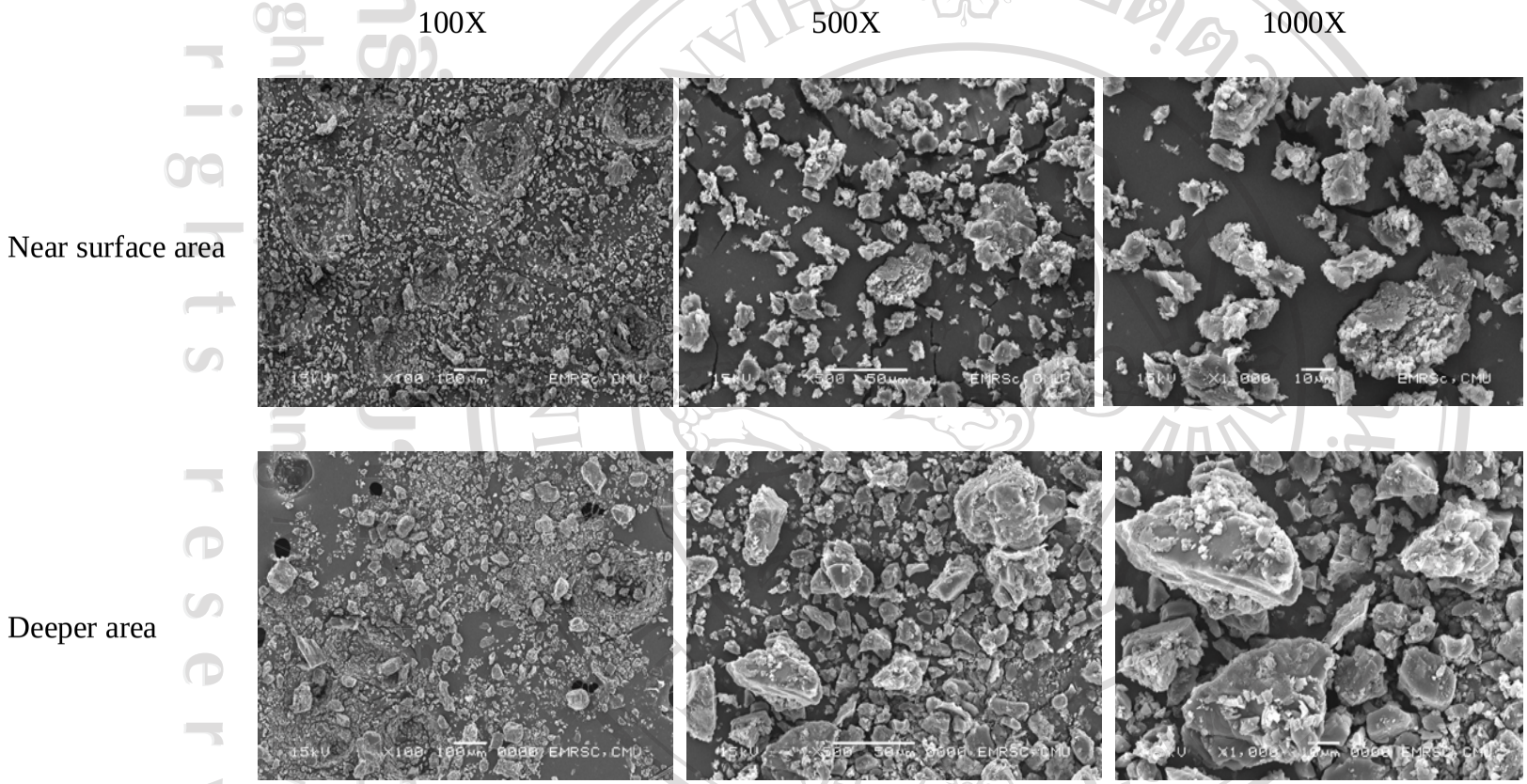


Figure 3.30 SEM morphology of powder scratched from near and deeper surface of CPM-solution-dropping tablet prepared from WG blank tablet compressed at 1000 kg CF

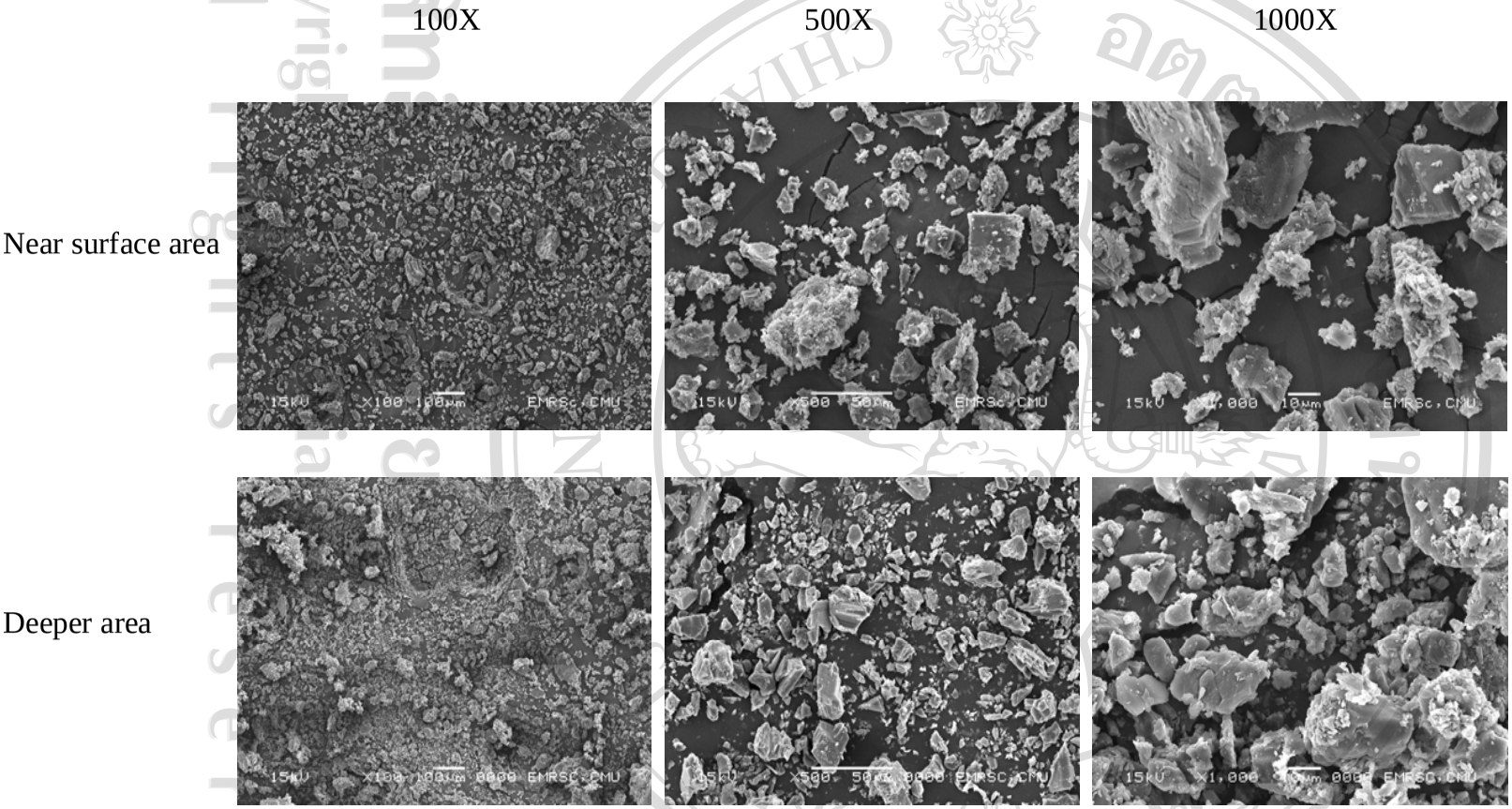
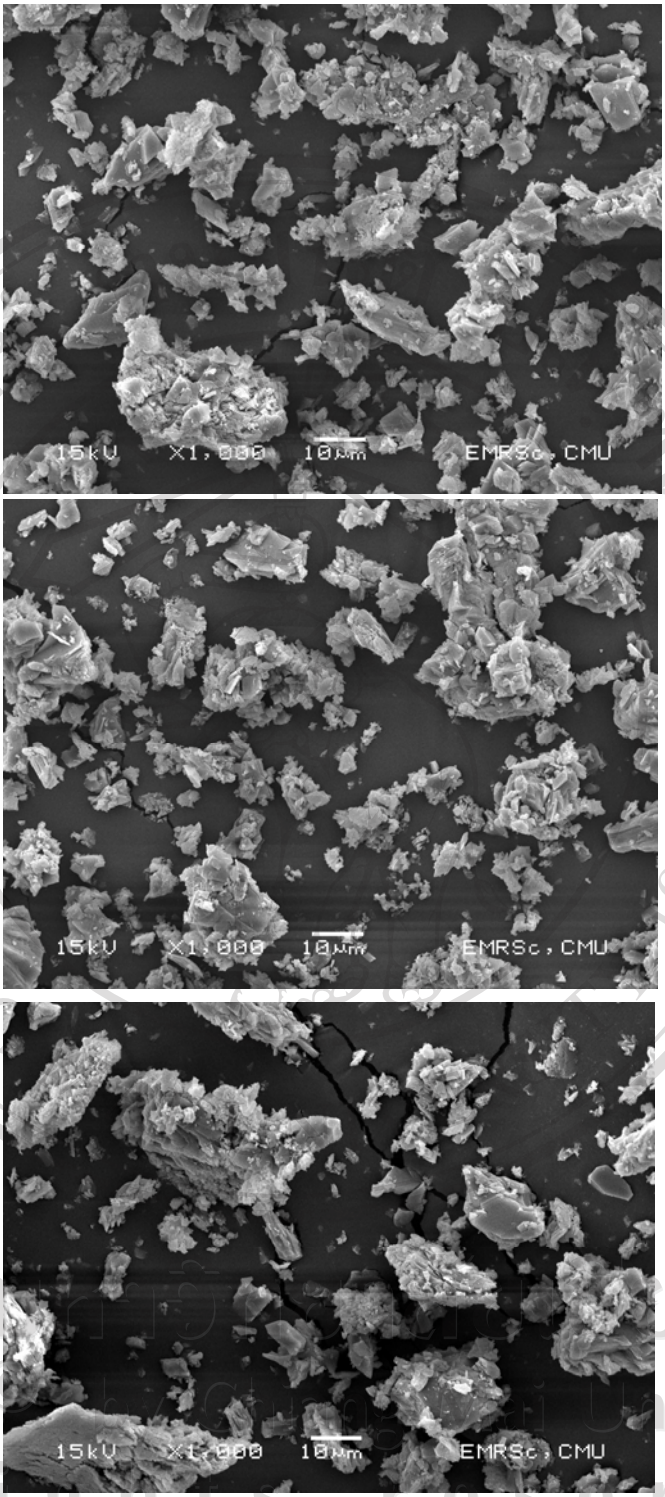


Figure 3.31 SEM morphology of powder scratched from near and deeper surface of CPM-solution-dropping tablet prepared from WG blank tablet compressed at 1400 kg CF

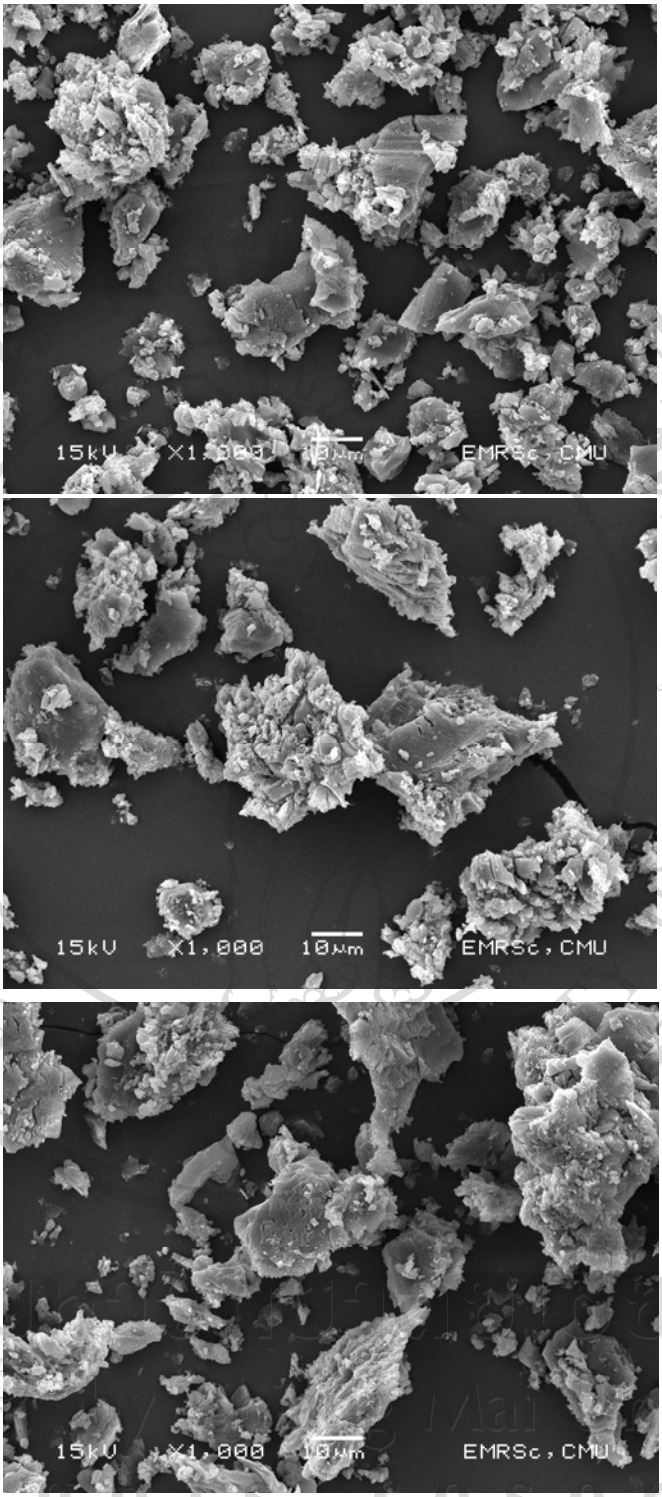


(a)

(b)

(c)

Figure 3.32 SEM morphology of powder scratched from near surface of DZP-solution-dropping tablet prepared from DC blank tablet (magnification 1000X) compressed at (a) 1000 kg (b) 1400 kg (c) 1800 kg



(a)

(b)

(c)

Figure 3.33 SEM morphology of powder scratched from near surface of DZP-solution-dropping tablet prepared from WG blank tablet (magnification 1000X) compressed at (a) 1000 kg (b) 1400 kg (c) 1800 kg

3.3.3 X-ray diffraction of powder

The powder characterization of CPM and diazepam were examined by using powder X-ray diffractometer (XRPD or XRD) and their patterns were shown in Figure 3.34 and 3.35 respectively. Both patterns show the crystalline forms of drug with clear peak at angle of 2Θ about 19.14, 20.00, 21.24, 24.89, 26.23 degrees for CPM and 18.67, 22.63 degree for diazepam. The excipients formulated in tablet were also examined the crystalline behavior which were shown in Figure 3.36 – 3.40. The diffraction pattern of the powder of each excipient shows the intensity peak at angle of 2Θ as the following paragraphs.

Many peaks of crystalline lattice at 2Θ belong to dicalcium phosphate dihydrate about 11.46, 20.78 and 29.13 degree as shown in Figure 3.36.

Pharmatose® occupied the dominant peak of crystal form about 19.73 degree as shown in Figure 3.37.

XRD pattern of Ac-Di-Sol® showed the distinct amorphous form with halo form as in Figure 3.38.

Magnesium stearate showed many peaks of crystalline lattice with the dominant peak at about 21.61 degrees as revealed in Figure 3.39.

Talcum showed the distinct crystal form with dominant peaks about 9.34 and 28.53 degree as shown in Figure 3.38.

The scratched surface powder from CPM-solution-dropping tablet prepared from prepared DC and WG blank tablet of 1000, 1400 and 1800 kg CF were examined by X-ray diffractometer and were shown in Figure 3.41 – 3.46. Their XRD patterns of powder scratched from the tablet surface were compared with the pattern of CPM, dicalcium phosphate dihydrate for preparing DC blank tablet and Pharmatose® for preparing WG blank tablet including other excipients such as Ac-Di-Sol®, magnesium stearate and talcum. In the same manner, the pattern of XRD of the scratched powder from the surface of DZP-solution-dropping tablet prepared from DC and WG blank tablet of 1000, 1400 and 1800 kg CF were shown in Figure 3.47 – 3.52. Their patterns were also compared with diazepam and the other tablet excipients as in CPM-solution-dropping tablet.

