CHAPTER 4

DISCUSSION AND CONCLUSION

In industrial pharmacy, the method development is important to improve the afficacy of pharmaceutical dosage forms and a better quality of product. Tablets are made from granular particulate solids, therefore granulation method can affect the granule characteristics, and there performance of the final tablets. There are many methods, manual, oscillating and fluid bed spray drying methods which process variables involved in the granulation step, therefore affect the granule and tablet characteristics.

A. Comparison of the properties of Diazepam granules

1. Bulk volume

The bulk volume of diazepam granules obtained by the three different methods(α =0.05) are differentiated by ANOVA and DUNCAN 's test in Table 16. The satisfied results are the granules which exhibit in low bulk volume. Smaller granules are closely packed whereas a less uniformly larger granules were loosely filled which may cause problems in compression. To compression the granules, smaller granules would be in the lower layer of feed shoe and the larger granules would be in the upper layer of feed shoe. The weight variation and the hardness of tablet could be varied.

Table 16 ANOVA and DUNCAN's test of the bulk volume of diazepam granules obtained by the three different methods ($\alpha = 0.05$).

sieve number	Manual method 12	16	20	25	30	Oscillating method 12	16	20	25	30
12	NS	S	S	S	S	NS	S	S	S	S
16	S	NS	S	S	S	S	NS	NS	S	S
20	S	S	NS	NS	NS	S	NS	NS	S	S
25	S	S	NS	NS	NS	S	S	S	NS	S
30	S	S	NS	NS	NS	S	S	S	S	NS

amount of PVP mg/tab	Fluid bed spray drying method 6	9	12	15
6	NS	NS	S	S
9	NS	NS	S	S
12	S	S	NS	S
15	S	S	S	NS

S Significant difference

NS Nonsignificant difference

1.1 Manual method

The bulk volume obtained by the sieve number 12 was significantly different from the bulk volumes obtained by all other sieves. The bulk volume obtained by the sieve number 16 was significantly different from those obtained by the sieve number 20,25 and 30.

The bulk volume obtained by the sieve number 20,25 and 30 were nonsignificantly different to each other.

The bulk volume of granule obtained by the sieve number 12 or 16 was different from each other and those of granules obtained by the other sieves. This can be attributed to a different weight distribution especially at > 840 μm. The granules obtained by these two sieves were of large sizes of 49.25% and 38.66%, respectively. Without the compressional force, the void space should increase as the granule size is increased, thereby increasing the bulk volume(13). The bulk volumes of the granules obtained by the sieve number 20, 25 and 30 were nonsignificantly difference to each other due to the size of the granules obtained by these sieve numbers were narrowly distributed. Upon ranking according to the bulk volume, granules by sieve numbers 20, 25 and 30 were the best, followed by those by sieve number 16. Granules by sieve number 12 were the worst. Because their bulk volumes were nearly equal.

1.2 Oscillating method

The bulk volumes obtained by all sieve number were significantly different from each other, except those obtained by the sieve number 16 and 20. The reasons were the same as in the manual method. The granules by different sieve numbers were then graded: 30 > 25 >20 = 16 >12.

1.3 Fluid bed spray drying method

The bulk volumes of granules prepared by using 6,9,12 and 15 mg/tab of PVP as the binder were significantly different from each other, except the bulk volume prepared by using 6 mg/tab and 9 mg/tab of PVP. This can be distributed the weight distribution of granules prepared by using different amount of PVP. The grading was granules by using 6 mg/tab of PVP = those using 9 mg/tab > those by 12 mg/tab > those by 15 mg/tab.

2. % Fine of granules

T - test of the % fine of diazepam granules obtained by the three different methods (α = 0.05) are demonstrated in Table 17.

2.1 Manual method

The granules obtained by all sieves were in the 10 - 20 % limit, except the granule obtained by the sieve number 30. Therefore, granules by all sieves except sieve number 30 were of good property.

