CHAPTER 3

RESULTS

A. EVALUATION OF GRANULES

1. Bulk Volume

1.1 Manual and oscillating methods

Comparison of the bulk volume of diazepam granule prepared by manual and oscillating method is shown in Figure 5 and Table 3. Both the oscillating and manual methods with different sieve size gave different bulk volumes. As the number of sieve increased the bulk volume of both granules decreased. The bulk volume of oscillating method was slightly larger than the bulk volume of manual method. As the number of sieve increased, the standard deviation also decreased in both manual and oscillating methods.

1.2 Fluid bed spray drying method

Figure 6 demonstrates the bulk volume of diazepam granule prepared by fluid bed spray drying method. Table 3 also lists the physical properties of diazepam granule prepared by this method. As the weight of PVP increased, the bulk volume and its standard deviation also increased especially when 15 mg/tab of the binder was used.

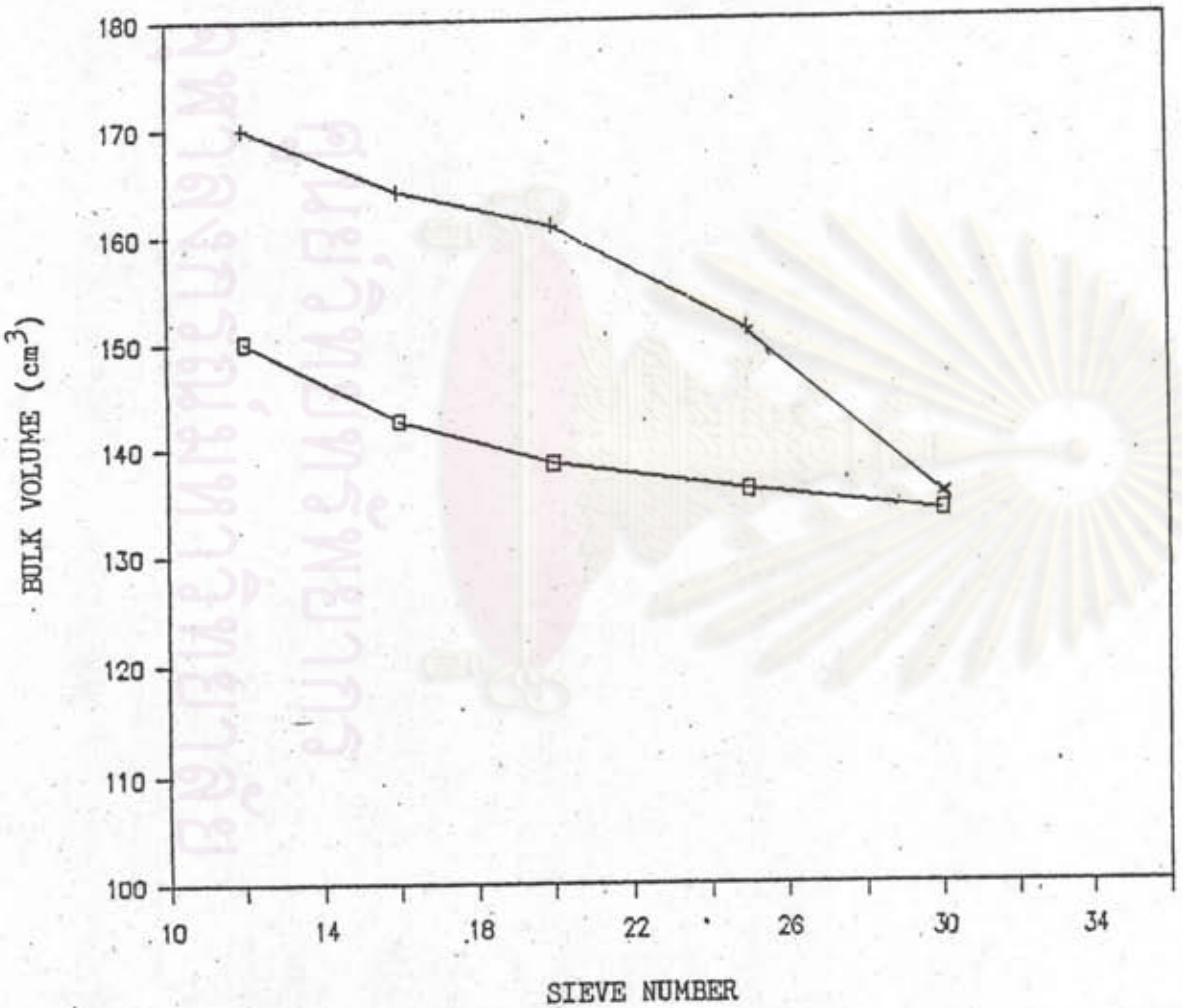

Figure 5 Comparison of bulk volume prepared by manual and oscillating methods: □ ,Manual and + ,Oscillating method.

Table 3 Comparison of bulk volume of diazepam granules prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (cm_3) ± SD.	P	Oscillating Mean* (cm^3) ± SD.	P_b
12	150.17 ± 2.91	0.499	170.00 ± 3.16	0.441
16	142.67 ± 2.24	0.526	164.14 ± 2.70	0.457
20	138.60 ± 2.06	0.543	161.00 ± 2.45	0.466
25	136.00 ± 1.90	0.551	151.14 ± 1.87	0.496
30	134.00 ± 1.42	0.560	130.40 ± 1.53	0.543

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (cm_3) ± SD.	P
6	144.00 ± 1.41	0.520
9	145.75 ± 1.75	0.515
12	154.40 ± 1.85	0.485
15	185.00 ± 3.28	0.405

* Average of 5 determinations

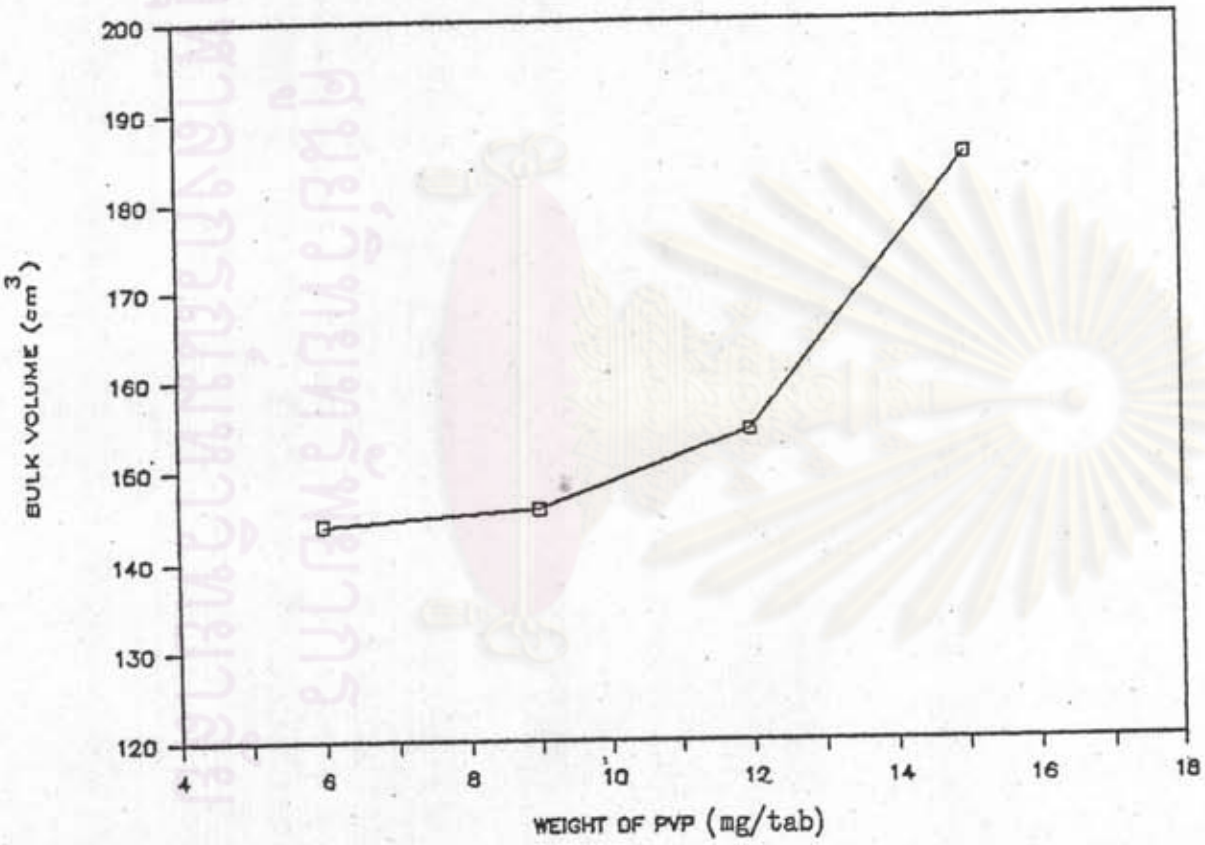

Figure 6 Comparison of bulk volume of diazepam granules prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

1.3 Comparison of bulk volume of diazepam granules prepared by manual, oscillating and fluid bed spray drying methods.

When 6 mg/tab of PVP used as binder in the three methods, it was found that the bulk volume from fluid bed spray drying method was lesser than oscillating method except the granule prepared by the sieve number 30 and larger than manual method except the granule prepared by the sieve number 12.

When increasing the amount of PVP to 9 mg/tab in fluid bed spray drying method the result was the same as previously mentioned. Further increasing the binder to 12 gm/tab, the bulk volume for fluid bed spray drying method was lesser than of oscillating method except the granule prepared by the sieve number 25 and 30 and greater than of the bulk volume of all granule prepared by manual method.

When the highest amount of the binder was used as 15 mg/tab the bulk volume for fluid bed spray drying method was the highest compared to manual and oscillating methods.

2. % Fine of Granule

2.1 Manual and oscillating method

Comparison of % fine of diazepam granule which prepared by manual and oscillating methods is shown in Figure 7 and listed in Table 4. The % fine of granule prepared by oscillating method was lower than the

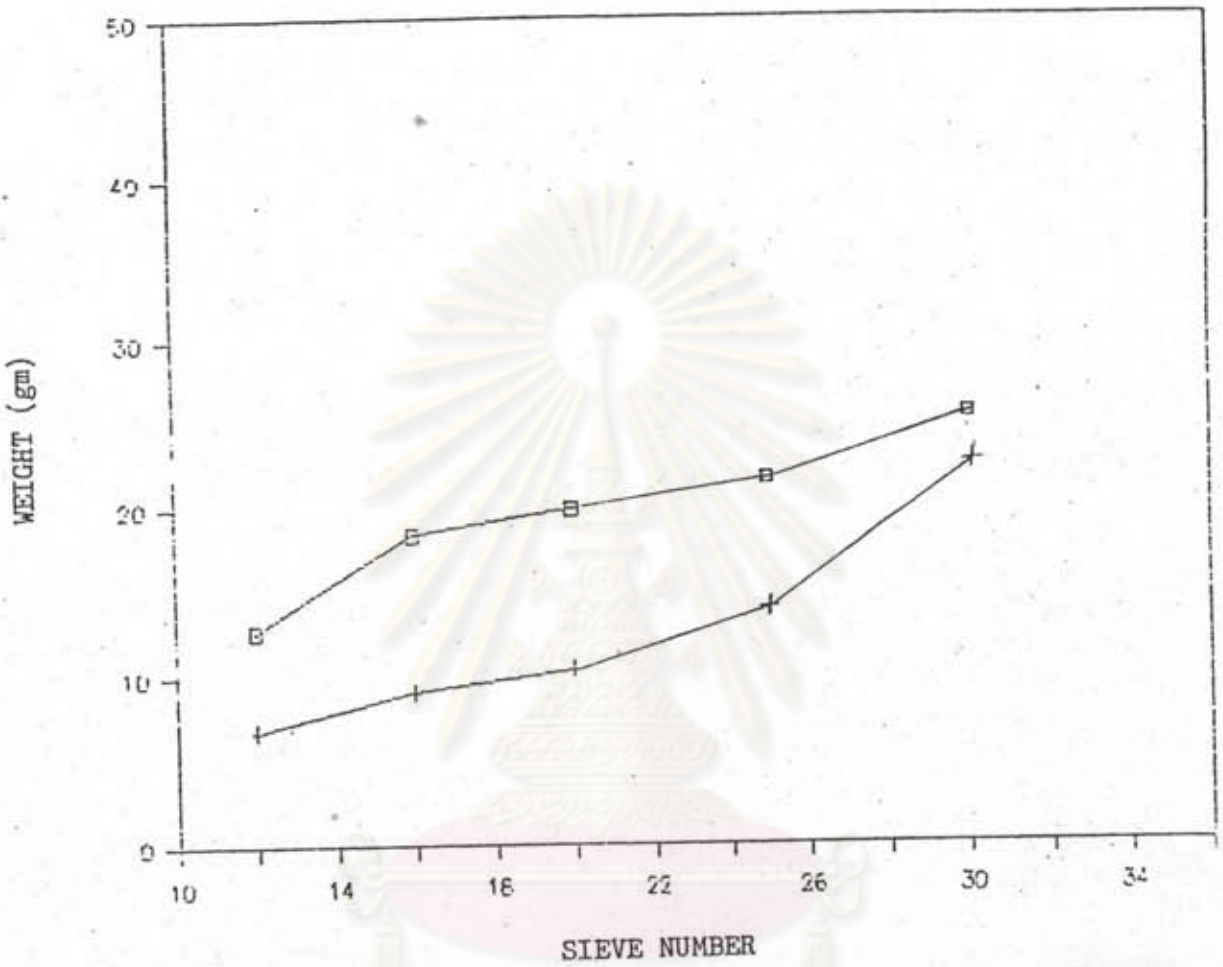

Figure 7 Comparison of %fine of diazepam granules prepared by manual and oscillating methods ; □ ,Manual and + ,Oscillating method

Table 4 Comparison of % fine of diazepam granules prepared by manual , oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (%) ± SD.	Oscillating Mean* (%) ± SD.
12	12.61 ± 1.23	6.75 ± 0.80
16	18.28 ± 1.45	8.98 ± 0.86
20	19.82 ± 1.58	10.28 ± 1.16
25	23.10 ± 1.95	11.64 ± 1.70
30	37.58 ± 2.95	23.27 ± 2.58

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (%) ± SD.
6	94.48 ± 9.48
9	84.33 ± 5.65
12	45.38 ± 3.13
15	27.30 ± 2.01

* Average of 5 determinations

% fine from manual method for all sieve sizes.

2.2 Fluid bed spray drying method

The % fine of diazepam granule prepared by fluid bed spray drying method is shown in Table 4 and Figure 8. As the weight of PVP increased from 6 to 15 mg/tab the % fine of granule extensively decreased.

2.3 Comparison of % fine of diazepam granules prepared by manual, oscillating and fluid bed spray drying methods

When 6 mg/tab of PVP was used in fluid bed spray drying method the % fine of diazepam granule was markedly higher than those from manual and oscillating methods.

When increasing PVP to 9-12 mg/tab in fluid bed spray drying method, the same result was obtained. Further increasing PVP to 15 mg/tab in fluid bed spray drying method the % fine of diazepam granule was still higher than the diazepam granule prepared by oscillating method and greater than by the manual method.

