CHAPTER III

RESULTS

Physical Properties of Granules Prepared with Ispaghula Husk and Various Binders.

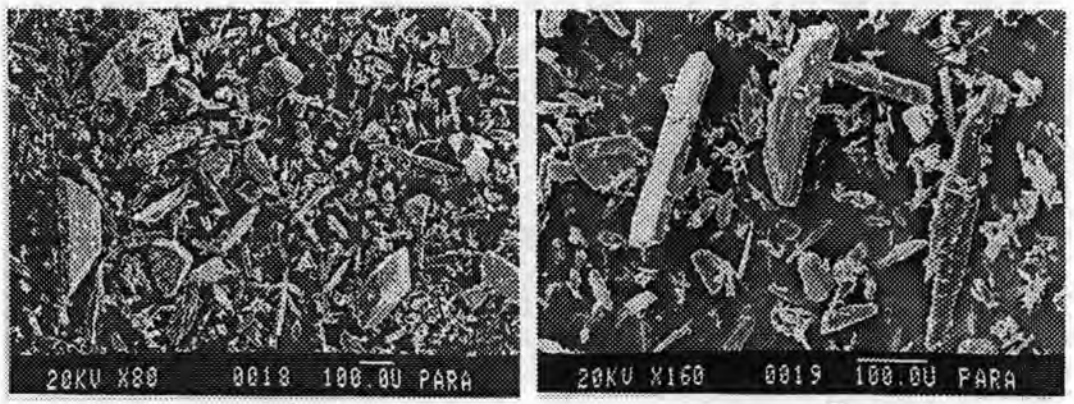
1. Morphology Examination

1.1 Paracetamol

The microscopic appearance of paracetamol powder, lactose and granules prepared by dry incorporation method in different appropriate magnification are shown in Figure 9 - 14. The shape of paracetamol powder consisted of large cylinder particles blend with small acicular particles. It had wide range of size distribution. In dry incorporation method, granules which prepared by various binders appeared to be similar and possessed quite round shape. The granules probably consisted of intact nonfractured paracetamol particles bound together by a sponge-like network solid binders. The similar results were observed with the granules prepared by solution incorporation method as shown in Figure 15 - 20.

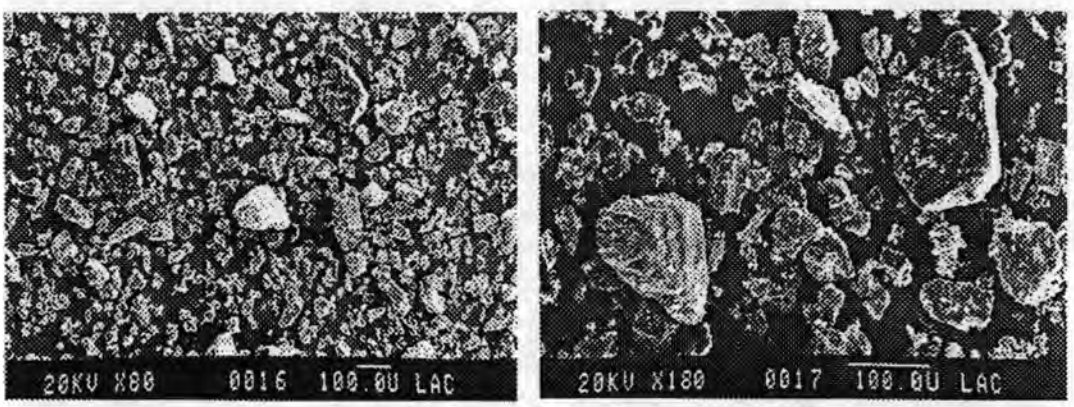
1.2 Nicotinamide

The microscopic appearance of nicotinamide powder, lactose and granules prepared by dry and solution incorporation method in different appropriate magnification are shown in Figure 21- 31. Nicotinamide powder composed of thick rod-shaped particles. It also showed wide range of size distribution. The granule characteristics for all cases were similar and had quite round shape. The granule surface appeared to consisted of intact nonfractured nicotinamide particles bound together by a sponge-like network solid binders and some particles that partially melted together.



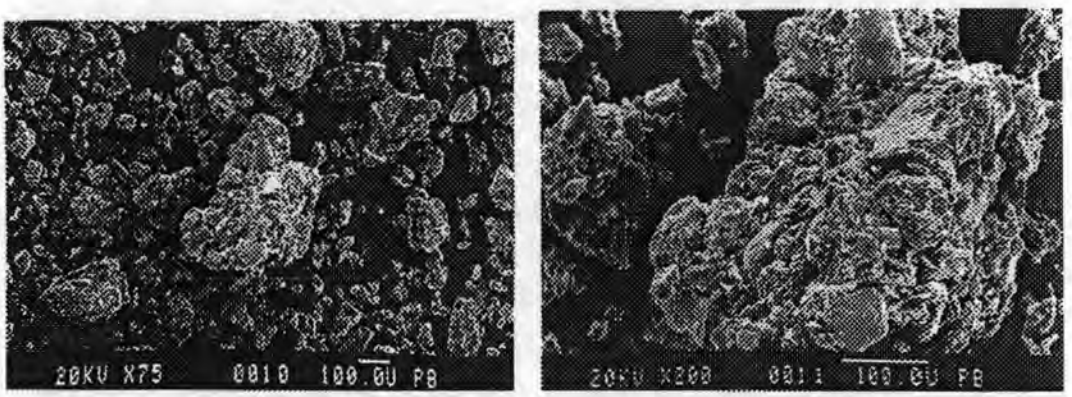
A B

Figure 9 Photomicrographs of Original Paracetamol Powders (Key : A X 80 , B X 160)



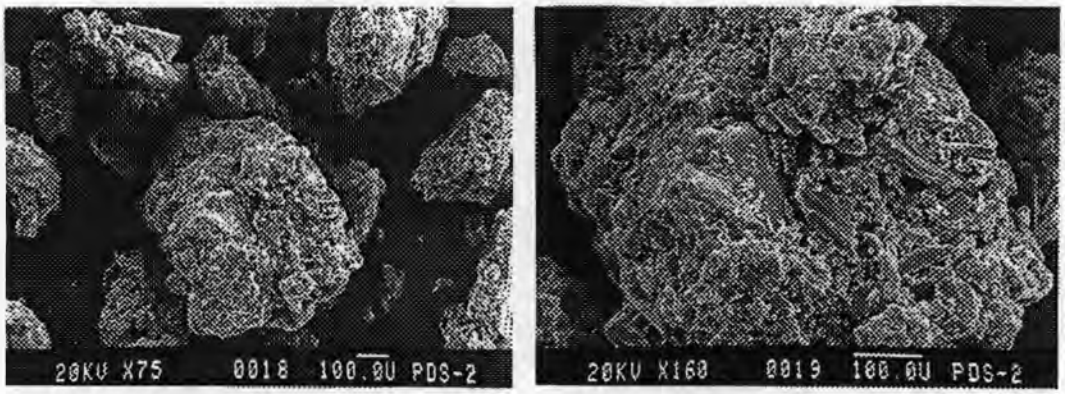
A B

Figure 10 Photomicrographs of Lactose Powders (Key : A X 80, B X160)



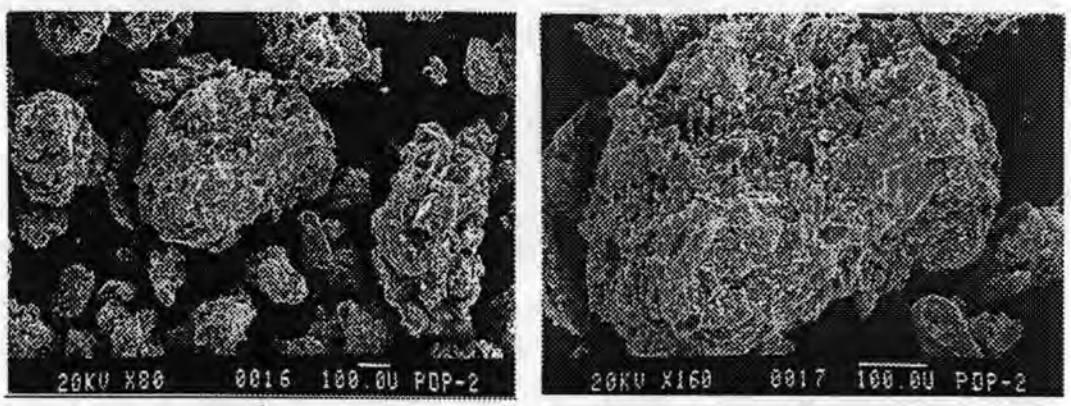
A B

Figure 11 Photomicrographs of Paracetamol Granules Prepared without Binder (Blank) (Key : A X 75 , B X 200)



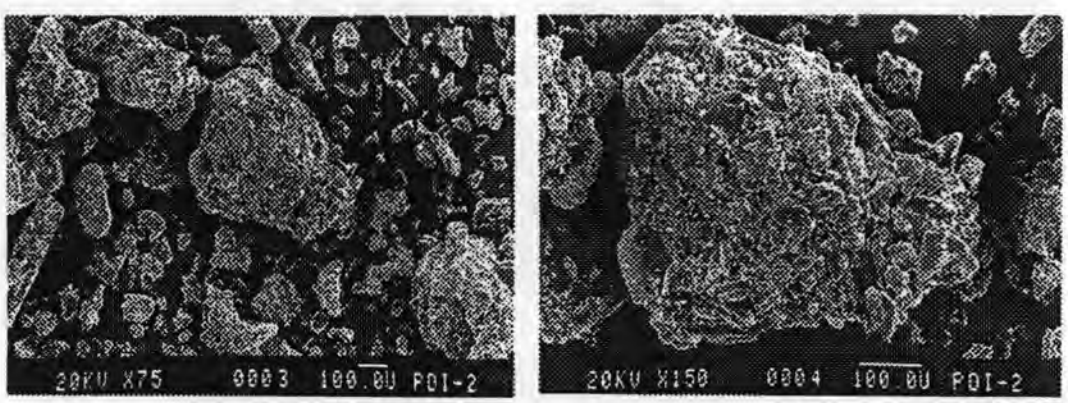
A B

Figure 12 Photomicrographs of Paracetamol Granules Prepared with 2 % Starch 1500® by Dry Incorporation Method
(Key : A X 75 , B X 160)



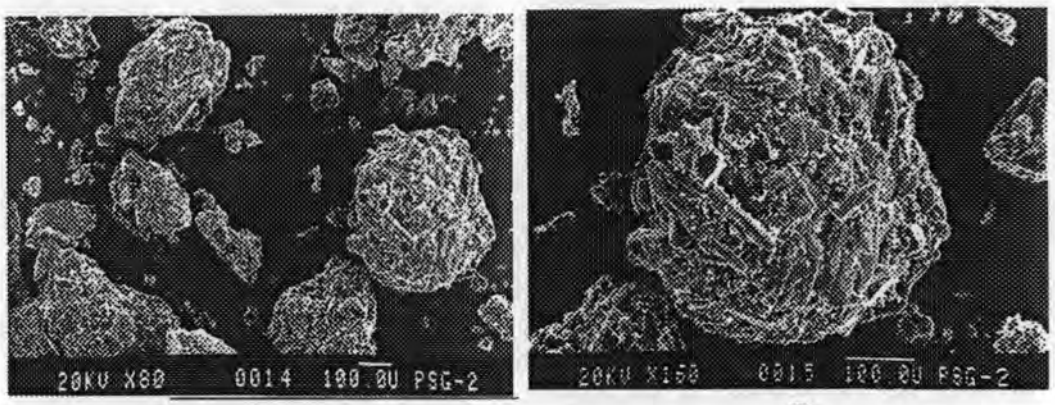
A B

Figure 13 Photomicrographs of Paracetamol Granules Prepared with 2 % PVP K 30 by Dry Incorporation Method
(Key : A X 80 , B X 160)



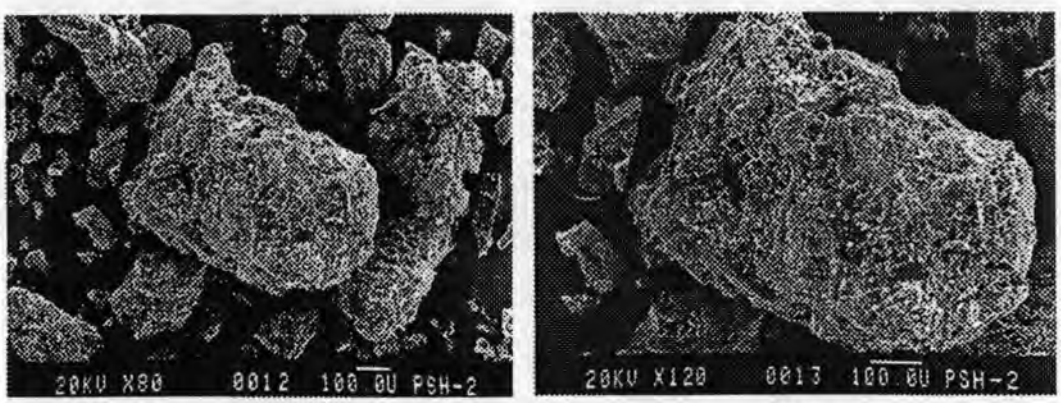
A B

Figure 14 Photomicrographs of Paracetamol Granules Prepared with 2 % Ispaghula Husk by Dry Incorporation Method
(Key : A X 75 , B X 150)



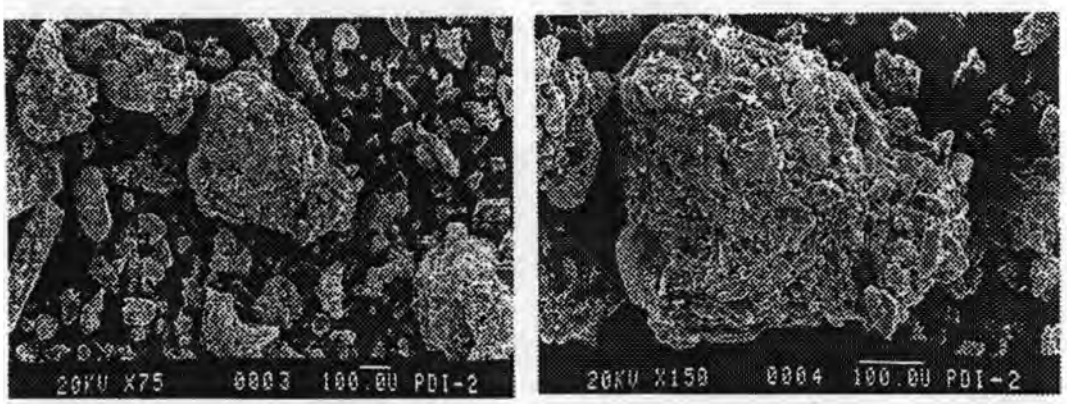
A B

Figure 15 Photomicrographs of Paracetamol Granules Prepared with 2 % Gelatin by Solution Incorporation Method
(Key : A X 80 , B X 160)



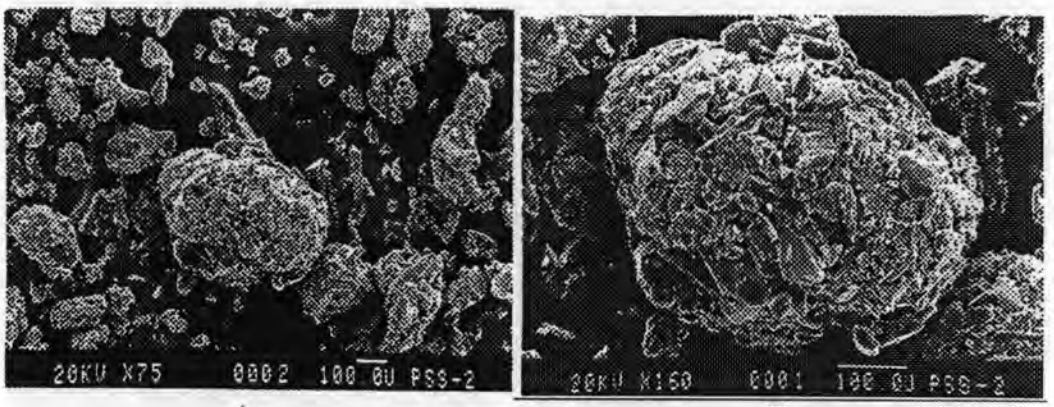
A B

Figure 16 Photomicrographs of Paracetamol Granules Prepared with 2 % HPC type L by Solution Incorporation Method
(Key : A X 80 , B X 120)



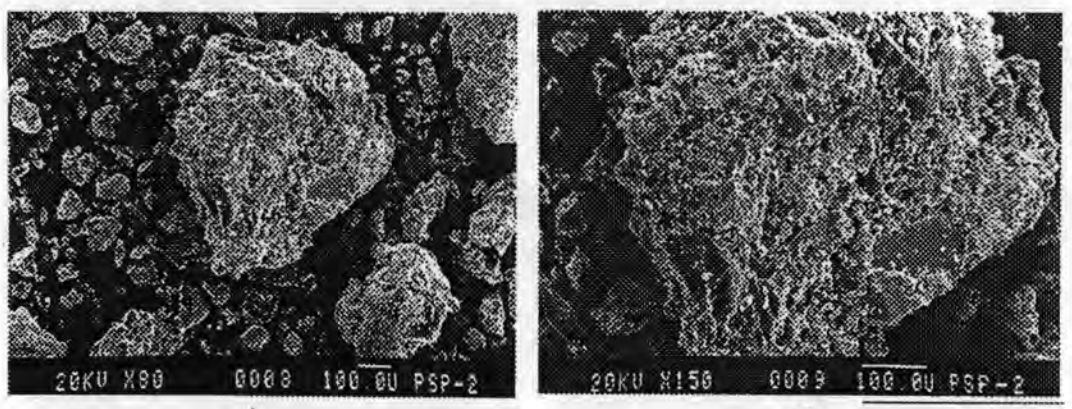
A B

Figure 17 Photomicrographs of Paracetamol Granules Prepared with 2 % Corn starch by Solution Incorporation Method
(Key : A X 80 , B X 200)



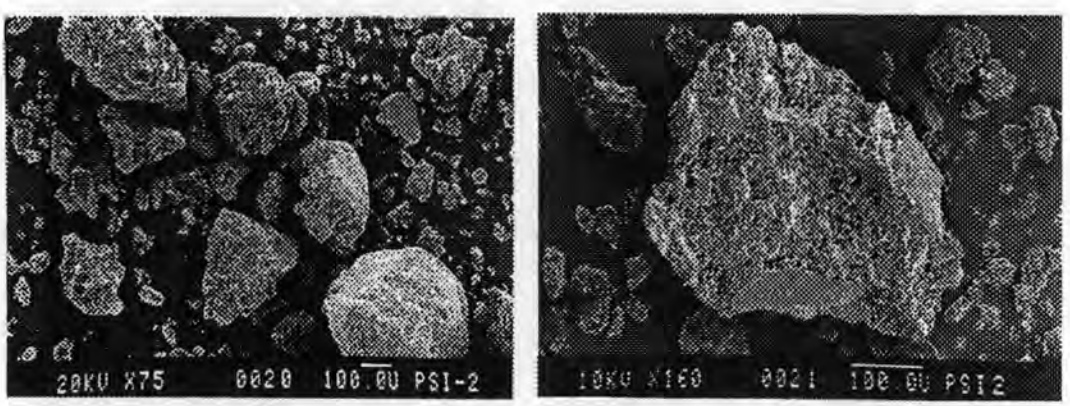
A B

Figure 18 Photomicrographs of Paracetamol Granules Prepared with 2% Starch 1500® by Solution Incorporation Method (Key : A X 75 , B X 160)



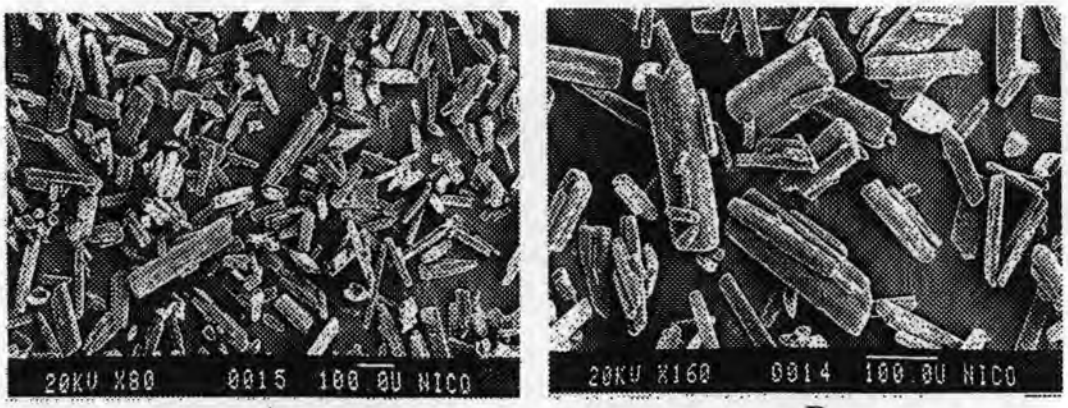
A B

Figure 19 Photomicrographs of Paracetamol Granules Prepared with 2% PVP K 30 by Solution Incorporation Method (Key : A X 80 , B X 150)



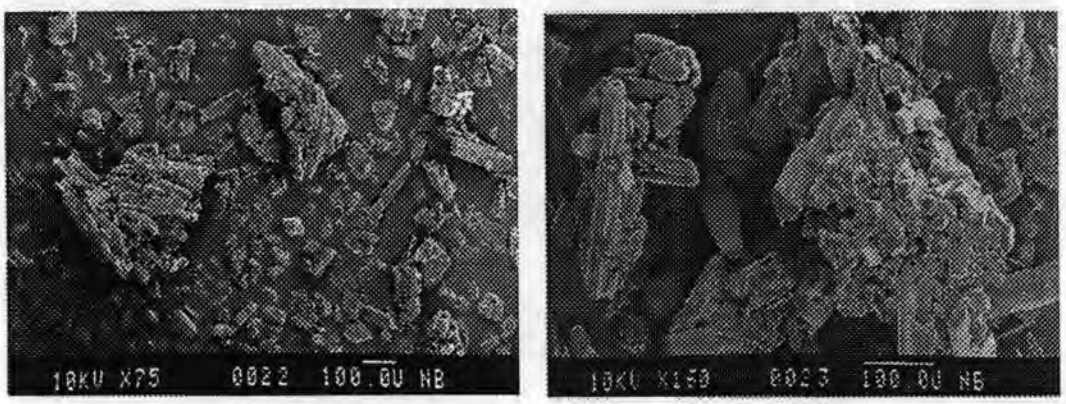
A B

Figure 20 Photomicrographs of Paracetamol Granules Prepared with 2% Ispaghula Husk by Solution Incorporation Method (Key : A X 75 , B X 160)



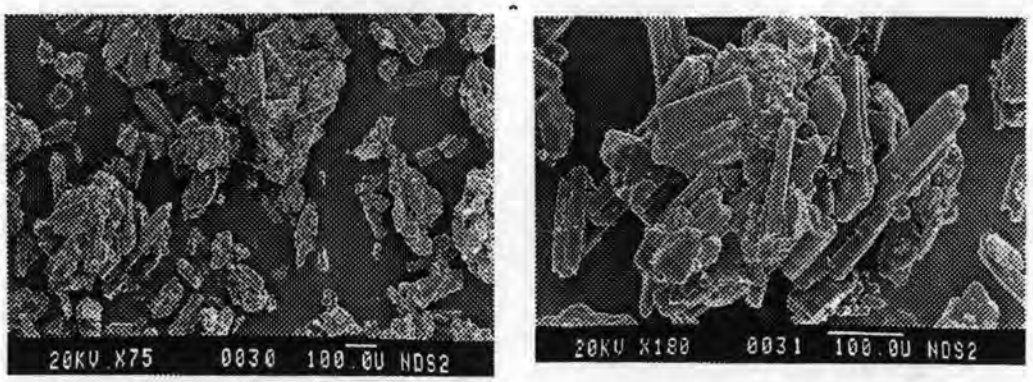
A B

Figure 21 Photomicrographs of Original Nicotinamide Powders (Key : A X 80 , B X 160)



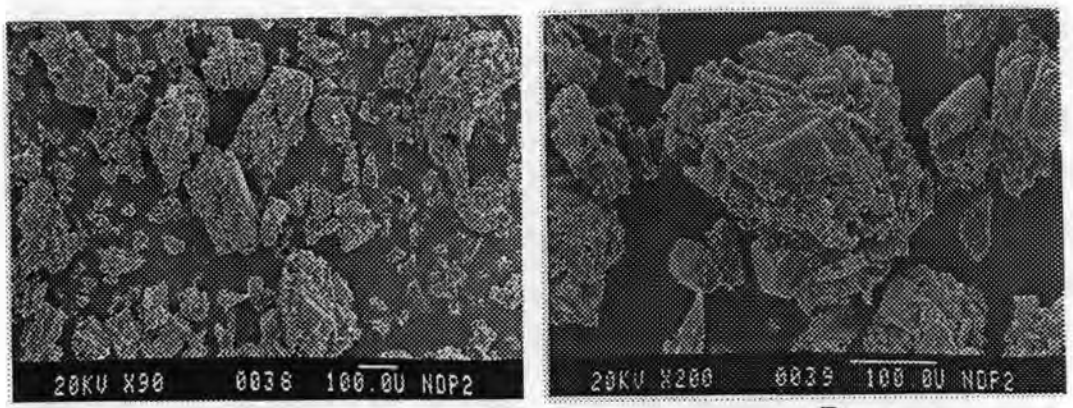
A B

Figure 22 Photomicrographs of Nicotinamide Granules Prepared without Binder (Blank) (Key : A X 75 , B X 160)