According to Gold, et al(22), 10 - 20 % fine of granules gave the best properties of tablet. This can be attributed the small particle in the granule in the

Table 17 T-test of % fine of diazepam granules prepared by manual, oscillating and fluid bed spray drying methods(α = 0.05) t = 3.495.

sieve number	Manual method t	Oscillating method t
12	0	9.104
16	0	2.656
20	0	0
25	1.195	0
30	3.878	2.521

weight of PVP mg/tab	Fluid bed spray drying method t
6	17.608
9	25.528
12	12.883
15	8.138

amount of appropriate there will help the flow of the granule and the fine particle will fill intergranular space to reduce the compressional force to form compacted mass. If the present of % fine of granule was too much or too little it will cause poor flow rate (19).

2.2 Oscillating method

The granules obtained by all the sieve number were in 10 - 20 % limit, except the granule obtained by the sieve number 12. Thus, all granules were of good property except granules by sieve number 12.

2.3 Fluid bed spray drying method

The granules obtained by using various amount of PVP were given the % fine outside the limit due to the reasons that

1) high temperature and an upward moving steam of air, therefore the water in spray binding fluid would lost before the granules were formed(50).

2) collision of blowing granules and falling granules resulting in increasing in % fine.

3. Granule size

3.1 Manual method

The granule obtained by sieve number 25 gave more normal size distribution than the granules obtained by other sieve numbers in the size analysis process. The causation of this phenomena was due to the aperture size of the sieve number 12, 16 and 20 were 1680, 1190 and 840 um respectively, a large size . The granules obtained by those sieves were also large size. The most

cumulation of granules were between 840 - 1680 um and shift to the right. The aperture size of sieve number 30 is 590 um. The granules obtained was smaller and gave narrower size distribution. The highest cumulation was between 45 - 840 um.

3.2 Oscillating method

The granules obtained by sieve number 20 gave more normal size distribution than those obtained by other sieve numbers. The causation of this phenomena was due to the aperture size similarly to the aforementioned method.

3.3 Fluid bed spray drying method

The granules prepared by using 15 mg/tab of PVP gave more normal size distribution than the others. The causation was possibly due to the appropriate amount of binder was required in this method.

3.4 The mean diameter of diazepam granule obtained by the three different methods as demonstrated in Table 6.

The mean diameter of granules obtained by the manual method was different from the mean diameter of granules obtained by oscillating method. This can be attributed that:

1) Shearing strength of oscillating method was greater than that of manual method.

2) By manual method, the granules were contacted with spatula directly, which in turn by oscillating method, there was a the space between sieve and

Table 18 ANOVA and DUNCAN'S test of the flow rate of diazepam granules obtained by the three different methods (α = 0.05).

sieve number	Manual method 12	16	20	25	30	Oscillating method 12	16	20	25	30
12	NS	S	S	S	S	NS	S	S	S	S
16	S	NS	NS	S	S	S	NS	S	S	S
20	S	NS	NS	S	S	S	S	NS	NS	S
25	S	S	S	NS	S	S	S	NS	NS	S
30	S	S	S	S	NS	S	S	S	S	NS

amount of PVP mg/tab	Fluid bed spraying drying method 6	9	12	15
6	NS	S	S	S
9	S	NS	S	S
12	S	S	NS	S
15	S	S	S	NS

S Significant difference

NS Nonsignificant difference

paddle.

3) While screening by oscillating method, the sieve was shaked thus the granules were passed through the sieve without rescreening.

The mean diameter of diazepam granules obtained by fluid bed spray drying method was much less than the granules obtained by the other methods. This can be attributed that:

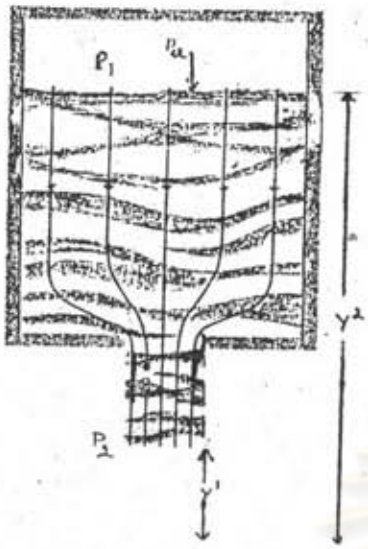
1) By the different methods of forming the granule. The size of granules obtained by the manual and oscillating method depended on pore size of the sieve. By the fluid bed spray drying method the size of granule depended on the quality of water in binding solution. Mehta et al.(50)report that the mean diameter of granules,obtained by fluid bed spray drying,increased with increased of water used.