3. Size Distribution

3.1 Manual and oscillating methods

Comparison of size distribution of diazepam granule prepared by manual and oscillating methods using the sieve number 12 is shown in Figure 9. The size distribution of diazepam granule prepared by manual method was in a higher frequency in the range of 0-149 and 840-1680 μm. and was in a lower frequency in the range of

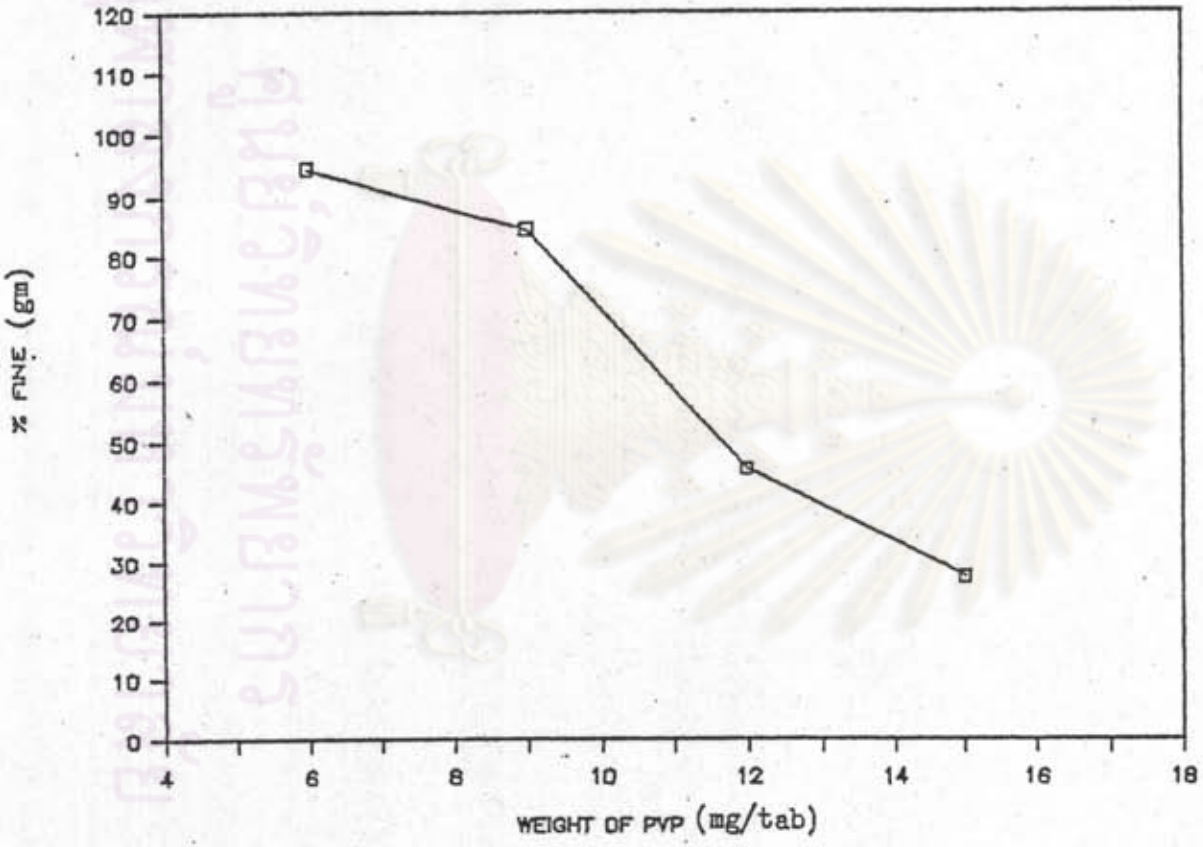

Figure 8 Comparison of % fine of diazepam granules prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

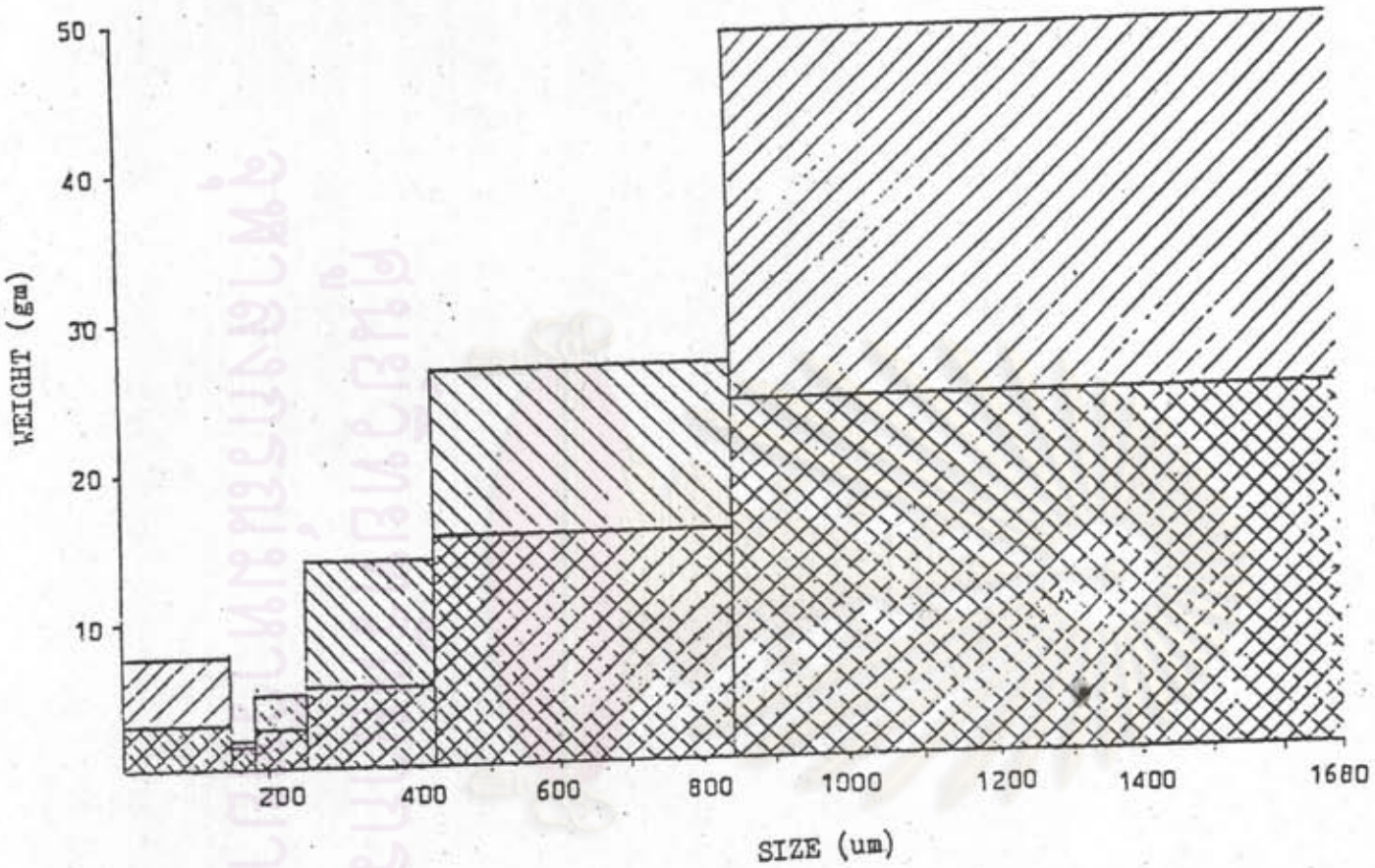

Figure 9 Comparison of size distribution of granule prepared by manual and oscillating method using sieve number 12: ▨ ,Manual method; ▨ ,Oscillating method.

149-177, 177-250, 250-420 and 420-840 μm. when compared to the diazepam granule prepared by oscillating method. Granules prepared by manual method had the greatest frequency in the range of 840-1680 μm. and the lowest in the range of 149-177 μm. Granules prepared by oscillating method had the greatest frequency in the range of 420-840 μm. and the lowest frequency the same as the granule prepard by manual method.

Comparison of size distribution of diazepam granule prepared by manual and oscillating method using sieve number 16 is shown in Figure 10. The size distribution of diazepam granule prepared by manual method showed higher frequency in the range of 0-149 and 840-1190 μm. and lower frequency in the same range as the granule prepared by sieve number 12 when compared to the diazepam granule prepared by oscillating method. Granules prepared by manual method had the greatest population in the range of 840-1190 μm. and the lowest in the range of 149-177 μm. Granules prepared by oscillating method had the greatest population in the range of 420-840 μm. and the lowest the same as the granule prepared by manual method.

Comparison of size distribution of diazepam granule prepared by manual and oscillating methods using sieve number 20 is shown in Figure 11. The size distribution of diazepam granule prepared by manual method showed higher frequency in the range of 0-149, 149-177 and 840-1190 μm. and lower in the range of 177-250, 250-420

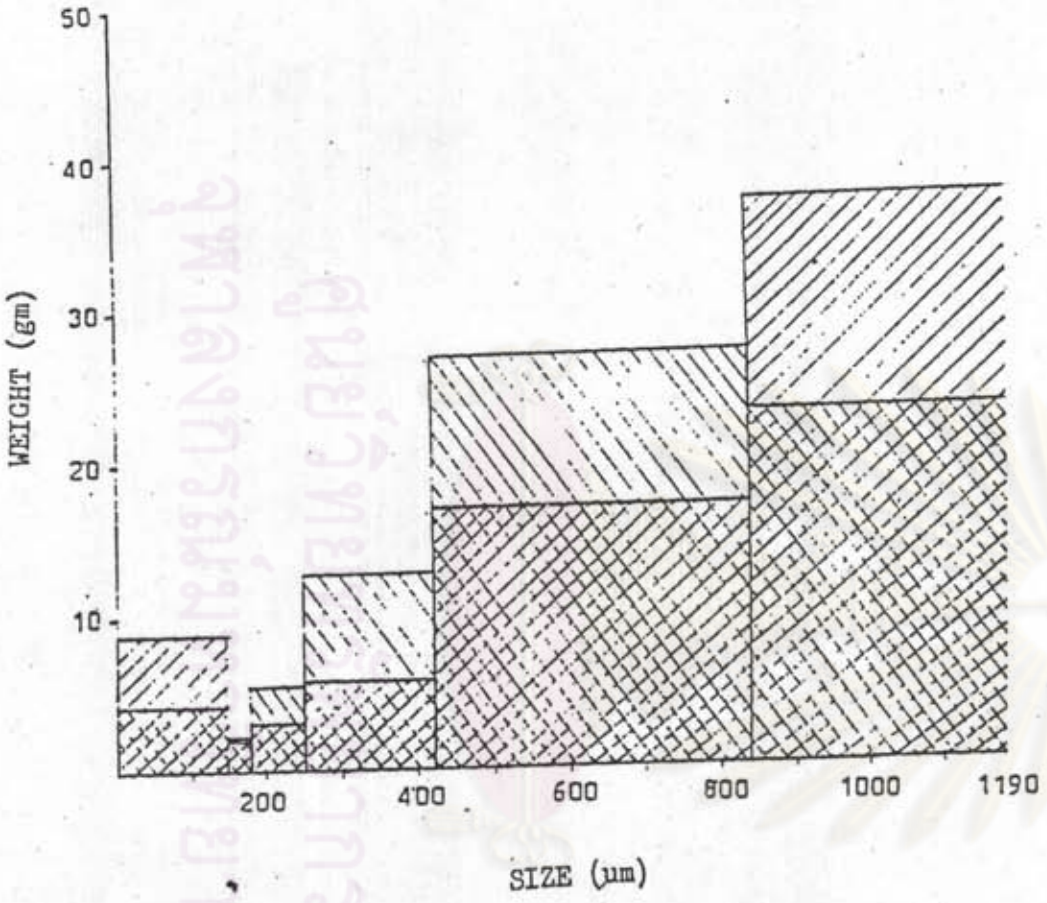

Figure 10 Comparison of size distribution of granule prepared by manual and oscillating method using sieve number 16: ▨ ,Manual method; ▧ ,Oscillating method.

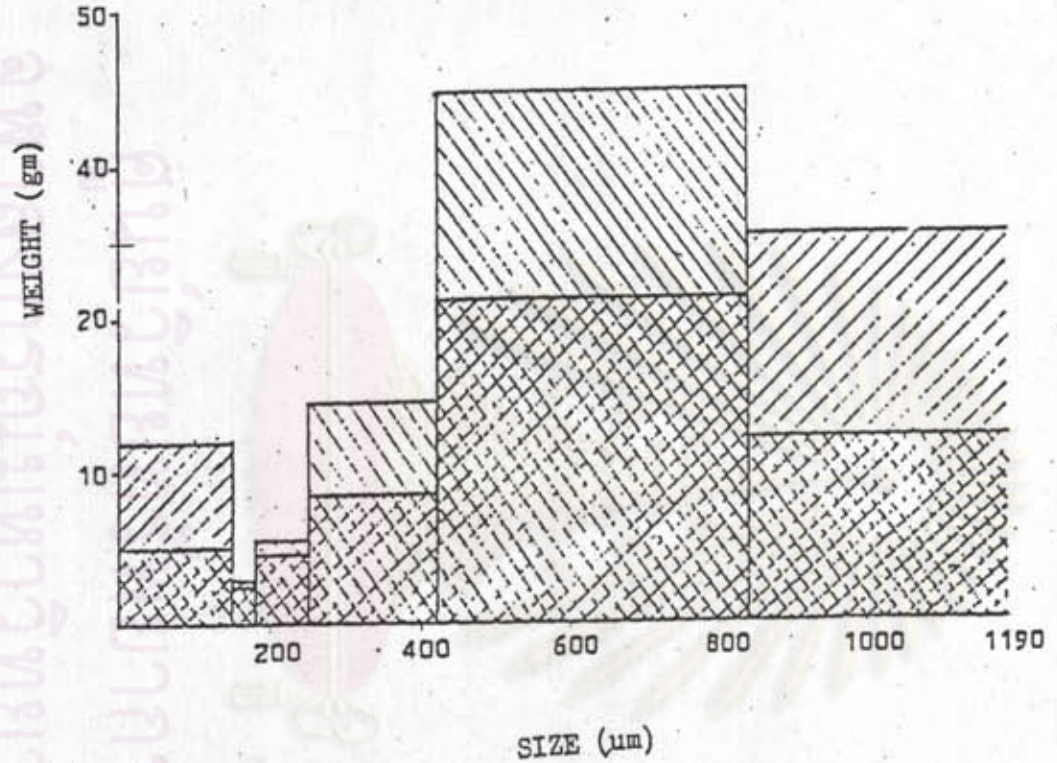

Figure 11 Comparison of size distribution of granule prepared by manual 1 and oscillating methods using sieve number 20: ▨ ,Manual method ; ▧ ,Oscillating method.

and 420-840 μm. when it was compared with the diazepam granule prepared by oscillating method. the diazepam granule had the greatest frequency in the range of 840-1190 μm. and the lowest in the range of 149-177 μm. The diazepam granule prepared by oscillating method had the greatest frequency in the range of 420-840 μm. and it had lowest size the same as the granule prepared by manual method.

