A Comparative Study of Novel Super Disintegrating Agent, Guar gum to existing Super Disintegrating Agent, Sodium Starch Glycolate on Release Rate of Drug from Fast Dissolving Tablet

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The aim of present study is to exist a novel super disintegrants in fast dissolving tablet. Guar gum is a natural substance and used in many pharmaceutical product and it can also used as a super disintegrating agent in fast dissolving tablet. The result is that it released the 99.21% drug in 15min as compared to Sodium Starch Glycolate (SSG), where only 97.51% drug was released. The onset of time was better for guar gum where, 84.79% of drug was released in 2min from F3 formulation as compared of F6 formulation where only 71.22% drug was released. The possible mechanism of disintegrating property was good swelling property of guar gum than SSG but when the concentration of guar gum was used above 8%, it created a problem on disintegration of tablet due to formation of gel layer around the tablet. All evaluating parameters were within range and no markedly difference was observed.

Keywords: Guar Gum, Super Disintegrating Agent, Sodium Starch Glycolate (SSG).

1. INTRODUCTION

Guar gum is a galactomannan, commonly used in cosmetics, food products, and pharmaceutical formulations. It has also been investigated in the preparation of sustained-release matrix tablets in the place of cellulose derivatives such as methylcellulose. In pharmaceuticals, guar gum is used in solid-dosage forms as a binder and disintegrant. Guar gum of natural origin is preferred over synthetic or semi synthetic substances because guar gum is relatively cheaper, abundantly available, nonirritating and nontoxic. Guar gum is widely used in foods and oral and topical pharmaceutical formulations [1].

Dispersible tablet is containing many synthetic or semi synthetic super disintegrants in formulation [2]. Due to impaired swallowing ability, many elderly patients find it difficult to take some conventional dosage form such as tablet, capsule and powders. In order to solve this problem development of solid dosage that disintegrate rapidly or dissolve even when taken orally without water is being undertaken [3,4,5,6]. These novel type of tablets that disintegrate/ dissolve/ disperse in saliva in less then a minute without the need of water [7]. Their characteristic advantage such as administration without water, any where, any time lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bed ridden, and patients who do not have easy access to

water [8,9]. The bioavailability of some drugs, especially those suffering from a high first pass metabolism, can be improved due pregastric absorption and local gastro intestinal side effects are also expected to be reduced by formulating such dosage form [10,11].

Migraine affects 13 to 18% of women and 3 to 6% of men, with peak prevalence between 35 and 45 years of age . Although there is considerable variation in the severity and frequency of migraine attacks among patients and within individuals, more than half of all patients with migraines have restricted their work and their social life significantly [12,13,14]. Zolmitriptan is a 5-HT1B/1D receptor agonists have been widely used for the treatment of moderate-to-severe migraine attacks. Zolmitriptan compound will be referred to as the second-generation triptans, since they are tryptamine derivatives and pharmacologically comparable to sumatriptan. Zolmitriptan is currently available in an oral dosage form [13,15].

2. MATERIALS AND METHODS

Guar gum was purchased from guar factory Jodhpur, other materials such as microcrystalline cellulose sodium starch glycolate, starch, talc, mannitol and magnesium stearate were laboratory grade.

2.1. Identification

For identification of drug, the λ_{max} was determined by U.V. spectrophotometer (CECIL) and HPLC (CECIL) as shown in Figure 1 and FTIR study was also performed for determination of drug as shown in Figure 2. The λ_{max} was found to be 224nm.