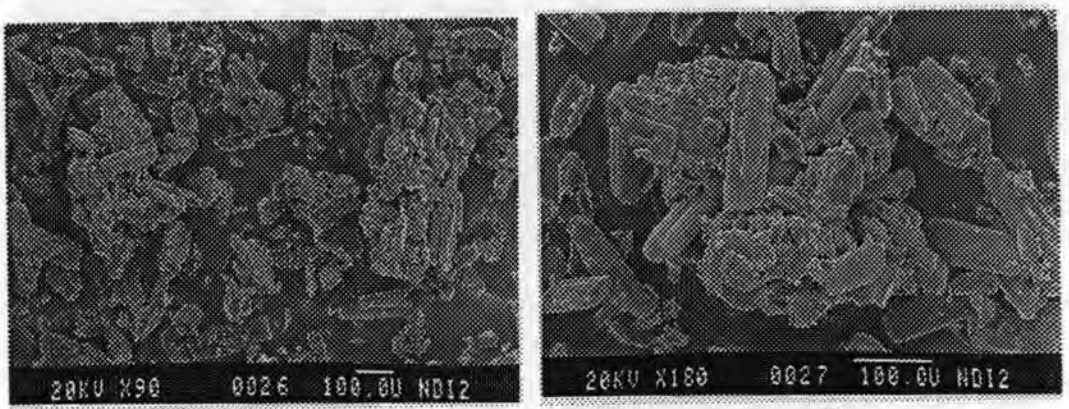
A B

Figure 23 Photomicrographs of Nicotinamide Granules Prepared with 2% Starch 1500® by Dry Incorporation Method (Key : A X 75 , B X 180)



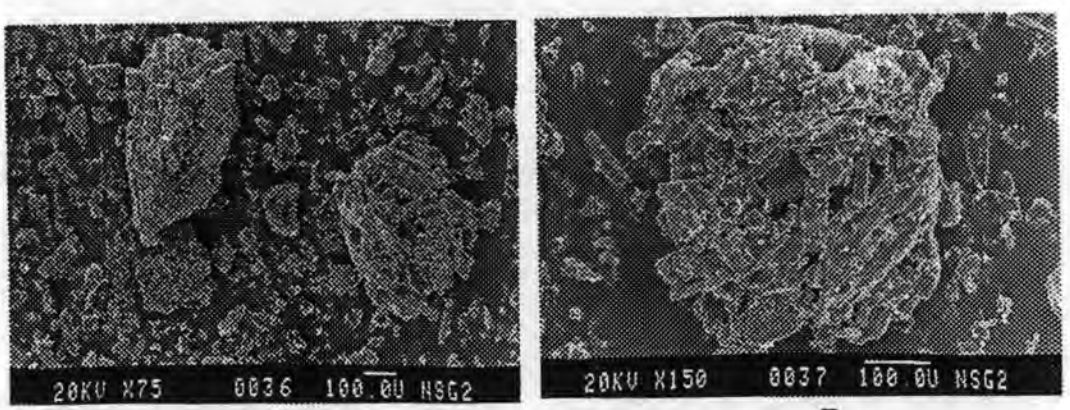
A B

Figure 24 Photomicrographs of Nicotinamide Granules Prepared with 2 % PVP K 30 by Dry Incorporation Method
(Key : A X 90 , B X 200)



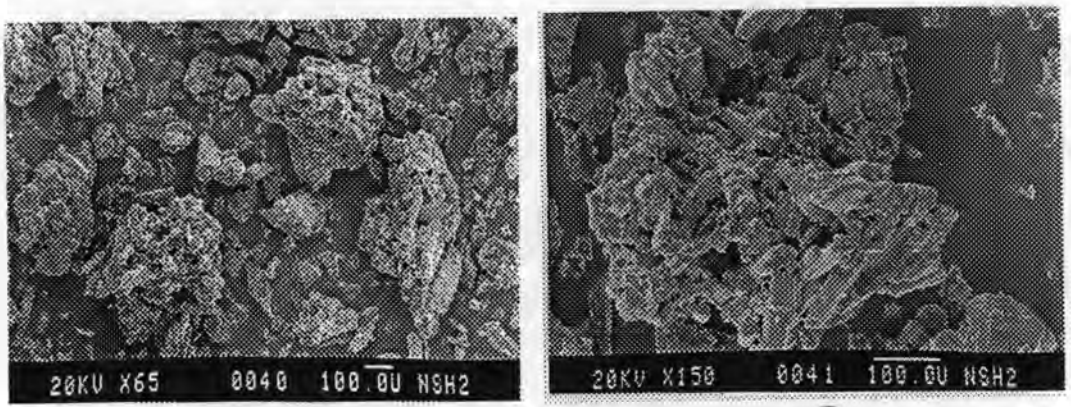
A B

Figure 25 Photomicrographs of Nicotinamide Granules Prepared with 2% Ispaghula Husk by Dry Incorporation Method
(Key : A X 90 , B X 180)



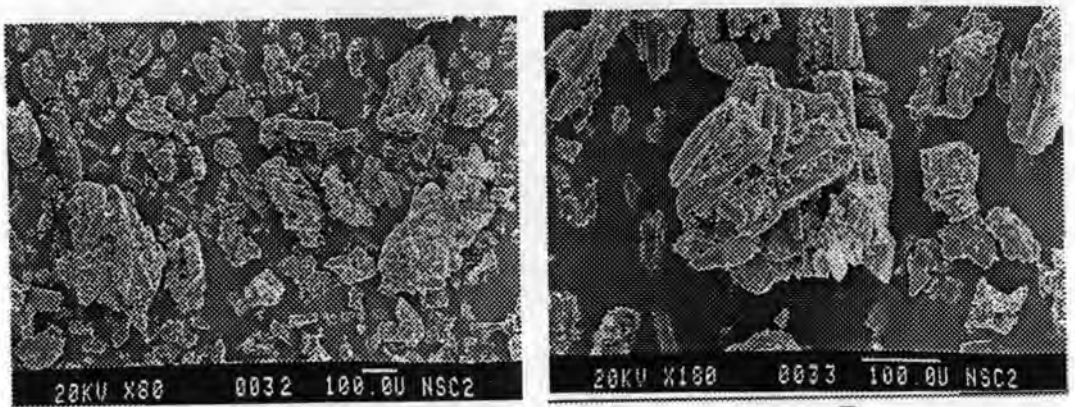
A B

Figure 26 Photomicrographs of Nicotinamide Granules Prepared with 2% Gelatin by Solution Incorporation Method
(Key : A X 75 , B X 150)



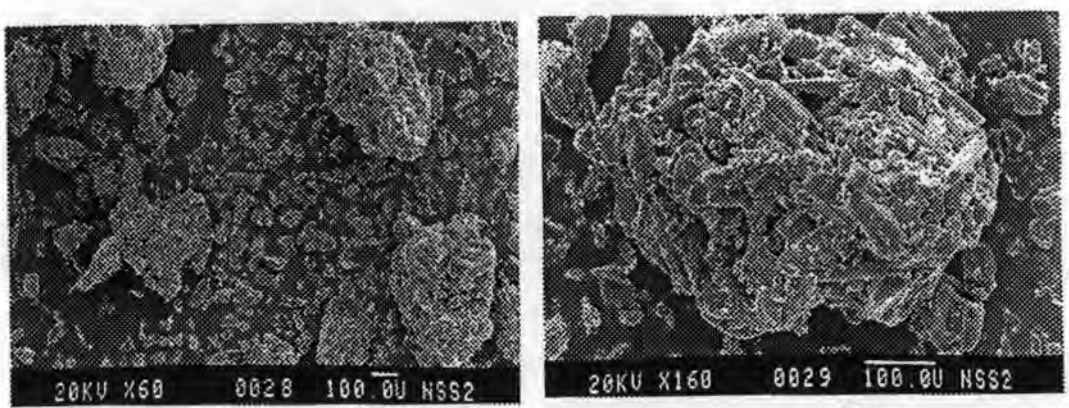
A B

Figure 27 Photomicrographs of Nicotinamide Granules Prepared with 2 % HPC type L by Solution Incorporation Method (Key : A X 65 , B X 150)



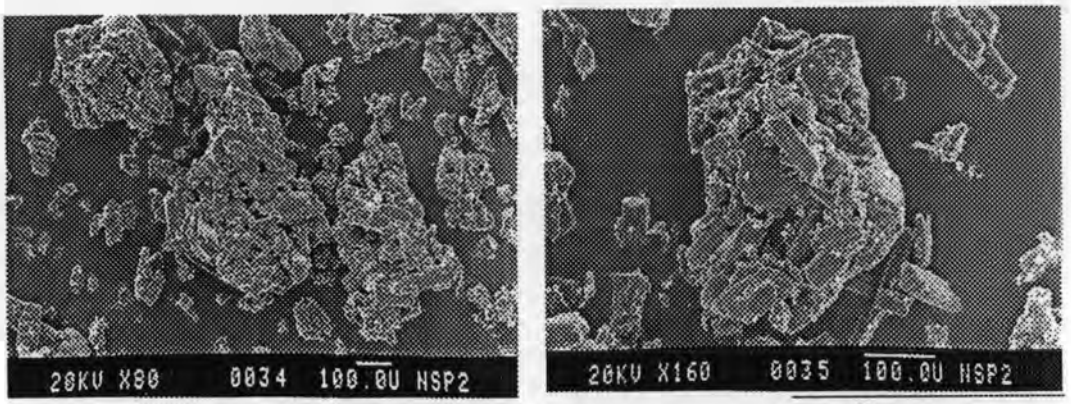
A B

Figure 28 Photomicrographs of Nicotinamide Granules Prepared with 2 % Corn Starch by Solution Incorporation Method (Key : A X 80 , B X 180)



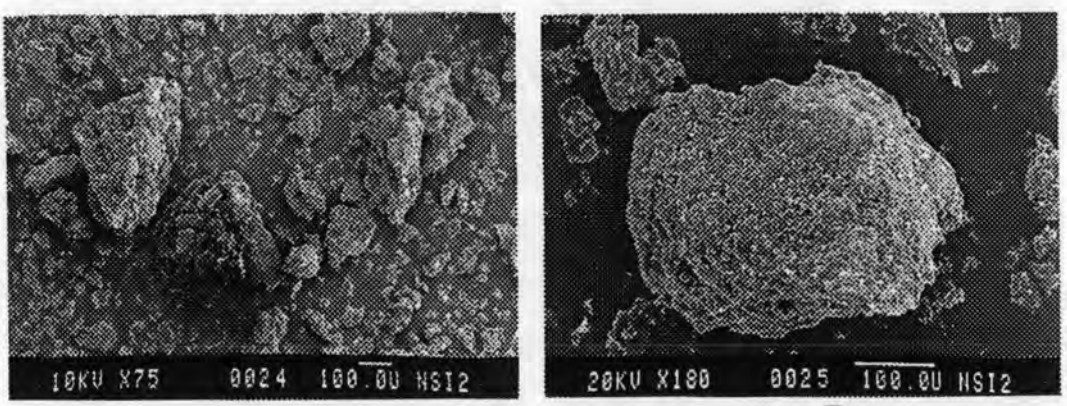
A B

Figure 29 Photomicrographs of Nicotinamide Granules Prepared with 2 % Starch 1500® by Solution Incorporation Method (Key : A X 60 ,B X 160)



A B

Figure 30 Photomicrographs of Nicotinamide Granules Prepared with 2 % PVP K30 by Solution Incorporation Method (Key : A X 80 ,B X 160)



A B

Figure 31 Photomicrographs of Nicotinamide Granules Prepared with 2 % Ispaghula Husk by Solution Incorporation Method (Key : A X 75 , B X 180)

2. Particle Size Distribution

2.1 Paracetamol

The average granule size was obtained by using the method introduced by El-Gindy et al (1988) . The average granule size and size distribution of paracetamol granules at various binder concentrations are illustrated in Table 5. In Figure 32,33, it obviously showed that the average granules size tend to increase when binder concentration increased (except for the granules prepared from Ispaghula husk by dry incorporation method) .

From the result presented in Table 5 and Figure 32,33. The average size of granules prepared by both incorporation method decreased in the following order ;

In dry incorporation method at
1 % w/w level: PVP K 30 > Ispaghula husk > Starch 1500®
2 % w/w level: PVP K 30 > Starch 1500® > Ispaghula husk
4 % w/w level: PVP K 30 > Starch 1500® > Ispaghula husk

In solution incorporation method at
0.5% w/w level : HPC type L > PVP K30 > gelatin > Ispaghula husk >Starch 1500®>corn starch
1 % w/w level : HPC type L > PVP K30 > gelatin > Ispaghula husk > corn starch >Starch 1500®
2 % w/w level : Ispaghula husk > PVP K 30 > HPC type L > gelatin > Starch 1500® > corn starch

2.2 Nicotinamide

The average granule size and size distribution of nicotinamide granules at various binder concentrations are illustrated in Table 6 . In Figure 34, 35, it obviously showed that the average granules size tend to increase when binder concentration increased .

From the result presented in Table 6 and Figure 34,35. The average size of granules prepared by both incorporation method decreased in the following order ;

In dry incorporation method at
1, 2 % w/w level : PVP K30 > Starch 1500® >Ispaghula husk
4 % w/w level : Starch 1500®> PVP K30 > Ispaghula husk

Table 5 Particle Size Distribution of Paracetamol Granules Prepared by Various Binders

Binder	Conc. (% w/w)	850 μm	425 μm	250 μm	180 μm	150 μm	smaller than 150 μm	Median size (μm)
Blank	-	1.88	41.12	18.28	24.37	8.32	6.03	352.65
Paracetamol Granules Prepared by Dry Incorporation Method								
Ispaghula Husk	1.0%	10.64	42.05	18.62	24.17	2.63	1.89	452.16
	2.0%	14.38	34.77	18.16	20.40	9.72	2.58	416.78
	4.0%	3.03	32.35	21.56	16.69	10.40	15.98	306.29
Pregelatinize Starch (Starch 1500 (R))	1.0%	7.51	44.98	27.57	14.95	2.26	2.73	448.53
	2.0%	4.60	51.09	31.83	10.12	1.57	0.79	472.33
	4.0%	5.90	50.91	24.30	13.54	3.12	2.23	481.85
Polyvinyl pyrolidone (PVP)	1.0%	5.14	55.36	20.94	15.15	1.73	1.67	505.61
	2.0%	5.46	56.04	19.95	8.05	6.89	3.61	512.22
	4.0%	19.98	59.33	14.63	3.58	1.33	1.14	634.99
Paracetamol Granules Prepared by Solution Incorporation Method								
Ispaghula Husk	0.5%	12.81	51.25	16.03	19.31	0.40	0.21	452.16
	1.0%	18.37	41.49	15.03	24.32	0.58	0.20	526.03
	2.0%	31.38	42.48	23.73	1.20	0.69	0.52	663.73
Pregelatinize Starch (Starch 1500 (R))	0.5%	3.57	48.35	24.64	19.68	2.41	1.35	441.85
	1.0%	8.89	44.43	23.90	20.00	1.63	1.15	456.82
	2.0%	5.83	56.61	17.08	12.91	6.35	1.23	518.37
Polyvinyl pyrolidone (PVP)	0.5%	15.52	44.66	13.80	8.43	4.91	12.68	521.87
	1.0%	16.08	51.01	17.49	14.98	0.31	0.14	567.36
	2.0%	23.10	45.39	14.40	13.79	2.86	0.46	598.10
Hydroxypropyl Cellulose (HPC type L)	0.5%	13.63	47.38	17.76	11.12	6.22	3.89	523.77
	1.0%	24.76	42.10	14.22	17.33	0.97	0.63	595.18
	2.0%	16.75	50.93	18.02	12.91	0.69	0.71	572.49
Corn Starch	0.5%	6.28	44.69	29.08	17.93	0.83	1.19	434.29
	1.0%	9.13	47.76	22.37	10.59	7.32	2.84	486.32
	2.0%	17.94	39.89	24.15	12.25	5.35	0.42	508.42
Gelatin	0.5%	12.69	47.70	21.12	11.20	6.36	0.94	517.52
	1.0%	21.34	42.73	16.89	17.71	0.82	0.51	564.92
	2.0%	16.85	46.73	20.90	9.71	4.88	0.94	548.50

Data averaged from three determinations is presented
(Determined by method of El-gindy et al., 1988)

Cumulative percent undersize plot see in Appendix II

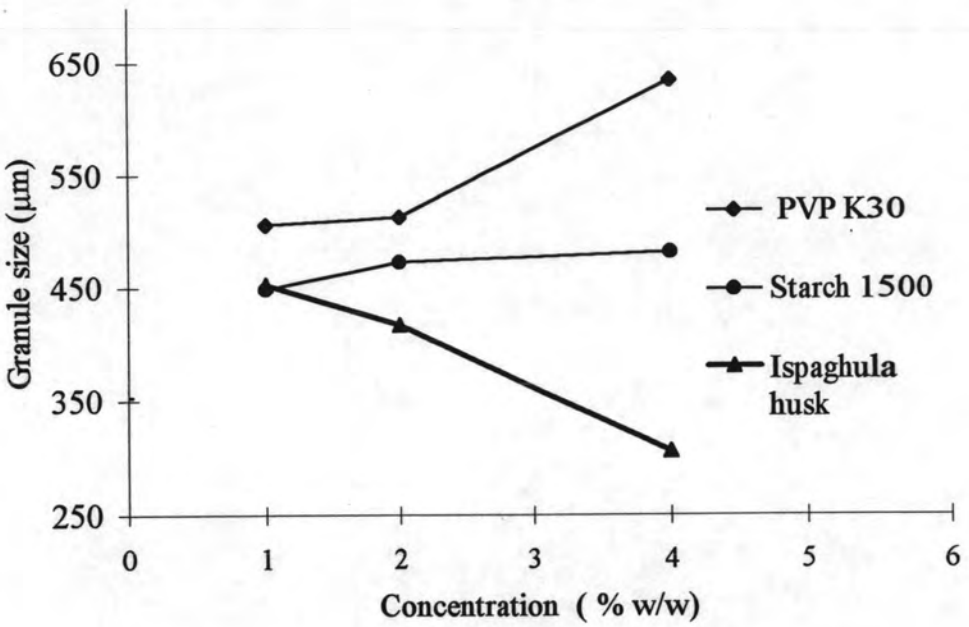


Figure 32 Effect of Binder Types and Concentrations on Average Size of Paracetamol Granules Prepared by Dry Incorporation Method

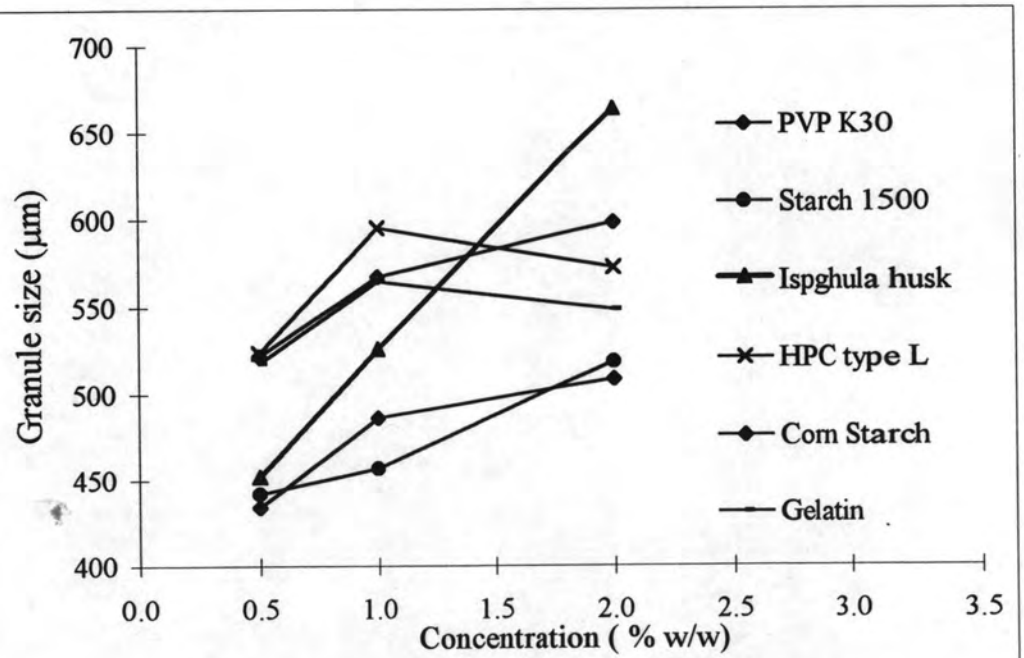


Figure 33 Effect of Binder Types and Concentrations on Average Size of Paracetamol Granules Prepared by Solution Incorporation Method

Table 6 Particle Size Distribution of Nicotinamide Granules Prepared by Various Binders

Binder	Conc. (%w/w)	850 μm	425 μm	250 μm	180 μm	150 μm	smaller than 150 μm	Median size (μm)
Blank	-	4.10	49.84	33.65	10.30	0.81	1.30	455.74
Nicotinamide Granules Prepared by Dry Incorporation Method								
Ispaghula Husk	1.0%	21.68	35.09	11.60	7.78	8.86	14.99	506.96
	2.0%	32.90	27.48	9.39	6.98	12.06	11.19	585.53
	4.0%	34.67	28.87	11.07	12.31	5.26	7.83	624.28
Pregelatinize Starch (Starch 1500 (R))	1.0%	20.09	37.70	10.90	6.40	7.76	17.15	512.82
	2.0%	22.90	39.08	10.90	6.40	7.76	12.96	617.34
	4.0%	24.78	40.26	11.78	8.06	8.96	6.16	648.59
Polyvinyl pyrolidone (PVP)	1.0%	35.58	24.50	8.98	23.88	3.26	3.80	599.86
	2.0%	37.49	24.68	10.56	23.27	2.28	1.72	634.57
	4.0%	38.50	23.48	8.58	18.30	2.66	8.48	641.84
Nicotinamide Granules Prepared by Solution Incorporation Method								
Ispaghula Husk	0.5%	27.38	42.70	9.99	4.18	4.26	11.49	624.86
	1.0%	28.30	41.70	9.48	5.08	7.46	7.98	628.84
	2.0%	22.49	56.28	9.99	3.60	2.66	4.98	642.26
Pregelatinize Starch (Starch 1500 (R))	0.5%	18.09	35.09	11.60	7.78	8.86	18.58	463.52
	1.0%	16.40	41.68	12.08	7.90	6.58	15.36	507.39
	2.0%	33.70	30.18	7.08	4.30	8.12	16.62	620.46
Polyvinyl pyrolidone (PVP)	0.5%	20.89	37.19	9.99	6.78	19.36	5.79	517.34
	1.0%	35.68	30.00	8.70	6.98	16.46	2.18	647.13
	2.0%	37.78	29.98	11.39	5.27	12.58	3.00	676.72
Hydroxypropyl Cellulose (HPC type L)	0.5%	18.27	36.08	12.48	7.80	8.06	17.31	476.24
	1.0%	24.33	40.16	11.39	4.75	12.58	6.80	578.31
	2.0%	28.90	40.16	11.39	4.41	12.58	2.56	626.71
Corn Starch	0.5%	18.29	38.98	11.49	6.43	7.37	17.44	504.27
	1.0%	20.09	37.19	11.69	6.60	9.06	15.37	508.19
	2.0%	24.88	41.48	9.69	4.98	6.78	12.19	592.62
Gelatin	0.5%	26.68	30.50	10.09	6.43	16.27	10.03	525.05
	1.0%	31.58	34.60	9.00	7.60	14.27	2.95	623.74
	2.0%	18.49	50.28	11.59	7.00	6.96	5.68.	583.66

Data averaged from three determinations is presented.
(Determined by method of El-gindy et al., 1988)

Cumulative percent undersize plot see in Appendix II

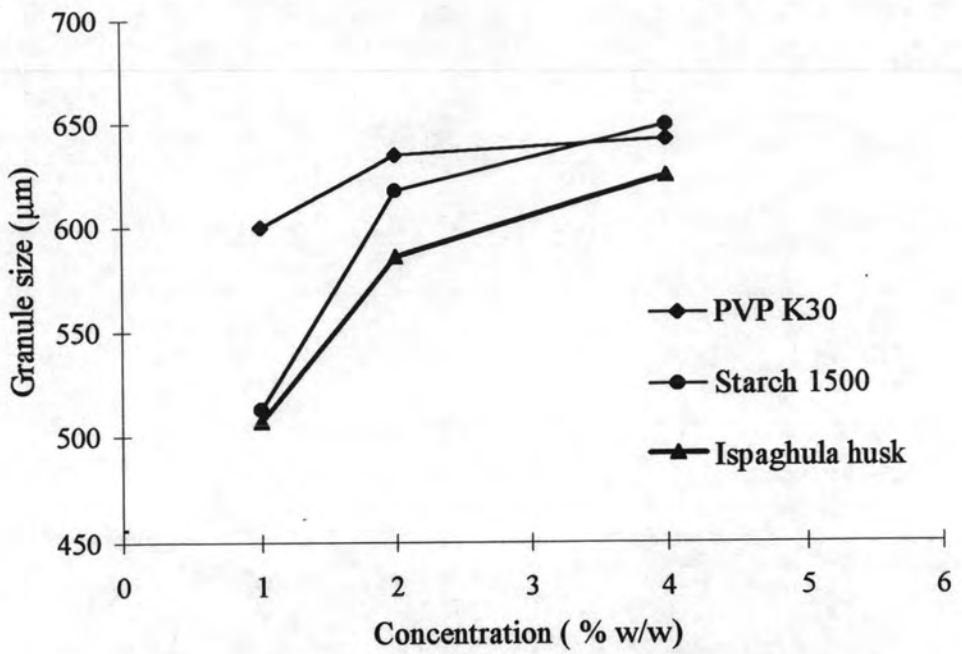


Figure 34 Effect of Binder Types and Concentrations on Average Size of Nicotinamide Granules Prepared by Dry Incorporation Method

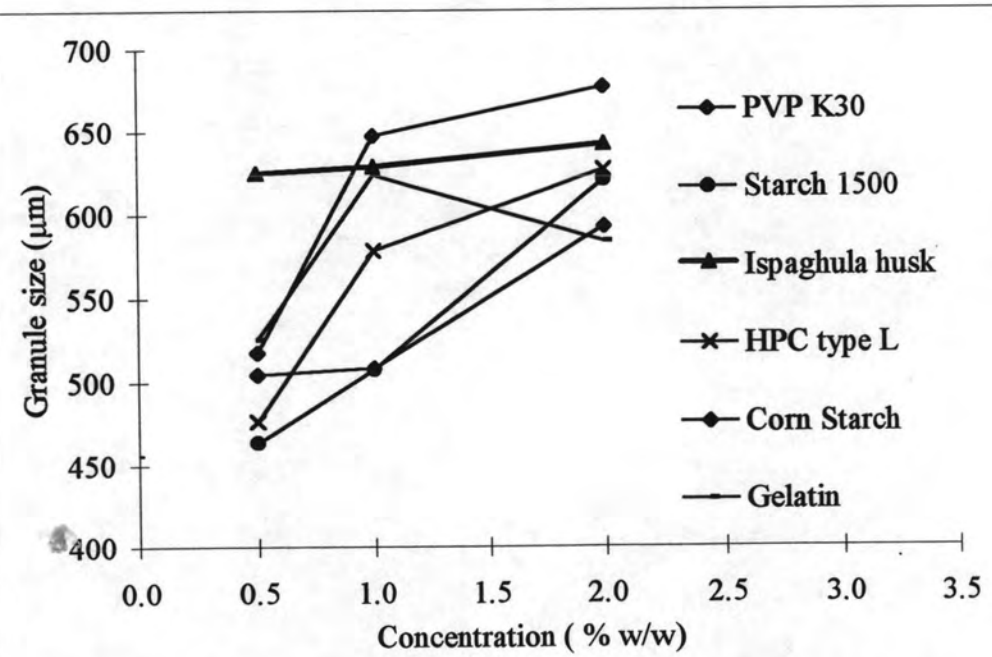


Figure 35 Effect of Binder Types and Concentrations on Average Size of Nicotinamide Granules Prepared by Solution Incorporation Method

In solution incorporation method at
0.5% w/w level : Ispaghula husk >gelatin >PVP K 30 > corn starch > HPC type L >Starch 1500®
1 % w/w level : PVP K30 > Ispaghula husk > gelatin > HPC type L > corn starch > Starch 1500®
2 % w/w level : PVP K30 > Ispaghula husk > HPC type L > Starch 1500® > corn starch > gelatin

3. Bulk Density , Tapped Density and Compressibility Determination

3.1 Paracetamol

The results of bulk density , tapped density and percent compressibility of granules prepared with various binders at three concentrations by both incorporation methods are illustrated in Table 7. The bulk density and tapped density slightly decreased when concentration of binder increased. For all cases , the bulk density and tapped density are distributed in the range of 0.45-0.51 g/ml and 0.50-0.62 g/ml, respectively. On the other hand, percent compressibility (Figure 36, 37) increased as percent binder used increased and ranging from 10.34 - 20.16. It could be noticed that the percent compressibility of granules produced by dry incorporation method were slightly lower than granules prepared by solution incorporation method .