Comparison of size distribution of diazepam granule prepared by manual and oscillating methods using sieve number 25 is shown in Figure 12. The size distribution of diazepam granule prepared by manual method demonstrated higher frequency than granule prepared by oscillating method except in the range of 149-420 um and 840-1190 μm. They had the greatest population in the range of 420-840 μm and the lowest in the range of 840-1190 μm. Granules prepared by oscillating method had the greatest and the lowest population the same as the granule prepared by manual method.

Comparison of size distribution of diazepam granule prepared by manual and oscillating methods using sieve number 30 is illustrated in Figure 13. The size distribution of diazepam granule prepared by manual method showed higher frequency than the diazepam granule prepared by oscillating method except the range of 149-420 μm. The diazepam granule prepared by manual method had the greatest population in the range of 420-840 μm. and

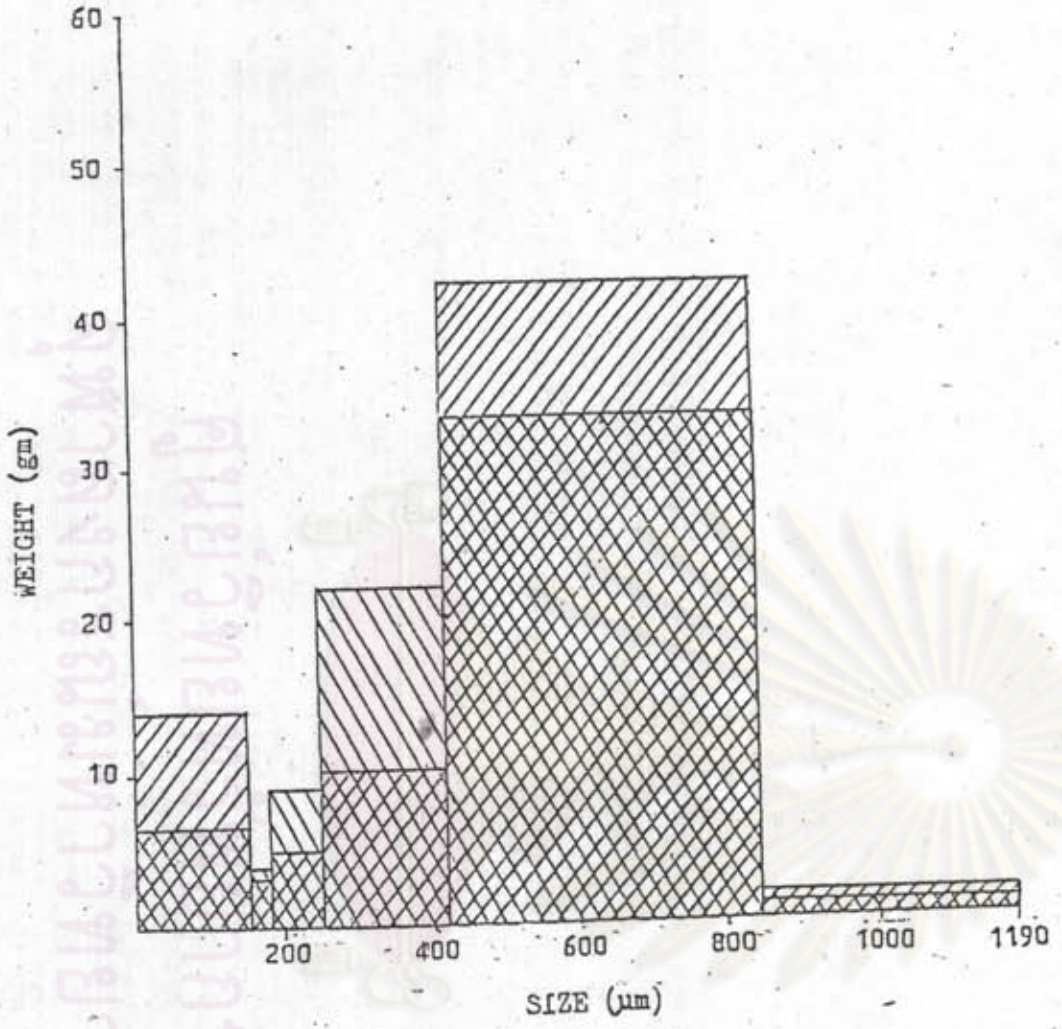

Figure 12 Comparison of size distribution of granule prepared by manual and oscillating methods using sieve number 25: ▨ ,Manual method; ▧ ,Oscillating method.

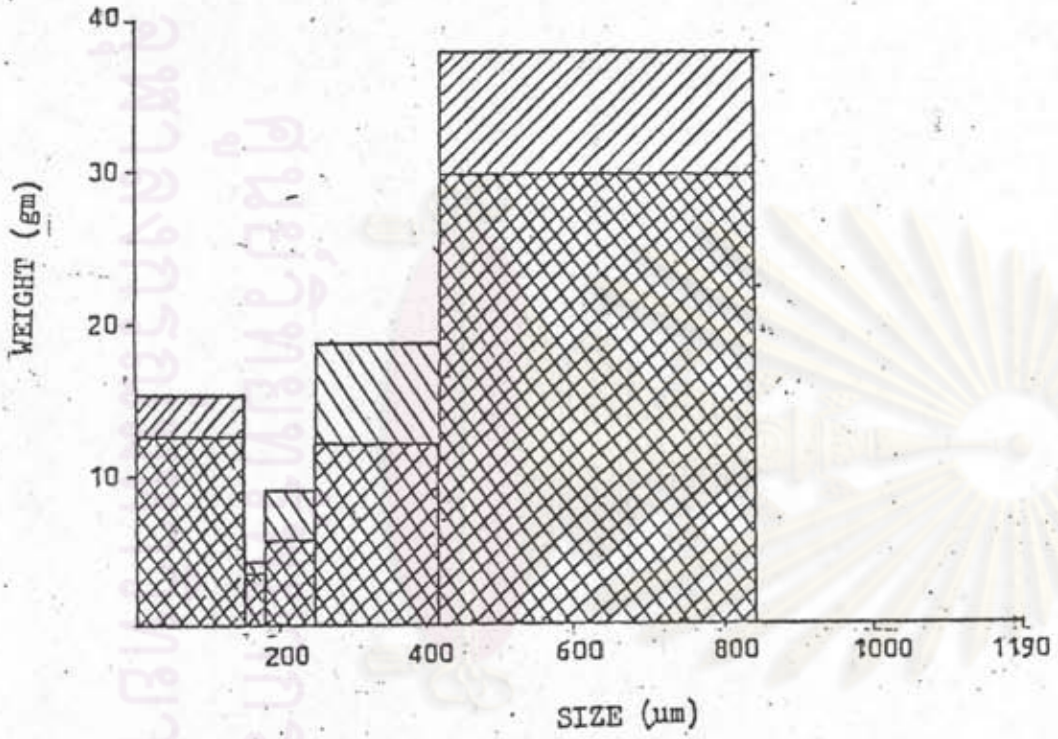

Figure 13 Comparison of size distribution of granule prepared by manual and oscillating methods using sieve number 30: ▨ , Manual method; ▧ , Oscillating method.

the lowest in the range of 840-1190 μm. The diazepam granule prepared by oscillating method had the greatest and the lowest population the same as the granule prepared by manual method.

3.2 The fluid bed spray drying method

Comparison of size distribution of diazepam granule prepared by fluid bed spray drying method using various amounts of PVP as granulating agent is shown in Figure 14 and Table 6. When 6 mg/tab of PVP was used the diazepam granules were highly accumulated in the size range of 0-149 μm. The granules were less accumulated in the range of 149-1190 μm. When increasing the amount of PVP to 9 mg/tab the result was the same. Further increasing PVP to 12 mg/tab the granule was less accumulated in the range of 840-1190 μm, when the highest amount of the binder was used, the granules were highly accumulated in the range of 250-420 μm.

3.3 Comparison of the mean diameter of diazepam granule prepared by manual, oscillating and fluid bed spray drying methods.

The mean diameters of diazepam granule prepared by the three methods are listed in Table 7 and 8. When 6 mg/tab of the binder was used in the three methods it was found that the granules from fluid bed spray drying method were more accumulated in the range of 0-149 μm and the mean diameter was 86.55 μm which it was smaller than the mean diameter of granules prepared by the other two methods.

Table 5 Comparison of the size distribution of diazepam granule prepared by fluid bed spray drying method using different levels of PVP.

Size (μm)	15 mg/tab	12 mg/tab	9 mg/tab	6 mg/tab
840-1680	0.06 gm.	0.06 gm.	0.06 gm.	0.02 gm.
420-840	11.93 gm.	10.60 gm.	0.84 gm.	0.23 gm.
250-420	22.15 gm.	15.80 gm.	4.06 gm.	0.64 gm.
177-250	20.42 gm.	14.48 gm.	6.93 gm.	2.02 gm.
149-177	10.93 gm.	12.31 gm.	8.36 gm.	3.42 gm.
0-149	9.11 gm.	21.28 gm.	54.23 gm.	68.10 gm.

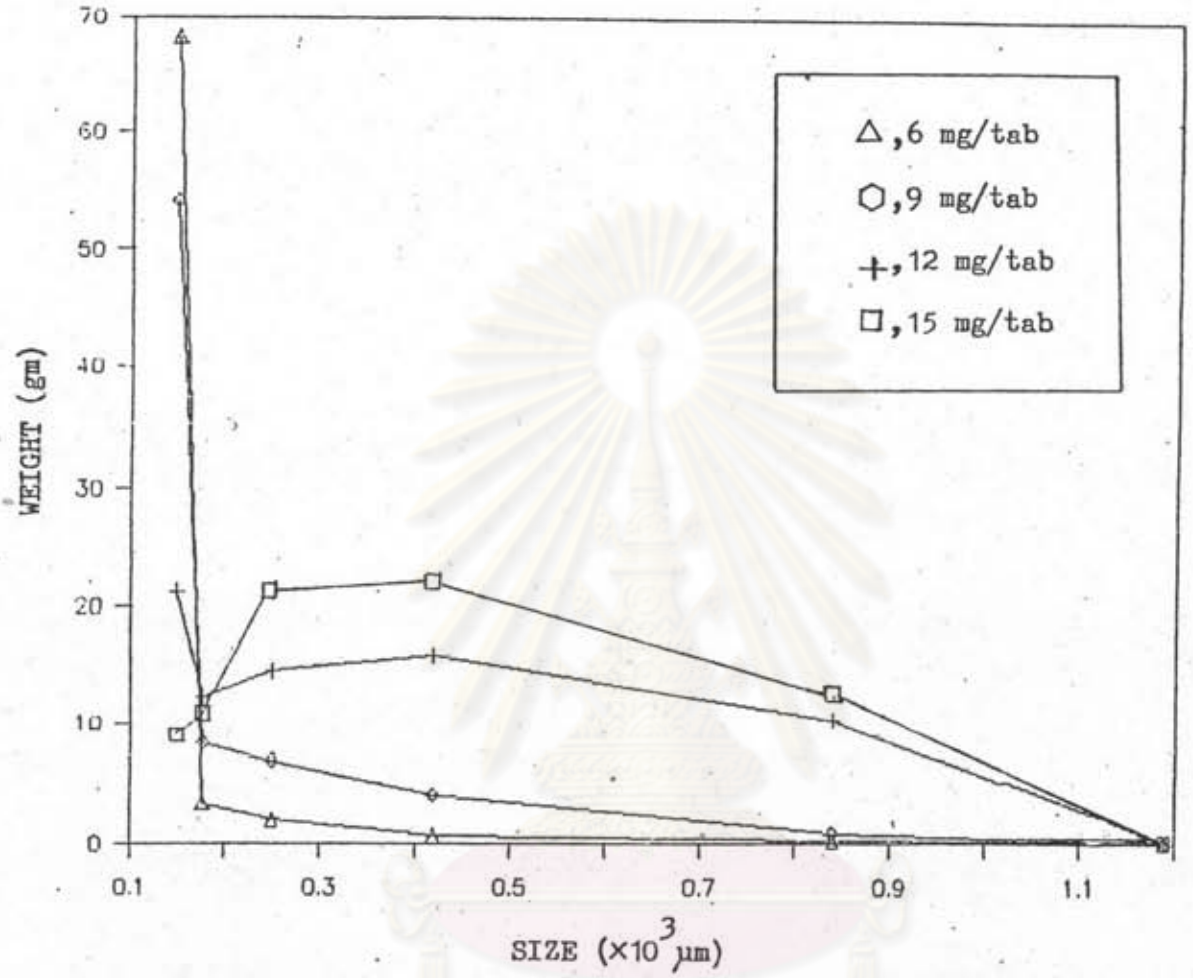

Figure 14 Comparison of size distribution of granule prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

Table 6 Influence of method of preparing on the mean diameter of diazepam granules prepared by manual and oscillating methods.

Sieve Number	Mean Diameter* (μm.) Manual Method	% CV	Oscillating Method	% CV
12	896.08 ± 34.02	3.80	713.32 ± 26.56	3.72
16	694.46 ± 30.52	4.39	621.77 ± 25.42	4.08
20	593.98 ± 29.50	4.97	550.94 ± 24.78	4.50
25	446.57 ± 25.45	5.44	523.85 ± 23.15	5.36
30	335.74 ± 24.60	5.91	433.85 ± 22.50	5.84

Table 7 Influence of amount of PVP as granulating agent on the mean diameter of diazepam granules prepared by fluid bed spray drying method.

Amount of PVP (mg)	Mean Diameter* (μm)	% CV
15	289.35 ± 16.50	5.70
12	251.11 ± 14.23	5.67
9	118.59 ± 6.25	5.27
6	86.55 ± 4.50	5.20

* Average of 5 determinations

When increasing the amount of PVP to 9 mg/tab in fluid bed spray drying method. The mean diameter of granules was 118.59 μm which it was a little higher than the mean size of granules prepared by using the binder 6 mg/tab but it was still smaller than the mean diameter prepared by other two methods.

Further increasing the amount of PVP to 12 mg/tab in fluid bed spray drying method. Although the population was well distributed in the range of 149-177, 177-250, 250-420 and 420-840 μm, the mean diameter was larger than the granule prepared by using lower amount of the binder but was still smaller than the mean diameter prepared by the other two methods.

When the highest of the binder was used in fluid bed spray drying method the mean diameter was bigger than those prepared by using less amount of PVP but was smaller than the mean diameter prepared by the other two methods.

4. Flow Rate

4.1 Manual and oscillating methods

Comparison of flow rate of diazepam granules prepared by manual and oscillating methods are shown in Figure 15 and Table 8.

As the number of sieve increased the flow rate increased. The flow rate of granule prepared by manual method was faster than the granule prepared by oscillating method.

