CHAPTER III

RESULTS

Physical Properties of Granules Prepared with Durian Rind Extracts (D_1, D_2) and Various Binders.

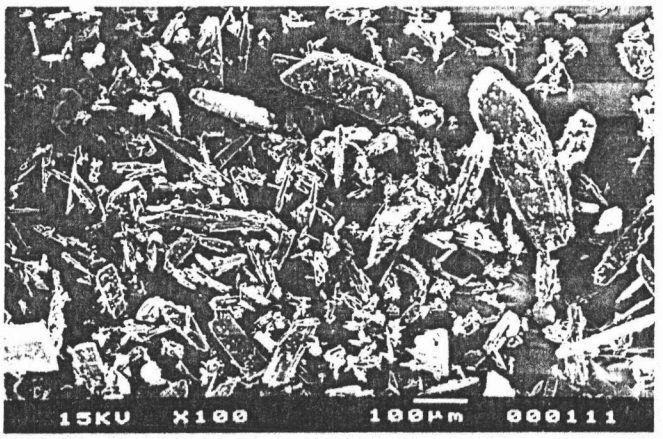
1. Determination of Granule Appearance

1.1 Paracetamol

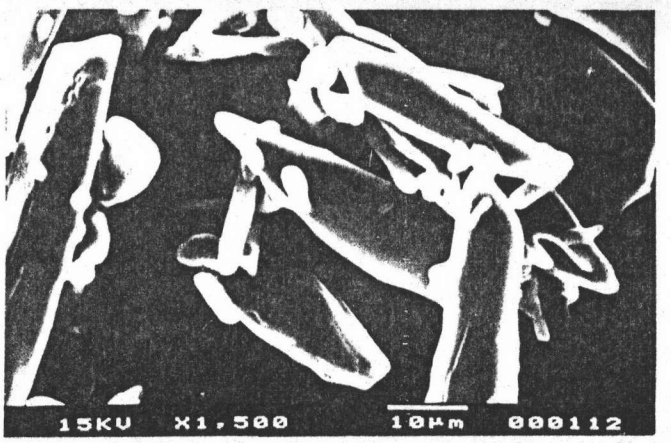
The microscopic appearance of paracetamol powder and granules in different magnification are shown in Figures 8-16. Paracetamol powder composed of many small acicular particles together with large cylinder particles. It consequently had wide range of size distribution. In the case of paracetamol granules which produced by various binders using solution incorporation method, appeared to be similar and possessed quite round shape. The granule consisted of intact nonfractured paracetamol particles bound together by a sponge-like network solid binders. The same results were observed with the granules prepared by dry incorporation method as given in Figures 17-20.

1.2 Pyridoxine hydrochloride

The microscopic appearance of pyridoxine hydrochloride powder and granules in different magnification are presented in Figures 21-33. Pyridoxine hydrochloride powder composed of thick rod and many fracture irregular-shaped particles. It also showed wide size distribution. The granule characteristics for all cases were similar and had quite round shape. However, granule surface appeared to consisted of particle that melted together and the original particles were not clearly seen.

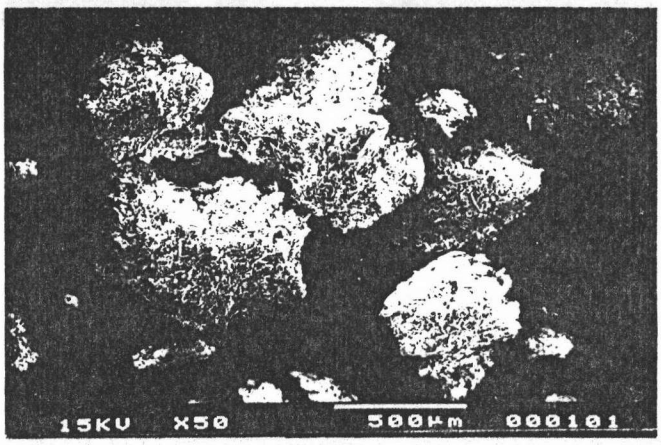


A

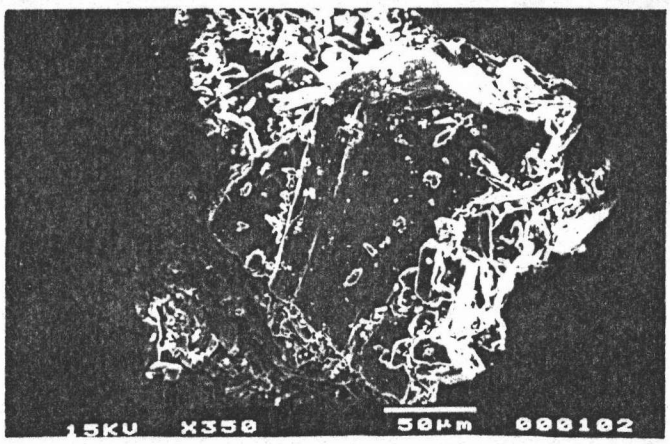


B

Figure 8 Photomicrographs of Original Paracetamol Powders (Key : A x 100, B x 1500).

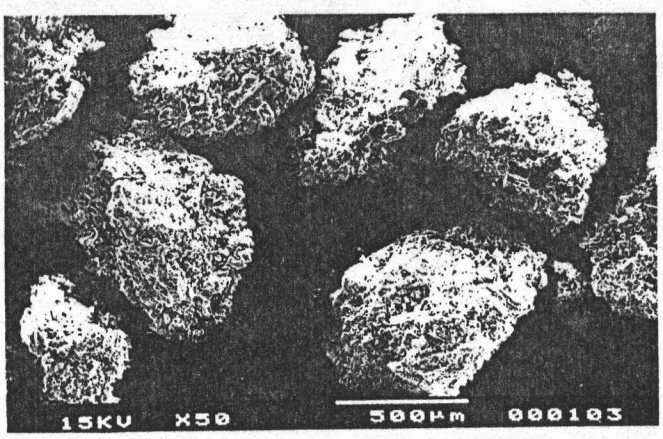


A

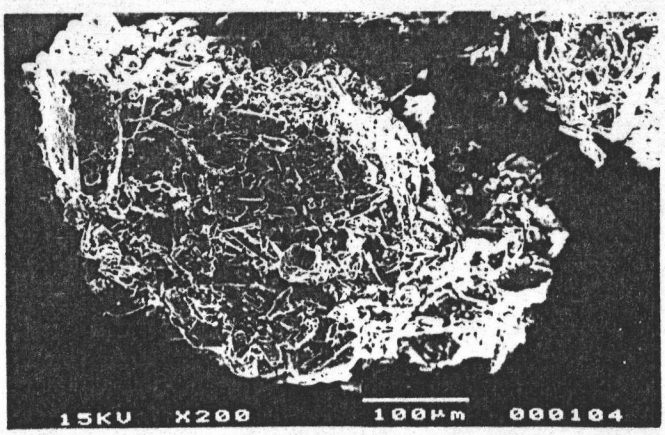


B

Figure 9 Photomicrographs of Paracetamol Granules Prepared with 2 % D_1 by Solution Incorporation Method (Key : A x 50 , B x 350).

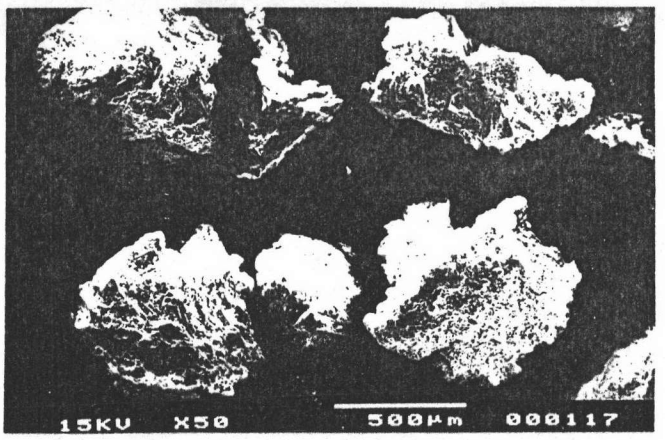


A

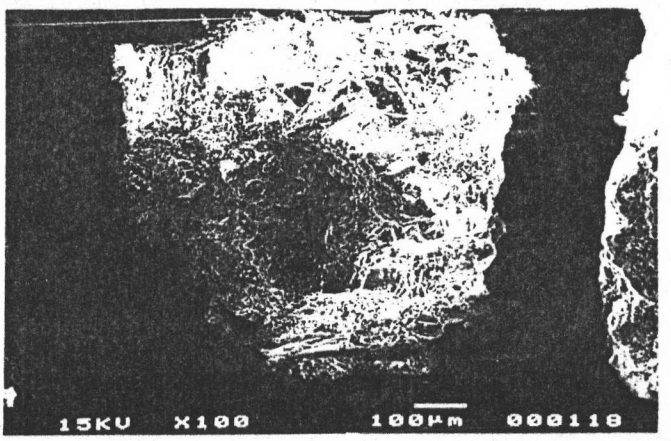


B

Figure 10 Photomicrographs of Paracetamol Granules Prepared with 2 % D_2 by Solution Incorporation Method (Key : A x 50 , B x200).

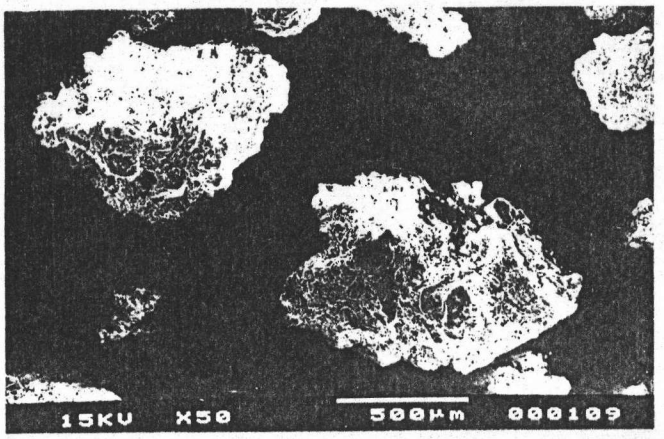


A

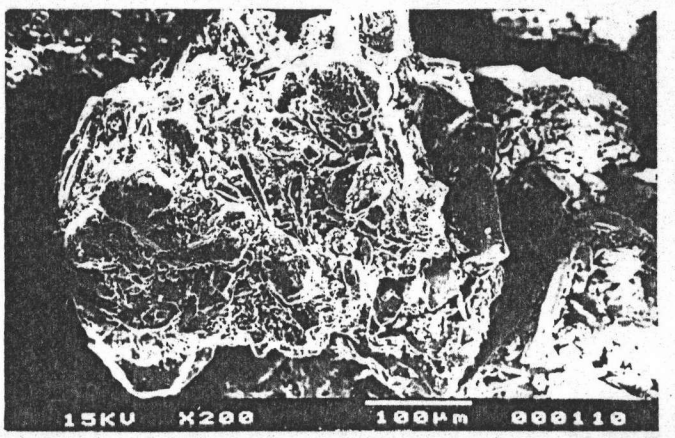


B

Figure 11 Photomicrographs of Paracetamol Granules Prepared with 2 % PVPK30 by Solution Incorporation Method (Key : A x 50, B x 100).

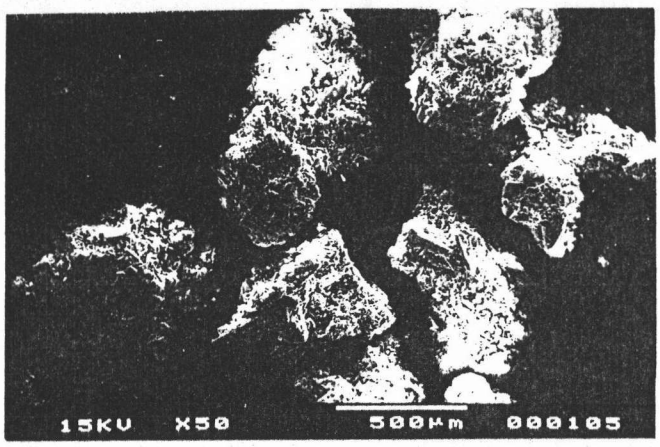


A

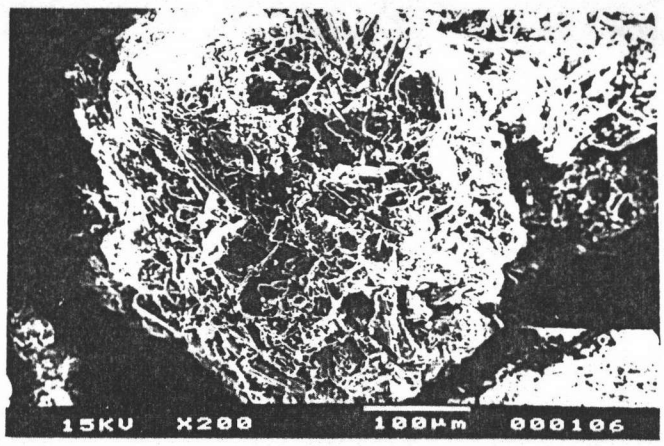


B

Figure 12 Photomicrographs of Paracetamol Granules Prepared with 2 % Corn Starch by Solution Incorporation Method (Key : A x 50 , B x 200).

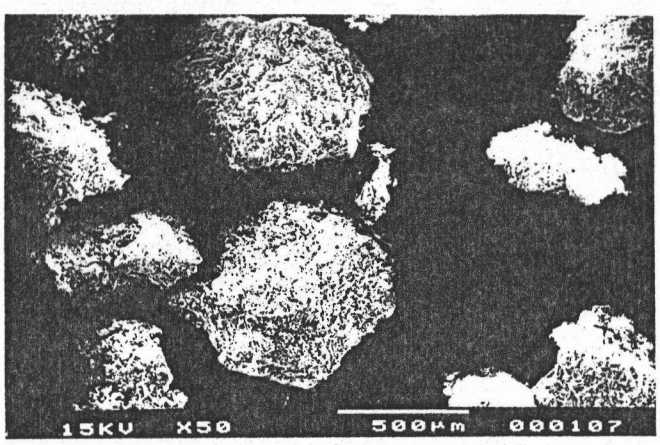


A

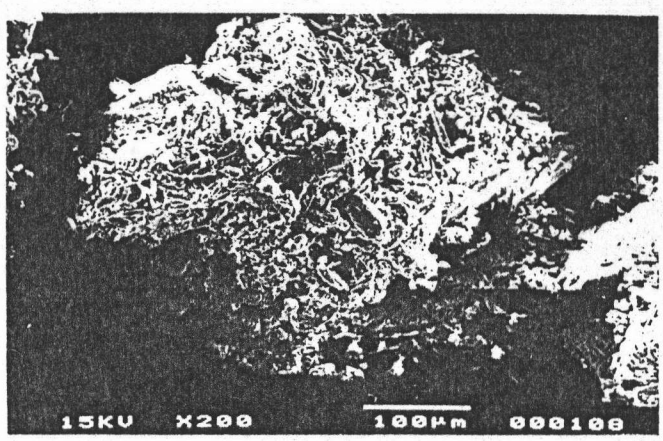


B

Figure 13 Photomicrographs of Paracetamol Granules Prepared with 2 % Starch 1500(R) by Solution Incorporation Method (Key : A x 50 , B x 200).

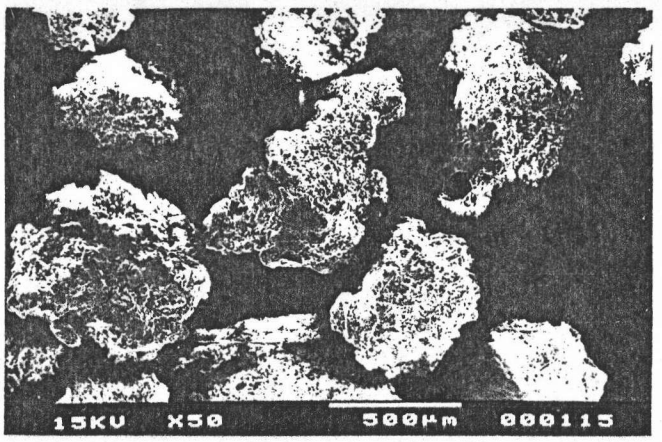


A

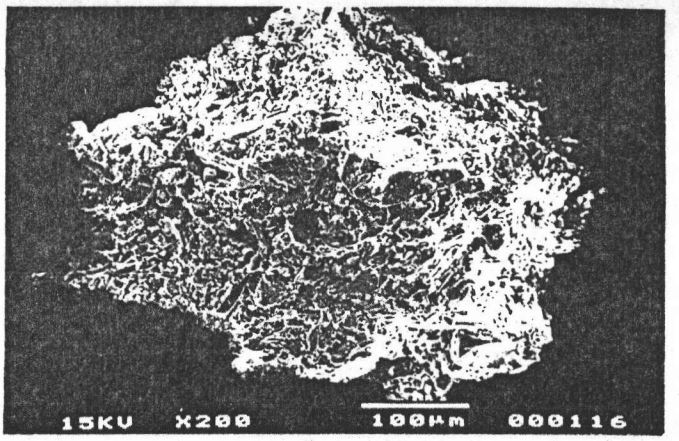


B

Figure 14 Photomicrographs of Paracetamol Granules Prepared with 2 % Gelatin by Solution Incorporation Method (Key : A x 50, B x 200).

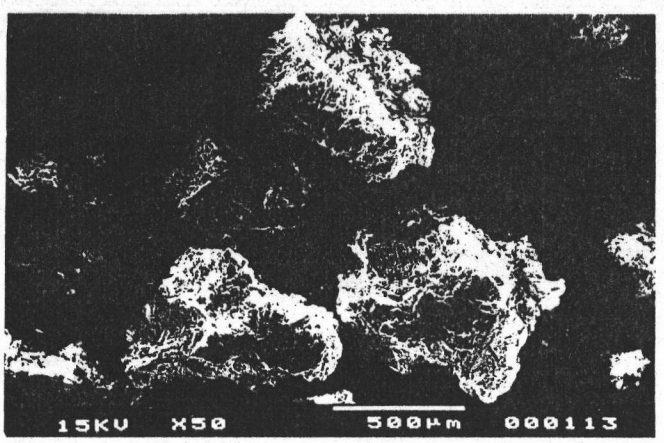


A

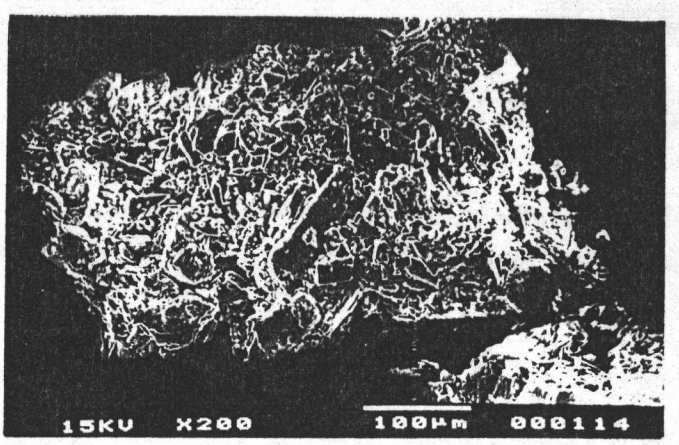


B

Figure 15 Photomicrographs of Paracetamol Granules Prepared with 2 % Methocel E15LV(R) by Solution Incorporation Method (Key : A x 50, B x 200).

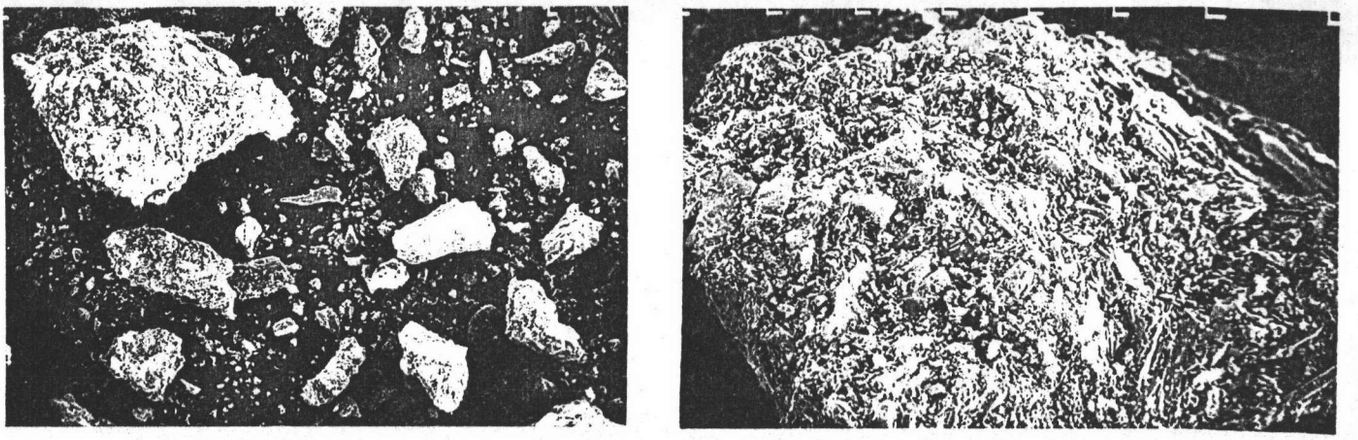


A



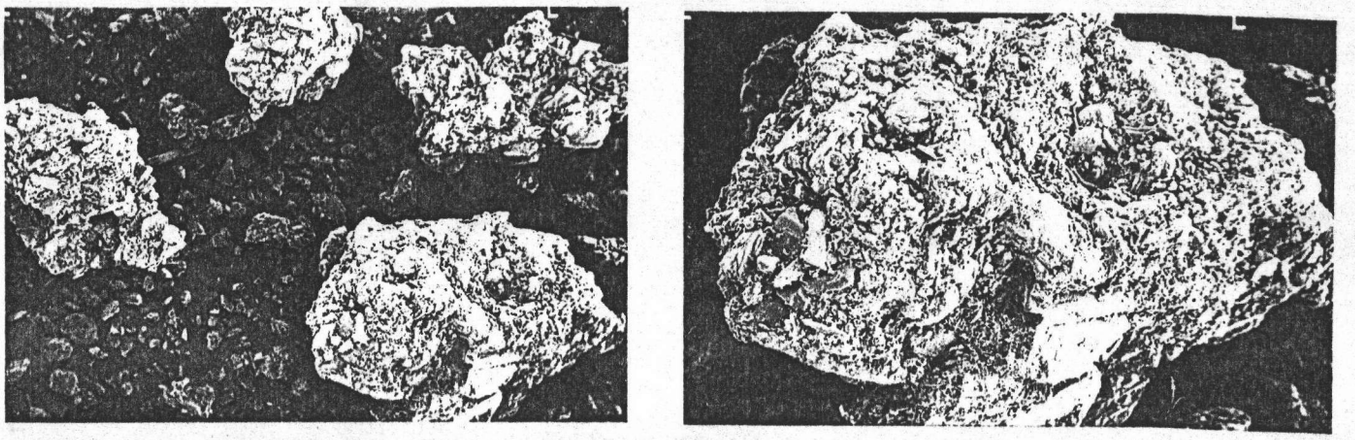
B

Figure 16 Photomicrographs of Paracetamol Granules Prepared without Binder (Blank) (Key : A x 50, B x 200).



A B

Figure 17 Photomicrographs of Paracetamol Granules Prepared with 2 % D_1 by Dry Incorporation Method (Key : A x 50, B x 100).



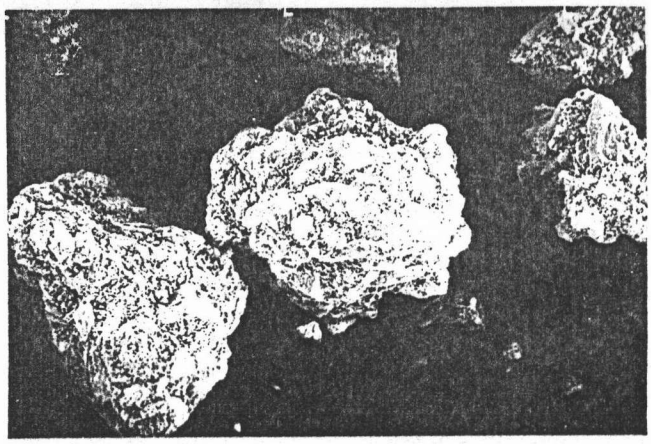
A B

Figure 18 Photomicrographs of Paracetamol Granules Prepared with 2 % D_2 by Dry Incorporation Method (Key : A x 50, B x 150).

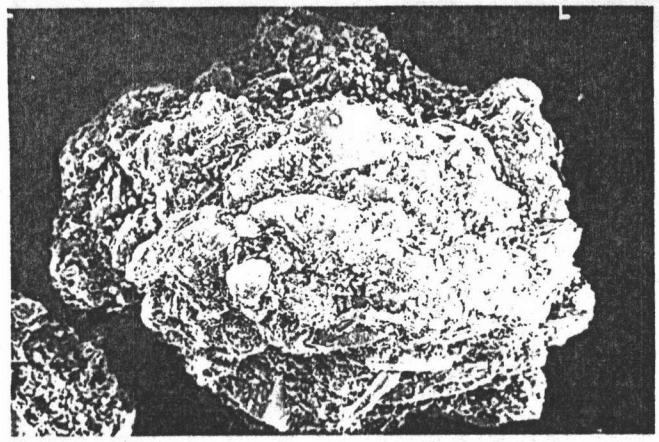
Micron marker = 1000 um at x 35 - x 100.

= 100 um at x 150 - x 1000.

(Figures 17 - 33).

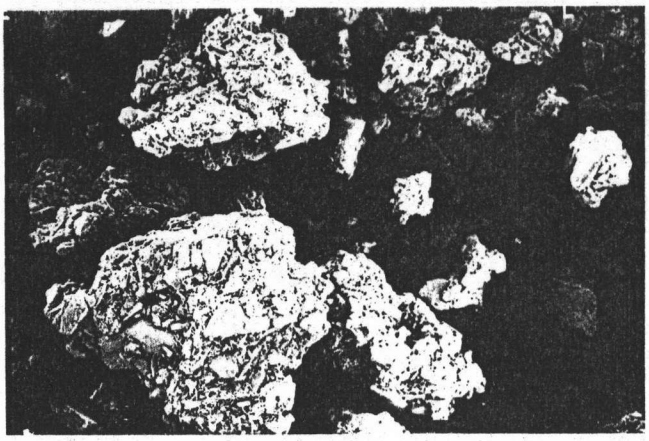


A

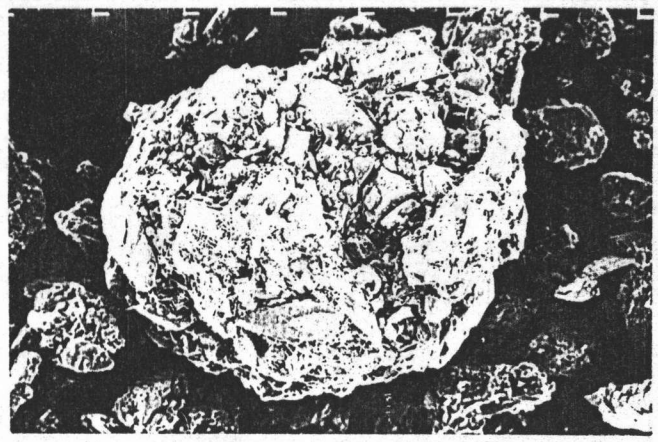


B

Figure 19 Photomicrographs of Paracetamol Granules Prepared with 2 % PVPK30 by Dry Incorporation Method (Key : A x 50, B x 100).

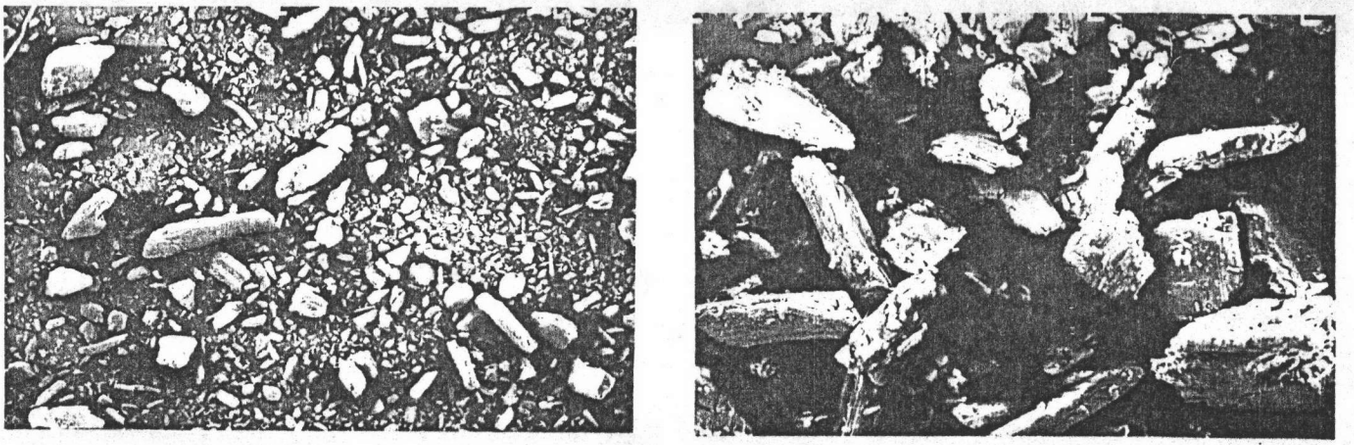


A



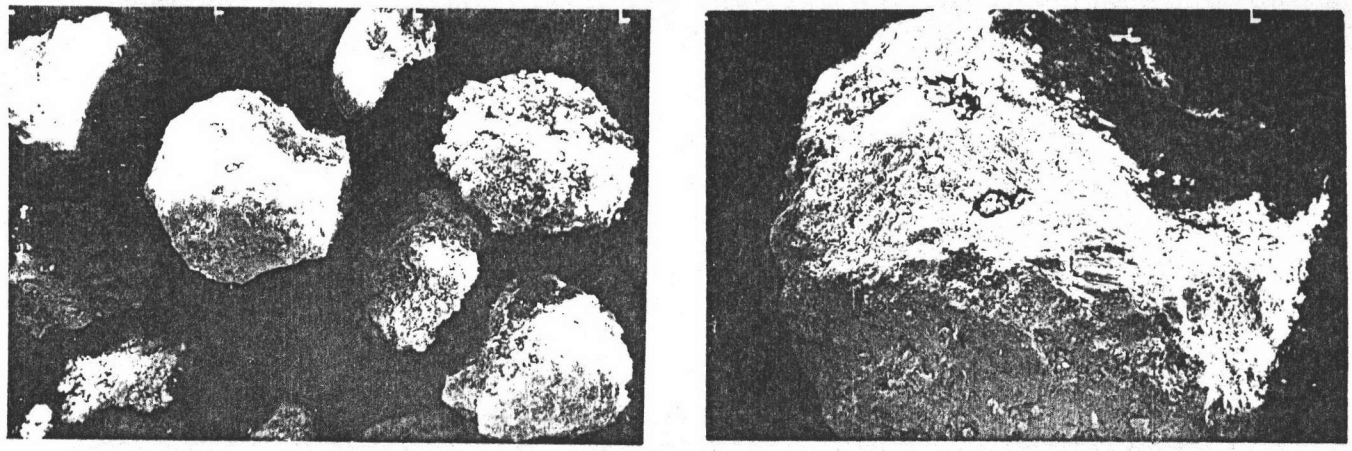
B

Figure 20 Photomicrographs of Paracetamol Granules Prepared with 2 % Starch 1500(R) by Dry Incorporation Method. (Key : A x 50, B x 100).