3.2 Nicotinamide

From the results presented in Table 8 decreasing in bulk density and tapped density with increasing binder concentration were noticed . The bulk density and tapped density were ranging from 0.40 - 0.59 g/ml and 0.48 - 0.70 g/ml , respectively . For percent compressibility of granules decreased with increasing of binder concentration except for granules prepared from dry incorporation metod and granule prepared with Ispaghula husk (Figure 38, 39). The range of percent compressibility was between 11.60 - 22.01 .

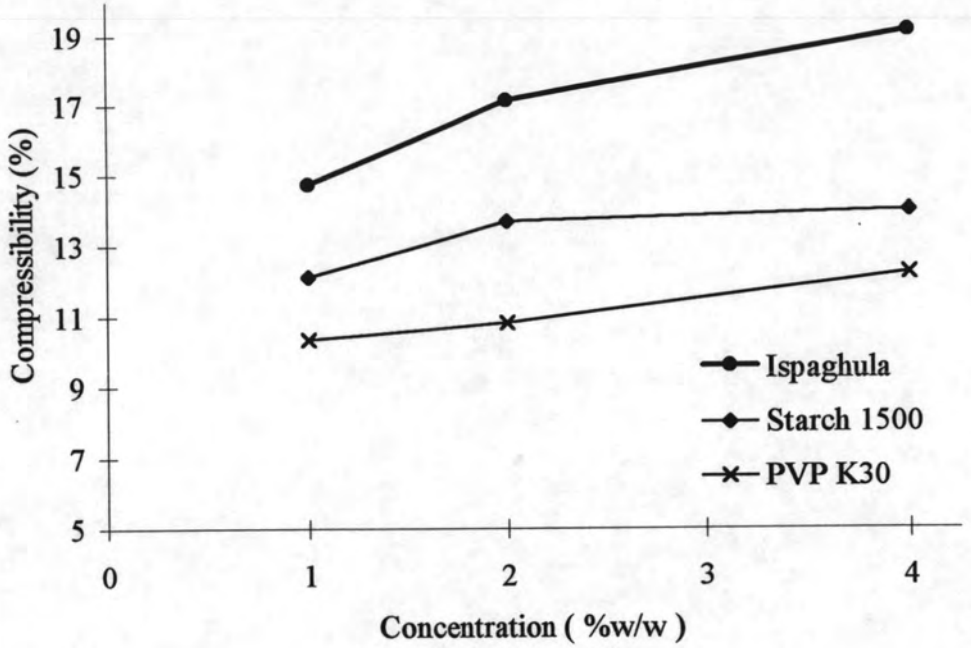


Figure 36 Compressibility of Paracetamol Granules Prepared by Dry Incorporation Method

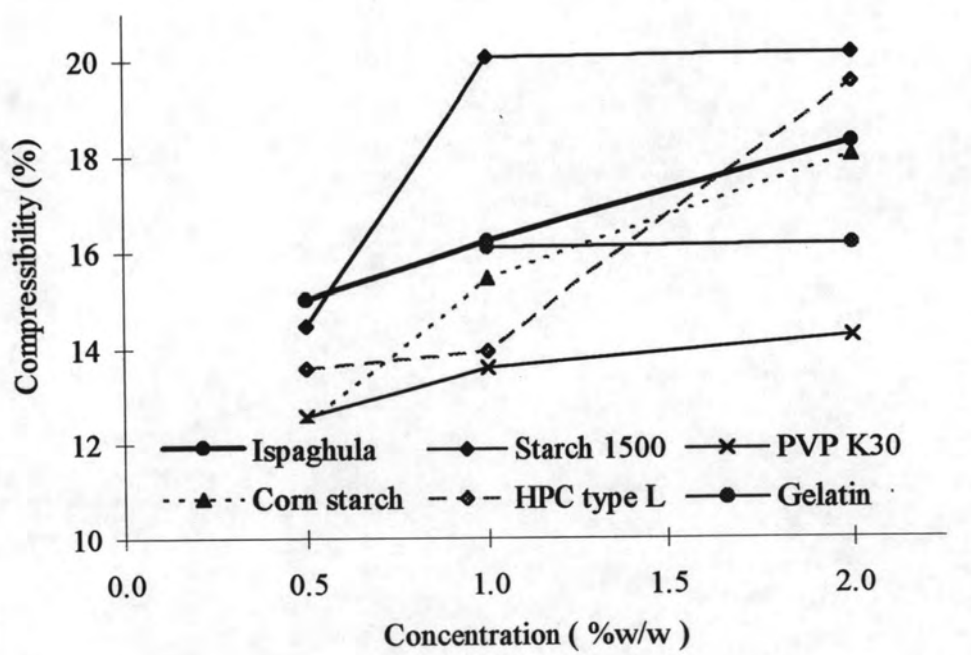


Figure 37 Compressibility of Paracetamol Granules Prepared by Solution Incorporation Method

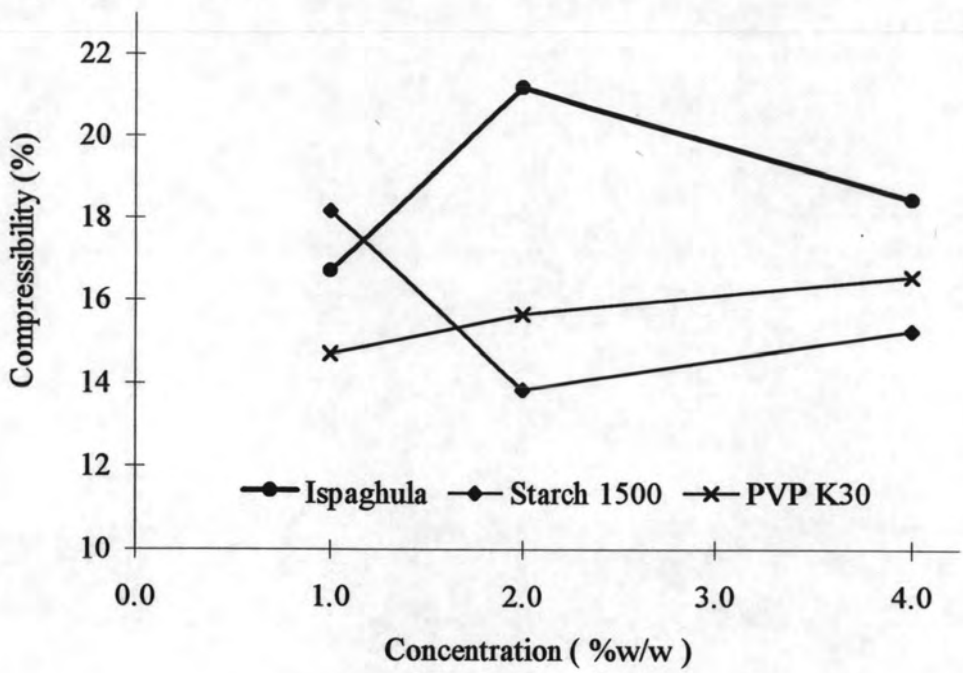


Figure 38 Compressibility of Nicotinamide Granules Prepared by Dry Incorportion Method

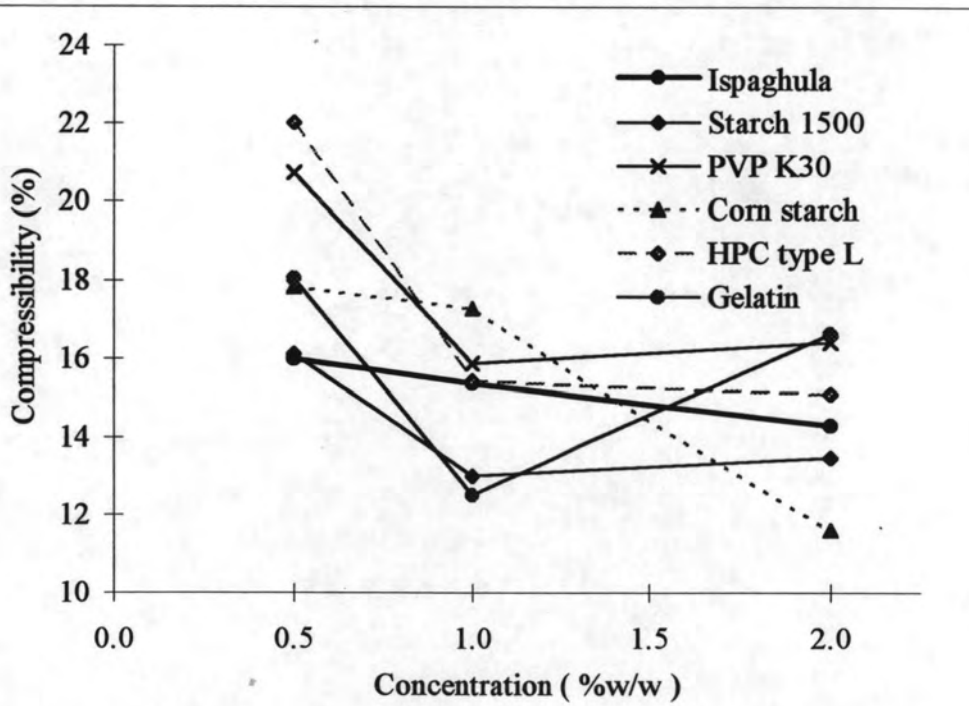


Figure 39 Compressibility of Nicotinamide Granules Prepared by Solution Incorportion Method

4. Flow Rate and Angle of Repose Determination

4.1 Paracetamol

The results of flowability and angle of repose are presented in Table 7 and Figure 40- 41. It revealed that flow rate reduced while angle of repose increased with increasing binder concentration except for granules prepared with Ispaghula husk by dry incorporation method (Figure 40).

They were ranked as follows ,
In dry incorporation method at
1 % w/w level: Starch 1500® > Ispaghula husk > PVP K 30
2, 4 % w/w level: Ispaghula husk > Starch 1500® > PVP K30

In solution incorporation method at
0.5% w/w level: HPC type L >Ispaghula husk > corn starch
PVP K 30 > Starch 1500® > gelatin
1, 2 %w/w level: Ispaghula husk >Starch 1500®> HPC type L
> gelatin > corn starch > PVP K30

From the data , it could be noticed that Ispaghula husk exhibited the best flow rate at concentration 1% w/w or over . The higher in flow rate of granules was noticed as comparing solution incorporation method with dry incorporation method .

4.2 Nicotinamide

The relationship between flow rate, angle of repose and binder concentration are noticed in Table 8 and Figure 42, 43. The flow rate did not linearly proportional to binder concentration. In both incorporation method , flowability of granules prepared with Ispaghula husk at 2 % w/w gave the optimal flow rate . The flow rate was ordered as follows ,

In dry incorporation method at
1 % w/w level : PVP K30 > Ispaghula husk >Starch 1500®
2 , 4 % w/w level : Ispaghula husk > PVP K30 >Starch 1500®

In solution incorporation method at
0.5 % w/w level : HPC type L > corn starch > PVP K30 >
Starch 1500® > Ispaghula husk > gelatin

1 % w/w level : Ispaghula husk >PVP K 30 > corn starch > HPC type L > Starch 1500® > gelatin

2 % w/w level : Ispaghula husk >HPC type L > PVP K30> corn starch > Starch 1500® > gelatin

From these data, it could be observed that Ispaghula husk exhibited the best flow rate at 2% w/w by dry incorporation method and 1-2% by solution incorporation metod.

Angle of repose of granules are presented in the Table 7,8. For all cases the values of lower than 40° were observed which indicated good flowing granules .

5. Comparison of Percent Fine

5.1 Paracetamol

The percent fine of all granules in the study are indicated in the Table 7. The relationship between binder concentration and percent fine are shown in Figure 44, 45 . The results showed that increasing the amount of binder utilized, decreasing percent fine of granule except for granules prepared with Ispaghula husk by dry incorporation method. Their ranks decrease in following order ;

In dry incorporation method at
all concentrations: Ispaghula husk >Starch 1500®> PVP K30

In solution incorporation method at

0.5 % w/w level : Ispaghula husk >PVP K30 > Starch 1500®> corn starch > gelatin > HPC type L

1 % w/w level : Starch 1500®> corn starch >Ispaghula husk > gelatin > PVP K 30 > HPC type L

2 % w/w level : Starch 1500®> corn starch > HPC type L > gelatin > Ispaghula husk > PVP K 30

All granules produced by dry incorporation method were less finer than granules prepared by solution incorporation except for granules prepared with Ispahula husk.

5.2 Nicotinamide

The results are illustrated in Table 8 and Figure 46, 47. I t was found that percent fine of granules reduced with the increase in

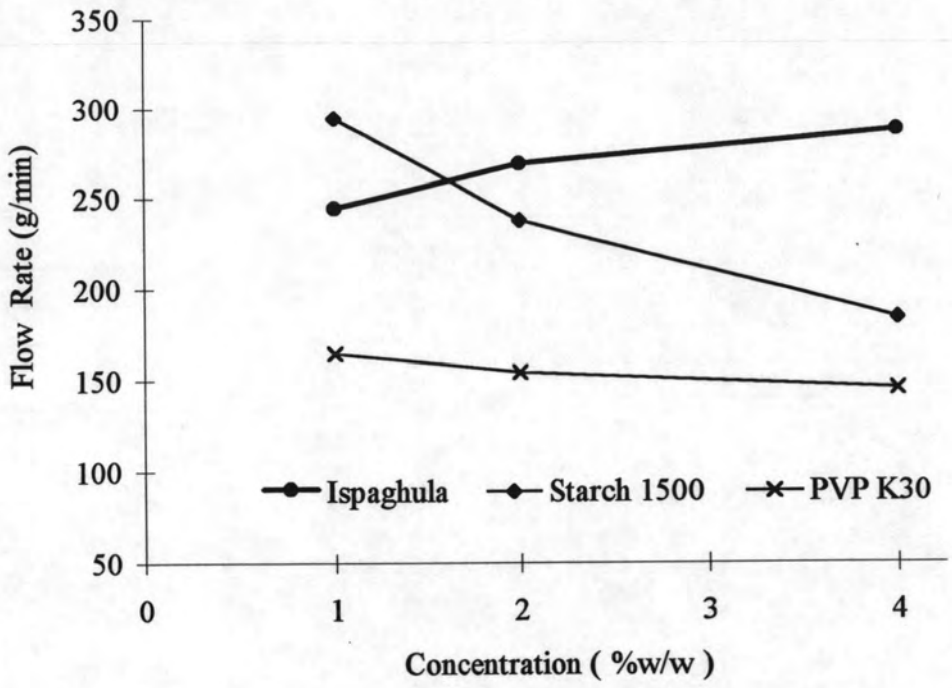


Figure 40 Flowability of Paracetamol Granules Prepared by Dry Incorporation Method

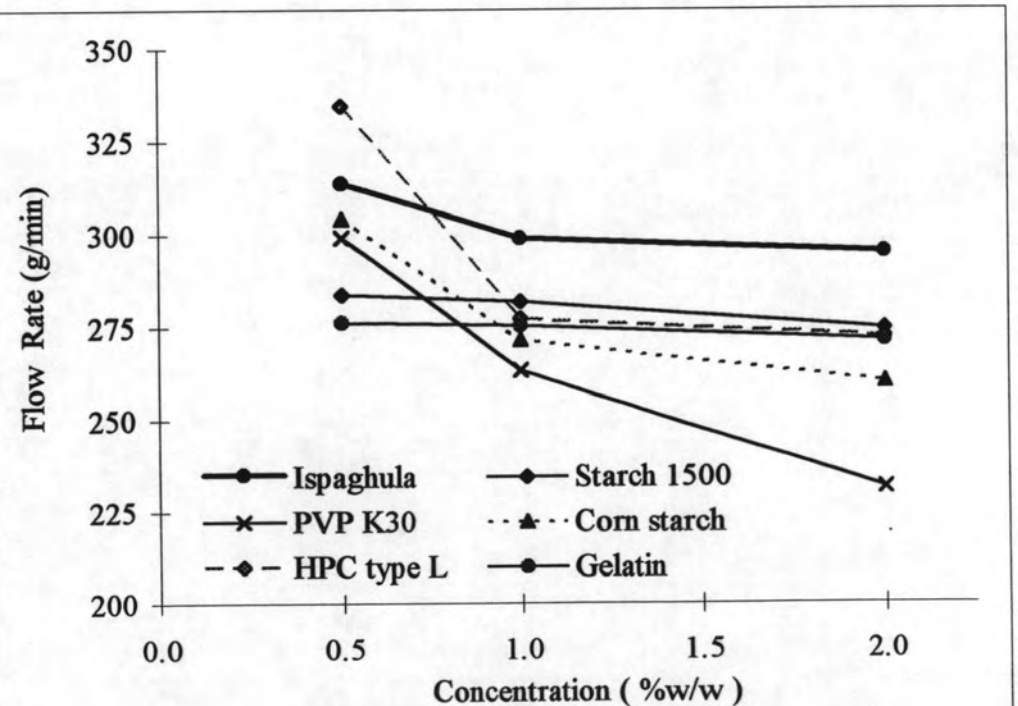


Figure 41 Flowability of Paracetamol Granules Prepared by Solution Incorporation Method

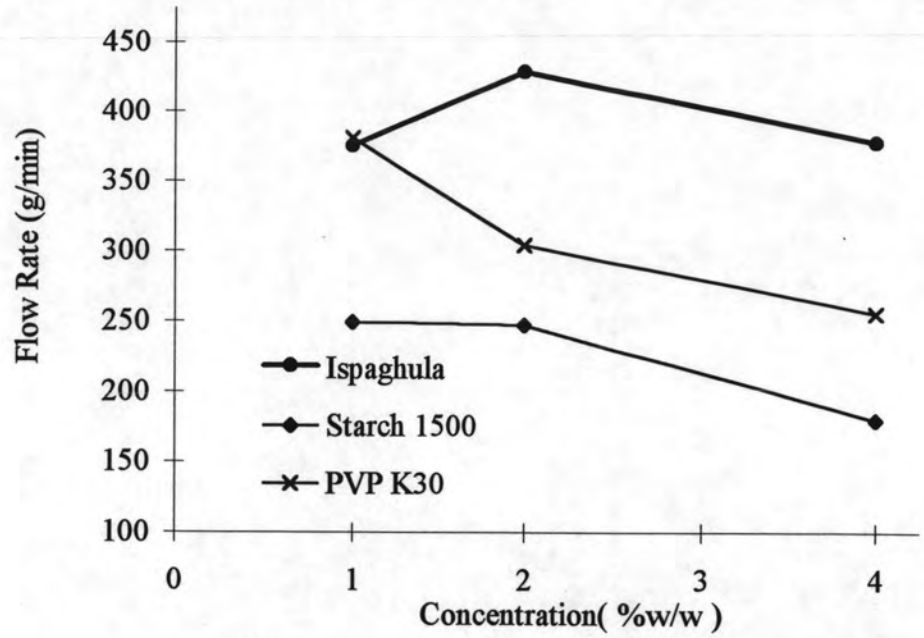


Figure 42 Flowability of Nicotinamide Grnules Prepared by Dry Incorportion Method

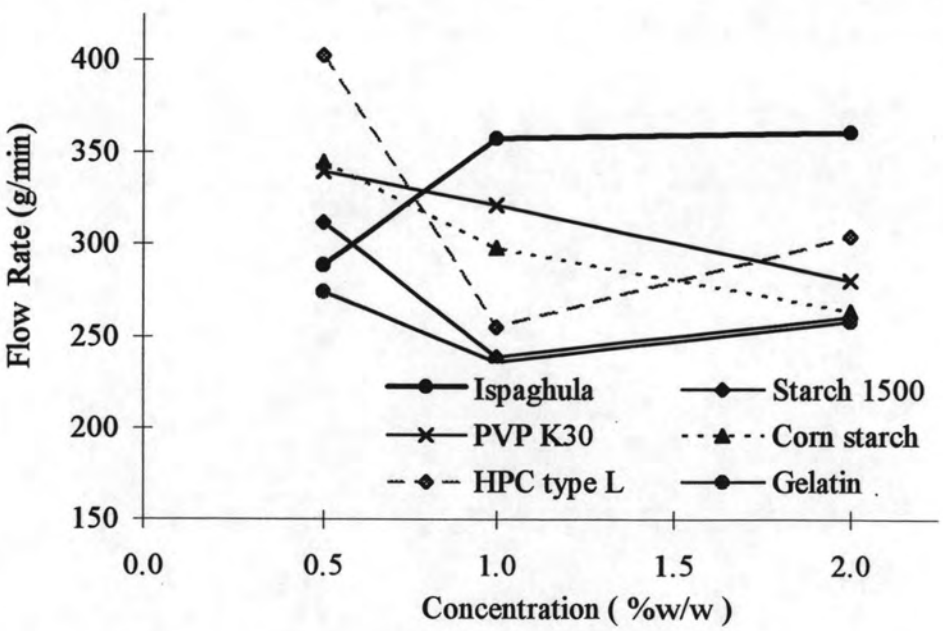


Figure 43 Flowbility of Nicotinamide Granules Prepared by Solution Incorportion Method

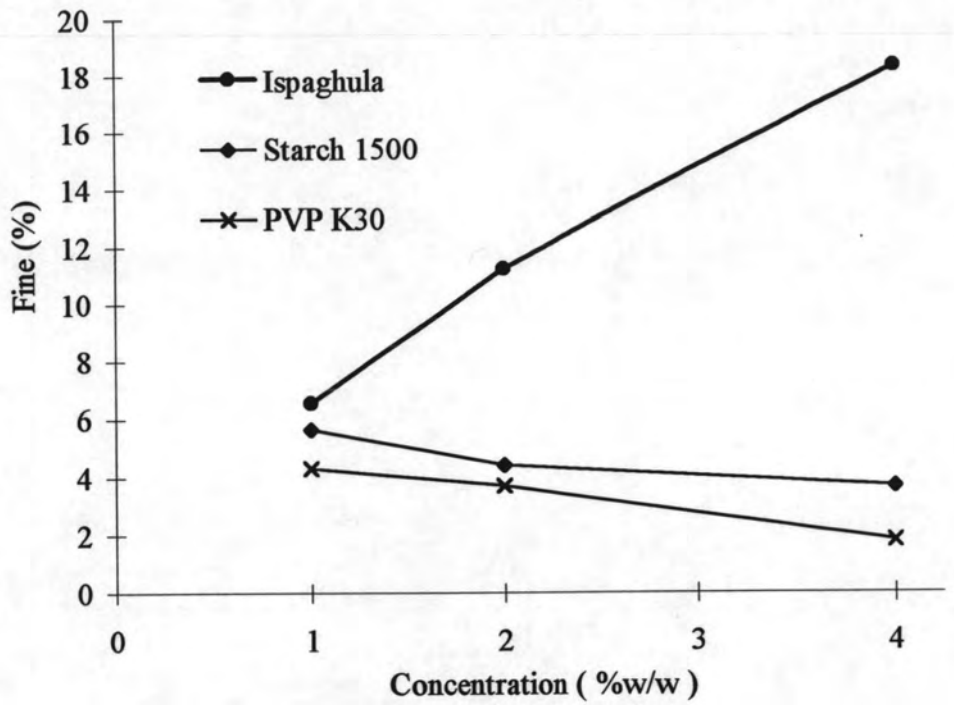


Figure 44 Percent Fine of Paracetamol Granules Prepared by Dry Incorporation Method