Table 8 Comparison of flow rate of diazepam granules prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (gm./sec) ± SD.	Oscillating Mean* (gm./sec) ± SD.
12	8.84 ± 0.19	8.65 ± 0.17
16	9.99 ± 0.24	9.19 ± 0.21
20	10.44 ± 0.28	10.28 ± 0.24
25	13.02 ± 0.30	10.56 ± 0.26
30	14.73 ± 0.34	13.53 ± 0.31

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (gm/sec) ± SD.
6	**
9	5.63 ± 1.41
12	14.06 ± 0.44
15	11.38 ± 0.86

* Average of 5 determinations

** Unmeasurable

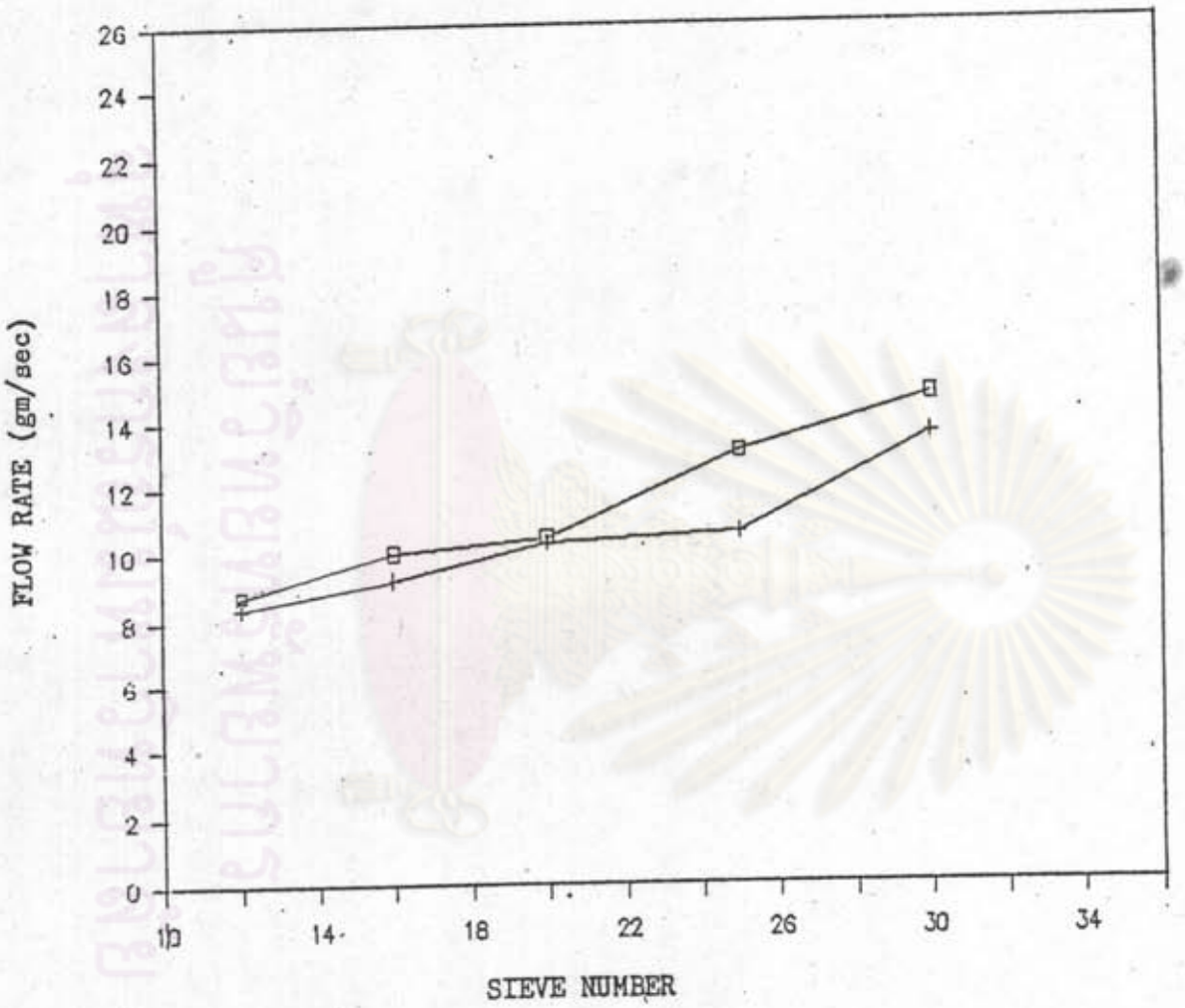

Figure 15 Comparison of flow rate of diazepam granules prepared by manual and oscillating methods: □, Manual and +, Oscillating method.

4.2 The flow rate of diazepam granules prepared by fluid bed spray drying method is listed in Table 8 and Figure 16. When using 6 mg/tab of PVP as the binder, nonflowable granule was obtained. When 9 mg/tab of the binder was used, the granule could flow but the flow rate was poor. Further increasing the amount of PVP to 12 mg/tab, the flow rate was extensively increased. However, further increasing the amount of binder to 15 mg/tab the flow rate was slightly decreased.

4.3 Comparison of flow rate of diazepam granules prepared by manual, oscillating and fluid bed spray drying methods are shown in Figure 15 and 16.

When the same amount of 6 mg/tab of PVP was used the granule from fluid bed spray drying method was nonflowable but the other three granules were flowable. When increasing the amount of PVP to 9 mg/tab in fluid bed spray drying method the flow rate of diazepam granules prepared by manual and oscillating were still faster than the granule prepared by fluid bed spray drying method.

Further increasing the amount of binder to 12 mg/tab in fluid bed spray drying method the diazepam granule flow faster than the diazepam granules prepared by oscillating and manual methods except that prepared by manual method with the sieve number 30. When the highest amount of the binder was used in fluid bed spray drying method the flow rate was still faster than granules prepared by other two methods except the granule prepared

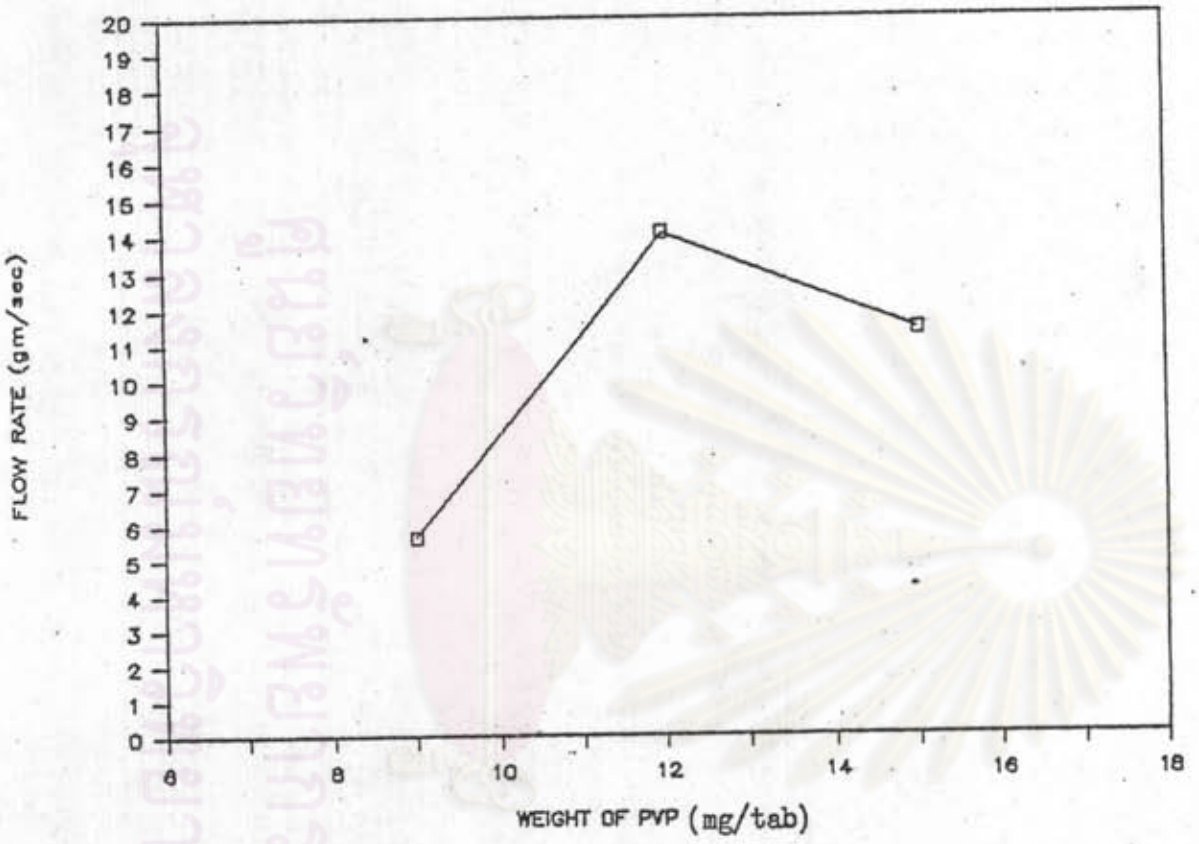

Figure 16 Comparison of flow rate of diazepam granules prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

by the sieve number 25 and 30 in manual method and the granule prepared by the sieve number 30 in oscillating method.

5. Repose Angle

5.1 Comparison of repose angle of diazepam granules prepared by manual and oscillating method

Comparison of repose angle of diazepam granules prepared by manual and oscillating method as illustrated in Figure 17, the repose angle increased as the sieve size increased both in manual and oscillating method. However the oscillating method gave larger angle than the manual method when using the same sieve number.

5.2 The repose angle of diazepam granules prepared by fluid bed spray drying method.

Comparison of the repose angle of diazepam granule prepared by fluid bed spray drying method was listed in Table 9. When 6 mg/tab of PVP was used as the binder the repose angle could not be measured because of the nonflowability of the granules. When 9, 12 and 15 mg/tab of PVP was used as the binder the repose angle was increased from 41.58 to 43.00. Increasing the amount of PVP would increase the repose angle of the granule.

5.3 Comparison of repose angle of diazepam granules prepared by manual, oscillating and fluid bed spray drying methods.

The repose angle of granules prepared by using 6

Table 9 Comparison of repose angle of diazepam grangules prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (°) ± SD.	Oscillating Mean* (°) ± SD.
12	34.90 ± 0.39	37.40 ± 0.41
16	35.75 ± 0.49	37.55 ± 0.51
20	36.55 ± 0.55	38.45 ± 0.77
25	37.50 ± 0.65	38.50 ± 0.76
30	38.25 ± 0.84	39.59 ± 0.87

Weight of PVP mg/tab	Fluid Bed Spray Drying Mean*(°) ± SD.
6	**
9	41.58 ± 0.95
12	42.42 ± 1.05
15	43.00 ± 1.20

* Average of 5 determinations

** Unmeasurable

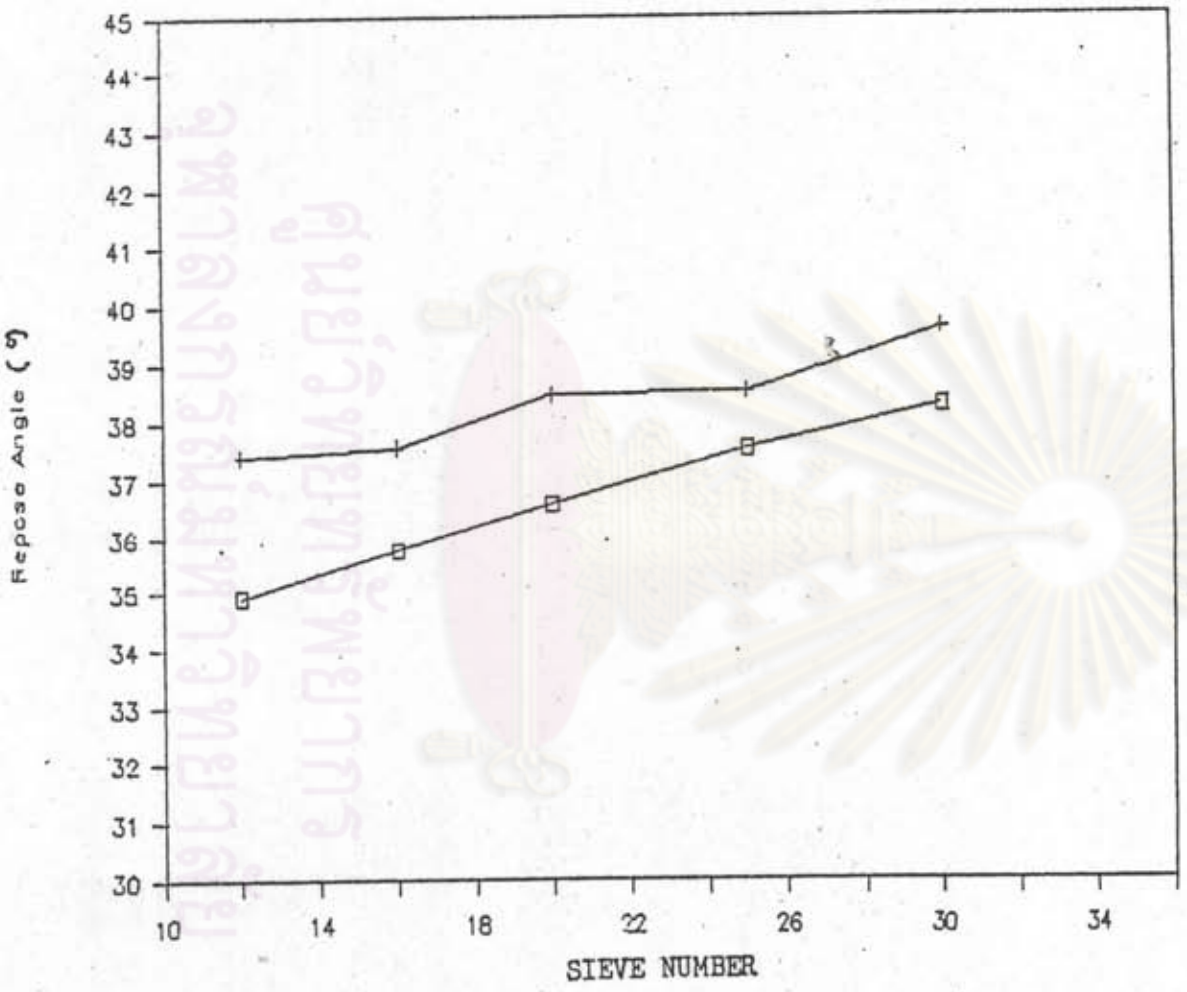

Figure 17 Comparison of repose angle of diazepam granules prepared by manual and oscillating methods : □ ,Manual and + , Oscillating method.

