Chapter 6

MODIFIED GUAR GUM

AS

TABLET DISINTEGRANT

6.1 INTRODUCTION

Tablet disintegration is a necessary first step to achieve rapid bioavailability of ingredients. Many compounds have been proposed as tablet disintegrants (1) that act through different mechanisms(2,3). GG, a naturally occurring macromolecular galactomannan polysaccharide, has been used as a tablet disintegrant(4) because of its cold water swellability. But its role as disintegrant is limited because it forms a cohesive gel on hydration, which hinders the disintegration of tablet.

In the present investigation OGGs were evaluated as tablet disintegrants. The important factors that influence disintegration use like rate and amount of water uptake, which control the penetration of liquid into the tablet matrix causing tablet disintegration, were evaluated and compared. Surface properties of tablets made with GG and OGGs as disintegrants were studied by scanning electron microscopy (SEM). Disintegration time (DT) of tablets made using GG, OGGs and disintegrants available in the market were determined and compared. The effect of tablet parameters such as composition, compressional forces and the pH of disintegration medium on DT of tablets made with OGG as disintegrant was also studied.

6.2 MATERIALS

Guar gum I.P. (National Chemicals, Bombay), sodium metaperiodate A.R., sodium hydroxide A.R., sodium chloride A.R. (S.D. Fine Chem Pvt. Ltd., Boisar), lactose I.P. (Suvidhinath Laboratories, Baroda), dibasic calcium phosphate I.P.(DCP), microcrystalline cellulose (MCC), starch I.P. (Modern Chemical Corporation, Bombay), magnesium stearate I.P., purified talc I.P. (Comet Chemicals, Bombay), sodium starch glycollate (SSG) (D.P. Chemicals, Bombay), bromocresol purple (B.D.H. Laboratory Chemicals Division, Poole, England), crosslinked polyvinylpyrrolidone (PVP-CL), crosslinked sodium carboxymethyl cellulose (NaCMC-CL) (courtesy M.J.

Institute of Research, Baroda), acetone A.R., hydrochloric acid A.R. (Emerck (India) Ltd., Bombay).

6.3 EQUIPMENTS

Single stroke compression machine (Cadmach Machinery, Ahmedabad), Tablet friability tester, Hardness tester (Magumps Instruments, Bombay), Tablet disintegration test apparatus (Veego Scientific Instruments, Bombay) Scanning Electron Microscope (JEOL JSM 300, Japan).

6.4 METHODS

6.4.1 Water Uptake :

The water uptake capacity of GG and modified GGs was determined using apparatus shown in Fig 6.1 (5) and calculated as under -

$$U = \frac{Wt_{\infty} - Wt_o}{Wt_o} X \frac{1}{\rho}$$

Where U is water uptake by powder bed (ml/g), wt_{∞} is final weight of the powder bed (g), Wt_o is the initial weight of the powder bed (g), ρ is the specific gravity of water (g/ml). The results of average water uptake from six samples of each of three batches alongwith standard error values are shown in Table 6.1.

6.4.2 Swelling characteristics of OGGs :

In the same apparatus (Fig 6.1) the swelling of powder bed with respect to time was calculated using the following equation -

$$S = \frac{h_t - h_o}{h_o} X \ 100$$

where S is the degree of swelling (%), h_t the height of powder bed at time t and h_o is the height of powder bed at time t = 0. The results are shown in Table 6.1 and Fig 6.2.

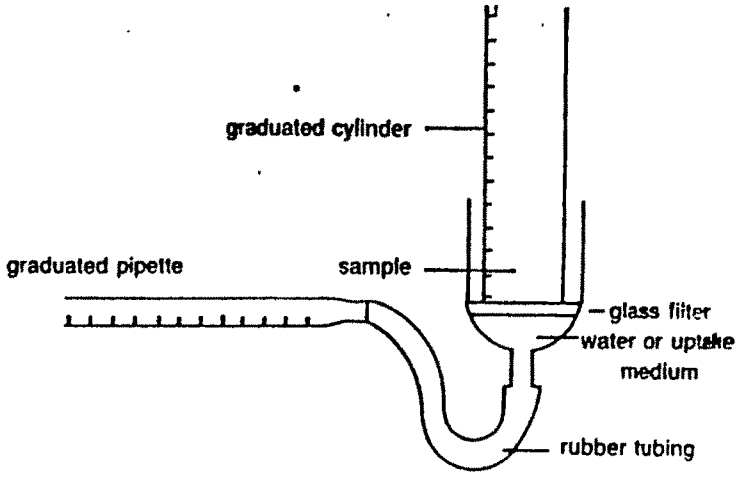

graduated cylinder
graduated pipette
sample
glass filter
water or uptake medium
rubber tubing