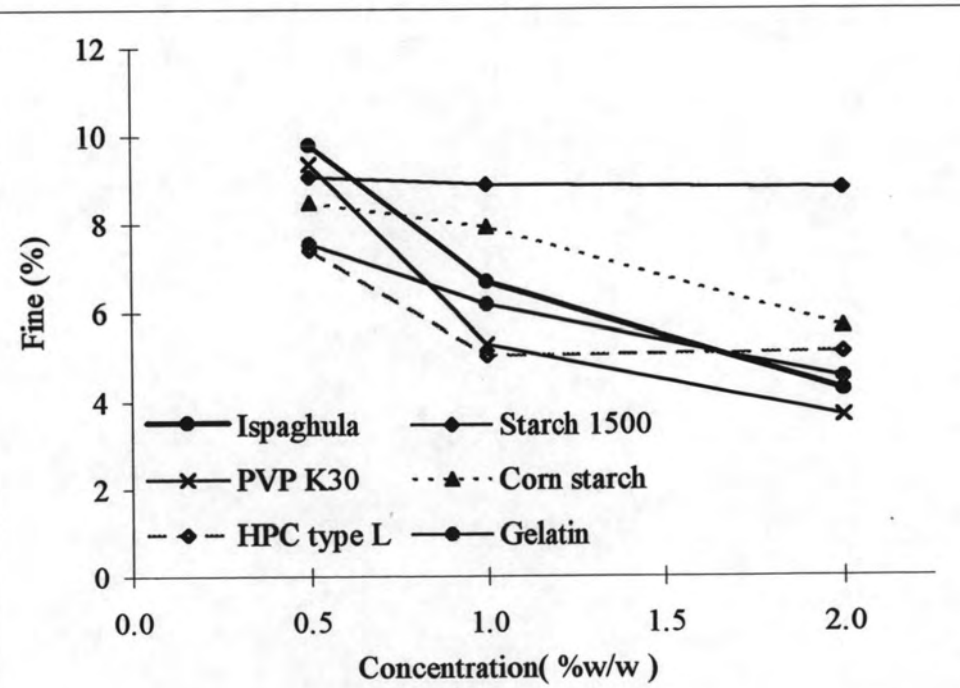


Figure 45 Percent Fine of Paracetamol Granules Prepared by Solution Incorporation Method

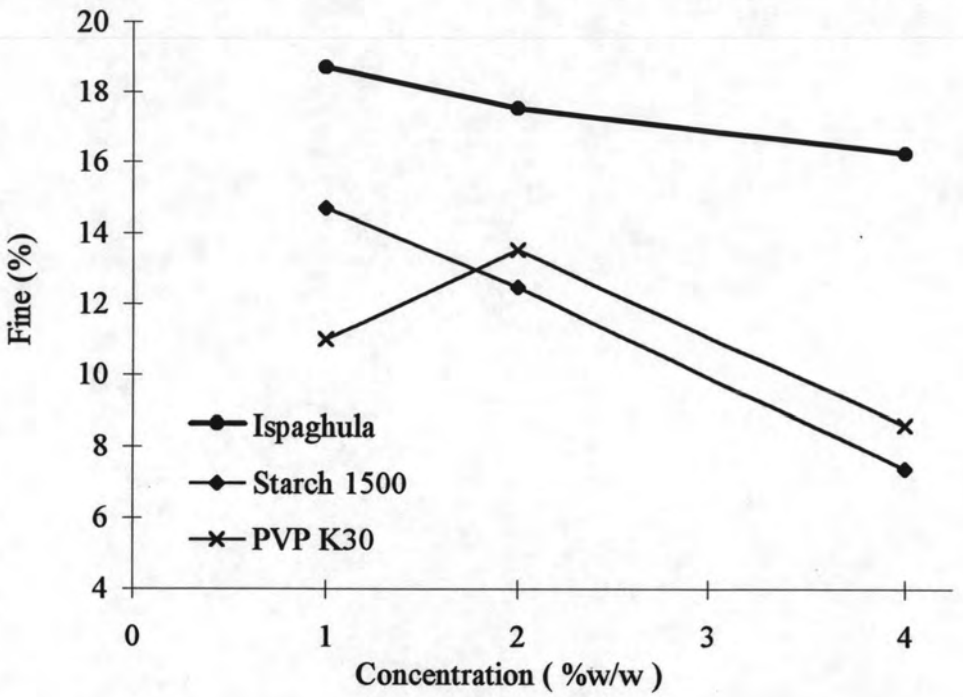


Figure 46 Percent Fine of Nicotinamide Granules Prepared by Dry Incorporation Method

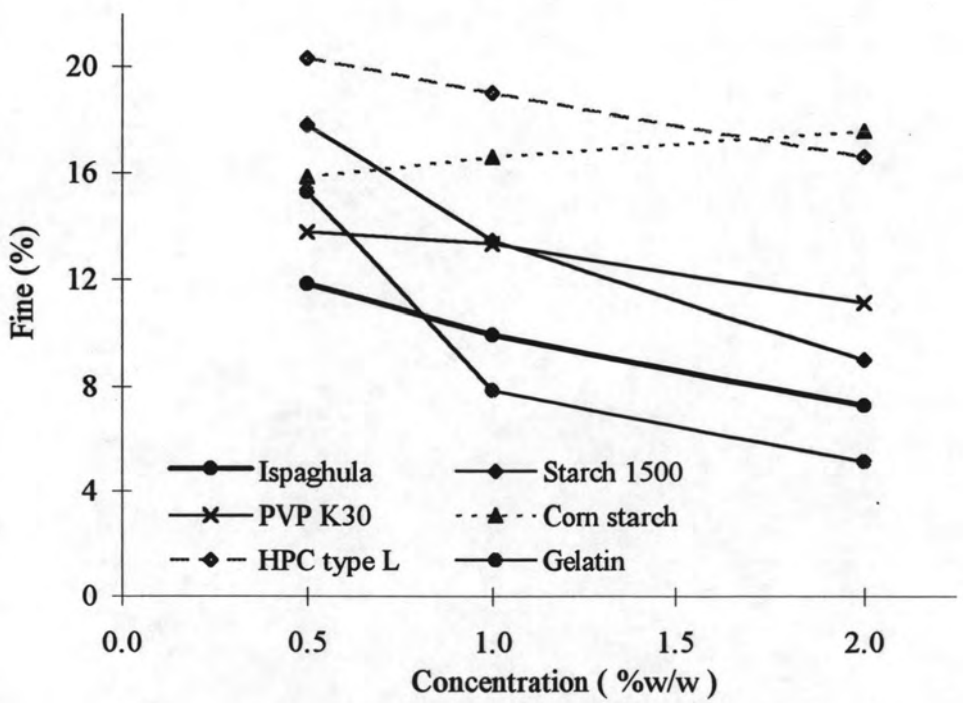


Figure 47 Percent Fine of Nicotinamide Granules Prepared by Solution Incorporation Method

binder concentration except corn starch by solution incorporation method and rank as follows ;

In dry incorporation method at
1 % w/w level: Ispaghula husk > Starch 1500® > PVP K30
2, 4 % w/w level: Ispaghula husk > PVP K30 > Starch 1500®

In solution incorporation method at
0.5 % w/w level : HPC type L > Starch 1500® > gelatin > corn starch > PVP K30 > Ispaghula husk
1 % w/w level : HPC type L >corn starch > Starch 1500® > PVP K 30 > Ispaghula husk > gelatin
2 % w/w level : corn starch > HPC type L > PVP K 30 > Starch 1500® > Ispaghula husk > gelatin

Comparing solution incorporation method with dry incorporation method, percent fine of granules were less. At low concentration (0.5% w/w), Ispaghula husk gave the least fine particles among six binders studied.

6. Comparison of Percent Friability

6.1 Paracetamol

The results from Table 7 and Figure 48,49 show the relation between the granule friability and binder concentration. The diminution of granule friability with the higher binder employed was obviously seen . The descending orders followed as ;

In dry incorporation method at
1,2 % w/w level: Starch 1500® > Ispaghula husk >PVP K30
4 % w/w level: Ispaghula husk > Starch 1500® > PVP K30

In solution incorporation method at
0.5 % w/w level : Starch 1500® >Ispaghula husk > HPC type L > PVP K 30 > corn starch > gelatin
1 % w/w level : Ispaghula husk > HPC type L > PVPK30 > Starch 1500® >corn starch > gelatin
2 % w/w level : Starch 1500® > corn starch > Ispaghula husk > PVP K 30 > gelatin >HPC type L

6.2 Nicotinamide

The similar results were observed (Table 8 and Figure 50, 51) that granule friability decrease with increasing of binder concentration . The declination of friability are in the following order ;

In dry incorporation method at
all concentrations : Starch 1500® > Ispaghula husk > PVP K30

In solution incorporation method at
0.5 % w/w level : Starch 1500® > corn starch > gelatin > HPC type L > Ispaghula husk > PVP K30
1, 2% w/w level : Starch 1500® > corn starch > HPC type L > gelatin > Ispaghula husk > PVP K 30

From the results in dry incorporation method , it could be noticed that granule prepared with Ispaghula husk possessed comparable friability with Starch 1500®. In solution incorporation method, granule friability of Ispaghula husk had pattern of declination like PVP K30.

7. Moisture Determination

Moisture content of all granules prepared with various binders and concentrations distributed in the range of 1.18 - 2.82 % and 1.09 - 2.12 % for paracetamol and nicotinamide , respectively (Table 7, 8).

Physical Properties of Tablets Prepared with Ispaghula Husk and Various Binders .

1. Weight Variation

The mean and standard deviation of tablet weight variation are shown in Table 9,10 .

2. Tablet Hardness

The mean and standard deviation of tablet hardness are presented in Table 9,10 . From the results presented in Figure 52, 53 they depicted the relationship between binder concentration and tablet hardness. Generally , it was found that the increase in binder concentration induced the increase in hardness of tablets .

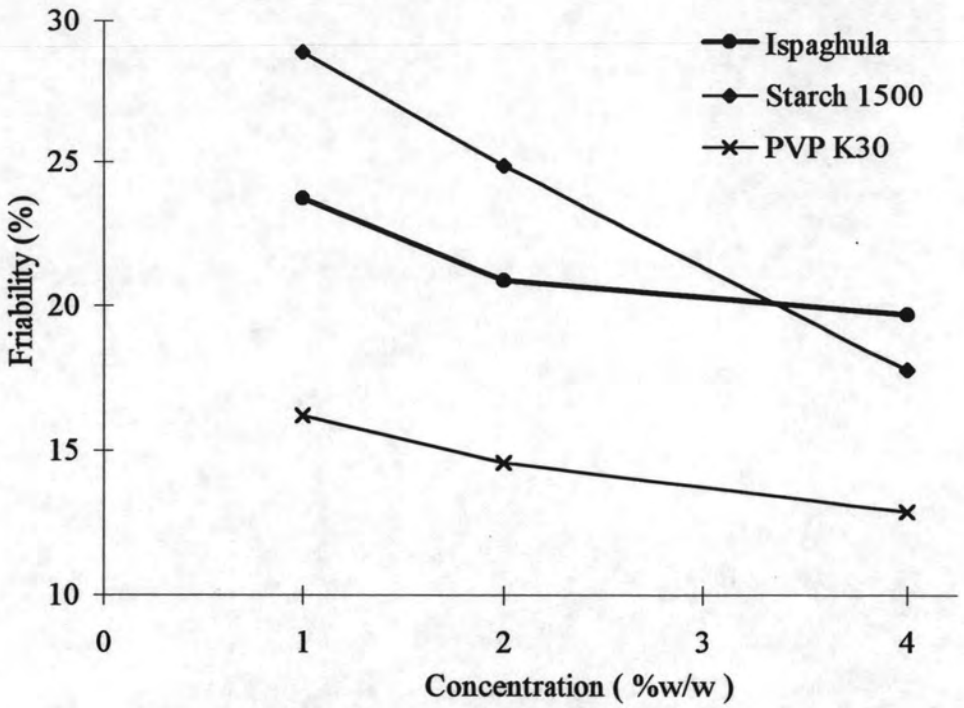


Figure 48 Fribility of Paracetamol Granules Prepared by Dry Incorporation Method

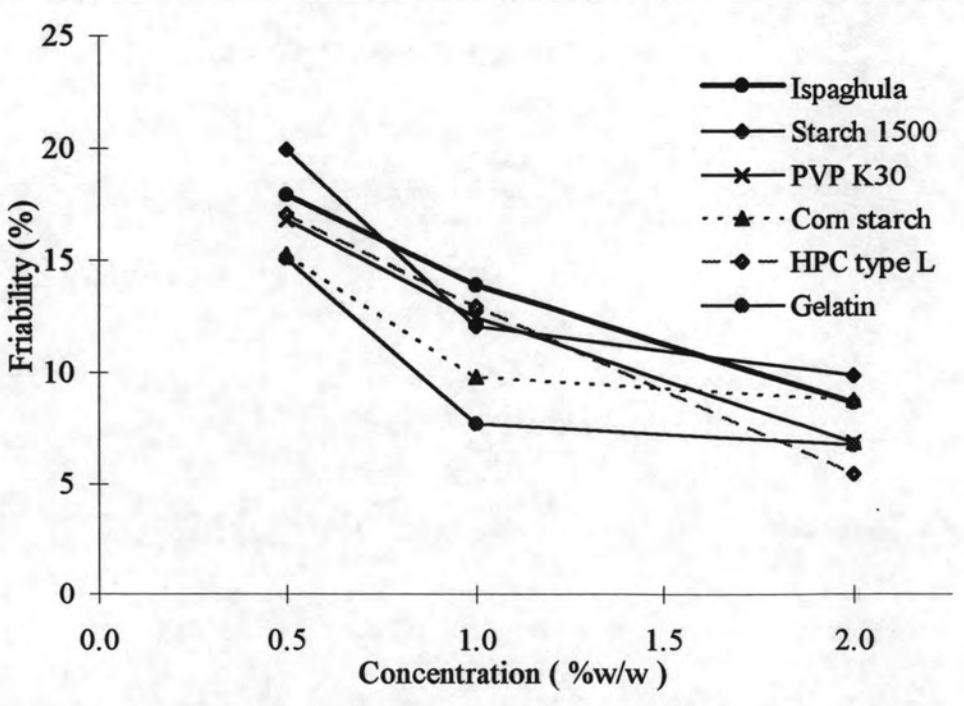


Figure 49 Friability of Paracetamol Granules Prepared by Solution Incorporation Method

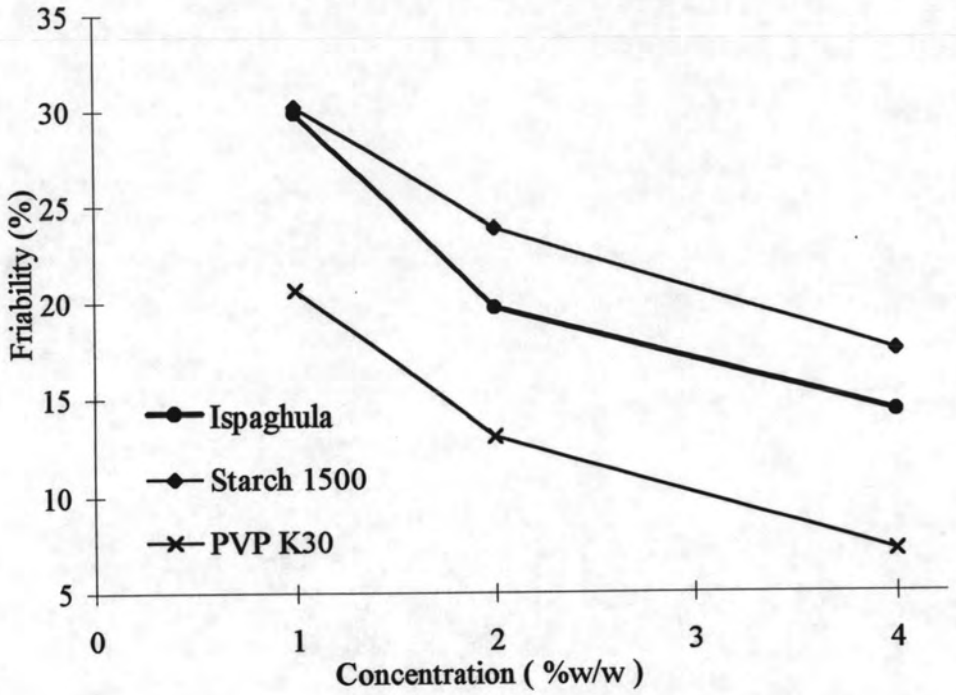


Figure 50 Friability of Nicotinamide Granules Prepared by Dry Incorporation Method

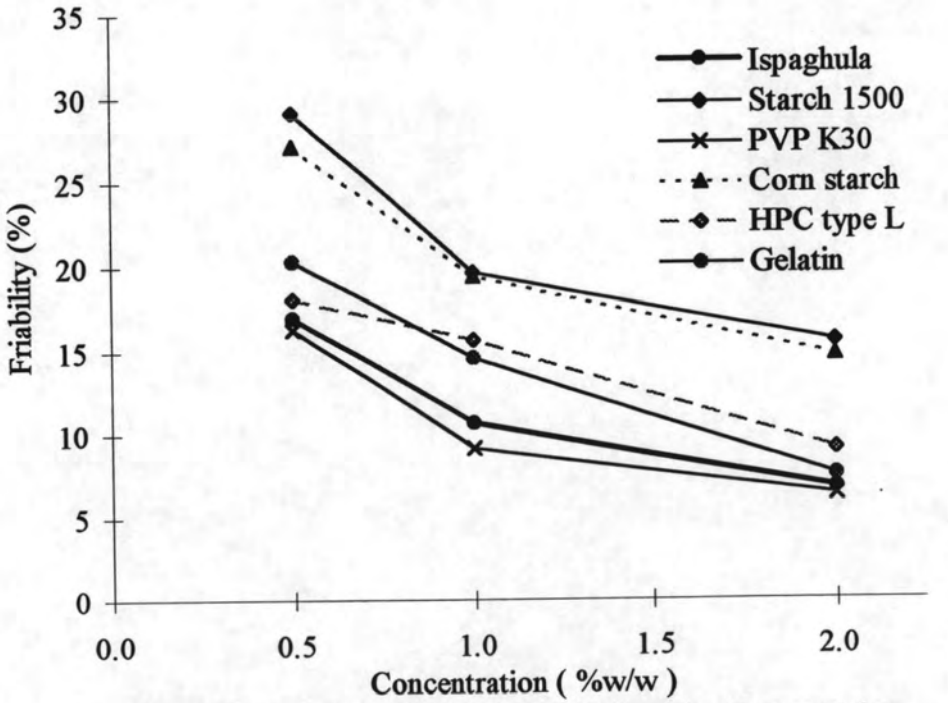


Figure 51 Friability of Nicotinamide Granules Prepared by Solution Incorporation Method

Table 7 Physical Properties of Paracetamol Granules Prepared with Various Binders and Concentrations

Paracetamol Granules Prepared by Solution Incorporation Method																	
Binder	Conc. (%w/w)	Granule Size [3] (μm)	Angle of Repose[2] (degree)	SD.	Flow Rate [3] (g/min)	SD.	Bulk density [3](g/ml)	SD.	Tap density [3] (g/ml)	SD.	Compressibility [3] (%)	SD.	Fine [3] (%)	SD.	Friabiity [3] (%)	SD.	Moisture Content [2] (%)
Blank	-	352.65	32.94	0.83	314.59	4.34	0.48	0.003	0.59	0.004	19.16	0.11	14.60	0.74	39.32	0.47	0.95
Ispaghula Husk	0.5	452.16	32.66	0.89	313.67	6.35	0.49	0.003	0.58	0.002	15.01	0.22	9.79	0.04	17.93	0.81	1.42
	1.0	526.03	34.07	0.63	298.90	3.35	0.48	0.000	0.56	0.003	16.22	0.38	6.68	0.71	13.90	0.26	1.75
	2.0	663.73	34.33	0.60	295.10	13.08	0.48	0.002	0.51	0.005	18.29	0.69	4.26	0.58	8.70	0.56	2.11
Polyvinyl pyrrolidone (PVP)	0.5	521.87	33.70	0.98	299.12	7.24	0.46	0.003	0.62	0.003	12.57	0.07	9.36	0.63	16.80	0.53	1.55
	1.0	567.36	35.43	0.71	263.23	8.19	0.51	0.003	0.59	0.003	13.59	0.29	5.28	0.61	12.47	0.25	1.74
	2.0	598.10	33.23	0.63	231.66	15.39	0.50	0.003	0.59	0.007	14.25	1.50	3.68	0.65	6.90	0.46	1.19
Pregelatinized Starch (Starch 1500(R))	0.5	441.85	32.71	1.47	283.54	8.87	0.45	0.001	0.59	0.002	14.47	0.52	9.07	1.06	19.93	0.67	1.40
	1.0	456.82	33.48	1.02	281.72	3.82	0.45	0.001	0.56	0.008	20.07	1.15	8.88	0.66	12.07	0.59	1.18
	2.0	518.37	35.43	0.71	274.41	2.90	0.47	0.003	0.55	0.002	20.16	0.18	8.81	0.56	9.90	0.60	1.77
Corn Starch	0.5	434.29	33.04	0.78	304.06	13.30	0.47	0.001	0.53	0.001	12.44	0.30	8.48	0.50	15.23	0.31	2.82
	1.0	486.32	33.18	0.52	271.51	2.98	0.44	0.002	0.52	0.007	15.44	0.64	7.93	0.68	9.80	0.30	2.33
	2.0	508.42	33.25	0.85	260.16	4.19	0.45	0.001	0.52	0.002	18.01	0.06	5.68	0.20	8.80	0.26	2.27
Hydroxypropyl Celluose (HPC type L)	0.5	523.77	32.36	1.00	334.59	2.66	0.49	0.000	0.56	0.010	13.58	1.54	7.41	0.72	17.03	0.68	1.55
	1.0	595.18	34.01	0.72	277.15	2.10	0.49	0.001	0.60	0.001	13.94	0.02	5.03	0.56	12.93	0.74	1.38
	2.0	572.49	33.80	0.85	272.37	12.06	0.48	0.001	0.60	0.002	19.53	0.31	5.11	0.36	5.50	0.80	1.91
Gelatin	0.5	517.52	33.53	0.78	276.18	1.15	0.48	0.001	0.59	0.000	13.19	0.11	7.54	0.43	15.07	1.24	1.89
	1.0	564.92	34.28	0.56	275.23	13.27	0.46	0.005	0.56	0.002	16.09	0.51	6.18	0.26	7.70	0.44	2.34
	2.0	548.50	34.34	0.80	271.23	14.94	0.48	0.003	0.58	0.002	16.16	0.27	4.54	0.14	6.80	0.40	2.08

Table 7 (Continue)

Paracetamol Granules Prepared by Dry Incorporation Method																
Binder	Conc. (%w/w)	Granule Size [3] (μm)	Angle of Repose [2] (degree)	SD.	Flow Rate [3] (g /min)	SD.	Bulk density [3] (g/ml)	SD.	Tap density [3] (g/ml)	SD.	Compressibility [3] (%)	SD.	Fine [3] (%)	SD.	Friability [3] (%)	SD.	Moisture Content [2] (%)
Blank	-	352.65	32.94	0.83	314.59	4.34	0.48	0.003	0.59	0.004	19.16	0.11	14.60	0.74	39.32	0.47	0.95
Ispaghula Husk	1.0	452.16	33.33	0.69	244.30	4.80	0.48	0.002	0.57	0.001	14.73	0.32	6.54	0.74	23.73	0.31	1.52
	2.0	416.78	33.25	0.95	268.88	7.14	0.48	0.003	0.58	0.002	17.13	0.23	11.23	0.69	20.87	0.49	1.76
	4.0	306.29	32.86	1.40	287.58	4.04	0.47	0.001	0.58	0.000	19.13	0.10	18.33	0.57	19.67	1.39	2.24
Polyvinyl pyrrolidone (PVP)	1.0	505.61	32.92	1.68	164.53	2.99	0.48	0.002	0.53	0.000	10.34	0.28	4.30	0.37	16.20	0.26	1.43
	2.0	512.22	33.78	1.08	154.43	5.36	0.47	0.002	0.52	0.007	10.81	1.43	3.69	0.25	14.57	0.25	1.64
	4.0	634.99	34.00	1.13	145.47	6.08	0.46	0.000	0.50	0.004	12.21	0.58	1.80	0.94	12.87	0.70	1.34
Pregelatinized Starch (Starch 1500$^{(R)}$)	1.0	448.53	33.52	0.79	294.28	4.51	0.47	0.002	0.53	0.004	12.11	0.66	5.64	0.70	28.90	1.18	1.38
	2.0	472.33	33.69	1.51	237.71	1.53	0.46	0.003	0.53	0.005	13.69	0.94	4.42	0.80	24.87	0.59	1.58
	4.0	481.85	33.79	0.95	183.92	4.01	0.46	0.005	0.53	0.005	13.98	0.21	3.68	0.10	17.77	0.57	1.19

Note : 2 Data was averaged from two determinations
3 Data was averaged from three determinations

Table 8 Physical Properties of Nicotinamide Granules Prepared with Various Binders and Concentrations