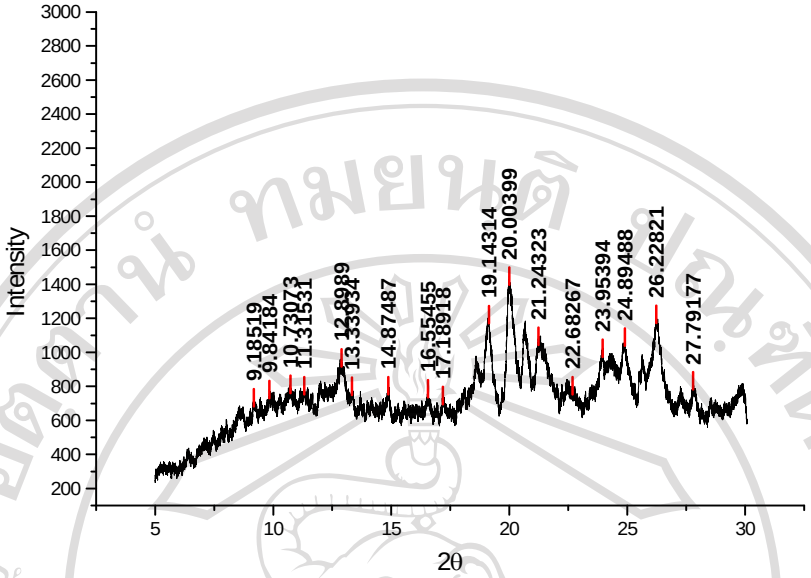


Figure 3.34 Powdered X-ray diffraction pattern of CPM

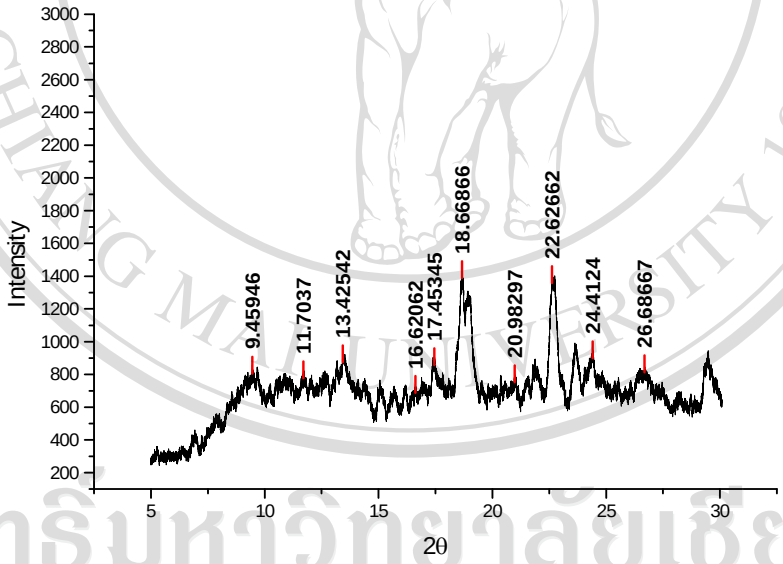


Figure 3.35 Powdered X-ray diffraction pattern of diazepam

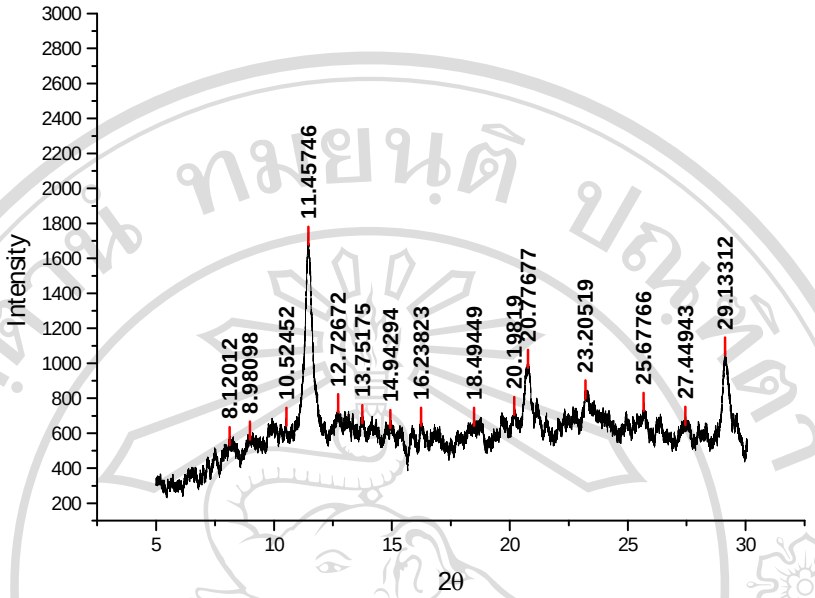


Figure 3.36 Powdered X-ray diffraction pattern of DCP dihydrate

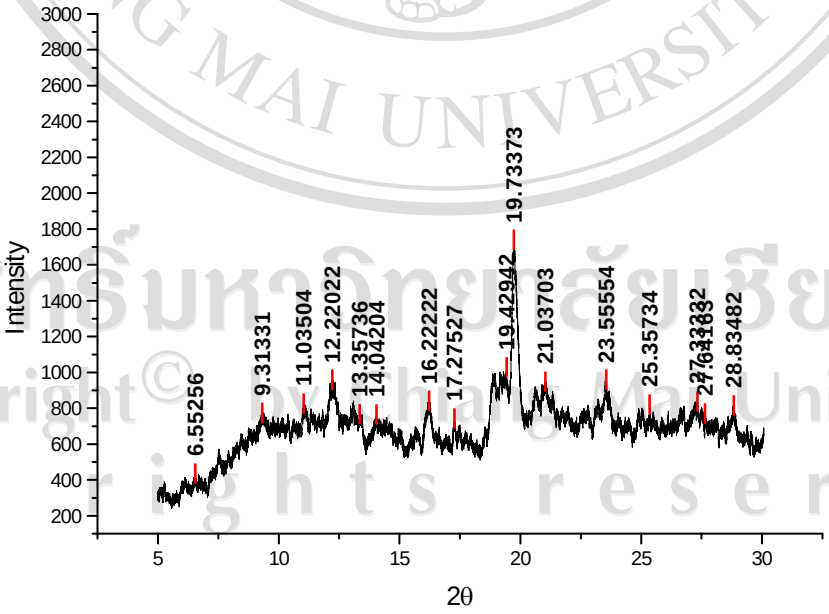


Figure 3.37 Powdered X-ray diffraction pattern of Pharmatose®

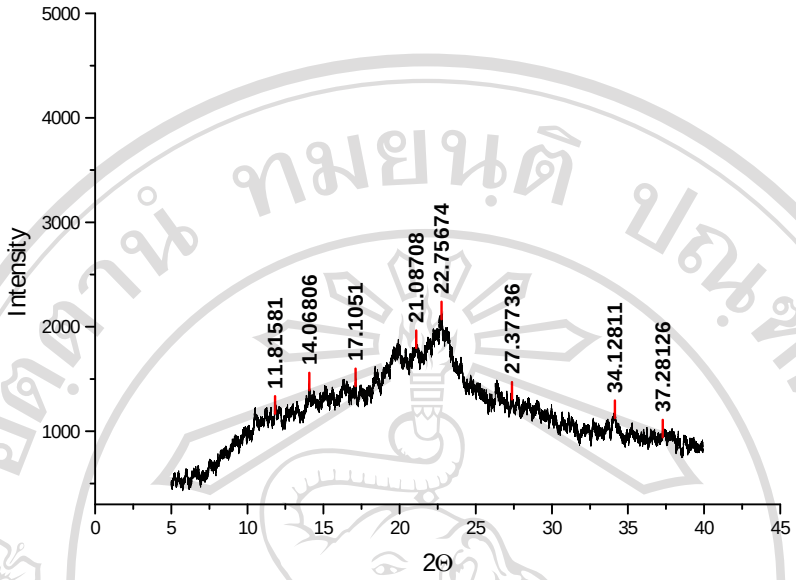


Figure 3.38 Powdered X-ray diffraction pattern of Ac-Di-Sol®

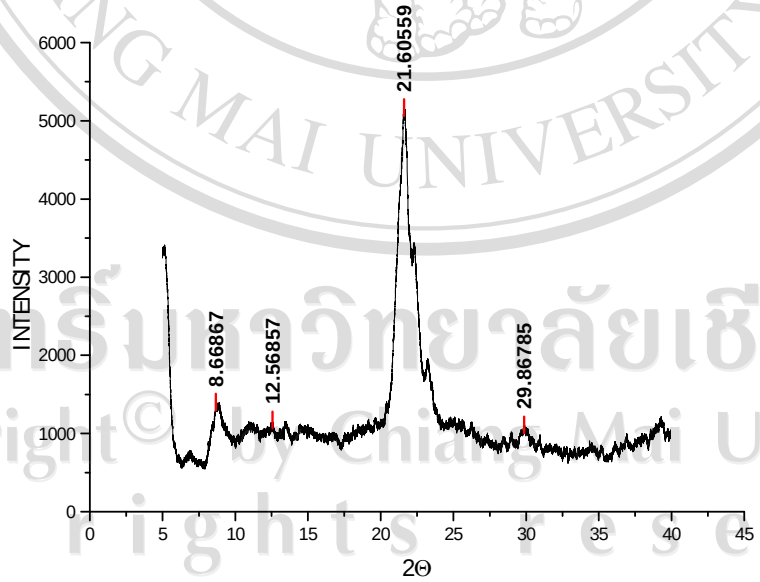


Figure 3.39 Powdered X-ray diffraction pattern of magnesium stearate

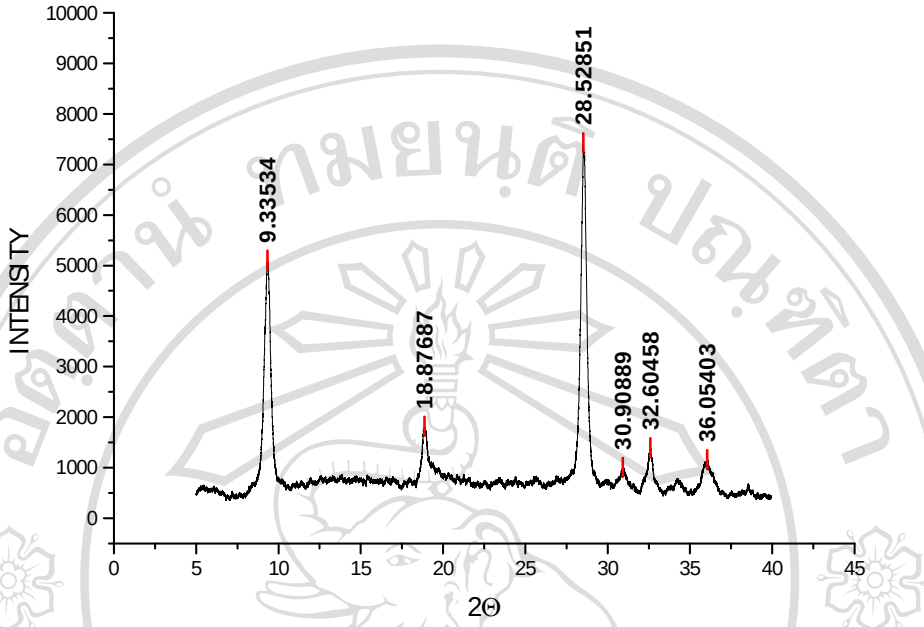


Figure 3.40 Powdered X-ray diffraction pattern of talcum

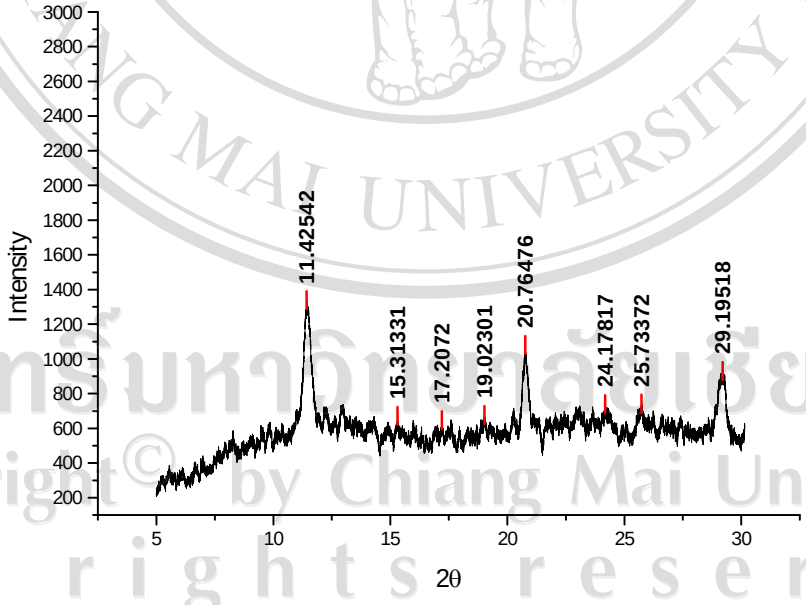


Figure 3.41 Powdered XRD pattern of scratched surface powder from CPM-solution-dropping tablet prepared from DC blank tablet of 1000 kg CF

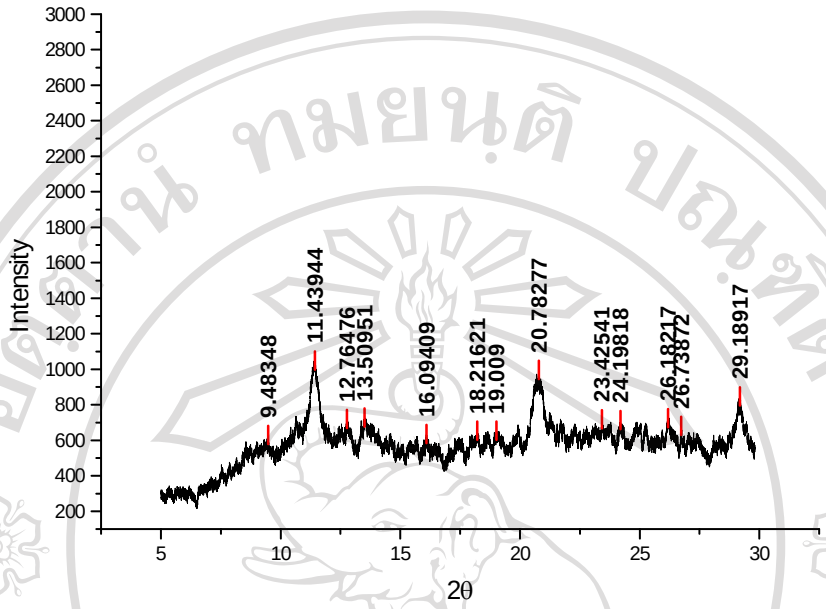


Figure 3.42 Powdered XRD pattern of scratched surface powder from CPM-solution-dropping tablet prepared from DC blank tablet of 1400 kg CF

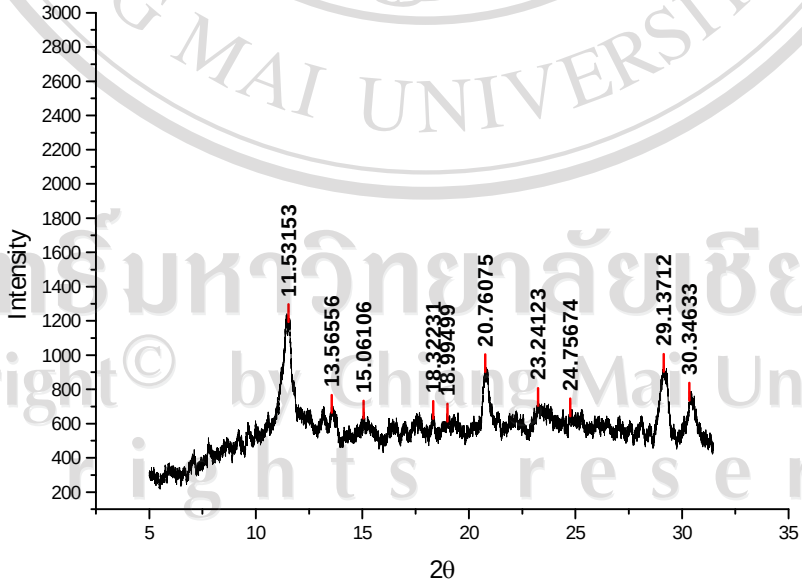


Figure 3.43 Powdered XRD pattern of scratched surface powder from CPM-solution-dropping tablet prepared from DC blank tablet of 1800 kg CF

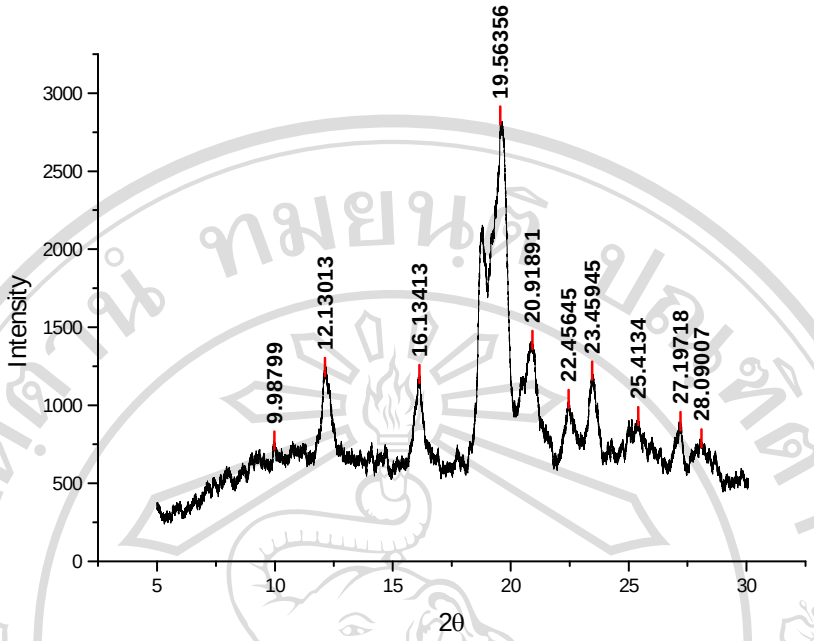


Figure 3.44 Powdered XRD pattern of scratched surface powder from CPM-solution-dropping tablet prepared from WG blank tablet of 1000 kg CF

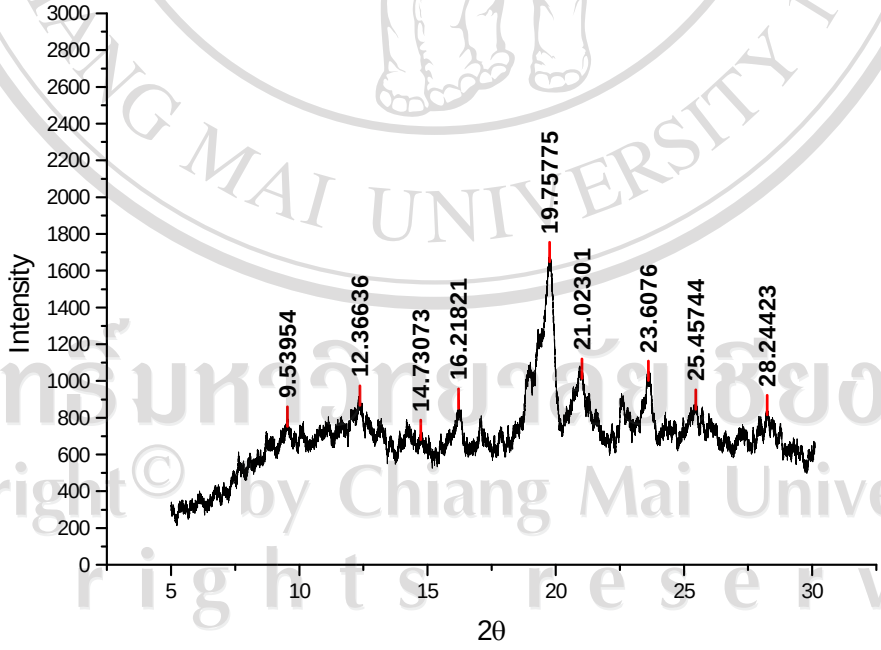


Figure 3.45 Powdered XRD pattern of scratched surface powder from CPM-solution-dropping tablet prepared from WG blank tablet of 1400 kg CF

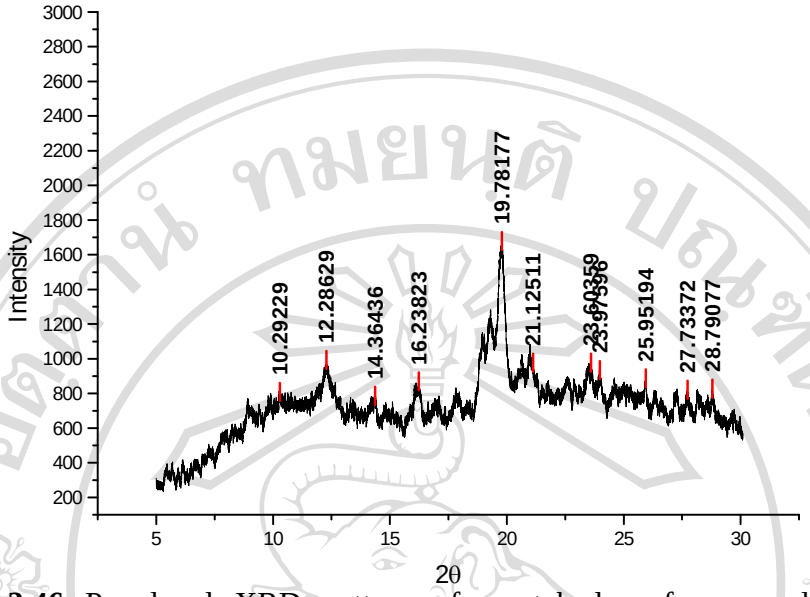


Figure 3.46 Powdered XRD pattern of scratched surface powder from CPM-solution-dropping tablet prepared from WG blank tablet of 1800 kg CF

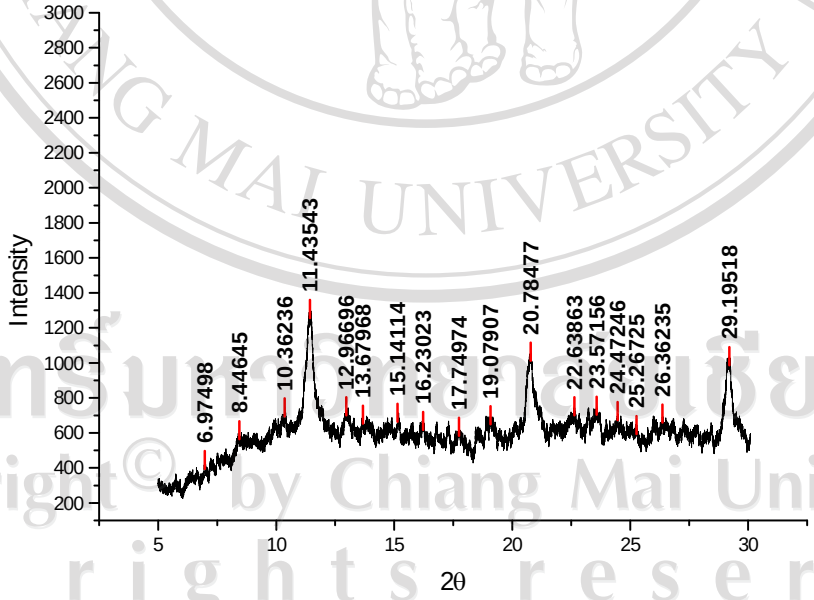


Figure 3.47 Powdered XRD pattern of scratched surface powder from DZP-solution-dropping tablet prepared from DC blank tablet of 1000 kg CF

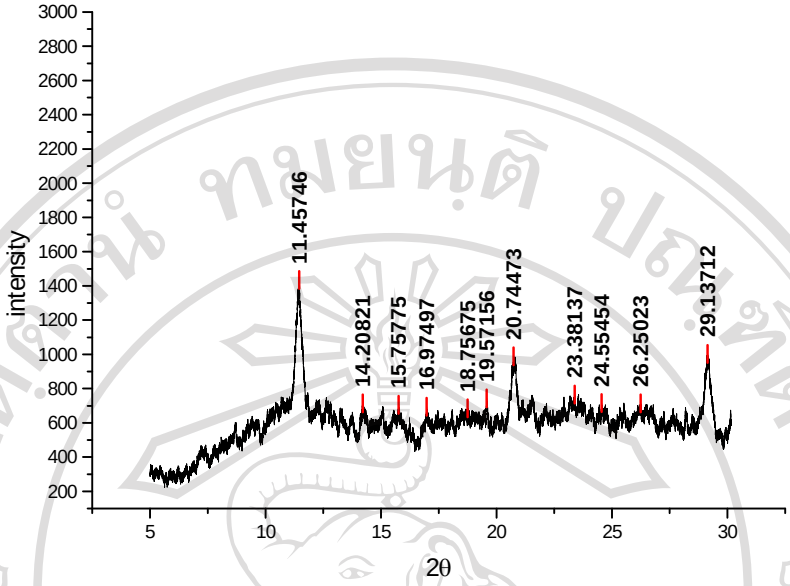


Figure 3.48 Powdered XRD pattern of scratched surface powder from DZP-solution-dropping tablet prepared from DC blank tablet of 1400 kg CF

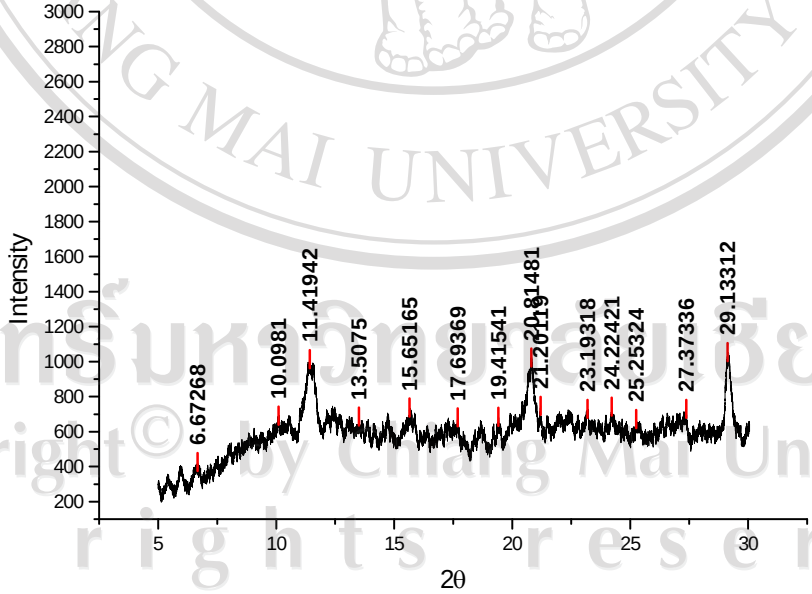


Figure 3.49 Powdered XRD pattern of scratched surface powder from DZP-solution-dropping tablet prepared from DC blank tablet of 1800 kg CF

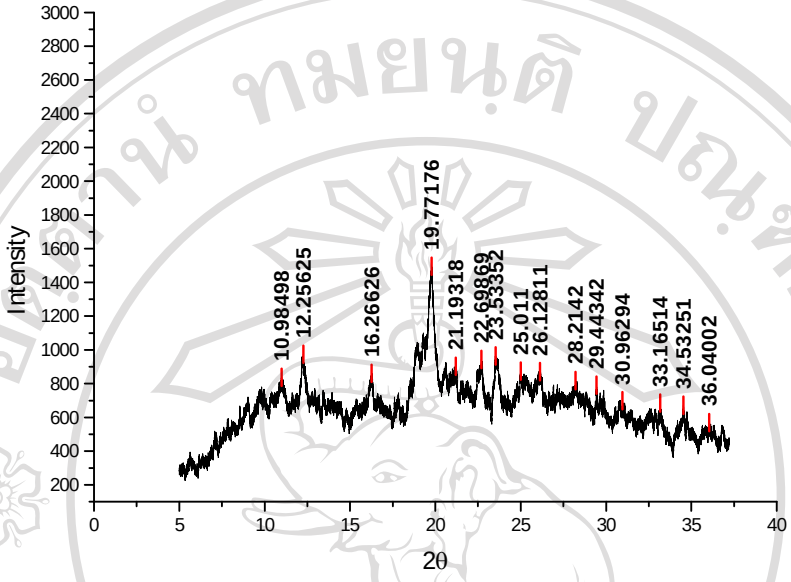


Figure 3.50 Powdered XRD pattern of scratched surface powder from DZP-solution-dropping tablet prepared from WG blank tablet of 1000 kg CF

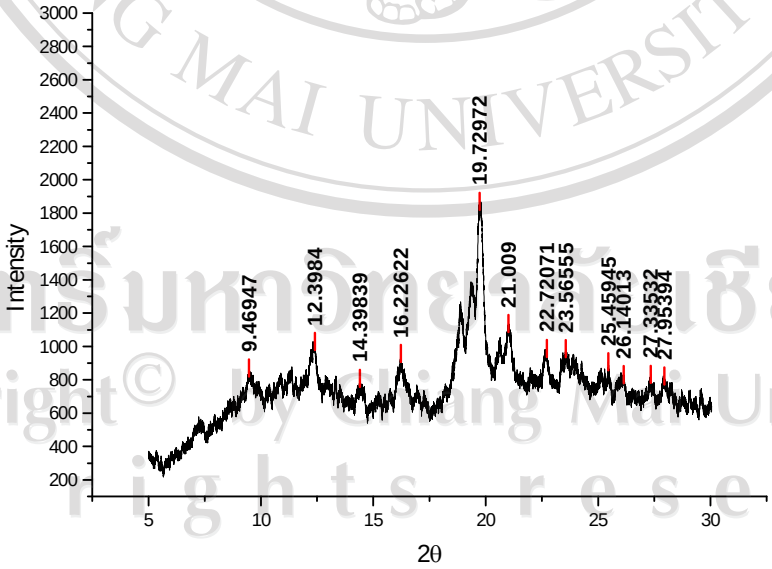


Figure 3.51 Powdered XRD pattern of scratched surface powder from DZP-solution-dropping tablet prepared from WG blank tablet of 1400 kg CF

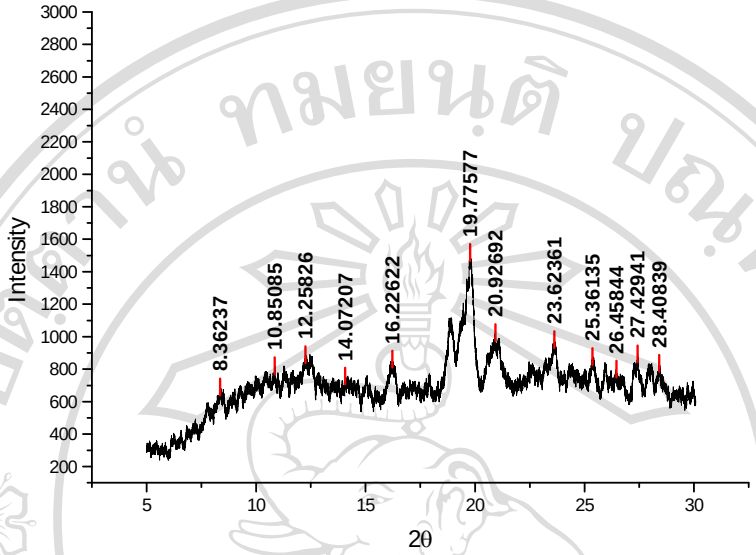


Figure 3.52 Powdered XRD pattern of scratched surface powder from DZP-solution-dropping tablet prepared from WG blank tablet of 1800 kg CF

From the study of the crystalline of CPM and diazepam in the powder scratched from the near surface area of DSDT by using powder X-ray diffractometer could not clearly support whether the crystalline form having of diffractogram different from those of the blank tablet. Single crystal X-ray diffraction was also an alternative method for the physical characterization of the powder from area of solution dropping on tablet surface as shown in Figure 3.53 – 3.70. The diffraction patterns of powder from the blank tablets have the similar pattern among the tablet of difference CF. DC blank tablet surface powder showed the same dominant peaks about 11.4, 20.8 and 29.1 degree of DCP dihydrate which was its filler in tablet as shown in Figure 3.53 – 3.55. WG blank tablet surface powder also had the dominant peak about 19.1, 19.7 degrees of Pharmatose® which act as diluent as shown in Figure 3.56 – 3.58. The diffraction patterns of powder from DSDT prepared from DC blank tablet compressed at all tested CF illustrated no peak of CPM and DZP which scratched from the tablet surface. The diffraction patterns was shown in Figure 3.59 – 3.61 and 3.62 – 3.64 respectively. Figure 3.65 – 3.67 showed the peak of CPM in the

diffractograms of CPM-solution-dropping tablets prepared from WG blank tablet compressed at 1000, 1400 and 1800 kg CF which was found at angle 2θ about 20.05, 20.02 and 20.01 degree respectively when compared with CPM and WG blank tablet patterns. For the patterns of powder from DZP-solution-dropping tablets prepared from WG blank tablet compressed at 1000, 1400 and 1800 kg CF had the different pattern of the peak at angle 2θ of about 22.89, 22.79 and 22.80 degree as shown in Figure 3.68 – 3.70 respectively when compared with diazepam and WG blank tablet patterns.