Fig 6.1

6.4.3 Tabletting :

Tablets of average weight 250 mg were prepared by wet granulation technique on single stroke compression machine using 8 mm die punch set. The composition of the formulations is shown in Table 6.2. 5% w/w polyvinylpyrrolidone was used as binder in the form of 25%w/v solution in isopropyl alcohol. The prepared granules were lubricated with 1%w/w magnesium stearate and 1%w/w talc .Disintegrants in the concentration of 5 %w/w of tablets were used in all cases.

OGGs showing promising results were further investigated for the effect of composition of formulation, compressional force and pH of the disintegration medium on DT of tablets.

6.4.4 Disintegration Test :

One tablet was placed in each of six tubes of the basket of USP XXII(6) disintegration test apparatus and the apparatus was operated using water, maintained at 37° ± 2° C, as the disintegration medium. The time required for the tablets to disintegrate completely was noted and are recorded in Table 6.2.

6.5 RESULTS AND DISCUSSIONS

GG, a natural macromolecular polysaccharide, consists of d-mannose unit with pendant d-galactose groups. Small amounts of periodate preferentially oxidize the galactose moiety and it has also been reported that reduction of galactose mannose ratio results in improved interaction properties of GG (7). Hence oxidation of GG was undertaken so as to improve its interaction coefficient . OGGs were evaluated as tablet disintegrants. The important factors that influence the disintegrant use like rate and amount of water uptake were evaluated and compared with those of the commercially available commonly used disintegrants which include crosslinked

polyvinylpyrrolidone, crosslinked sodium carboxymethylcellulose, sodium starch glycollate, starch and microcrystalline cellulose.

6.5.1 Water Uptake :

The amount of water uptake in 2 h was determined using the apparatus shown in Fig 6.1 and the results are recorded in Table 6.1. GG shows poor amount of water uptake (0.51 ± 0.02 ml/g) due to its gelling at the interface and formation of obstructive cohesive gel layer which prevents penetration of water inside the GG bed. Oxidation of GG reduces the gelling tendency of the gum and thereby helps in water uptake by capillary action due to unchanged hydrophilicity. The degree of oxidation also influences the amount of water uptake by OGGs. The amount of water uptake increases with increase in the degree of oxidation upto carboxyl content value of 71.38 ± 1.54 meq/g (2.60 ± 0.23 ml/g) and then reduces. Increasing the degree of oxidation further, leads to oxidation of mannose backbone reducing the chain-length as well as the molecular size and weight of the polymer hence reducing the water uptake.

6.5.2 Swelling Characteristics :

In the same apparatus (Fig 6.1) the swelling characteristics of products were studied. The data of rate and degree of swelling of GG/OGGs (Fig 6.2) suggest that swelling behaviour follows a pattern similar to that found for the amount of water uptake. The rate of swelling increased with increase in degree of oxidation but the degree of swelling reduced beyond OGG2. This phenomenon may be explained in similar lines as described before, that the reduction in molecular size/weight increases hydrophilicity but reduces water swellability.

Table 6.1 Swelling Cahracteristics and Water Uptake of OGGs.

Sr. No.	Time (Min)	Per cent Swelling of powder bed					
		GG	OGG1	OGG2	OGG3	OGG4	OGG5
1	1	5.26	26.31	52.63	63.16	68.42	78.95
2	2	5.26	52.36	73.7	78.95	78.95	105.26
3	5	10.53	84.21	105.26	119.79	126.32	126.32
4	10	10.53	84.21	126.32	121.79	131.58	131.58
5	120	10.53	126.32	168.42	157.89	152.63	147.27
Water Uptake (ml)	240	0.51±0.02	1.61±0.12	2.60±0.23	2.35±0.07	2.21±0.13	2.00±0.04