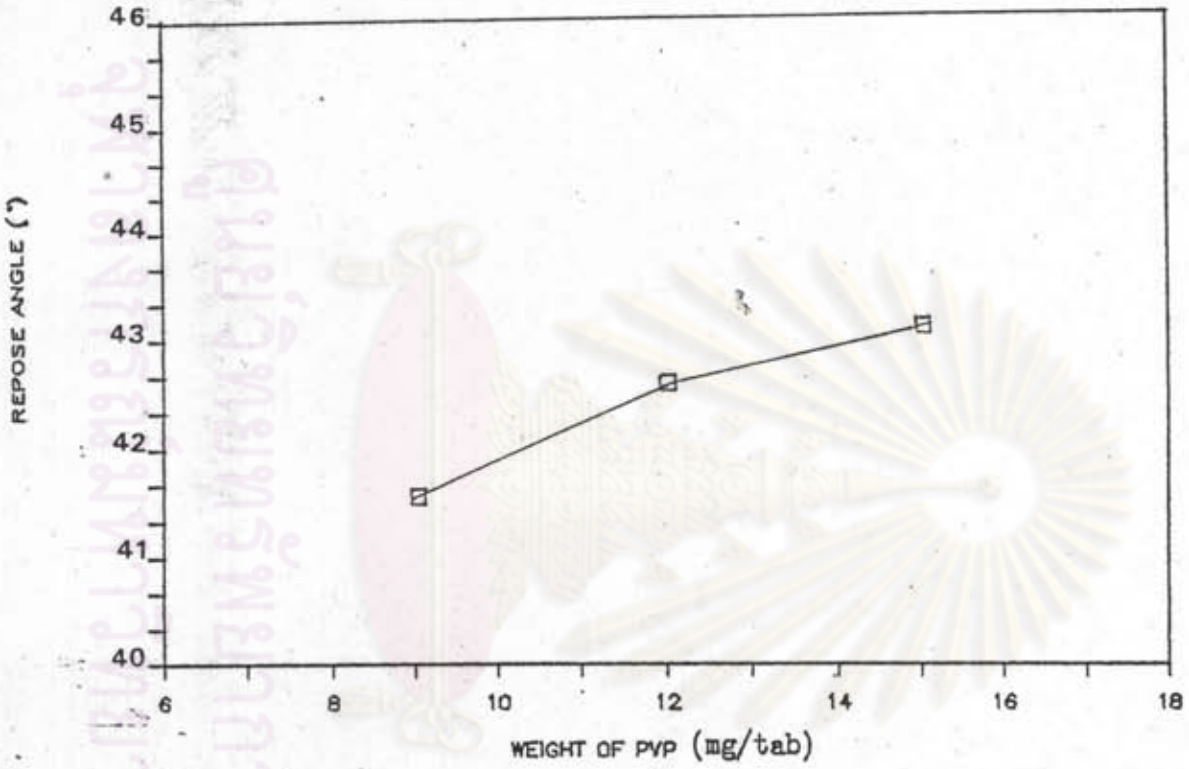

Figure 18 Comparison of repose angle of diazepam granules prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

mg/tab of PVP the repose angle was uncomparable. When increasing the amount of PVP to 9 mg/tab the repose angle was large amount the granules obtained by fluid bed spray drying , manual and oscillating methods.

Further increasing PVP to 12 mg/tab in fluid bed spray drying method the repose angle was larger than all the granule which prepared by manual and oscillating methods.

When the highest amount of the binder was used in fluid bed spray drying method as 15 mg/tab the repose angle was highest compared to all granules obtained by manual and oscillating methods.

B. EVALUATION OF TABLET

1. Weight Variation of Diazepam Tablet

1.1 Comparison of weight of diazepam tablet prepared by manual and oscillating methods

Comparison of weight of diazepam tablet prepared by manual and oscillating method as illustrated in Figure 19. In manual method the mean weight of diazepam tablet was a little lower than the mean weight of diazepam tablet prepared by oscillating method except the tablet prepared by the sieve number 25. The tablet prepared by larger sieve size showed larger weight deviation than that prepared by smaller the sieve size. The weight variation of diazepam tablet prepared by oscillating method gave lower weight variation than manual

Table 10 Comparison of weight of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (mg.) ± SD.	% CV	Oscillating Mean* (mg.) ± SD.	% CV
12	217.90 ± 4.55	2.09	221.50 ± 3.32	1.50
16	212.60 ± 4.24	1.99	217.40 ± 2.64	1.43
20	213.80 ± 2.61	1.22	217.60 ± 2.33	1.07
25	217.30 ± 2.47	1.14	215.60 ± 2.09	0.97
30	213.80 ± 1.80	0.84	220.60 ± 1.72	0.73

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (mg ± SD.)	% CV
6	216.20 ± 1.42	0.89
9	211.90 ± 1.15	0.73
12	219.55 ± 0.42	0.48
15	213.75 ± 0.94	0.71

* Average of 20 determinations

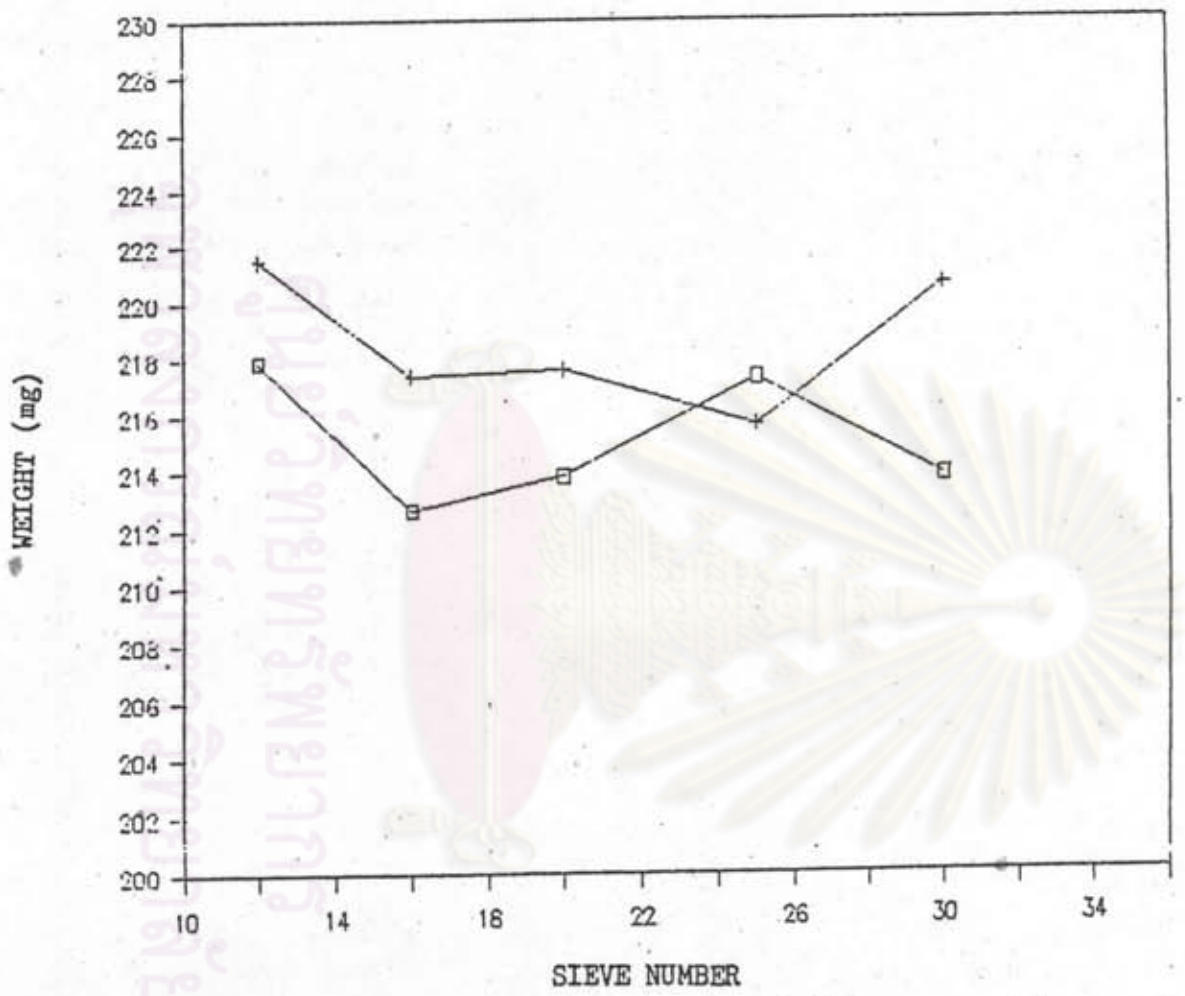

FIgure 19 Comparison of weight of diazepam tablets prepared by manual and oscillating methods: □, Manual and +, Oscillating method.

method.

1.2 The weight of diazepam tablet prepared by fluid bed spray drying method

Comparison of the weight of diazepam tablets prepared by fluid bed spray drying method is listed in Table 10 and Figure 20. When 6, 9, 12 and 15 mg/tab of PVP was used as the binder the mean weight was within the limit of + 10% from the mean weight. When 12 mg/tab of PVP was used the weight variation was the lowest. When 6 mg/tab of PVP was used the weight variation was the highest.

1.3 Comparison of weight of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods

All tablets weighed within the limit of + 10% from the mean weight.

The mean weight of tablets using 6 mg/tab as the binder in fluid bed spray drying method was found to be lower than the tablets prepared by the sieve number 12 and 25 but higher than all other tablets in manual method, and lower than all tablets prepared by oscillating method except those prepared by the sieve number 25.

When increasing the amount of PVP to 9 mg/tab the mean weight was the lowest amount the tablet prepared by fluid bed spray drying, manual and oscillating methods.

Further increasing the amount of PVP to 12 mg/tab in fluid bed spray drying method the mean weight was the

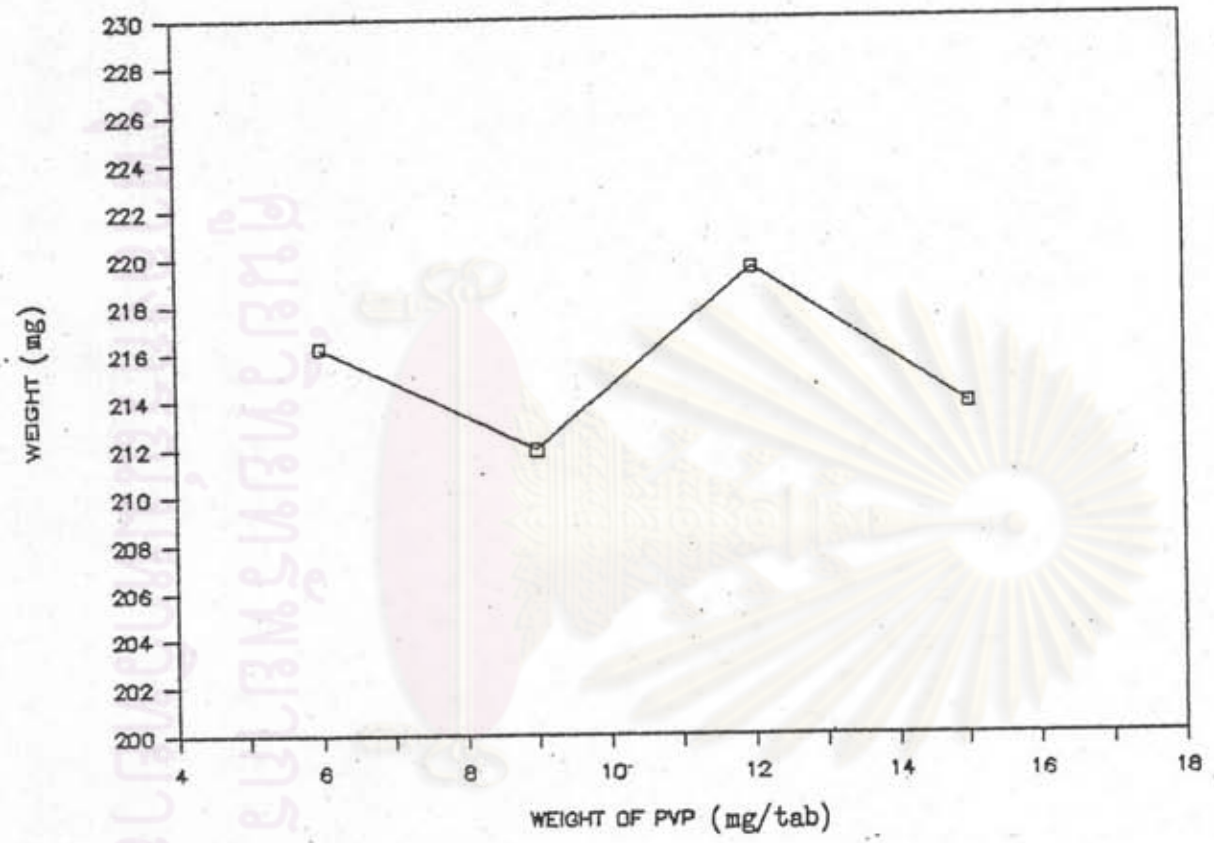

Figure 20 Comparison of weight of diazepam tablets prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

highest when compared to all tablets in the other two methods except the tablets prepared by the sieve number 12 and 30 in oscillating method.

When it was compared to the manual and oscillating methods the tablet which prepared by using 15 mg/tab as the binder in fluid bed spray drying method had the lowest of the mean weight except the tablet which prepared by the sieve number 16 in manual method.

2. Hardness of Tablet

2.1 Comparison of hardness of diazepam tablets prepared by manual and oscillating methods

Comparison of hardness of diazepam tablet prepared by manual and oscillating method was shown in Figure 21 and Table 11 the mean hardnesses of tablet which prepared by manual and oscillating methods were within the limit of 3-6 Kps. The standard deviation was increased when the tablet was prepared by using an larger sieve size and was decreased when the tablet prepared by a smaller the sieve size. The hardness of tablet prepared by manual method had a higher standard deviation than that prepared by oscillating method.

2.2 Comparison of hardness of diazepam tablets prepared by the fluid bed spray drying method

Comparison of hardness of diazepam tablet prepared by the fluid bed spray drying method was listed in Table 11 and Figure 22. When 6, 9, 12 and 15 mg/tab of PVP were used. The mean hardnesses of all tablets were

Table 11 Comparison of hardness of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (Kp.) ± SD.	% CV	Oscillating Mean* (Kp.) ± SD.	% CV
12	4.85 ± 0.91	18.76	4.73 ± 0.69	16.70
16	4.12 ± 0.73	17.96	5.02 ± 0.54	16.33
20	3.88 ± 0.61	14.18	5.14 ± 0.50	13.62
25	4.34 ± 0.48	13.82	4.29 ± 0.47	12.12
30	3.77 ± 0.42	11.94	4.92 ± 0.41	9.75

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (Kp.) ± SD.	% CV
6	4.74 ± 0.83	17.51
9	4.18 ± 0.46	13.40
12	4.72 ± 0.26	7.63
15	4.60 ± 0.56	10.87