2) By fluid bed drying method, there was collision of some granules resulting in decreasing the size of granules.

4. Flow rate

The flow property of granules behaves the same as the flow property of fluid.

From the fluid dynamic, the flow is described by the Bernoulli'equation



$P1 - P2 = \rho g (Y2 - Y1)...(eq\ 2)$

P1 = upper pressure of air (Pa) and granule

P2 = lower pressure of air

g = gravitational force

ρ = density of granule

Y1 = distance between P2 to base

Y2 = distance between P1 to base

When g, Y1, Y2 and P2 are constant

$$P1 - P2 = \rho$$

If increased when P1 increase, therefore flow rate would increased.

The flow rate of diazepam granules obtained by the three different methods($\alpha = 0.05$) are differentiated by ANOVA and DUNCAN 's test in Table 18.

4.1 Manual method

The flow rate of the granules obtained by all the sieve numbers were significantly different from each other, except those obtained by the sieve number 16 and 20. This can be attributed to a different bulk density.

The flow rate of the granules obtained by the sieve number 30 was more rapid than the flow rate of the granules obtained by the other sieve. This can be attributed that their bulk density were greater than their

density obtained by the other sieve. When ranking granules by sieve number 30 > 25 > 20 = 16 > 12.

4.2 Oscillating method

This flow rate of the granules obtained by all the sieve number were significantly different from each other, except those obtained by the sieve number 20 and 25. The reasons were the same as in the manual method.

The flow rate of the granules obtained by manual method was more rapid than the flow rate of the granules obtained by oscillating method. The reason was due to higher bulk density of granules of manual method. Upon ranking, granules by sieve number 20 > 25 = 20 > 16 > 12.

4.3 Fluid bed spray drying method

The flow rate of the granules obtained by using different amount of PVP as the binder were significantly different from each other. The causation of this phenomena was due to the bulk density similarly to the aforementationed method.

The flow rate of the granules obtained by using 12 mg/tab of PVP as the binder was the fastest. This can be attributed to two reasons; various forces such as frictional forces, surface-tension forces, mechanical forces caused by inter-locking of particles of irregular shape, electrostatic forces, cohesive force or wan der waals' forces, occurs to too fine or irregular granules prepared by insufficient amount of binder(6 mg/tab and 9 mg/tab of PVP), whereas too large amount of binder (15

Table 19 T-test of repose angle of diazepam granules prepared by manual, oscillating and fluid bed spray drying methods (α = 0.05) t = 3.495.

sieve number	Manual method t	Oscillating method t
12	0	0
16	0	0
20	0	0
25	0	0
30	0	1.06

weight of PVP mg/tab	Fluid bed spray drying method t
6	*
9	3.726
12	5.160
15	5.597

* unmeasurable

mg/tab of PVP) produced bulkier granules, therefore less bulk density. When ranking granules by 12 mg/tab of PVP > 15 mg/tab > 9 mg/tab.

5. Repose angle

Pipel(19) reported the granule which had the repose angle of 30 or below indicated that the flow was free, angle of 40 or above the flow was broken and the phenomenon of balling might occur.

5.1 Manual and oscillating methods

The repose angles of the granules obtained by all the sieve number were < 40 . Therefore all granules were free-flowing

5.2 Fluid bed spray drying method

The repose angle of granules prepared by using different amount of PVP as the binder were greater than 40 , except the granules prepared by using 6 mg/tab of PVP, which was unmeasurable.

The repose angle of granules prepared by the three different methods could conclude that:

1) The repose angle of the large granules were less than the small granules as the amount of binder were equals. This can be attributed the smaller granules would more contact one another than larger ones, therefore increased in frictional force, surface tension force, mechanical forces caused by interlocking of particles of irregular shape, electrostatic force and cohesive or Van der Waals' forces. Its repose angle was

more than the large ones.

2) The repose angle value of granules obtained by oscillating method was more than the granules obtained by manual method. The reason that the granule size of the granules obtained by oscillating method were slightly smaller than those obtained by manual method.