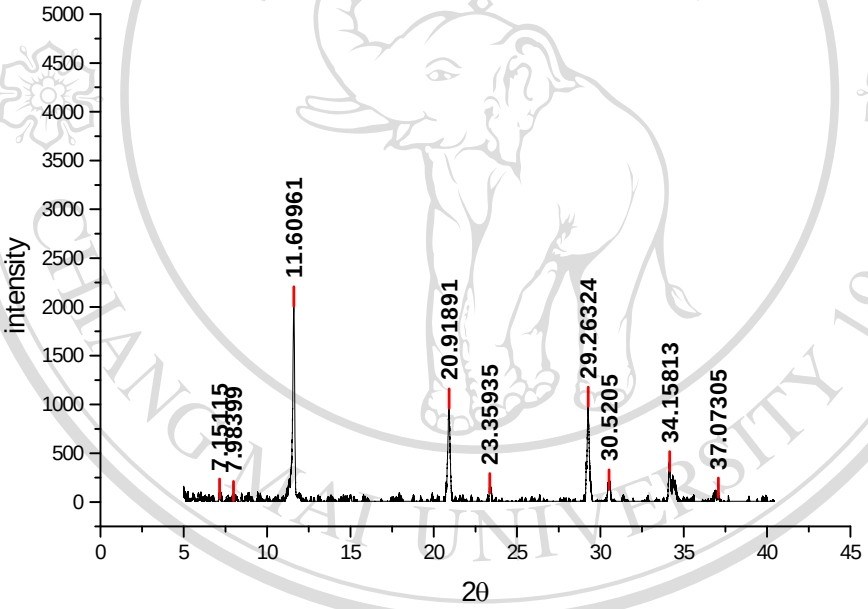


Figure 3.53 Single crystal XRD pattern of powder from the surface of DC blank tablet compressed at 1000 Kg CF

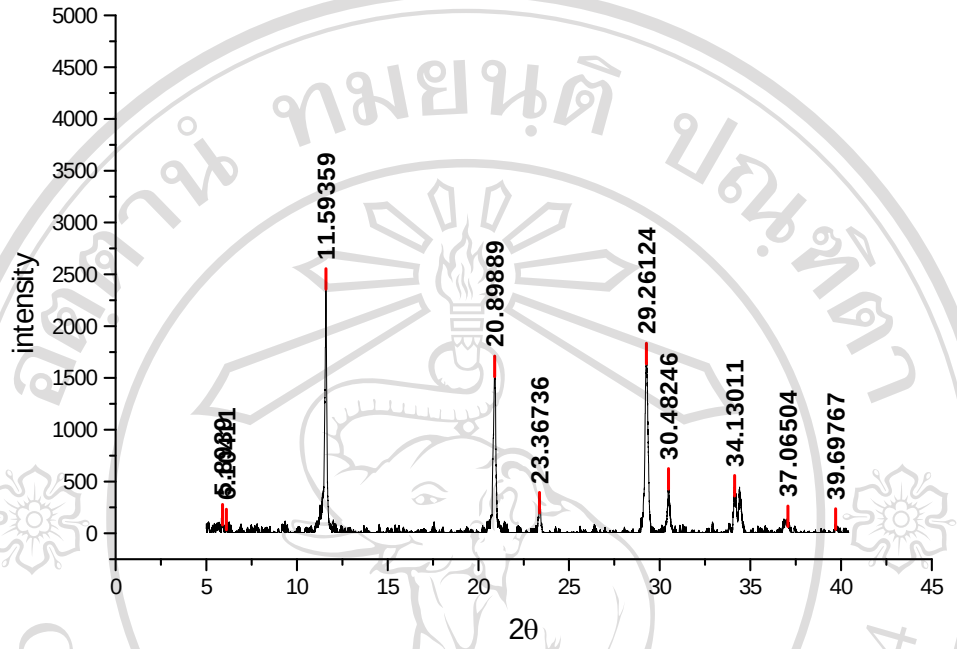


Figure 3.54 Single crystal XRD pattern of powder from the surface of DC blank tablet compressed at 1400 Kg CF

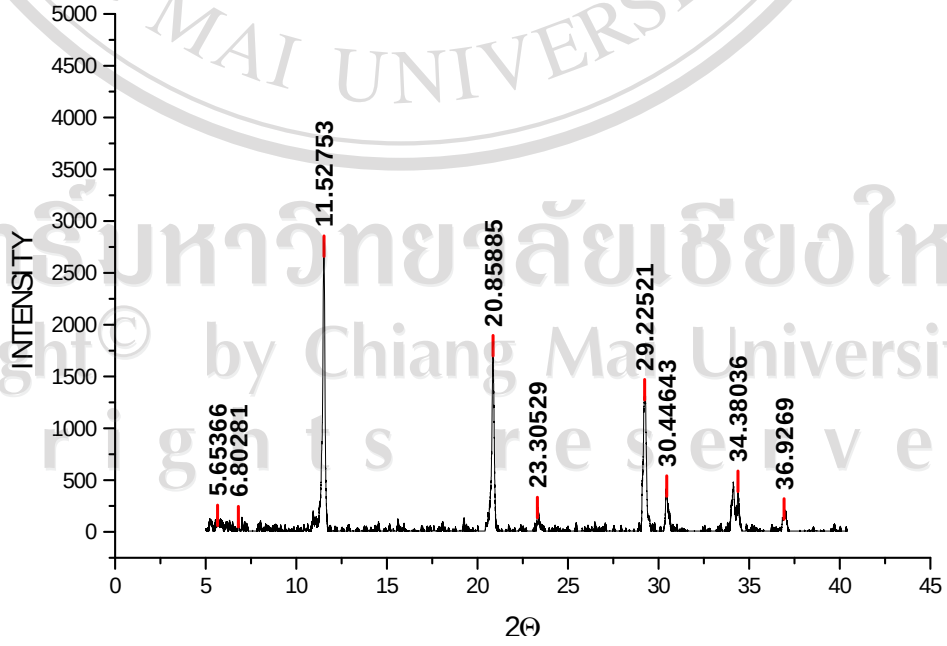


Figure 3.55 Single crystal XRD pattern of powder from the surface of DC blank tablet compressed at 1800 Kg CF

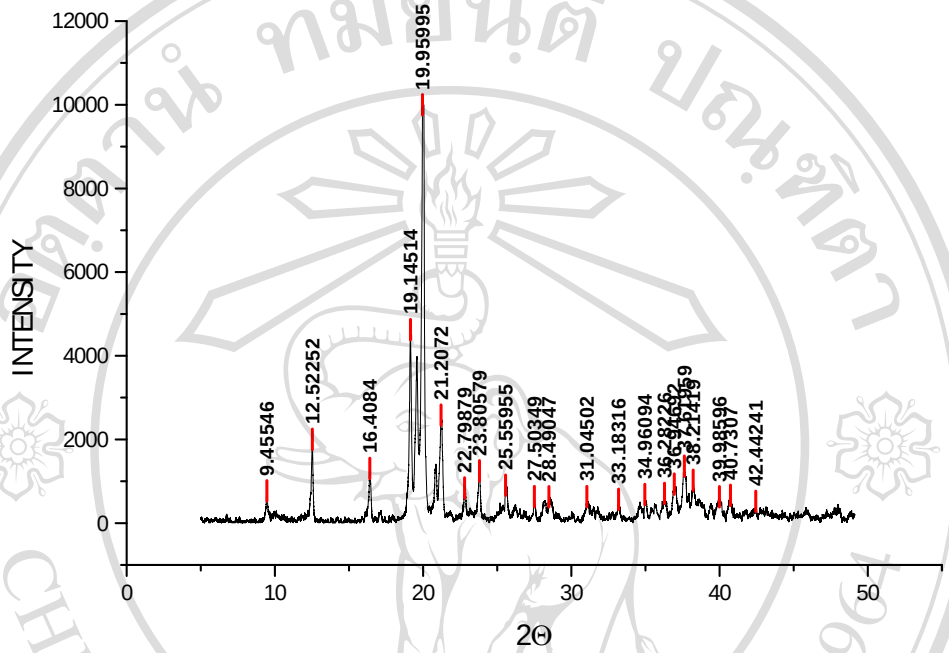


Figure 3.56 Single crystal XRD pattern of powder from the surface of WG blank tablet compressed at 1000 Kg CF

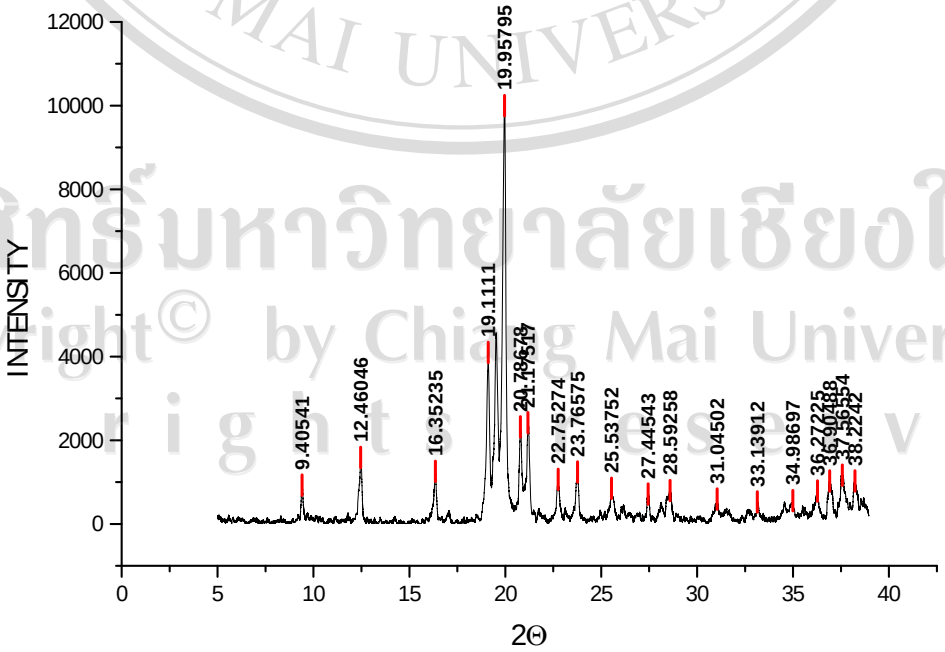


Figure 3.57 Single crystal XRD pattern of powder from the surface of WG blank tablet compressed at 1400 Kg CF

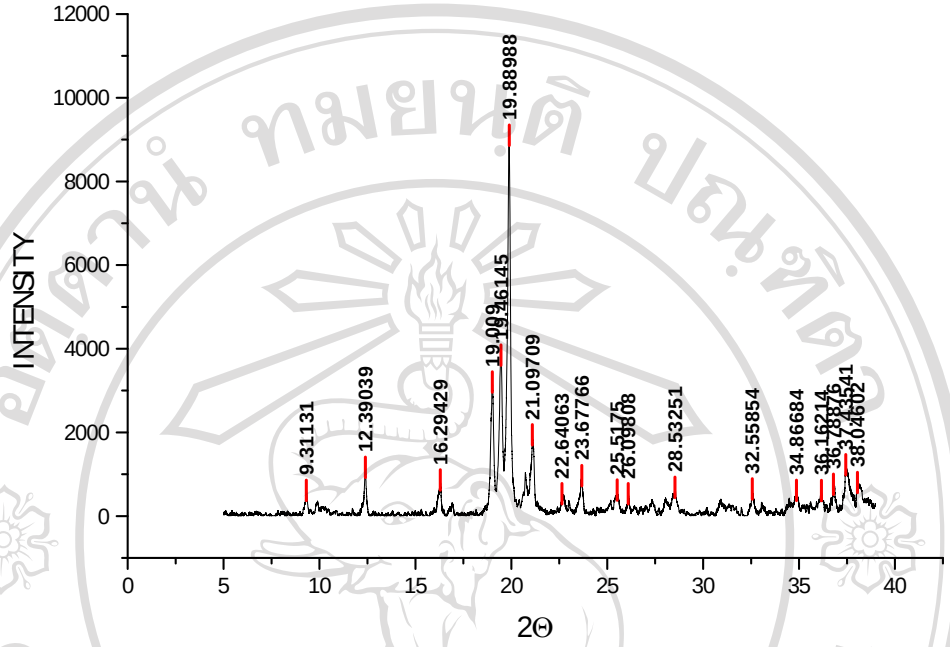


Figure 3.58 Single crystal XRD pattern of powder from the surface of WG blank tablet compressed at 1800 Kg CF

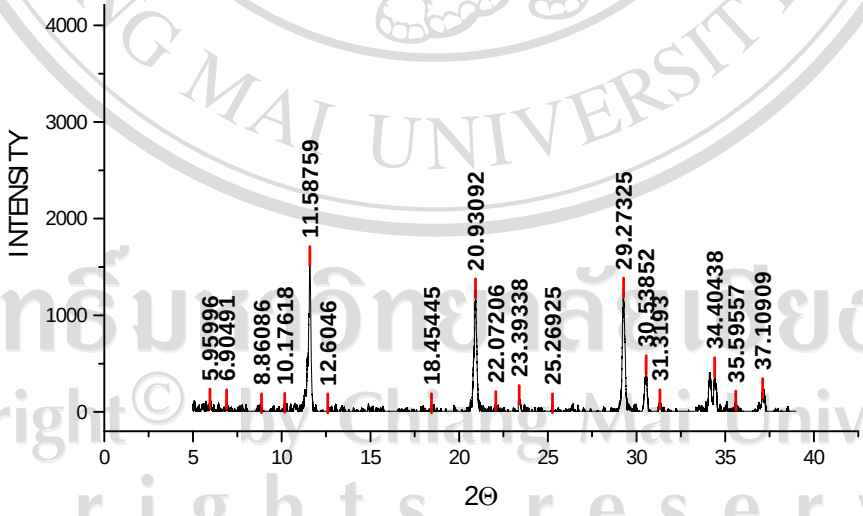


Figure 3.59 Single crystal XRD pattern of the powder from the surface of CPM-solution-dropping tablet prepared from DC blank tablet compressed at 1000 Kg CF

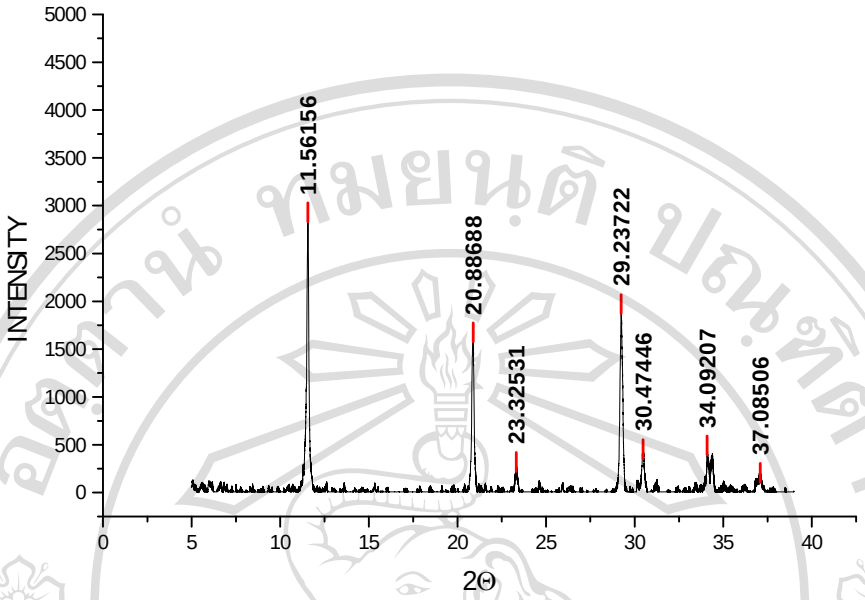


Figure 3.60 Single crystal XRD pattern of the powder from the surface of CPM-solution-dropping tablet prepared from DC blank tablet compressed at 1400 Kg CF

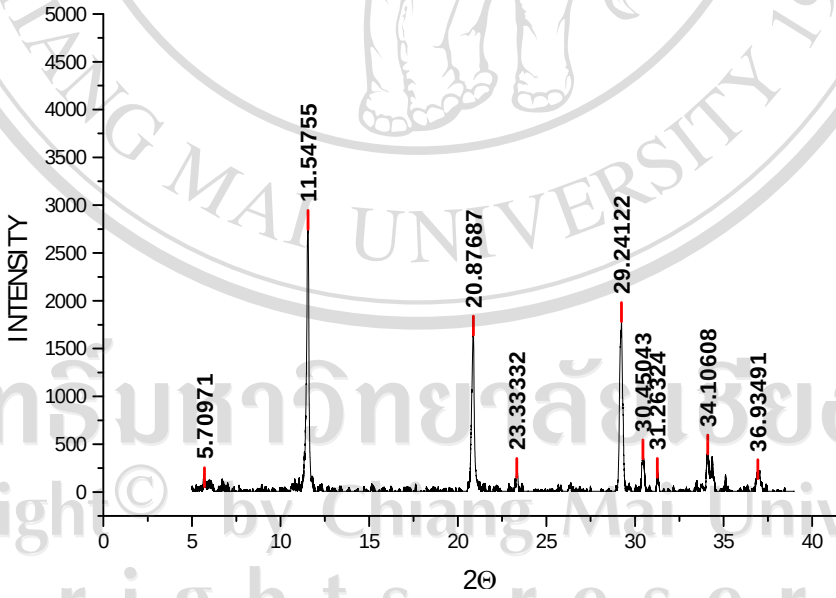


Figure 3.61 Single crystal XRD pattern of the powder from the surface of CPM-solution-dropping prepared tablet from DC blank tablet compressed at 1800 Kg of CF

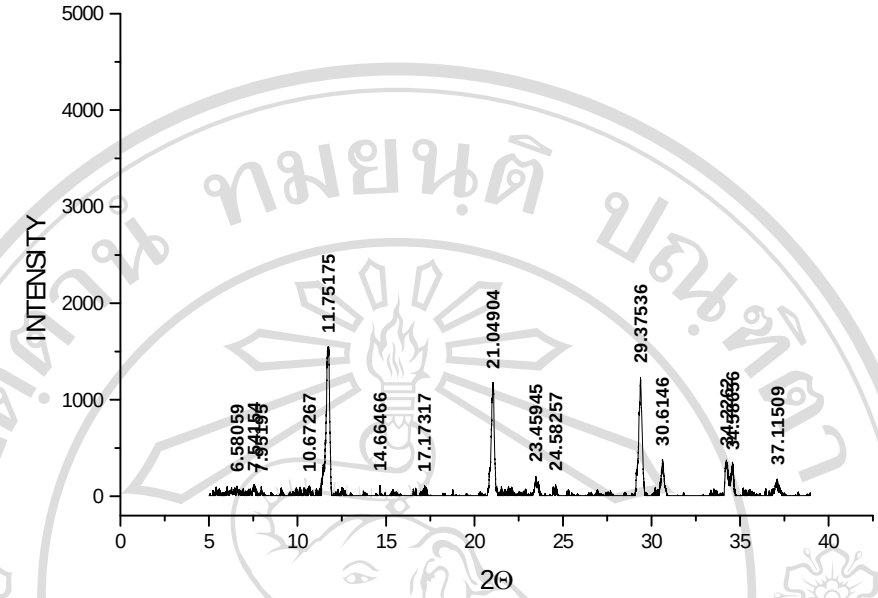


Figure 3.62 Single crystal XRD pattern of the powder from the surface of DZP-solution-dropping tablet prepared from DC blank tablet compressed at 1000 Kg CF

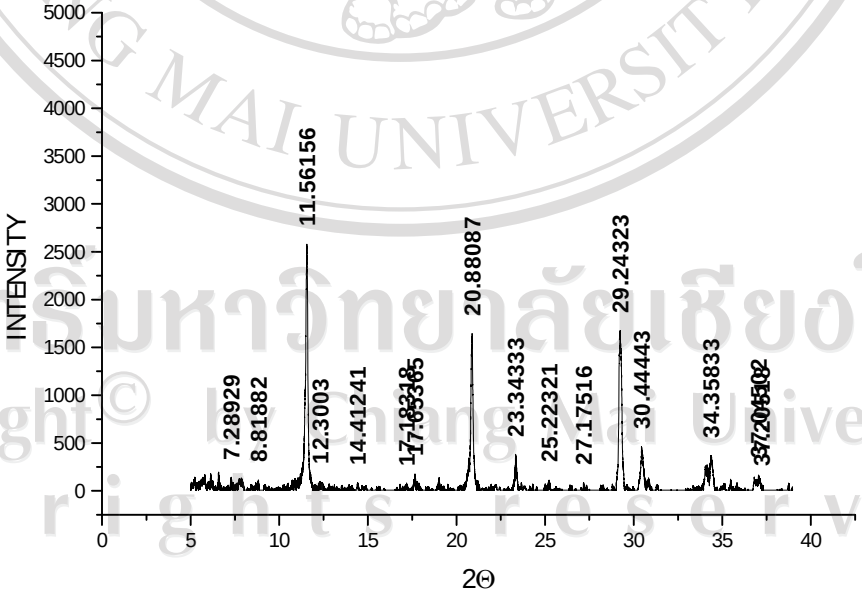


Figure 3.63 Single crystal XRD pattern of the powder from the surface of DZP-solution-dropping tablet prepared from DC blank tablet compressed at 1400 Kg CF