Nicotinamide Granule Prepared by Solution Incorporation Method																	
Binder	Conc. (%w/w)	Granule Size [3] (μm)	Angle of Repose [2] (degree)	SD.	Flow Rate [3] (g/min)	SD.	Bulk density [3] (g/ml)	SD.	Tap density [3] (g/ml)	SD.	Compressibility [3] (%)	SD.	Fine [3] (%)	SD.	Friability [3] (%)	SD.	Moisture Content [2] (%)
Blank	-	455.74	31.78	0.92	418.61	1.11	0.50	0.006	0.62	0.019	18.76	1.485	23.73	0.671	36.40	1.929	1.35
Ispaghula Husk	0.5	624.86	33.95	0.94	288.66	6.10	0.55	0.001	0.65	0.003	16.00	0.384	11.83	0.576	17.00	0.346	1.37
	1.0	628.84	33.47	1.08	357.72	5.07	0.59	0.001	0.70	0.006	15.36	0.749	9.93	0.391	10.67	0.611	1.66
	2.0	642.26	32.51	1.42	361.13	5.02	0.57	0.000	0.67	0.001	14.29	0.012	7.29	0.820	6.77	0.586	2.07
Polyvinyl pyrrolidone (PVP)	0.5	517.34	33.55	1.23	339.48	3.31	0.46	0.000	0.58	0.004	20.72	0.577	13.77	0.166	16.30	0.854	1.35
	1.0	647.13	33.35	0.63	321.30	8.82	0.46	0.011	0.54	0.011	15.87	0.660	13.33	0.101	9.13	0.404	1.62
	2.0	676.72	32.16	1.04	280.41	3.78	0.46	0.001	0.54	0.004	16.42	0.577	11.13	0.214	6.33	0.503	1.88
Pregelatinized Starch (Starch 1500(R))	0.5	463.52	33.61	0.67	311.56	1.82	0.45	0.005	0.62	0.018	16.12	1.899	17.83	0.325	29.17	0.651	1.09
	1.0	507.39	33.95	1.07	239.00	3.34	0.42	0.003	0.54	0.001	12.99	0.616	13.46	0.188	19.67	0.764	1.46
	2.0	620.46	34.32	1.61	260.83	4.60	0.40	0.005	0.49	0.007	13.48	0.653	9.00	0.198	15.60	0.656	1.56
Corn Starch	0.5	504.27	31.77	1.22	344.68	3.02	0.56	0.003	0.59	0.002	17.83	0.210	15.85	0.000	27.17	0.757	2.12
	1.0	508.19	33.68	0.90	298.05	3.89	0.54	0.003	0.60	0.014	17.27	1.370	16.60	0.000	19.43	0.404	1.80
	2.0	592.62	33.67	0.96	264.03	1.74	0.49	0.001	0.58	0.002	11.60	0.100	17.60	0.000	14.77	0.493	1.45
Hydroxypropyl Celluose (HPC type L)	0.5	476.24	33.73	1.30	402.72	4.42	0.43	0.005	0.56	0.010	22.01	0.511	20.33	0.052	18.10	0.624	1.76
	1.0	578.31	33.56	0.97	255.32	1.25	0.42	0.009	0.50	0.015	15.42	0.883	19.03	0.413	15.67	0.503	1.60
	2.0	626.71	34.13	0.68	304.32	1.61	0.42	0.003	0.49	0.001	15.11	0.328	16.63	0.319	9.10	0.529	1.82
Gelatin	0.5	525.05	34.49	0.96	274.30	2.80	0.47	0.006	0.57	0.010	18.04	1.193	15.31	0.072	20.33	1.102	1.08
	1.0	623.74	35.13	1.13	236.40	2.91	0.42	0.011	0.48	0.013	12.50	0.130	7.84	0.113	14.60	0.265	1.34
	2.0	583.66	34.67	1.81	258.38	4.03	0.45	0.002	0.55	0.005	16.63	0.962	5.12	0.243	7.53	0.651	1.44

Table 8 (Continue)

Nicotinamide Granule Prepared by Dry Incorporation Method																
Binder	Conc. (%w/w)	Granule Size [3] (μm)	Angle of Repose[2] (degree)	SD.	Flow Rate [3] (g /min)	SD.	Bulk density [3](g/ml)	SD.	Tap density [3] (g/ml)	SD.	Compressibility [3] (%)	SD.	Fine [3] (%)	SD.	Friability [3] (%)	SD.	Moisture Content [2] (%)
Blank	-	455.74	31.78	0.92	418.61	1.11	0.50	0.006	0.62	0.019	18.76	1.485	23.73	0.671	36.40	1.93	1.35
Ispaghula Husk	1.0	506.96	33.70	0.91	375.06	5.86	0.50	0.002	0.60	0.001	16.71	0.429	18.70	0.363	29.83	1.35	1.41
	2.0	618.45	32.62	0.92	428.79	11.92	0.49	0.003	0.62	0.009	21.18	0.737	17.53	1.475	19.70	1.50	1.54
	4.0	639.06	33.20	0.59	378.03	6.60	0.48	0.002	0.66	0.006	18.45	0.954	16.23	0.375	14.33	1.06	1.87
Polyvinyl pyrrolidone (PVP)	1.0	599.86	32.08	0.68	380.59	4.89	0.50	0.003	0.58	0.006	14.70	0.439	11.01	0.628	20.63	0.67	1.22
	2.0	634.57	32.36	0.96	304.31	0.80	0.49	0.003	0.58	0.009	15.66	0.739	13.53	0.303	13.10	0.82	1.44
	4.0	641.84	33.55	0.71	255.36	3.90	0.48	0.002	0.61	0.001	16.55	0.158	8.59	0.690	7.17	0.84	1.66
Pregelatinized Starch (Starch 1500®)	1.0	463.52	32.29	0.72	249.21	5.32	0.46	0.001	0.56	0.004	18.19	0.597	14.68	0.374	30.20	1.18	1.16
	2.0	617.34	32.85	0.79	247.11	6.52	0.45	0.005	0.52	0.010	13.84	2.669	12.48	0.217	23.87	0.67	1.54
	4.0	648.59	33.80	0.87	179.57	2.08	0.42	0.003	0.49	0.003	15.25	0.189	7.38	0.313	17.47	1.30	1.77

Note : 2 Data was averaged from two determinations
3 Data was averaged from three determinations

2.1 Paracetamol

Consideration through the data of statistic analysis, it was found that types of binders significantly effect on hardness of paracetamol tablets at the same concentration employed (P < O.O5, F > F crit). The ranks of hardness decreased as follow;

In dry incorporation method at
1,2 % w/w level : PVP K30 > Ispaghula husk >Starch 1500®
4 % w/w level : PVP K30 > Starch 1500® > Ispaghula husk

In solution incorporation method at
0.5 % w/w level: Ispaghula husk > gelatin > HPC type L ≅ PVP K30 > corn starch ≅ Starch 1500®
1 % w/w level : PVP K30 ≅ HPC type L >Ispaghula husk > gelatin > corn starch > Starch 1500®
2 % w/w level : HPC type L > PVPK30 > Ispaghula husk > gelatin > corn starch > Starch 1500®

Comparative data showed that Ispaghula husk give the hardest tablet at low concentration employed. In addition the hardness of tablets produced by solution incorporation method were greater than dry incorporation method.

As was expected, capping was occurred during tabletting blank granules. Consequently, no evaluated data was obtained.

2.2 Nicotinamide

According to the data from statistic value, at the same binder concentration utilized, the influence of binder types on hardness of nicotinamide were significantly different (P < O.O5, F > F crit). The hardness of nicotinamide tablets decreased as follows (Figure 53);

In dry incorporation method at
all concentrations : PVP K30 >Ispaghula husk > Starch 1500® > Blank

In solution incorporation method at
0.5 % w/w level: gelatin > Ispaghula husk ≅ PVP K30 ≅ HPC type L ≅ corn starch ≅ Starch 1500® > Blank
1 % w/w level: HPC type L > PVP K30 > gelatin ≅ Ispaghula husk >corn starch ≅ Starch 1500®> Blank
2 % w/w level: HPC type L > PVP K 30 > Ispaghula husk ≅ gelatin > Starch 1500® ≅ corn starch > Blank

The tablet produced by dry incorporation method had inferior hardness to solution incorporation method .

3. Tablet Thickness

The mean and standard deviation of tablet hardness are presented in Table 9, 10. The standard deviation of all tablets never exceeds ± 0.05.

4. Tablet Tensile Strength

The results of tablet tensile strength are reported in Table 9,10. Tensile strength of tablets increased with the increasing amount of binder employed (Figure 54, 55). This manner is corresponding to the result of tablet hardness .

4.1 Paracetamol

For all cases the tensile strength ranged from 5.18 to 15.84 kp/cm^2 . The tendency of high tensile strength was found on the tablet prepared with HPC type L and PVP K 30. On the other hand , corn starch and Starch 1500® showed the lowest value. From this result , tablet produced by solution incorporation method possessed slightly greater tensile strength than dry incorporation method .

4.2 Nicotinamide

The range of tensile strength were between 5.16-17.37 kp/cm^2. According to the results presented in Table 10, HPC type L gave the maximum tensile strength . As comparing tensile strength of tablet produced by solution incorporation method with dry incorporation method, it could be noticed that tablets produced by the first method had tensile strength more than the latter.

Table 9 Physical Properties of Paracetamol Tablets Prepared with Various Binders and Concentrations

Paracetamol Tablets Prepared by Solution Incorporation Method																		
Binder	Conc. (%w/w)	Average Weight [1] (mg)	SD.	Thickness [2] (mm)	SD.	Hardness [2] (kp)	SD.	Friability [3] (%)	SD.	Porosity [2] (%)	SD.	Tensile Strength [2] (kp/cm^2)	SD.	Disintegration Time [4] (min)	SD.	T 50 % of dissolved drug [3] (min)	SD.	Labeled Amount [5] (%)	Binder Index (kp x 10^{-2}/cm^2.min)
Blank	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ispaghula Husk	0.5	499.99	4.76	3.23	0.02	5.21	0.12	1.11	0.11	4.11	0.08	8.34	0.94	42.87	2.52	241.80	5.53	99.95	12.77
	1.0	502.78	3.18	3.28	0.02	6.18	0.18	0.91	0.10	4.08	0.16	9.57	1.26	59.33	1.58	272.88	7.42	100.42	15.72
	2.0	499.65	5.50	3.25	0.03	6.55	0.08	0.83	0.06	4.36	0.18	10.44	0.87	64.04	7.36	330.45	14.46	99.96	16.60
Polyvinyl pyrrolidone (PVP)	0.5	499.40	6.21	3.26	0.03	4.28	0.07	1.14	0.09	4.48	0.19	6.85	0.77	16.12	2.22	57.13	1.78	99.84	47.12
	1.0	497.70	5.74	3.25	0.03	6.46	0.06	1.02	0.07	4.36	0.14	9.94	0.45	27.97	1.65	67.62	0.95	99.65	62.84
	2.0	496.45	5.62	3.20	0.02	9.07	0.11	0.76	0.02	5.13	0.21	14.36	1.15	33.58	0.81	102.01	3.66	99.33	95.02
Pregelatinized Starch (Starch 1500$^{(R)}$)	0.5	499.68	4.55	3.25	0.02	3.97	0.09	Capping		3.16	0.07	5.18	0.82	30.27	0.56	132.82	5.36	99.94	-
	1.0	501.74	4.01	3.30	0.01	4.24	0.09	Capping		3.92	0.12	6.57	0.48	33.64	1.98	172.35	9.14	100.42	-
	2.0	498.34	3.79	3.24	0.01	5.07	0.11	1.25	0.07	3.57	0.09	7.95	0.29	47.94	1.50	243.60	13.70	99.67	9.32
Corn Starch	0.5	501.70	3.58	3.30	0.03	4.03	0.07	Capping		3.56	0.09	5.24	0.75	30.34	0.95	42.73	1.93	100.34	-
	1.0	498.62	4.95	3.22	0.03	4.35	0.04	Capping		3.30	0.07	6.82	1.08	35.69	0.98	66.49	1.49	99.72	-
	2.0	504.52	3.38	3.30	0.01	5.57	0.09	1.16	0.04	3.57	0.18	7.57	0.76	44.13	2.67	286.19	13.45	100.11	8.14
Hydroxypropyl Celluose (HPC type L)	0.5	497.62	3.51	3.19	0.02	4.33	0.08	1.17	0.05	4.57	0.03	6.98	0.84	8.49	0.58	77.97	2.90	99.17	34.97
	1.0	500.76	4.44	3.24	0.02	6.38	0.07	0.87	0.06	4.47	0.22	9.92	0.33	11.49	0.86	113.67	4.31	100.19	44.84
	2.0	500.60	4.61	3.23	0.02	10.14	0.18	0.62	0.03	4.91	0.16	15.84	0.97	25.74	1.22	132.63	3.46	100.21	94.58
Gelatin	0.5	496.84	4.67	3.21	0.02	4.66	0.08	1.73	0.06	4.55	0.21	7.33	0.12	27.85	1.97	78.95	5.21	99.45	24.42
	1.0	496.77	3.42	3.24	0.02	5.33	0.09	1.05	0.08	4.42	0.18	8.45	0.38	36.81	0.92	98.85	2.71	99.34	35.98
	2.0	503.72	3.17	3.24	0.03	6.13	0.15	0.94	0.09	4.36	0.15	9.64	0.72	28.69	0.71	122.14	8.49	100.88	36.61

Table 9 (Continue)

Paracetamol Tablets Prepared by Dry Incorporation Method																		
Binder	Conc. (%w/w)	Average Weight [1] (mg)	SD.	Thickness [2] (mm)	SD.	Hardness [2] (kp)	SD.	Friability [3] (%)	SD.	Porosity [2] (%)	SD.	Tensile Strength [2] (kp/cm^2)	SD.	Disintegration Time [4] (min)	SD.	T 50 % of dissolved drug [3] (min)	SD.	Labeled Amount [5] (%)	Binder Index (kp x 10^{-2}/cm^2.min)
Blank	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ispaghula Husk	1.0	497.18	4.40	3.26	0.03	4.72	0.09	2.34	0.07	4.27	0.06	7.37	0.11	46.09	2.85	159.17	3.92	99.44	8.45
	2.0	502.09	3.54	3.31	0.02	5.06	0.09	1.32	0.12	4.52	0.14	7.75	0.62	64.02	2.87	202.73	5.49	100.64	13.09
	4.0	498.76	2.98	3.27	0.01	5.29	0.08	0.98	0.05	4.60	0.09	8.26	0.74	74.96	2.46	254.77	6.14	99.75	15.22
Polyvinyl pyrrolidone (PVP)	1.0	501.10	4.42	3.26	0.03	5.72	0.05	1.08	0.08	4.67	0.17	8.02	1.02	20.05	1.39	55.22	2.38	98.22	62.80
	2.0	496.24	3.71	3.24	0.03	8.52	0.09	0.82	0.04	4.89	0.11	12.23	0.41	27.51	1.52	77.50	1.86	99.25	94.10
	4.0	500.12	4.30	3.24	0.01	9.73	0.08	0.69	0.12	5.27	0.24	15.26	0.53	32.86	2.45	109.01	2.65	100.18	106.92
Pregelatinized Starch (Starch1500$^{(R)}$)	1.0	497.68	3.21	3.25	0.02	4.14	0.16	Capping		4.59	0.05	6.44	0.24	17.44	1.90	129.87	5.30	99.54	-
	2.0	498.95	4.48	3.24	0.02	4.85	0.06	2.21	0.20	4.43	0.13	7.62	0.15	35.48	1.74	169.87	4.17	99.89	8.99
	4.0	505.76	3.18	3.20	0.02	5.37	0.04	1.56	0.15	4.68	0.10	8.51	0.36	36.22	3.40	272.90	14.29	101.13	9.36

Note : 1 mean data was averaged from twenty determinations
2 mean data was averaged from ten determinations
3 mean data was averaged from three determinations
4 mean data was averaged from six determinations
5 mean data was averaged from two determinations

Table 10 Physical Properties of Nicotinamide Tablets Prepared with Various Binders and Concentrations

Nicotinamide Tablets Prepared by Solution Incorporation Method																			
Binder	Conc. (%w/w)	Average Weight [1] (mg)	SD.	Thickness [2] (mm)	SD.	Hardness [2] (kp)	SD.	Friability [3] (%)	SD.	Porosity [2] (%)	SD.	Tensile Strength [2] (kp/cm^2)	SD.	Disintegration Time [4] (min)	SD.	T 50 % of dissolved drug [3] (min)	SD.	Labeled Amount [5] (%)	Binder Index ($kp \times 10^{-2}/cm^2 \cdot min$)
Blank	-	501.45	4.22	3.05	0.03	4.04	0.22	1.77	0.15	4.08	0.05	6.74	0.91	4.47	0.10	9.06	0.19	100.32	1.72
Ispaghula Husk	0.5	503.04	5.97	3.06	0.03	5.14	0.16	0.85	0.10	4.81	0.17	8.51	0.87	5.37	0.22	13.96	0.55	100.74	3.45
	1.0	498.59	5.30	3.03	0.03	6.38	0.15	0.62	0.08	4.30	0.05	10.62	0.69	6.38	0.17	19.67	0.23	99.82	3.75
	2.0	500.76	5.99	3.03	0.05	7.24	0.29	0.48	0.04	4.76	0.09	12.03	0.62	7.88	0.23	20.96	0.79	100.23	5.69
Polyvinyl pyrrolidone (PVP)	0.5	496.59	4.64	3.06	0.04	5.13	0.18	0.78	0.07	5.07	0.13	8.51	1.04	4.27	0.12	9.20	0.18	99.47	6.01
	1.0	500.12	5.16	3.06	0.03	7.06	0.18	0.67	0.06	5.16	0.04	11.62	1.21	4.85	0.10	9.50	0.23	100.04	9.42
	2.0	501.46	4.50	3.06	0.03	10.08	0.19	0.54	0.03	6.53	0.30	16.60	0.48	5.25	0.07	9.73	0.21	100.33	20.64
Pregelatinized Starch (Starch 1500 (R))	0.5	500.25	5.28	3.05	0.02	4.96	0.21	1.20	0.08	4.59	0.05	8.17	0.68	6.07	0.17	16.92	0.48	100.11	1.85
	1.0	499.40	4.69	3.09	0.03	5.11	0.17	0.94	0.14	4.91	0.16	8.33	1.29	5.58	0.12	22.18	1.03	99.68	1.96
	2.0	500.38	5.29	3.07	0.02	6.33	0.12	0.71	0.05	4.64	0.10	10.37	1.36	7.25	0.18	23.28	0.55	100.02	2.91
Corn Starch	0.5	503.32	4.19	3.06	0.02	4.98	0.20	1.31	0.03	3.91	0.07	8.18	0.82	5.62	0.12	12.81	0.02	100.76	1.91
	1.0	500.90	4.73	3.07	0.03	5.23	0.18	1.12	0.07	4.53	0.06	8.62	0.45	6.32	0.10	17.27	0.34	100.28	2.02
	2.0	499.18	3.75	3.05	0.03	6.17	0.17	0.89	0.13	4.31	0.13	10.22	0.48	8.38	0.23	20.74	0.84	99.89	2.39
Hydroxypropyl Celluose (HPC type L)	0.5	497.67	5.66	3.03	0.03	5.07	0.17	0.83	0.10	4.18	0.09	8.45	0.88	4.47	0.17	9.56	0.33	99.65	4.45
	1.0	498.60	6.72	3.05	0.03	7.31	0.16	0.56	0.07	4.59	0.07	12.15	0.47	4.90	0.18	10.01	0.42	99.82	9.95
	2.0	501.74	5.51	3.08	0.02	10.65	0.16	0.45	0.05	4.79	0.26	17.37	0.61	6.35	0.23	13.51	0.31	100.44	13.69
Gelatin	0.5	497.92	4.79	3.05	0.02	5.33	0.18	0.90	0.08	4.69	0.17	8.84	1.12	4.37	0.22	8.87	0.17	99.75	5.19
	1.0	501.46	4.76	3.09	0.02	6.46	0.18	0.74	0.09	4.33	0.16	10.51	1.30	4.78	0.28	9.08	0.53	100.54	6.77
	2.0	497.85	4.03	3.05	0.02	7.19	0.23	0.62	0.11	4.52	0.07	11.92	0.80	5.12	0.18	11.99	0.49	99.47	7.25

Table 10 (Continue)

Nicotinamide Tablets Prepared by Dry Incorporation Method																	
Binder	Conc. (%w/w)	Average Weight [1] (mg)	SD.	Thickness [2] (mm)	SD.	Hardness [2] (kp)	SD.	Friability [3] (%)	SD.	Porosity [2] (%)	SD.	Tensile Strength [2] (kp/cm^2)	SD.	Disintegration Time [4] (min)	SD.	T 50 % of dissolved drug [3] (min)	SD.	Labeled Amount [5] (%)	Binder Index ($kp \times 10^{-2}/cm^2 \cdot min$)
Blank	-	501.45	4.22	3.05	0.03	4.04	0.22	1.77	0.15	4.08	0.05	6.74	0.91	4.40	0.10	9.06	0.19	100.32	1.72
Ispaghula Husk	1.0	497.375	6.74	3.00	0.03	5.69	0.14	0.85	0.04	4.33	0.06	9.75	0.13	7.42	0.40	18.29	1.48	99.56	2.72
	2.0	499.60	7.47	3.07	0.02	6.76	0.12	0.66	0.09	4.53	0.13	11.25	0.46	8.52	0.12	26.89	0.84	99.94	2.87
	4.0	499.43	7.69	3.06	0.03	7.28	0.15	0.53	0.18	4.85	0.11	12.14	0.85	17.17	0.67	37.45	0.93	99.78	2.97
Polyvinyl pyrrolidone (PVP)	1.0	500.93	5.83	3.04	0.03	6.73	0.21	0.75	0.05	4.02	0.17	11.37	1.08	4.68	0.20	9.60	0.27	100.21	6.35
	2.0	497.37	4.69	2.99	0.01	9.36	0.18	0.61	0.14	4.85	0.09	15.84	1.16	5.97	0.27	10.03	0.32	99.45	12.56
	4.0	500.13	4.67	3.03	0.02	10.25	0.26	0.52	0.16	4.97	0.18	17.13	0.67	6.90	0.17	10.64	0.54	100.10	15.38
Pregelatinized Starch (Starch 1500 (R))	1.0	495.80	4.46	3.01	0.01	5.04	0.19	1.27	0.13	4.61	0.05	5.16	0.98	6.92	0.27	9.87	0.12	99.18	1.90
	2.0	497.39	4.66	3.02	0.03	5.48	0.17	0.86	0.09	4.42	0.14	7.84	0.35	7.73	0.37	14.66	0.37	98.97	2.75
	4.0	498.14	5.42	3.04	0.03	6.12	0.18	0.69	0.10	4.69	0.14	9.25	0.73	14.62	0.20	16.96	0.63	99.70	3.71

Note : 1 mean data was averaged from twenty determinations
2 mean data was averaged from ten determinations
3 mean data was averaged from three determinations
4 mean data was averaged from six determinations
5 mean data was averaged from two determinations

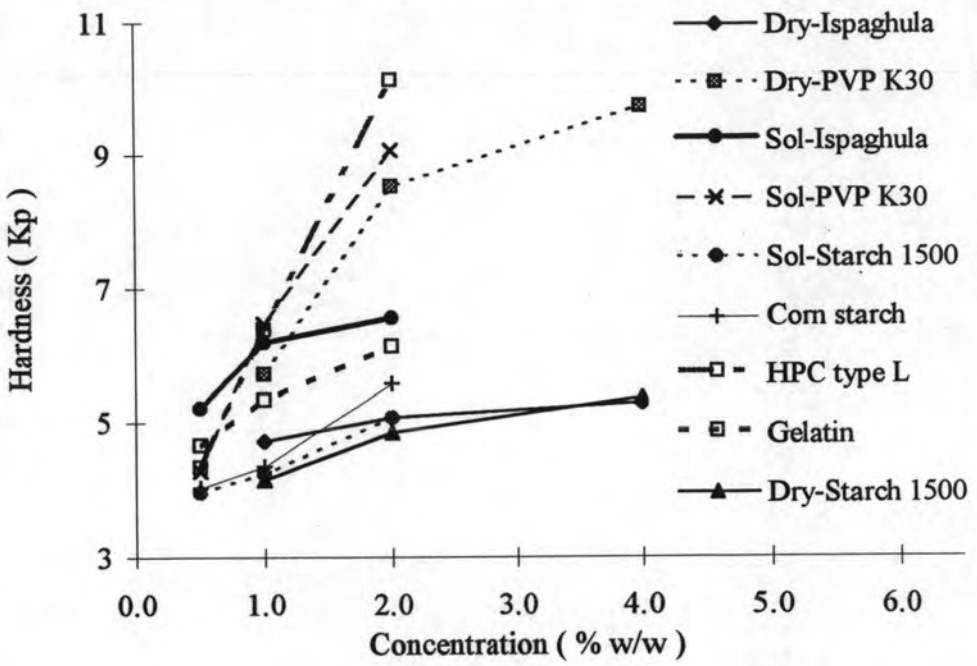


Figure 52 Effect of Various Binders and Concentrations on Hardness of Paracetamol Tablets