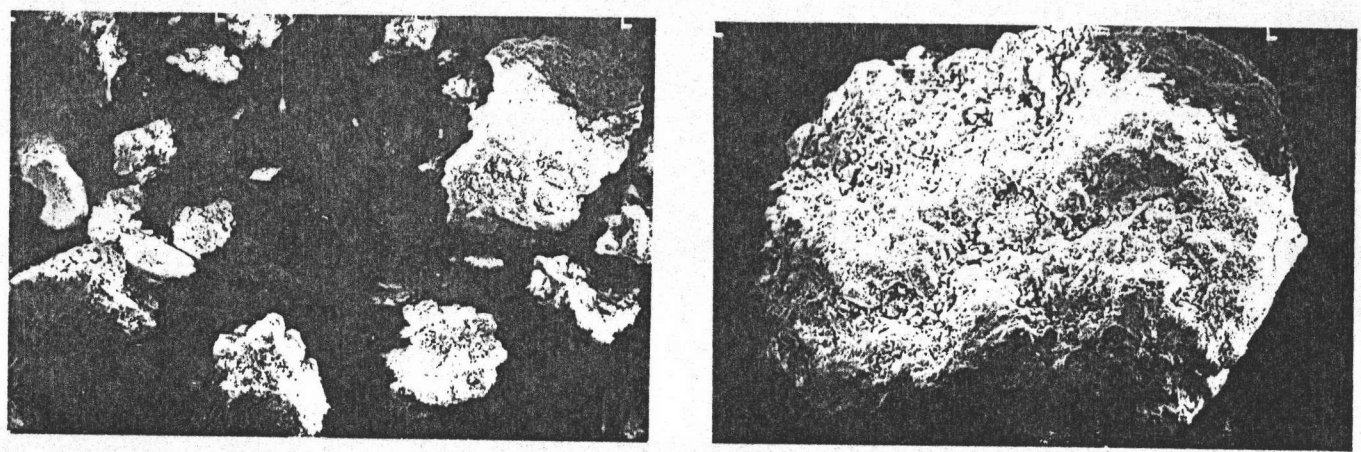
A B

Figure 21 Photomicrographs of Original Pyridoxine Hydrochloride Powders (Key : A x 50, B x 350).



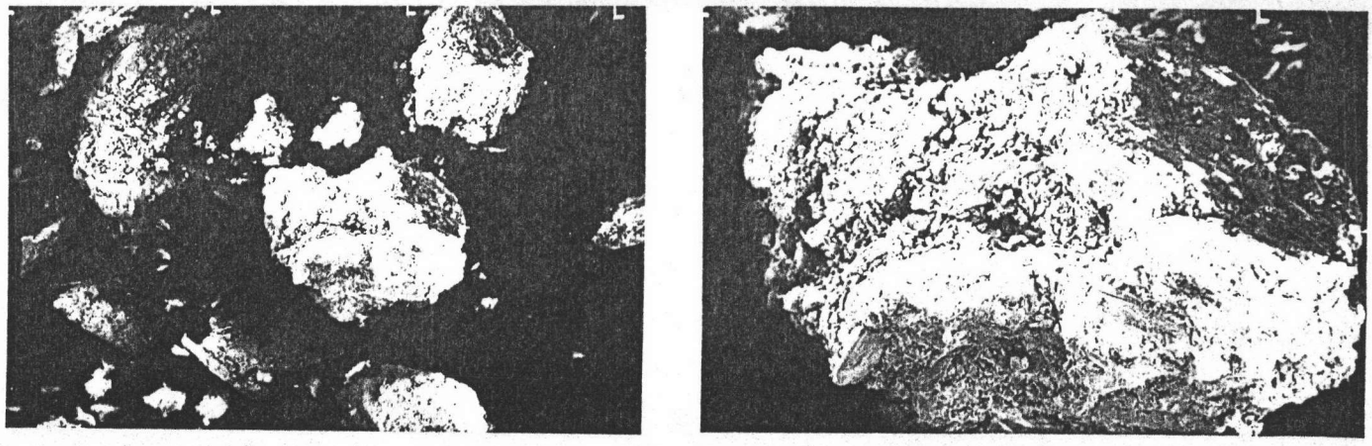
A B

Figure 22 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% D_1 by Solution Incorporation Method (Key : A x 35, B x 100).



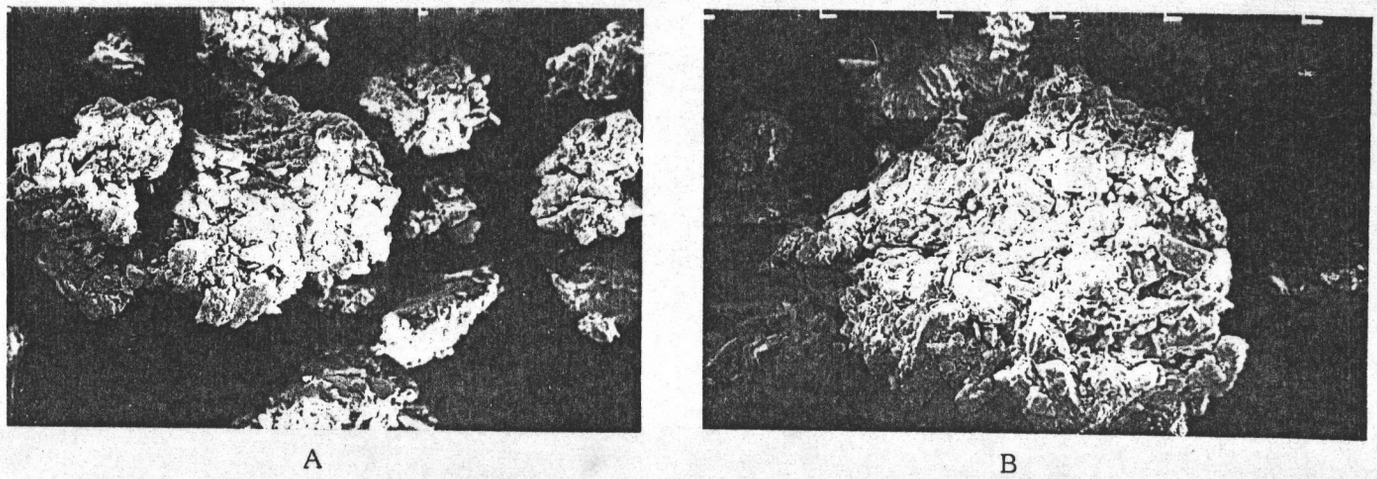
A B

Figure 23 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% D_2 by Solution Incorporation Method (Key : A x 35, B x 100).



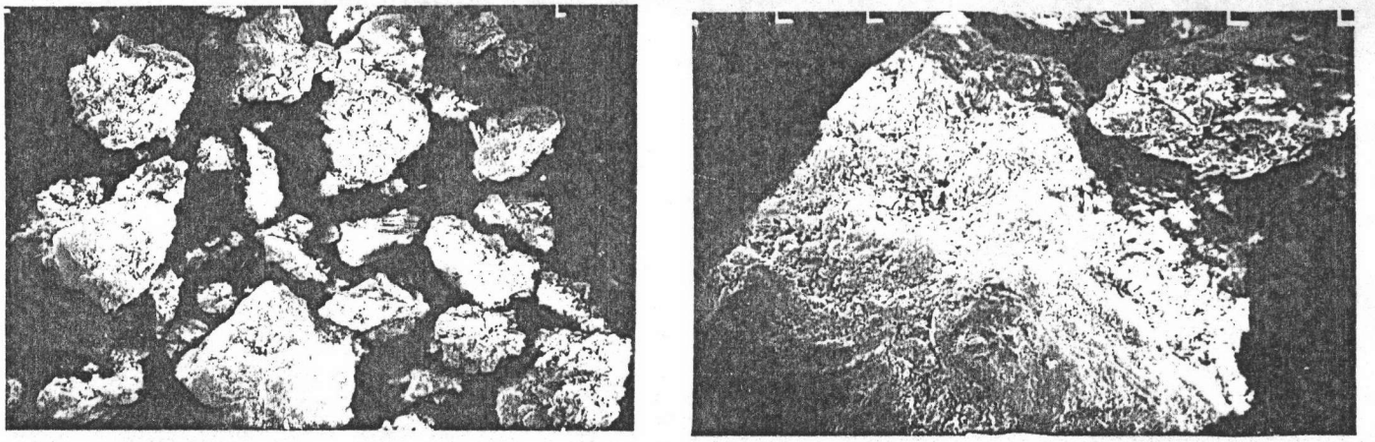
A B

Figure 24 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% PVPK30 by Solution Incorporation Method (Key : A x 35, B x 100).



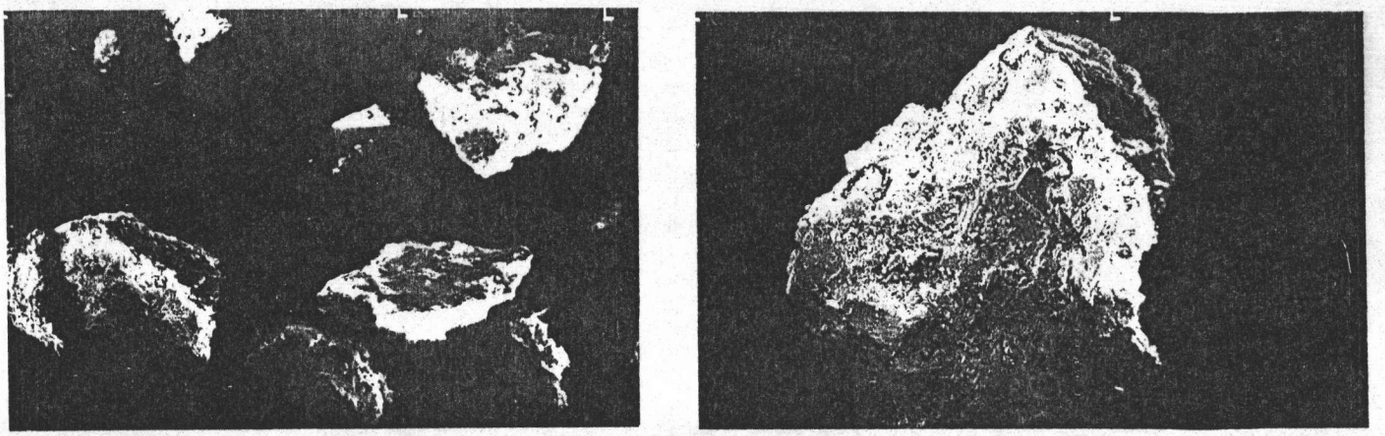
A B

Figure 25 Photomicrographs of Pyridoxine Hydrochloride Granuled Prepared with 2% Corn Starch by Solution Incorporation Method(Key : A x 75, B x 200)



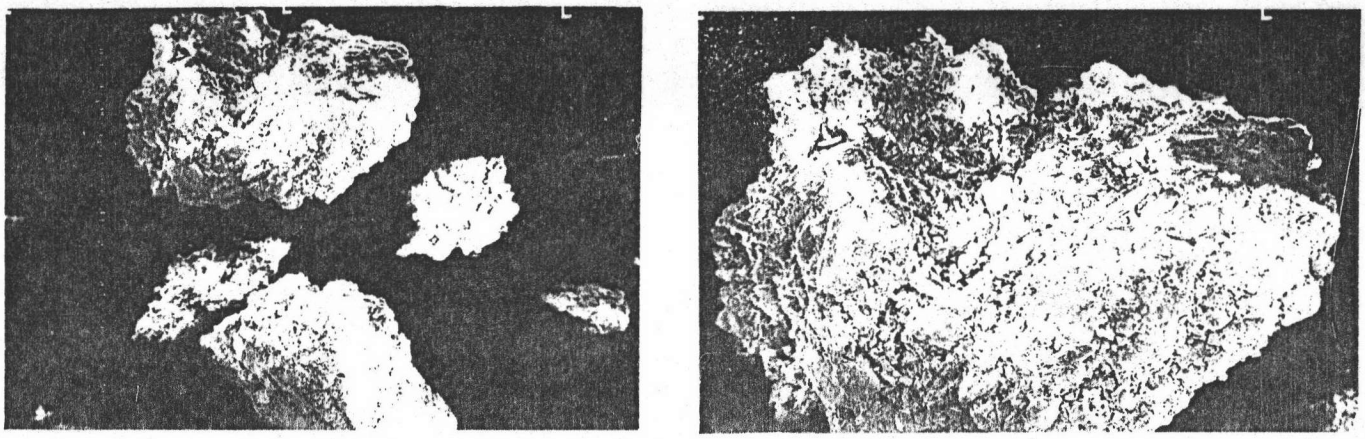
A B

Figure 26 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% Starch 1500(R) by Solution Incorporation Method(Key : A x 50, B x 150).



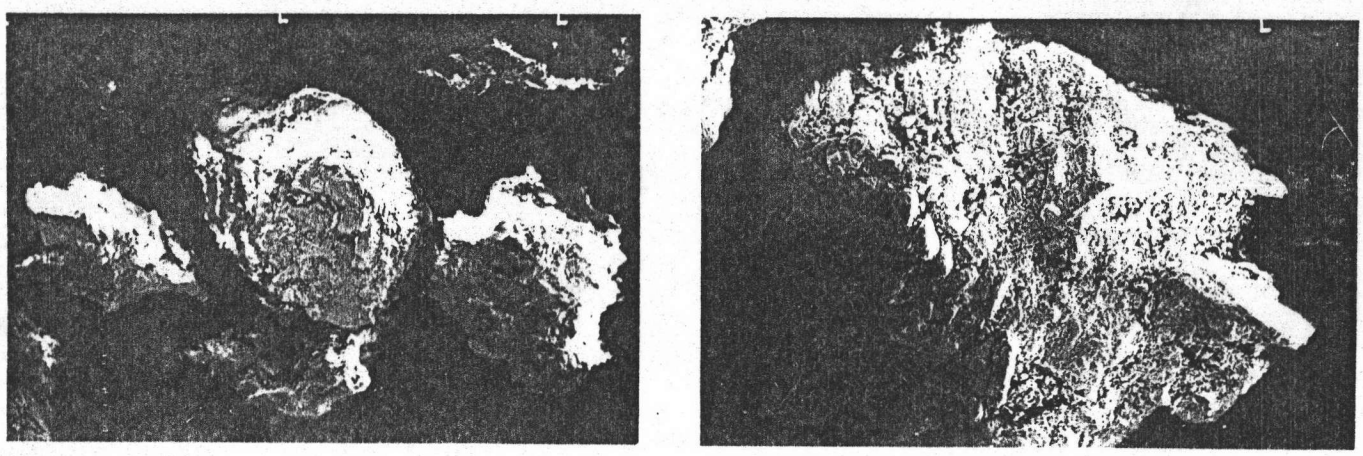
A B

Figure 27 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% Gelatin by Solution Incorporation Method (Key : A x 35, B x 75).



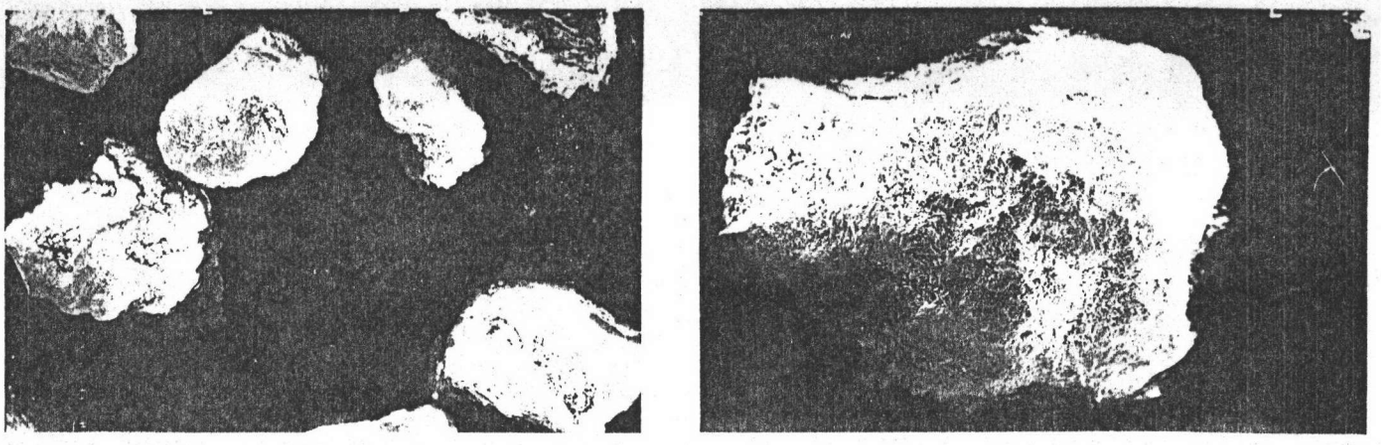
A B

Figure 28 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% Methocel E15LV(R) by Solution Incorporation Method(Key : A x 50, B x 100).



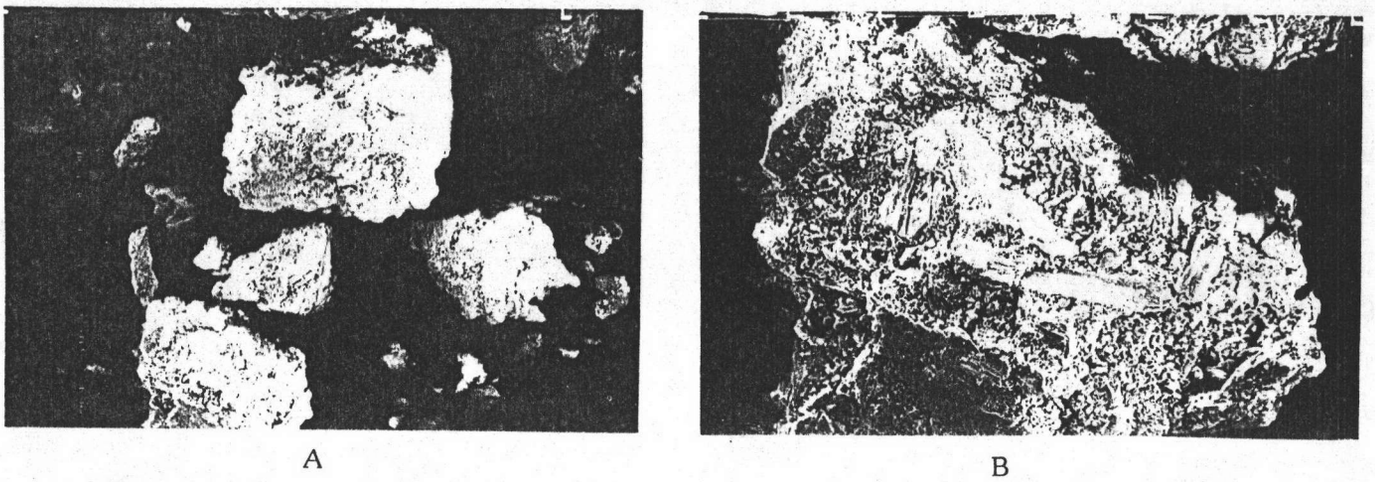
A B

Figure 29 Photomicrographs of Pyridoxine Hydroloride Granules Prepared without Binder (Blank) (Key : A x 50, B x 100).



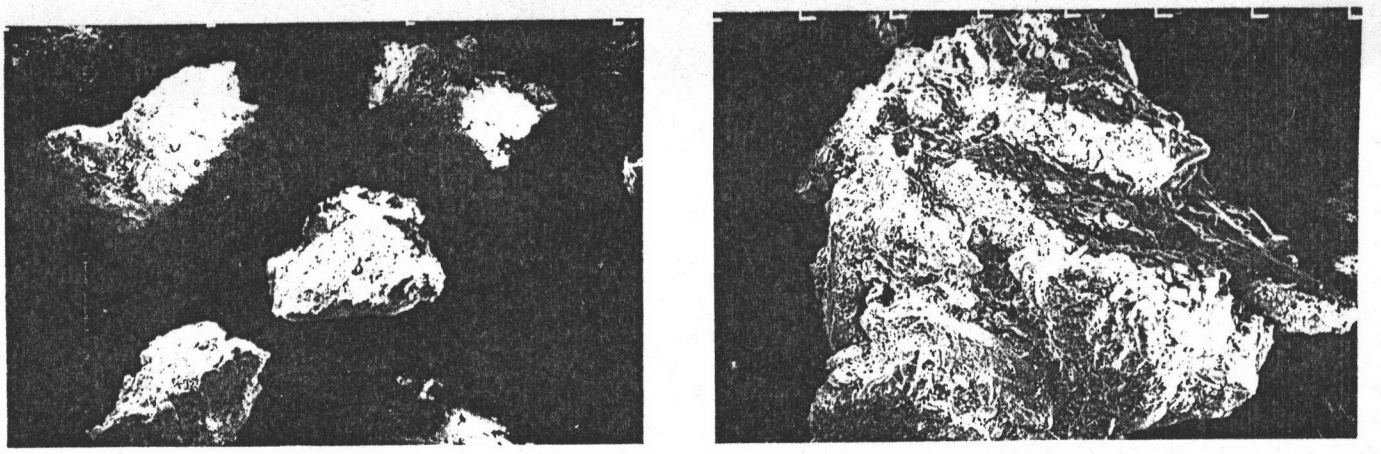
A B

Figure 30 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% D_1 by Dry Incorporation Method (Key : A x 35, B x 100).



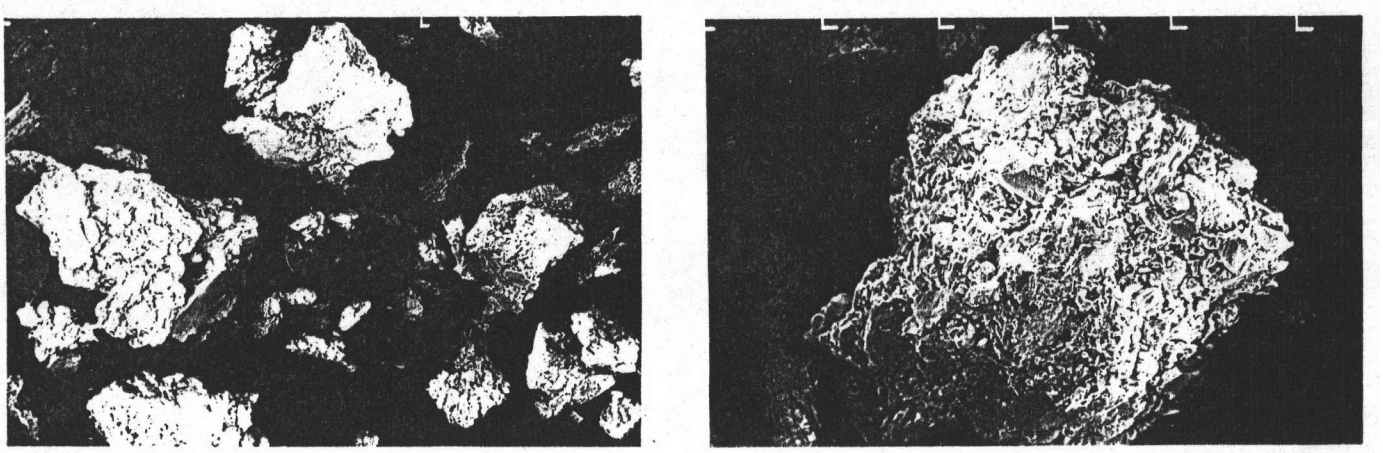
A B

Figure 31 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% D_2 by Dry Incorporation Method (Key : A x 35, B x 150).



A B

Figure 32 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% PVPK30 by Dry Incorporation Method (Key : A x 35, B x 150).



A B

Figure 33 Photomicrographs of Pyridoxine Hydrochloride Granules Prepared with 2% Starch 1500(R) by Dry Incorporation Method (Key : A x 75, B x 200).

2. Particle Size Distribution

2.1 Paracetamol

The cumulative percent undersize of paracetamol granules at various binder concentrations are illustrated in Table 4 and Figure 34-41. It clearly revealed that the average granule size tend to increase as binder concentration increased(Figure 43). Owing to the linear correlationship between granule size and cumulative percent underzide was not seen as plotting in log-probability scale As a result, the average granule size was obtained using the method introduced by El-Gindy et al (10). The average granule size decreased in the following order, at 1% level : PVPK30 > D_2 >Methocel E15LV$^{(R)}$ > gelatin > D_1 >Starch 1500$^{(R)}$ >corn starch. At 2 % level : PVPk30 > D_2 > Starch 1500$^{(R)}$ > gelatin $\simeq$ Methocel E15LV$^{(R)}$ > D_1 > corn starch. In the case of 4 % level : D_2 > PVPk30 $\simeq$ gelatin > Methocel E15LV$^{(R)}$ $\simeq$ D_1 > Starch 1500$^{(R)}$ > corn starch, respectively. At all cencentrations studied PVPk30 and D_2 were considered to produce larger granules than other binders , while corn starch produced the smallest granules. In addition, D_2 possesed greater granules than D_1.

From the results of dry incorporation method at 2 % concentration (Table 5 and Figure 42), the order of decrease in average granule sizes are follow, PVPk30 > Starch 1500$^{(R)}$ $\simeq$ D_1 > D_2. By comparing with the solution incorporation method, D_2 and Starch 1500$^{(R)}$ possessed smaller granules but D_1 gave converse result. In the case of PVPk30 no change in average particle size was observed.

2.2 Pyridoxine Hydrochloride

The same relationships between cumulative percent undersize of granules and binder concentration were observed (except for D_1) as shown in Table 6 and Figures 44-51,53. The results were ranked in the following order, at 1 % level : D_2 > Methocel E15LV$^{(R)}$

Table 4

Sieve Analysis of Paracetamol Granules Prepared with Various Binders and Concentrations by Solution Incorporation Method

Binders	% (w/w)	% Weight Retained[a]					
		Sieve Size (μm)					
		850	425	250	180	150	Pan
D_1	1	3.79	45.34	20.47	12.80	6.07	11.53
	2	2.88	49.34	21.94	8.14	7.04	10.66
	4	7.57	53.25	15.21	19.76	2.23	1.98
D_2	1	6.28	51.54	18.02	7.66	5.16	11.35
	2	8.64	53.51	15.50	6.20	5.47	10.38
	4	13.18	55.93	12.94	5.12	4.24	8.58
PVPK30	1	4.69	54.58	18.89	9.37	3.45	9.02
	2	5.69	59.17	15.64	18.09	0.49	0.92
	4	6.23	62.07	15.96	14.15	1.22	0.37
Corn Starch	1	1.76	44.05	23.06	10.76	14.26	6.11
	2	3.51	49.50	21.29	12.37	7.36	5.97
	4	3.03	51.02	21.87	12.25	6.87	5.36
Starch 1500®	1	1.96	45.81	22.61	9.84	8.10	3.42
	2	3.61	53.22	19.92	10.94	11.68	4.20
	4	4.54	53.40	21.48	13.92	3.24	3.42
Gelatin	1	2.28	48.35	23.09	9.69	15.76	0.83
	2	4.36	49.21	19.66	25.23	1.26	0.28
	4	10.89	53.93	32.31	0.83	1.59	0.45
Methocel E15LV®	1	2.89	48.60	19.65	7.94	6.02	14.90
	2	2.65	50.90	20.08	7.98	5.40	12.99
	4	3.03	60.90	15.70	6.17	3.65	10.55
Blank		2.03	40.97	18.37	24.54	8.28	5.22

(a) averaged from two determinations.

Table 5

Sieve Analysis of Paracetamol Granules Prepared with Various Binders at 2% Concentration by Dry Incorporation Method.

Binders	% Weight Retained[a]					
	Sieve Size (μm)					
	850	425	250	180	150	Pan
D_1	3.25	53.42	18.51	21.15	3.42	0.25
D_2	2.33	51.63	20.40	8.86	6.28	10.50
PVPK30	7.00	56.86	32.70	2.10	1.24	0.10
Starch 1500®	2.74	54.48	20.18	11.80	10.17	0.63

(a) averaged from two determinations.