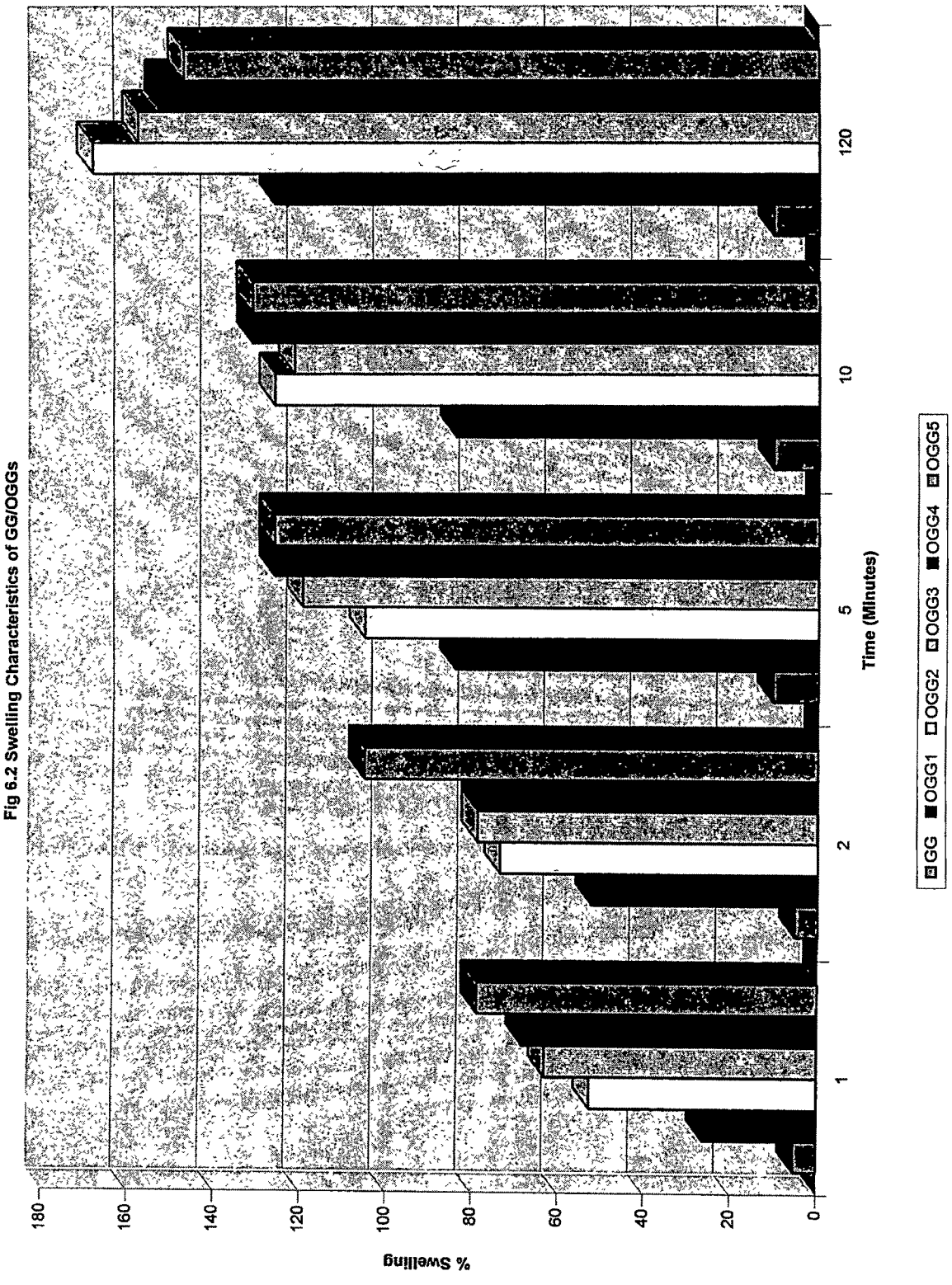


Fig 6.2 Swelling Characteristics of GG/OGGs

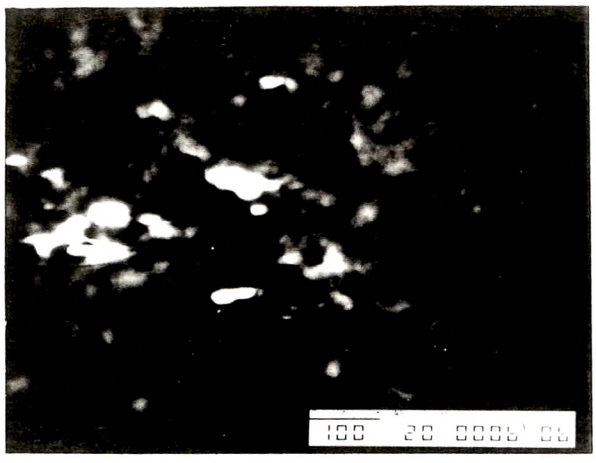
6.5.3 Disintegration Test :