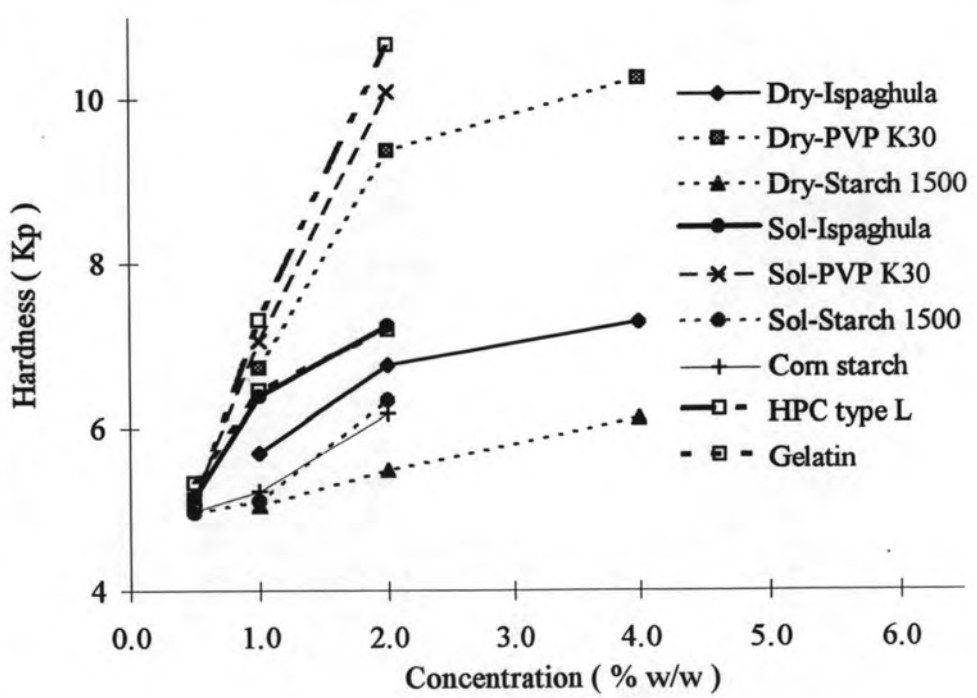


Figure 53 Effect of Various Binders and Concentrations on Hardness of Nicotinamide Tablets

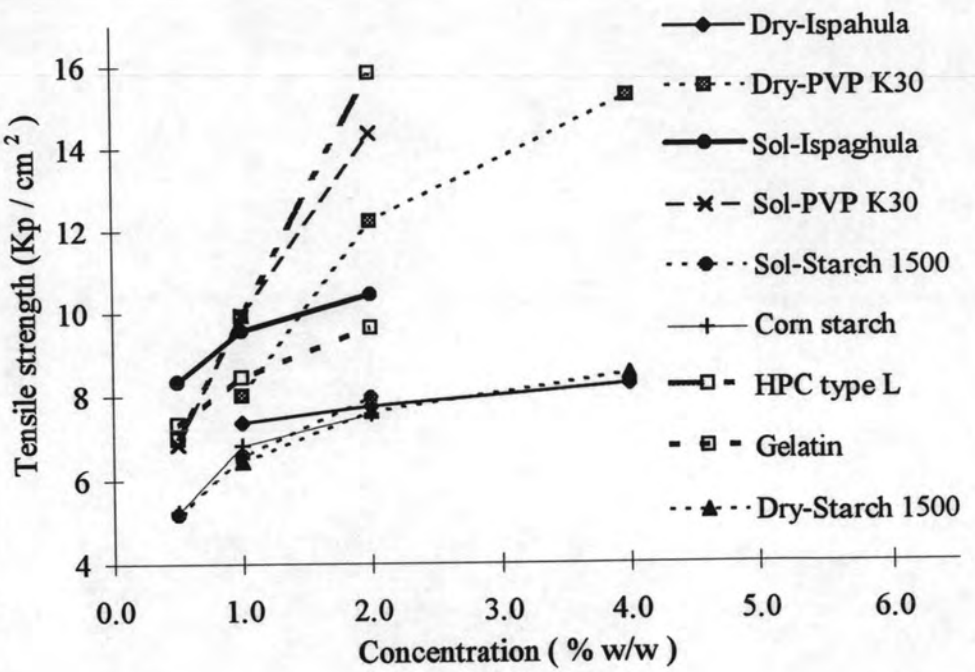


Figure 54 Effect of Various Binders and Concentrations on Tensile strength of Paracetamol Tablets

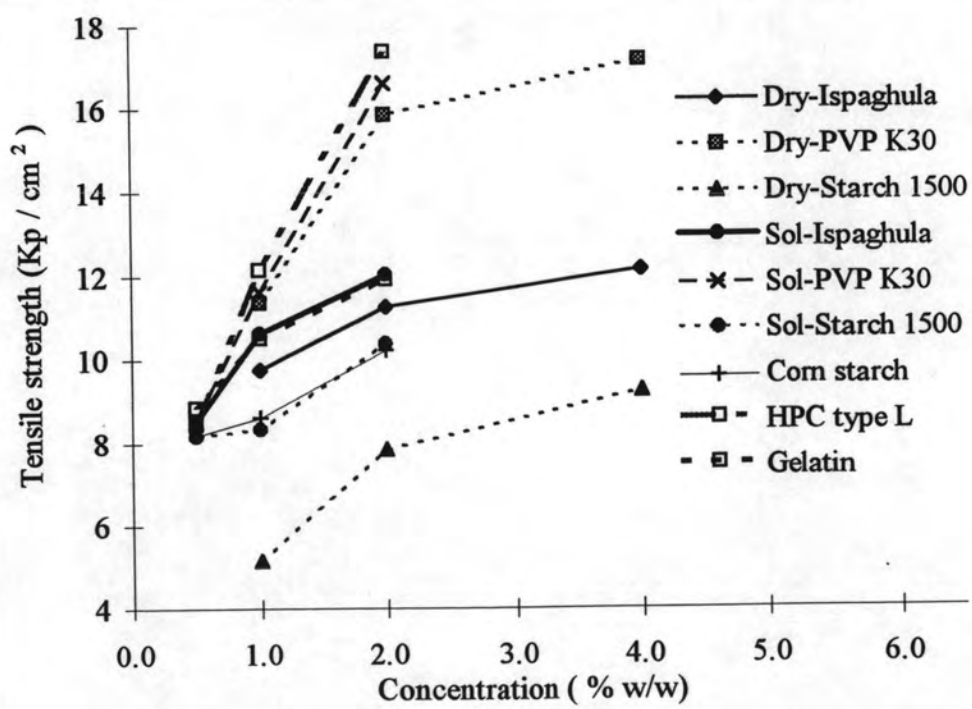


Figure 55 Effect of Various Binders Concentrations on Tensile strength of Nicotinamide Tablets

5. Tablet Friability

The result which shown in Table 9, 10 and Figure 56, 57 obviously revealed that increasing binder concentration, decreasing friability of tablets .

5.1 Paracetamol

The relationship between binder concentration and tablet friability are presented in Figure 76. The friability of paracetamol tablets decreased as follows ;

In solution incorporation method at
0.5 % w/w level : corn starch (capping) ≅ Starch 1500® (capping) > gelatin > HPC type L > PVP K 30 > Ispaghula husk
1 % w/w level : corn starch (capping) ≅ Starch 1500® (capping) > gelatin > PVP K 30 > Ispaghula husk > HPC type L
2 % w/w level : Starch 1500® > corn starch > gelatin > Ispaghula husk > PVP K 30 > HPC type L

It could be noted that at 2 % w/w level friability of tablets were less than 1% except for corn starch and Starch 1500®. In dry incorporation method , only tablets prepared with PVP K30 at 2 and 4 % w/w as well as Ispaghula husk 4 % gave friability less than 1 % .

Moreover , it could be noticed that tablet prepared by dry incorporation method obviously possessed more friable than the other incorporation method .

5.2 Nicotinamide

The same relationship between tablet friability and binder concentration were observed (Figure 57). It is interesting that friability of nicotinamide tablets produced with various binder at all concentration studies were less than paracetamol tablets . Friability of tablets were decreased as follows ;

In solution incorporation method at
0.5 % w/w level : corn starch > Starch 1500® > gelatin > Ispaghula husk > HPC type L > PVP K30
1, 2 % w/w level : corn starch > Starch 1500® > gelatin > PVP K 30 >Ispaghula husk > HPC type L

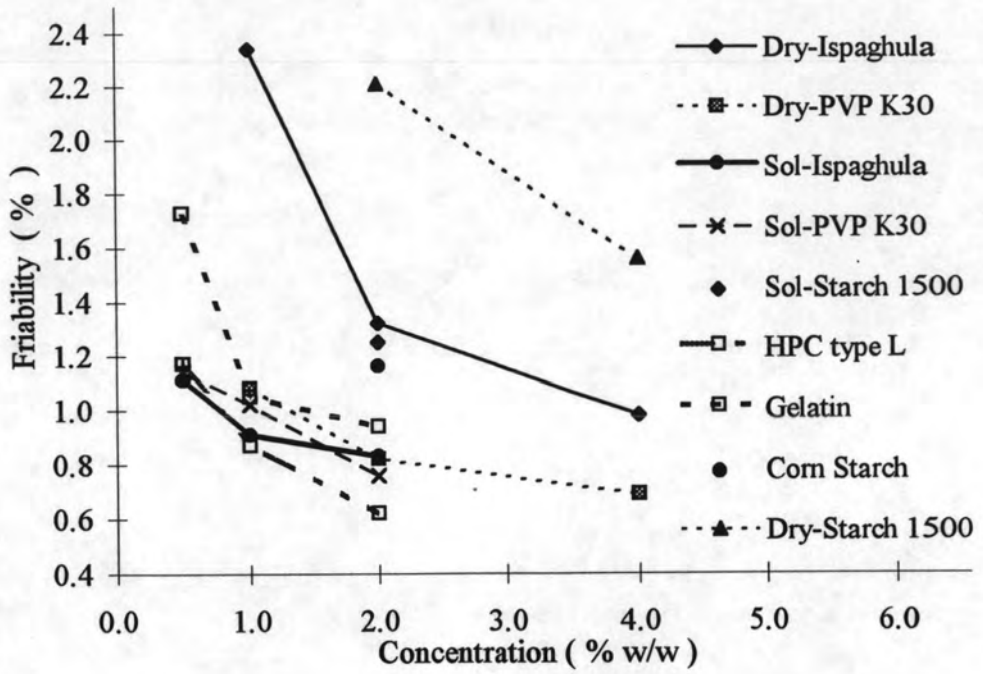


Figure 56 Effect of Various Binders and Concentrations on Friability of Paracetamol Tablets

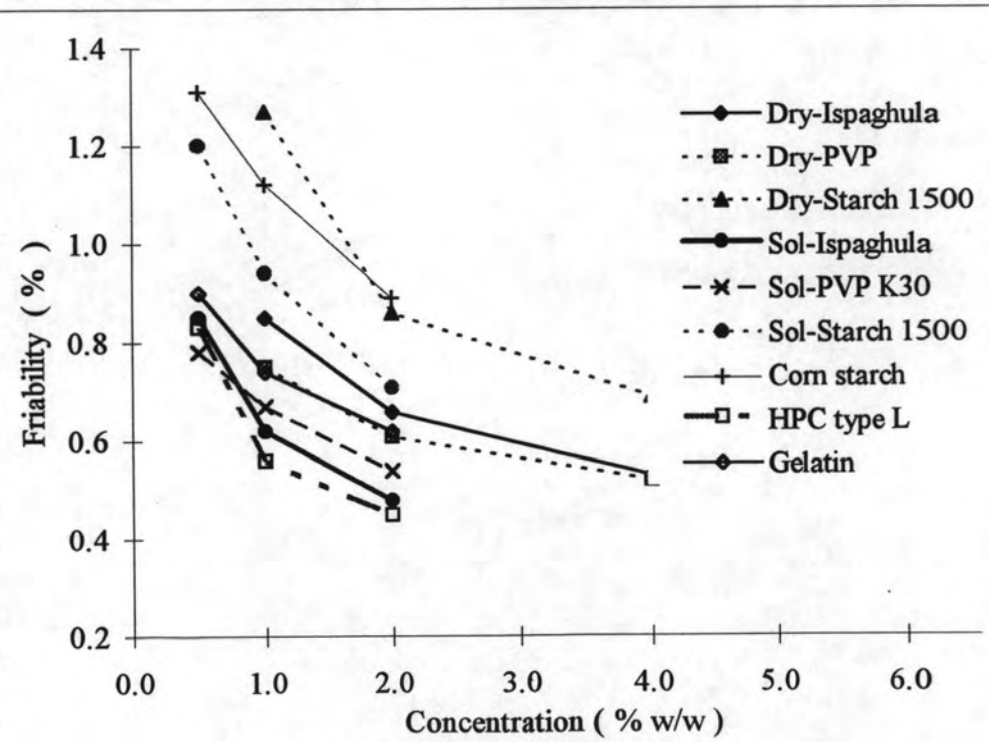


Figure 57 Effect of Various Binders and Concentrations on Friability of Nicotinamide Tablets

In dry incorporation method, friability of tablet were less than 1 % except for Starch 1500®at 1% level. Furthermore, tablets produced by dry incorporation method tend to friable than solution incorporation method.

6. Tablet Porosity

The results are presented in Table 9,10 and Figure 58, 59. The relationship between tablet porosity and binder concentration were not clearly seen .

6.1 Paracetamol

From the results shown in Figure 58 , both corn starch and Starch 1500® showed lower porosity than other tablets in this study. On the other hand , the high porous tablets were given by PVP K30. Tablet porosity were between 3.16 and 5.27 % .

6.2 Nicotinamide

The results of porosity (Figure 59) were 3.91 and 6.53 %. It was noticed that tablet produced by PVP K30 was the highest porosity.

7. Disintegration Time

The disintegration time of tablets increased with increasing in binder concentration .

7.1 Paracetamol

The results are shown in Table 9 and Figure 60. Obviously prolonged disintegration time as binder concentration increased was noticed in all cases. Disintegration time decreased with the following order ;

In solution incorporation method at
0.5% w/w level : Ispaghula husk >corn starch > Starch 1500®> gelatin > PVP K30 > HPC type L
1 % w/w level : Ispaghula husk > gelatin > corn starch > Starch 1500®> PVP K 30 > HPC type L
2 % w/w level : Ispaghula husk >Starch 1500®> corn starch > PVP K30 > gelatin > HPC type L

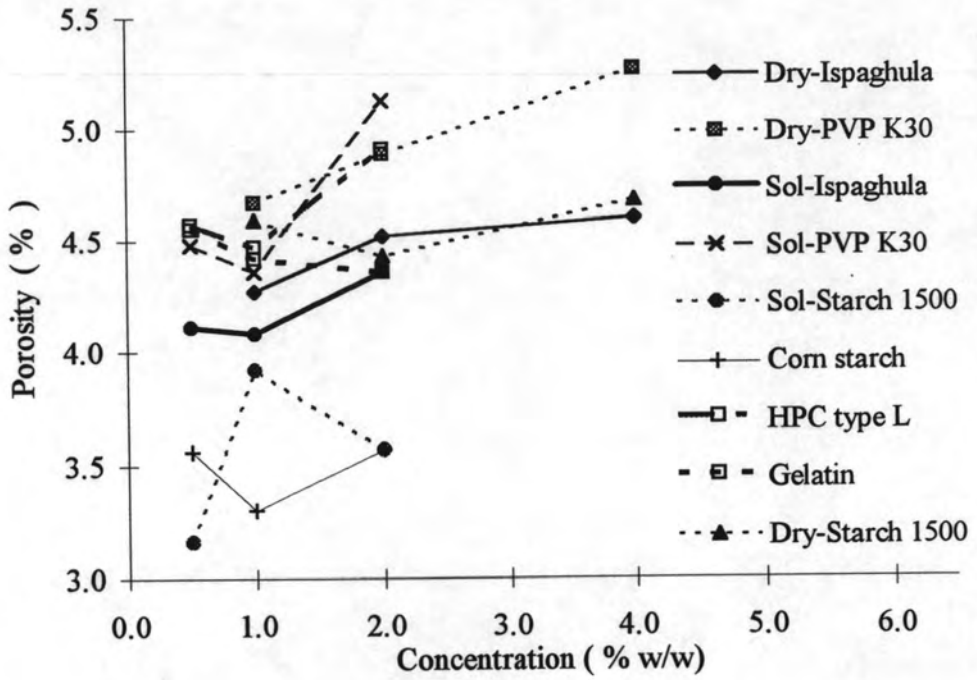


Figure 58 Effect of Various Binders and Concentrations on Porosity of Paracetamol Tablets

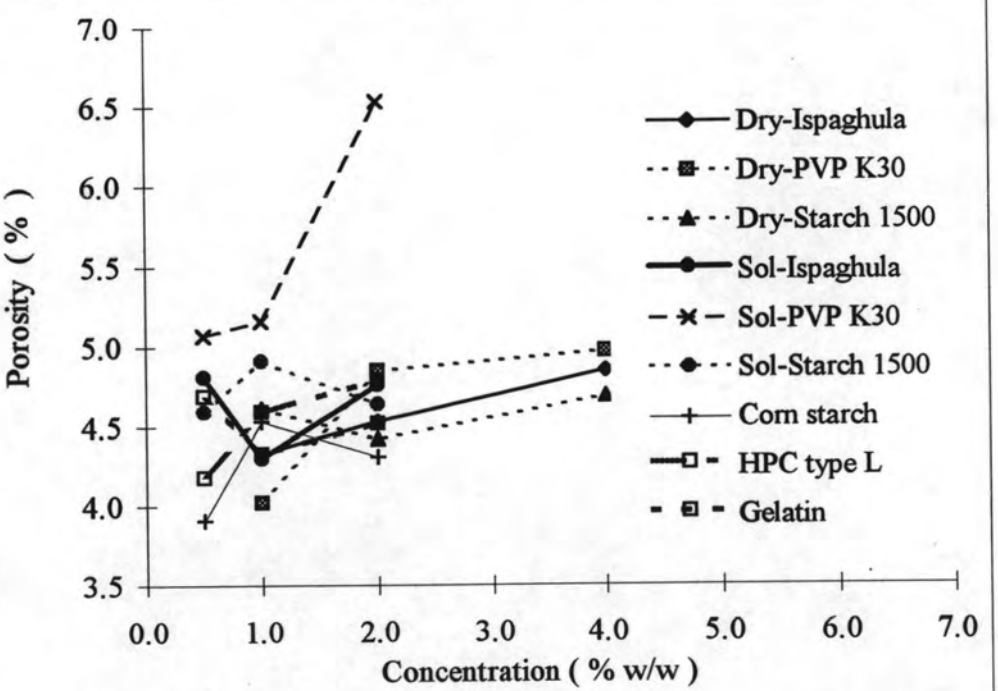


Figure 59 Effect of Various Binders and Concentrations on Porosity of Nicotinamide Tablets

The fastest and slowest disintegration time were given by HPC type L and Ispaghula husk, respectively. In addition tablet produced by dry incorporation method outstandingly showed rapid disintegration than tablet produced by solution incorporation method . The shorter disintegration time did not mean better efficacy or better formulation. In this study, the longer disintegrated formulation may be better binding properties of binder than faster formulation . In addition , besides disintegration time many important factors, such as hardness, friability, dissolution time must also be considerated all together to evaluate binder efficacy .

7.2 Nicotinamide

The same trend as above was noticed but in solution incorporation method the disintegration was slightly influenced with the increase in binder concentration (Figure 61 and Table 10). Disintegration time decreased with the following order ;

In solution incorporation method at
0.5 % w/w level: Starch 1500® > corn starch > Ispaghula husk > HPC type L > gelatin > PVP K30
1 % w/w level : Ispaghula husk > corn starch > Starch 1500® > HPC type L > PVP K 30 > gelatin
2 % w/w level : corn starch > Ispaghula husk > Starch 1500® > HPC type L > PVP K 30 > gelatin

From the previous results , it indicated that tablet prepared with gelatin showed the shortest disintegration time, in contrast to Ispaghula husk. The tablet prepared by dry incorporation method were slightly slower than solution incorporation method (except for at 4 % level). It was clearly seen that nicotinamide tablets disintegrated faster than paracetamol tablets .

8. Dissolution Time

The median dissolution time (T50%) and dissolution rate profiles of tablets produced with various binders are presented in Table 9,10 and Figure 62 - 82. It obviously indicated how dissolution rate can be affected by altering the concentration of binder. The same results as in disintegration studies, the prolong dissolution rate mean better formulation for evaluation of binding properties of binders .

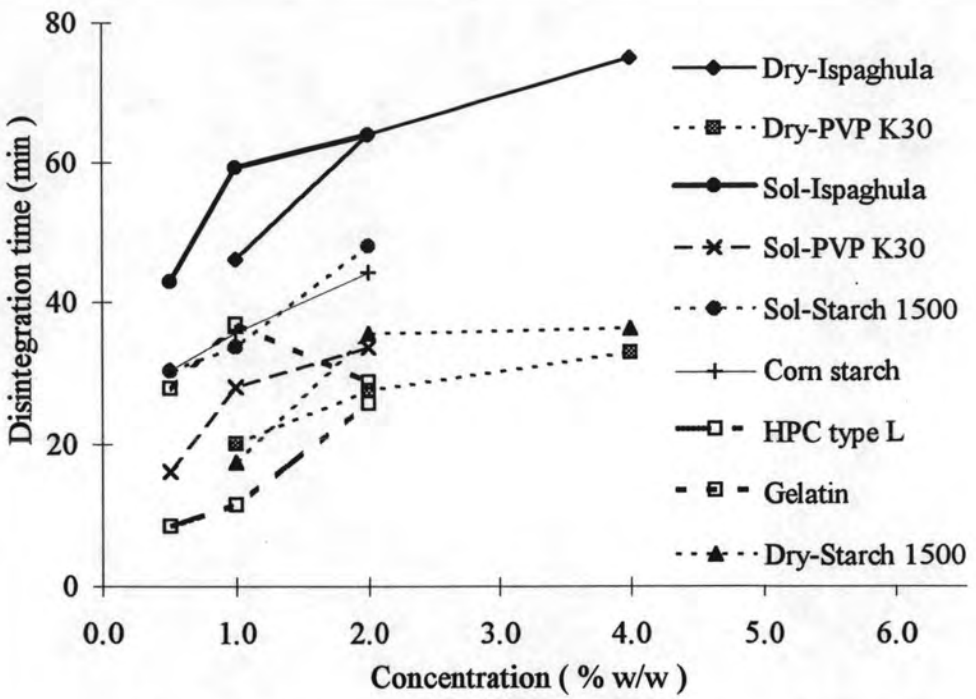


Figure 60 Effect of Various Binders and Concentrations on Disintegration Time of Paracetamol Tablets

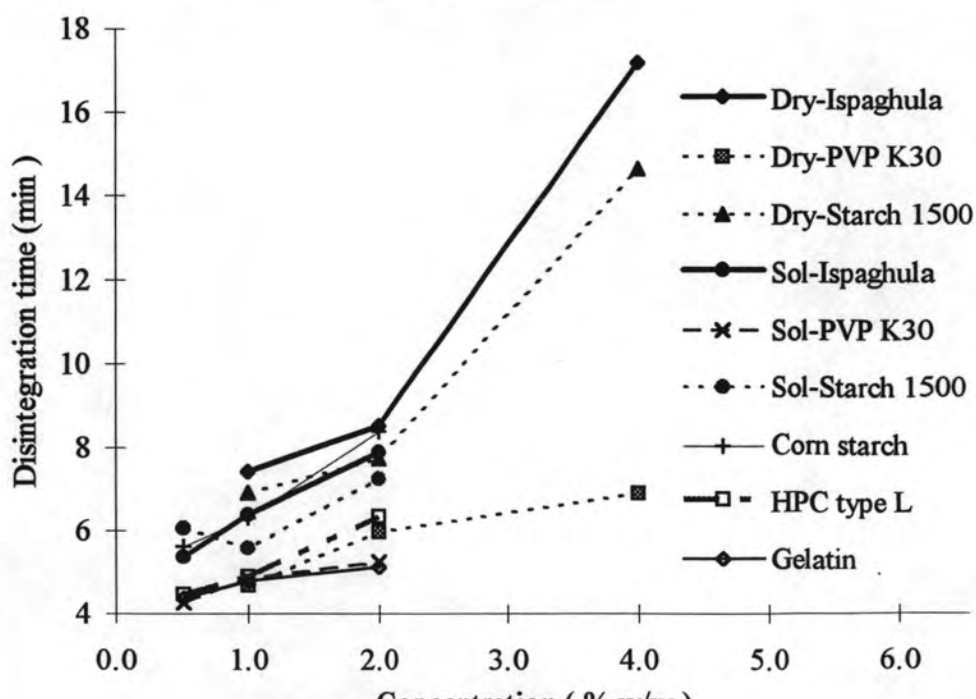


Figure 61 Effect of Various Binders and Concentrations on Disintegration Time of Nicotinamide Tablets

8.1 Paracetamol

The median dissolution time (T 50%) of paracetamol tablets was increased with increase in binder concentration (Figure 81). The ranks of T 50% were decreased as follows,

In dry incorporation method at
1,2 % w/w level : Ispaghula husk > Starch 1500® > PVP K30
4 % w/w level : Starch 1500® > Ispaghula husk > PVP K30

In solution incorporation method at
0.5% w/w level : Ispaghula husk >Starch 1500®> gelatin > HPC type L > PVP K30 > corn starch
1 % w/w level : Ispaghula husk >Starch 1500®>HPC type L > gelatin > PVP K 30 > corn starch
2 % w/w level : Ispaghula husk >corn starch > Starch 1500® > HPC type L > gelatin > PVP K30

The slowest dissolution rate was given by Ispaghula husk. Regarding to incorporation method, tablet produced by dry incorporation method clearly exhibited faster dissolution rate than solution incorporation method.

8.2 Nicotinamide

The declination of dissolution rates of nicotinamide tablets were less effected by increasing binder concentration (except for Ispaghula husk) when compared with paracetamol tablets (Figure 81, 82). The median dissolution time were decreased as follows,

In solution incorporation method at
0.5,1%w/w level: Starch 1500®>Ispaghula husk >corn starch > HPC type L > PVP K30 > gelatin
2 % w/w level: Starch 1500®>Ispaghula husk >corn starch > HPC type L > gelatin > PVP K 30

The slight difference in dissolution rate was observed with tablet produced by dry incorporation method comparing with solution incorporation method. In this study, tablet prepared with Ispaghula husk by dry incorporation gave the slowest dissolution rate, in contrast to PVP K30. As was expected, blank tablet showed the fastest dissolution rate.