* Average of 20 determinations

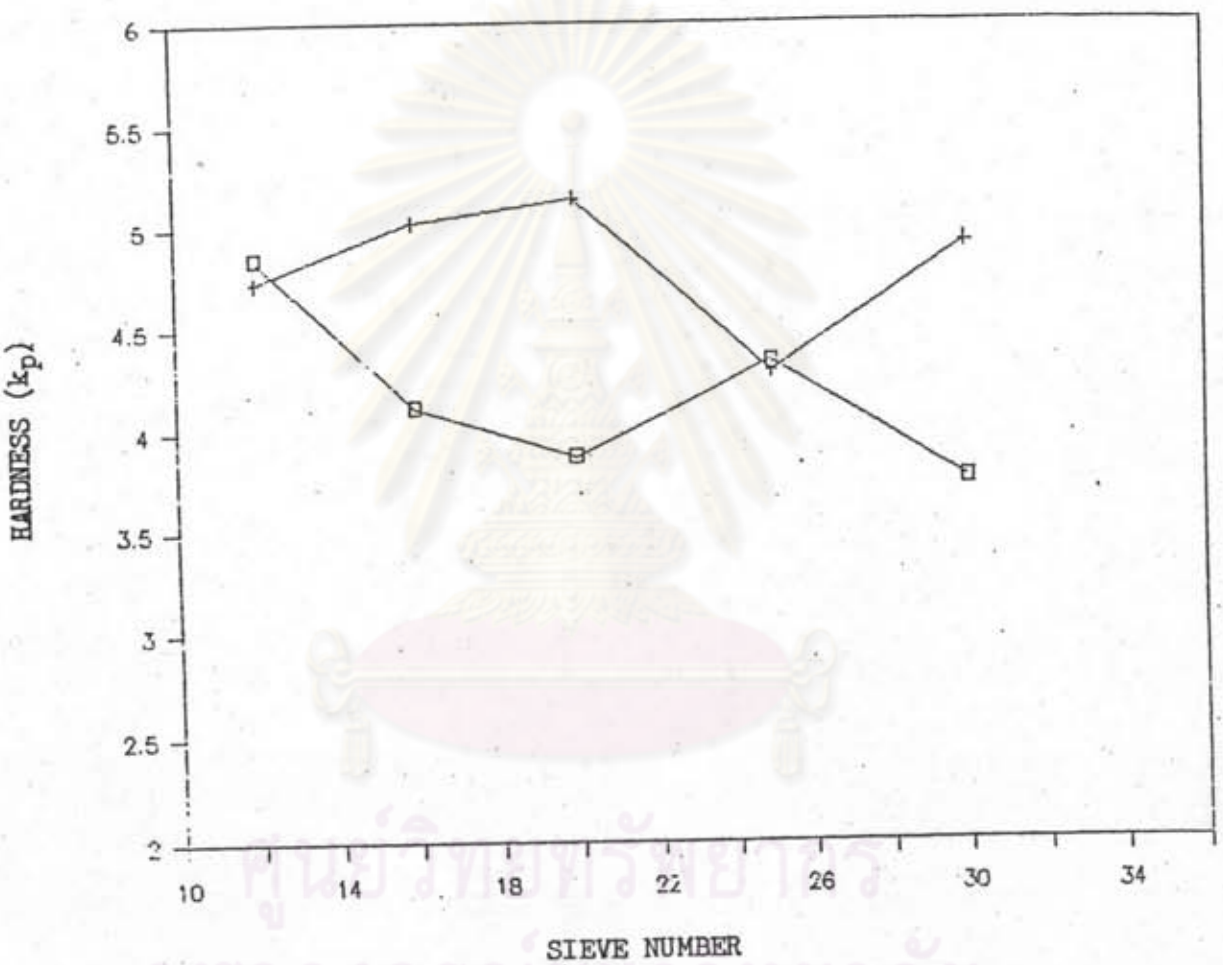

Figure 21 Comparison of hardness of diazepam tablets prepared by manual and oscillating methods : □ ,Manual and + , Oscillating method

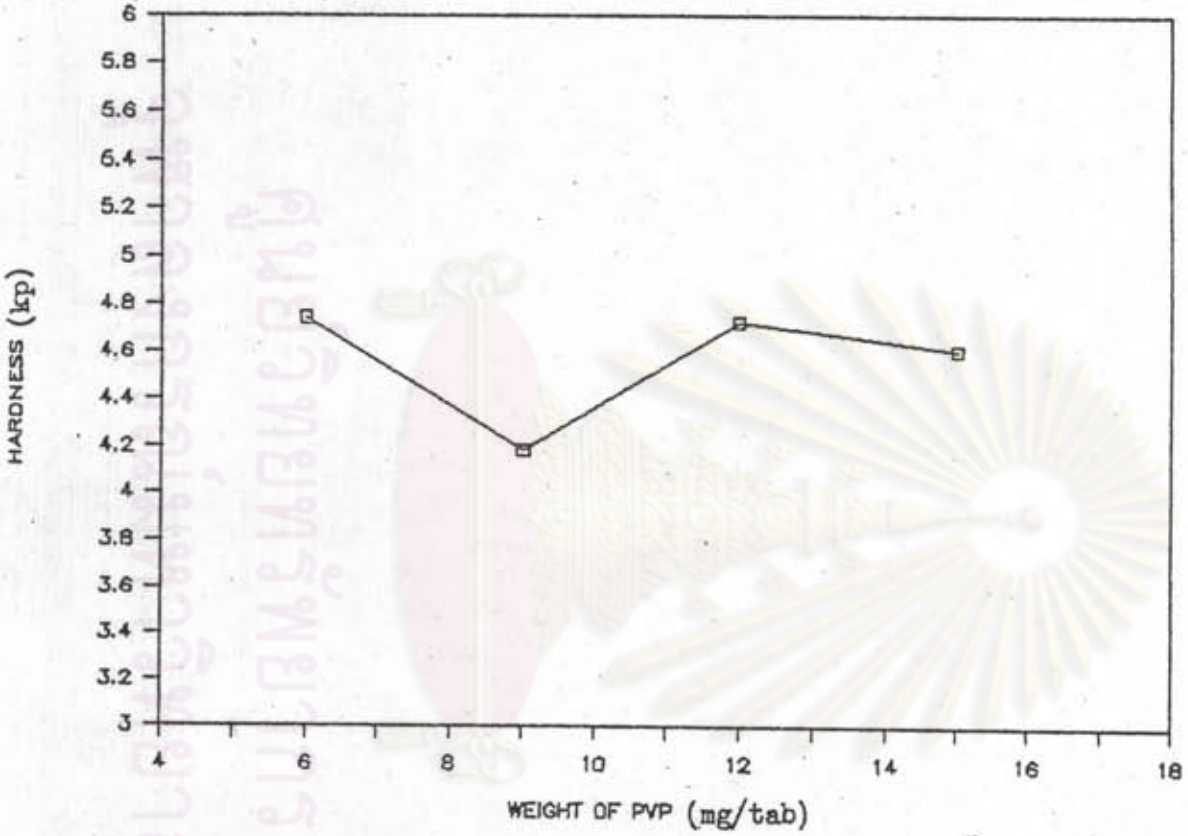

Figure 22 Comparison of hardness of diazepam tablets prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

within the limit of 3-6 Kps. When smaller amount PVP was used the standard deviation of the hardness was quite large and it was decreased when the tablet prepared by using 12 mg/tab. When increasing the amount of PVP to 15 mg/tab the standard deviation of the hardness was increased again.

2.3 Comparison of hardness of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods

When the hardnesses of tablets prepared by using 6 mg/tab of the binder was compared it was found that the hardness of tablets from fluid bed spray drying method was higher than all tablets from manual method except the tablet prepared by the sieve number 12, was only higher than the tablet which prepared by the sieve number 12 and 25 in oscillating method.

When the tablet was prepared by 9 mg/tab of the binder fluid bed spray drying method it was found that the hardness was lower than all tablets prepared by manual and oscillating methods except the tablet prepared by the sieve number 16 from manual method.

Further increasing the amount of PVP to 12 mg/tab the hardness of tablets was higher than those by manual method except the tablet prepared by the sieve number 12. was lower than the tablets prepared by oscillating method except the tablet prepared by the sieve number 25.

When the tablets were prepared by using 15 mg/tab

of the binder in fluid bed spray drying method the hardness of the tablet was higher than all tablets except the tablet prepared by the sieve number 12 from manual method.

3. Disintegration Time

3.1 Comparison of disintegration time of diazepam tablet prepared by manual and oscillating methods

Comparison of disintegration time of diazepam tablet prepared by manual and oscillating method was listed in Table 12. Larger sieve number decreased the disintegration time of tablets from both manual and oscillating methods. The tablet prepared by oscillating method showed higher disintegration time than the tablet prepared by manual method.

The disintegration time of tablets which prepared by manual method showed higher standard deviation than that by the oscillating method.

3.2 The disintegration time of diazepam tablets prepared by fluid bed spray drying method

The disintegration time of diazepam tablets prepared by fluid bed spray drying method was shown in Table 12 and Figure 19. The tablet prepared by less amount of PVP showed faster disintegration time than the tablet using higher amount of PVP. The tablet prepared by 12 mg/tab of PVP showed the lowest standard deviation than the tablet containing by the other three amount of PVP.

3.3 Comparison of disintegration time of diazepam

Table 12 Comparison of disintegration time of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (sec.) ± SD.	Oscillating Mean* (sec.) ± SD.
12	575.46 ± 59.05	525.98 ± 47.16
16	484.02 ± 50.63	466.14 ± 39.57
20	394.05 ± 38.05	392.82 ± 23.89
25	336.11 ± 24.29	310.24 ± 20.80
30	274.54 ± 15.58	268.52 ± 14.33

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (Sec.) ± SD.
6	269.00 ± 18.50
9	279.42 ± 15.02
12	515.19 ± 12.08
15	532.53 ± 23.45

* Average of 5 determinations

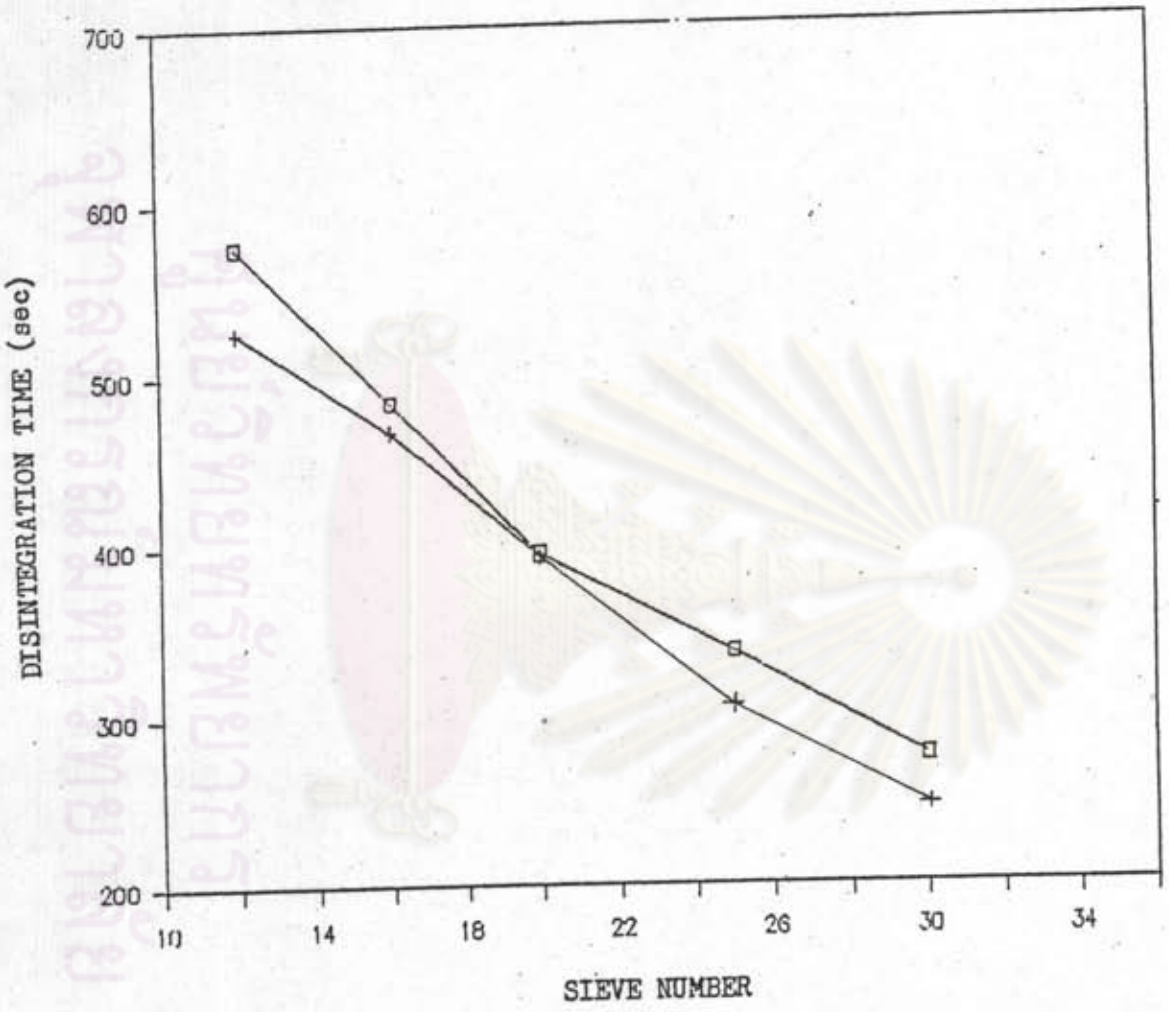

Figure 23 Comparison of disintegration time of dizepam tablets prepared by manual and oscillating methods : □ ,Manual and + ,Oscillating method.

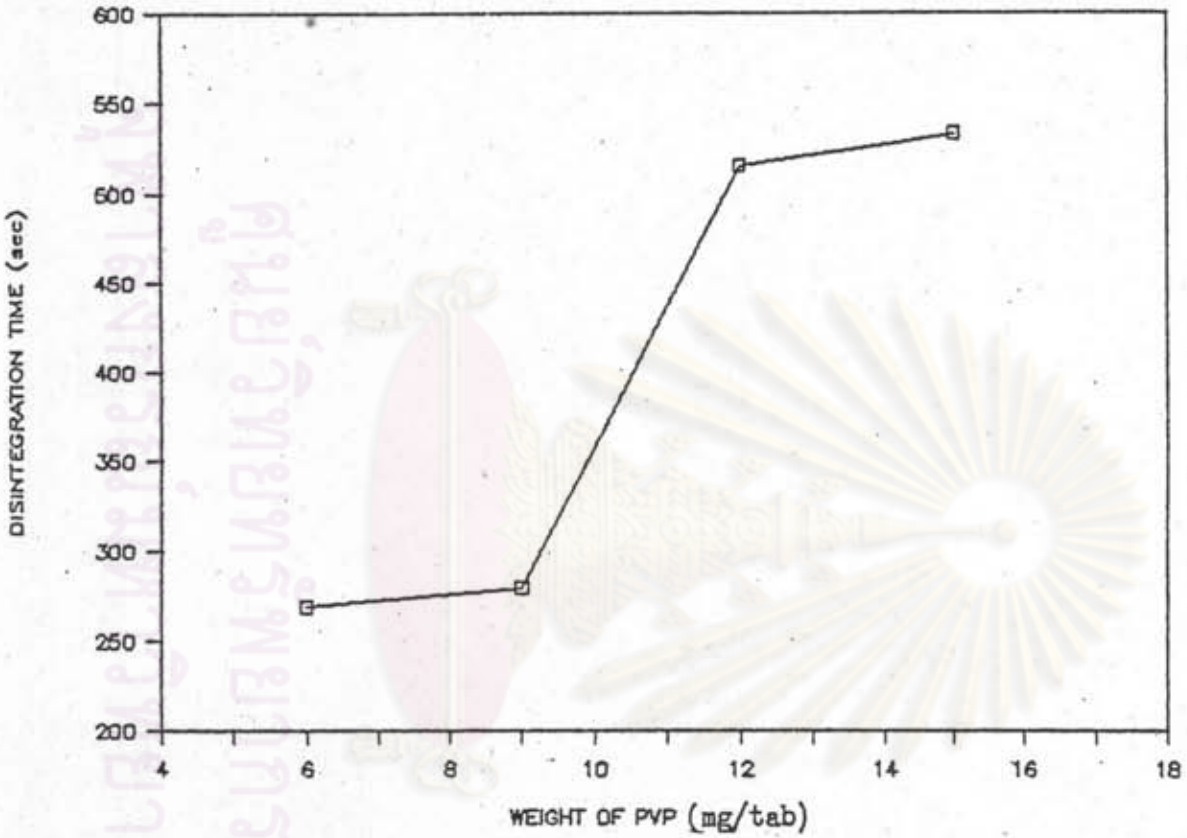

Figure 24 Comparison of disintegration time of diazepam tablets prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone asgranulating agent.

tablets prepared by manual, oscillating and fluid bed spray drying methods

Comparison of disintegration time of diazepam tablet prepared by manual, oscillating and fluid bed spray drying methods were shown in Table 12. When 6 mg/tab of PVP was used the disintegration time of tablet prepared by fluid bed spray drying method was the fastest.