All the formulations were subjected to disintegration test using USP XXII disintegration test apparatus. Effect of composition of tablets, compressional force and pH of disintegration media were studied.

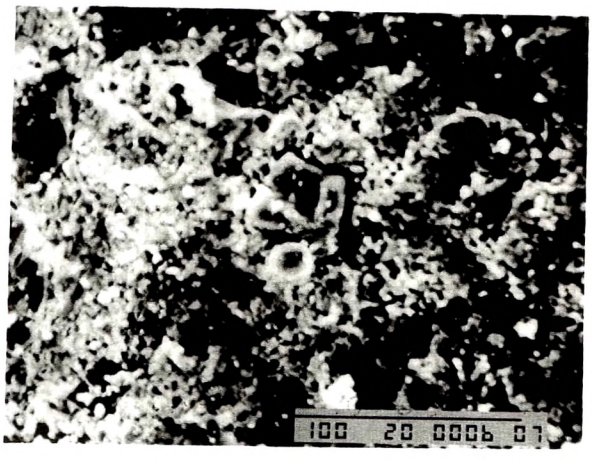
6.5.3.1 Comparison of GG and OGGs as disintegrants :

The tablets made with 5 % GG show DT of 13 (±2) min compared to the tablets made without any disintegrant having DT of more than half an hour. Tablets containing 5 % of OGGs as disintegrants show a noticeable reduction in DT (1.75 ± 0.25 min to 5.5 ± 0.5 min) compared to the tablets containing GG as disintegrant. This signifies that the rate and amount of water uptake and the degree of swelling are the important factors responsible for the disintegration of the tablets. The degree of oxidation of OGGs shows a significant influence on the DT of tablets. With increase in degree of oxidation of OGGs DT of tablets decreased to a minimum of 1.75 ± 0.25 min (OGG2) and then increased to a maximum of 5.5 ± 0.5 min. This implies that faster uptake of water through enhanced capillary action alongwith increased degree of swelling is responsible for the better performance of OGG2 compared to other OGGs.

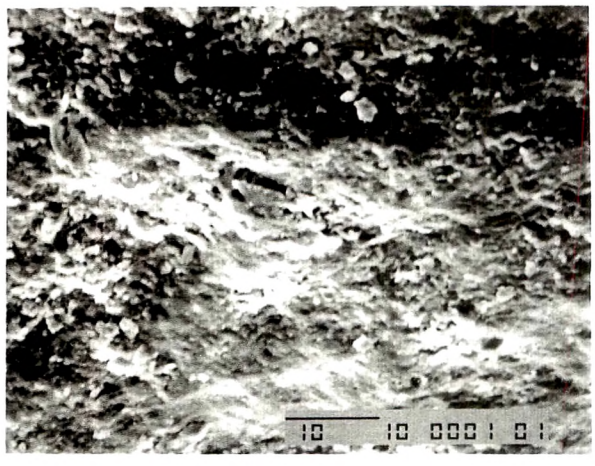
Surface properties of the tablets were studied using SEM, shown in Fig 6.3 a, b and c, where magnification was adjusted to see F#1 (tablets without any disintegrants) tablets as continuous matrix. Scanning electron microphotographs of the formulations containing disintegrants show uniform distribution of disintegrants (GG/OGGs) on the surface of the tablets. The faster uptake of water by the disintegrants reduces the DT of tablets. OGGs, with improved water uptake capacity and swelling characteristics compared to GG, contribute to significant reduction in DT.



A



B



C

Fig 6.3

TABLE 6.2.1 Composition of tablets and their evaluation for DT.