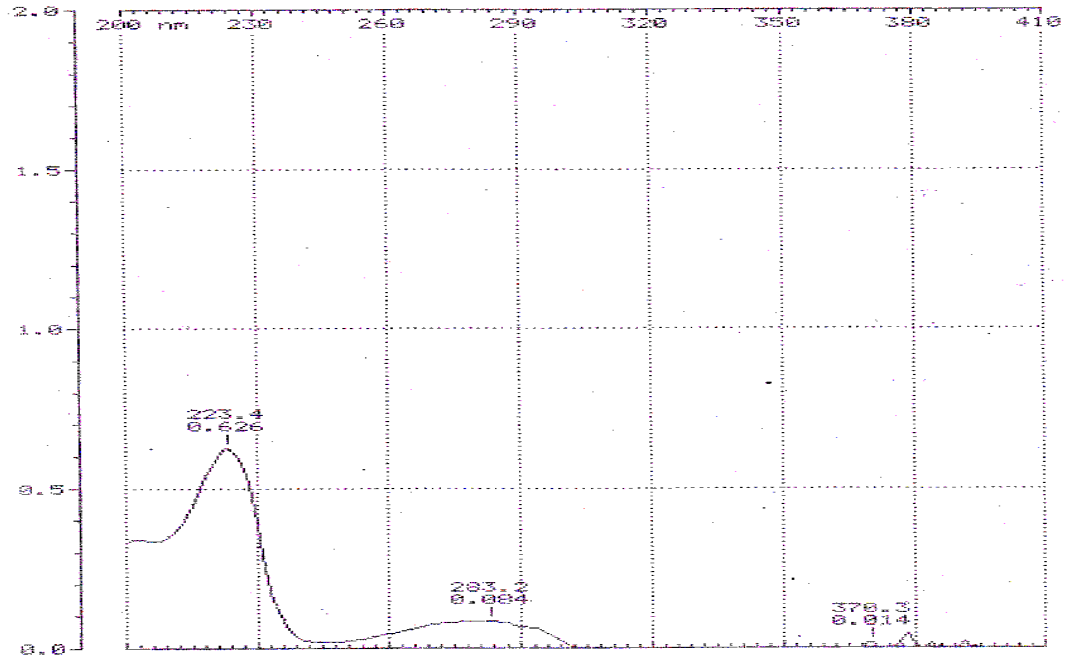

Fig. 1: Determination of λ_{max}.

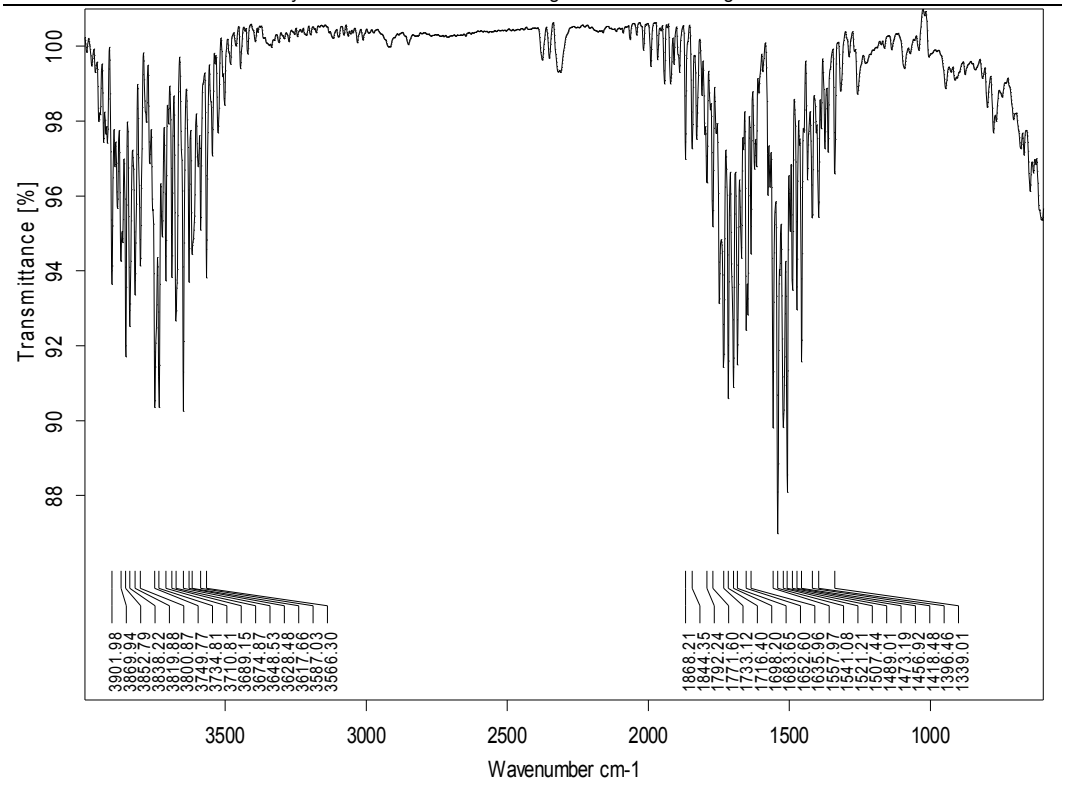

Fig. 2: FTIR study of the drug.