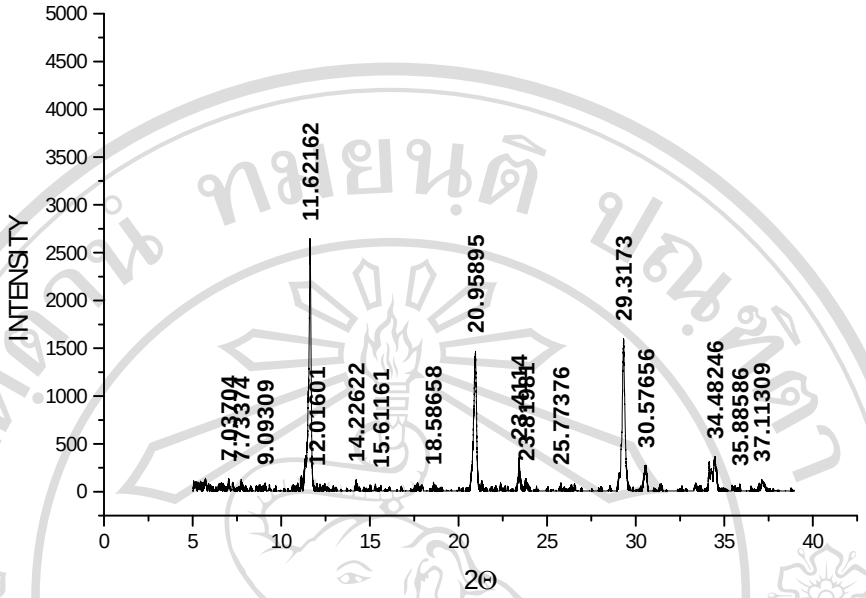


Figure 3.64 Single crystal XRD pattern of the powder from the surface of DZP-solution-dropping tablet prepared from DC blank tablet compressed at 1800 Kg CF

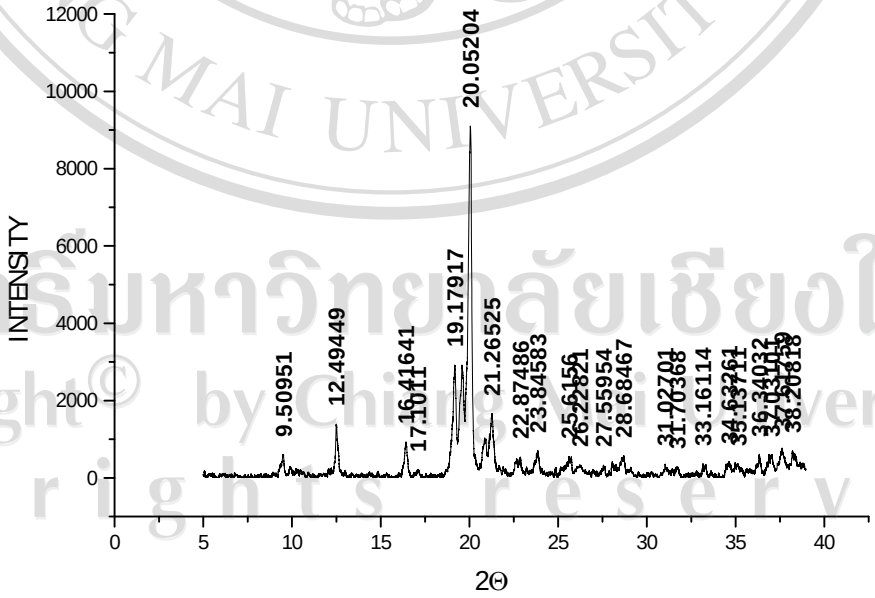


Figure 3.65 Single crystal XRD pattern of the powder from the surface of CPM-solution-dropping tablet prepared from WG blank tablet compressed at 1000 Kg CF

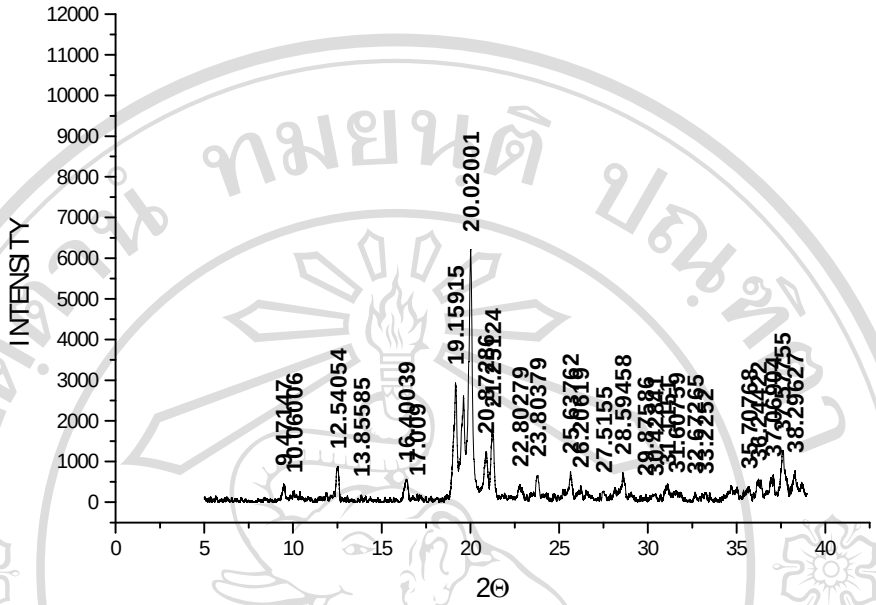


Figure 3.66 Single crystal XRD pattern of the powder from the surface of CPM-solution-dropping tablet prepared from WG blank tablet compressed at 1400 Kg CF

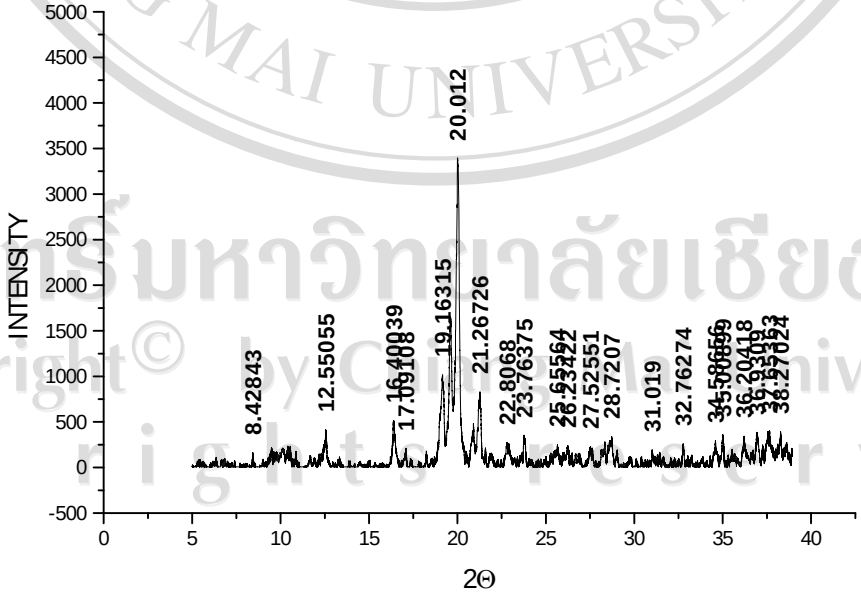


Figure 3.67 Single crystal XRD pattern of the powder from the surface of CPM-solution-dropping tablet prepared from WG blank tablet compressed at 1800 Kg CF

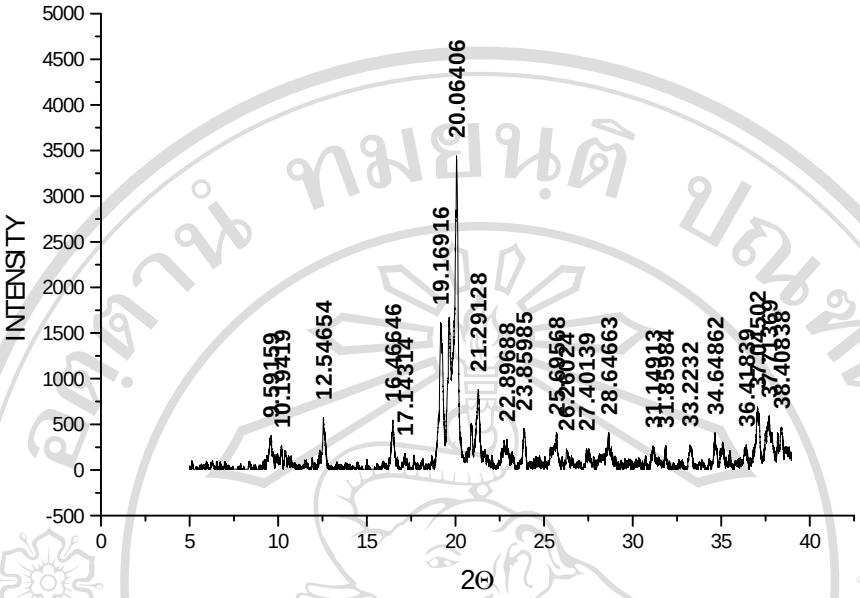


Figure 3.68 Single crystal XRD pattern of the powder from the surface of DZP-solution-dropping tablet prepared from WG blank tablet compressed at 1000 Kg CF

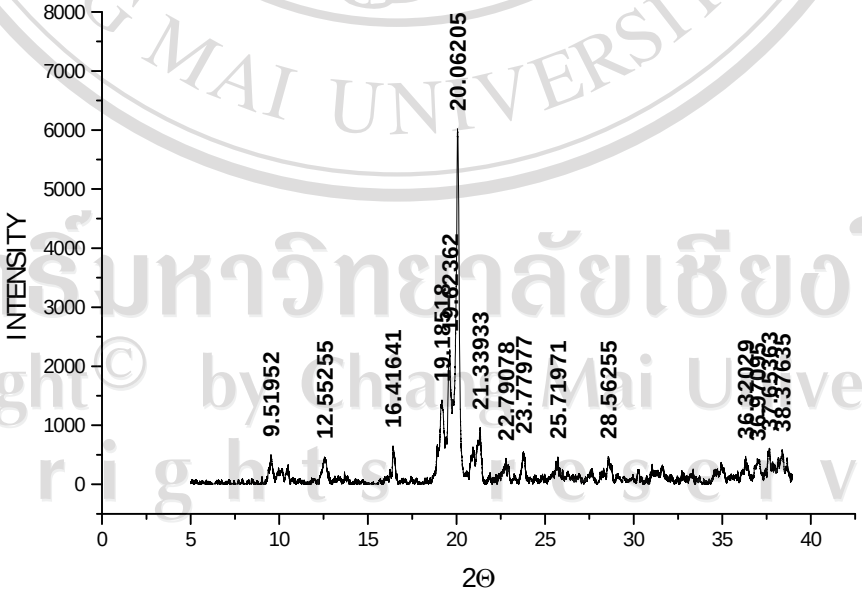


Figure 3.69 Single crystal XRD pattern of the powder from the surface of DZP-solution-dropping tablet prepared from WG blank tablet compressed at 1400 Kg CF

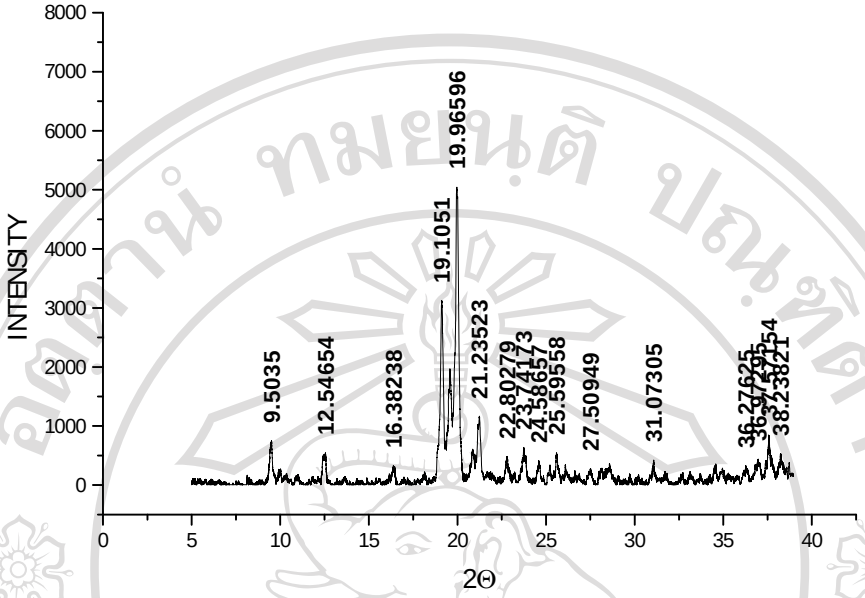


Figure 3.70 Single crystal XRD pattern of the powder from the surface of DZP-solution-dropping tablet prepared from WG blank tablet compressed at 1800 Kg CF

3.3.4 Differential scanning calorimetry

The thermal behavior of the powder scratched from the tablet surface of DSDT prepared from DC or WG blank tablet of 1000 kg CF were compared to CPM, DZP and excipients used in preparing tablet. The DSC thermatogram of powder from CPM-solution-dropping tablet surface prepared from DC blank tablet was shown in Figure 3.71 which displayed the peaks at 132.4 and 139.3^{o} C. The mentioned peaks were in the range of melting point of CPM, 135.7^{o} C, and DCP dihydrate at 138.9^{o} C as shown in Figure 3.72 and 3.73 respectively.

For the powder from the surface of CPM-solution- dropping tablet prepared from WG blank tablet showed its thermogram with two distinct peaks at 142.6 and 170.6^{o} C as in Figure 3.74 which corresponded to endothermic peak of Pharmatose® at 147.8 – 161.3^{o}C as shown in Figure 3.75. DSC thermogram pointed out clearly the presence of DCP dihydrate and lactose which were the major ingredients in the CPM-solution-dropping tablets prepared from the blank tablets.

The thermal behavior of the powder scratched from the surface of DZP-solution-dropping tablet originated from DC blank tablet of 1000 kg CF was shown in Figure 3.76 which displayed the endothermic peaks at 110.7, 116.8 and 154.8^{o} C as maximum peak. These peaks did not correspond to the range of melting point of DZP, 132.3^{o} C, and DCP dihydrate at 138.9^{o} C as shown in Figure 3.77 and 3.73 respectively.

As shown in Figure 3.78, DSC thermogram of the scratched powder from the surface of DZP-solution-dropping tablet prepared from WG blank tablet of 1000 kg CF showed the same peaks of diazepam, at 130.4 and 144.5^{o} C.

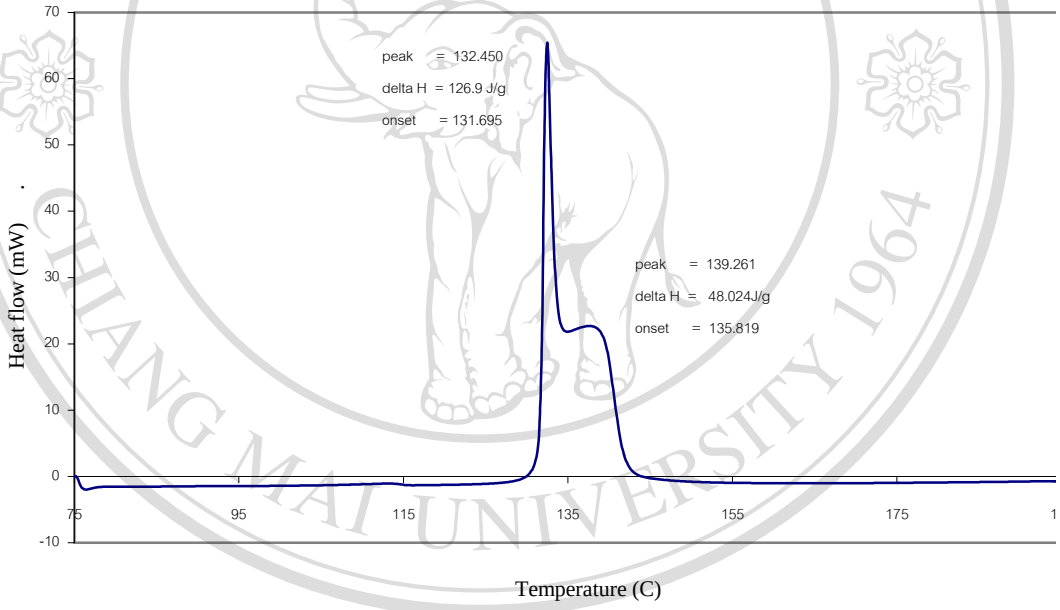


Figure 3.71 DSC thermogram of CPM-solution-dropping tablet prepared from DC blank tablet compacted at 1000 kg CF

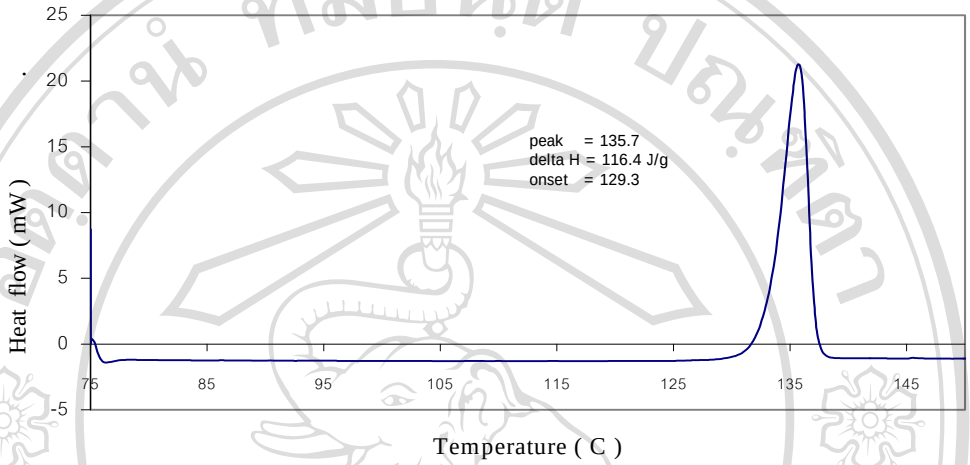


Figure 3.72 DSC thermogram of CPM

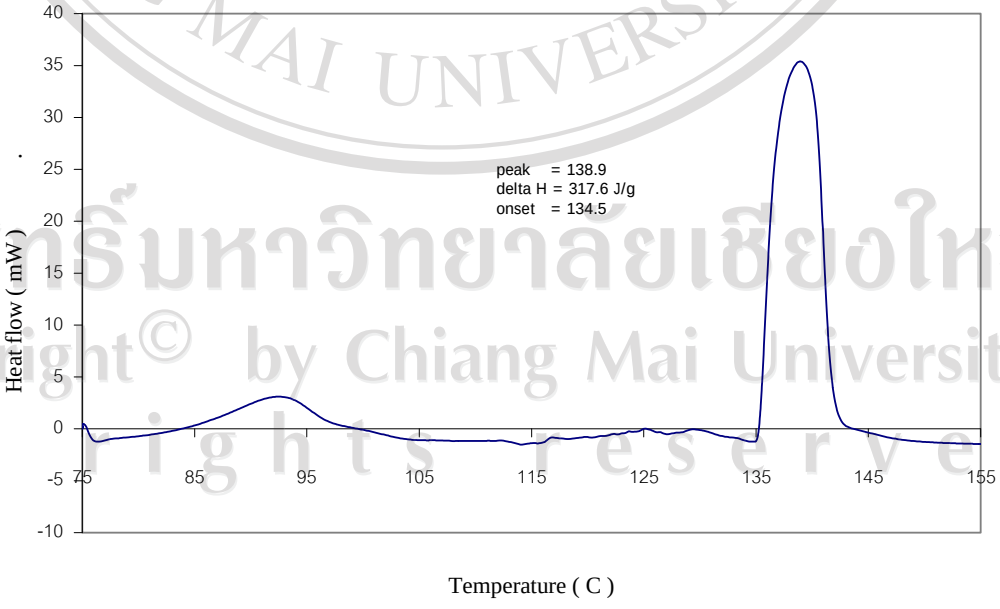


Figure 3.73 DSC thermogram of DCP dihydrate

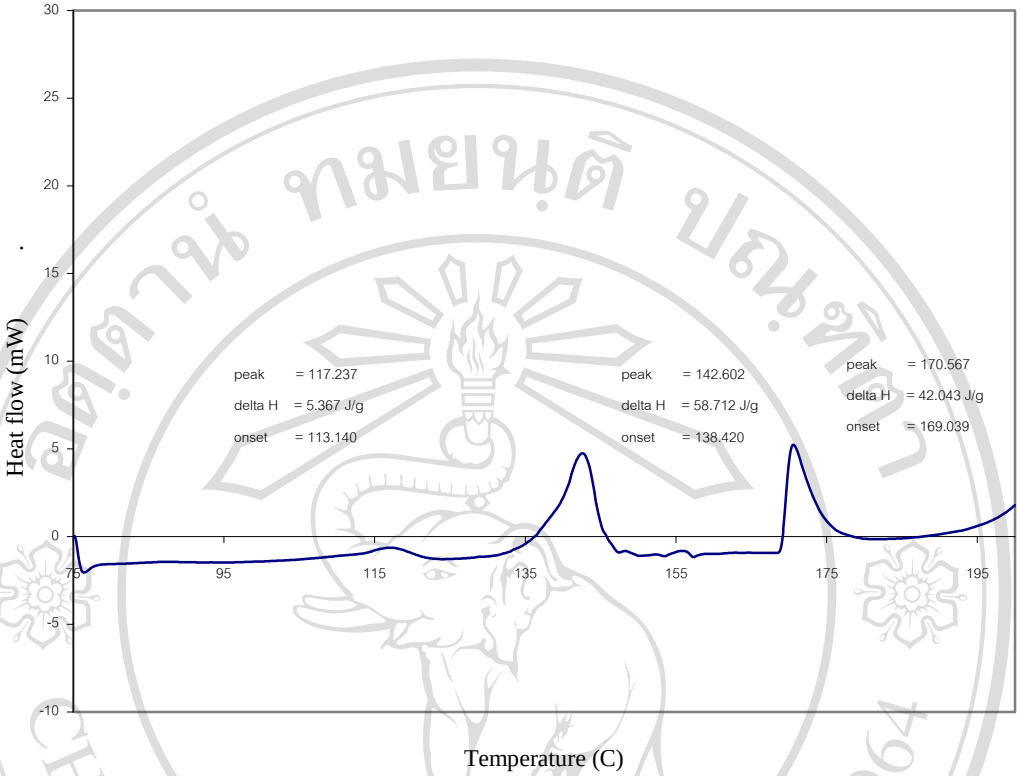


Figure 3.74 DSC thermogram of CPM-solution-dropping tablet prepared from WG blank tablet compacted at 1000 kg CF