When increasing the amount of PVP to 9 mg/tab in fluid bed spray drying method it was found that the disintegration time was slightly increased. However, it was faster than those from manual method except the tablets prepared by the sieve number 30 and faster than all tablets prepared by oscillating method. Except the tablets prepared by the sieve number 25 and 30.

Further increasing PVP to 12 mg/tab the disintegration time was increased, and slower than those of the tablets prepared by all sieve number except number 12 both in manual and oscillating methods.

When the highest amount of the binder was used the disintegration was slower than all the tablets prepared by manual and oscillating methods except the tablet using sieve number 12 from manual method.

4. % Friability

4.1 Comparison of % friability of diazepam tablets prepared by manual and oscillating methods

Comparison of % friability of diazepam

tablets prepared by manual and oscillating method was shown in Figure 25 and Table 13. Tablets prepared by manual method using the sieve number 12, 16, 20, 25 and 30 gave 0.92, 0.48, 0.43, 0.50 and 0.59 % friability respectively. The % friability and its standard deviation were the least for tablet prepared by the sieve number 20. The tablet prepared by the sieve number 12 gave the highest % friability and its standard deviation.

For tablets prepared by oscillating method, as the sieve size increased the % friability was slightly increased. And its standard deviation was also increased except the tablet prepared by the sieve number 12.

4.2 The % friability of diazepam tablet prepared by fluid bed spray drying method

The % friability of diazepam tablet prepared by fluid bed spray drying method was summarized in Table 13 and Figure 26. The lesser amount of PVP as the binder produced greater % friability of the tablets and its standard deviation.

4.3 Comparison of % friability of diazepam tablet prepared by manual, oscillating and fluid bed spray drying methods

The % friability of all diazepam tablet prepared by manual, oscillating and fluid bed spray drying method were less than 0.75% except the tablet prepared by manual method which the sieve number 12.

The % friability of diazepam tablet prepared by 6 mg/tab in fluid bed spray drying method was compared to

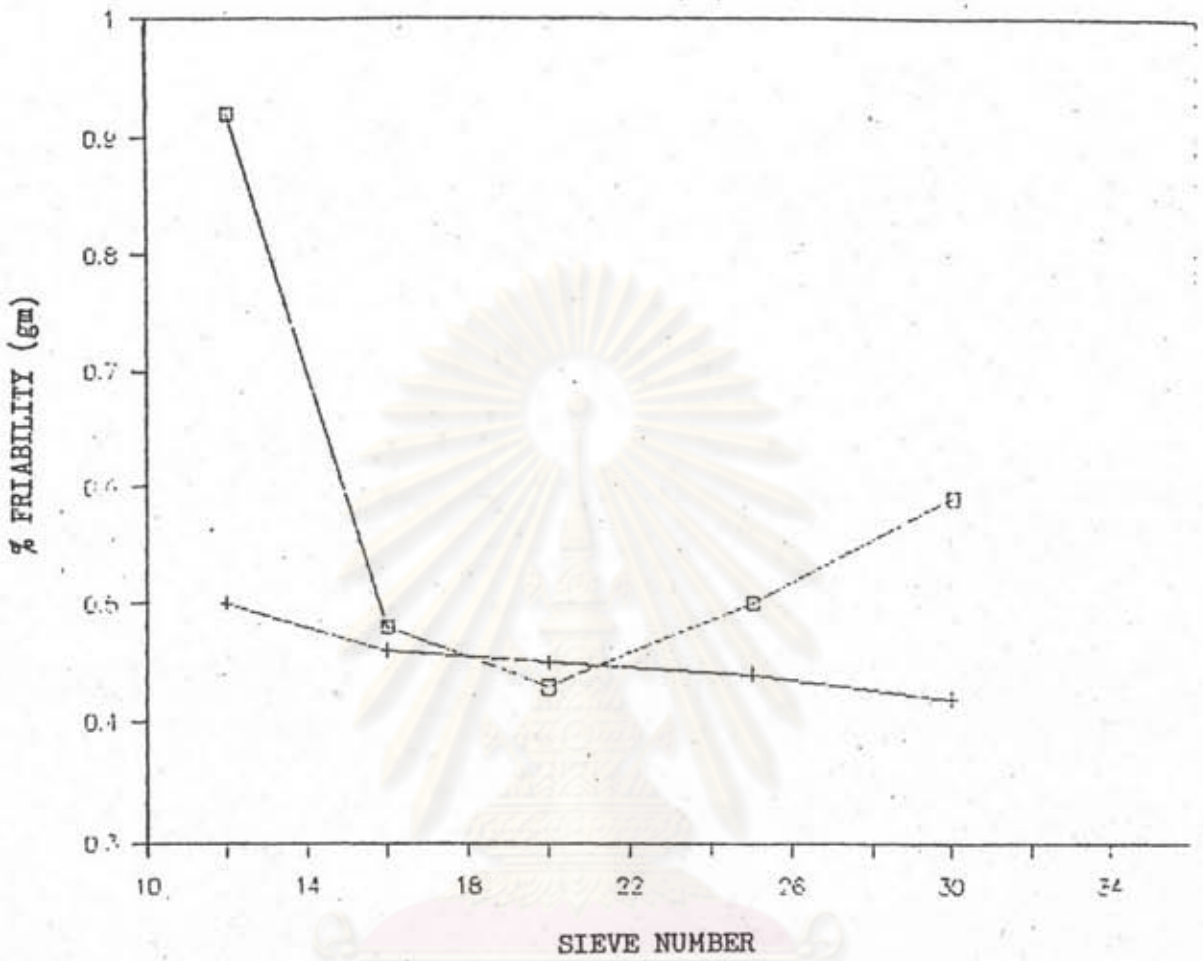

Figure 25 Comparison of % friability of diazepam tablets prepared by manual and oscillating methods : □ ,Manual and + ,Oscillating method.

Table 13 Comparison of % friability of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (%) ± SD.	Oscillating Mean* (%) ± SD.
12	0.92 ± 0.37	0.50 ± 0.02
16	0.48 ± 0.02	0.46 ± 0.07
20	0.43 ± 0.01	0.45 ± 0.02
25	0.50 ± 0.10	0.44 ± 0.03
30	0.59 ± 0.18	0.42 ± 0.01

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (%) ± SD.
6	0.57 ± 0.08
9	0.50 ± 0.05
12	0.35 ± 0.03
15	0.34 ± 0.02

* Average of 5 determinations

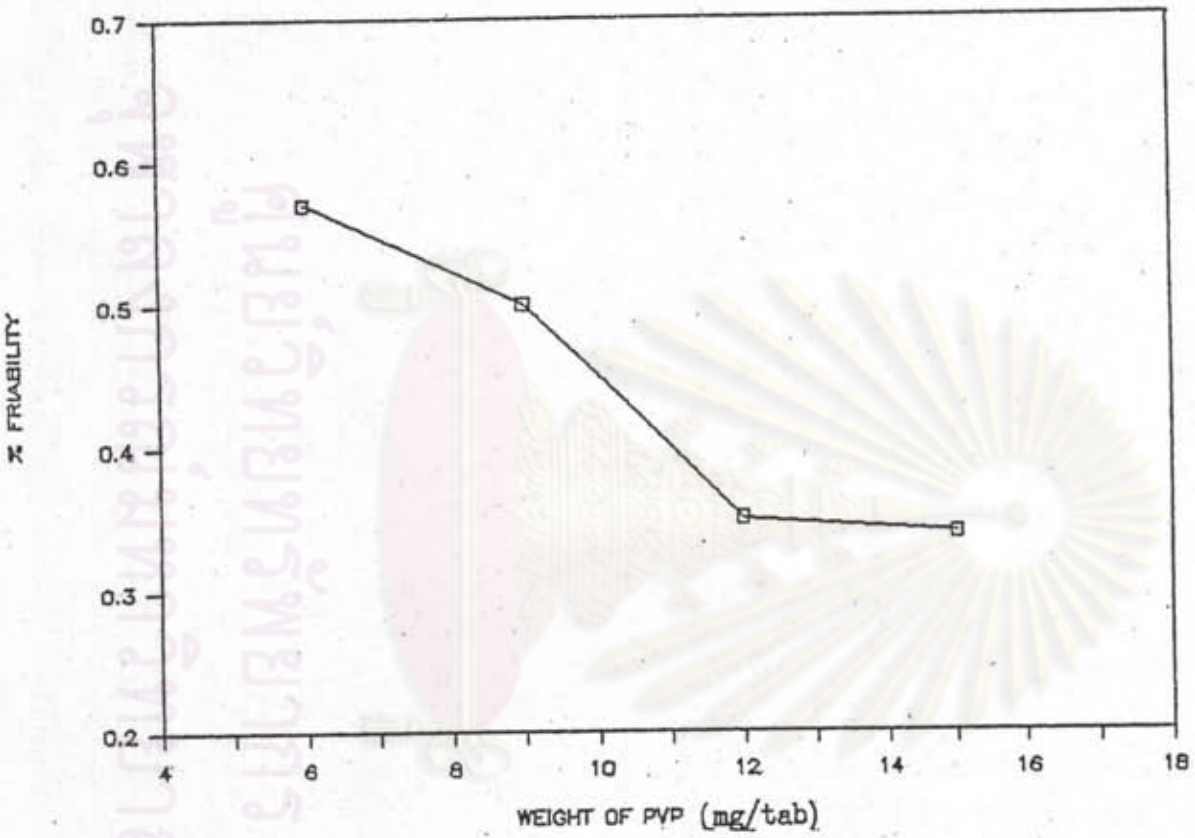

Figure 26 Comparison of % friability of diazepam tablets prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

the tablet prepared by manual method it was found that the % friability was higher than the tablet prepared by the sieve number 16, 20 and 25 but it was lower than the tablet prepared by the sieve number 12 and 30.

When compared to the tablet prepared by oscillating method it was shown that its % friability was the highest of all.

When increasing PVP to 9 mg/tab in fluid bed spray drying method its % friability was lower than those from the tablet of manual method prepared by the sieve number 12 and 30 higher than the tablet prepared by the sieve number 16 and 20 and equal to the tablet prepared by the sieve number 30.

When compared to the tablet prepared by oscillating method its % friability was equal to the tablet prepared by the sieve number 12 and higher than the tablet prepared by all other the sieve number.

Further increasing PVP to 12 and 15 mg/tab the % friability was lower when compared to those from manual and oscillating methods.

5. Content Uniformity

5.1 Comparison of content uniformity of diazepam tablet prepared by manual and oscillating methods

Comparison of content uniformity of diazepam tablets prepared by manual and oscillating method was shown in Figure 27 and Table 14. The content of requirment drug in all diazepam tablet was within the limit of 90-110 %. When increasing the sieve number in both methods the standard deviation of the drug content was decreased.

5.2 The content uniformity of diazepam tablet prepared by fluid bed spray drying method

The content uniformity of diazepam tablet prepared by fluid bed spray drying method was shown in the Figure 27 and Table 14. All tablets prepared by fluid bed spray drying method also showed the content of drug within the limit of 90-110 %. The standard deviation of tablets contains 12 mg/tab of PVP showed the lowest standard deviation.

5.3 Comparison of content uniformity of diazepam tablets prepared by manual, oscillating and fluid bed spray drying method

Comparison of content uniformity of diazepam tablets prepared by manual, oscillating and fluid bed spray drying method were shown in Table 14. The content of drug in diazepam tablets prepared by the three methods were within the USP limit of 90-110%.

Table 14 Comparison of content uniformity of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (%) ± SD.	% CV	Oscillating Mean* (%) ± SD.	% CV
12	100.48 ± 5.34	5.31	102.80 ± 5.63	5.48
16	100.49 ± 5.25	5.22	94.71 ± 5.00	5.28
20	100.59 ± 4.54	4.51	98.36 ± 4.60	4.68
25	99.92 ± 4.50	4.50	97.79 ± 3.89	3.98
30	101.56 ± 3.80	3.74	101.46 ± 3.10	3.06

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (%) ± SD.	% CV
6	90.50 ± 6.32	6.98
9	93.02 ± 4.84	5.20
12	97.10 ± 2.60	2.68
15	100.04 ± 4.90	4.90

* Average of 5 determinations

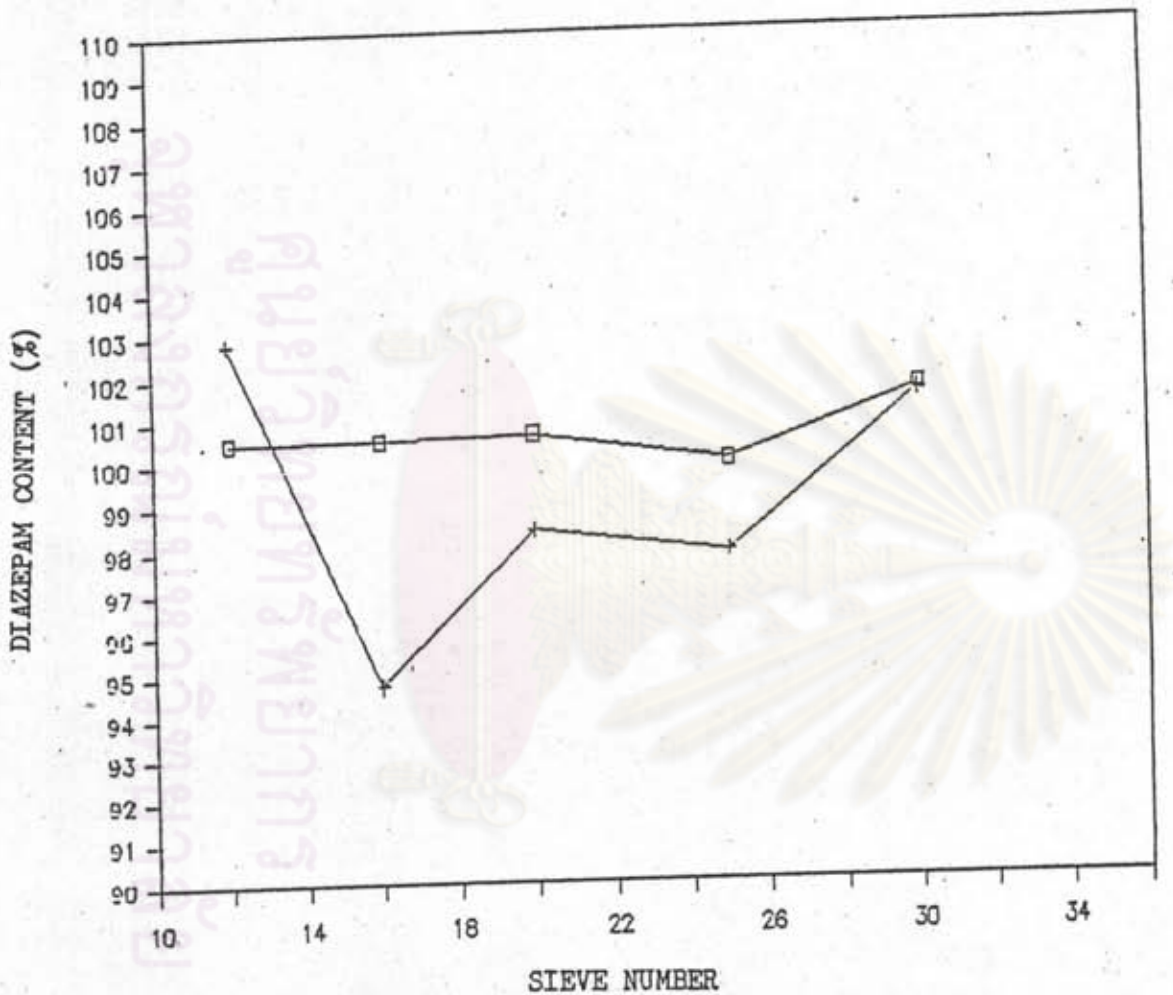

Figure 27 Comparison of content uniformity of diazepam tablets prepared by manual and oscillating methods : □ ,Manual and + , Oscillating method.