3) Increased in the too large amount of binder, increased in the repose angle value due to there were intergranular force and increased in frictional force.

4) As the amount of binder were equal to 6 mg/tab of PVP, the granules obtained by the fluid bed spray drying method gave the repose angle value more than the repose angles of the granules obtained by manual and oscillating methods.

6. Weight variation

The best properties of tablets should have the mean weight in the USP limit of 7.5 % according to standard deviation of weight, the tablets which had the lowest standard deviation of weight would have the best properties of tablets.

The ANOVA and DUNCAN's test % cv of tablet weight prepared by the three different method (α= 0.05) were shown at Table 20.

6.1 Manual method

The % cv of tablet weight prepared by all the sieve number were significantly different from each

Table 20 ANOVA and DUNCAN's test of % cv of weight of diazepam tablet obtained by the three different methods (α = 0.05).

sieve number	Manual method 12	16	20	25	30	Oscillating method 12	16	20	25	30
12	NS	NS	S	S	S	NS	NS	S	S	S
16	NS	NS	S	S	S	NS	NS	S	S	S
20	S	S	NS	NS	S	S	S	NS	S	S
25	S	S	NS	NS	S	S	S	S	NS	S
30	S	S	S	S	NS	S	S	S	S	NS

amount of PVP mg/tab	Fluid bed spray drying method 6	9	12	15
6	NS	S	S	S
9	S	NS	S	NS
12	S	S	NS	S
15	S	NS	S	NS

S Significant difference

NS Nonsignificant difference

other, except those of tablets obtained by sieve number 12 and 16, 20 and 25. This can be attributed the weight variation of the tablets prepared from the granules obtained by larger sieve size was higher than those obtained by the smaller sieve size. During tablet compression, the hopper shoe was vibrated different sizes of granule were separated to different layers. The flow property was unsteady, therefore the % cv value of tablet weights prepared by larger sieve size was high. On the other hand the weight variation of tablet prepared from granules obtained by smaller sieve size was low due to the sizes of granules were nearly equal.

When ranking, granules by sieve number 30 > 25 = 20 > 16 = 12.

6.2 Oscillating method

The standard deviation of tablet weight obtained by all sieve numbers were significantly different from each others, except those of tablet obtained by the sieve number 16 and 20. The possible reason was the same as in the manual method.

Upon ranking, granules by sieve number 30 > 25 > 20 = 16 > 12.

6.3 Fluid bed spray drying method

The standard deviation of the tablet weights prepared by using different amount of PVP as the binder were significantly different from each other, except those prepared by using 9 and 15 mg/tab of PVP. The

granules obtained by using 6 mg/tab of PVP as binder were the smallest granules. The flow of granules was almost uncomplete. Therefore, the % cv of tablet weight was high. For the granule obtained by using 9 mg/tab of PVP as binder. The flow of granules was poor also. For the granule obtained by using 12 mg/tab of PVP as binder. The flow of granules was complete, the granules filled the die completely. The % cv of tablet weight was the lowest. For the granules obtained by using 15 mg/tab of PVP as binder were of large size bulky. There were much void space, therefore the weight variation of tablets were high.

When ranking, granules by 12 mg/tab of PVP > 9 mg/tab > 6 mg/tab.

7. Hardness variation

The required hardness of the test tablet was aimed to have the mean hardness in the limit of 3 - 6 Kp. All tablets according to % cv of hardness the tablets which had the lowest % cv of hardness would gave the best properties of tablets.

ANOVA and DUNCAN's test of hardness variation of diazepam tablet prepared by the three different methods(α = 0.05) were shown at Table 21.