2.2. Method of Preparation of fast Dissolving Tablets by Wet Granulation Method

The fast dissolving tablets were prepared by wet granulation method. Micro crystalline cellulose (MCC) and mannitol was used as diluents, Guar gum and sodium starch glycolate were used as a disintegrating agent, starch paste was used as a binder and talc and magnesium stearate were used as a flow promoter. Micro crystalline cellulose (MCC) and mannitol were mixed together and a sufficient quantity of starch paste at different concentrations were added and mixed them to form a coherent mass. The wet mass was granulated using sieve no. 22 and regranulated after drying through sieve no. 44 and called as base granules. Guar gum, Mg- sterate, talc and were added as extra granularly. The all ingredients were mixed and compressed in to tablet using 6 mm punches on 8 station rotary tablet machine (Hardik engineers, Ahmadabad). Data were shown in Table 1.

Table 1: Formulation of fast dissolving tablet of zolmitriptan.

S. No.	Ingredients	F1	F2	F3	F4	F5	F6
1	Zolmitriptan	5	5	5	5	5	5
2	Mannitol	60	57	54	57	54	60
3	Guar gum	2	5	8	-	-	-
4	Sodium starch glycolate	-	-	-	2	5	8
5	MCC	30	30	30	30	30	30
6	Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5
7	Talc	1.5	1.5	1.5	1.5	1.5	1.5
8	Starch paste (10%)	q.s	q.s	q.s	q.s	q.s	q.s

3. EVALUATION PARAMETER

Weight variation (I.P monograph 1996) Friability (Roche fribilator), Hardness (Monsanto hardness tester) and thickness (vernier calipers) were determined. Drug contents were calculated using 6.8 phosphate buffers at 224nm (CECIL UV spectrometer). Wetting and swelling time were determined for tablet because wetting time is required for complete wetting of tablet in buccal cavity and swelling time is required for destruction of tablet in buccal cavity. Wetting time was determined by covering the tablet in tissue paper and applied the eosin dye on surface of tablet and placed it in Petri dish which containing 10 ml phosphate (6.8 pH) buffer. Swelling time was determined by placing the tablet in 10 ml phosphate buffer and noted the time when the tablet was swelled.

4. RESULT AND DISCUSSION

The precompression parameters of all the batches were determined and tabulated in Table 2**.** All parameters of granules were showing better results. The angles of repose of all the formulation (21.34±0.6 to 24.68±0.6) were within limit which shown the good flow ability. The bulk density (0.50±0.05 to 0.59±0.06) and tape density (0.552±0.05 to 0.66±0.07) data were showing good dye fill capacity. The Carr's index (5.61±0.2 to 11.84±0.6) and hausner's ratio (1.04±0.06 to 1.14±0.05) were showing excellent flow and compressibility properties of granules.

The evaluation parameters of all the batches were determined and tabulated in Table 3. It is found that weight variation test for all the batches were from 100.5±1.5 to 102±2.44, friability was found from 0.790 to 0.998, tablet hardness was from 3.0 to 5.0, wetting time was from 2.0 to 4.0 sec., swelling time was 4.0 to 7.0 sec. and disintegration time was from 10.0 to 16.0 sec. for all the batches.

The data were showing that guar gum containing tablet demonstrated better swelling property than sodium starch glycolate containing tablet and it demonstrate that tablet was disintegrated by swelling mechanism.

Table 2: Pre compression Parameters.

S. No.	Parameters	F1	F2	F3	F4	F5	F6
1	Angle of repose (º)	24.27	24.77	25.74	23.12	22.95	22.09
2	Bulk density(gm/cm^3)	0.272	0.254	0.244	0.250	0.221	0.225
3	Tapped density(gm/cm^3)	0.334	0.310	0.310	0.280	0.270	0.291
4	Carr's index (%)	18.56	18.06	21.29	24.32	18.14	22.68
5	Hausner's ratio	1.22	1.22	1.27	1.12	1.22	1.29

Table 3: Evaluation Parameters.