Formul. No.	Ingredients (% w/w)						
	Lact.	DCP	MCC	Starch	Disint.[a]	D.T.(min)[b]	Times Red.[c]
F#1	68.0	25.0	-	-	-	>30	-
F#2	63.0	25.0	-	-	GG	13.0±1.50	1.00±0.00
F#3	63.0	25.0	-	-	OGG1	3.50±0.50	3.71±0.44
F#4	63.0	25.0	-	-	OGG2	1.75±0.50	7.43±1.75
F#5	63.0	25.0	-	-	OGG3	2.50±0.50	5.20±0.90
F#6	63.0	25.0	-	-	OGG4	3.50±0.50	3.71±0.44
F#7	63.0	25.0	-	-	OGG5	4.00±0.70	3.25±0.51
F#8	63.0	25.0	-	-	PVP-CL	1.25±0.20	10.40±1.78
F#9	63.0	25.0	-	-	NaCMG-CL	3.00±0.50	4.33±0.61
F#10	63.0	25.0	-	-	SSG	5.50±0.50	2.36±0.17
F#11	63.0	25.0	-	-	MCC	9.00±1.00	1.44±0.13
F#12	63.0	25.0	-	-	Starch	8.00±1.00	1.63±0.13

[a] 5%w/w of the disintegrants have been used in all cases.
[b] Measured at constant hardness (4.5±0.05 kg/cm^2) and pH of the disintegration media (6.8).
[c] 13.0 ± 1.5 /D.T.(min) of respective formulation.

The performance of OGG2 was compared with disintegrants commonly available in the market (Table 6.2.1). The tablets with OGG2 as disintegrant show the least DT compared to the tablets with other disintegrants except those with PVP-CL. The examination of the physical parameters show that the density of PVP-CL (0.35) is very less compared to that of OGG2 (0.71), which means that for the same amount of the material the number of particles of PVP-CL will be very high. This leads to better distribution of PVP-CL particles in the tablet matrix and provides a continuous network which can convey water from one grain to other and so on thus reducing DT.

6.5.3.2 Effect of Diluents :

The composition of water soluble/insoluble excipients was varied and the DT of tablets with and without OGG2 as disintegrant (F#13 to F#28) was determined. The results (Table 6.2.2) of these variations reveal that the composition of the tablet matrix has significant effect on DT of the tablets and OGG2 reduces DT effectively in all cases.

6.5.3.3 Effect of compressional forces :

Tablets containing GG, OGG2 and other disintegrants were prepared at varying compressional forces and subjected to hardness and DT tests (Table 6.2.3). An increase in DT was observed with increase in hardness of the tablets and the disintegrants can be ranked, with respect to the effect of hardness, as-

PVP-CL < Starch < SSG < OGG2 < NaCMC-CL < MCC

The rate of penetration of fluids into a tablet is proportional to mean pore diameter or porosity when other factors are constant, which decreases with increase in compressional forces. Further, the change in degree of deformation of disintegrant under pressure increases

Table 6.2.2 Effect of diluents on DT.

Formul. No.	Ingredients (% w/w)						
	Lact.	DCP	MCC	Starch	Disint.[a]	D.T.(min)[b]	Times Red.[c]
F#13	-	68.0	-	25.0	-	1.25±0.20	10.40±1.78
F#14	-	63.0	-	25.0	OGG2	0.80±0.10	16.25±2.59
F#15	-	68.0	25.0	-	-	1.50±0.20	8.67±1.22
F#16	-	63.0	25.0	-	OGG2	0.25±0.00	52.0±10.49
F#17	25.0	68.0	-	-	-	>30	-
F#18	25.0	63.0	-	-	OGG2	4.00±0.50	3.25±0.33
F#19	-	25.0	68.0	-	-	2.50±0.50	5.20±0.89
F#20	-	25.0	63.0	-	OGG2	0.25±0.00	52.0±8.92
F#21	-	-	68.0	25.0	-	0.15±0.00	86.67±15.8
F#22	-	-	63.0	25.0	OGG2	0.15±0.00	86.67±15.8
F#23	25.0	-	68.0	-	-	22.0±2.00	0.59±0.04
F#24	25.0	-	25.0	-	OGG2	6.00±1.00	2.17±0.30
F#25	68.0	-	25.0	-	-	>30	-
F#26	63.0	-	25.0	-	OGG2	2.00±0.50	6.50±1.43
F#27	63.0	-	-	25.0	-	>30	-
F#28	63.0	-	-	25.0	OGG2	2.50±0.50	5.20±0.90

[a] 5%w/w of the disintegrants have been used in all cases.
[b] Measured at constant hardness (4.5±0.05 kg/cm^2) and pH of the disintegration media (6.8).
[c] 13.0 ± 1.5 /D.T.(min) of respective formulation.

with increase in compressional forces and hence reduces the rate of penetration of fluids into the tablet.