7.1 Manual method

The % cv of hardness obtained by all the sieve number were significantly different from each other, except the % cv of hardness obtained by the sieve numbers 12 and 16, 20 and 25. The reason of % cv of

Table 21 ANOVA and DUNCAN's test of % cv of hardness of diazepam tablets obtained by the three different methods(α = 0.05).

sieve number	Manual method 12	16	20	25	30	Oscillating method 12	16	20	25	30
12	NS	NS	S	S	S	NS	NS	S	S	S
16	NS	NS	S	S	S	NS	NS	S	S	S
20	S	S	NS	NS	S	S	S	NS	S	S
25	S	S	NS	NS	S	S	S	S	NS	S
30	S	S	S	S	NS	S	S	S	S	NS

amount of PVP mg/tab	Fluid bed spray drying method 6	9	12	15
6	NS	S	S	S
9	S	NS	S	NS
12	S	S	NS	S
15	S	NS	S	NS

S Significant difference

NS Nonsignificant difference

hardness obtained by all the sieve were significantly from each other was the same as the reason of % cv of weight in the manual method.

7.2 Oscillating method

The % cv of hardness obtained by all the sieve number were significantly different from each other, except those obtained by the sieve number 12 and 16. The reason of that was the same as in the manual method.

7.3 Fluid bed spray drying method

The standard deviations of hardness prepared by using different amount of PVP were significantly different, except the standard deviation of hardness prepared by using 9 and 15 mg/tab of PVP. The reason was the same as in the weight variation by Fluid bed spray drying method.

8. Disintegration time

The satisfied results are the tablets which exhibit the shortest disintegration time to rapidly distribute and affect at the desired site of action.

ANOVA and DUNCAN's test of disintegration time of diazepam tablets prepared by the three different method(α = 0.05) were shown at Table 22.

8.1 Manual method

The disintegration time of diazepam tablets obtained by the sieve number 12, 16, 20, 25 and 30 were significantly different. This can be attributed the disintegration time of tablets prepared from granule

Table 22 ANOVA and DUNCAN's test of disintegation time of diazepam tablets obtained by the three different methods(α = 0.05).

sieve number	Manual method 12	16	20	25	30	Oscillating method 12	16	20	25	30
12	NS	S	S	S	S	NS	S	S	S	S
16	S	NS	S	S	S	S	NS	S	S	S
20	S	S	NS	S	S	S	S	NS	S	S
25	S	S	S	NS	S	S	S	S	NS	S
30	S	S	S	S	NS	S	S	S	S	NS

amount of PVP mg/tab	Fluid bed spray drying method 6	9	12	15
6	NS	S	S	S
9	S	NS	S	S
12	S	S	NS	S
15	S	S	S	NS

S Significant difference

NS Nonsignificant difference

different sizes were significantly different. Tablets prepared from smaller granules give more rapid disintegration time followed Kassem and Sahrs'theory(28).

8.2 Oscillating method

The disintegration time of diazepam tablet obtained by all the sieve number were significantly different from each other. The reason of that was the same as the manual method.

8.3 Fluid bed spray drying method

The disintegration time of diazepam tablets prepared by 6, 9, 12 and 15 mg/tab of PVP as binder were significantly different from each other due to different amount of binder. Kassem and Sahr(28)reported that increasing the amount of binder. It would cause the tablet to increase disintegration time.

9. % Friability

The % friability of tablets is usually considered satisfactory when the product exhibits a weight of less than 0.8 % (28) because friability is related to a tablet ability to withstand both shock and abrasion without crumbling during handling or manufacturing.

According to T-test method in Table 23 the % friability of tablets obtained by manual oscillating and fluid bed spray drying methods were in the 0.8 % limit.

Table 23 T-test of % Friability of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods(α = 0.05) t = 3.495.

sieve number	Manual method t	Oscillating method t
12	0.727	0
16	0	0
20	0	0
25	0	0
30	0	0

weight of PVP mg/tab	Fluid bed spray drying method t
6	0
9	0
12	0
15	0

10. Content uniformity

According to the pharmacopoeia tablets should have the mean % content of drug in the limit of 85 - 115 %. Tablets having the lowest standard deviation would be the best.

ANOVA test of % content of diazepam tablets prepared by the three different methods($\alpha = 0.05$) were shown in Table 24.

10.1 Manual method

The standard deviation of % content of tablets obtained by all the sieve number were significantly different from each other, except the tablets obtained by the sieve number 12 and 16, 20 and 25. Due to the weight variation of tablets prepared from the granules obtained by smaller sieve number was higher than those obtained by the larger sieve number, therefore the % content of tablets were different. Whereas the weight variation of tablets by sieve number 12 and 16, 20 and 25 were nonsignificantly different, threrefore % content uniformity of tablets were not different.