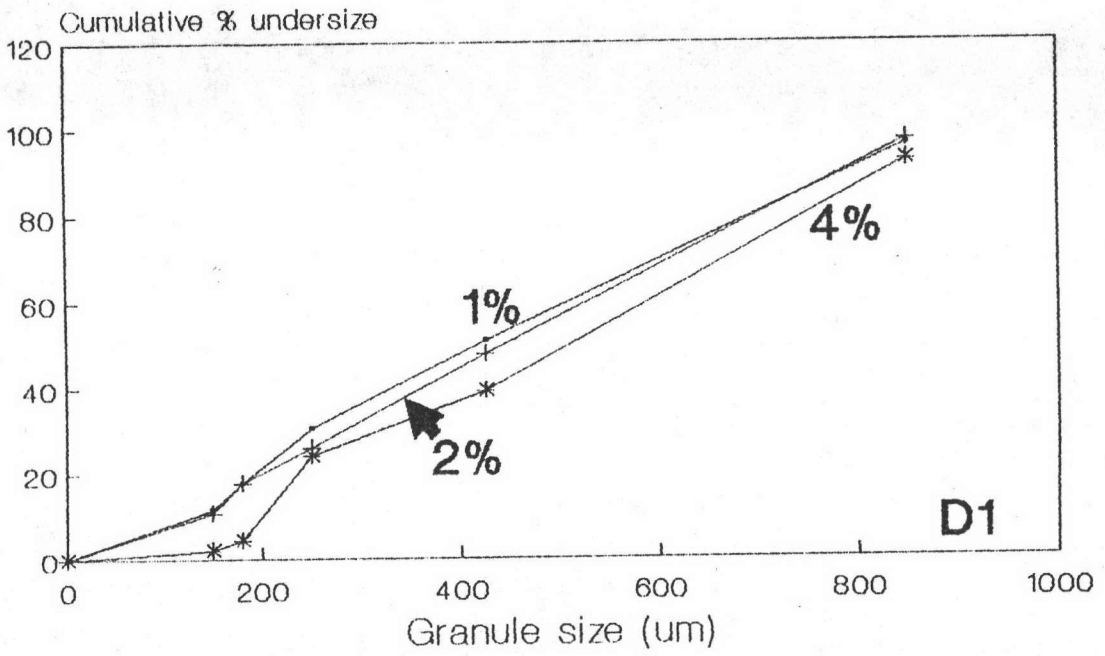


Figure 34 Effect of D_1 Concentration on the Cumulative Percent Undersize for Paracetamol Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

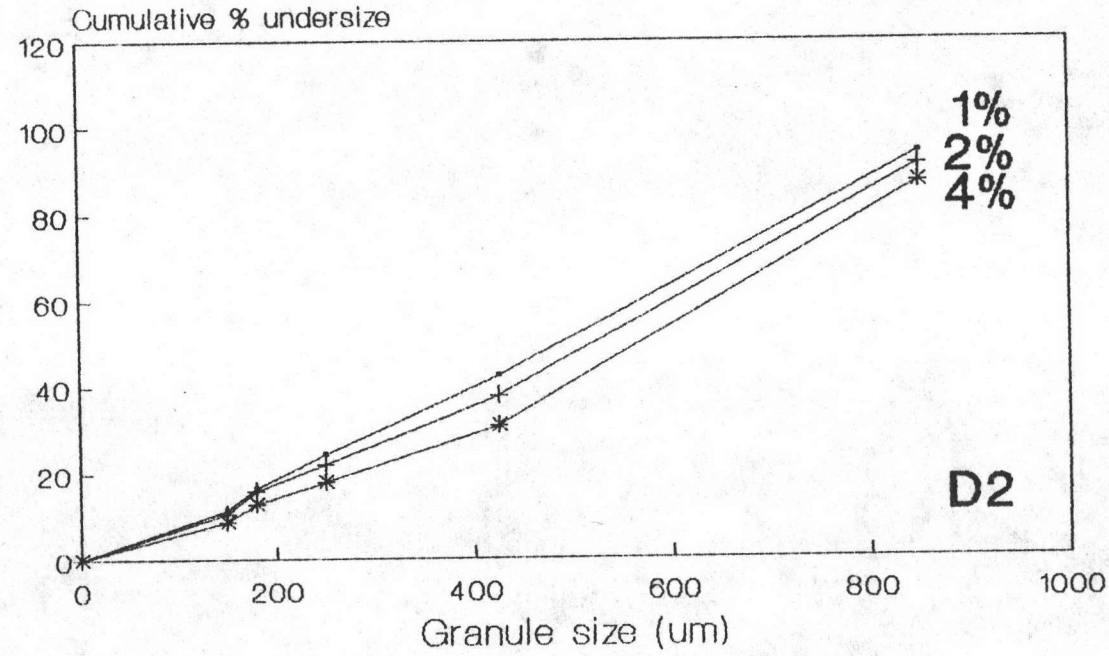


Figure 35 Effect of D_2 Concentration on the Cumulative Percent Undersize for Paracetamol Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

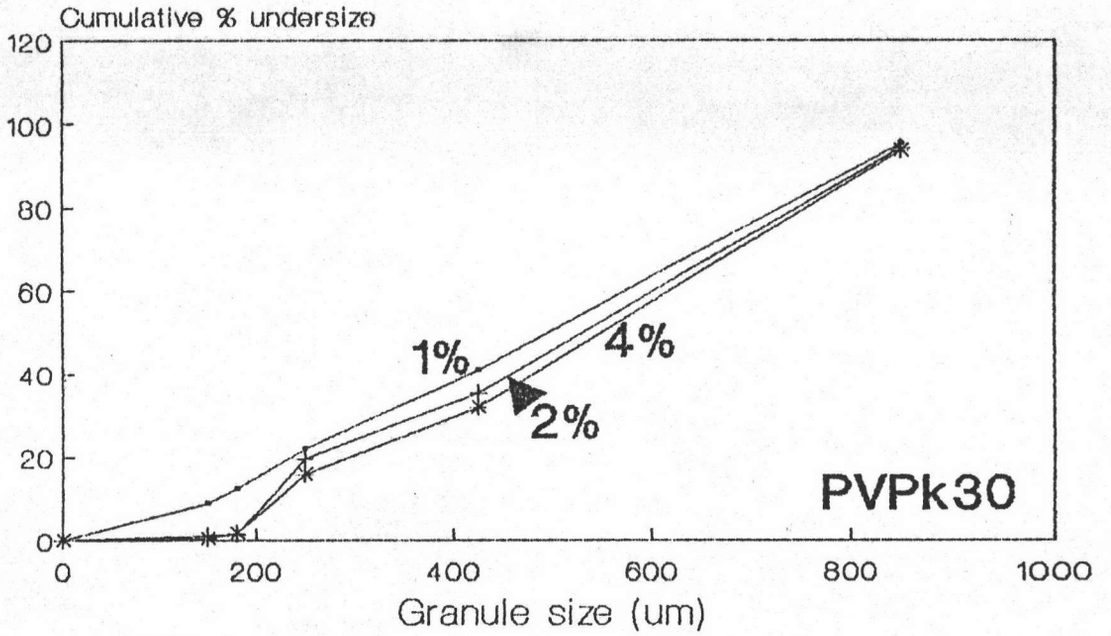


Figure 36 Effect of PVPK30 Concentration on the Cumulative Percent Undersize for Paracetamol Granules by solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

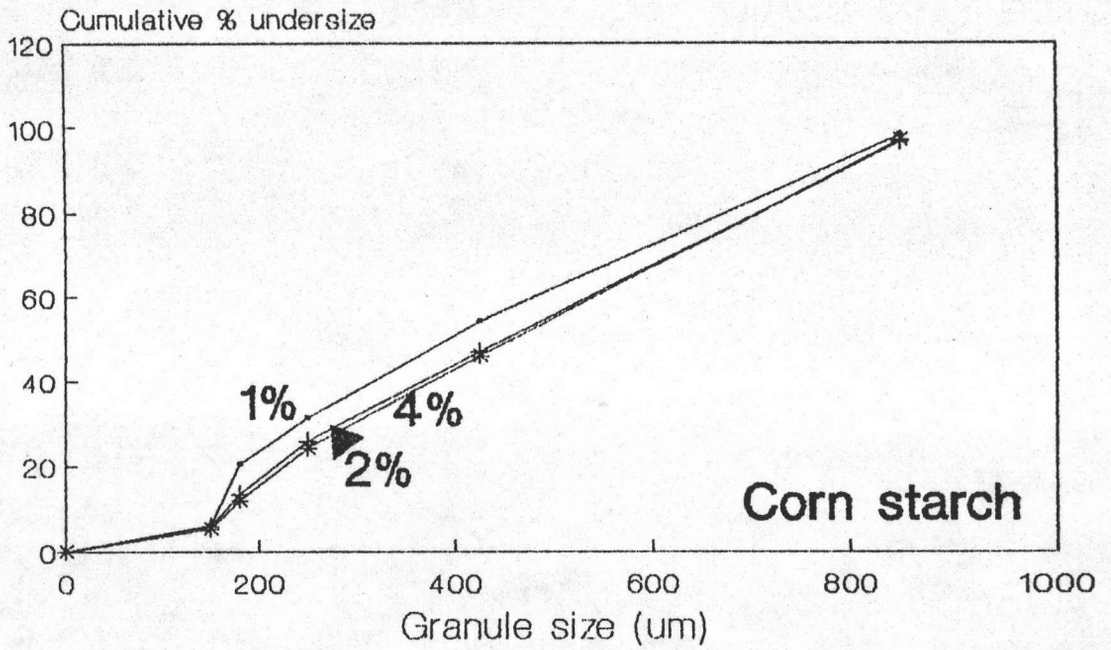


Figure 37 Effect of Corn Starch Concentration on the Cumulative Percent Undersize for Paracetamol Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

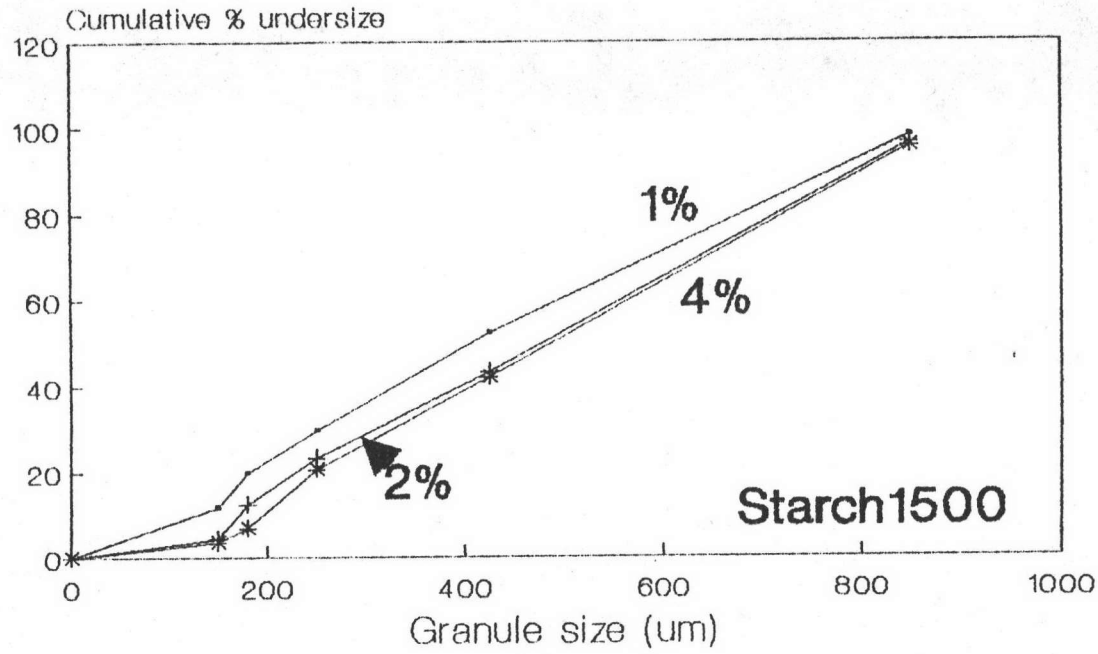


Figure 38 Effect of Starch 1500(R) Concentration on the Cumulative Percent Undersize for Paracetamol Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

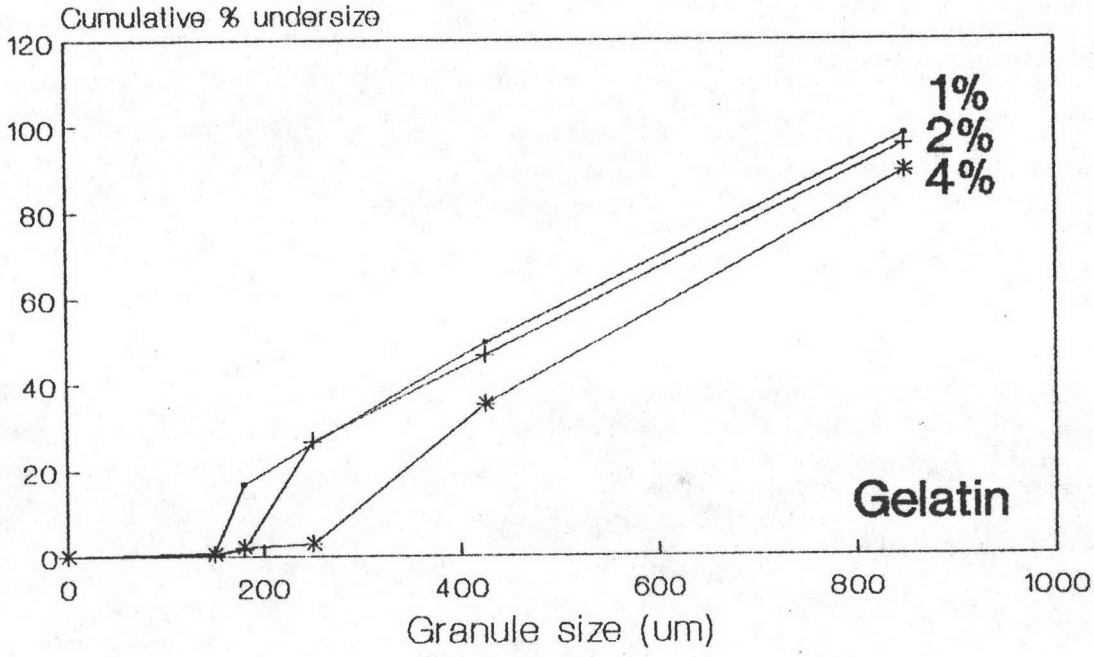


Figure 39 Effect of Gelatin Concentration on the Cumulative Percent Undersize for Paracetamol Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

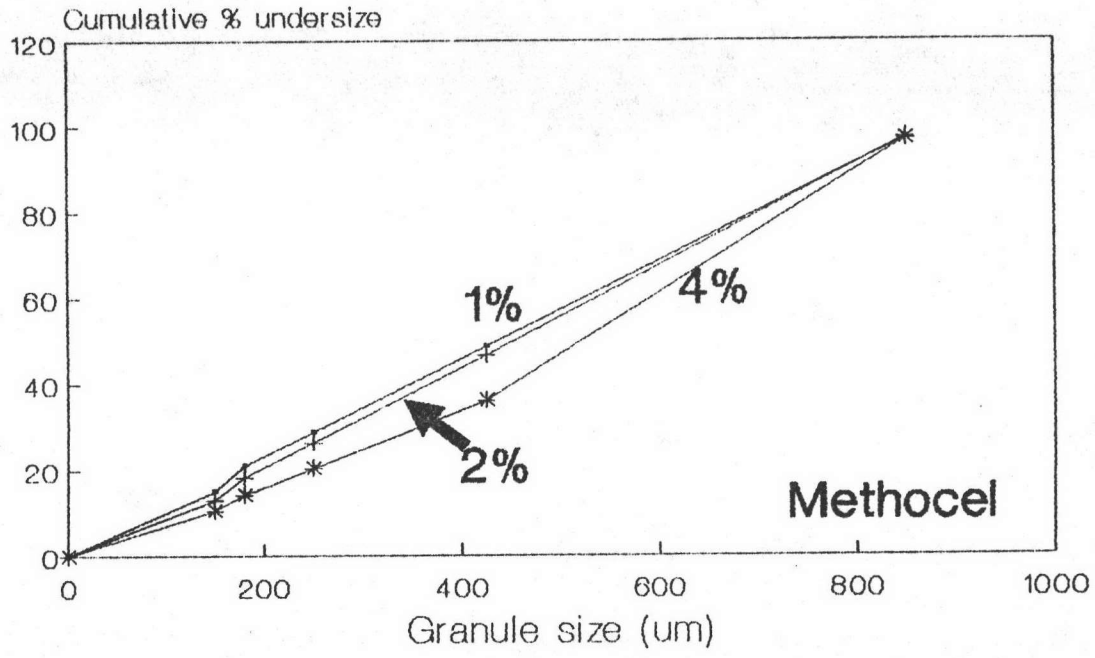


Figure 40 Effect of Methocel E15LV(R) Concentration on the Cumulative Percent Undersize for Paracetamol Granules by Solution Incorporation method (Key : —•— 1%, —┼— 2%, —*— 4%).

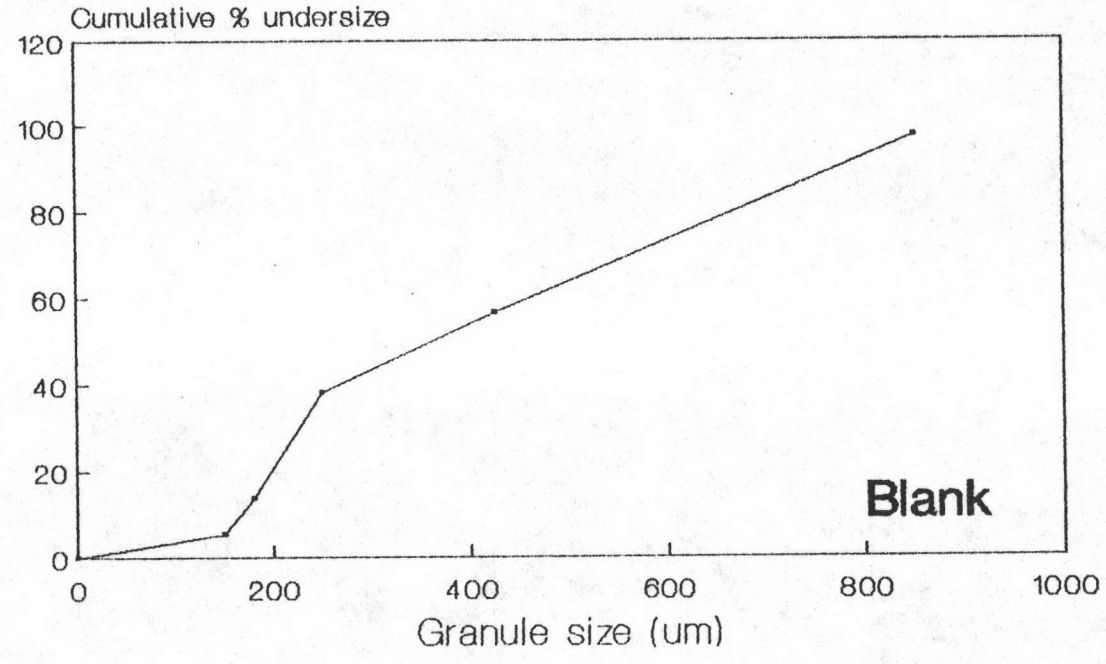


Figure 41 Cumulative Percent Undersize for Blank Paracatamol Prepared with Purified Water.

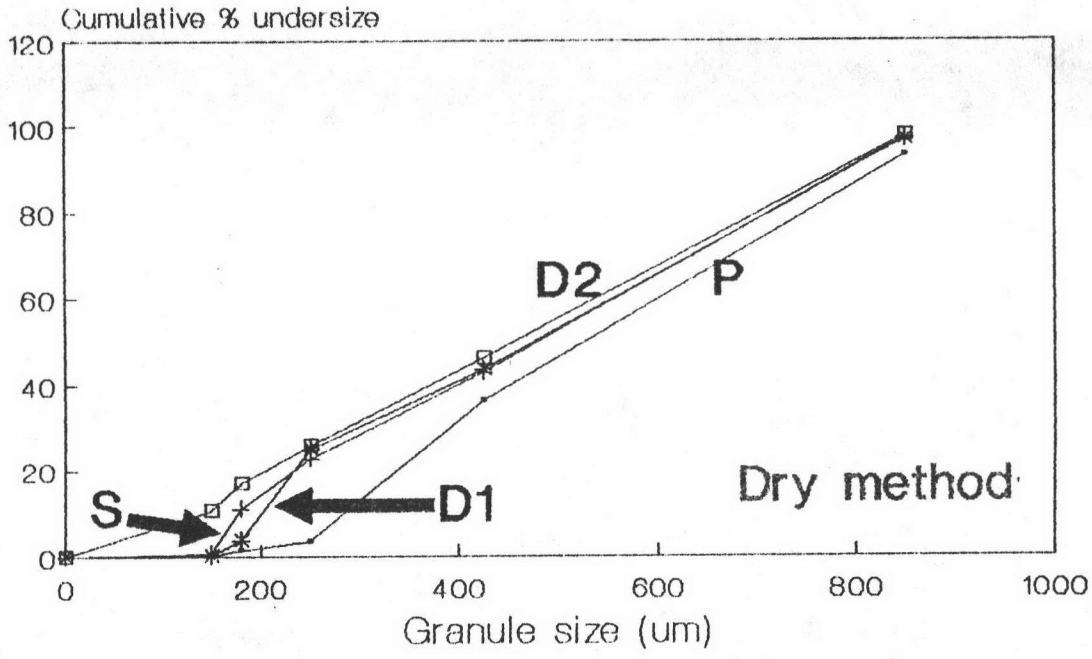


Figure 42 Effect of Various Binders at 2% Concentration on the Cumulative Percent Undersize for Paracetamol Granules by Dry Incorporation Method (Key : ✳ D_1, ⊞ D_2, —•— PVPK30, —|— Starch 1500$^{(R)}$)

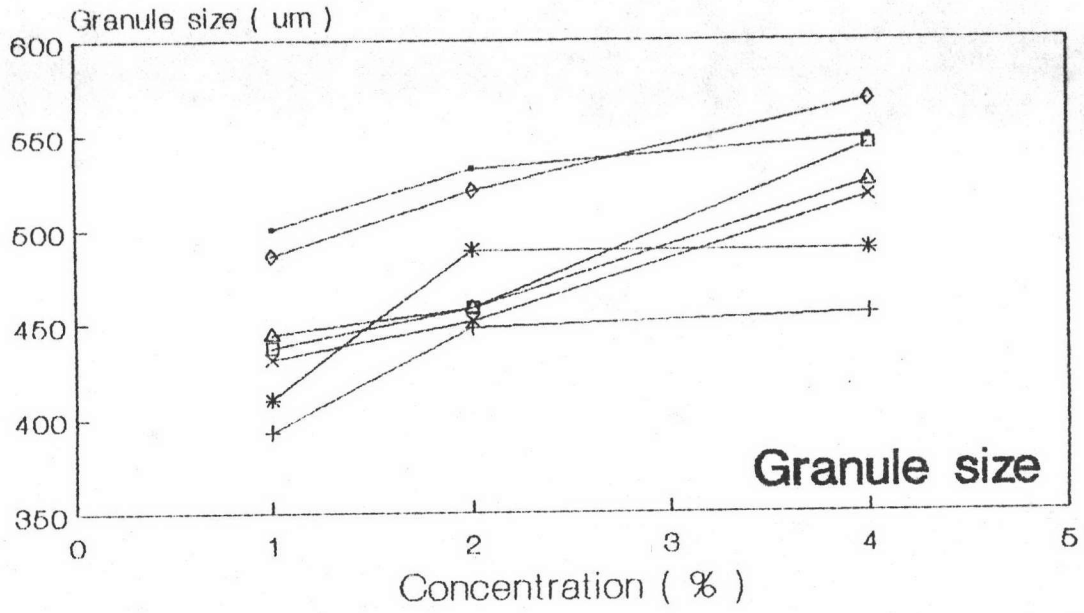


Figure 43 Effect of Binder Types and Concentrations on Average Granule Size of Paracetamol Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®)

Table 6

Sieve Analysis of Pyridoxine Hydrochloride Granules Prepared with Various Binders and Concentrations by Solution Incorporation Method.

Binders	% (w/w)	% Weight Retained[a]					
		Sieve Size (μm)					
		850	425	250	180	150	Pan
D_1	1	6.03	46.60	13.33	4.91	3.42	25.71
	2	8.15	44.79	18.50	8.08	18.23	2.25
	4	16.72	35.82	13.50	6.24	5.33	22.39
D_2	1	12.52	49.64	14.99	5.68	3.56	13.61
	2	10.74	56.77	14.48	4.89	2.66	10.46
	4	21.60	43.68	13.14	4.95	3.37	13.26
PVPK30	1	7.98	49.69	12.99	5.43	3.27	20.64
	2	9.47	50.81	14.35	6.00	3.28	16.09
	4	17.86	44.36	11.28	5.05	2.99	18.46
Corn Starch	1	1.75	48.27	20.40	10.71	6.33	12.54
	2	1.93	50.44	23.33	9.36	4.19	10.75
	4	2.22	54.92	23.57	7.75	3.36	8.19
Starch 1500(R)	1	2.08	48.68	21.76	10.70	5.64	11.14
	2	4.39	50.75	20.65	8.66	3.84	11.71
	4	5.71	53.46	20.69	7.85	3.84	8.45
Gelatin	1	8.79	40.10	11.14	8.02	6.56	25.40
	2	10.24	42.10	11.67	7.84	6.14	22.02
	4	12.19	43.15	12.61	4.61	4.27	23.18
Methocel E15LV(R)	1	7.26	51.64	12.26	8.03	5.98	14.83
	2	9.56	54.48	12.95	5.00	2.93	15.07
	4	17.12	47.93	10.15	4.14	2.98	17.67
Blank		11.24	41.07	12.68	5.61	3.35	25.95

(a) averaged from two determinations.

Table 7

Sieve Analysis of Pyridoxine Hydrochloride Granules Prepared with Various Binders at 2% Concentration by Dry Incorporation Method.

Binders	% Weight Retained[a]					
	Sieve Size (μm)					
	850	425	250	180	150	Pan
D_1	14.80	46.22	13.54	8.28	3.96	13.70
D_2	15.96	42.96	12.52	5.36	3.49	19.68
PVPK30	11.45	51.45	12.48	4.96	2.92	16.74
Starch 1500[R]	9.33	52.82	15.78	5.45	3.02	13.60

(a) averaged from two determinations.

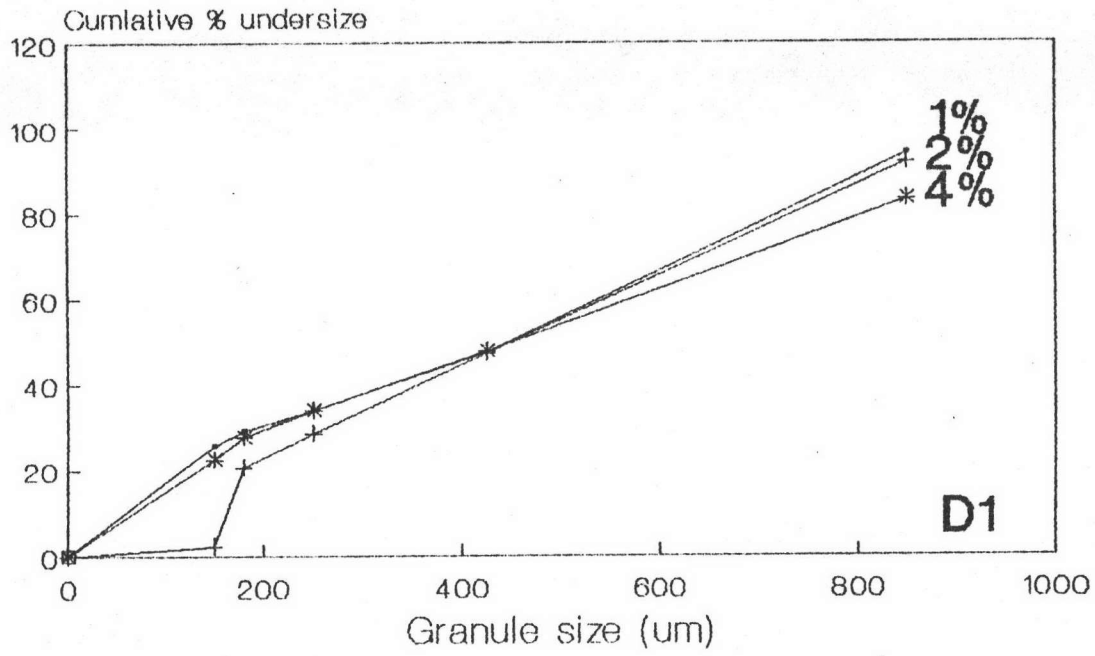


Figure 44 Effect of D_1 Concentration on the Cumulative Percent Undersize for Pyridoxine Hydrochloride Granules by Solution Incorporation Method (Key : —•— 1%, —+— 2%, —*— 4%).

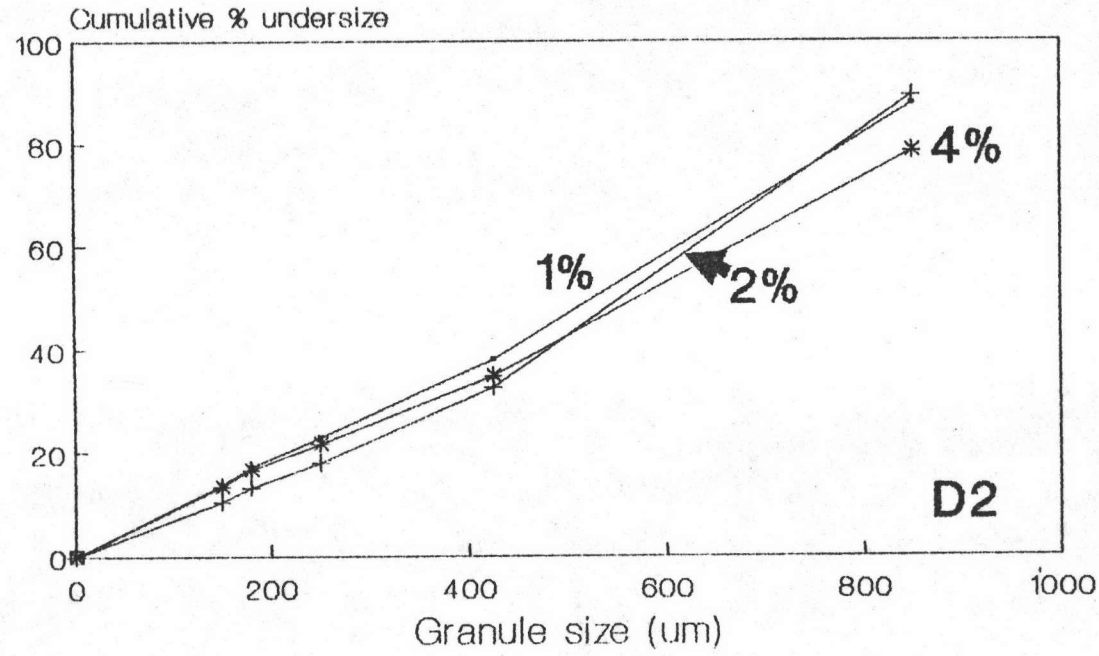


Figure 45 Effect of D_2 Concentration on the Cumulative Percent Undersize for Pyridoxine Hydrochloride Granules by Solution Incorporation Method (Key : —•— 1%, —+— 2%, —*— 4%).