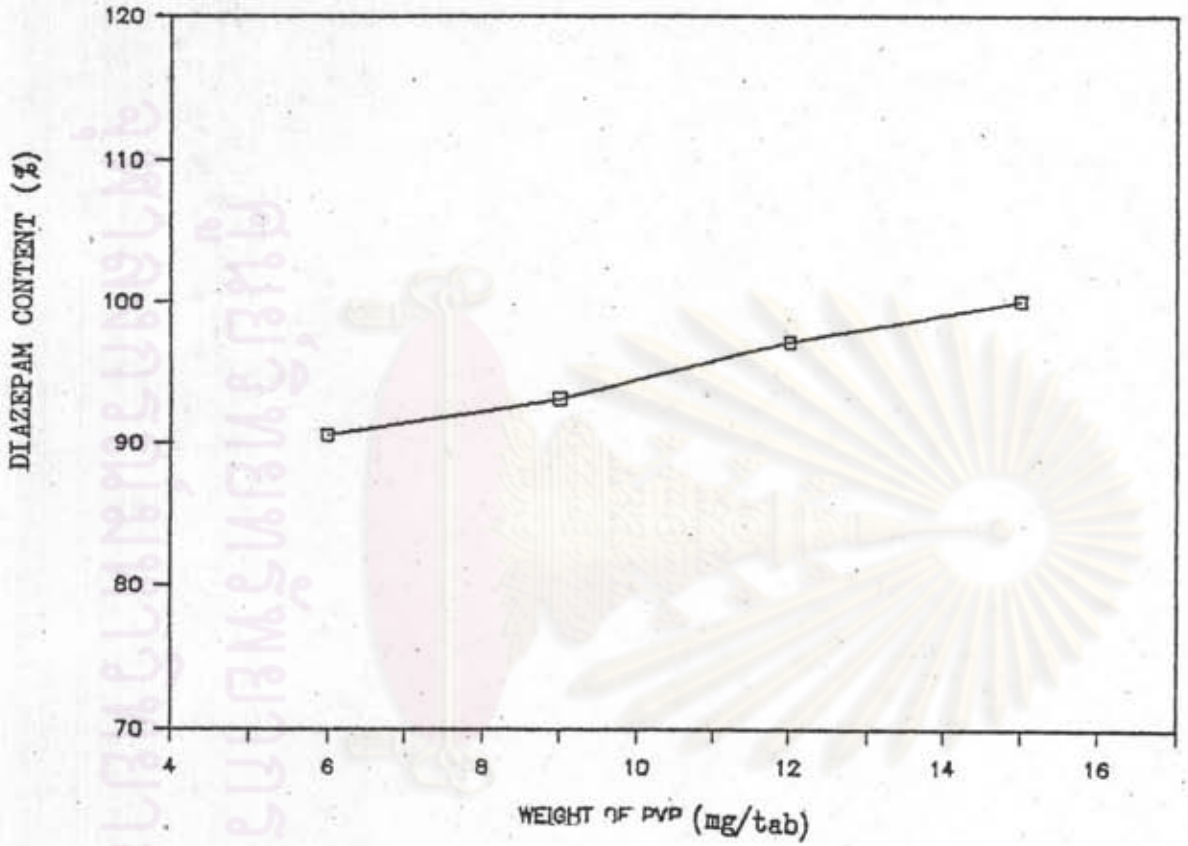

Figure 28 Comparison of content uniformity of diazepam tablets prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

When 6 mg/tab of PVP was used in all tablets that the variation of drug content from tablets prepared by fluid bed spraying drying method showed the highest. When increasing the amount of PVP to 9 mg/tab in spraying drying method the deviation of drug content was still higher than those of tablets prepared by both manual and oscillating methods except those by the sieve number 12 and 16 both in manual and oscillating methods.

Further increasing the binder to 12 mg/tab in spray drying method the deviation of drug content was the lowest.

When the highest amount of the binder was used the standard deviation was markedly increased. And it was higher than all these tablets prepared by both methods except the tablets prepared by the sieve number 12 and 16.

6. % Drug Dissolved

6.1 Comparison of % drug dissolved of diazepam tablet prepared by manual and oscillating method

Comparison of % drug dissolved of diazepam tablet prepared by manual and oscillating method as illustrated in Figure 29 and Table 15. The % drug dissolved after 30 minutes was under the limit of 85% which not meet the USP XX requirement. Its standard deviations was increased as the number of sieve decreased in both manual and oscillating methods.

Table 15 Comparison of % drug dissolved from diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods.

Sieve Number	Manual Mean* (%) ± SD.	Oscillating Mean* (%) ± SD.
12	69.39 ± 5.32	67.97 ± 5.44
16	69.04 ± 5.25	65.28 ± 5.25
20	67.36 ± 4.64	68.37 ± 4.90
25	69.64 ± 4.59	68.16 ± 4.52
30	71.93 ± 4.02	69.61 ± 4.30

Weight of PVP mg/tab	Fluid Bed Spray Drying mean* (Sec.) ± SD.
6	70.25 ± 5.79
9	68.40 ± 4.50
12	67.53 ± 3.65
15	65.15 ± 4.48

* Average of 5 determinations

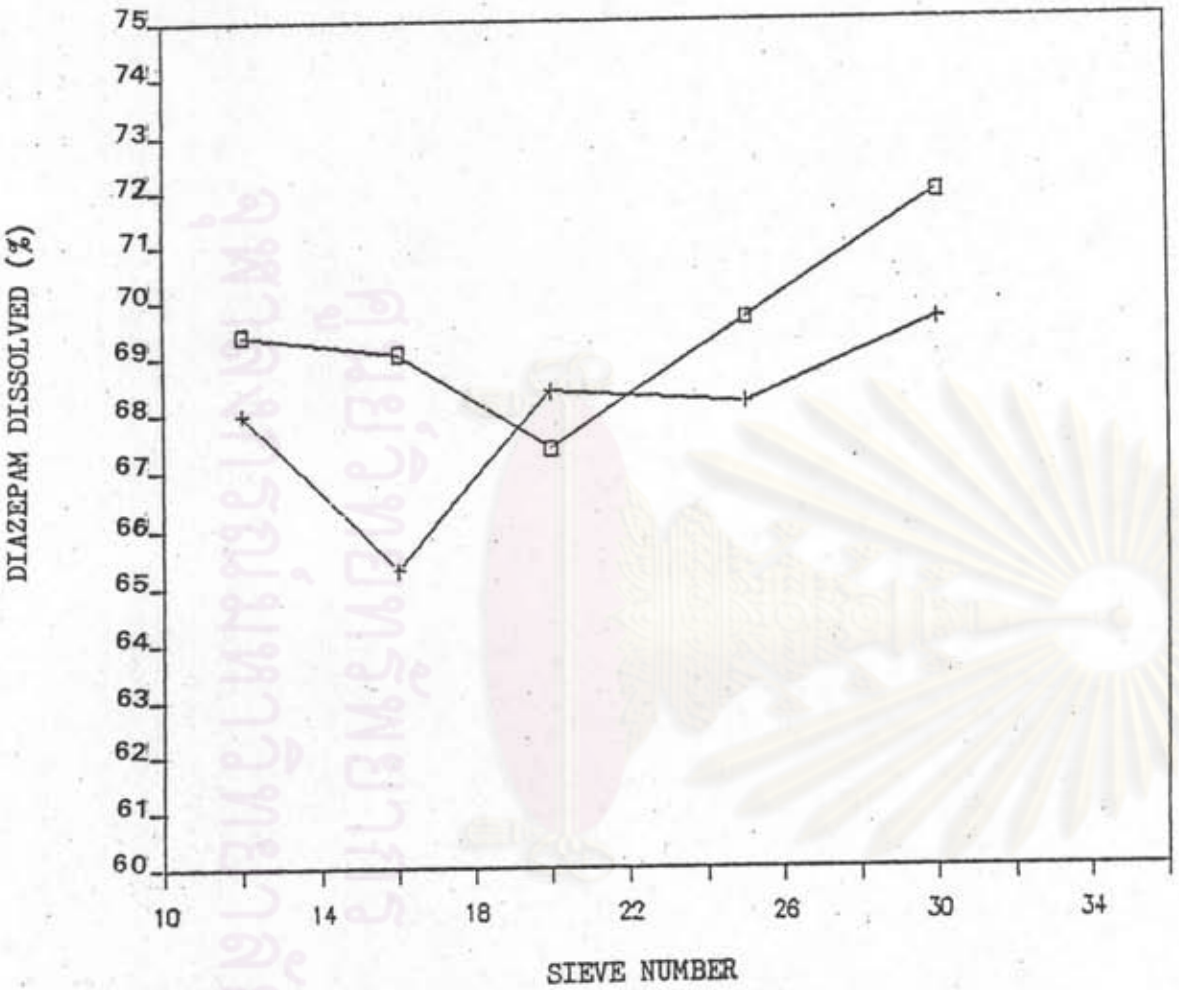

Figure 29 Comparison of % drug dissolved of diazepam tablets prepared by manual and oscillating methods: □,Manual and +,Oscillating method.

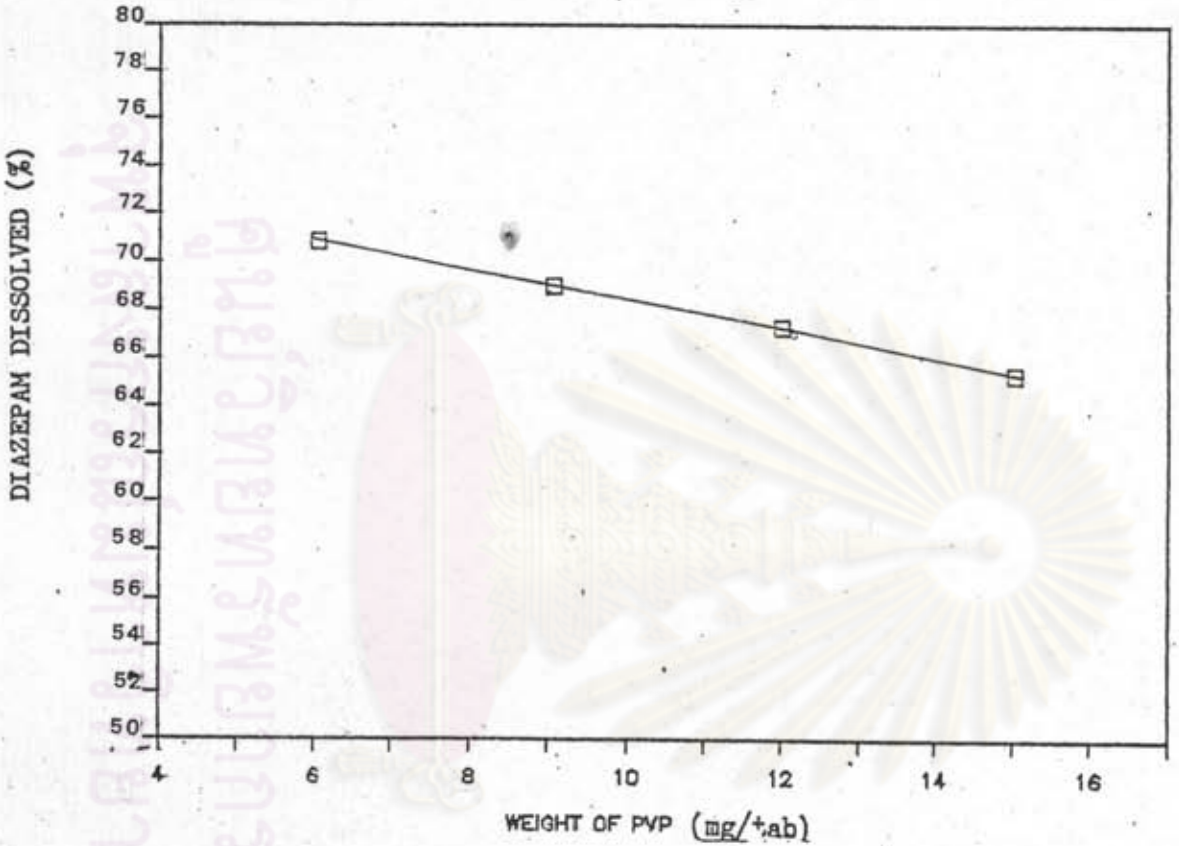

Figure 30 Comparison of % drug dissolved of diazepam tablets prepared by fluid bed spray drying method using various amounts of polyvinylpyrrolidone as granulating agent.

6.2 The % drug dissolved of diazepam tablets prepared by fluid bed spray drying method

The % drug dissolved of diazepam tablet prepared by fluid bed spray drying method was listed in Table 12. All tablets prepared by fluid bed spray drying method also showed the % drug dissolved under the USP requirement of 85%. The tablet prepared by using 12 mg/tab of PVP showed the lowest standard deviation of % drug dissolved.

6.3 Comparison of % drug dissolved of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods

Comparison of % drug dissolved of diazepam tablets prepared by manual, oscillating and fluid bed spray drying method as listed in Table 15, the % drug dissolved of diazepam tablet prepared by manual, oscillating and fluid bed spray drying methods were under the limit of 85%.

When 6 mg/tab of PVP was used in three methods, it was found that the % drug dissolved from tablets of fluid bed spray drying method was higher than those from the other two methods. When increasing the amount of PVP to 9 mg/tab in fluid bed spray drying method its % drug dissolved was still lower than all the tablet prepared by the manual method. except the tablets prepared by the sieve number 20 and oscillating methods except the tablets prepared by the sieve number 12-25.

Further increasing PVP to 12 mg/tab, it was shown that the % drug diassolved was the lower than all the tablet prepared by oscillating and manual methods except the tablet prepared by the seive number 20. And its standard deviation of % drug dissolved was the lowest when it was compared with manual and oscillating method.

When the highest amount of the binder was used as 15 mg/tab in fluid bed spray drying method its % drug dissolved was lower than oscillating and manual methods.