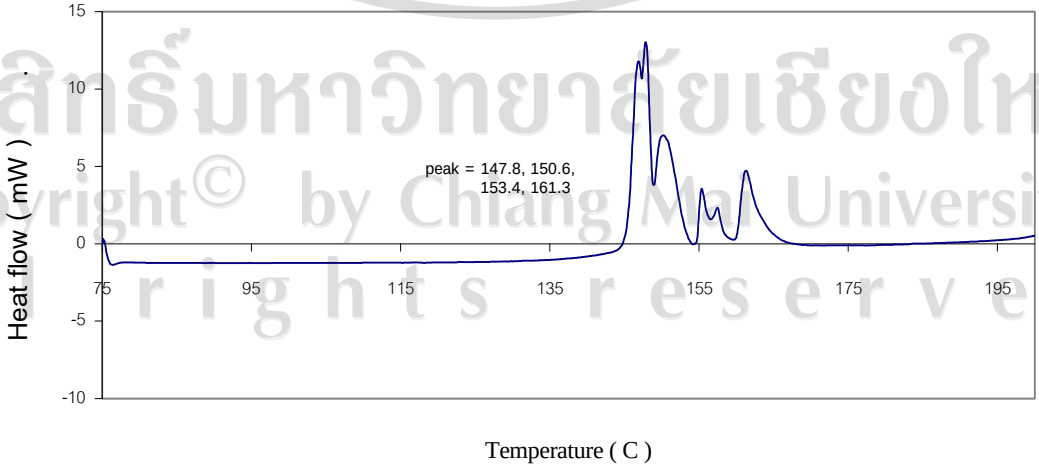


Figure 3.75 DSC thermogram of Pharmatose®

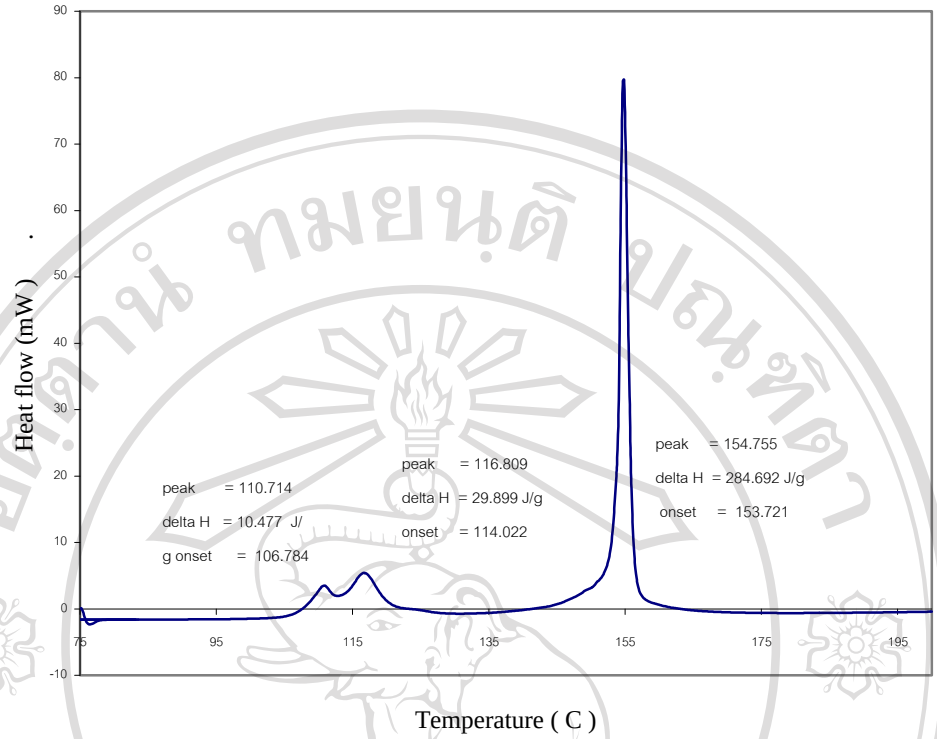


Figure 3.76 DSC thermogram of DZP-solution-dropping tablet prepared from DC blank tablet compressed at 1000 kg CF

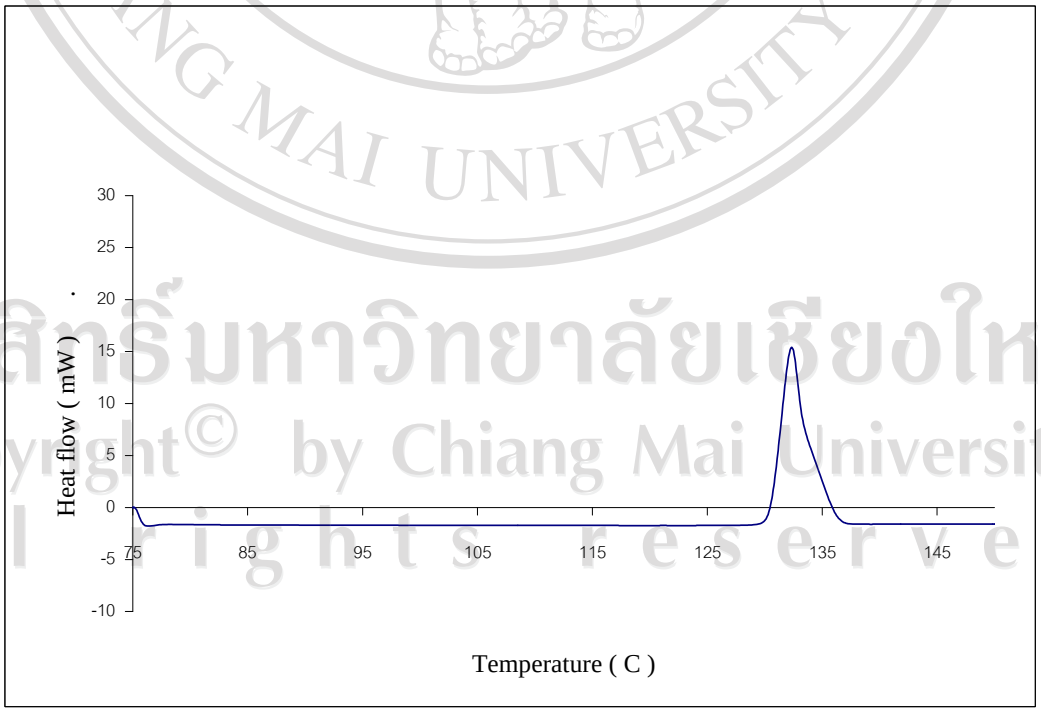


Figure 3.77 DSC thermogram of diazepam

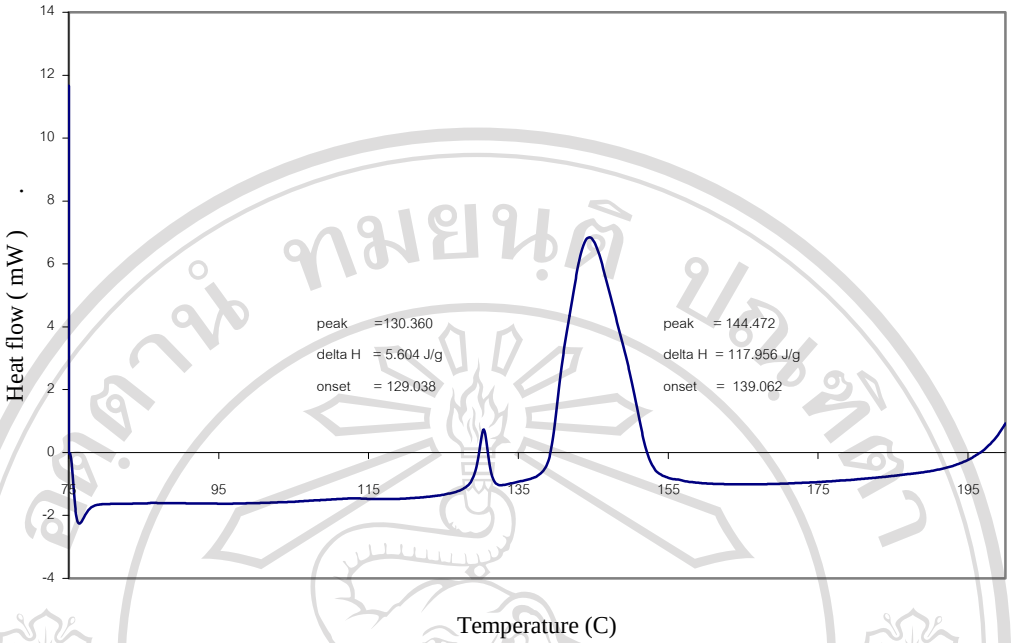


Figure 3.78 DSC thermogram of DZP-solution-dropping tablet prepared from WG blank tablet compressed at 1000 kg CF

3.4 Determination of the active ingredient content

The analytical method for determination the quantity of active ingredient in DSDT was followed the Pharmacopoeia as in APPENDIX A and B. It was found that CPM-solution-dropping tablet contained the average amount 94.96 percent of the labeled amount of CPM ($C_{16}H_{19}ClN_2$. $C_4H_4O_4$). The average content of diazepam ($C_{16}H_{13}ClN_2O$**)** in DZP-solution-dropping tablet was 104.54 percent of the stated amount. Both active ingredients CPM and diazepam complied with the range stated in the Pharmacopoeia. The USP is 90 – 110 percent of the labeled amount and the BP is 92.5 – 107.5 percent of the stated amount.

3.5 Content uniformity

The portion of 40 µl of 10% CPM solution and 50 µl of 10% DZP solution was dropped on the surface of each blank tablet to obtain 4 mg of CPM and 5 mg of diazepam per tablet respectively. Content uniformity of the both DSDT was determined to convince the uniformity of each dropping of drug solution. The content uniformity test method in USP 30 and BP 2007 were used for CPM and DZP tablet

respectively. Table 3.5 showed the amount of the active ingredients in 10 DSDT and followed the range of 85.0% to 115% of label claim (% LA) of CPM and diazepam and the relative standard deviation is acceptable which was less than 6.0%.

Table 3.5 The amount of CPM and DZP in 10 tablets of CPM- and DZP-solution-dropping tablets which prepared from DC blank tablet of 1000 kg CF

Tablet number	**CPM (% LA)**	**Diazepam (% LA)**
1	95.22	107.80
2	98.69	105.50
3	99.27	103.42
4	99.41	104.41
5	94.65	105.07
6	96.38	105.29
7	97.10	106.49
8	96.23	107.36
9	99.41	102.99
10	96.52	107.36
Average ($\bar{X}$)	97.29	105.57
SD	1.79	1.67
RSD	1.84	1.59

3.6 Dissolution Profiles Studies

3.6.1 Effect of time of solvent dropping

Drug dissolution of DSDT prepared from DC and WG blank tablets of 1000 kg CF after dropping 0, 2, 4 or 6 times of blank solvent were studied. Figure 3.79 showed the drug dissolution profiles of the CPM-solution-dropping tablets prepared from DC blank tablets which were different in times of dropping of blank solvent 0, 2, 4 or 6 times after dropping CPM solution. It was found that drug dissolution at first ten minutes were not different between 0 and 2 times of blank

solvent dropping. Nevertheless, it was shown the tendency of slow down dissolution when the tablet was dropped with blank solvent 4 and 6 times. It was similar as the preparation from WG blank tablet, i.e. the dissolution profiles of the tablet after dropping blank solvent 2, 4 or 6 times were in lower range than tablet without blank solvent dropping. Apparently at 4 and 6 times, it showed drug dissolution less than 80% of 4 mg of CPM within 30 minutes as shown in Figure 3.80. For DZP-solution-dropping tablet prepared from DC blank tablet, the dissolution profiles of tablets after repeat of dropping blank solvent 2, 4 or 6 times were not different but in comparison with that of without blank solvent dropping they showed less dissolution as shown in Figure 3.81. In the case of tablet prepared from WG blank tablet, all cases behaved the similar profile as shown in Figure 3.82. All of data were shown in Table C1 – C4 in Appendix C.

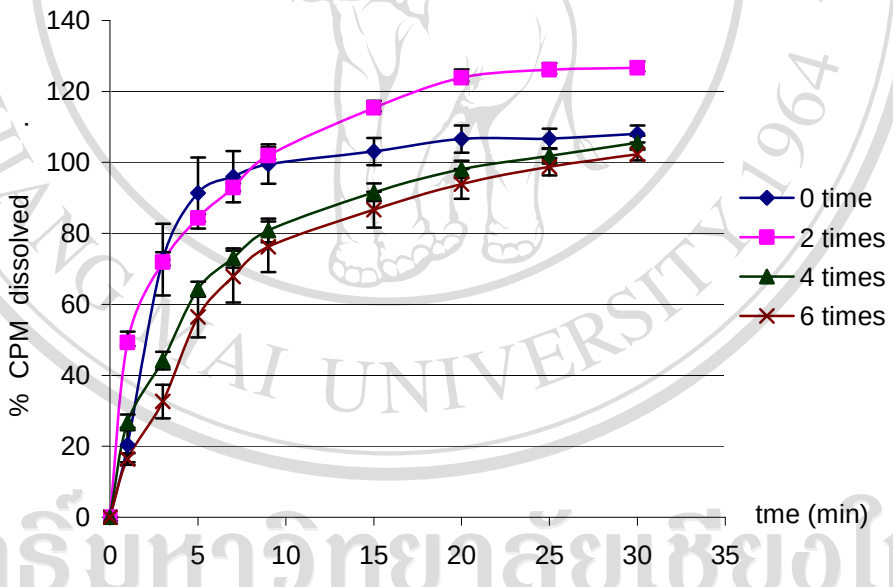


Figure 3.79 CPM dissolution profiles of the CPM-solution dropping tablet prepared from DC blank tablet at the same 1000 kg CF after repeat blank solvent dropping of 0, 2, 4 or 6 times

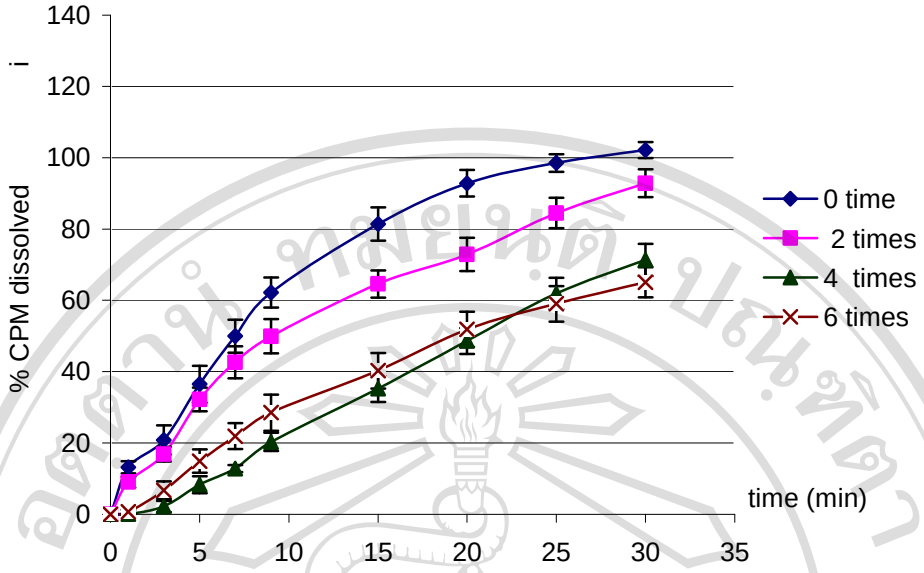


Figure 3.80 CPM dissolution profiles of the CPM-solution dropping tablet prepared from WG blank tablet at the same 1000 kg CF after repeat blank solvent dropping of 0, 2, 4 or 6 times

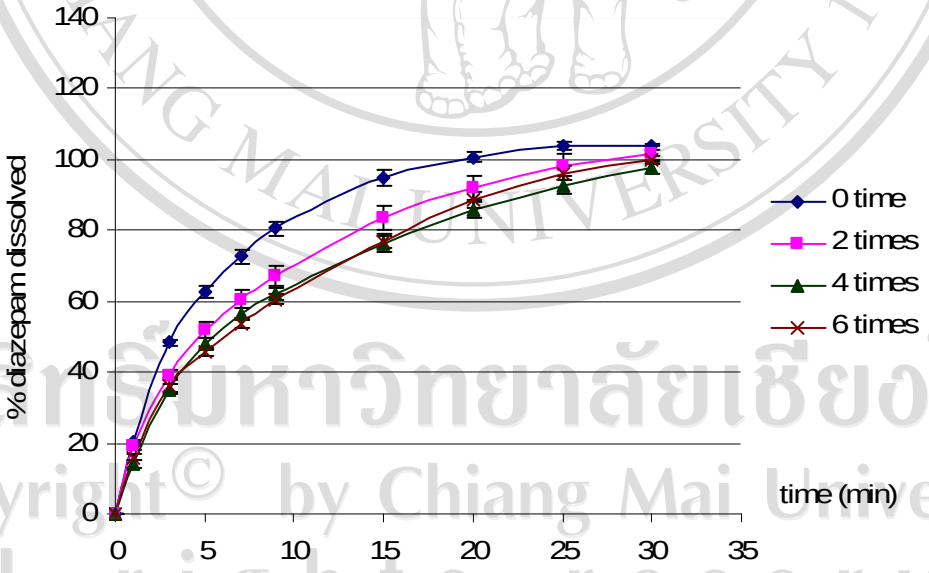


Figure 3.81 DZP dissolution profiles of the DZP-solution dropping tablet prepared from DC blank tablet at the same 1000 kg CF after repeat blank solvent dropping of 0, 2, 4 or 6 times

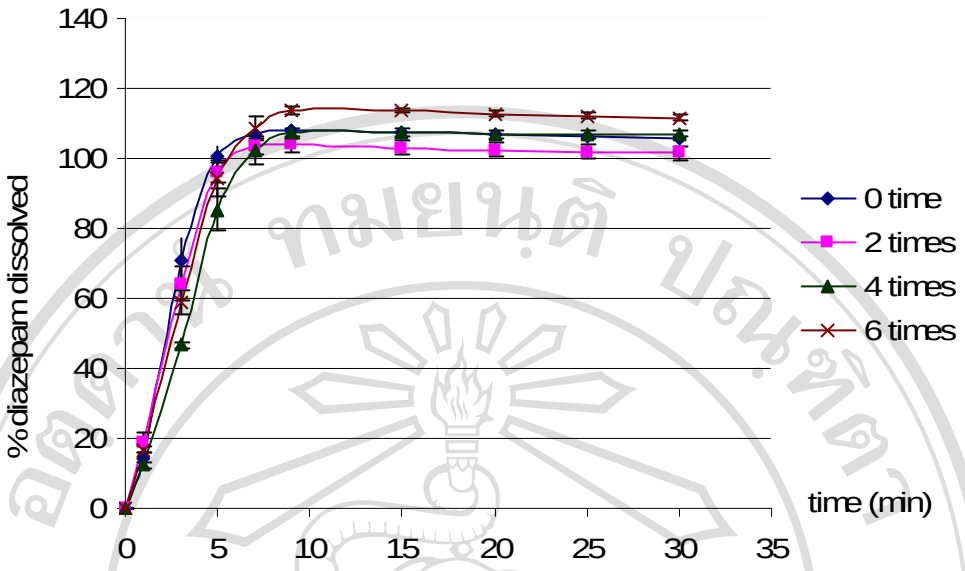


Figure 3.82 DZP dissolution profiles of the DZP-solution dropping tablet prepared from WG blank tablet at the same 1000 kg CF after repeat blank solvent dropping of 0, 2, 4 or 6 times

3.6.2 Dissolution profiles of CPM-solution-dropping tablet

Amount of drug dissolution rate from CPM-solution-dropping tablets prepared from DC and WG blank tablets at 1000, 1400 and 1800 kg CF were compared with CPM tablet prepared by conventional method of the same CF. Figure 3.83 – 3.85 showed the dissolution profiles of CPM-solution-dropping tablets prepared from DC blank tablets in comparison with CPM tablet prepared by direct compression method (CPM DC tablet) compressed at the same CF, 1000, 1400 and 1800 kg CF respectively and also with commercial CPM tablets. All of them comply to the requirement in monograph of USP that not less than 80% of 4 mg of CPM is dissolved within 30 minutes. Of 1000 kg CF, 90% of CPM was dissolved from the CPM-solution-dropping tablet within 5 minutes and significantly faster than CPM DC tablet ($p<0.01$) as shown in Figure 3.83. At 1400 and 1800 kg CF, the dissolved amount of drug was not significantly different between the CPM DC tablet and CPM-solution-dropping tablet ($p>0.01$) as shown in Figure 3.84 -3.85. CPM dissolution of commercial CPM tablet was shown to be slower than CPM DC and CPM-solution-dropping tablet. All of data were shown in Table C5 – C6 in Appendix C.