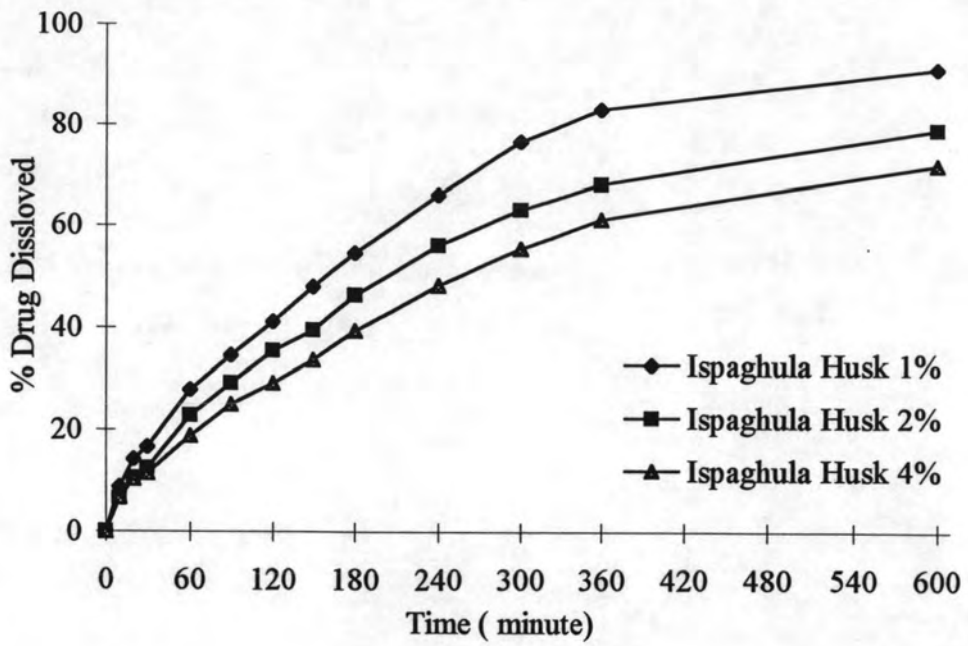


Figure 62 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Ispaghula Husk by Dry Incorporation Method

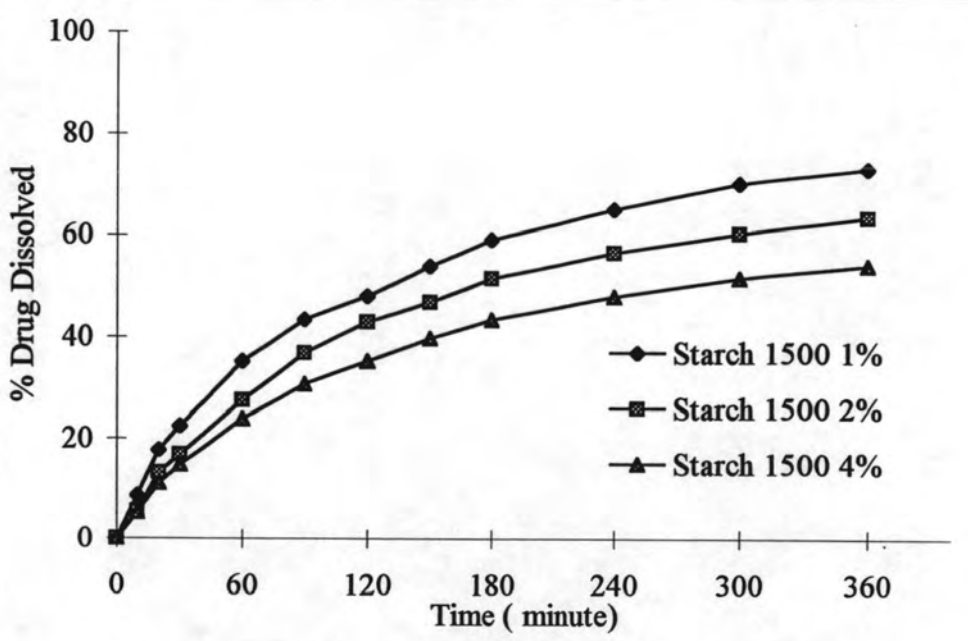


Figure 63 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Pregelatinized Starch by Dry Incorporation Method

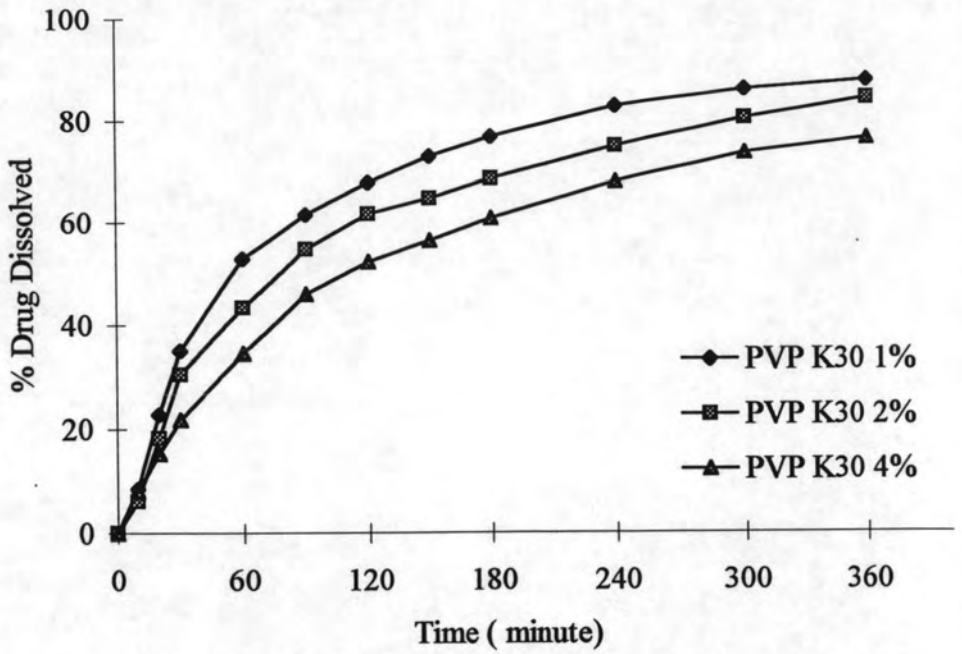


Figure 64 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Polyvinylpyrrolidone by Dry Incorporation Method

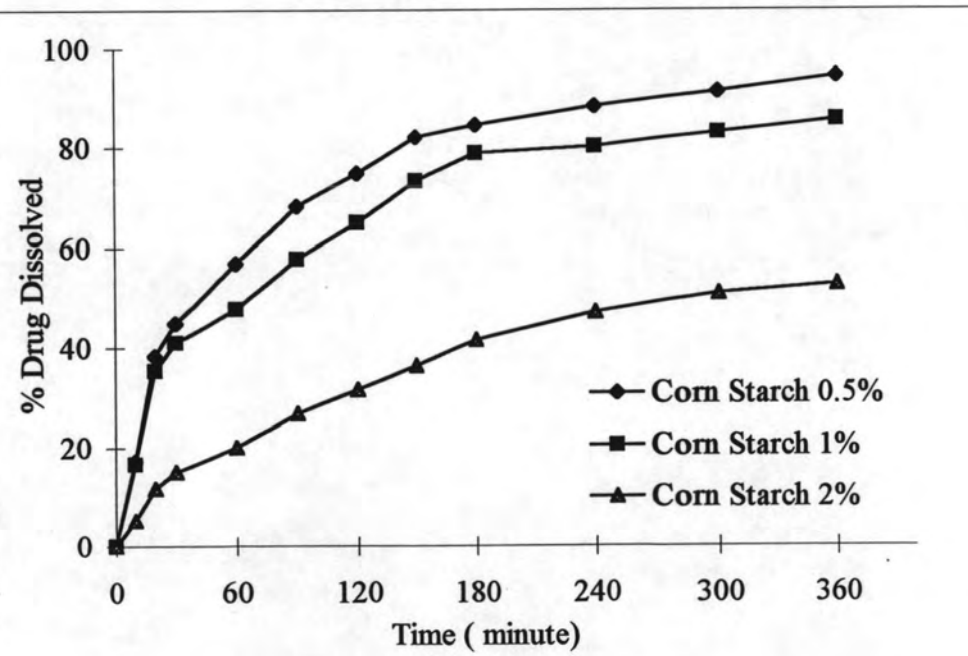


Figure 65 Dissolution Rate Profies of Paracetamol Tablets Prepared with Corn Starch by Solution Incorporation Method

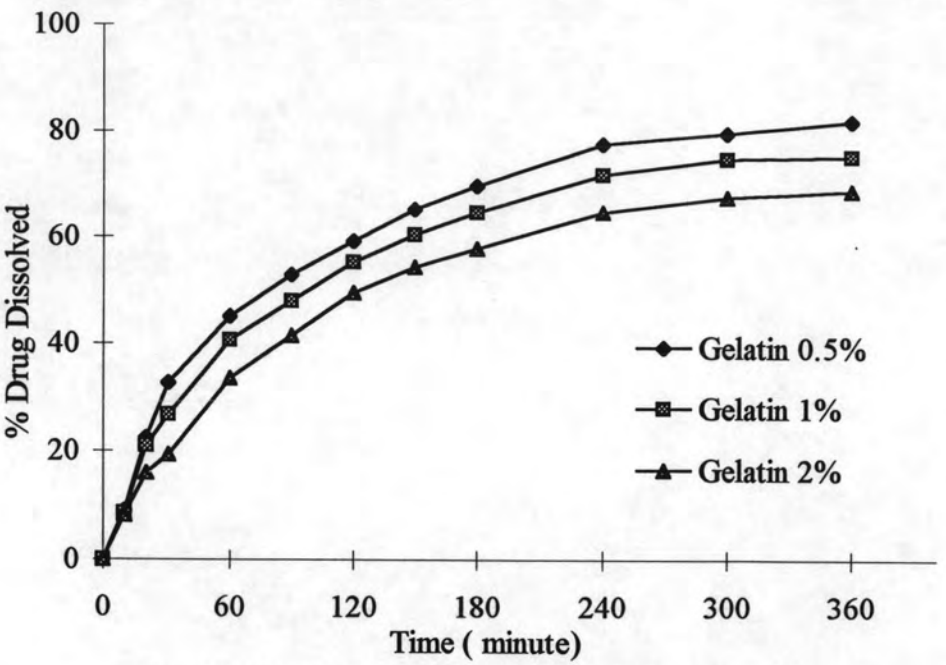


Figure 66 Dissolution Rate Profies of Paracetamol Tablets Prepared with Gelatin by Solution Incorporation Method

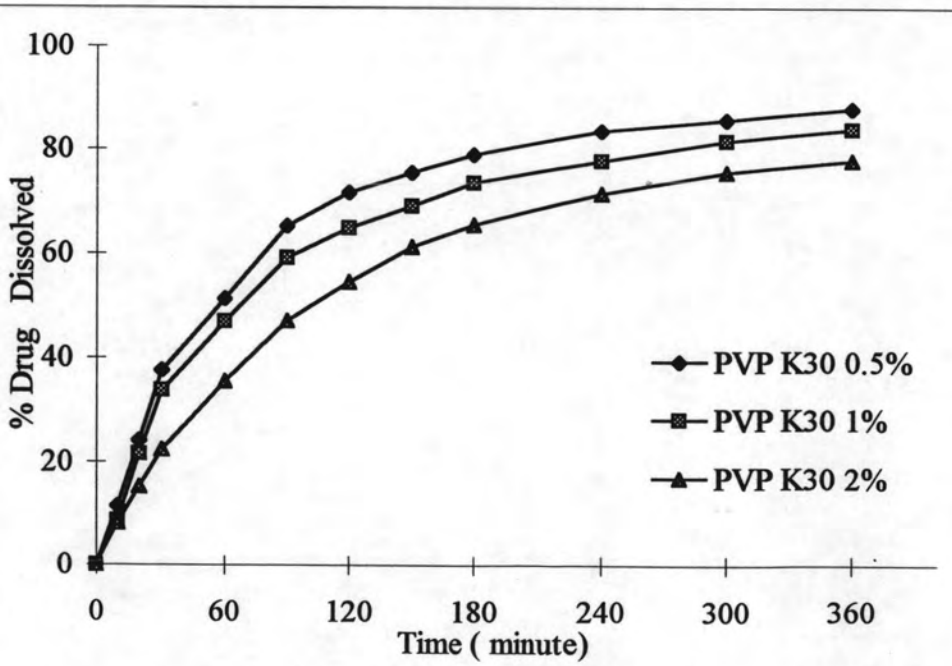


Figure 67 Dissolution Rate Profile of Paracetamol Tablets Prepared with Polyvinylpyrrolidone by Solution Incorporation Method

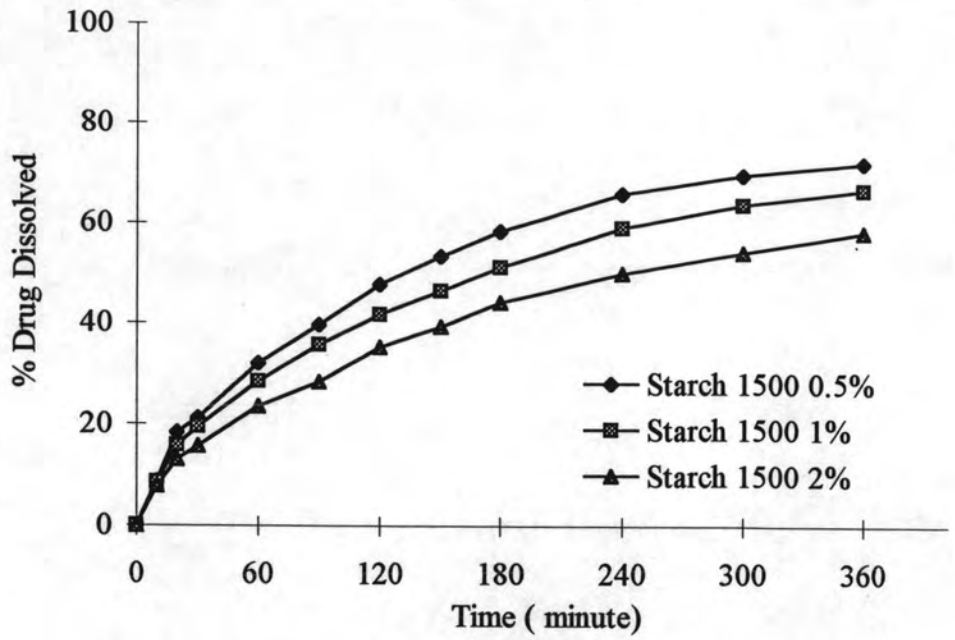


Figure 68 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Pregelatinized Starch by Solution Incororation Method

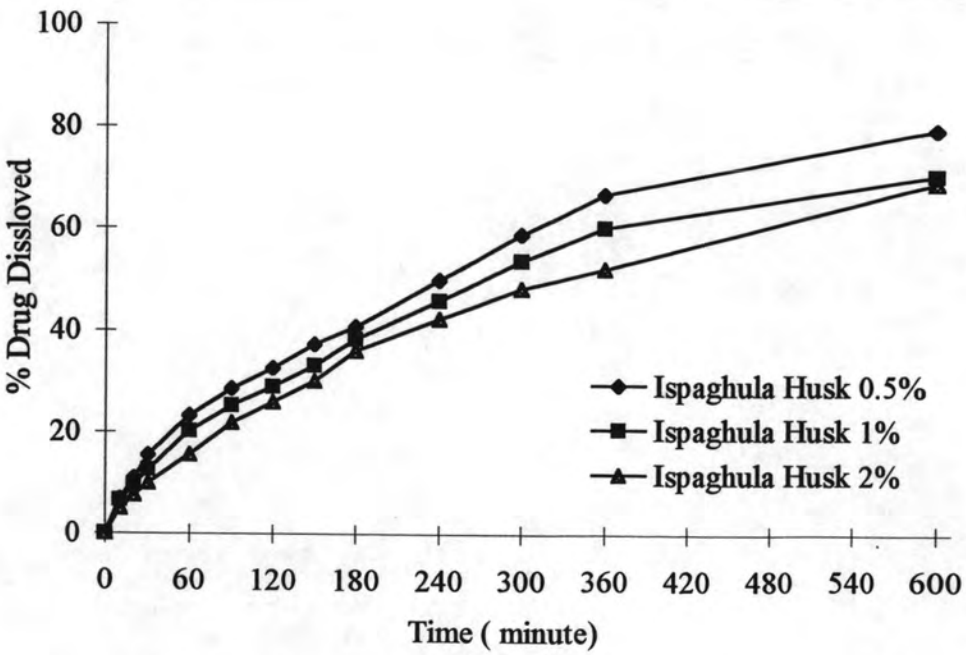


Figure 69 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Ispaghula Husk by Solution Incorporation Method

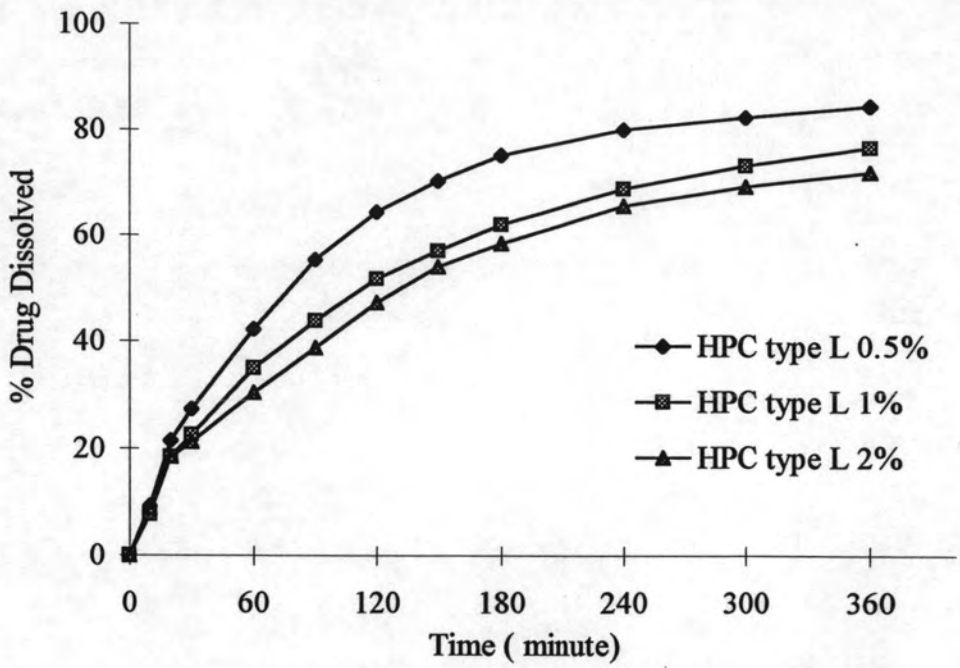


Figure 70 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Hydroxypropyl Cellulose by Solution Incorporation Method

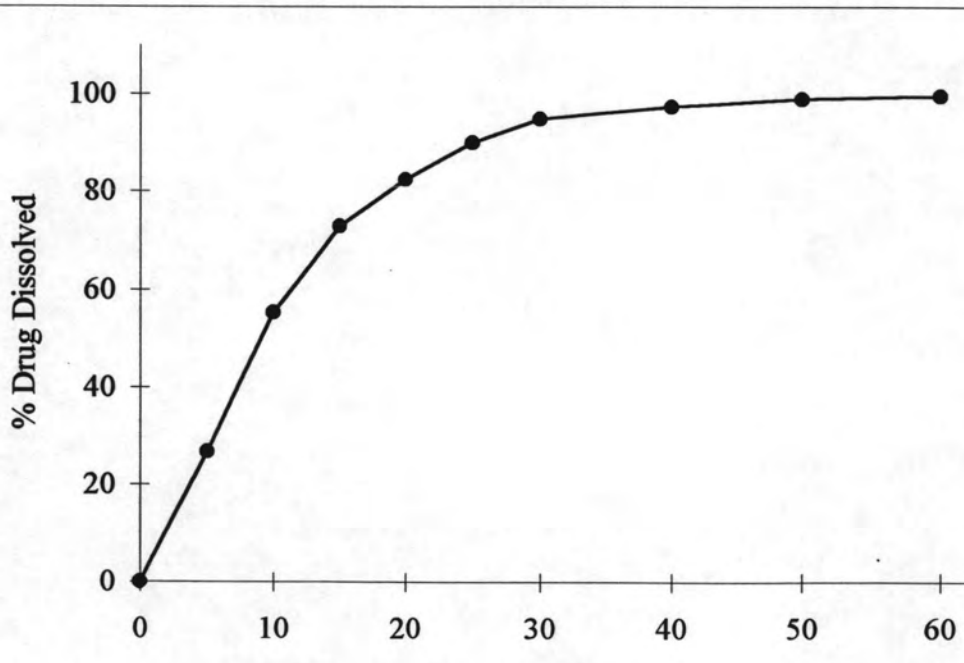


Figure 71 Dissolution Rate Profile of Nicotinamide Tablets Prepared without Binder

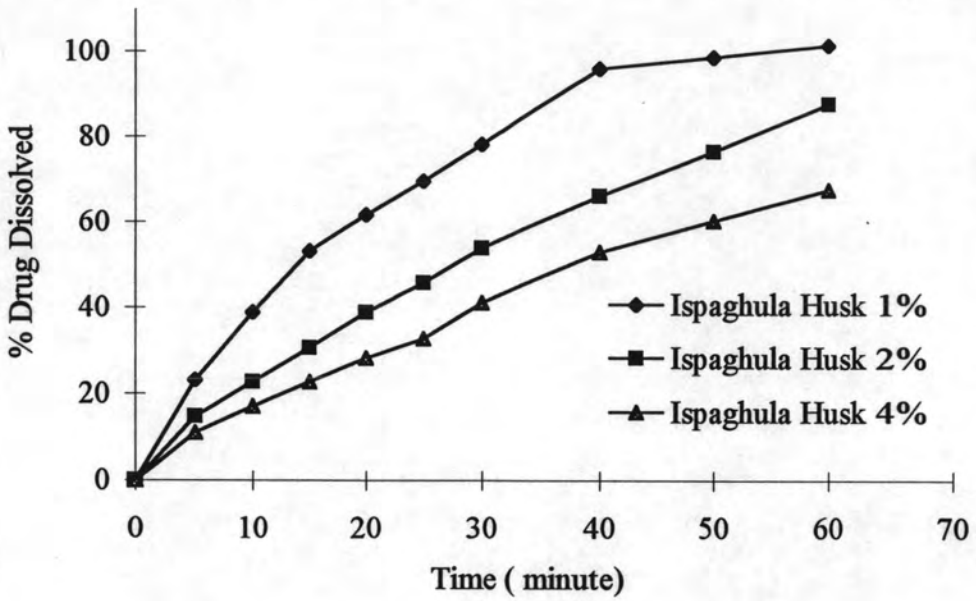


Figure 72 Dissolution Rate Profiles of Nicotinamide Tablets Prepared with Ispaghula Husk by Dry Incorporation Method

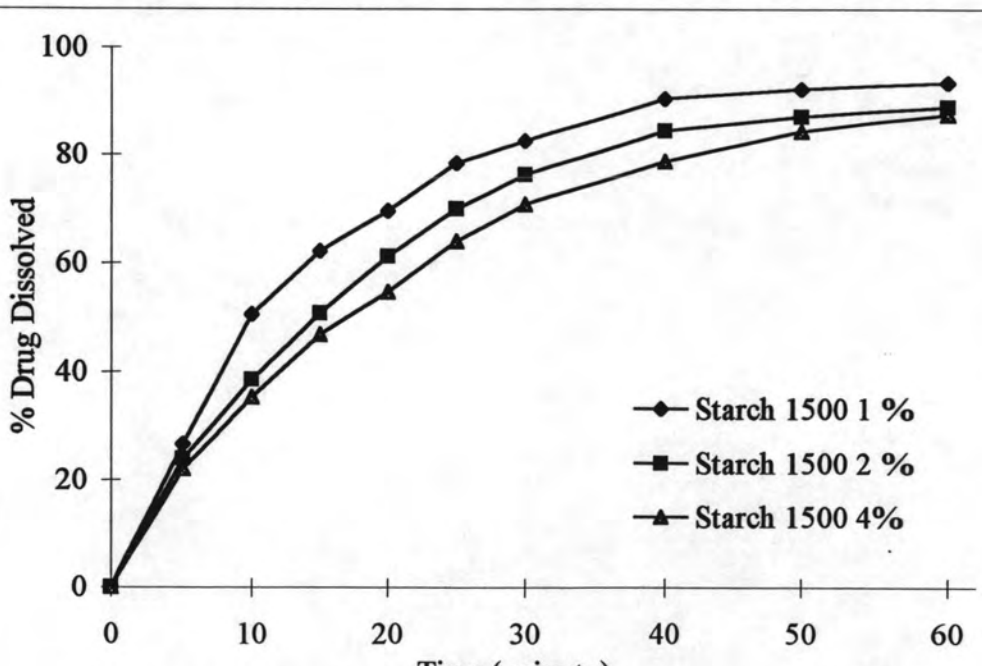


Figure 73 Dissolution Rate Profiles of Nicotinamide Tablets Prepared with Pregelatinized Starch by Dry Incorporation Method