10.2 Oscillating method

The standard deviation of % tablets obtained by all the sieve number were significantly different from each other, except those obtained by the sieve numbers 12 and 16. The explanation was the same as in the manual method.

10.3 Fluid bed spray drying method

The standard deviation of % content of

Table 24 ANOVA and DUNCAN's test of % cv of content uniformity of diazepam tablets obtained by the three differrent methods(α = 0.05).

sieve number	Manual method 12	16	20	25	30	Oscillating method 12	16	20	25	30
12	NS	NS	S	S	S	NS	NS	S	S	S
16	NS	NS	S	S	S	NS	NS	S	S	S
20	S	S	NS	NS	S	S	S	NS	S	S
25	S	S	NS	NS	S	S	S	S	NS	S
30	S	S	S	S	NS	S	S	S	S	NS

amount of PVP mg/tab	Fluid bed spray drying method 6	9	12	15
6	NS	S	S	S
9	S	NS	S	NS
12	S	S	NS	S
15	S	NS	S	NS

S Significant difference

NS Nonsignificant difference

Table 25 T-test of % drug dissolved of diazepam tablets prepared by manual, oscillating and fluid bed spray drying methods(α = 0.05) t = 3.495.

sieve number	Manual method t	Oscillating method t
12	6.573	7.011
16	6.809	7.974
20	8.518	7.601
25	7.496	8.345
30	7.281	8.016

weight of PVP mg/tab	Fluid bed spray drying method t
6	5.706
9	8.263
12	10.724
15	9.925

diazepam tablets prepared by using different amount of PVP were significantly different from each other, except those prepared by using 9 and 15 mg/tab of PVP. This can be attributed the % cv of weight of tablet as in the aforementioned method.

11. % Drug dissolved

The best tablets should have the % drug dissolved within the 85 % USP limit, after 30 minutes in dissolution medium.

11.1 Manual oscillating and fluid bed spray drying methods

According to T-test method. The % drug dissolved of diazepam tablets obtained by all methods were outside the USP limit.

Comparison of All Properties

Evaluation of all properties of diazepam granules prepared by manual and oscillating methods were demonstrated in Table 26, 27. For manual method, the granules prepared by the sieve number 12 had the poorest properties. The granules prepared by the sieve number 25 gave the best properties. For oscillating method, the best granules were prepared by sieve number 30 while the poorest were prepared by sieve number 12.

Evaluation of the properties of diazepam tablets prepared by manual method was demonstrated in Table 28. The properties of diazepam tablets prepared by the sieve

number 12, 16, 20, 25 and 30 were ranked as the following:by sieve number 30 > by sieve number 25 >by sieve number 20 > by sieve number 16 > by sieve number 12.

The ranking of properties of diazepam tablets prepared by oscillating method was demonstrated in Table 29. The properties of tablets prepared by the sieve number 12,16,20,25 and 30 were ranked in the same order as in the manual method.

For both properties of granules and tablets, the granules prepared by the sieve number 30 of manual and oscillating methods was considered satisfactory and found to be the best among the tablets prepared by the five different sieve numbers.

The ranking of properties of diazepam granules prepared by fluid bed spray drying method using various amount of PVP as granulating agent was demonstrated in Table 30. The properties of the granules prepared by using different amount of PVP was ranked as the following: the properties of the granules prepared by using 12 mg/tab of PVP > the properties of the granules prepared by using 9 mg/tab of PVP : the properties of the granules prepared by using 15 mg/tab of PVP > the properties of the granules prepared by using 6 mg/tab of PVP.

Comparison of properties of diazepam tablets prepared by fluid bed spray drying method using various amount of PVP as granulating agents was demonstrated in

Table 31. The properties of the tablets prepared by using 6,9,12 and 15 mg/tab of PVP was ranked as the following : the properties of the tablets prepared by using 12 mg/tab of PVP > the properties of the tablets prepared by using 15 mg/tab > the properties of the tablets prepered by using 9 mg/tab of PVP.

For both properties of the granules and tablets, the granules prepared by using 12 mg/tab of PVP was considered satisfactory and found to be the best among tablets prepared by four different binder concentrations.