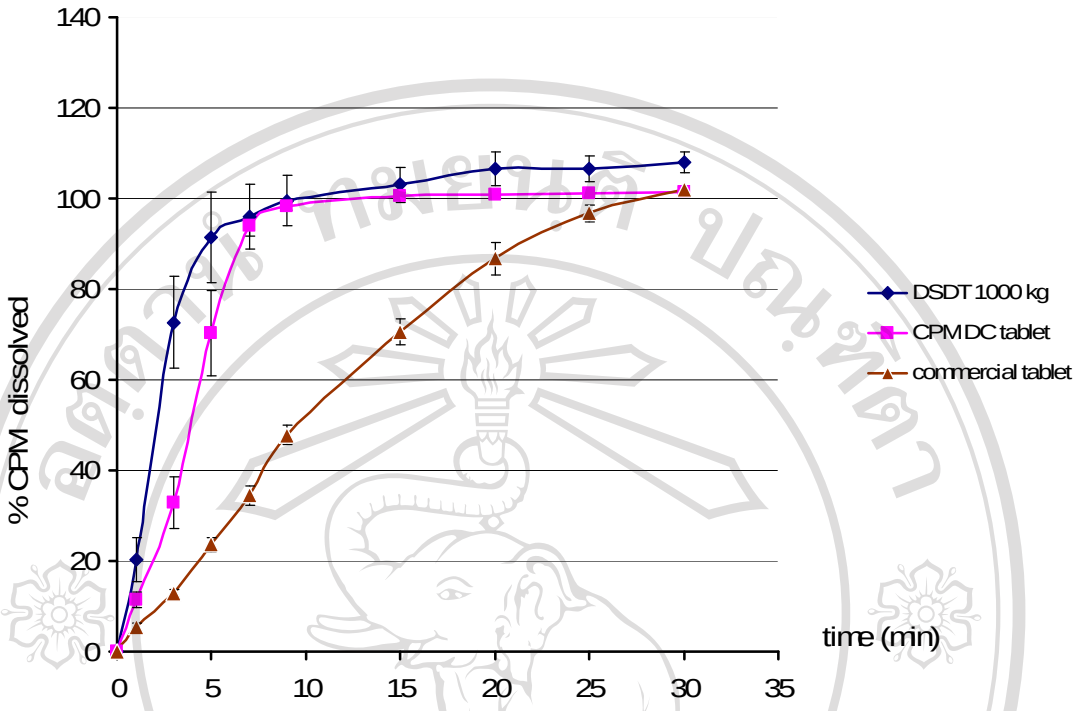


Figure 3.83 CPM dissolution profiles of CPM-solution-dropping tablet prepared from DC blank tablet compared with CPM DC tablet at the same 1000 kg CF and commercial CPM tablet

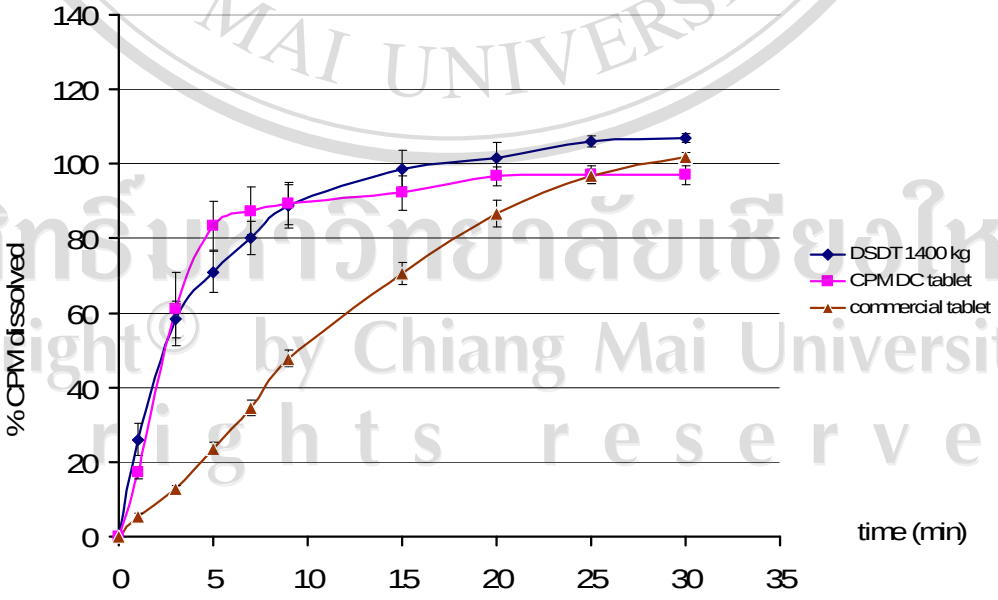


Figure 3.84 CPM dissolution profiles of CPM-solution dropping tablet prepared from DC blank tablet compared with CPM DC tablet at the same 1400 kg CF and commercial CPM tablet

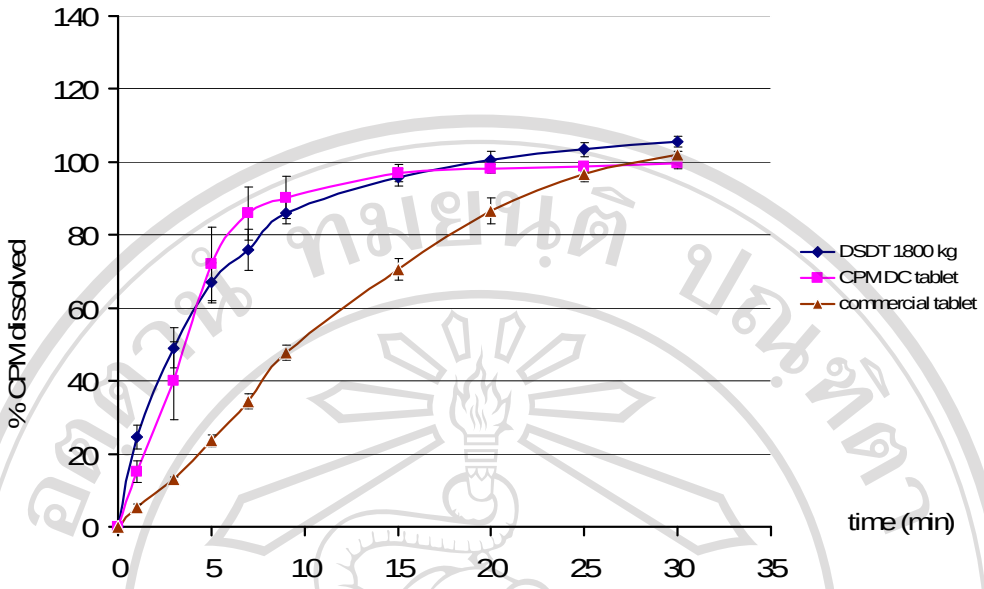


Figure 3.85 CPM dissolution profiles of CPM-solution dropping tablet prepared from DC blank tablet compared with CPM DC tablet at the same 1800 kg CF and commercial CPM tablet

The drug dissolution profiles of the CPM-solution-dropping tablets prepared from WG blank tablets and the CPM WG tablets as illustrated in Figure 3.86 - 3.88 showed the amount of CPM which met the requirement in monograph of USP. The dissolution rates were not significantly different except that of the tablet of 1000 kg CF which the CPM dissolution rate from CPM-solution-dropping tablets were significantly slower than that of the CPM WG tablets, especially at 3 and 5 minutes ($p<0.01$) as shown in Figure 3.86. Of 1400 and 1800 kg CF, the CPM which was dissolved at 1 minute from CPM-solution-dropping tablets were significantly faster than that of the CPM WG tablets ($p<0.01$) as shown in Figure 3.87 and 3.88 respectively. In case of commercial CPM tablets, the dissolution rates only at 1, 3 and 5 minutes of the CPM-solution-dropping-tablets of 1000 and 1400 kg CF were significant faster than of commercial CPM tablets ($p<0.01$). But for CPM-solution-dropping tablets of 1800 kg CF, CPM was dissolved faster than of commercial CPM tablet at all range of times studied. All of data were shown in Table C7 – C8 in Appendix C.

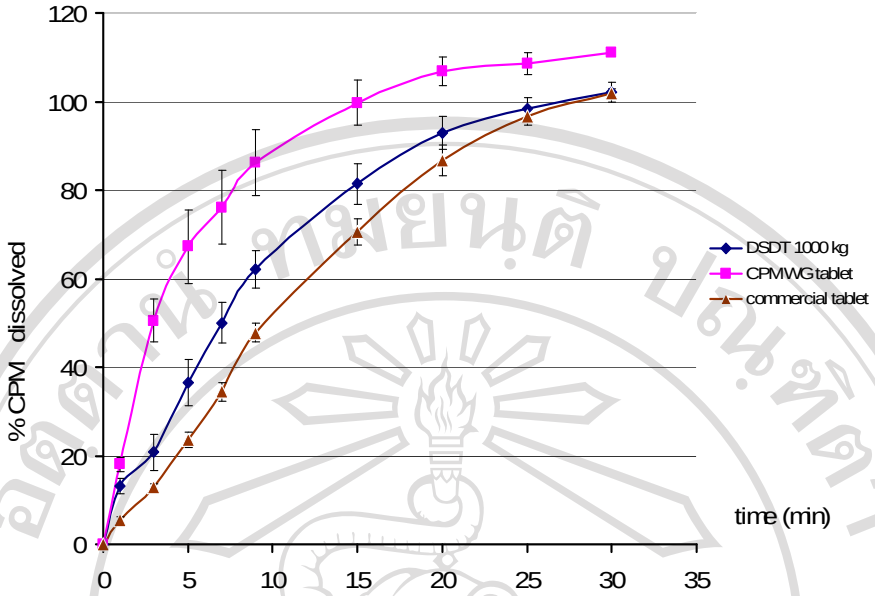


Figure 3.86 CPM dissolution profiles of CPM-solution dropping tablet prepared from WG blank tablet compared with CPM WG tablet at the same 1000 kg CF and commercial CPM tablet

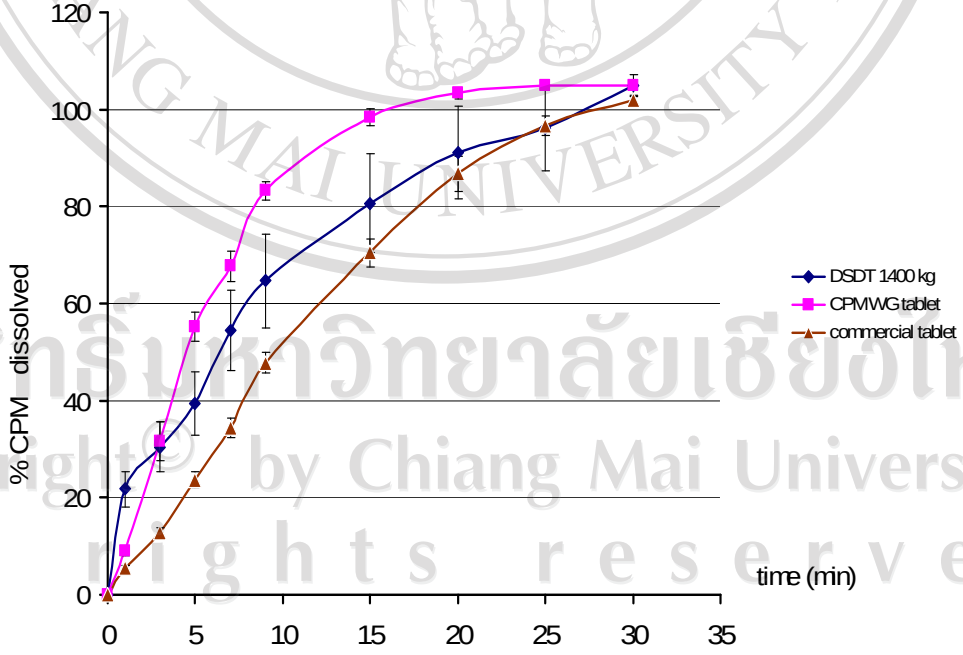


Figure 3.87 CPM dissolution profiles of CPM-solution dropping tablet prepared from WG blank tablet compared with CPM WG tablet at the same 1400 kg CF and commercial CPM tablet

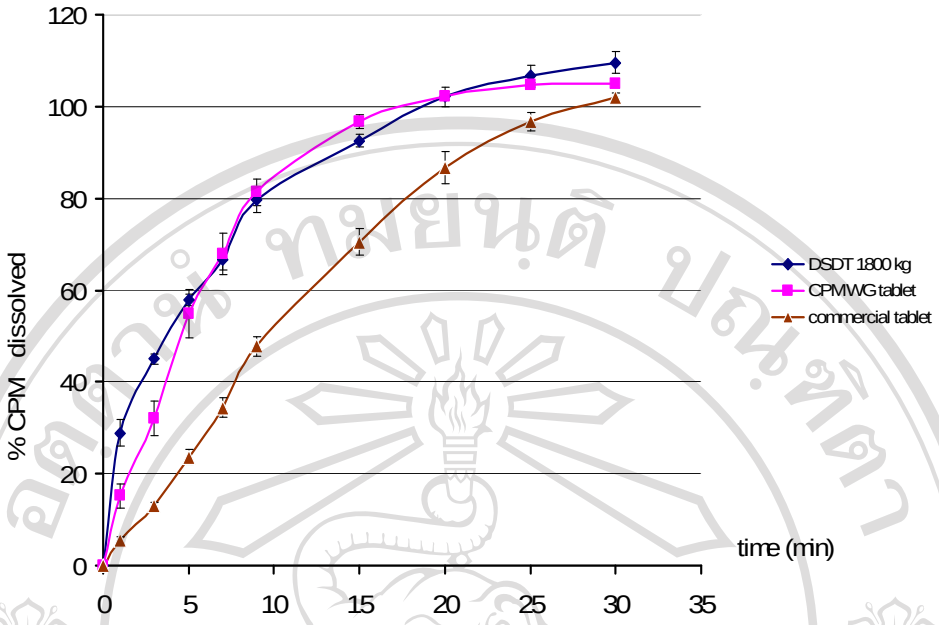


Figure 3.88 CPM dissolution profiles of CPM-solution dropping tablet prepared from WG blank tablet compared with CPM WG tablet at the same 1800 kg CF and commercial CPM tablet

3.6.3 Dissolution profiles of DZP-solution-dropping tablet

The dissolution profiles of DZP-solution-dropping tablet prepared from DC and WG blank tablets in comparison with the profiles of diazepam tablets prepared by conventional DC and WG method of all tested CF were shown in Figure 3.89 – 3.94. All of them meet the requirement in monograph of USP 30 that not less than 85% of 5 mg of diazepam is dissolved within 30 minutes.

DZP-solution-dropping tablet prepared from DC blank tablet, diazepam was dissolved significantly faster than that of the DZP DC tablets at 3 and 5 minutes of 1000 kg CF tablet and at 3 minutes of 1800 kg CF tablet ($p<0.01$) as shown in Figure 3.89 and 3.91 respectively. Diazepam was dissolved from DZP-solution-dropping tablets of all tested CF and DZP DC tablet slower than commercial diazepam tablet at all points of study except for at 1 minute of 1000 kg CF for DZP-solution-dropping tablet and DZP DC tablet, DZP was dissolved in the same rate as diazepam tablet from market.

Of 1400 kg CF tablet, the dissolution rate of DZP-solution-dropping tablet was significantly slower than of DZP DC tablet at all point ($p<0.01$) as shown in Figure 3.90. However from the performance in 1800 kg CF tablet, the dissolution rate of DZP-solution-dropping tablet was non significant different from DZP DC tablet ($p>0.01$). All of data were shown in Table C9 – C10 in Appendix C.

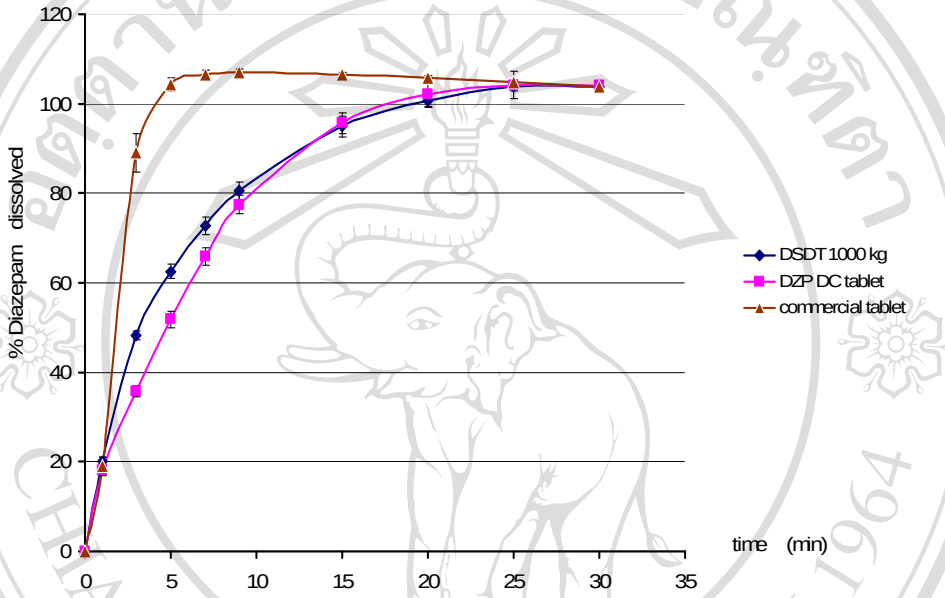


Figure 3.89 DZP dissolution profiles of DZP-solution dropping tablet prepared from DC blank tablet compared with DZP DC tablet at the same 1000 kg CF and commercial diazepam tablet

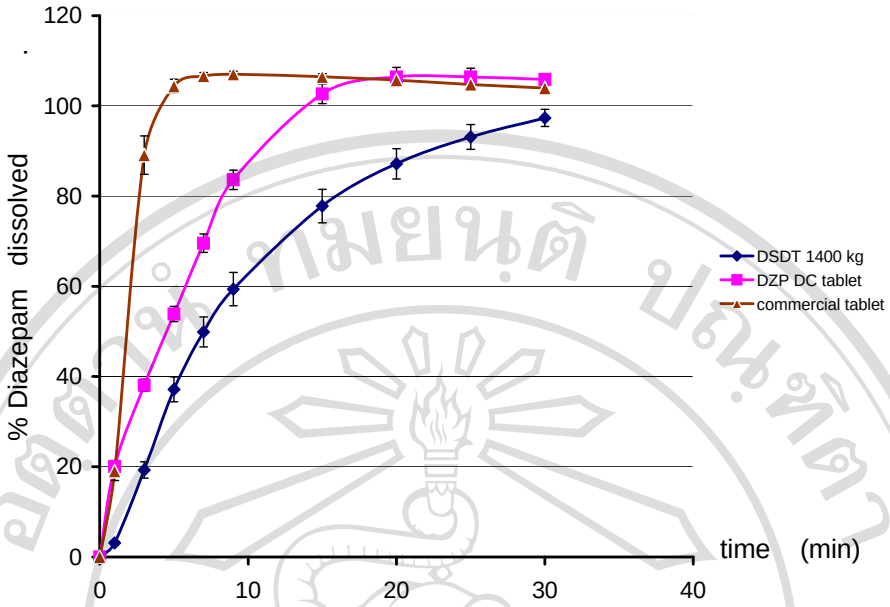


Figure 3.90 DZP dissolution profiles of DZP-solution dropping tablet prepared from DC blank tablet compared with DZP DC tablet at the same 1400 kg CF and commercial diazepam tablet

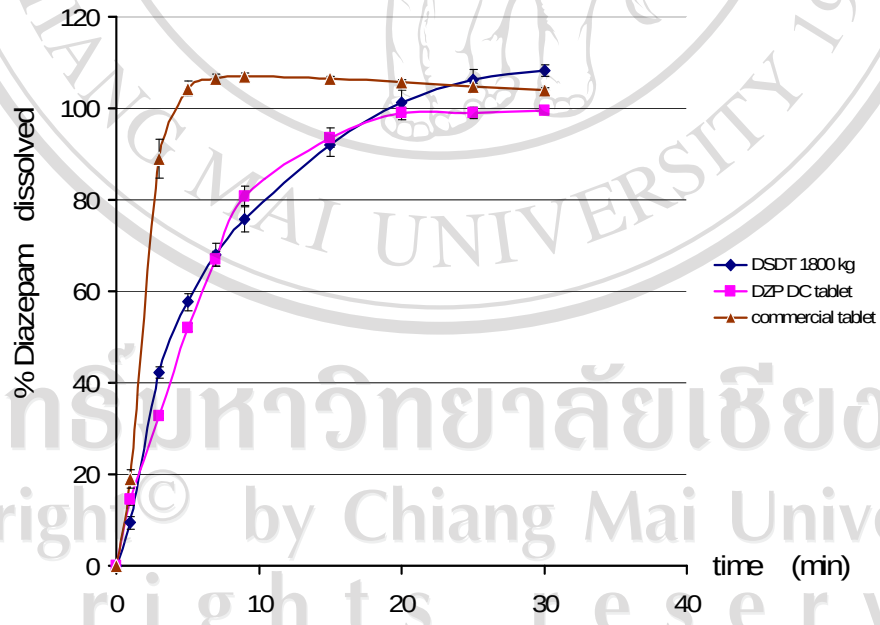


Figure 3.91 DZP dissolution profiles of DZP-solution dropping tablet prepared from DC blank tablet compared with DZP DC tablet at the same 1800 kg CF and commercial diazepam tablet

For WG method, the DZP-solution-dropping tablet of 1000 Kg CF, it was found that the dissolution rate after 3 minutes was not significantly difference comparing to DZP WG tablet ($p>0.01$) as shown in Figure 3.92. At CF of 1400 and 1800 kg, the dissolution rate of DZP-solution-dropping tablet was apparently lower than of DZP WG tablet except for 1 minute as shown in Figure 3.93 and 3.94 respectively. DZP was dissolved from DZP WG tablet with the same rate as commercial diazepam tablet especially of 1400 and 1800 kg CF. All of data were shown in Table C11 – C12 in Appendix C.

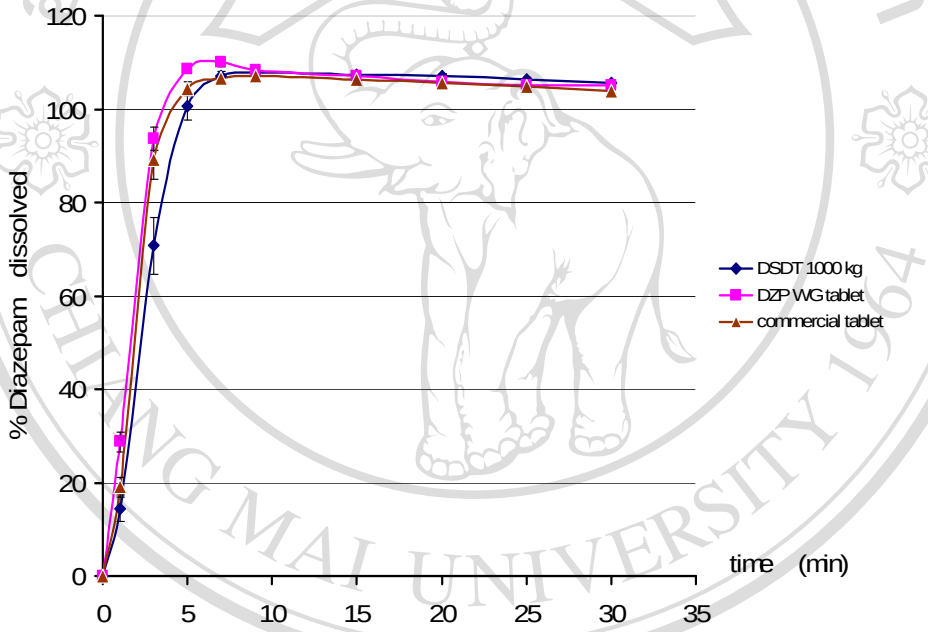


Figure 3.92 DZP dissolution profiles of DZP-solution dropping tablet prepared from WG blank tablet compared with DZP WG tablet at the same 1000 kg CF and commercial diazepam tablet

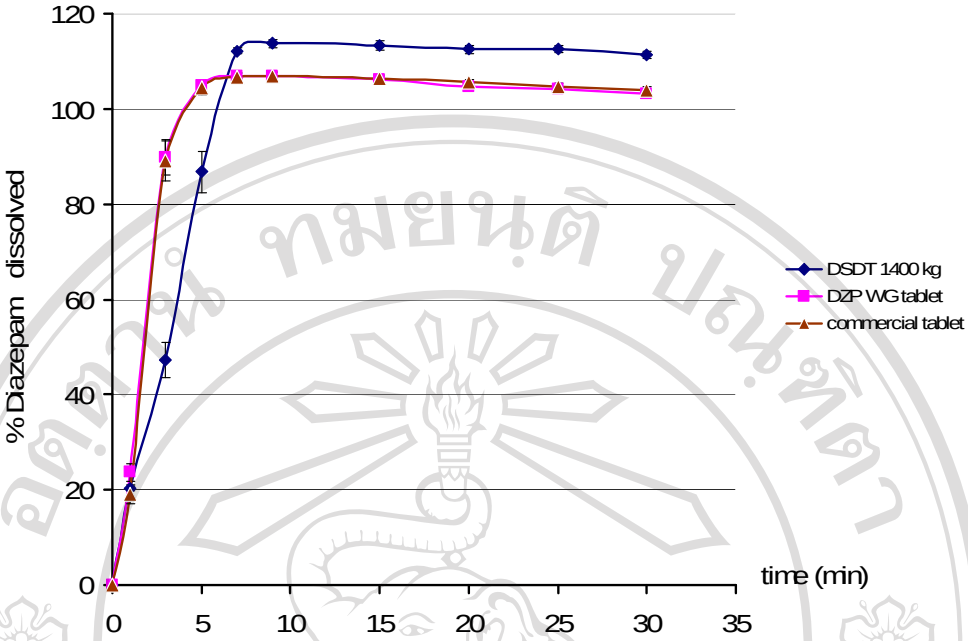


Figure 3.93 DZP dissolution profiles of DZP-solution dropping tablet prepared from WG blank tablet compared with DZP WG tablet at the same 1400 kg CF and commercial diazepam tablet

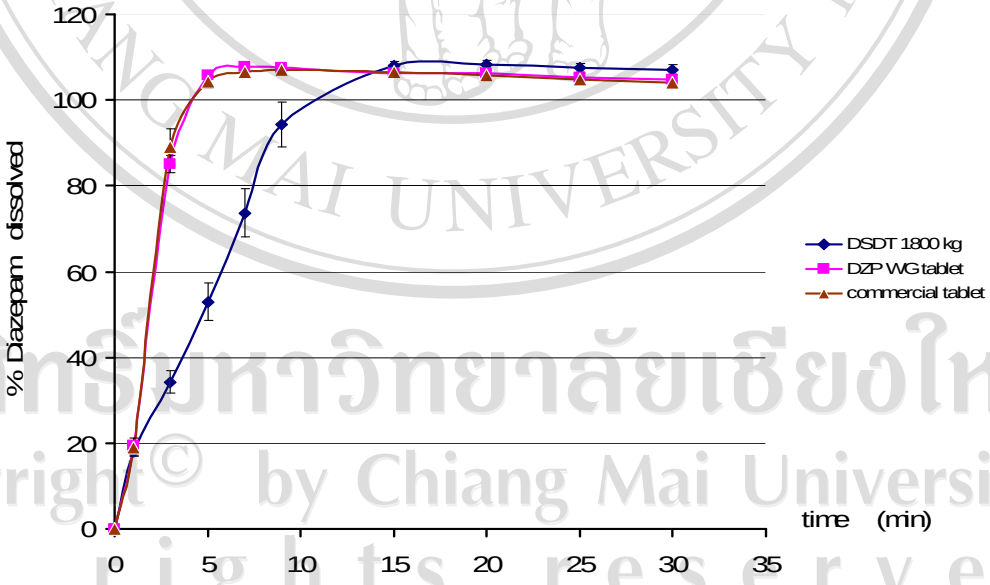


Figure 3.94 DZP dissolution profiles of DZP-solution dropping tablet prepared from WG blank tablet compared with DZP WG tablet at the same 1800 kg CF and commercial diazepam tablet

3.6.4 Effect of compression force on drug dissolution of DSDT

Figure 3.95 - 3.96 showed the effect of compression force on CPM dissolution of CPM-solution dropping tablet prepared from DC and WG blank tablet respectively. The result revealed the dissolution rate of CPM-solution-dropping tablet prepared from DC blank tablet compressed at 1000 kg CF was faster than of tablet at 1400 and 1800 CF respectively. Dissolution rate from CPM-solution-dropping tablet prepared from WG blank tablet compressed at 1800 kg CF was significantly faster than tablet both of 1000 and 1400 kg CF ($p<0.01$). All of data were shown in Table C5 and C7 of Appendix C respectively.