6.5.3.4 Effect of pH :

DT of tablets, with OGG2 as disintegrant, determined at physiological pH range, to study the influence of pH (Table 6.2.4), suggest no significant variation in DT with change in pH of disintegration media.

In conclusion, it may be said that the oxidation of GG results in a hydrophilic and water-insoluble products, which have fast rate of water uptake, good swelling ability and poor gelling tendency. The products are non-ionic in nature and so are pH-independent. These properties are the requisites for an ideal tablet disintegrant, hence OGGs can serve as excellent tablet disintegrants and can be valuable alternative to the commonly used expensive tablet disintegrants.

Table 6.2.3 Effect of compression forces on DT.

Formul. No.	D.T (min) at Hardness (kg/cm^2)[a]				
	3.5 ± 0.5	4.5 ± 0.5	5.5 ± 0.5	6.5 ± 0.5	8.0 ± 0.5
F#4	1.25 ± 0.1	1.75 ± 0.5	2.25 ± 0.2	2.75 ± 0.3	3.50 ± 0.2
F#8	1.00 ±0.0	1.25 ± 0.2	1.50 ± 0.2	1.50 ± 0.2	1.75 ± 0.5
F#9	2.00 ± 0.2	3.00 ± 0.5	3.50 ± 0.5	4.50 ± 0.1	6.00 ± 0.7
F#10	5.25 ± 0.2	5.50 ± 0.5	6.00 ± 0.5	6.50 ± 0.6	7.25 ± 0.2
F#11	8.00 ± 0.8	9.00 ± 1.0	10.00 ± 1.0	12.00 ± 0.7	13.00 ± 0.5
F#12	7.00 ± 1.5	8.00 ± 1.0	8.00 ± 0.5	8.25 ± 0.5	8.50 ± 1.0

[a] pH of disintegration media kept constant (6.8)

Table 6.2.4 Effect of pH of disintegration media on DT.

Formul. No.	D.T (min) at pH[a]				
	1.2	5.8	6.8	7.4	9.0
F#4	1.25 ± 0.2	1.75 ± 0.2	1.75 ± 0.2	1.75 ± 0.3	1.75 ± 0.2
F#8	1.00 ±0.1	1.25 ± 0.2	1.25 ± 0.2	1.25 ± 0.5	1.50 ± 0.1
F#9	3.00 ± 0.5	3.00 ± 0.5	3.25 ± 0.5	3.50 ± 0.2	3.50 ± 0.1
F#10	5.25 ± 0.5	5.50 ± 0.5	5.50 ± 0.7	6.00 ± 0.5	6.00 ± 0.5
F#11	8.50 ± 0.5	8.50 ± 0.7	8.75 ± 0.7	9.00 ± 0.2	90 ± 0.2
F#12	8.00 ± 1.0	8.00 ± 0.5	8.00 ± 0.5	8.00 ± 0.2	8.25 ± 0.2

[a] Hardness of Tablets kept constant (4.5 ± 0.5 kg/cm^2)

6.6 REFERENCES

1. Lowenthal,W., *J. Pharm. Sci.*, 1972, *61*, 1695.
2. Guyot-Hermann,A.M., Rengard,D.J., *Drug Dev. Ind. Pharm.*, 1981, 7, 155.
3. Rudnic,E.M., Rhodes,C.T., Welch,S., Bernardo,P., *Drug Dev. Ind. Pharm.*, 1982, *8*, 87.
4. Feinstein,W., Bartilucci,A.J., *J. Pharm. Sci.*, 1966, *55*, 332.
5. Nogami,H., Nagai,T., Fukuoka,E., Sonabe,T., *Chem. Pharm. Bull.*, 1969, *17*, 1450.
6. **United States Pharmacopoeia,** Pharmacopoeial Convention, Inc., Rockville, 1995, 22, p 1577.
7. Whistler,R.L., Li,T.K., Dvanch,W., *J. Am. Chem. Soc.*, 1948, *70*, 3144.