S. No.	Parameters	F1	F2	F3	F4	F5	F6
1	Weight Variation	102±2.44	101.5±2.29	100.5±1.5	102±2.44	101±2.0	101.5±2.29
2	Friability (%)	0.996±0.2	0.834±0.1	0.790±0.2	0.998±0.3	0.887±0.2	0.887±0.3
3	Hardness	4.5±0.3	5.0±0.2	5.0±0.3	3.5±0.2	4.0±0.4	4.0±0.3
4	Wetting Time(sec)	22±0.1	16±0.1	12±0.2	19±0.2	15±0.1	12±0.2
5	Swelling time(sec)	27±0.2	20±0.1	15±0.4	33±0.2	24±0.2	19±0.3
6	D.T.(Sec.)	65±2.44	48±1.12	20±1.23	68±2.56	52±3.23	22±1.28
7	Drug content	95±0.57	96±0.69	99±0.54	94±0.86	96±0.67	99±0.64

4.1. Dissolution Studies

The Invitro dissolution studied was performed in 900 ml 6.8 pH phosphate buffer (Electro lab eight station paddle type dissolution apparatus) at 50rpm and samples (5ml) were withdrawn at specified time interval and filtered. Samples were analyzed by UV spectrophotometer at 224 nm. Comparative studies were performed between release rate of guar gum and SSG. It was found that after one hours the rate of release of drug from the dosage form was almost same but a significantly change was observed up to 15min, the rate of release of drug was 99.21% in F3 formulation as compared to F6 formulation where only 97.51% drug was released. A markedly difference was also observed on onset of time where 84.79% of drug was released in 2 min. as compared of F6 formulation where 71.22% drug was released. The reason was behind that the high swelling property of guar gum as compared of SSG, as shown in Table 4. It was also seen that increment in the concentration of guar gum, create the disintegration problem

of tablet. The reason was behind that formation of viscous gel layer by guar gum that create a problem for tablet disintegration [16]. The comparison of release of drug by guar gum and SSG are shown in Figure 3 and Figure 4 respectively.

Table 4: In Vitro Dissolution Studies.

Time (min)	% DRUG RELEASED					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
2	78.13	81.79	84.79	55.82	62.30	71.22
4	87.23	88.26	90.56	68.23	74.94	80.76
6	91.93	92.16	93.52	73.17	82.76	85.94
8	92.34	93.97	95.05	76.35	83.35	88.23
10	92.67	95.39	96.70	78.77	86.61	93.49
15	97.42	98.78	99.21	90.74	92.43	97.51
20	99.84	99.42	99.84	92.64	96.88	98.57
25	99.95	99.63	99.90	96.45	99.84	99.74
30	99.84	99.74	99.95	98.47	99.52	99.42
60	99.87	99.02	99.84	98.39	99.45	99.39