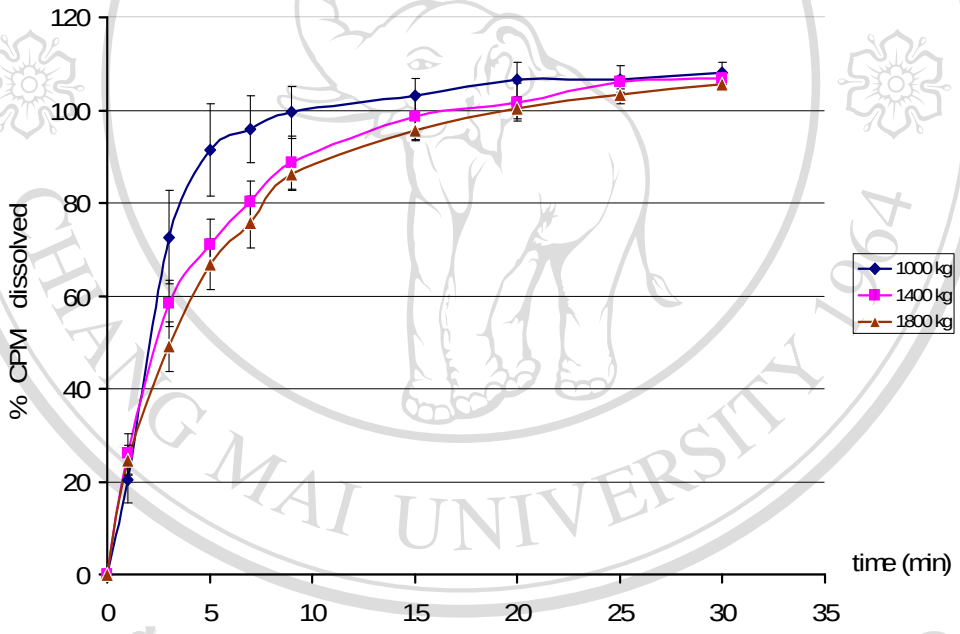


Figure 3.95 The effect of CFs on CPM dissolution profiles of CPM-solution-dropping tablet prepared from DC blank tablet

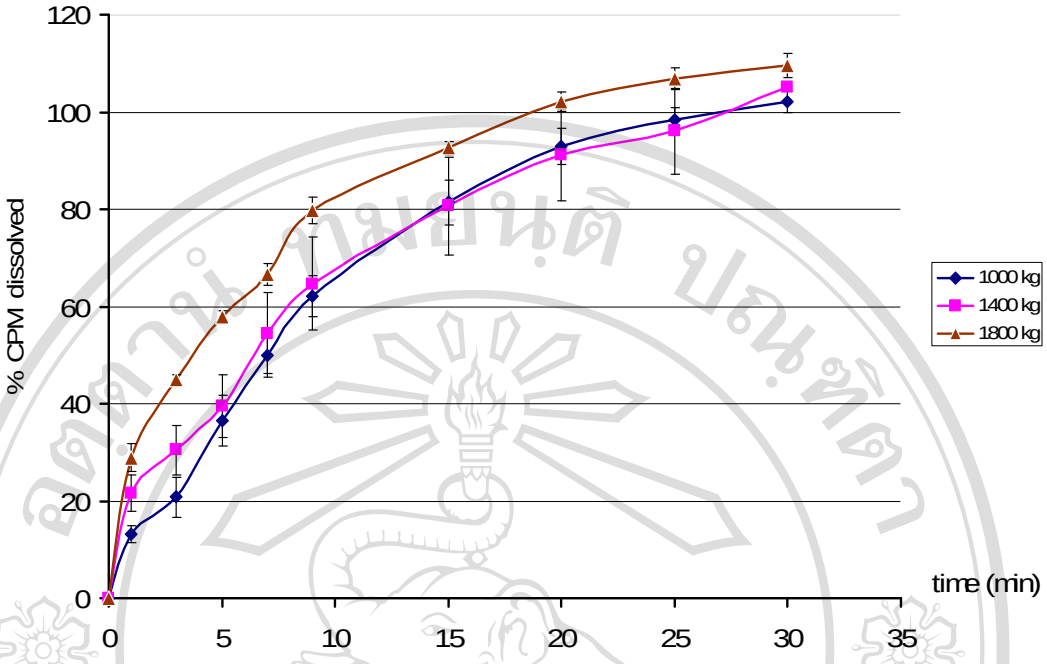


Figure 3.96 The effect of CFs on CPM dissolution profiles of CPM-solution-dropping tablet prepared from WG blank tablet

Figure 3.97 - 3.98 showed the effect of compression force on diazepam dissolution of DZP-solution dropping tablet prepared from DC and WG blank tablet respectively. It was found that the dissolution rate of DZP-solution-dropping tablet prepared from DC blank tablet compressed at 1000 and 1800 kg CF were significantly faster than tablet of 1400 CF ($p<0.01$). Drug dissolution rate of DZP-solution-dropping tablet prepared from WG blank tablet compressed at 1000 kg CF was faster than that of tablet at 1400 and 1800 kg respectively ($p<0.01$). All of data were shown in Table C9 and C11 of Appendix C respectively.

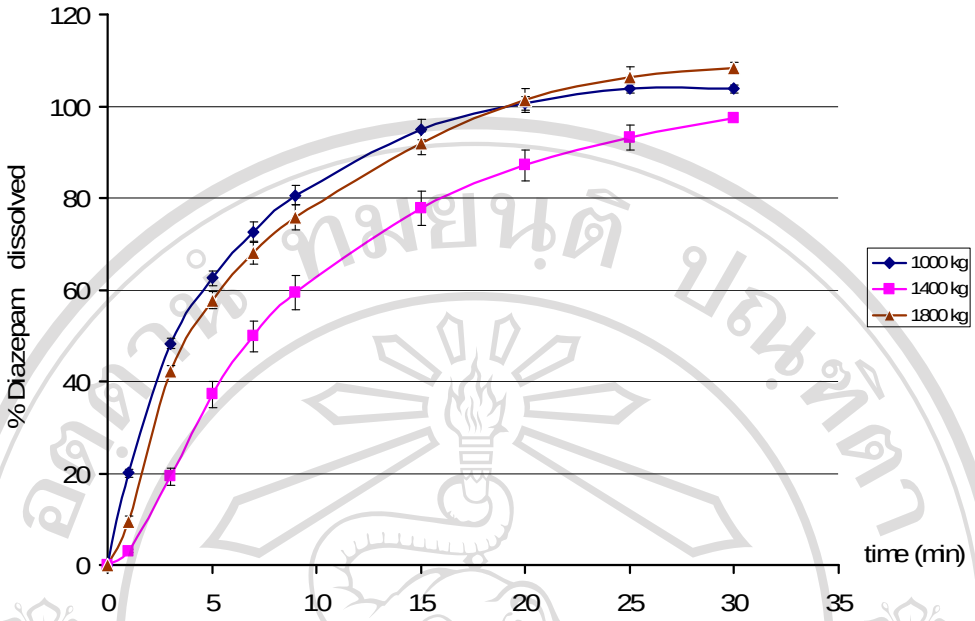


Figure 3.97 The effect of CFs on DZP dissolution profiles of DZP-solution-dropping tablet prepared from DC blank tablet

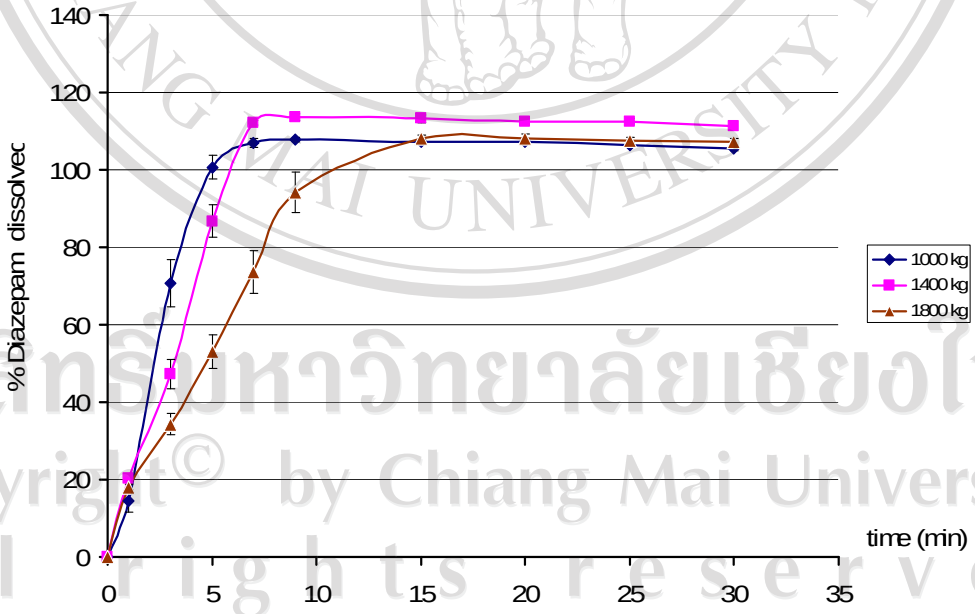


Figure 3.98 The effect of CFs on DZP dissolution profiles of DZP-solution-dropping tablet prepared from WG blank tablet

3.6.5 Comparison of DSDT dissolution profiles of tablets prepared from DC and from WG blank tablet

Figure 3.99 showed the dissolution profiles of CPM-solution-dropping tablet prepared from DC blank tablet compared with tablet prepared from WG blank tablet of 1000, 1400 and 1800 kg CF respectively. It was found that CPM from the tablet prepared from DC blank tablet compressed at all tested CF was dissolved faster than that of tablet prepared from WG blank tablet especially of 1000 kg CF. Of DZP-solution-dropping tablet from the both blank tablets, the DZP dissolution rate of DZP-solution-dropping tablet prepared from WG blank tablets were faster than of DZP-solution-dropping tablet prepared from DC blank tablets of 1000 and 1400 kg CF. However, of 1800 kg CF, the dissolution rate exhibited not significantly different between the DZP-solution-dropping tablet prepared from WG and DC blank tablet ($p>0.01$) as shown in Figure 3.98.

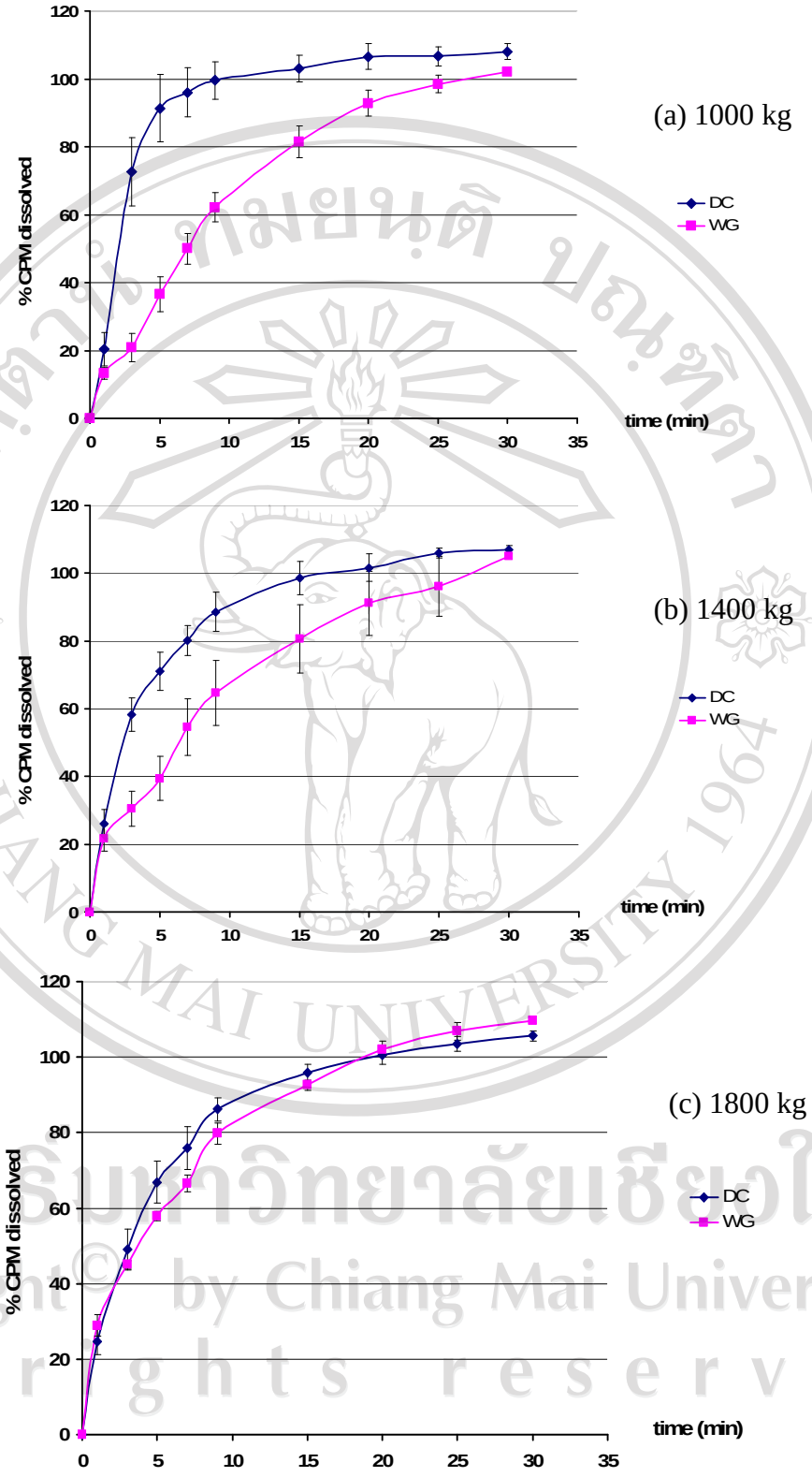


Figure 3.99 CPM dissolution profiles of CPM-solution-dropping tablet prepared from DC blank tablet and WG blank tablet at all tested CF.

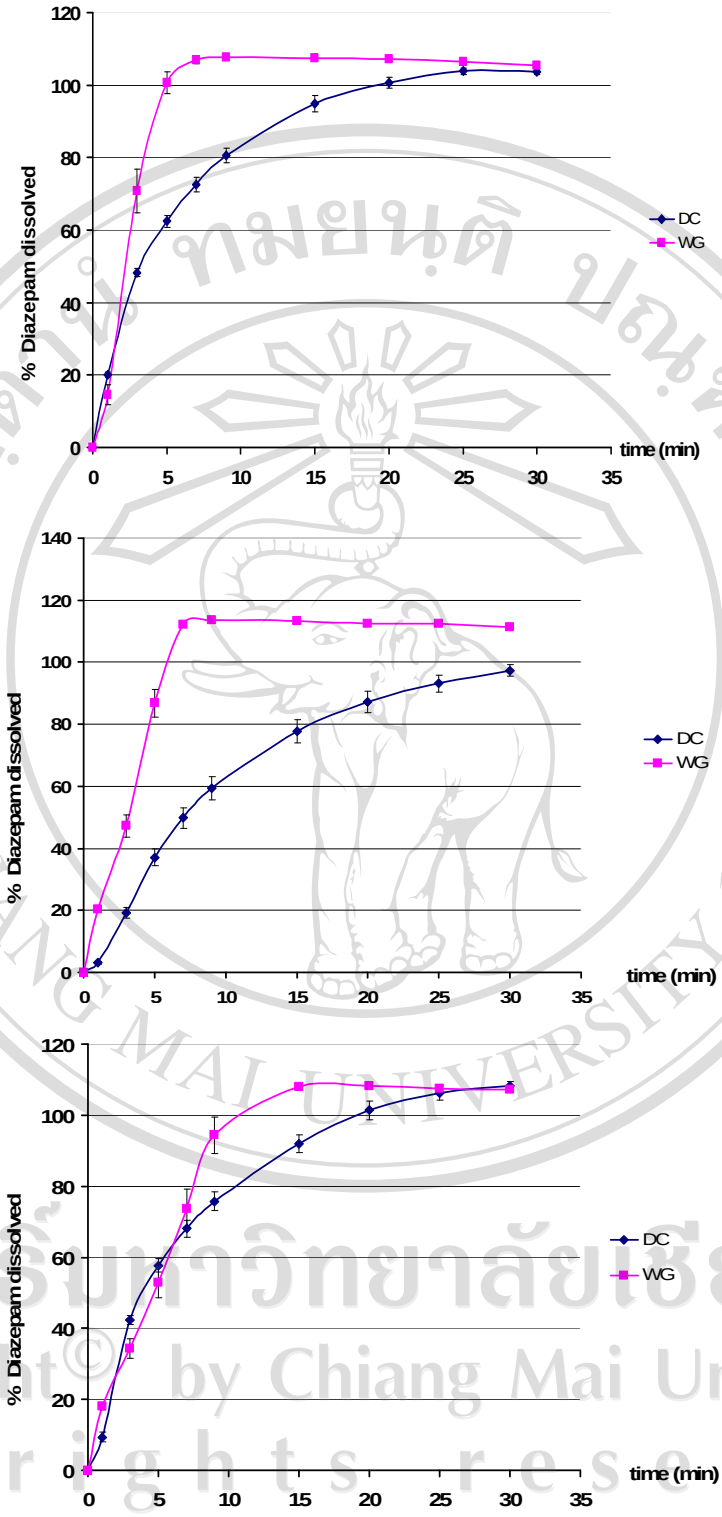


Figure 3.100 DZP dissolution profiles of DZP-solution-dropping tablet prepared from DC blank tablet and WG blank tablet at all tested CF

3.7 Stability Studies

3.7.1 Drug contents

The contents of drug from DSDT prepared from DC blank tablet of 1000 kg CF were determined after 0, 1, 2 and 3 months of the storage at room temperature. The analytical results were shown in Table 3.8 and it was found that the drug content were not different from the beginning at 0 month.

Table 3.6 The amount of CPM and diazepam in DSDT after 0, 1, 2 and 3 months of the storage

Tablet preparation	% LA of drug at each storage time			
	0 month	1 month	2 months	3 months
CPM-solution-dropping tablet	97.74	96.72	96.90	99.20
DZP-solution-dropping tablet	103.74	103.84	107.59	105.04

3.7.2 Dissolution profiles

Dissolution studies of CPM and diazepam tablet prepared by various methods after storage at 0, 1, 2 and 3 months were performed. Figure 3.101 showed the CPM dissolution profile of CPM-solution-dropping tablet prepared from DC blank tablet of all tested CF. The dissolution rates were fluctuated with the storage time. However all of them complied with the monograph of USP that not less than 80% of 4 mg of CPM is dissolved within 30 minutes. CPM was dissolved within 7 minutes in amount of 80% of 4 mg from tablet of 1000 kg and 1400 kg CF except for 1000 kg CF tablet at 2 months of storage it reached within 15 minutes at as shown in Figure 3.101 (a) and (b). Of 1800 kg CF tablet, CPM was dissolved within 5 minutes as shown in Figure 3.101 (c) except at 0 and 1 month of storage, it was dissolved within 9 minutes. The 80% CPM was dissolved from CPM DC tablet of 1000 or 1800 kg CF within 15 minutes except of 1000 kg CF tablet of 2 months storage within 30 minutes as shown in Figure 3.102 (a) and (c) respectively. Of 1400 kg CF, CPM dissolution

profile complied monograph of USP within 9 minutes as shown in Figure 3.102 (b) except at 2 and 3 months of storage they took 30 minutes and 15 minutes respectively. All of data were shown in Table C13 – C18 in Appendix C.

Figure 3.103 showed the dissolution profile of CPM-solution-dropping tablet prepared from WG blank tablet of all tested CF after 3 months storage. The dissolution rates were slower along the longer storage time. However all of them met the requirement in monograph of USP. CPM was dissolved 80% of 4 mg within 15 minutes from tablet 1000 and 1400 kg CF except tablet at 1400 kg CF of 3 months of storage which was dissolved of 80% CPM within 25 minutes as shown in Figure 3.103 (a) and (b). The dissolution profile of tablet of 1800 kg CF was not evaluated because of dark brown spot appearance on tablet surface. All of data were shown in Table C19 – C20 in Appendix C.