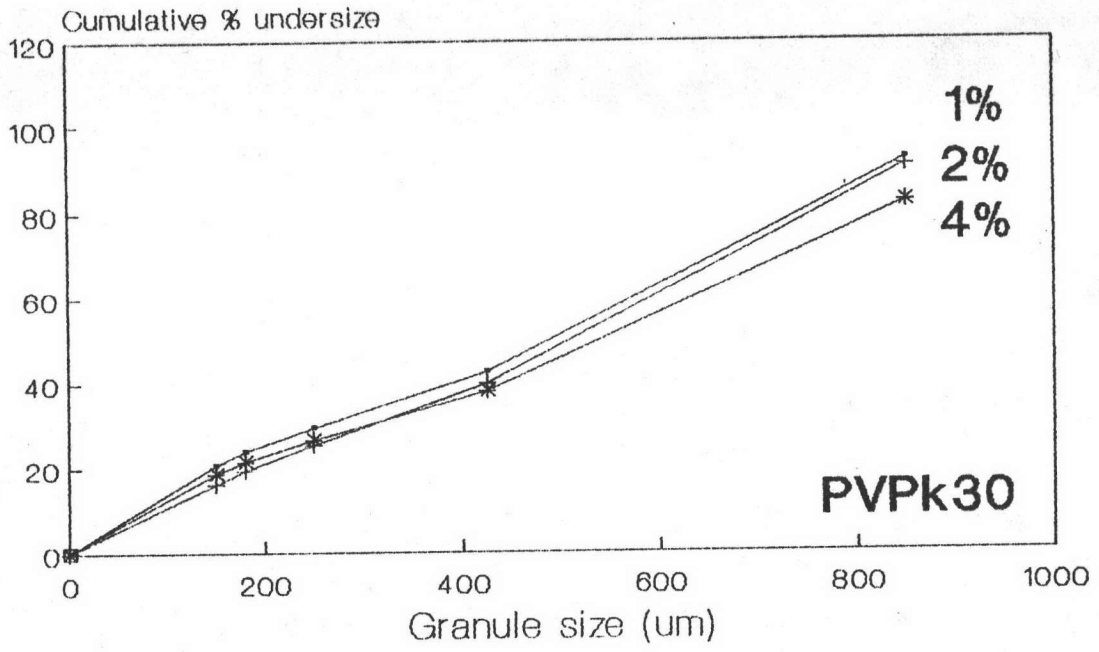


Figure 46 Effect of PVPK30 Concentration on the Cumulative Percent Undersize for Pyridoxine Hydrochloride Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

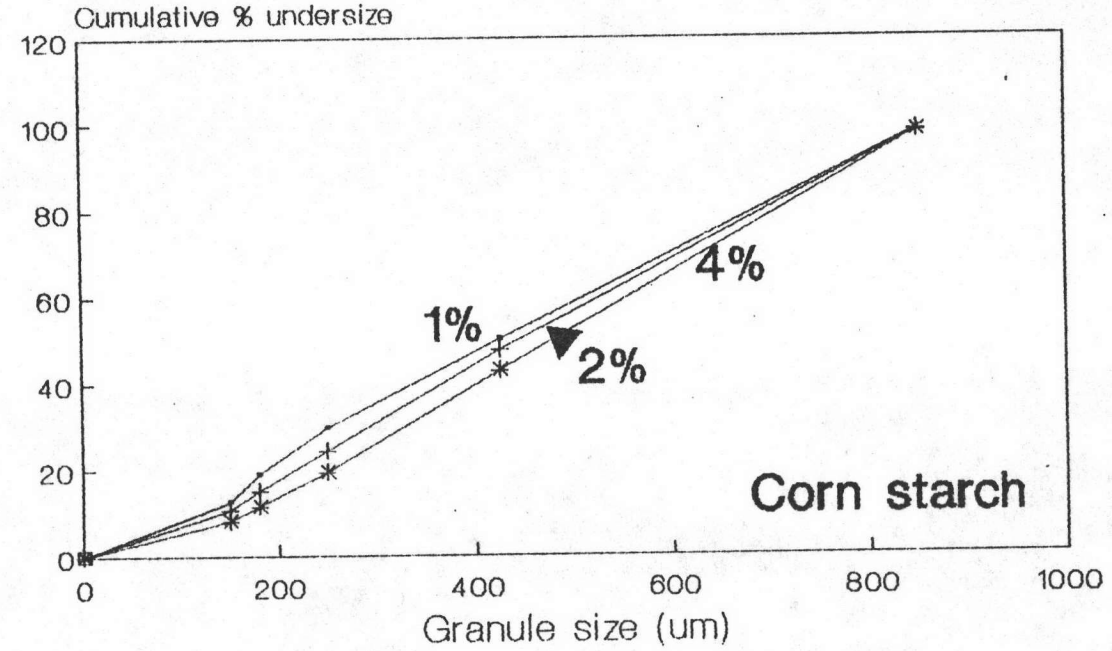


Figure 47 Effect of Corn Starch Concentration on the Cumulative Percent Undersize for Pyridoxine Hydrochloride Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

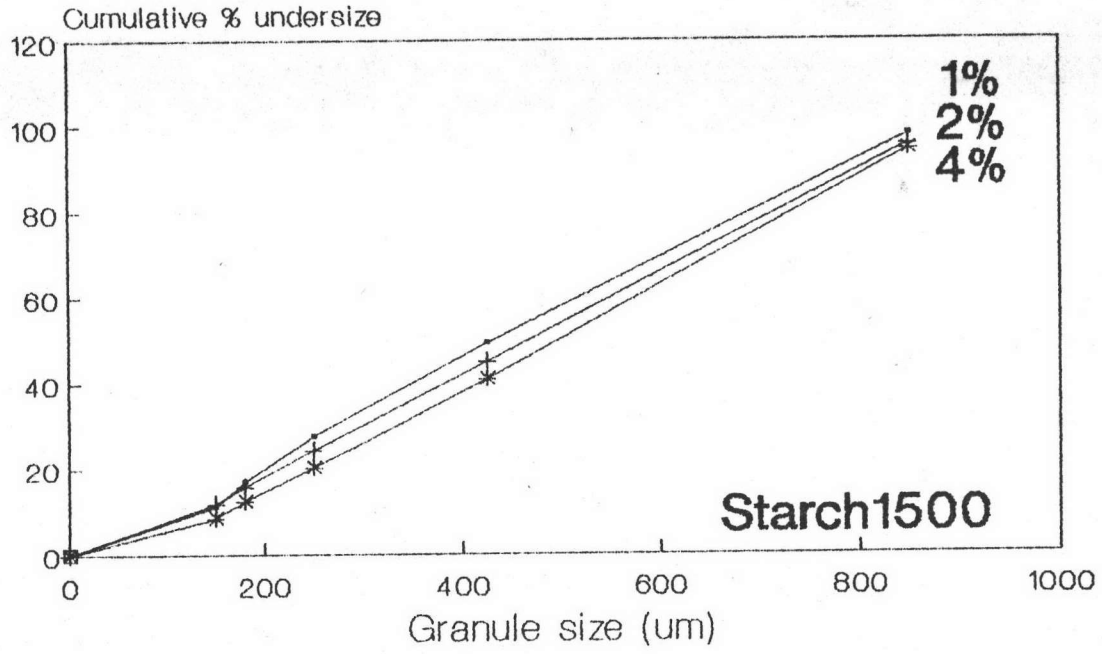


Figure 48 Effect of Starch 1500(R) Concentration on the Cumulative Percent Undersize for Pyridoxine Hydrochloride Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

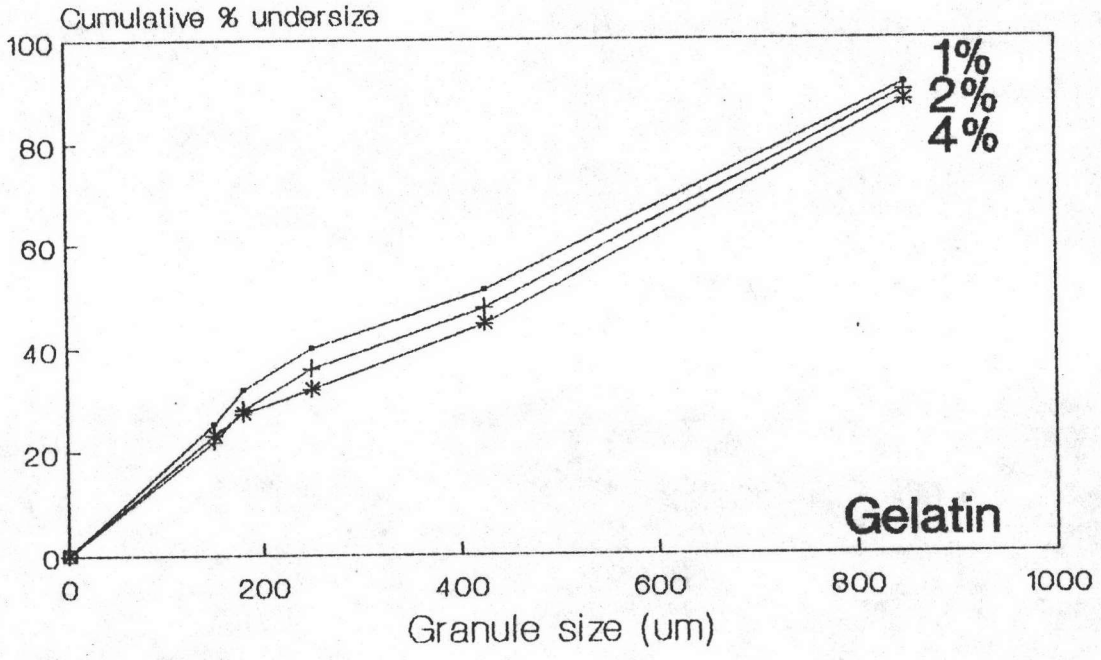


Figure 49 Effect of Gelatin Concentration on the Cumulative Percent Undersize for Pyridoxine Hydrochloride Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

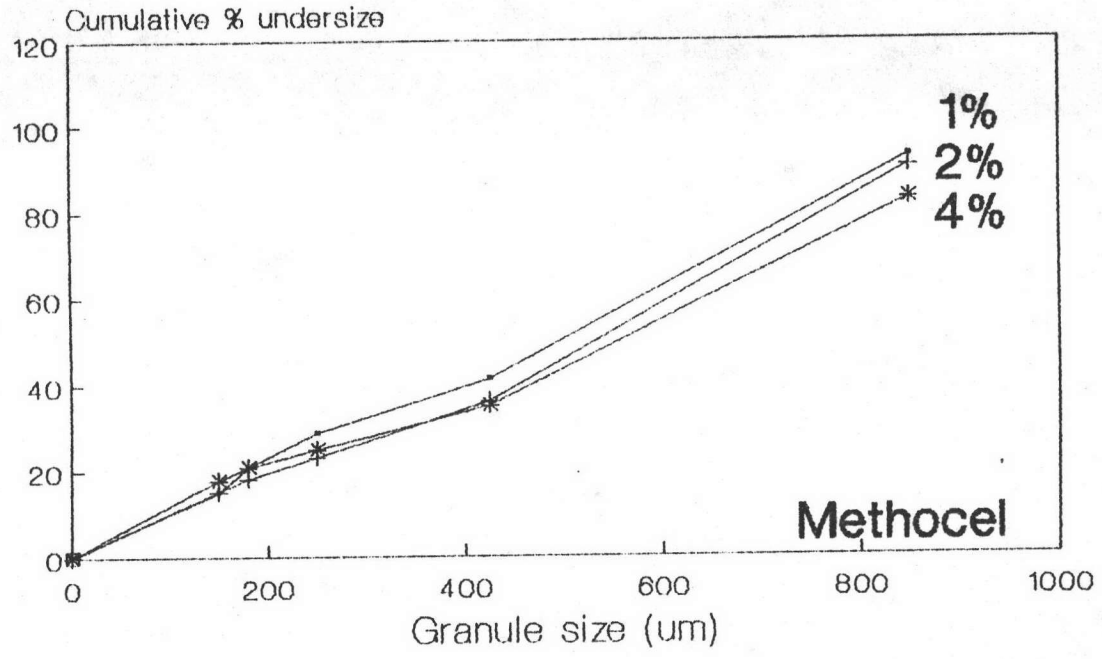


Figure 50 Effect of Methocel E15LV(R) Concentration on the Cumulative Percent Undersize for Pyridoxine Hydrochloride Granules by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

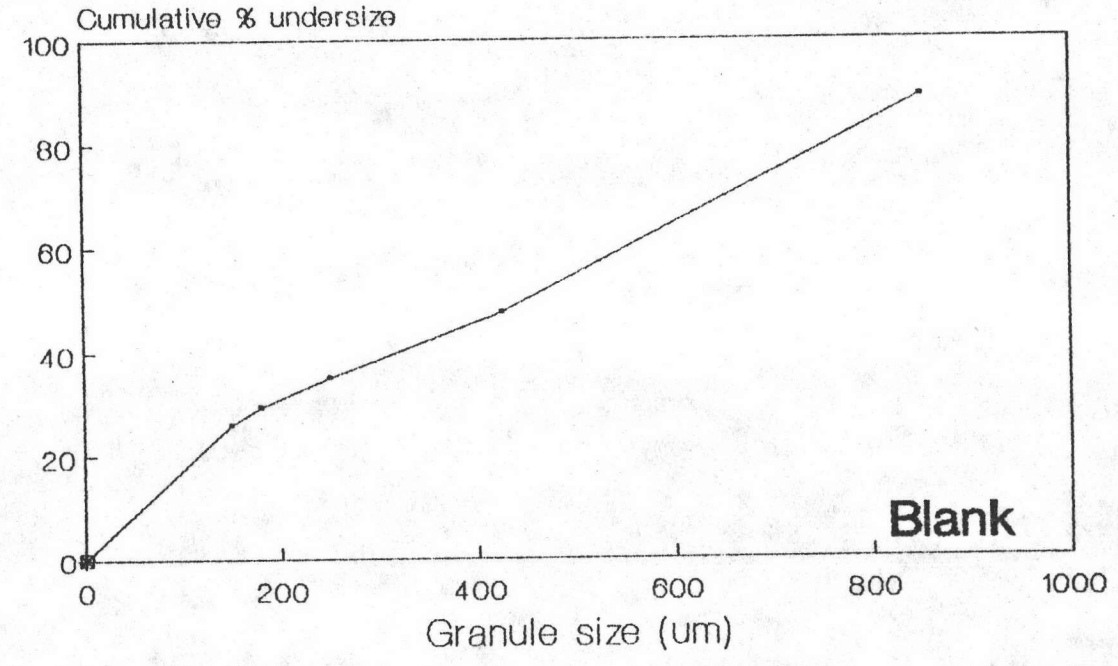


Figure 51 Cumulative Percent Undersize for Blank Pyridoxine Hydrochloride Prepared with Purified Water.

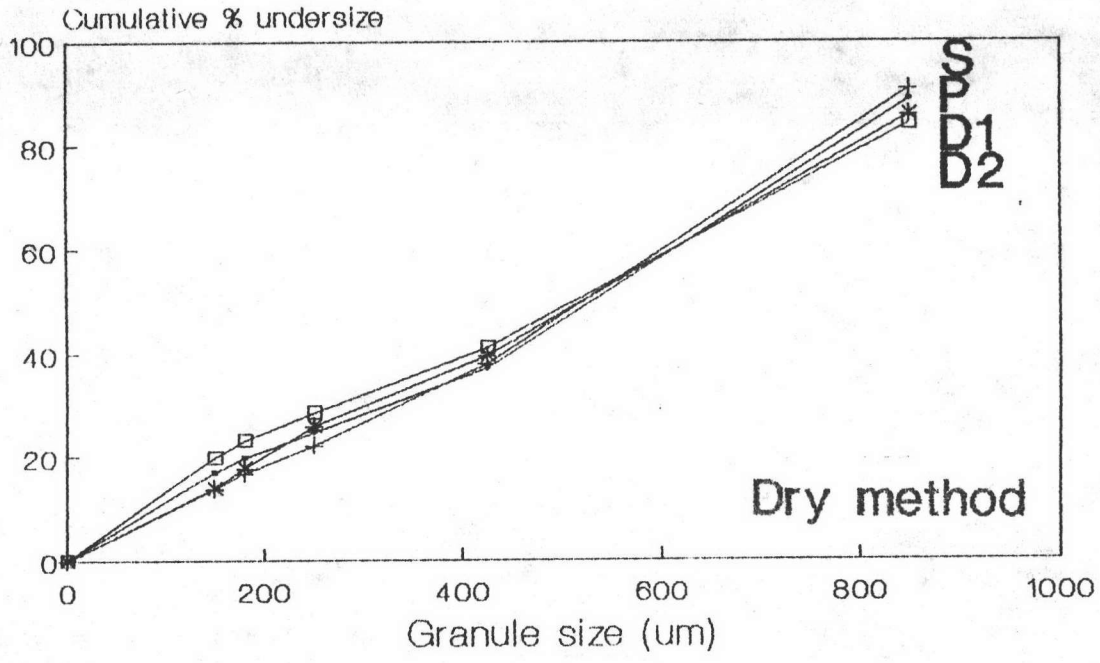


Figure 52 Effect of Various Binders at 2% Concentration on the Cumulative Percent Underzide for Pyridoxine Hydrochloride Granules by Dry Incorporation Method (Key : ✳ D_1, ⊟ D_2, • PVPK30, + Starch 1500$^{(R)}$).

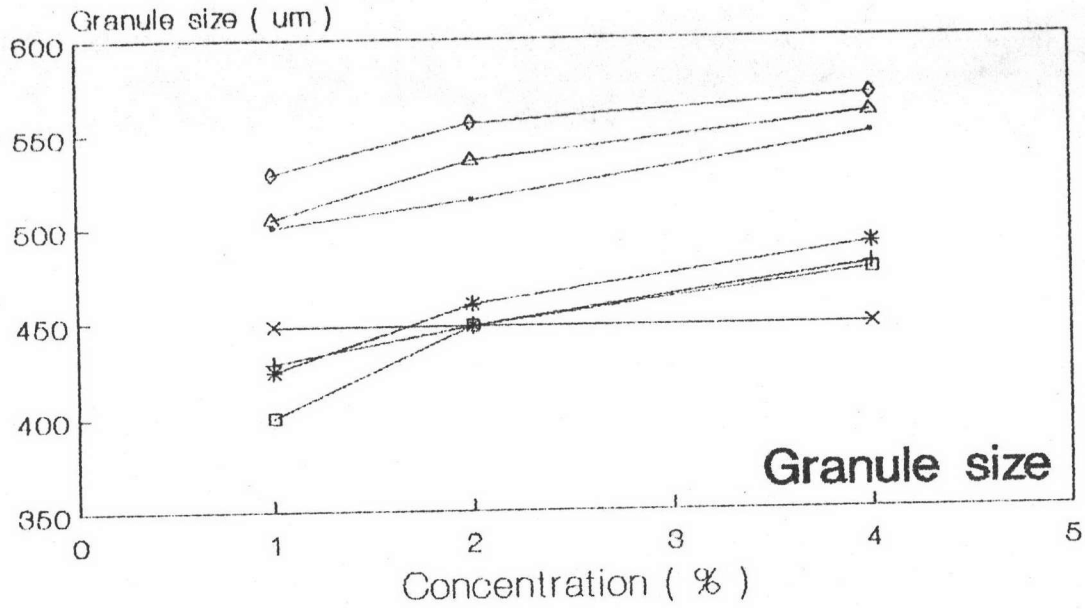


Figure 53 Effect of Binder Types and Concentrations on Average Granule Size of Pyridoxine Hydrochloride Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$).

$\simeq$ PVPk30 > D_1 > corn starch $\simeq$ Starch 1500(R) > gelatin. At 2 % level: D_2 > Methocel E15LV(R) > PVPk30 > Starch 1500(R) > gelatin $\simeq$ D_1 $\simeq$ Corn starch. In the case of 4 % level : D_2 > Methocel E15LV(R) > PVPk30 > Starch 1500(R) > corn starch > gelatin > D_1. The greatest granule size was given by D_2 . The granule produced by dry incorporation method (Table 7 and Figure 52) exhibited larger size than solution method except for D_2 .

The blank granules of both cases (except for pyridoxine hydrochloride prepared with corn starch , Starch 1500(R) and gelatin at 1 %) showed smaller in size than granule obtained from various binders in this study, regarding the process of preparations.

3. Bulk Density , Tapped Density and Compressibility Determination

3.1 Paracetamol

The effect of binder types and concentrations on bulk density , tapped density and percent comperssibility of granules are shown in Tables 8-9. Slightly decreasing in bulk density and tapped density with increasing binder concentration were noticed. For all cases, the bulk density and tapped density are ranging from 0.42 - 0.64 g / ml and 0.53 - 0.77 g/ml , respectively. On the other hand , percent compressibility (Figure 54) of granules are decreased as percent binder used increased and ranging from 13.00 to 20.75 %. The percent compressibility of granules produced by dry incorporation method were slightly lower than prepared by solutiuon incorporation method expect for D_2

3.2 Pyridoxine hydrochloride

From Tables 10-11, correlation between density and binder concentration were also observed . The bulk density and tapped density were ranging from 0.43 - 0.61 g/ml and 0.52 - 0.78

Table 8

Physical Properties of Paracetamol Granules Prepared with Various Binders and Concentrations by Solution Incoporation Method.

Binders	Physical Properties of Granules								
	Granule Size (μm) *	Bulk Density (g/ml, ±SD) **	Tapped Density (g/ml, ±SD) **	Compressibility (%)	Flow Rate (g/min, ±SD) **	Angle of Repose (°, ±SD) **	Friability (%) *	Fine (%) *	Moisture Content (%) *
D1	431	0.45 (0.00)	0.55 (0.02)	18.18	288.00 (3.34)	33.96 (0.48)	27.60	10.80	1.90
	451	0.43 (0.00)	0.53 (0.01)	18.86	274.80 (5.15)	34.75 (0.41)	23.22	8.04	1.40
	517	0.42 (0.01)	0.53 (0.00)	20.75	264.00 (2.98)	35.40 (0.43)	9.02	5.13	2.00
D2	486	0.48 (0.00)	0.58 (0.00)	17.24	292.68 (3.80)	33.82 (0.24)	21.64	11.68	1.00
	520	0.46 (0.00)	0.57 (0.01)	19.30	289.70 (4.59)	34.40 (0.49)	20.30	10.29	1.90
	568	0.45 (0.00)	0.56 (0.00)	19.64	279.00 (3.01)	34.75 (0.19)	6.60	8.42	2.10
PVPK30	500	0.53 (0.10)	0.61 (0.02)	13.11	267.00 (3.21)	33.26 (0.50)	10.10	9.43	1.50
	531	0.50 (0.00)	0.60 (0.00)	16.67	250.20 (10.25	33.83 (0.00)	7.31	7.45	1.20
	548	0.48 (0.00)	0.60 (0.02)	20.00	154.40 (2.14)	35.82 (0.25)	4.64	4.33	2.10
Corn Starch	393	0.49 (0.00)	0.59 (0.02)	16.95	308.40 (7.52)	32.25 (0.50)	22.60	12.05	2.40
	448	0.47 (0.00)	0.57 (0.01)	17.54	255.60 (9.85)	33.73 (0.10)	20.79	8.00	2.10
	455	0.47 (0.00)	0.57 (0.02)	17.54	237.00 (4.23)	34.96 (0.48)	18.62	9.90	1.70
Starch 1500(R)	410	0.64 (0.00)	0.77 (0.02)	13.00	434.40 (5.14)	22.42 (0.27)	22.42	12.25	1.10
	489	0.62 (0.01)	0.75 (0.01)	17.33	342.80 (2.22)	21.37 (0.46)	21.37	10.10	1.50
	489	0.60 (0.00)	0.74 (0.01)	18.92	340.80 (7.89)	20.00 (0.47)	20.00	9.85	1.20
Gelatin	437	0.50 (0.00)	0.62 (0.01)	19.35	319.80 (3.11)	33.54 (0.24)	18.19	12.70	2.10
	458	0.49 (0.00)	0.61 (0.02)	19.67	297.00 (5.22)	33.75 (0.92)	8.45	11.45	1.80
	544	0.49 (0.00)	0.61 (0.00)	19.67	270.60 (4.30)	35.04 (0.97)	7.04	5.05	1.40
Methocel E151V(R)	444	0.48 (0.00)	0.58 (0.00)	17.24	309.00 (10.25)	33.40 (0.00)	9.50	15.05	1.30
	458	0.46 (0.00)	0.56 (0.01)	17.86	298.80 (6.39)	33.54 (0.25)	6.60	12.05	2.00
	524	0.46 (0.00)	0.56 (0.02)	17.86	267.00 (8.46)	33.69 (0.25)	3.38	7.90	1.60
Blank	361	0.49(0.01)	0.62 (0.01)	20.97	333.60 (11.1)	33.19 (0.03)	35.78	20.81	1.10

* averaged from two determinations.
** averaged from three determinations.

Table 9

Physical Properties of Paracetamol Granules Prepared with Various Binders at 2% Concentrations by Dry Incoporation Method

Binders	Physical Properties of Granules								
	Granule Size (μm)*	Bulk Density (g/ml, ±SD)**	Tapped Density (g/ml, ±SD)**	Compressibility (%)	Flow Rate (g/min, ±SD)*	Angle of Repose (°, ±SD)*	Friability (%)*	Fine (%)*	Moisture Content (%)*
D1	479	0.50 (0.01)	0.60 (0.02)	16.67	266.67(11.21)	35.06(0.01)	12.35	4.56	1.60
D2	458	0.45 (0.00)	0.56 (0.01)	19.64	230.77(2.48)	37.90(0.24)	24.84	13.32	2.00
PVPK30	531	0.51 (0.00)	0.64 (0.01)	13.00	208.70(6.01)	38.28(0.42)	7.79	1.95	1.70
Starch 1500(R)	479	0.49 (0.02)	0.56 (0.00)	12.50	235.29(5.13)	35.51(0.21)	17.90	7.40	1.90

* averaged from two determinations.
** averaged from three determinations.

Tables 10

Physical Properties of Pyridoxine Hydrochloride Granules Prepared with Various Binders and Concentrations by Solution Incorporation Method.

Binders	% (w/w)	Physical Properties of Granules								
		* Granule Size (μm)	** Bulk Density (g/ml, ±SD)	** Tapped Density (g/ml, ±SD)	Compressibility (%)	** Flow Rate (g/ml, ±SD)	** Angle of Repose (°, ±SD)	* Friability (%)	* Fine (%)	* Moiture Content (%)
D1	1	448	0.60(0.02)	0.71(0.01)	15.49	352.94(6.44)	34.29(0.02)	8.69	7.98	1.40
	2	448	0.58(0.00)	0.68(0.03)	14.71	387.10(3.21)	33.84(0.10)	7.70	11.93	1.70
	4	448	0.61(0.00)	0.78(0.02)	21.79	347.83(2.15)	34.39(0.10)	6.45	22.63	2.00
D2	1	528	0.52(0.01)	0.63(0.00)	17.46	244.90(5.54)	34.73(0.01)	11.08	8.33	1.50
	2	555	0.58(0.02)	0.63(0.03)	7.94	258.06(3.68)	33.84(0.00)	7.19	12.15	1.90
	4	569	0.58(0.04)	0.67(0.00)	13.43	279.27(10.11)	33.84(0.02)	6.79	13.15	1.60
PVPK30	1	500	0.57(0.00)	0.71(0.02)	19.72	315.79(5.12)	35.00(0.14)	7.66	17.43	1.10
	2	514	0.56(0.01)	0.70(0.02)	20.00	302.94(4.12)	35.20(0.39)	6.99	16.33	1.30
	4	548	0.56(0.00)	0.69(0.00)	18.84	296.3(3.44)	36.16(0.55)	4.28	14.00	1.50
Corn Starch	1	428	0.47(0.00)	0.56(0.04)	16.07	184.60(6.15)	37.88(0.42)	18.08	8.18	1.90
	2	448	0.45(0.00)	0.53(0.02)	15.09	226.42(11.21)	36.02(0.41)	16.22	6.95	1.20
	4	479	0.46(0.01)	0.55(0.01)	16.36	206.90(2.22)	36.26(0.15)	12.94	7.90	1.40
Starch 1500(R)	1	424	0.46(0.00)	0.52(.0.00)	11.54	245.72(7.21)	36.87(0.02)	20.77	6.60	1.20
	2	458	0.45(0.02)	0.52(0.02)	13.46	231.55(5.52)	37.28(0.15)	17.70	5.00	1.40
	4	489	0.44(0.01)	0.51(0.03)	13.73	203.39(2.11)	37.45(0.59)	10.82	5.50	1.10
Gelatin	1	400	0.52(0.00)	0.67(0.00)	22.39	320.00(7.10)	34.00(0.10)	11.57	20.00	1.20
	2	448	0.53(0.05)	0.68(0.07)	22.01	375.00(5.20)	33.84(0.04)	7.96	21.12	1.30
	4	476	0.51(0.10)	0.66(0.00)	22.72	333.33(3.12)	34.29(0.03)	6.90	25.15	1.50
Methocel E15LV(R)	1	504	0.40(0.04)	0.52(0.01)	17.31	222.22(8.42)	36.87(0.02)	11.12	10.83	1.50
	2	535	0.51(0.00)	0.62(0.01)	17.74	230.77(10.10)	36.45(0.00)	9.17	14.50	1.60
	4	229	0.53(0.01)	0.63(0.00)	15.87	315.79(2.34)	36.03(0.10)	5.26	15.53	1.40
Blank		448	0.58(0.00)	0.71(0.02)	18.31	393.44(5.21)	35.16(0.05)	28.59	22.03	1.20

* averaged from two determinations
** averaged from three determinations

Tables 11

Physical Properties of Pyridoxine Hydrochloride Granules Prepared with Various Binders at 2% Concentration by Dry Incorporation Method.

Binders	Physical Properties of Granules								
	* Granule Size (μm)	** Bulk Density (g/ml, ±SD)	** Tapped Density (g/ml, ±SD)	Compressibility (%)	** Flow Rate (g/ml, ±SD)	** Angle of Repose (°, ±SD)	* Friability (%)	* Fine (%)	* Moiture Content (%)
D1	517	0.57(0.01)	0.66(0.02)	16.67	352.94(10.12)	33.39(0.87)	7.78	12.22	1.50
D2	510	0.58(0.01)	0.71(0.02)	18.31	313.79(8.18)	34.93(0.17)	11.24	14.28	1.60
PVPK30	528	0.58(0.01)	0.66(0.04)	12.12	272.23(4.48)	34.73(0.21)	10.46	19.28	1.20
Starch 1500(R)	517	0.58(0.02)	0.62(0.02)	6.45	333.33(4.12)	35.16(0.15)	13.74	14.73	1.30

* averaged from two determinations
** averaged from three determinations

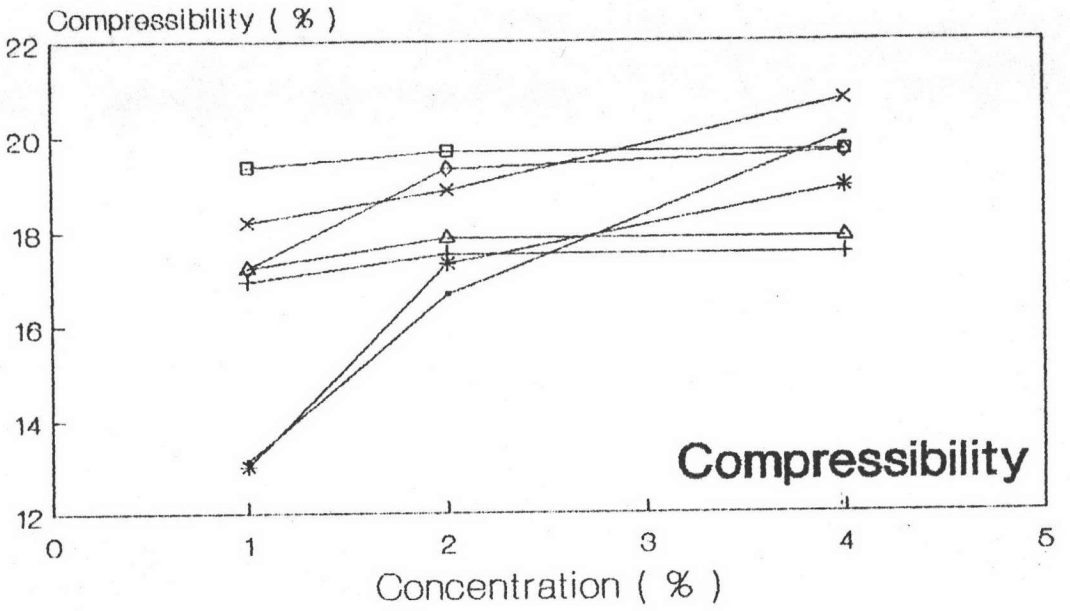


Figure 54 Effect of Binder Types and Concentrations on Percent Compressibility of Paracetamol Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®).