B. Selection of the best granule and tablet

The granules by the sieve number 30 of manual and oscillating methods and by 12 mg/tab of binder from fluid bed spray drying method as the best granules obtained by each method were compared using ANOVA and DUNCAN's test for each aforementioned property as shown in Table 32-37. Each property of granules and tablets was scored and ranked in Table 38-39. Among three types of granules, granules obtained by 12 mg/tab of binder from fluid bed spray drying method gave the highest total score although granules obtained from manual method produced the best granular property. Therefore, it would be concluded that among various method and amount of binder used, fluid bed spray drying method using 12 mg/tab of binder gave the best granule and tablet.

Table 26 Comparison properties of diazepam granules prepared by manual method.

Properties	sieve number				
	12	16	20	25	30
1. Bulk volume***	1	2	3	3	3
2. % Fine granule**	2	2	2	2	1
3. Granule size distribution***	1	1	1	2	1
4. Flow rate***	1	2	2	3	4
5. Repose angle**	2	2	2	2	2
Total score	7	9	10	12	11

* use % cv to calculate the point

** use T-test to calculate the point

*** use ANOVA and DUNCAN 's test to calculate the point

The large number was shown the best property, the small number was shown the worst property.

Table 27 Comparison of properties of diazepam granules prepared by oscillating method.

Properties	sieve number				
	12	16	20	25	30
1. Bulk volume***	1	2	2	3	4
2. % Fine granule**	1	2	2	2	2
3. Granules size distribution***	1	1	2	1	1
4. Flow rate***	1	2	3	3	4
5. Repose angle**	2	2	2	2	2
Total score	6	9	11	11	13

* use % cv to calculate the point

** use T-test to calculate the point

*** use ANOVA and DUNCAN's test to calculate the point

The large number was shown the best property, the small number was shown the worst property.

Table 28 Comparison of properties of diazepam tablets prepared by manual method.

Properties	sieve number				
	12	16	20	25	30
1. Weight variation*	1	1	2	2	3
2. Hardness variation*	1	1	2	2	3
3. Disintegration time***	1	2	3	4	5
4. % Friability**	2	2	2	2	2
5. Content uniformity*	1	1	2	2	3
6. % Drug dissolve**	1	1	1	1	1
Total score	7	8	12	13	17

* use % cv to calculate the point

** use T-test to calculate the point

*** use ANOVA and DUNCAN 's test to calculate the point

The large number was shown the best property, the small number was shown the worst property.

Table 29 Comparison of properties of diazepam tablets prepared by oscillating method.

Properties	sieve number				
	12	16	20	25	30
1. Weight variation*	1	1	2	3	4
2. Hardness variation*	1	1	2	3	4
3. Disintegration time***	1	2	3	4	5
4. % Friability**	2	2	2	2	2
5. Content uniformity*	1	1	2	3	4
6. % Drug dissolved*	1	1	1	1	1
Total score	7	8	12	16	20

* use % cv to calculate the point

** use T-test to calculate the point

*** use ANOVA and DUNCAN's test to calculate the point

The large number was shown the best property, the small number was shown the worst property.

Table 30 Comparison of properties of diazepam granules prepared by fluid bed spray drying method using various amount of PVP as granulating agents.

Properties	weight of PVP (mg/tab)			
	6	9	12	15
1. Bulk volume***	3	3	2	1
2. % Fine of granule**	1	1	1	1
3. Granule size distribution***	1	1	1	2
4. Flow rate ***	1	2	4	3
5. Repose angle**	1	1	1	1
Total score	7	8	9	8

* use % cv to calculate the point

** use T-test to calculate the point

*** use ANOVA and DUNCAN's test to calculate the point

The large number was shown the best property, the small number was shown the worst property.

Table 31 Comparison of properties of diazepam tablets prepared by fluid bed spray drying method using various amount of PVP as granulating agents.