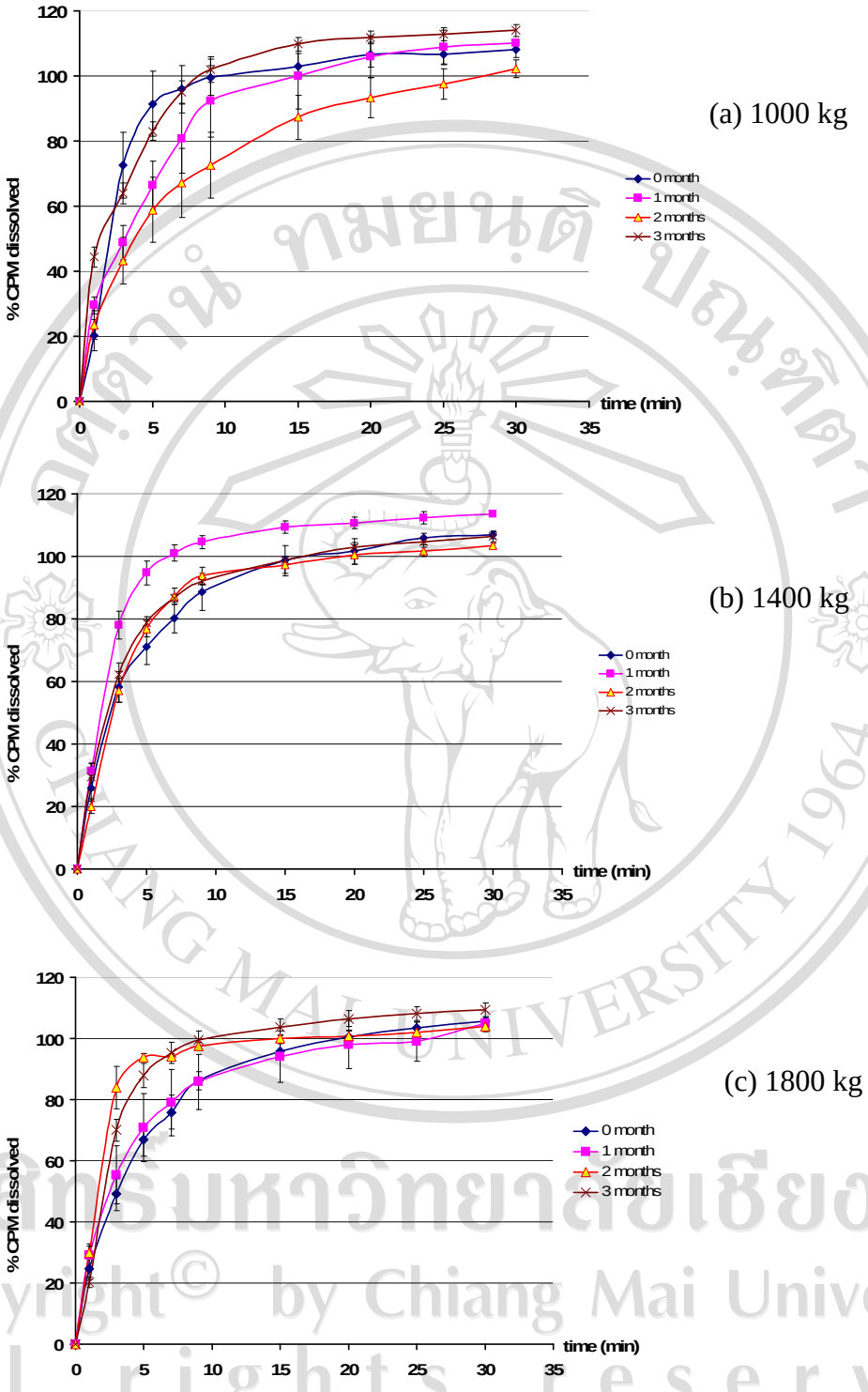


Figure 3.101 Dissolution profiles of CPM-solution-dropping tablet prepared from DC blank tablet at all tested CF after storage 0, 1, 2 and 3 months

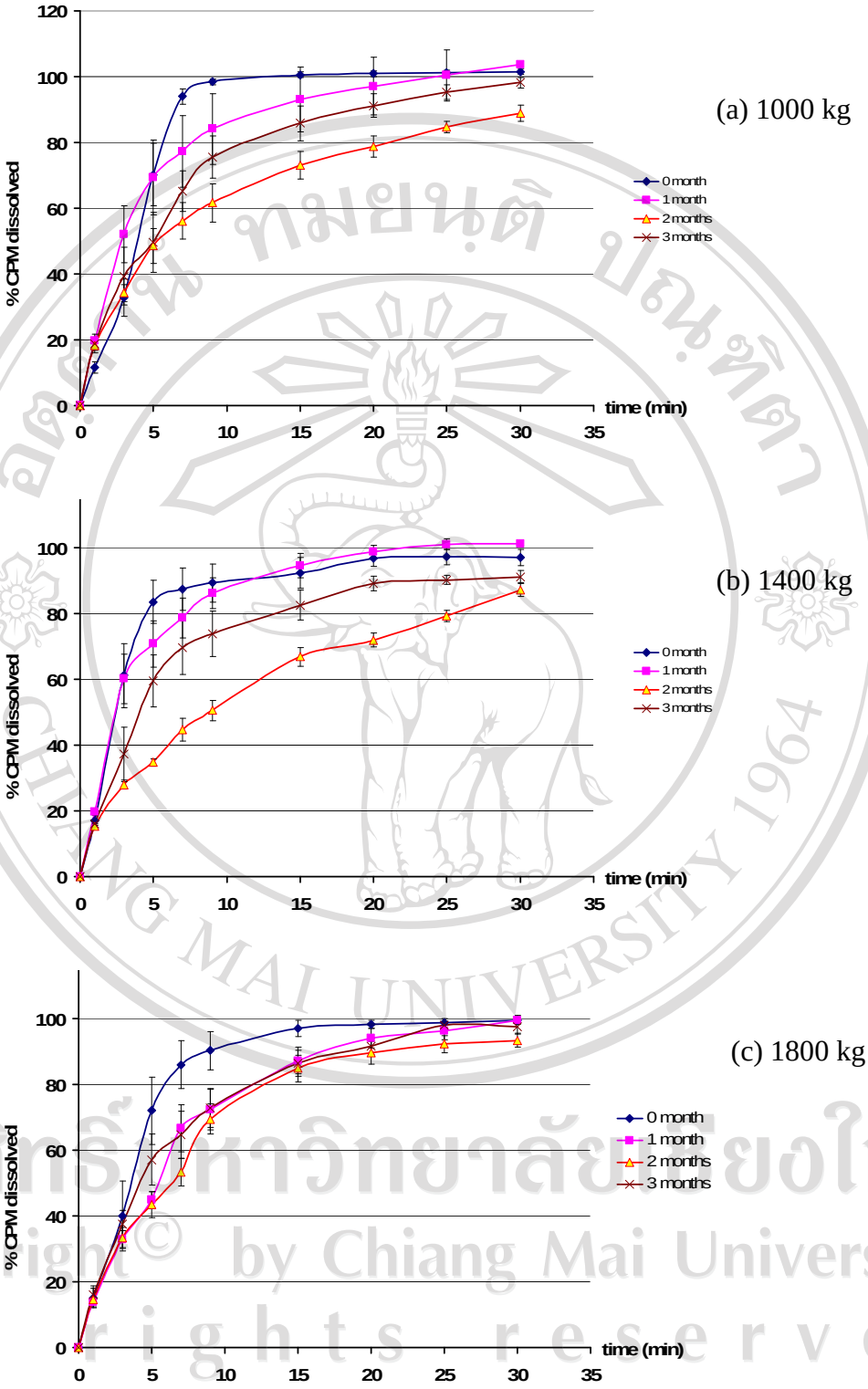


Figure 3.102 Dissolution profiles of CPM DC tablet at all tested CF after storage 0, 1, 2 and 3 months

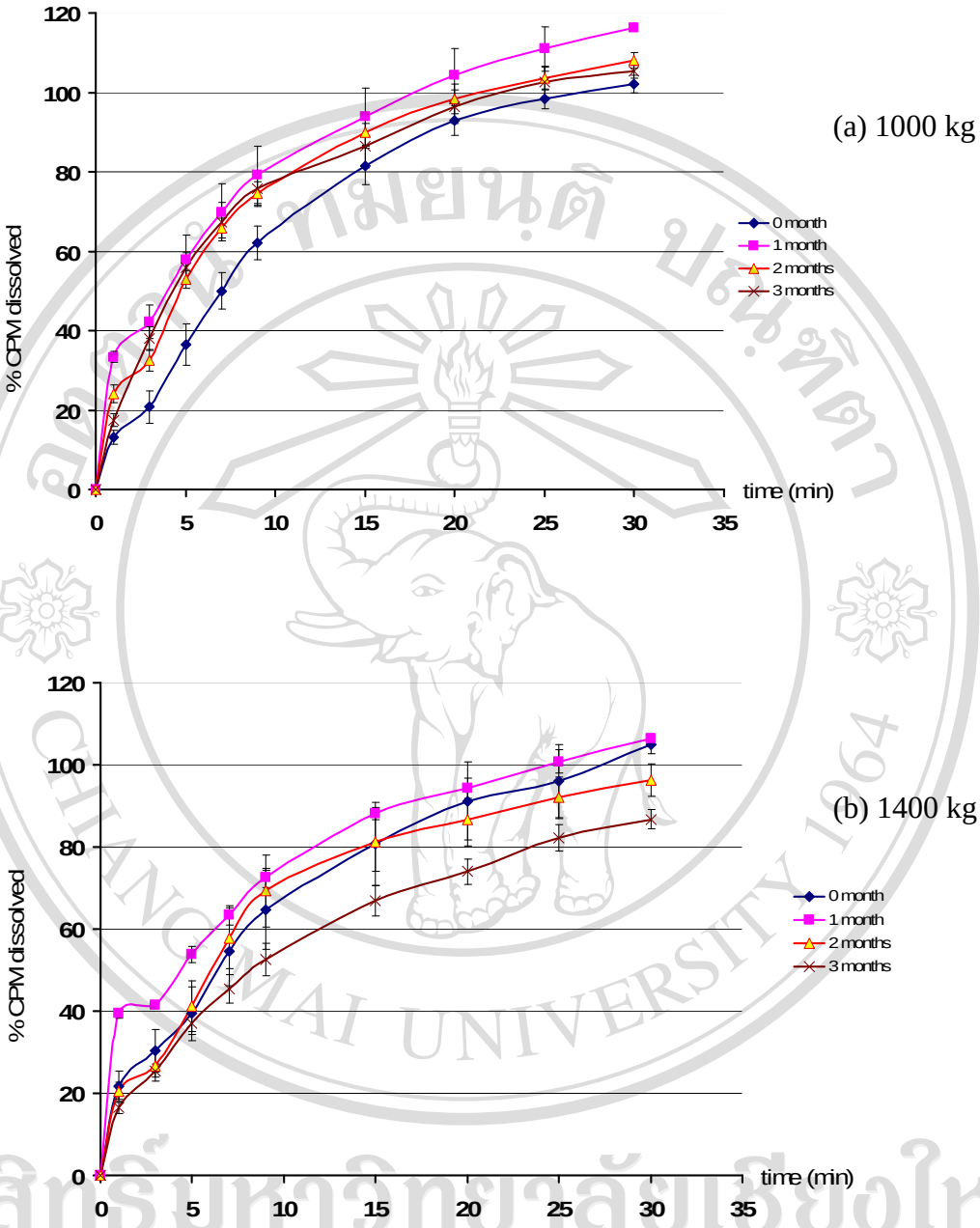


Figure 3.103 Dissolution profiles of CPM-solution-dropping tablet prepared from WG blank tablet at 1000 and 1400 kg of CF after storage 0, 1, 2 and 3 months

Figure 3.104 showed the diazepam dissolution profiles of DZP-solution-dropping tablet prepared from DC blank tablet of all tested CF after storage of 1, 2 and 3 months comparing with those of 0 month. The dissolution rate was slower as the storage time was longer. The requirement in monograph of USP i.e. not less than 85% of 5 mg diazepam is dissolved within 45 minutes. For tablet of 1000 and 1800 kg CF diazepam was dissolved 85% of 5 mg within 15 minutes except at 1800 kg CF tablet at 3 months of storage within 20 minutes as shown in Figure 3.104 (a) and (c). Of 1400 kg CF tablet, diazepam was dissolved more than 85% within 25 minutes as shown in Figure 3.104 (b) except at 2 and 3 months of storage. In case of 1000 kg CF, DZP DC tablet, diazepam was dissolved within 20 minutes except at 3 months storage within 30 minutes as shown in Figure 3.105 (a). Of 1400 and 1800 kg CF of DZP DC tablet, diazepam was dissolved within 25 and 15 minutes as shown in Figure 3.105 (b) and (c) respectively except at 1 and 3 months storage of tablet compressed at 1800 kg CF. All of data was shown in Table C21–C 26 in Appendix C.

Figure 3.106 showed the diazepam dissolution profiles of DZP-solution-dropping tablet prepared from WG blank tablet of all tested CF after storage of 1, 2 and 3 months comparing with those of 0 month. The dissolution rates were fluctuated with the storage time. All of them met the requirement in monograph of USP. Diazepam was dissolved 85% of 5 mg from tablet of 1000 kg and 1400 kg CF within 5 and 7 minutes except for tablet at 1400 kg CF of 1 month of storage taking time of 9 minutes as shown in Figure 3.106 (a) and (b) respectively. The dissolution profile of tablet of 1800 kg CF showed more than 85% diazepam was dissolved within 9 minutes except at 2 months reaching the level later which confirmed as in Figure 3.106 (c). All of data was shown in Table C27 - C29 in Appendix C.

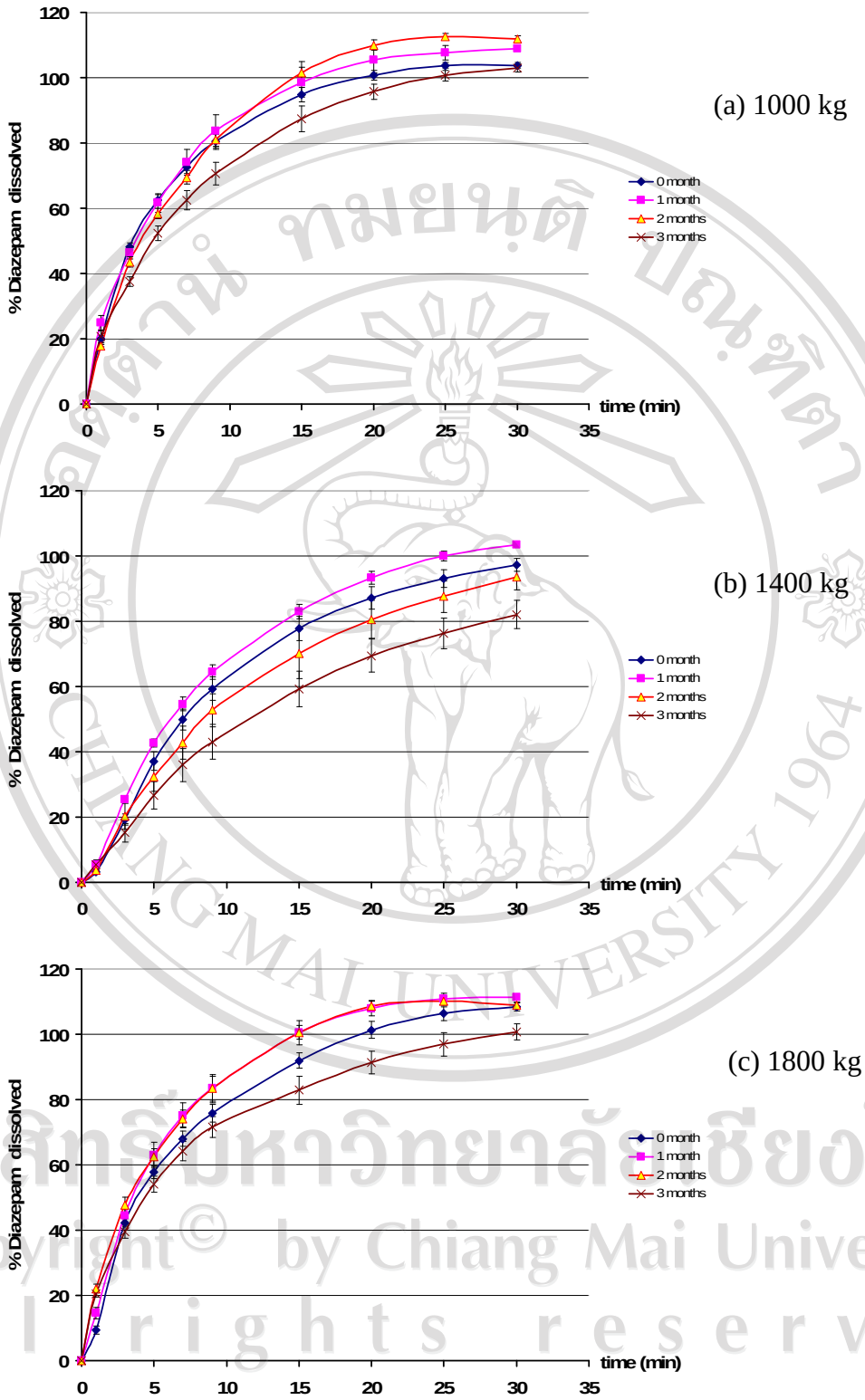


Figure 3.104 Dissolution profiles of DZP-solution-dropping tablet prepared from DC blank tablet of all tested CF after storage 0, 1, 2 and 3 months

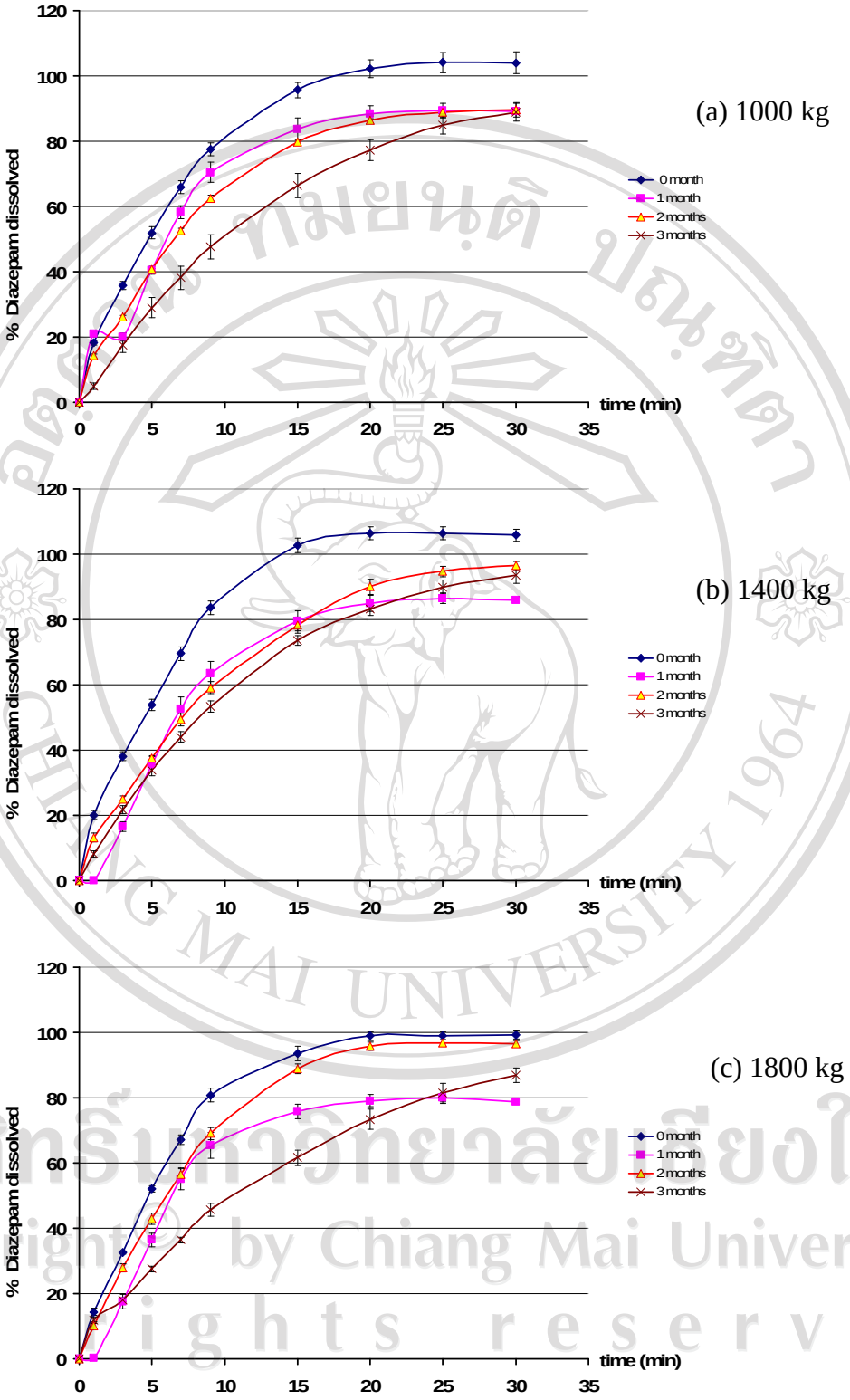


Figure 3.105 Dissolution profiles of DZP DC tablet at all tested CF after storage 0, 1, 2 and 3 months

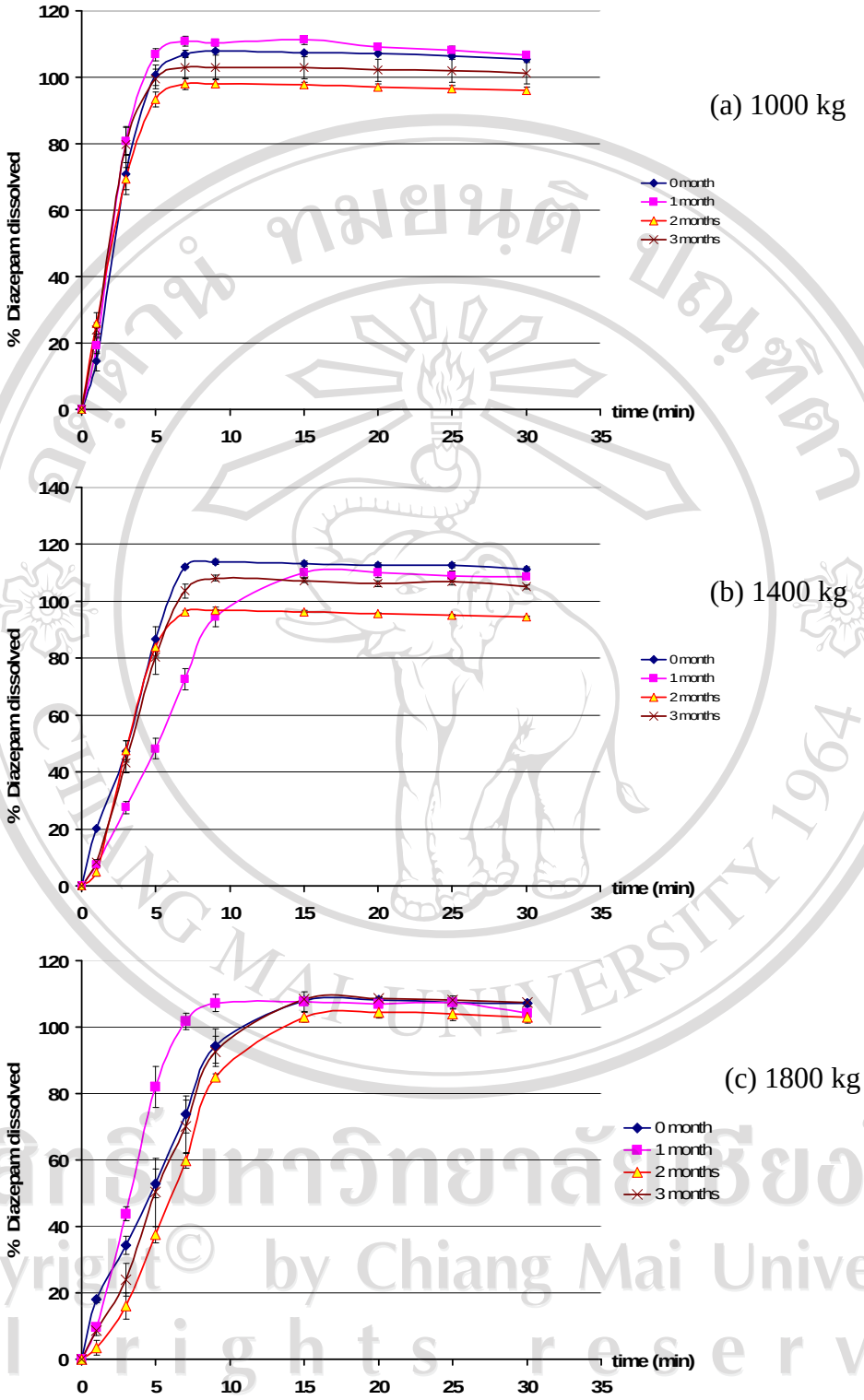


Figure 3.106 Dissolution profiles of DZP-solution-dropping tablet prepared from WG blank tablet of all tested CF after storage 0, 1, 2 and 3 months