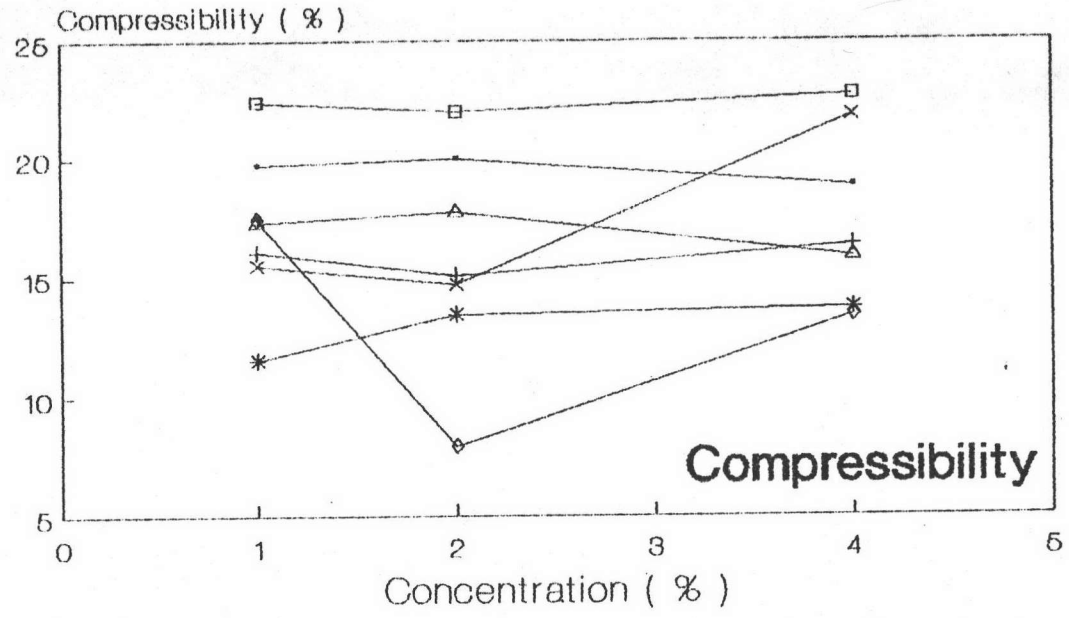


Figure 55 Effect of Binder Types and Concentrations on Percent Compressibility of Pyridoxine Hydrochloride Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$).

g/ml , respectively. However, percent compressibility of granules decreased with increasing of binder concentration (Figure 55) . The range of percent compressibility was between 7.94 - 22.72 %. The results of density and percent compressibility by dry incorporation method are showed in Table 25. Comparing with solution incorporation method, percent compressibility of PVPk30 and Starch 1500$^{(R)}$ were lower but inversely for D_1 and D_2 .

It was noticed that most of granules in this study had percent compressibility of less than 21% with indicated good flowability (15).

4. Flow Rate and Angle of Repose

4.1 Paracetamol

The results of these two properties in Tables 8-9 and Figure 56, revealed that flow rate reduced with increasing binder concentration in the formulation. They were ranked as follow, at 1% level : Starch 1500$^{(R)}$ > gelatin > Methocel E15LV$^{(R)}$ $\simeq$ corn starch > D_2 $\simeq$ D_1 > PVPK30. At 2% level : Starch 1500$^{(R)}$ > Methocel E15LV$^{(R)}$ $\simeq$ gelatin $\simeq$ D_2 > D_1 > corn starch $\simeq$ PVPK30. In the case of 4% level : Starch 1500$^{(R)}$ > D_2 > gelatin > Methocel E15LV$^{(R)}$ > D_1 > corn starch > PVPK30, respectively. From the data, it could be noted that Starch 1500$^{(R)}$ exhibited the best flow rate. On the other hand, PVPK30 which superior granule size possessed the lowest flow rate. For D_2, however showed better flow rate than D_1. The significantly higher in flow rate of granules was noticed as comparing solution incorporation method with dry incorporation method.

4.2 Pyridoxine Hydrochloride

The relationship between granule flow rate and binder concentraton are noticed in Tables 10-11 and Figure 57. However, the flow rate did not linearly proportional to binder

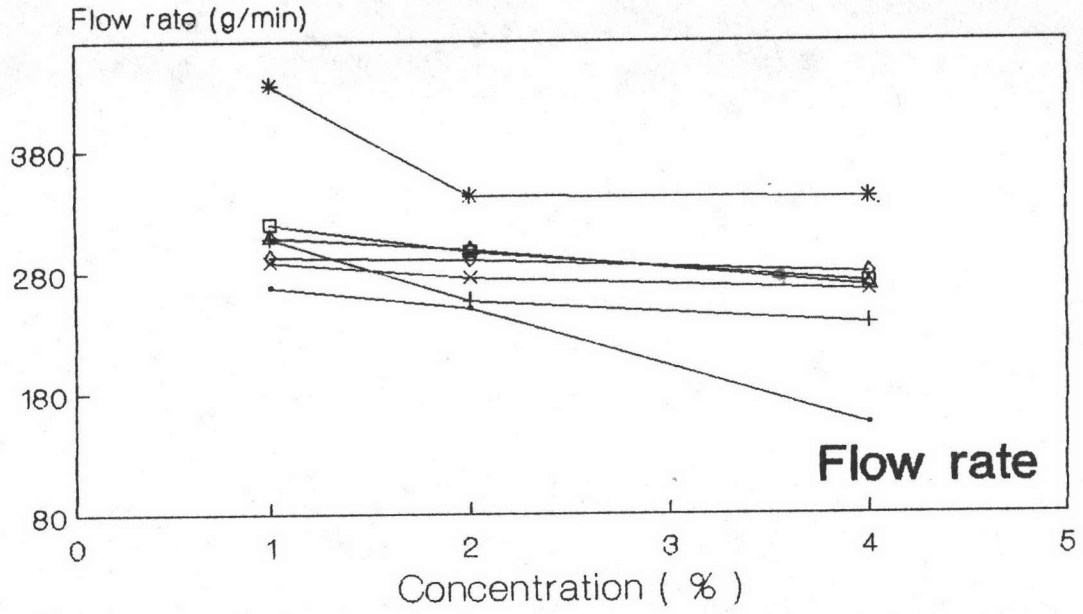


Figure 56 Effect of Binder Types and Concentrations on Flow Rate of Paracetamol Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®)

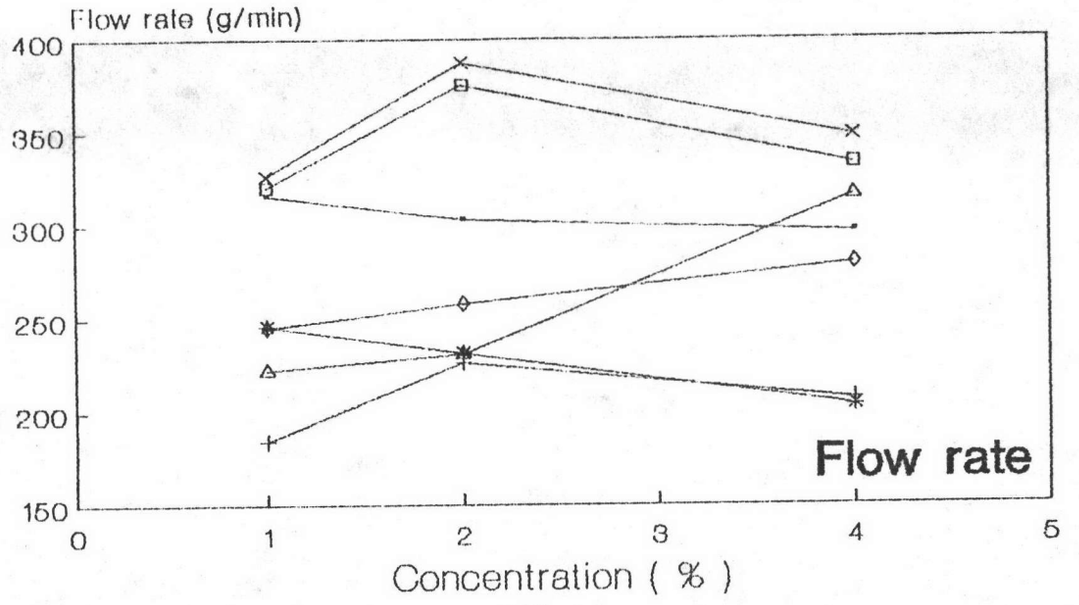


Figure 57 Effect of Binder Types and Concentrations on Flow Rate of Pyridoxine Hydrochloride Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$)

concentration. As binder concentration increased, flowability of granules prepared with D_2 and Methocel E15LV(R) were increased whereas Starch 1500(R) showed inverse results. Nevertheless, slight change in flow rate was noticed in granule produced with PVPK30. In addition, the optimal flowability was observed in the case of D_1, corn starch and gelatin. The flow rate was ordered as follow, at 1% level : D_1 > gelatin $\simeq$ PVPK30 > Starch 1500(R) $\simeq$ D_2 > Methocel E15LV(R) > corn starch. At 2% level: D_1 > gelatin > PVPK30 > D_2 > Starch 1500(R) > Methocel E15LV(R) > corn starch. In the case of 4%: D_1 > gelatin > Methocel E15LV(R) > PVPK30 > D_2 > corn starch > Starch 1500(R), respectively. D_1 represented the best flowing granules while corn starch granules were the poorest. The significant difference in flow property was found between dry incorporation method and solution incorporation method. For D_2 and Starch 1500(R) granules prepared from dry incorporation method, imparted the higher flow rate than that prepared from solution incorporation method. In contrast, D_1 and PVPK30 showed inverse results. Both paracetamol granules and pyridoxine hydrochloride granules obsiously possessed inferior flow rate than blank granules.

Angle of repose are reported in the tables 8-11. For all cases the values of lower than 40° were observed which indicate good flowing granules (15). It was interesting to notice that granules with high angle of repose had the inferior flow rate.

5. Comparision of Percent Friability

5.1 Paracetamol

Tables 8-9 and Figure 58 show the association between the granule friability and binder concentration. The declination of granule friability with the higher binder concetration was clearly seen. The orders followed as, at 1% level: D_1 > corn starch $\simeq$ Starch 1500(R) $\simeq$ D_2 > gelatin > PVPK30 $\simeq$ Methocel E15LV(R). At 2% level the order of decrease are, D_1 > Starch 1500(R)

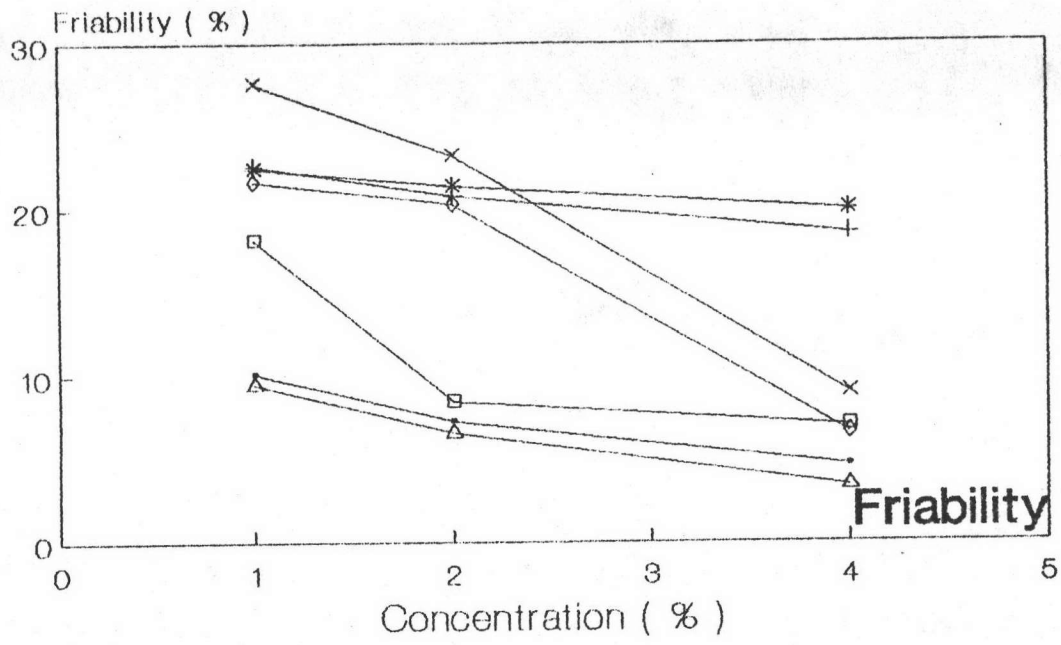


Figure 58 Effect of Binder Types and Concentrations on Percent Friability of Paracetamol Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$)

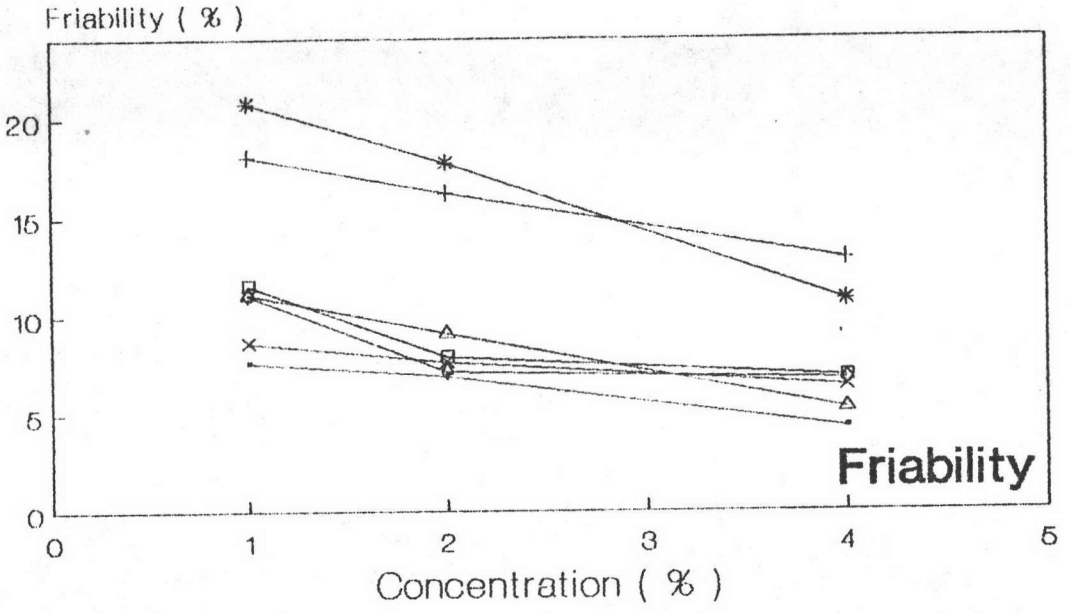


Figure 59 Effect of Binder Types and Concentrations on Percent Friability of Pyridoxine Hydrochloride Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$)

≃ corn starch ≃ D_2 > gelatin > PVPK30 ≃ Methocel E15LV$^{(R)}$. In the case of 4%: Starch 1500$^{(R)}$ > corn starch > D_1 > gelatin ≃ D_2 > PVPK30 > Methocel E15LV$^{(R)}$. Methocel E15LV$^{(R)}$ and PVPK30 were the two lowest fribility values. D_2 possessed stronger granules than D_1. For dry incorporation method at the same binder concentration, D_1 gave more friability values than solution incorporation method, nevertheless, the inverse results were found for D_2 and Starch 1500$^{(R)}$. On the other hand, PVPK30 showed comparable results. However, blank granules were the most friable granules.

5.2 Pyridoxine Hydrochloride

The similar correlations were observed (Tables 10-11 and Figure 59) and granule friability decreased in the following order, at 1% level:Starch 1500$^{(R)}$ ≃ corn starch > gelatin ≃ Methocel E15LV$^{(R)}$ ≃ D_2 > D_1 > PVPK30. At 2% level : Starch 1500$^{(R)}$ ≃ corn starch > Methocel E15LV$^{(R)}$ ≃ gelatin ≃ D_1 ≃ D_2 ≃ PVPK30. In the case of 4% : corn starch > Starch 1500$^{(R)}$ > gelatin ≃ D_2 ≃ D_1 > Methocel E15LV$^{(R)}$ > PVPK30, respectively. The minimum and maximum friability values were PVPK30 and Starch 1500$^{(R)}$ (except at 4% level), respectively. For PVPK30 and D_2 dry incorporation method, gave weaker granules, than solution incorporation method. In the case of Starch 1500$^{(R)}$ the reverse result was observed.

From data in Tables 10-11,it is clearly seen that granules produced without binder possessed the highest friability value.

6. Comparison of Percent Fine

6.1 Paracetamol

The percent fine of all formulations in this study are indicated in Tables 8-9 and approximately less than 15%. Figure 60 depicts the relationships between the amount of binder utilized and percent fine which tended to decrease as binder concentration

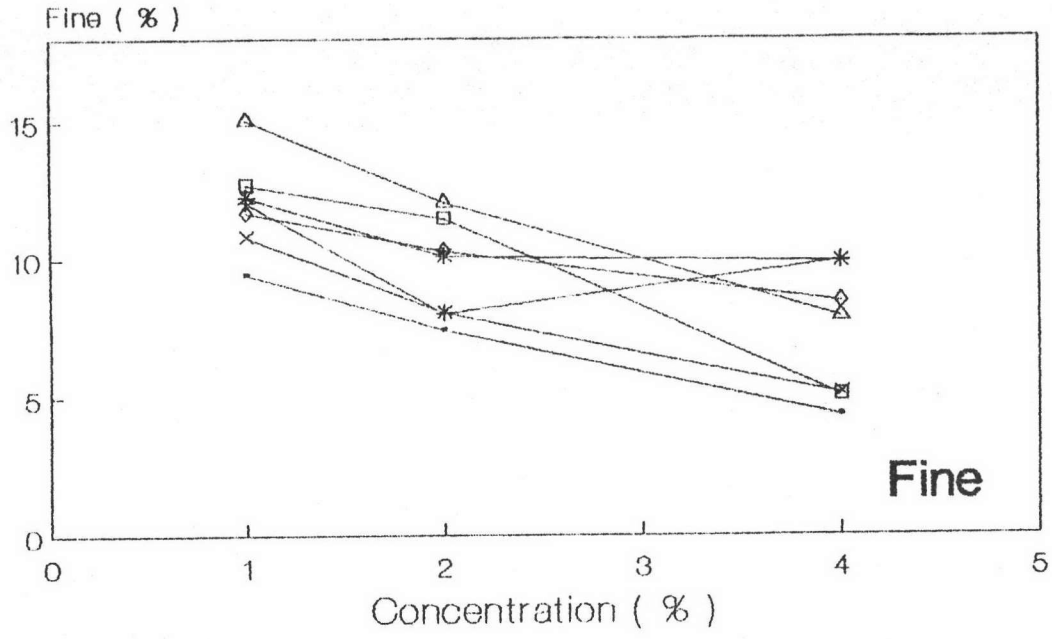


Figure 60 Effect of Binder Types and Concentrations on Percent Fine of Paracetamol Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500(R), Gelatin, Methocel E15LV(R))

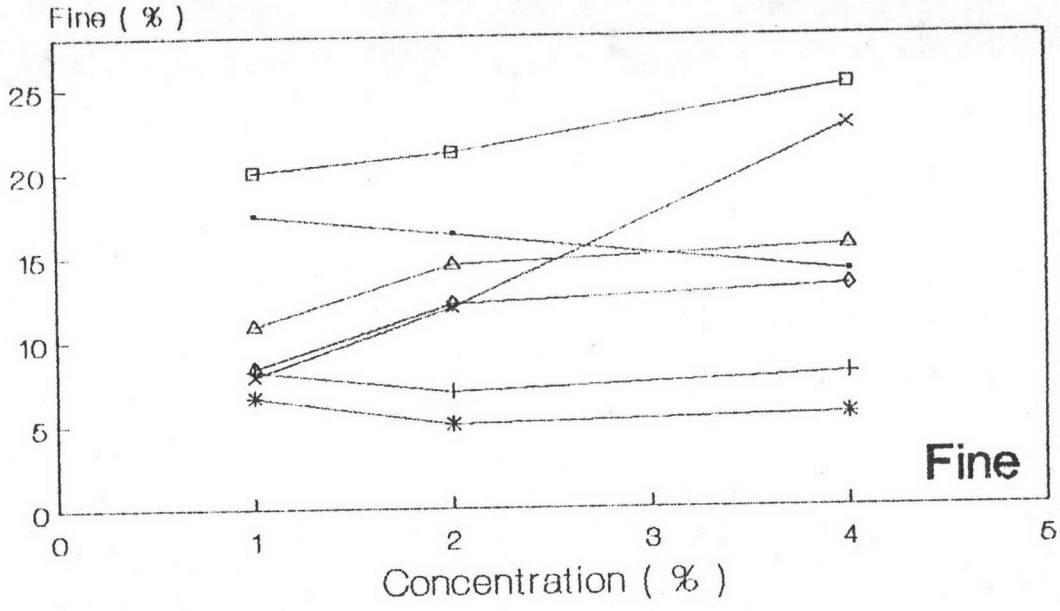


Figure 61 Effect of Binder Types and Concentrations on Percent Fine of Pyridoxine Hydrochloride Granules Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$)

increased. Their ranks are in the following order, at 1% level : Methocel E15LV$^{(R)}$ > gelatin $\simeq$ Starch 1500$^{(R)}$ $\simeq$ corn starch $\simeq$ D_2 $\simeq$ D_1 > PVPK30. At 2% level: Methocel E15LV$^{(R)}$ $\simeq$ gelatin > D_2 > Starch 1500$^{(R)}$ > corn starch $\simeq$ D_1 $\simeq$ PVPK30. In the case of 4% level : corn starch $\simeq$ Starch 1500$^{(R)}$ > D_2 > Methocel E15LV$^{(R)}$ > D_1 $\simeq$ gelatin $\simeq$ PVPK30. Consideration with all level of concentration studies, PVPK30 gave the least percent fine but Methocel E15LV$^{(R)}$ and gelatin showed the most fine particles, except at 4% level. In addition, D_2 imparted finer granules than D_1. All granules except for D_2 which produced by dry incorporation method were less finer than prepared by solution incorporation method. Blank granules, nevertheless, composed of the greatest fine particles.

6.2 Pyridoxine Hydrochloride

The results are illustrated in Tables 10-11 and Figure 61 . It was found that amount of fine particles of PVPK30, corn starch and Starch 1500$^{(R)}$ reduced with the increase in binder concentration. In the case of D_1, D_2, gelatin and Methocel E15LV$^{(R)}$ the inverse results were seen. The percent fine of granules were ranked as follow, at 1% level : gelatin > PVPK30 > Methocel E15LV$^{(R)}$ > D_2 $\simeq$ corn starch $\simeq$ D_1 > Starch 1500$^{(R)}$. At 2% level : gelatin > PVPK30 > Methocel E15LV$^{(R)}$ > D_2 $\simeq$ D_1 > corn starch > Starch 1500$^{(R)}$. In the case of 4% level : gelatin > D_1 > Methocel E15LV$^{(R)}$ > PVPK30 $\simeq$ D_2 > corn starch > Starch 1500$^{(R)}$. Gelatin gave the most finest granules. D_2 was more finer than D_1 except at 2% level. All granules produced with dry incorporation method imparted more percent fine than prepared by solution incorporation method. Blank granules (like paracetamol) also showed the highest percent fine comparing with other granules.(except for gelatin and D_1 at 4 %).

7. Moisture Determination

The range of moisture content for all granules obtained from various binder solutions were between 1.10-2.40% and 1.10-2.20% for paracetamol and pyridoxine hydrochloride, respectively.(Tables 8-11) Slightly difference in moisture content of granules prepared by two methods was noticed.

The Physical Properties of Tablets Prepared with Durian Rind Extracts (D_1 ,D_2) and Various Binders

1. Weight Variation

The mean and standard deviation of Tablet weight variation are shown in Tables 12-15. They were all within the limit of USP standard.

2. Tablet Thickness

The results of tablet thickness are presented in Tablets 12-15. The standard deviation never exceeded ± 0.06 for all batchs tested.

3. Tablet hardness

The mean and standard deviation of tablet hardness are presented in Tables 12-15. Figures 62-63 depict the relationship between binder concentration and tablet hardness. Generally,it was found that the increase in binder concentration caused increase in hardness values.

3.1 Paracetamol

Consideration through the data in Appendices VI-XI, it was found that types of binders significantly effect on hardness of paracetamol tablets at the same concentration employed ($P < 0.005$). The ranks of hardness decreased as follow, at 1 % level : Methocel E15LV$^{(R)}$ $\simeq$ PVP K30 > gelatin > $D_1 \simeq D_2 \simeq$ Starch 1500$^{(R)}$

Table 12

Physical Properties of Paracetamol Tablets Prepared with Various Binders and Concentrations by Solution Incorporation Method.

Binders	% (w/w)	Physical Properties of Tablets									
		* Weight Variation (mg, ±SD)	** Thick ness (mm, ±SD)	** Hard ness (kp, ±SD)	*** Friabi lity (%)	*** Tensile Strength ($MN*10/m^2$)	Poro sity (%)	**** Disinte gration (min, ±SD)	T50% (min)	** Content Uniformity (%, ±SD)	Binder Index ($MN*10^2/m^2.min$)
D1	1	508.20(1.83)	4.25(0.01)	5.35(0.38)	1.41	6.30	4.02	60.25(4.49)	140.90	99.79(0.77)	1.27
	2	496.60(2.25)	4.23(0.00)	7.12(0.56)	0.71	7.70	4.05	62.51(3.55)	203.70	101.29(1.19)	2.28
	4	500.70(2.08)	4.23(0.01)	8.30(0.45)	0.50	8.80	4.99	63.40(2.67)	271.40	99.43(1.05)	3.24
D2	1	498.60(1.71)	4.24(0.03)	5.25(0.51)	1.59	6.60	4.71	63.12(3.10)	226.00	100.93(1.43)	0.87
	2	501.70(0.01)	4.24(0.01)	6.74(0.41)	0.84	7.73	4.26	64.40(3.92)	260.90	101.14(1.99)	1.66
	4	494.80(1.99)	4.23(0.01)	7.56(0.67)	0.52	8.00	4.73	65.01(3.10)	281.90	100.05(1.66)	2.58
PVPK30	1	503.90(1.21)	4.23(0.01)	8.15(0.80)	0.91	7.90	4.25	52.21(2.45)	80.80	99.20(1.05)	5.64
	2	494.00(2.33)	4.22(0.01)	9.76(0.71)	0.34	9.20	6.16	55.08(1.58)	104.60	100.45(0.94)	15.94
	4	490.00(1.90)	4.22(0.01)	11.15(0.82)	0.24	9.70	5.53	58.55(3.12)	145.10	98.20(1.13)	14.57
Corn Starch	1	498.20(1.37)	4.25(0.02)	4.80(0.38)	c	4.70	3.53	67.79(3.57)	180.90	100.90(0.86)	-
	2	495.50(1.24)	4.22(0.01)	6.06(0.57)	1.34	5.90	3.77	70.55(1.88)	270.70	102.41(1.62)	0.61
	4	491.20(2.31)	4.22(0.01)	7.53(0.53)	0.85	7.40	4.25	79.31(1.98)	294.40	99.78(2.01)	1.26
Starch 1500(R)	1	503.20(1.14)	4.23(0.01)	4.83(1.00)	c	6.20	3.32	62.10(2.78)	177.50	99.59(0.50)	-
	2	497.10(2.03)	4.22(0.03)	5.64(0.98)	1.17	6.80	3.33	65.74(2.36)	237.20	100.10(0.61)	0.88
	4	497.20(2.20)	4.22(0.00)	7.80(0.29)	0.72	8.00	4.74	69.10(2.14)	274.90	102.30(1.99)	1.92
Gelatin	1	497.20(1.82)	4.24(0.01)	6.55(0.59)	2.67	6.70	4.25	47.30(2.38)	107.43	98.99(1.90)	0.99
	2	504.70(1.71)	4.24(0.01)	7.75(0.61)	1.09	7.80	4.01	53.45(1.67)	147.90	101.34(1.58)	1.94
	4	495.20(2.14)	4.23(0.01)	7.77(0.54)	0.80	8.80	4.95	55.57(1.56)	167.40	100.20(1.57)	3.25
Methocel E15LV(R)	1	499.10(2.22)	4.21(0.01)	8.28(0.74)	1.03	7.40	4.04	47.00(1.95)	97.70	99.90(1.01)	2.97
	2	495.50(2.35)	4.21(0.01)	10.47(1.12)	0.47	7.80	5.45	60.02(3.15)	131.20	100.50(0.97)	6.89
	4	501.20(2.35)	4.21(0.01)	11.74(1.05)	0.39	10.60	5.82	62.24(2.77)	164.60	101.20(1.37)	9.61
Blank		-	-	-	-	-	-	-	-	-	-

c capping.
- no data was obtained.
* averaged from twenty determinations.
** averaged from ten determinations.
*** averaged from two determinations.
**** averaged from six determinations.

Table 13

Physical Properties of Paracetamol Tablets Prepared with Various Binders at 2% Concentration by Dry Incorporation Method.