Properties	weight of PVP (mg/tab)			
	6	9	12	16
1. Weight variation*	1	2	3	2
2. Hardness variation*	1	2	3	2
3. Disintegration time***	4	3	2	1
4. % Friability**	2	2	2	2
5. Content uniformity*	1	2	3	2
6. % Drug dissolved**	1	1	1	1
Total score	10	12	14	10

* use % cv to calculate the point

** use T-test to calculate the point

*** use ANOVA and DUNCAN's test to calculate the point

The large number was shown the best property, the small number was shown the worst property.

Table 32 ANOVA and DUNCAN 's test of the bulk volume of diazepam granules obtained by the three different methods(α 0.05).

	Manual*	Oscillating**	Fluid bed***
Manual	NS	S	S
Oscillating	S	NS	S
Fluid bed	S	S	NS

S Significant difference

NS Nonsignificant difference

* manual method : sieve number 30

** oscillating method : sieve number 30

*** fluid spray drying method: 12 mg/tab

Table 33 ANOVA and DUNCAN's test of flow rate of diazepam tablets prepared by the three different methods(α = 0.05).

	Manual*	Oscillating**	Fluid bed***
Manual	NS	S	NS
Oscillating	S	NS	S
Fluid bed	NS	S	NS

S Significant difference

NS Nonsignificant difference

* manual method : sieve number 30

** oscillating method : sieve number 30

*** fluid spray drying method: 12 mg/tab

Table 34 ANOVA and DUNCAN's test of % cv of diazepam tablet prepared by the three different methods ($\alpha = 0.05$).

	Manual*	Oscillating**	Fluid bed***
Manual	NS	S	S
Oscillating	S	NS	S
Fluid bed	S	S	NS

S Significant difference

NS Nonsignificant difference

* manual method : sieve number 30

** oscillating method : sieve number 30

*** fluid spray drying method: 12 mg/tab

Table 35 ANOVA and DUNCAN's of % cv of diazepam hardness obtained by the three different methods ($\alpha = 0.05$).

	Manual*	Oscillating**	Fluid bed***
Manual	NS	S	S
Oscillating	S	NS	S
Fluid bed	S	S	NS

S Significant difference

NS Nonsignificant difference

* manual method : sieve number 30

** oscillating method : sieve number 30

*** fluid spray drying method: 12 mg/tab

Table 36 ANOVA and DUNCAN's test of disintegation time of diazepam tablets obtained by the three different methods(α = 0.05).

	Manual*	Oscillating**	Fluid bed***
Manual	NS	NS	S
Oscillating	NS	NS	S
Fluid bed	S	S	NS

S Significant difference

NS Nonsignificant difference

* manual method : sieve number 30

** oscillating method : sieve number 30

*** fluid spray drying method: 12 mg/tab

Table 37 ANOVA and DUNCAN's test of % cv of content uniformity of drug of diazepam tablets obtained by the three different methods ($\alpha = 0.05$).

	Manual*	Oscillating**	Fluid bed***
Manual	NS	S	S
Oscillating	S	NS	S
Fluid bed	S	S	NS

S Significant difference

NS Nonsignificant difference

* manual method : sieve number 30

** oscillating method : sieve number 30

*** fluid spray drying method: 12 mg/tab

Table 38 Comparison of properties of diazepam by manual, oscillating and fluid bed spray drying methods.

Properties	Method		
	manual	oscillating	fluid bed
1. Bulk volume***	3	2	1
2. % Fine of granule**	1	2	1
3. Granule size distribution***	1	1	1
4. Flow rate ***	2	1	2
5. Repose angle**	2	2	1
Total score	9	8	7

* use % cv to calculate the point

** use T-test to calculate the point

*** use ANOVA and DUNCAN's test to calculate the point

The large number was shown the best property, the small number was shown the worst property.

Table 39 Comparison of properties of diazepam tablets prepared by manual ,oscillating and fluid bed spray drying methods.

Properties	Method		
	manual	oscillating	fluid bed
1. Weight variation*	1	2	3
2. Hardness variation*	1	2	3
3. Disintegration time***	2	2	1
4. % Friability**	2	2	2
5. Content uniformity*	1	2	3
6. % Drug dissolved**	1	1	1
Total score	8	11	13

* use % cv to calculate the point

** use T-test to calculate the point

*** use ANOVA and DUNCAN's test to calculate the point

The large number was shown the best property, the small number was shown the worst property.