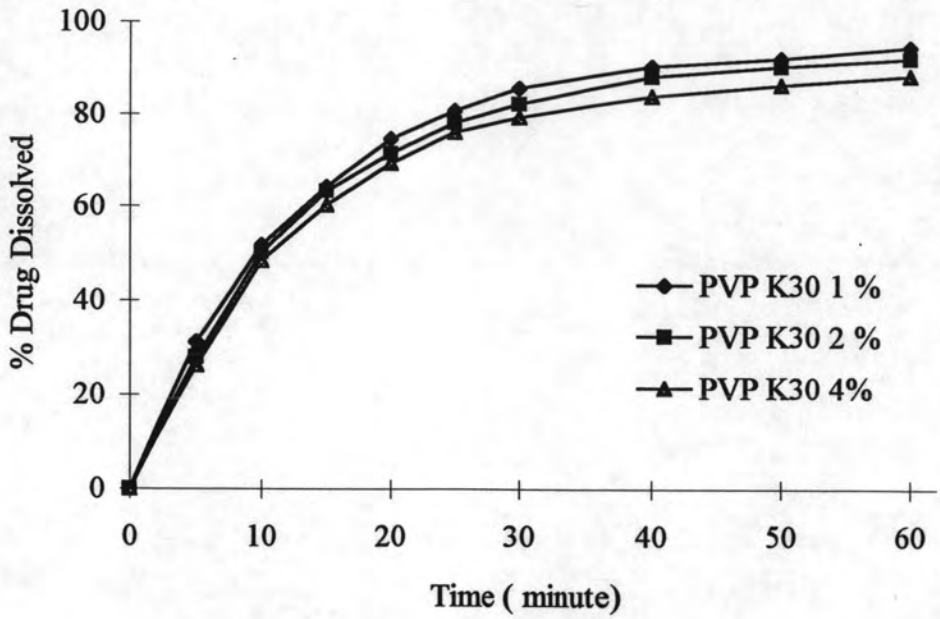


Figure 74 Dissolution Rate Profiles of Nicotinamide Tablets Prepared with Polyvinylpyrrolidone by Dry Incorporation Method

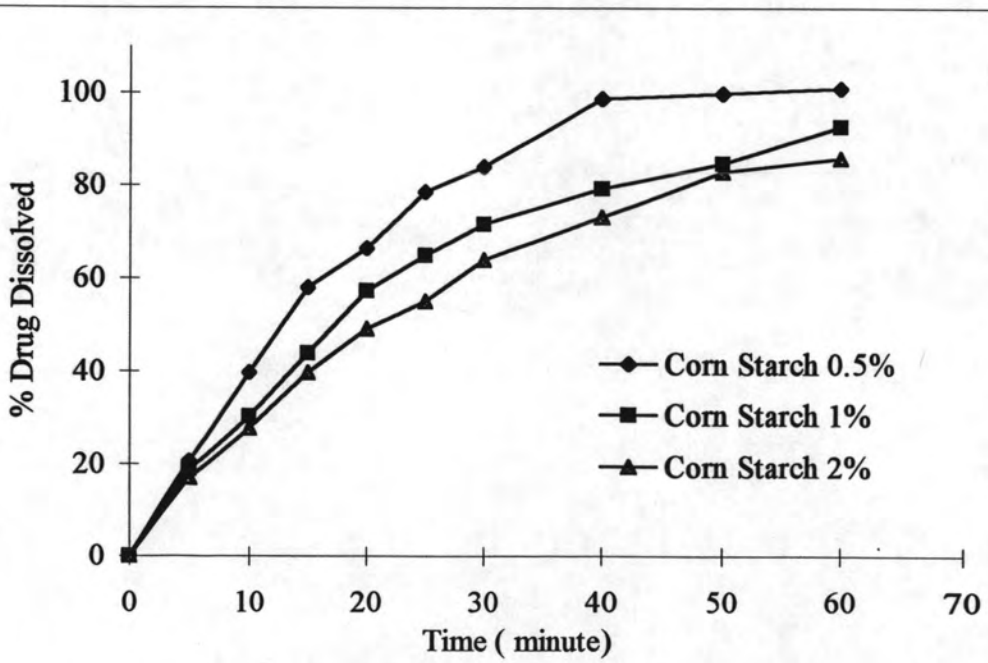


Figure 75 Dissolution Rate Profiles of Nicotinamide Tablets Prepared with Corn Starch by Solution Incorporation Method

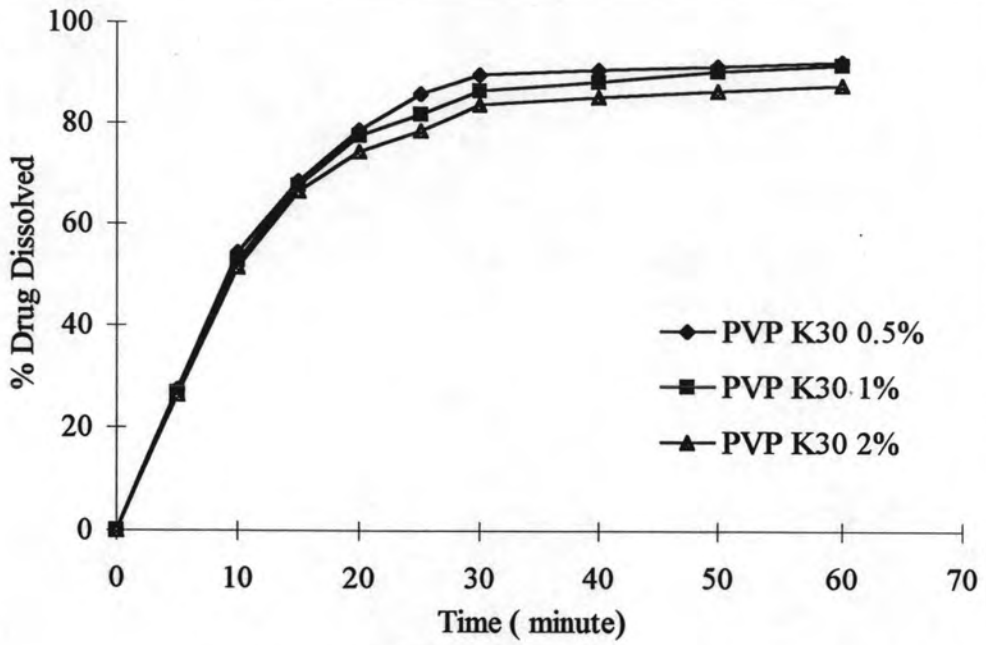


Figure 76 Dissolution Rate Profiles of Nicotinamide Tablets Prepared with PVP K30 by Solution Incorporation Method

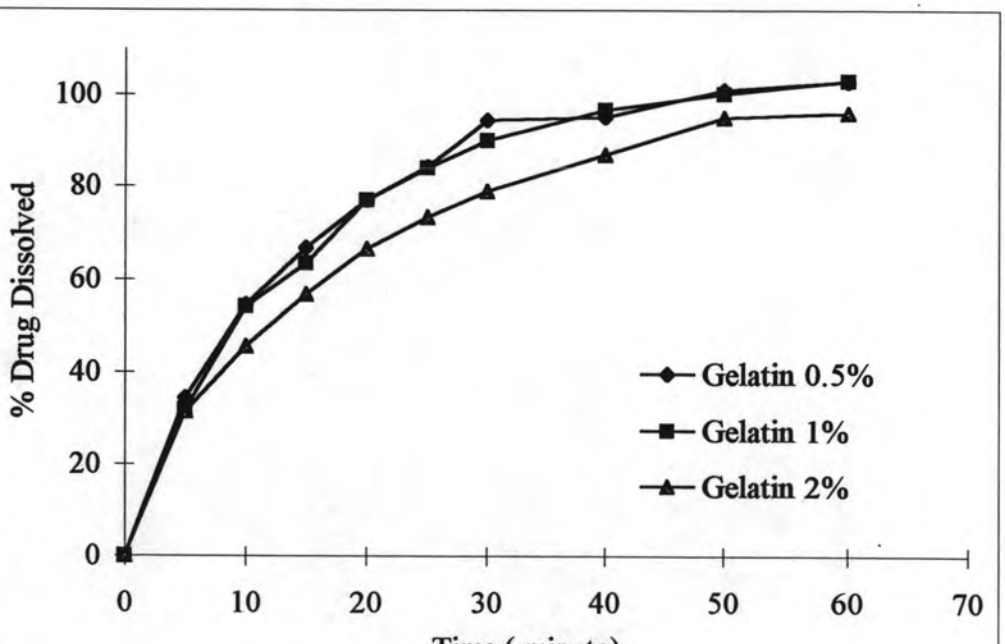


Figure 77 Dissolution Rate Profiles of Nicotinamide Tablets Prepared with Gelatin by Solution Incorporation Method

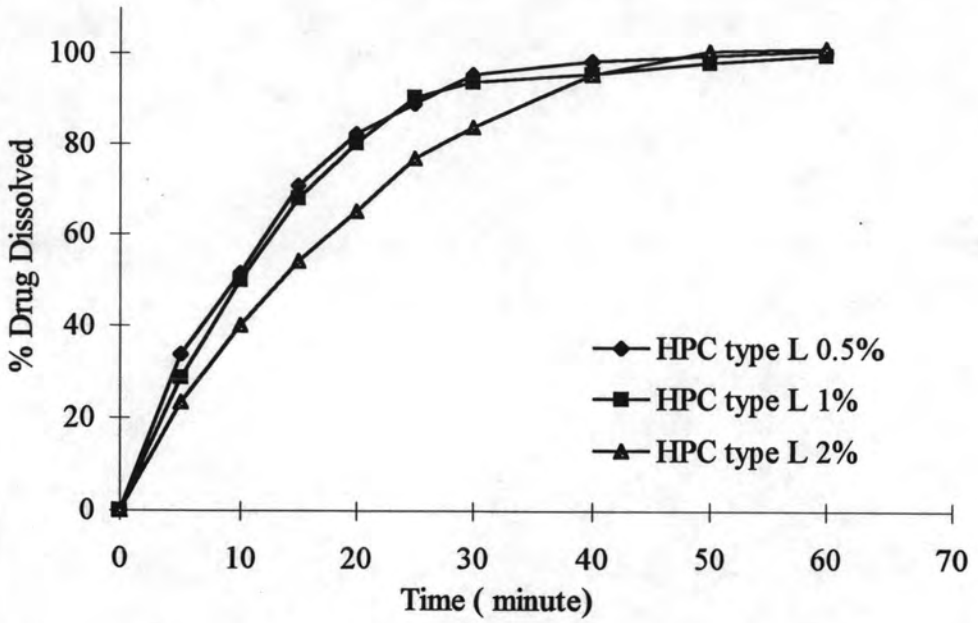


Figure 78 Dissolution Rate Profiles of Nicotinamide Tablets Prepared with HPC type L by Solution Incorporation Method

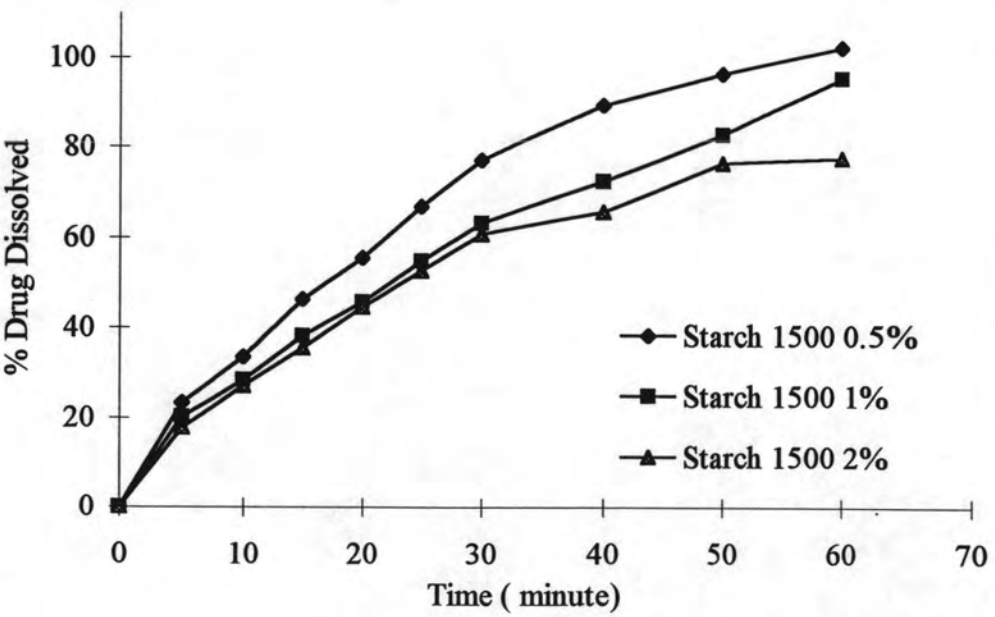


Figure 79 Dissolution Rate Profile of Nicotinamide Tablets Prepared with Starch 1500 (R) by Solution Incorporation Method

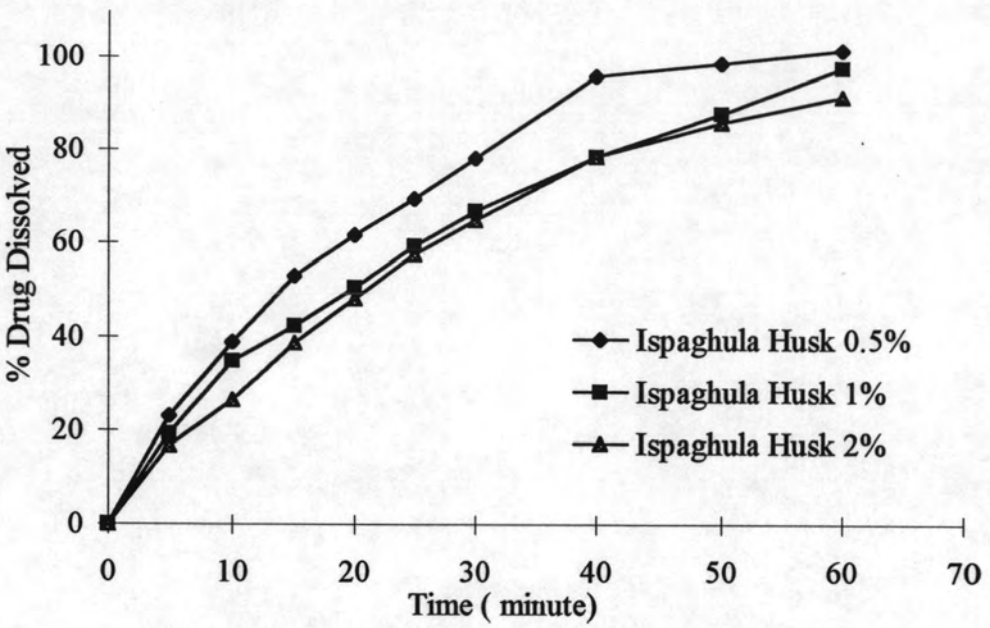


Figure 80 Dissolution Rate Profile of Nicotinamide Tablets Prepared with Ispaghula Husk by Solution Incorporation Method

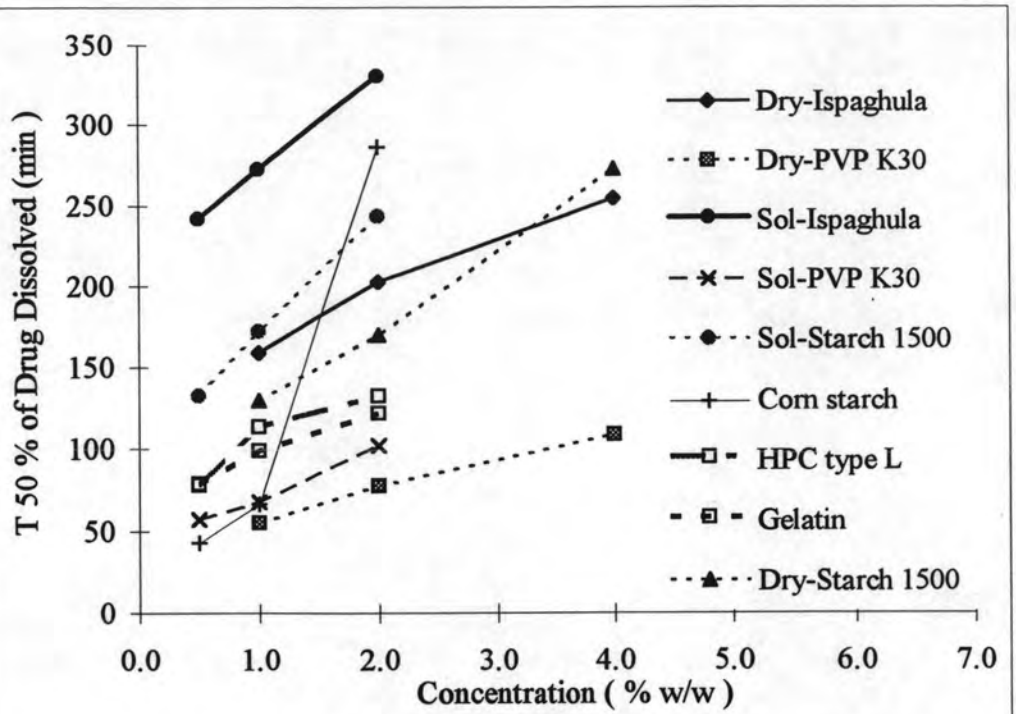


Figure 81 Effect of Various Binders and Concentrations on Median Dissolution Time of Paracetamol Tablets

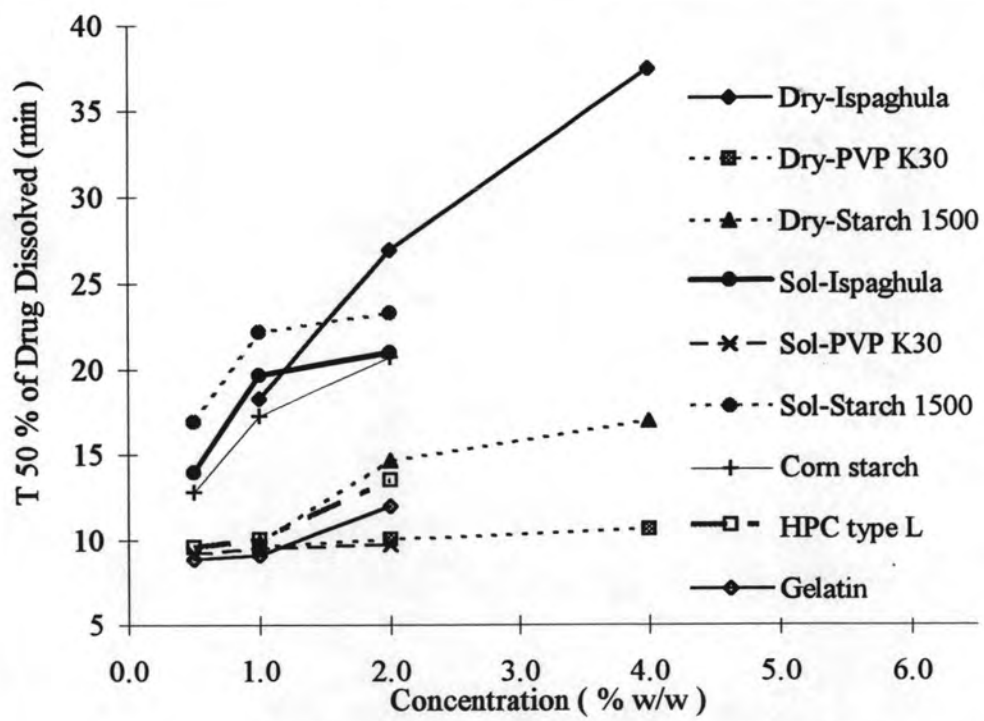


Figure 82 Effect of Various Binders and Concentrations on Median Dissolution Time of Nicotinamide Tablets

9. Label Amount

The percent labeled amount of paracetamol and nicotinamide tablets are illustrated in Table 9-10. The results were all within the range of USP XIII standard (90-110 %) .

10. Binder Index Determination

The results of binder index (Table 9,10 and Figure 83, 84) clearly indicated that binder index increased as the binder concentration increased .

10.1 Paracetamol

The ranks of binder index decreased as follow,
In dry incorporation method at
1 % w/w level: PVP K30 > Ispaghula husk
2, 4 % w/w level: PVP K30 >Ispaghula husk>Starch 1500®

In solution incorporation method at
0.5,1%w/w level: PVP K30 > HPC type L > gelatin > Ispaghula husk
2 %w/w level: PVP K30 > HPC type L > gelatin > Ispaghula husk >Starch1500®>corn starch

Consideration for all concentration studied, PVP K30 showed the highest binder index while corn starch gave the lowest value. From data in Table 9, tablets produced by dry incorporation method gave inferior binder index than solution incorporation method .

10.2 Nicotinamide

According to the results presented in Table10, binder index of various binders and concentrations employed in nicotinamide seemed to be higher than paracetamol tablets formulations . The order of binder index were decreased as follow ,

In dry incorporation method at
1,2 % w/w level: PVP K30 >Ispaghula husk >Starch 1500®
4 % w/w level: PVP K 30 >Starch 1500® >Ispaghula husk

In solution incorporation method at
0.5% w/w level: PVP K30 > gelatin > HPC type L > Ispaghula husk >corn starch > Starch 1500®
1% w/w level: HPC type L > PVP K 30 > gelatin > Ispaghula husk >corn starch > Starch 1500®
2% w/w level: PVP K 30 > HPC type L > gelatin > Ispaghula husk > Starch 1500® >corn starch

It also found that at 2 % w/w level the highest and lowest binder index were tablet prepared with PVP K30 and corn starch, respectively. The inferior binder values were found for dry incorporation method as comparing with solution incorporation method except for Starch 1500® . In addition , blank tablet was customarily the least binder index values.

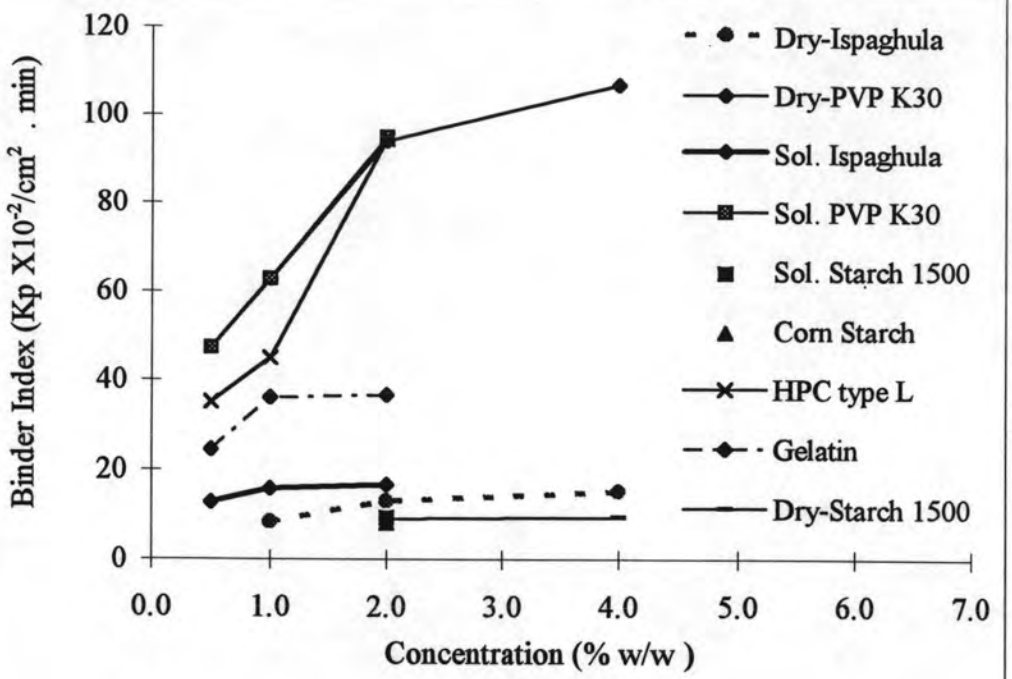


Figure 83 Effect of Various Binders and Concentrations on Binder Index of Paracetamol Tablets

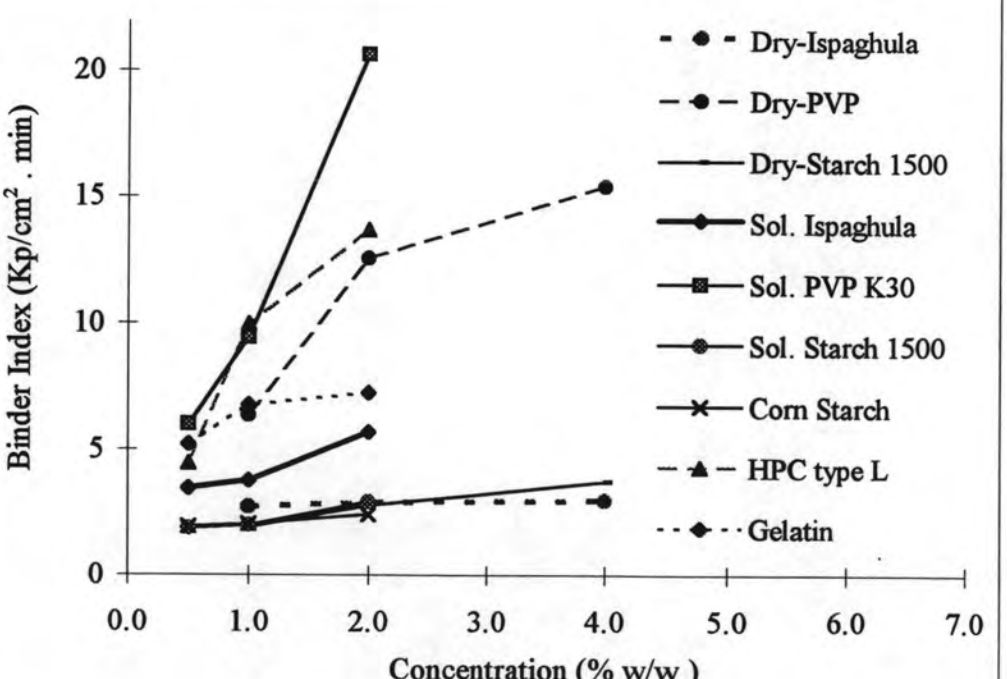


Figure 84 Effect of Various Binders and Concentrations on Binder Index of Nicotinamide Tablets