Binders	Physical Properties of Tablets									
	* Weight Variation (mg, ±SD)	** Thick ness (mm, ±SD)	** Hard ness (kp, ±SD)	*** Friabi lity (%)	*** Tensile Strength ($MN*10/m^2$)	Poro sity (%)	**** Disinte gration (min, ±SD)	**** T50% (min)	** Content Uniformity (%, ±SD)	Binder Index ($MN*10^2/m^2.min$)
D1	497.10(1.117)	4.23(0.02)	6.89(0.30)	2.58	7.10	4.95	44.17(2.24)	176.60	99.05(1.11)	1.26
D2	502.90(2.18)	4.24(0.07)	4.61(0.27)	2.73	6.00	3.55	33.92(1.88)	68.75	100.10(0.79)	2.32
PVPK30	491.50(2.35)	4.22(0.01)	9.05(0.39)	0.73	8.40	5.21	33.66(2.10)	84.38	100.40(1.20)	8.64
Starch 1500 (R)	496.90(2.01)	4.23(0.01)	5.21(0.16)	2.45	6.50	4.49	57.15(3.75)	196.92	101.19(1.82)	0.74

* averaged from twenty determinations.
** averaged from ten determinations.
*** averaged from two determinations.
**** averaged from six determinations.

Table 14

Physical Properties of Pyridoxine Hydrochloride Tablets Prepared with Various Binders and Concentrations by Solution Incorporation method.

Binders	% (w/w)	Physical Properties of Tablets									
		* Weight Variation (mg, ±SD)	** Thick ness (mm, ±SD)	** Hard ness (kp, ±SD)	*** Friabi lity (%)	*** Tensile Strength ($MN*10/m^2$)	Poro sity (%)	**** Disinte gration (min, ±SD)	T50% (min)	** Content Uniformity (%)	Binder Index ($MN*10^2/m^2.min$)
D1	1	298.10(1.69)	3.10(0.02)	6.55(0.30)	0.77	8.60	3.89	7.81(0.30)	18.70	99.02(1.11)	23.33
	2	298.40(1.32)	3.11(0.02)	9.28(0.29)	0.64	11.80	3.87	8.75(0.38)	20.00	100.16(0.93)	35.68
	4	301.40(1.05)	3.11(0.01)	9.50(0.43)	0.56	12.30	3.90	10.75(0.09)	23.00	99.54(1.07)	37.24
D2	1	310.30(2.50)	3.20(0.04)	6.77(0.39)	0.84	8.70	4.24	7.36(0.50)	13.50	98.90(0.47)	32.53
	2	302.50(2.31)	3.12(0.04)	7.00(0.38)	0.71	10.60	4.30	8.10(0.12)	15.10	99.95(0.44)	42.51
	4	297.90(1.87)	3.07(0.02)	7.70(0.38)	0.59	11.30	4.95	10.67(0.15)	15.10	99.95(0.44)	62.78
PVPK30	1	304.70(1.64)	3.11(0.01)	7.89(0.63)	0.69	10.00	5.96	5.98(0.30)	9.50	99.50(0.88)	90.92
	2	299.90(2.05)	3.10(0.01)	7.93(0.20)	0.59	11.20	5.59	6.14(0.13)	10.00	99.11(0.58)	106.12
	4	290.10(1.69)	3.08(0.03)	8.50(0.25)	0.31	11.40	6.62	6.20(0.15)	10.00	100.04(1.01)	243.45
Corn Starch	1	308.40(1.81)	3.11(0.02)	6.24(0.34)	0.84	10.60	3.90	6.01(0.32)	20.27	99.24(0.92)	24.28
	2	292.90(1.60)	3.10(0.19)	6.95(0.51)	0.75	11.10	4.59	6.05(0.44)	23.00	99.20(1.02)	29.54
	4	299.60(1.88)	3.12(0.11)	7.91(0.15)	0.69	11.30	4.95	6.92(0.18)	23.00	100.04(1.10)	31.69
Starch 1500 (R)	1	308.70(1.44)	3.11(0.03)	6.24(0.42)	0.81	10.30	4.24	6.71(0.53)	18.90	99.48(0.66)	28.53
	2	291.70(1.69)	3.09(0.04)	7.82(0.10)	0.72	11.00	5.96	8.34(0.10)	21.10	99.59(1.23)	43.15
	4	294.90(2.26)	3.10(0.03)	8.29(0.18)	0.63	11.50	5.63	8.59(0.10)	25.90	99.89(0.79)	39.68
Gelatin	1	295.00(2.21)	3.10(0.07)	7.81(0.60)	0.68	10.80	4.27	5.08(0.31)	7.60	100.02(1.07)	89.92
	2	297.80(1.30)	3.10(0.02)	8.02(0.53)	0.55	12.00	4.95	5.25(0.55)	9.70	99.90(0.69)	111.34
	4	298.10(1.90)	3.12(0.06)	8.96(0.47)	0.33	12.70	4.56	6.09(0.68)	10.50	99.21(1.15)	167.13
Methocel E15LV (R)	1	292.50(2.37)	3.11(0.02)	8.89(0.27)	0.77	11.50	4.25	6.25(0.28)	10.00	100.28(0.48)	63.47
	2	293.50(2.05)	3.13(0.02)	9.08(0.36)	0.64	11.80	4.23	6.92(0.19)	11.10	99.49(1.55)	70.26
	4	301.60(1.21)	3.12(0.16)	10.61(0.49)	0.35	13.80	4.61	8.58(0.48)	11.10	99.33(0.77)	156.65
Blank		302.40(1.12)	3.34(0.03)	3.58(0.69)	1.93	1.90	4.29	4.50(0.84)	21.10	99.88(1.82)	5.12

* averaged from twenty determinations.
** averaged from ten determinations.
*** averaged from two determinations.
**** averaged from six determinations.

Table 15

Physical Properties of Pyridoxine Hydrochloride Tablets Prepared with Various Binders at 2 % Concentrations by dry Incorporation method.

Binders	Physical Properties of Tablets									
	* Weight Variation (mg,±SD)	** Thick ness (mm,±SD)	** Hard ness (kp,±SD)	*** Friabi lity (%)	*** Tensile Strength ($MN*10/m^2$)	Poro sity (%)	**** Disinte gration (min,±SD)	**** T50% (min)	** Content Uniformity (%)	Binder Index ($MN*10^2/m^2.min$)
D1	298.40(1.61)	3.05(0.02)	7.10(0.44)	0.74	9.50	4.15	7.44(0.28)	17.89	100.02(0.55)	29.56
D2	296.50(1.93)	3.03(0.01)	6.83(0.36)	0.77	9.50	4.64	6.10(0.03)	14.93	99.92(0.87)	38.34
PVPK30	303.00(2.31)	3.16(0.02)	7.75(1.10)	0.55	11.00	4.96	5.17(0.42)	10.00	99.74(0.88)	90.93
Starch 1500(R)	303.80(1.75)	3.12(0.02)	7.60(0.55)	0.74	10.50	4.05	7.33(0.31)	15.10	99.55(1.02)	38.06

* averaged from twenty determinations.
** averaged from ten determinations.
*** averaged from two determinations.
**** averaged from six determinations.

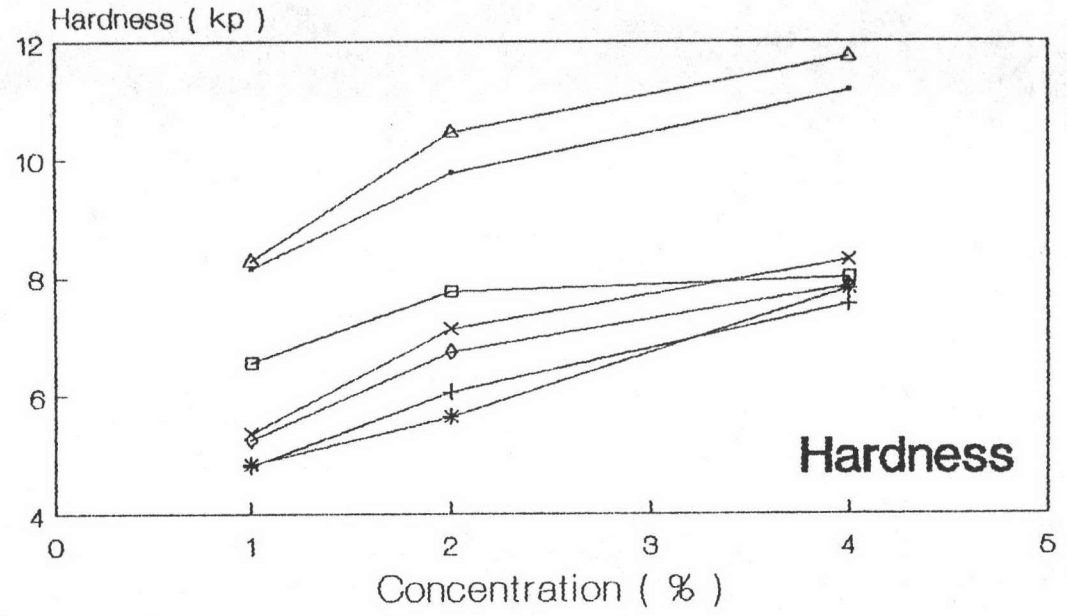


Figure 62 Effect of Binder Types and Concentrations on Hardness of Paracetamol Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500(R), Gelatin, Methocel E15LV(R))

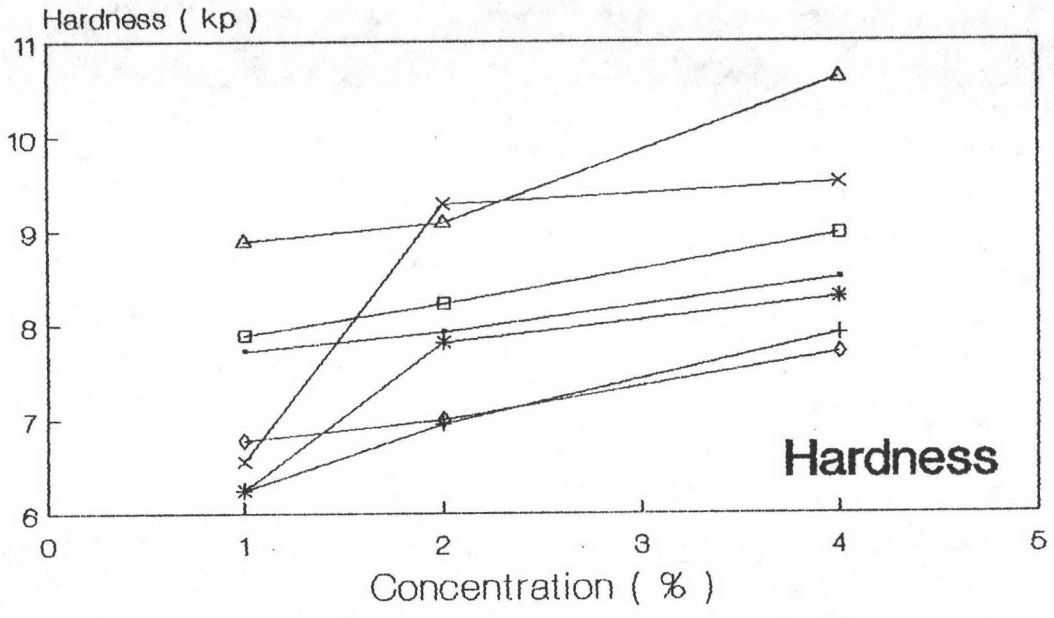


Figure 63 Effect of Binder Types and Concentrations on Hardness of Pyridoxine Hydrochloride Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®)

$\simeq$ corn starch. At 2% level : Methocel E15LV$^{(R)}$ $\geqslant$ PVPK30 $\geqslant$ gelatin $\geqslant$ D_1 $\simeq$ D_2 $\geqslant$ corn starch $\simeq$ Starch 1500$^{(R)}$. In the case of 4% level : Methocel E15LV$^{(R)}$ $\geqslant$ PVPK30 > D_1 $\simeq$ gelatin $\simeq$ Starch 1500$^{(R)}$ $\simeq$ D_2 $\simeq$ corn starch. Comparative data showed that tablets made with Methocel E15LV$^{(R)}$ were strongest. On the other hand, corn starch exhibited the weakest tablet except at 2% level. D_1 possessed slightly harder tablet than D_2. In addition the hardness values 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.

3.2 Pyridoxine Hydrochloride

At the same binder concentration used, the influence of binder types on pyridoxine hydrochloride tablet hardness were significantly difference ($P < 0.005$) (Appendices XII-XVII). The hardness values could be ordered as follow, at 1% level : Methocel E15LV$^{(R)}$ > gelatin $\simeq$ PVPK30 > D_2 $\simeq$ D_1 $\simeq$ Starch 1500$^{(R)}$ $\simeq$ corn starch > Blank. At 2% level : D_1 $\simeq$ Methocel E15LV$^{(R)}$ > gelatin $\simeq$ PVPK30 $\simeq$ Starch 1500$^{(R)}$ > D_2 $\simeq$ corn starch > Blank. In the case of 4% level : Methocel E15LV$^{(R)}$ > D_1 $\geqslant$ gelatin $\simeq$ PVPK30 $\simeq$ Starch 1500$^{(R)}$ $\simeq$ corn starch $\simeq$ D_2 > Blank. As was expected, tablets formulated with Methocel E15LV$^{(R)}$ also strongest, nevertheless, blank tablets were the weakest. At 1% level, both D_1 and D_2 had comparable tablet hardness but at higher level, D_1 imparted greater hardness than D_2.

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

4. Tablet Friability

The results which presented in Tables 12-15 clearly

revealed that tablet friability decreased with increasing binder concentration.

4.1 Paracetamol

The relationships between binder concentration and tablet friability are shown in Figure 64. At 1% level, they decreased in the following order : corn starch (capping) ≃ Starch 1500$^{(R)}$ (capping) > gelatin > D_2 > D_1 > Methocel E15LV$^{(R)}$ > PVPK30. Only tablets prepared with PVPK30 gave friability values within acceptable limit of less than 1% (8). In addition, capping was occurred with corn starch and Starch 1500$^{(R)}$. At 2% level, the orders are : corn starch > Starch 1500$^{(R)}$ > gelatin > D_2 > D_1 Methocel E15LV$^{(R)}$ > PVPK30. It could be noted that tablet friabilities of PVPK30, Methocel E15LV$^{(R)}$, D_1 and D_2 were less than 1%. In the case of 4% level : corn starch ≃ gelatin ≃ Starch 1500$^{(R)}$ > D_2 ≃ D_1 > Methocel E15LV$^{(R)}$ > PVPK30. Neither of the tablet at 4% level showed the friability values of more than 1%. Although the tablet prepared by dry incorporation method clearly possessed more friable than solution incorporation method, only PVPK30 gave friability value in acceptable range.

4.2 Pyridoxine Hydrochloride

The same correlations between tablet friability and binder concentration were observed (Figure 65). It is interesting that friability value of tablets at all binder concentration studies were less than 1% except for blank tablets. They were decreased in following order, at 1% level : corn starch = D_2 ≃ Starch 1500$^{(R)}$ ≃ Methocel E15LV$^{(R)}$ = D_1 ≃ PVPK30 ≃ gelatin. At 2% level : corn starch ≃ Starch 1500$^{(R)}$ ≃ D_2 ≃ D_1 = Methocel E15LV$^{(R)}$ ≃ PVPK30 ≃ gelatin. In the case 4% level : corn starch ≃ Starch 1500$^{(R)}$ ≃ D_2 ≃ D_1 > Methocel E15LV$^{(R)}$ ≃ gelatin ≃ PVPK30. According to the results, PVPK30 and gelatin were considered to produced less friable tablets but inversely for corn starch. D_1 slightly gave more

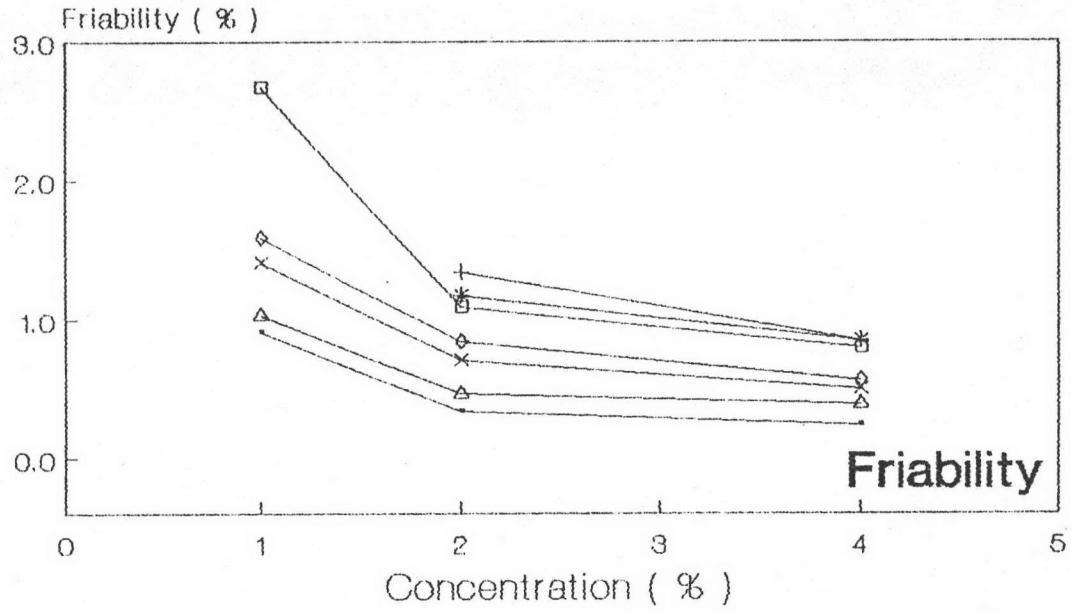


Figure 64 Effect of Binder Types and Concentrations on Friability of Paracetamol Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®)

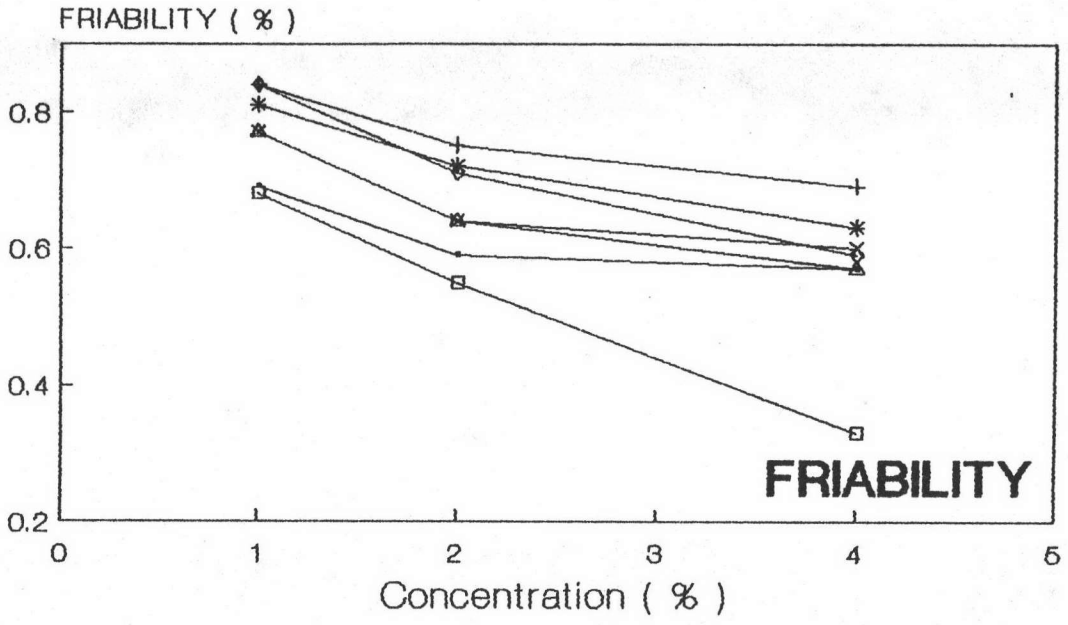


Figure 65 Effect of Binder Types and Concentrations on Friability of Pyridoxine Hydrochloride Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$)

friability values than D_2. Furthermore, tablets produced by dry incorporation method tended to friable than solution incorporation method.

5. Tablet Tensile Strength

The results of tablet tensile strength are reported in Tables 12-15. They slightly increased with the increasing of binder concentration (Figures 66-67). This behavior are corresponding to the result of tablet hardness.

5.1 Paracetamol

For all cases the tensile strength ranged from 4.7 to 10.6 $MN*m^{-2}*10$. The tendency of high tensile strength was found on the tablet prepared with Methocel E15LV$^{(R)}$ and PVPK30. On the other hand, corn starch showed the lowest value. D_1 and D_2 were slightly difference in tensile strength. Tablets produced by solution incorporation method possessed mildly greater tensile strength than dry incorporation method.

5.2 Pyridoxine Hydrochloride

The range of tensile strength were between 8.6 to 13.8 $MN*m^{-2}*10$. Methocel E15LV$^{(R)}$, however, gave the maximum tensile strength . As comparing tensile strength of tablet produced by solution incorporation method with dry incorporation method , slightly different was observed.

6. Tablet Porosity

The results are preseted in Tables 12-15 and Figures 68-69. The Relationship between tablet porosity and binder concentration were not clearly seen.

6.1 Paracetamol

Tablet porosity values were between 4.02 and 5.53 % .

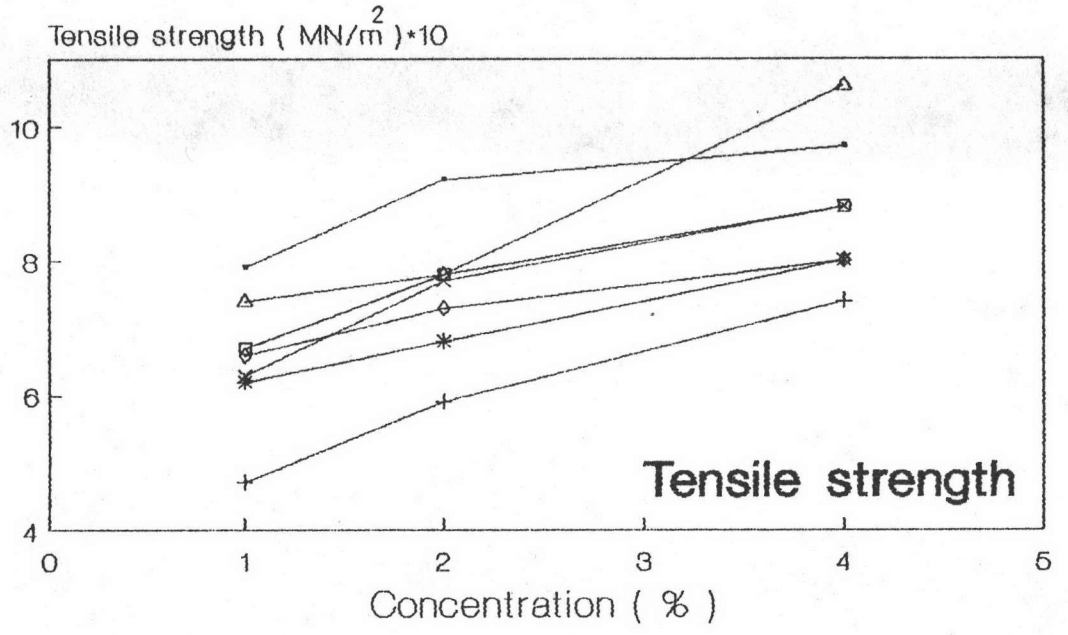


Figure 66 Effect of Binder Types and Concentrations on Tensile Strength of Paracetamol Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500(R), Gelatin, Methocel E15LV(R))

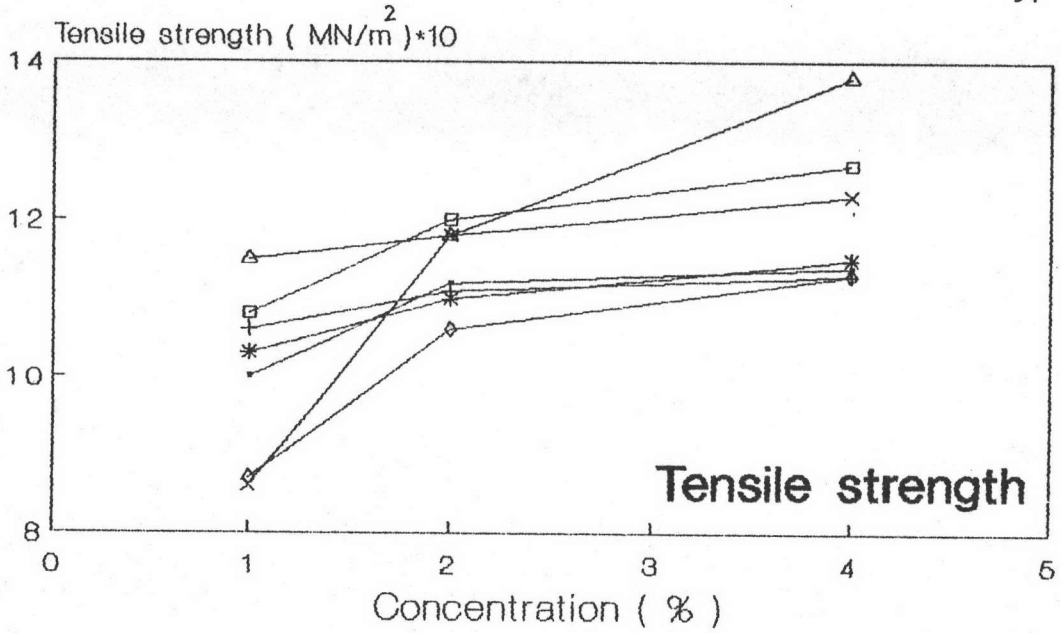


Figure 67 Effect of Binder Types and Concentrations on Tensile Strength of Pyridoxine Hydrochoride Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500(R), Gelatin, Methocel E15LV(R))

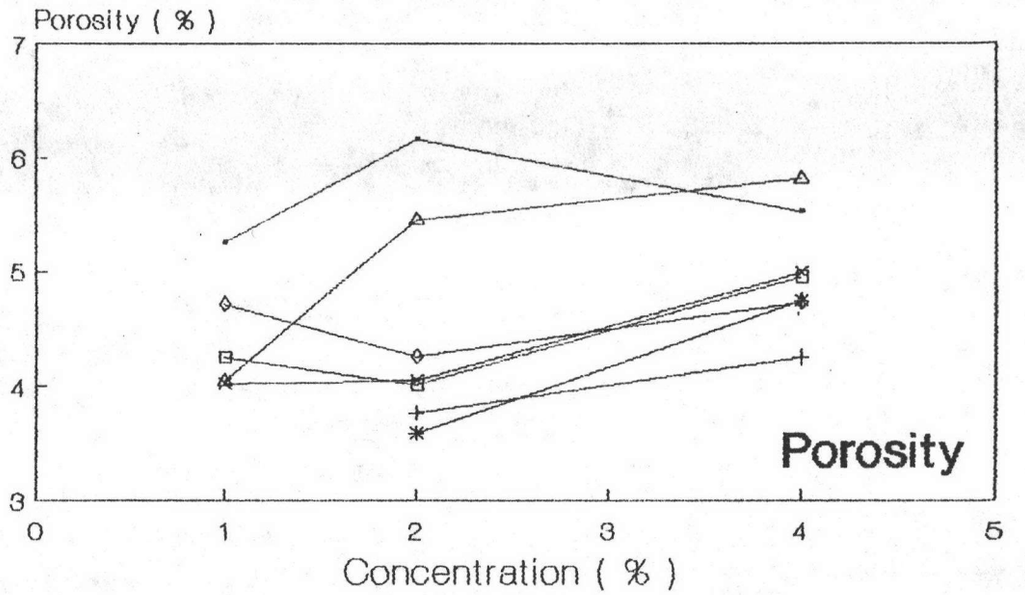


Figure 68 Effect of Binder Types and Concentrations on Porosity of Paracetamol Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®)

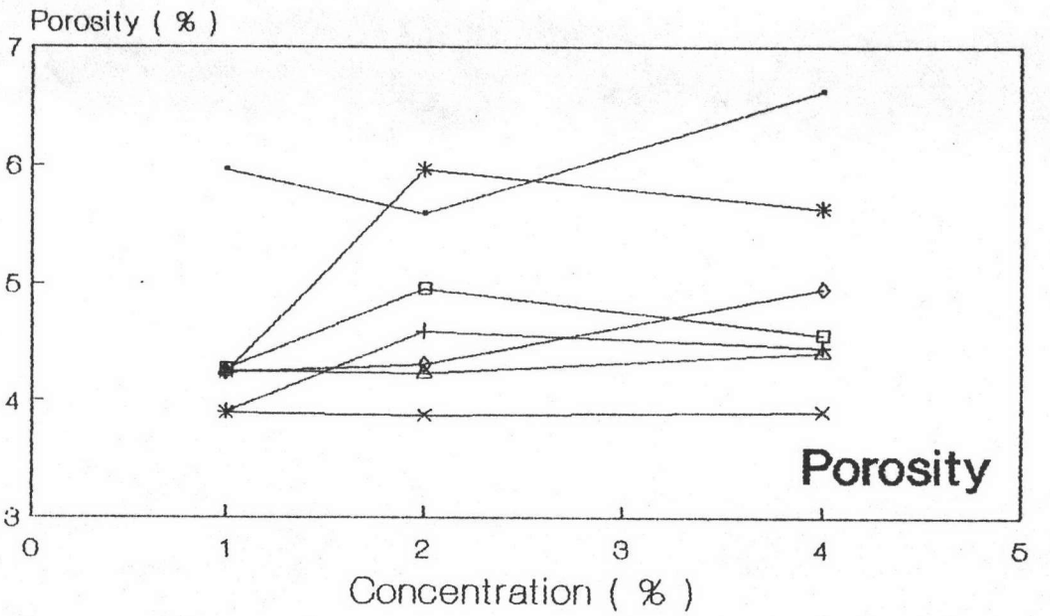


Figure 69 Effect of Binder Types and Concentrations on Porosity of Pyridoxine Hydrochloride Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$)

At 1% level , lamination was occurred for the tablets prepared with corn starch and Starch 1500$^{(R)}$ at highest compression pressure to obtain zero porosity thus no data were resulted. In addition at higher binder concentration , both corn starch and Starch 1500$^{(R)}$ showed lower porosity values than other tablets in this study . On the other hand, the high porous tablets were given by PVPK30.

6.2 Pyridoxine Hydrochloride

The results of porosity value were between 3.87 and 6.62%. It was noticed that tablets produced by PVPk30 and D_1 were the two highest and lowest porosity values, respectively.

7. Disintegration time

As was expected from previous reports (29-31), the disintegration time of tablets increased with increasing in binder concentration (Tables 12-15).

7.1 Paracetamol

The results are illustrated in Tables 12-15 and Figure 70. Significantly prolonged disintegration time as binder concentration increased was noticed in all cases. It increased with the following order, at 1% level : corn starch > D_2 > Starch 1500$^{(R)}$ > D_1 > PVPK30 > gelatin $\simeq$ Methocel E15LV$^{(R)}$. At 2% level : corn starch > Starch 1500$^{(R)}$ > D_2 > D_1 > Methocel E15LV$^{(R)}$ > PVPK30 > gelatin. In the case of 4% level : corn starch > Starch 1500$^{(R)}$ > D_2 > D_1 $\simeq$ Methocel E15LV$^{(R)}$ > PVPK30 > gelatin. The most quickest and slowest disintegration time were given by gelatin and corn starch, respectively. It was found that D_2 disintegrated more rapid than D_2. In addition, tablet produced by dry incorporation method clearly showed rapid disintegration than solution incorporation method. The quicker disintegrated formulation did not mean better efficacy or better formulation. In this study. however, the longer disintegrated formulation mean better binding properties of

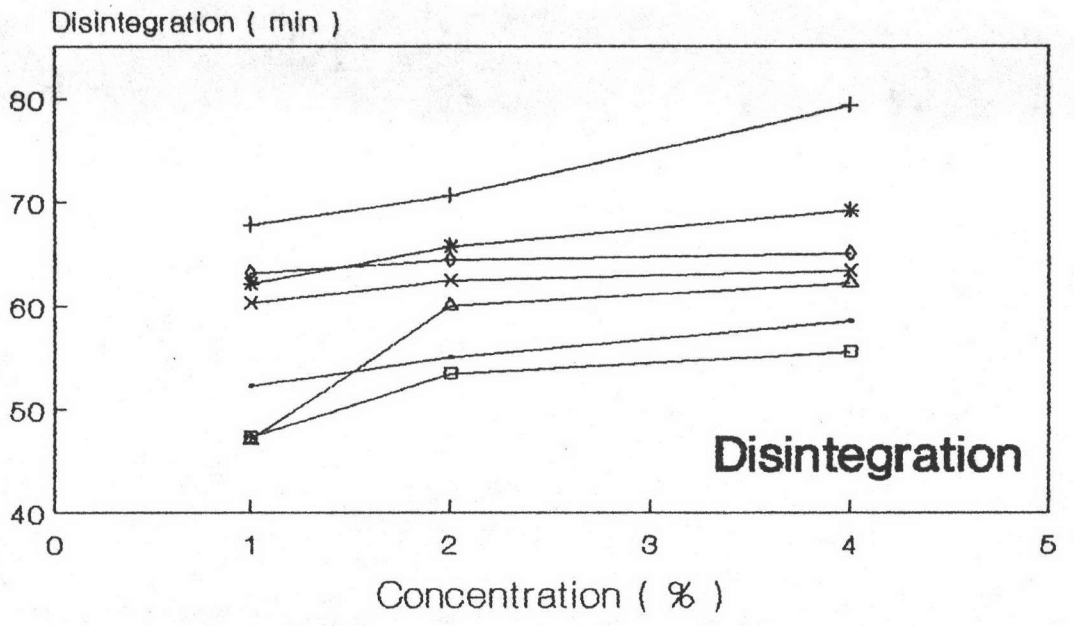


Figure 70 Effect of Binder Types and Concentrations on Disintegration Time of Paracetamol Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®)

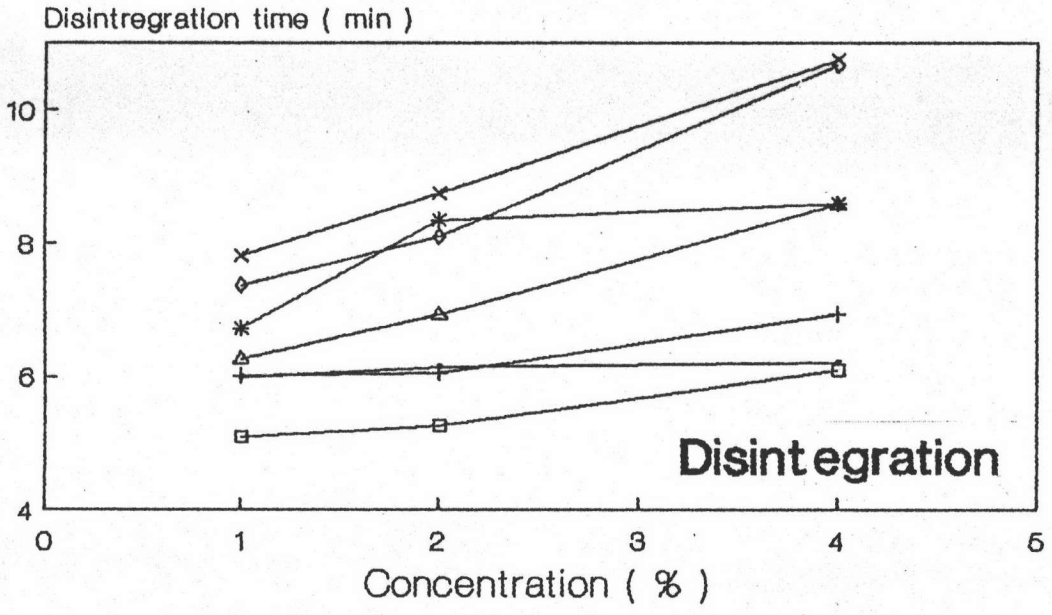


Figure 71 Effect of Binder Types and Concentrations on Disintegration Time of Pyridoxine Hydrochloride Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®)

binder than slower formulation. In addition, beside disintegration time many important factors, such as hardness, friability, dissolution rate must also be considerated all together to evaluate binder efficacy.

7.2 Pyridoxine Hydrochloride

The similar correlation as above was noticed but the disintegration values were unsignificantly influenced with the increase in binder concentration (Figure 71). The orders followed as, at 1% level : $D_1 \simeq D_2$ > Starch 1500(R) > Methocel E15LV(R) $\simeq$ corn starch $\simeq$ PVPK30 > gelatin. At 2% level : D_1 > Starch 1500(R) > D_2 > Methocel E15LV(R) > PVPK30 > corn starch > gelatin. In the case of 4% level : $D_1 \simeq D_2$ > Starch 1500(R) $\simeq$ Methocel E15LV(R) > corn starch > PVPK30 $\simeq$ gelatin. From the previous results, indicated that gelatin tablets showed the fastest disintegration time, in contrast to corn starch. Comparable data were obtained in the cases of D_1 and D_2. The tablet made by dry incorporation method disintegrated faster than solution incorporation method. Nevertheless, the fastest disintegration was blank tablets. In addition, it was clearly seen that pyridoxine hydrochloride disintegrated quicker than paracetamol tablets.

8. Dissolution Time

The median dissolution time (T50%) and dissolution rate profile of tablets produced with various binders are presented in Tables 12-15 and Figures 72-90. It obviously indicated how dissolution rates can be affected by altering the concentration of binder. The same as in disintegration studies, the prolong dissolution rate mean better formulation for evaluation of binding properties of binders.

8.1 Paracetamol

The dissolution rate of paracetamol tablets were

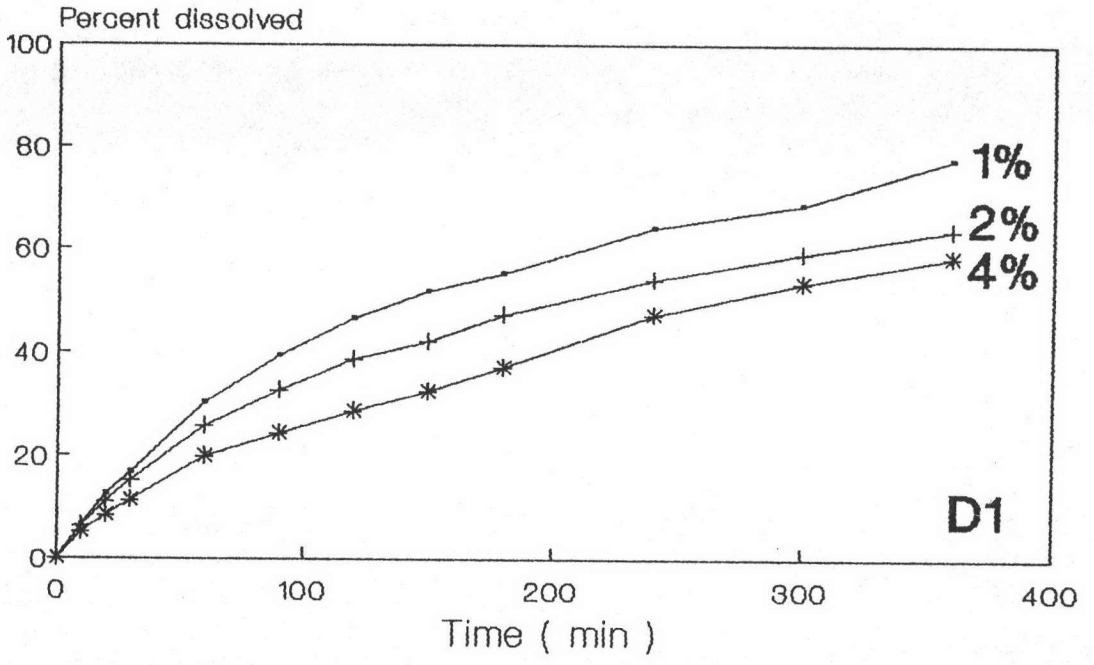


Figure 72 Dissolution Rate Profiles of Paracetamol Tablets Prepared with D_1 by Solution Incorporation Method (Key : —•— 1%, —+— 2%, —*— 4%).

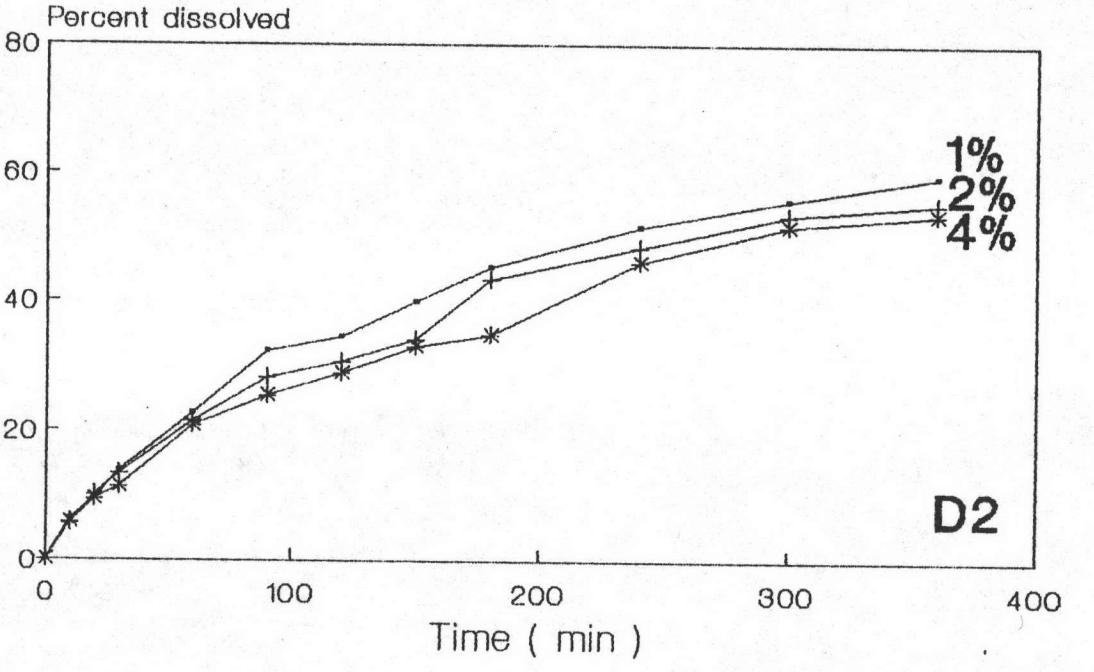


Figure 73 Dissolution Rate Profiles of Paracetamol Tablets Prepared with D_2 by Solution Incorporation Method (Key : —•— 1%, —+— 2%, —*— 4%).

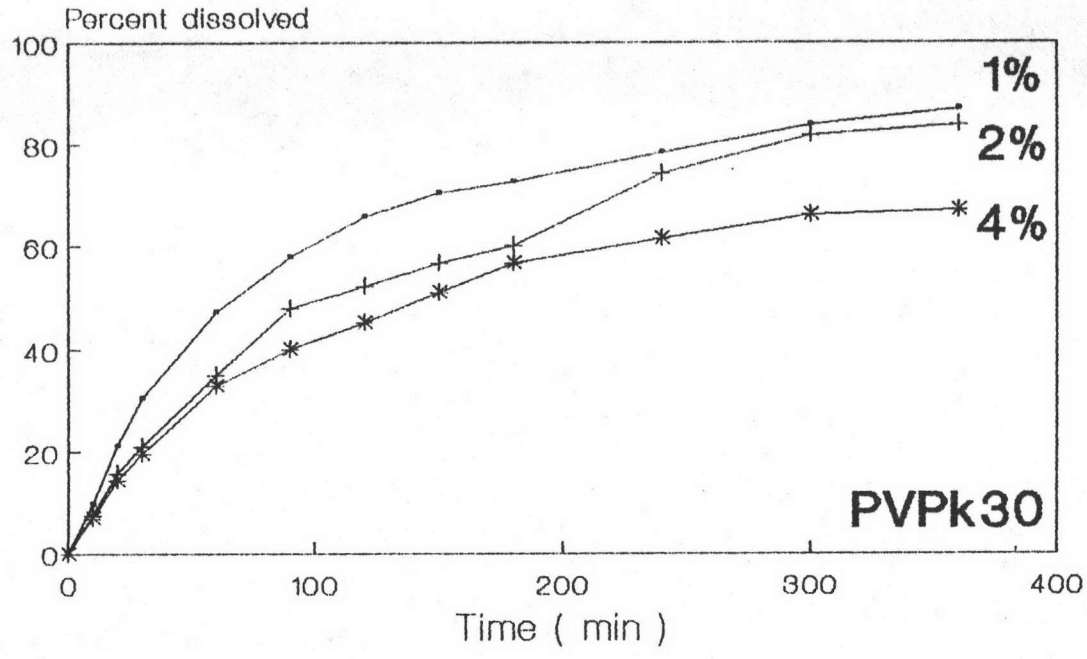


Figure 74 Dissolution Rate Profiles of Paracetamol Tablets Prepared with PVPK30 by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

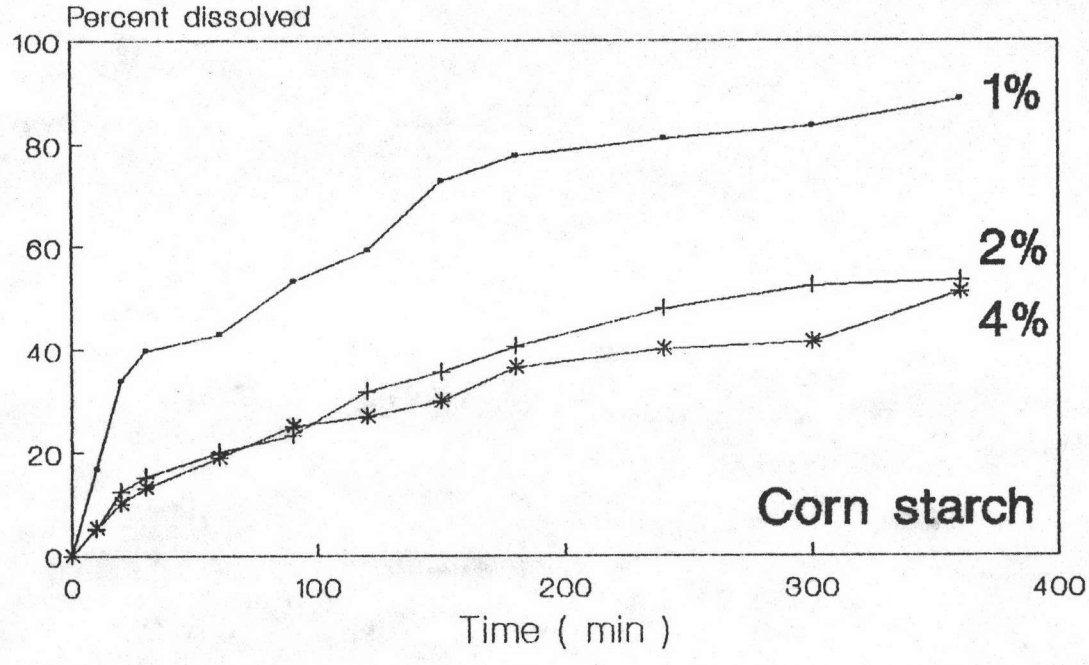


Figure 75 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Corn Starch by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

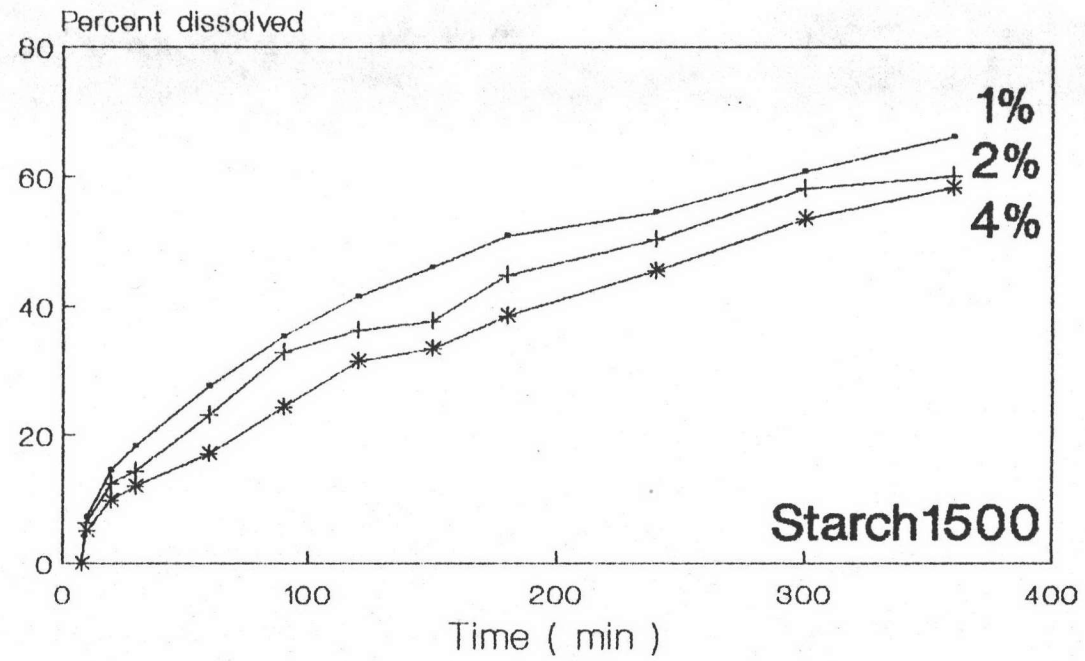


Figure 76 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Starch 1500(R) by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

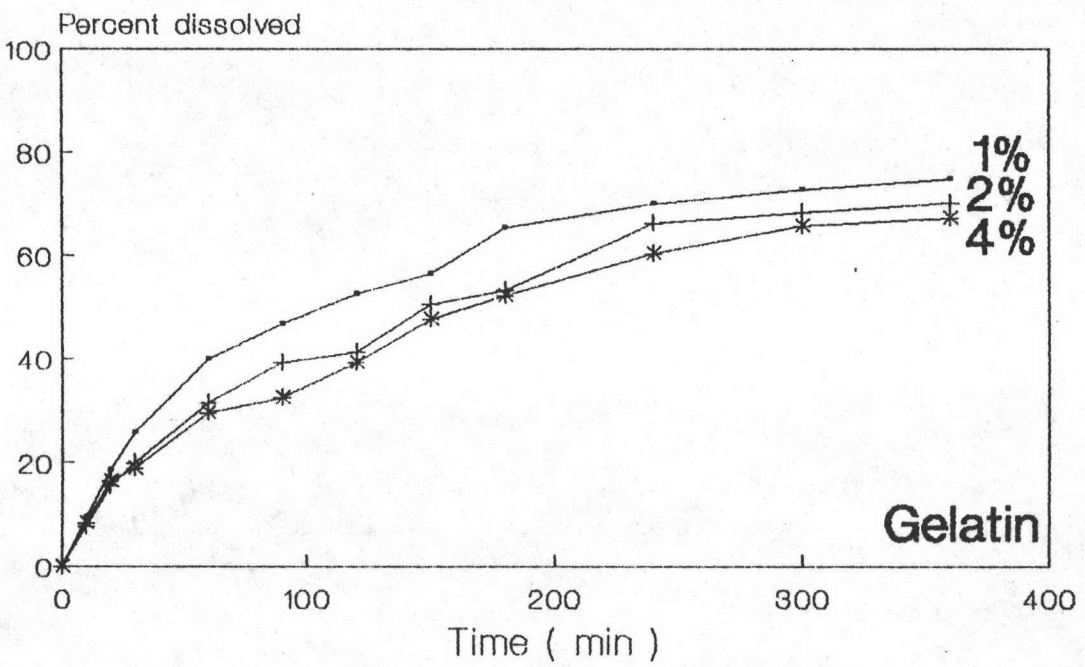


Figure 77 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Gelatin by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

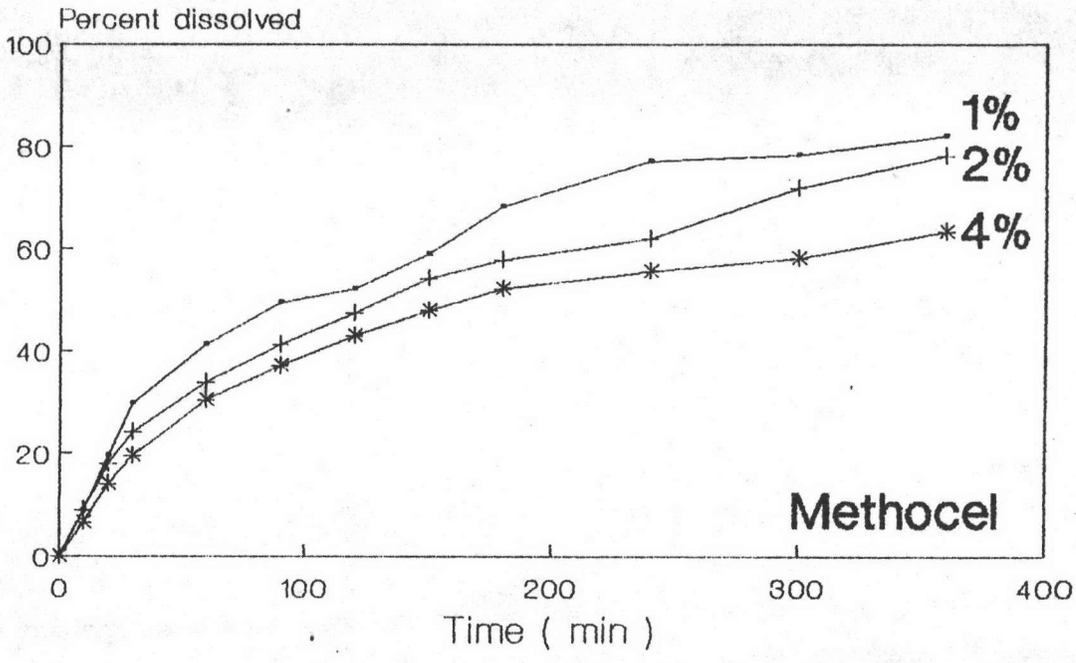


Figure 78 Dissolution Rate Profiles of Paracetamol Tablets Prepared with Methocel E15LV$^{(R)}$ Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

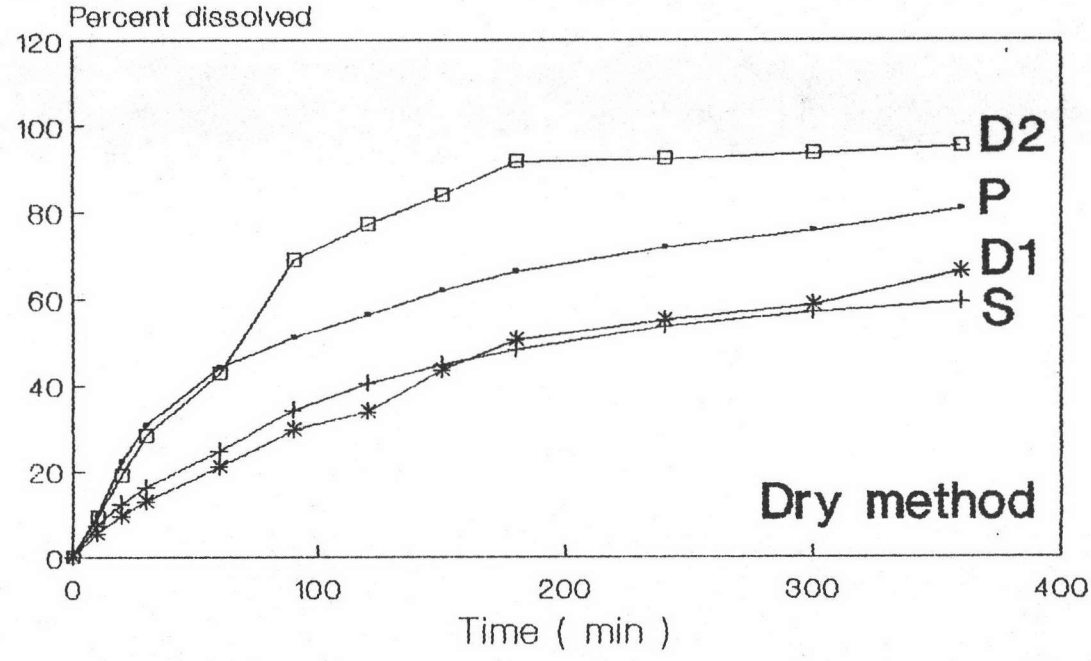


Figure 79 Dissolution Rate Profiles of Paracetamol Tablet Prepared with Various Binders at 2% Concentration by Dry Incorporation Method (Key : D_1, D_2, PVPK30, Starch 1500$^{(R)}$)

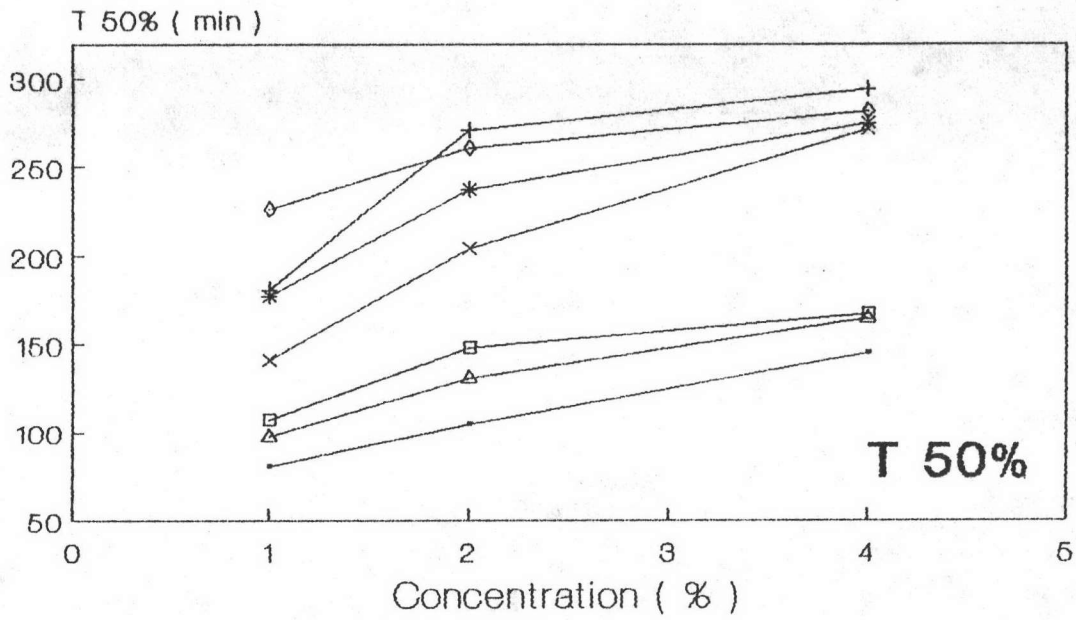


Figure 80 Effect of Binder Types and Concentrations on T50% of Paracetamol Tablets Prepared by Solution Incorporation Method (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500(R), Gelatin, Methocel E15LV(R))

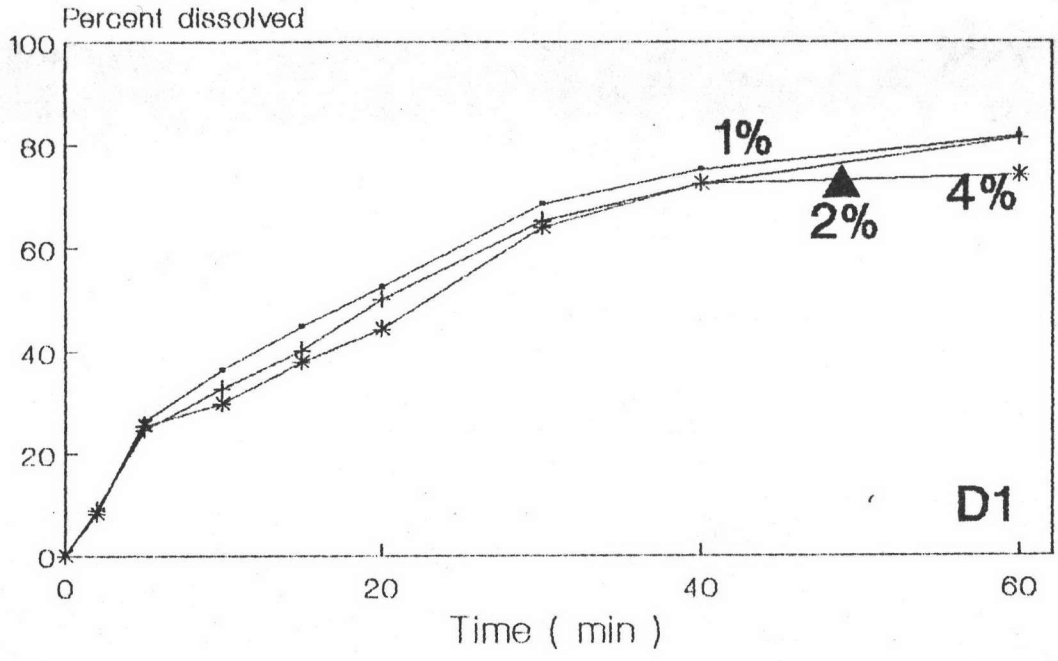


Figure 81 Dissolution Rate Profiles of Pyridoxine Hydrochloride Tablets Prepared with D_1 by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

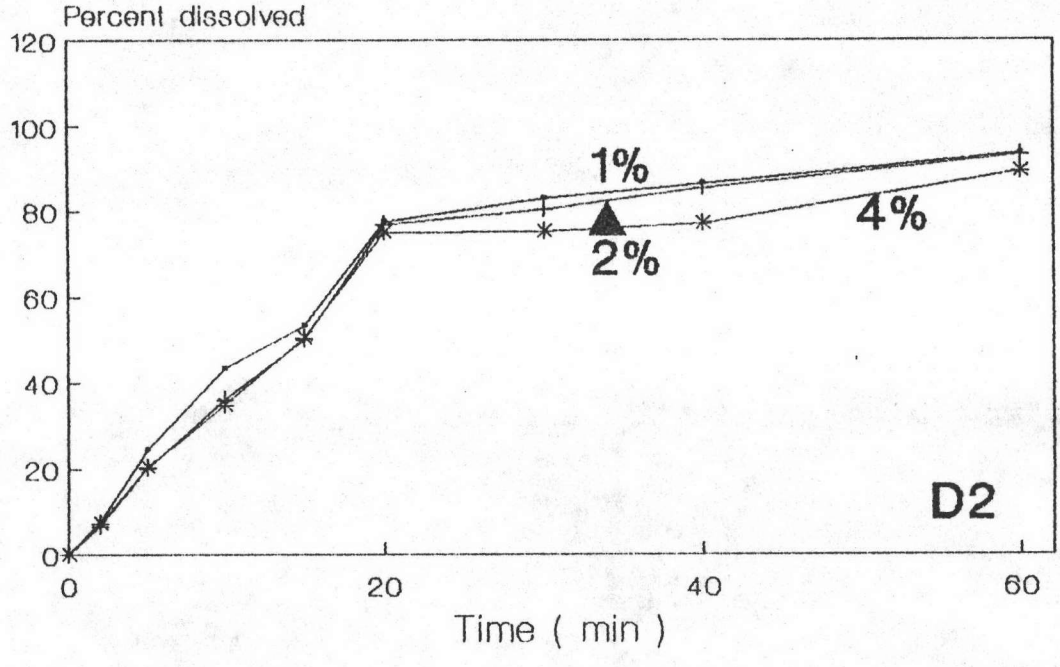


Figure 82 Dissolution Rate Profiles of Pyridoxine Hydrochloride Tablets Prepared with D_2 by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

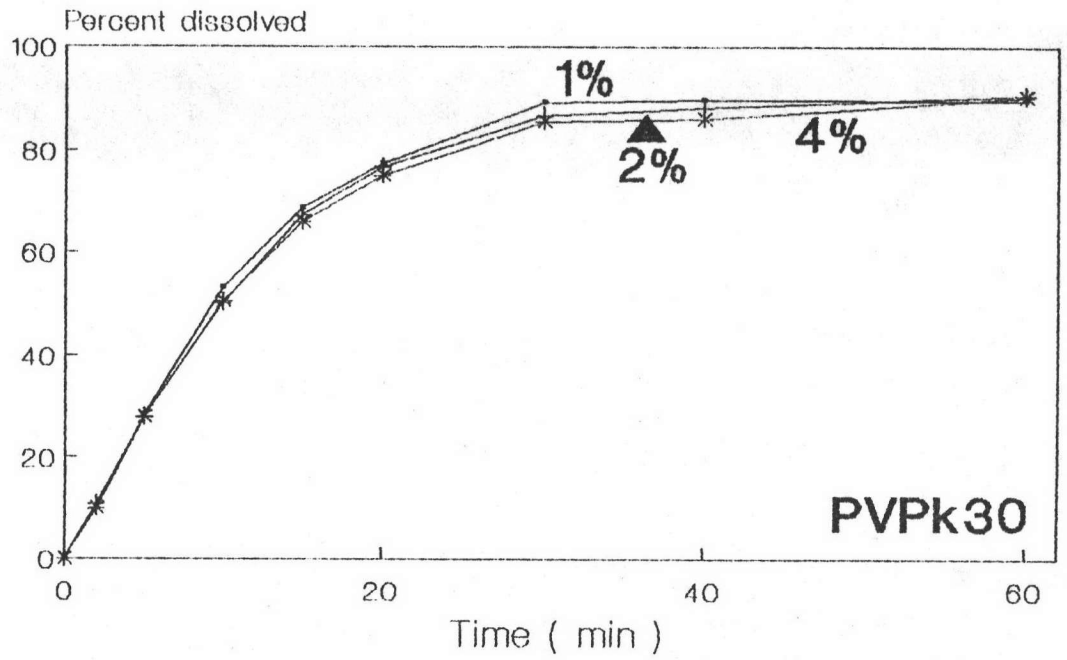


Figure 83 Dissolution Rate Profiles of Pyridoxine Hydrochloride Tablets Prepared with PVPK30 by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

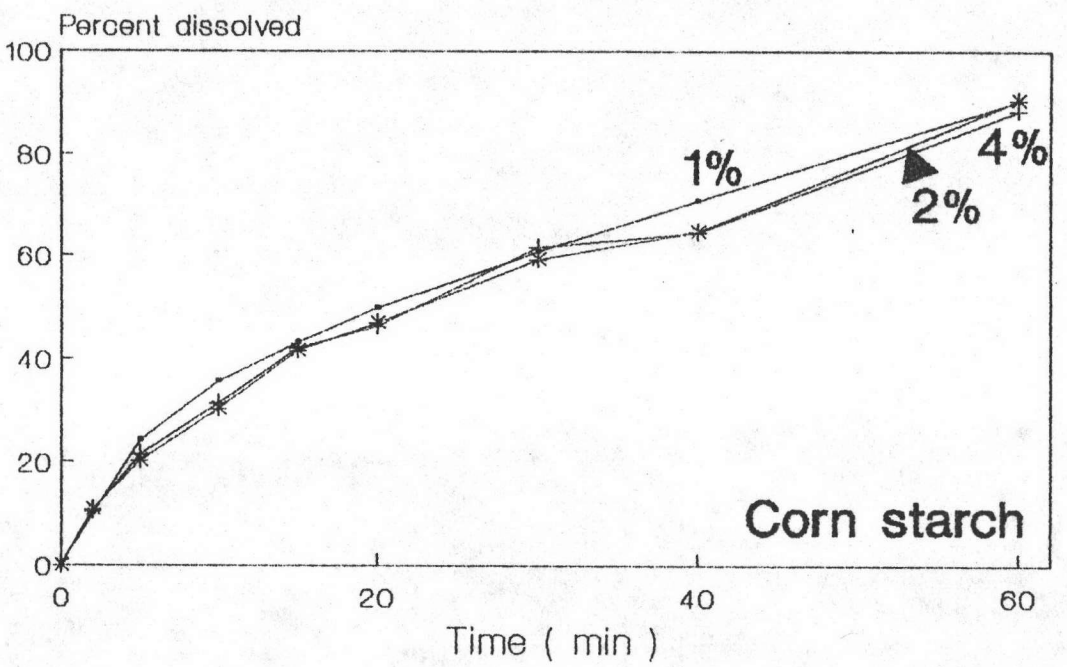


Figure 84 Dissolution Rate Profiles of Pyridoxine Hydrochloride Tablets Prepared with Corn Starch by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

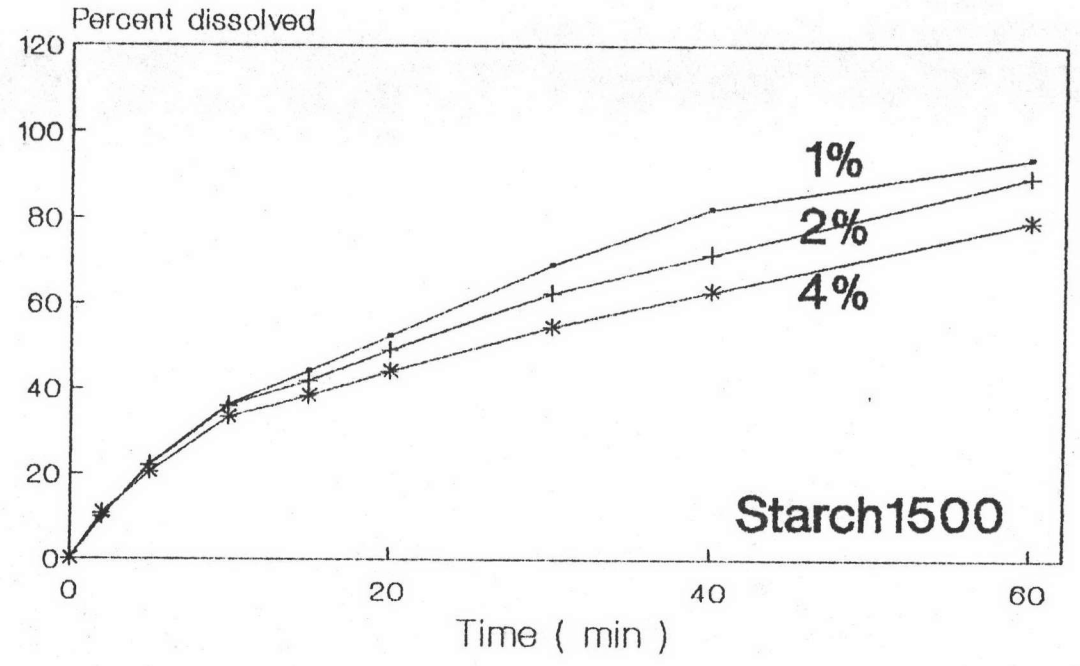


Figure 85 Dissolution Rate Profiles of Pyridoxine Hydrochloride Tablets Prepared with Starch 1500(R) by Solution Incorporation Method (Key : —•— 1%, —+— 2%, —*— 4%).

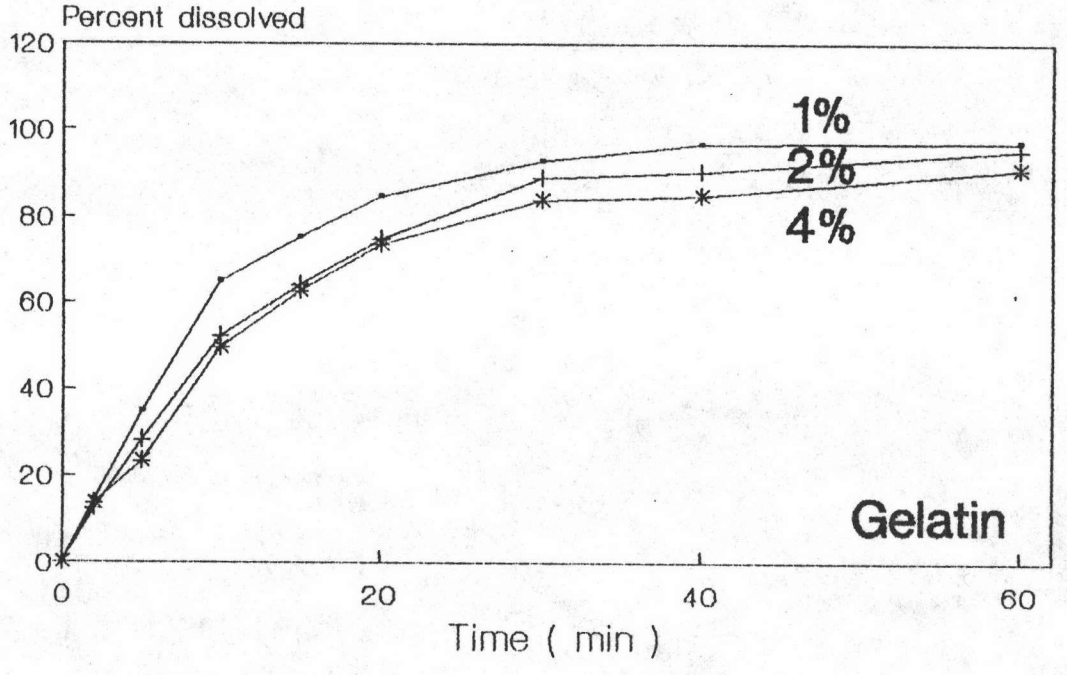


Figure 86 Dissolution Rate Profiles of Pyridoxine Hydrochloride Tablets Prepared with Gelatin by Solution Incorporation Method (Key : —•— 1%, —+— 2%, —*— 4%).

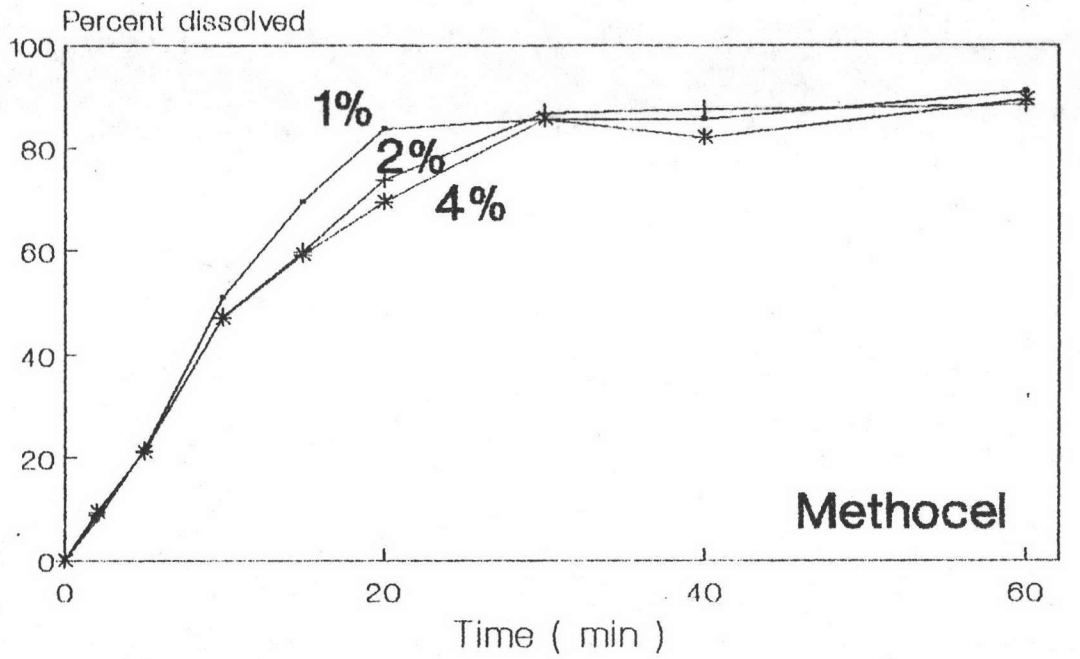


Figure 87 Dissolution Rate Profiles of Pyridoxine Hydrochloride Tablets Prepared with Methocel E15LV(R) by Solution Incorporation Method (Key : —•— 1%, —┼— 2%, —*— 4%).

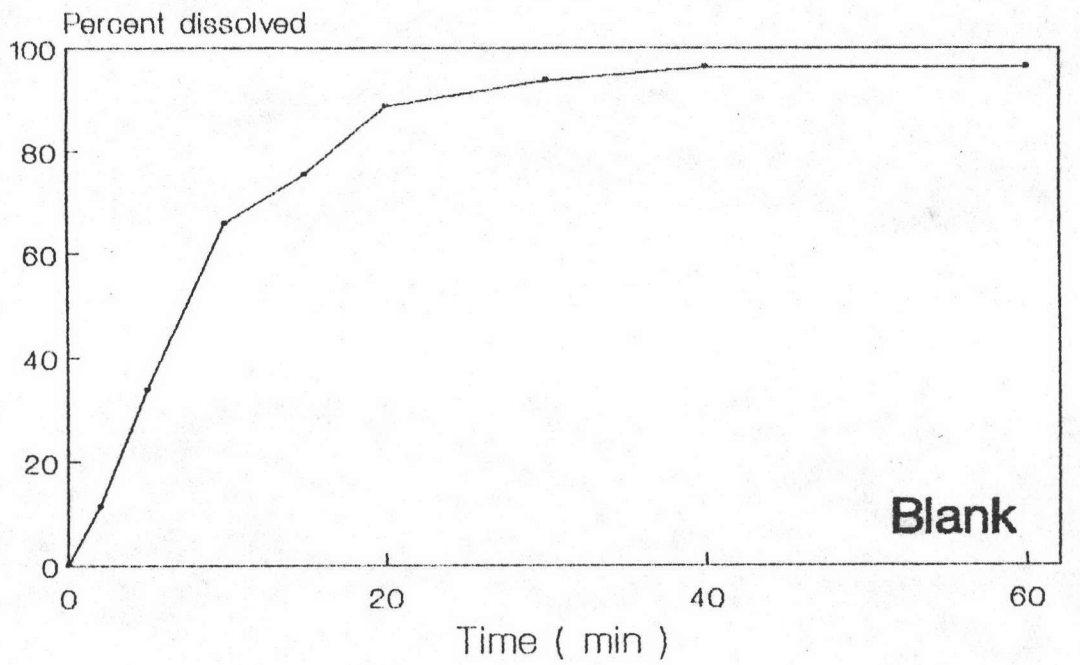


Figure 88 Dissolution Rate Profile of Pyridoxine Hydrochloride Tablet Prepared without Binder (Blank).

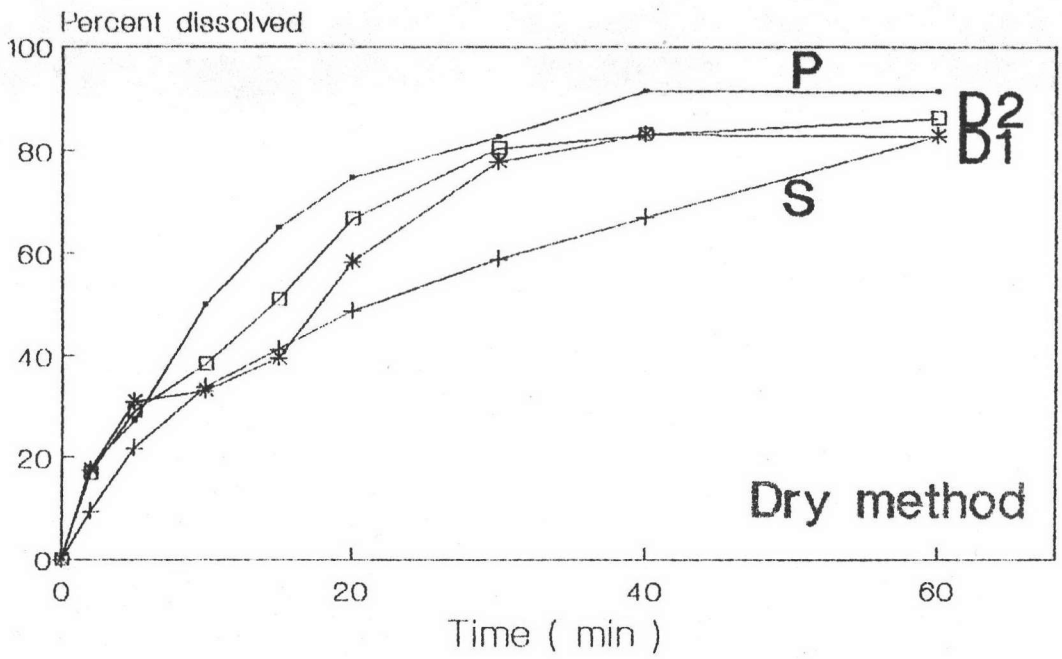


Figure 89 Dissolution Rate Profiles of Pyridoxine Hydrochloride Tablets Prepared Various Binders at 2% Concentration by Dry Incorporation Method (Key : ✳ D_1, ⊞ D_2, —•— PVPK30, —+— Starch 1500$^{(R)}$).

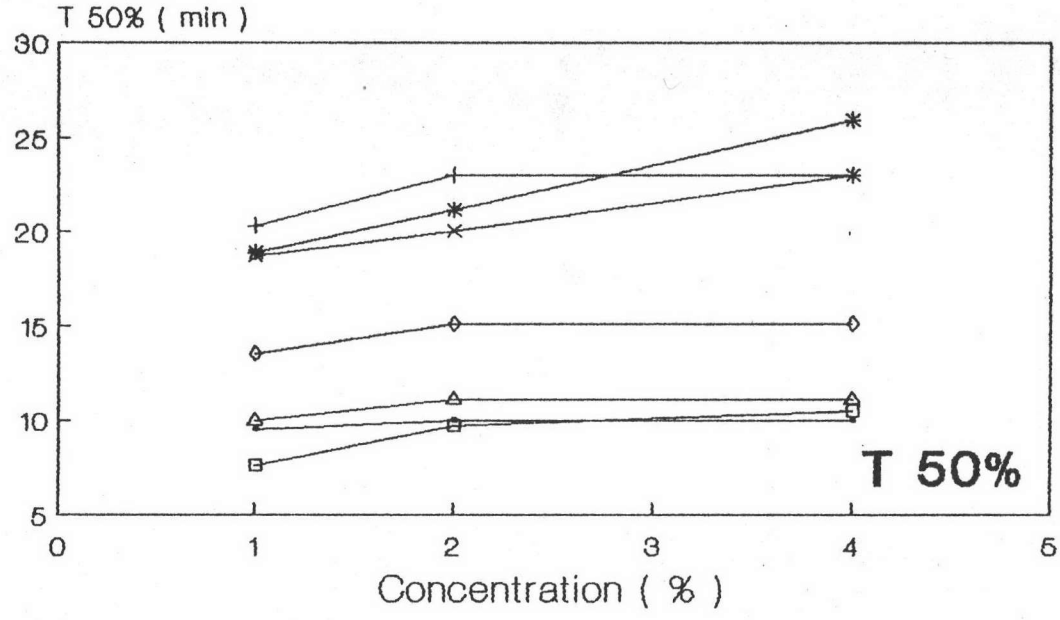


Figure 90 Effect of Binder Types and Concentrations on T50% of Pyridoxine Hydrochloride Tablets Prepared by Solution Incorporation Method. (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500(R), Gelatin, Methocel E15LV(R)).

diminished with the increase in binder concentration (Figure 8Ø). The ranks of T5Ø% were decreased as follow, at 1% level : D_2 > corn starch > Starch 15ØØ$^{(R)}$ > D_1 > gelatin > Methocel E15LV$^{(R)}$ > PVPK3Ø. At 2% level : corn starch > D_2 > Starch 15ØØ$^{(R)}$ > D_1 > gelatin > Methocel E15LV$^{(R)}$ > PVPK3Ø. In the case of 4% level : corn starch > D_2 > Starch 15ØØ$^{(R)}$ > D_1 > gelatin > Methocel E15LV$^{(R)}$ > PVPK3Ø. The quickest dissolution rate was given by PVPK3Ø. While D_1 tended to dissolved better than D_2. Regarding to incorporation method, tablet prepared by dry incorporation method clearly exhibited faster dissolution rate than solution incorporation method.

8.2 Pyridoxine Hydrochloride

The declination of dissolution rates of pyridoxine hydrochloride were less affected by increasing binder concentration (Figure 9Ø). T5Ø% values were decreased in the following order, at 1% level : corn starch > Starch 15ØØ$^{(R)}$ $\simeq$ D_1 > D_2 > Methocel E15LV$^{(R)}$ > PVPK3Ø > gelatin. At 2 % level : corn starch > Starch 15ØØ$^{(R)}$ > D_1 > D_2 > Methocel E15LV$^{(R)}$ > PVPk3Ø > gelatin. In the case of 4 % level : Starch 15ØØ$^{(R)}$ > corn starch = D_1 > D_2 > Methocel E15LV$^{(R)}$ > gelatin > PVPk3Ø . At all concentrations studies , the most rapid dissolution were seen in tablets prepared with gelatin and PVPk3Ø. D_1 gave the superior dissolution as comparing with D_2. The slightly better in dissolution rate was observed with tablet produced by dry incorporation method comparing with solution incorporation method. As was expected, blank tablet which showed the fastest disintegrating time, represented the best dissolution rate.

9. Content Uniformity

The mean and standard deviation of content uniformity of paracetamol and pyridoxine hydrochloride tablets are illustrated in tables 12-15. The results were all within the range of USP standard (85-115%).

10. Binder Index

According to the results of binder index, they increased as the binder concentration increased (Tables 12-15 and Figure 91-92).

10.1 Paracetamol

The ranks of binder index decreased as follow, at 1% level : PVPk30 > Methocel E15LV$^{(R)}$ > D_1 > gelatin > D_2 > , At 2 % level : PVPk30 > Methcel E15LV$^{(R)}$ > D_1 > gelatin > D_2 > Starch 1500$^{(R)}$ > corn starch. In the case of 4% level : PVPk30 > Methocel E15LV$^{(R)}$ > gelatin > D_1 > D_2 > Starch 1500$^{(R)}$ > corn starch. Consideration for all concentration studies, PVPk30 showed the greatest binder index whearas corn starch gave the lowest value. It could be noticed that D_1 had higher binder index than D_2. From data in Tables, all the tablet produced by dry incorporation method exhibited inferior binder index than solution incorporation method except for D_2.

10.2 Pyridoxine hydrochloride

In this study, binder index of pyridoxine hydrochloride tablet seemed to be higher than paracetamol tablet. Their orders were decreased as follow , at 1 % level : PVPk30 > gelatin > Methocel E15LV$^{(R)}$ > D_2 > Starch 1500$^{(R)}$ > corn starch > D_1. At 2 % level : gelatin > PVPK30 > Methocel E15LV$^{(R)}$ > Starch 1500$^{(R)}$ > D_2 > D_1 > corn starch. In the case of 4 % level : PVPK30 > gelatin > Methocel E15LV$^{(R)}$ > D_2 > Starch 1500$^{(R)}$ > D_1 > corn starch. It also noted that the highest and lowest binder index were tablet produced with PVPk30 (except at 2 %) and corn starch, respectively. However, D_2 showed higher binder index than D_1. The inferior binder index values were found for dry incorporation method as comparing wwith solution incorporation method. In addition, blank tablet was typically the least binder index values.

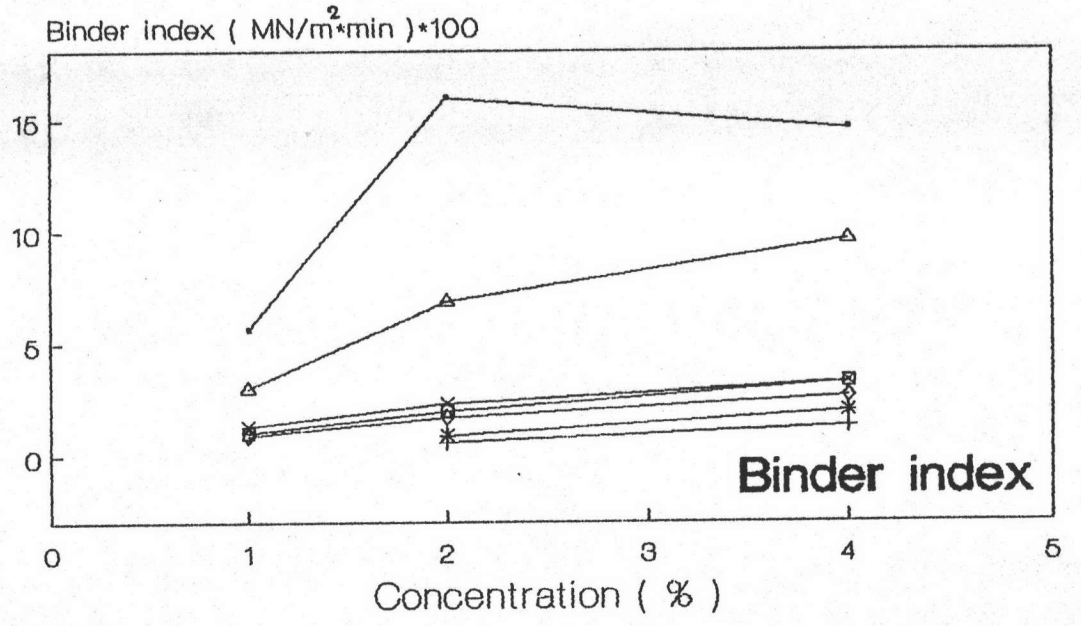


Figure 91 Effect of Binders Types and Concentrations on Binder Index of Paracetamol Tablets Prepared by Solution Incorporation Method. (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500®, Gelatin, Methocel E15LV®).

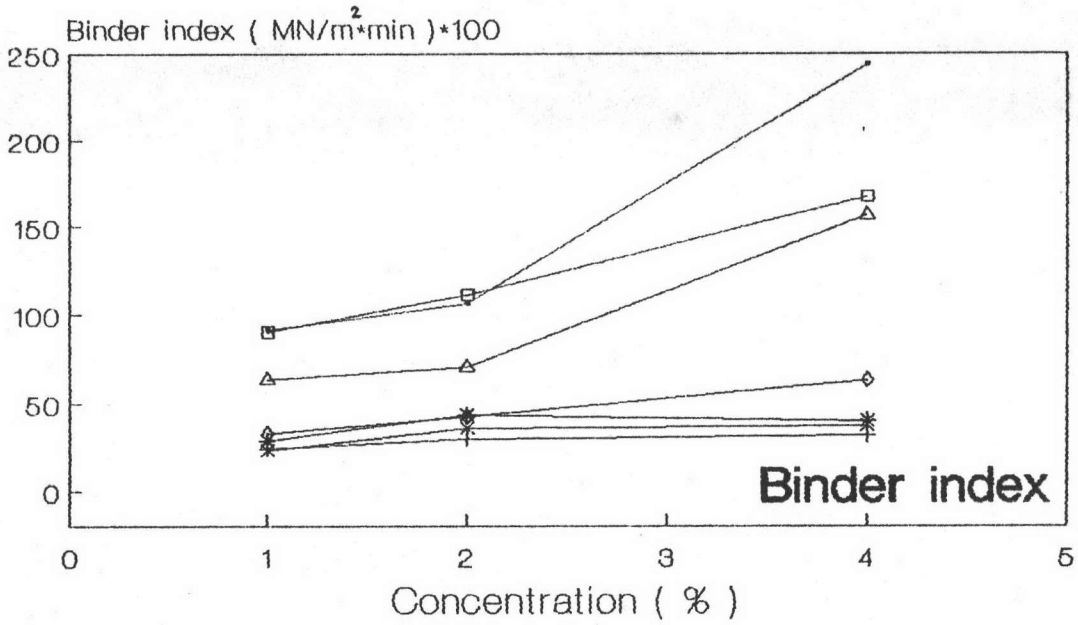


Figure 92 Effect of Binders Types and Concentrations on Binder Index of Pyridoxine Hydrochloride Tablets Prepared by Solution Incorporation Method. (Key : D_1, D_2, PVPK30, Corn starch, Starch 1500$^{(R)}$, Gelatin, Methocel E15LV$^{(R)}$).