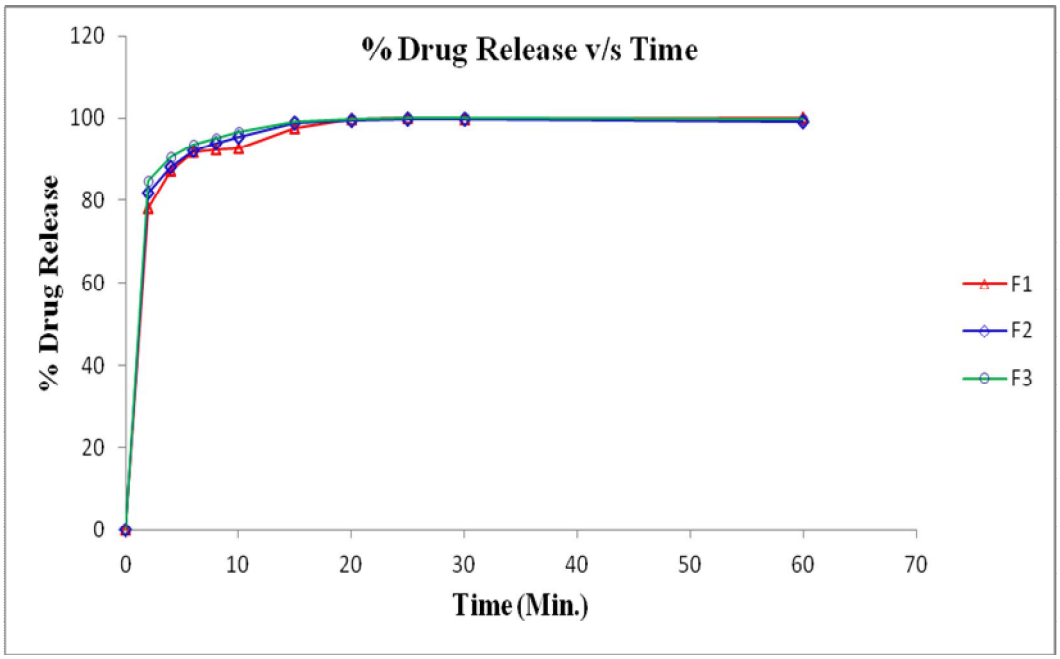

Fig. 3: Dissolution study for Batch 1, 2 and 3.

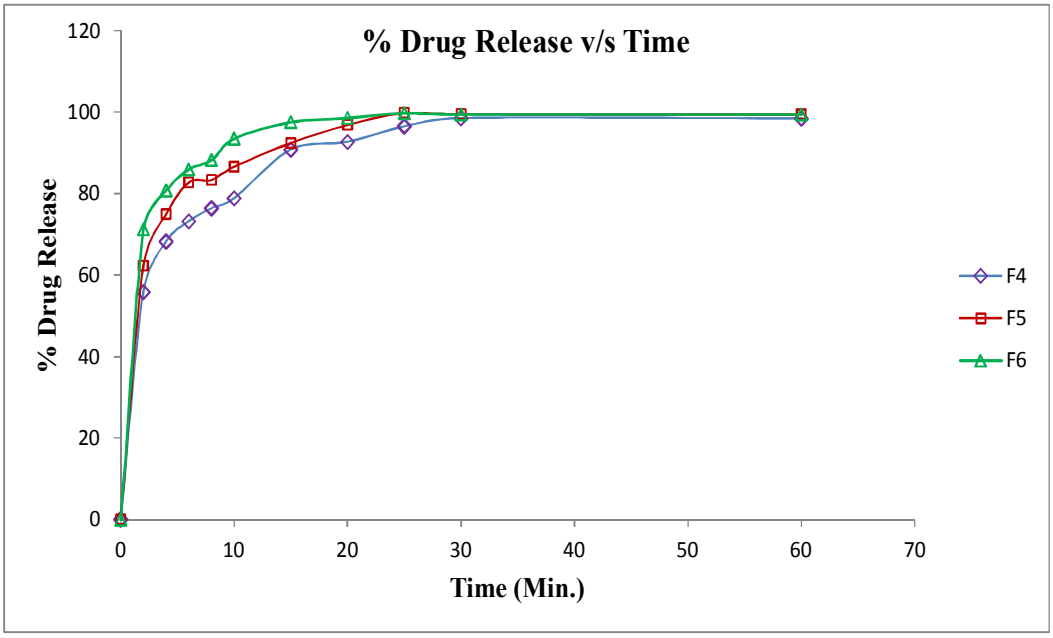

Fig. 4: Dissolution study for Batch 4,5,6.

4.2. Dissolution Studies Table

**Dunette`s Multiple comparison test**: The dinette`s multiple test was performed for comparison of release data of guar gum to release data of SSG and a significant difference was observed in release rate of drug as shown in Table 5.

Table 5: Dunett's multiple comparison test.

Sr.No.	Formulation	Mean difference	Q	P-Valve	95% CI of difference	Effect
1.	F1v/s F4	10.02	64.09	P<0.01	6.157 to 13.88	Significant
2	F1v/sF5	5.558	3.556	P<0.01	1.698 to 9.414	Significant
3	F1 v/s F6	2.268	1.451	P>0.05	-1.592 to 6.129	Not significant
4	F2 v/s F4	10.83	6.236	P<0.01	6.540 to15.12	Significant
5	F2 v/s F5	6.371	3.668	P<0.01	2.081 to 10.66	Significant
6	F2 v/s F6	3.081	1.774	P>0.05	-1.1029 to 7.371	Not significant
7	F3 v/s F4	11.85	6.279	P<0.01	7.187 to 16.51	Significant
8	F3 v/s F5	7.389	3.916	P<0.01	2.728 to 12.05	Significant
9	F3 v/s F6	4.099	2.172	P>0.05	-0.5617 to	Not

					8.760	significant

The data indicated that, Formulation F1, F2 and F3 were given a significant difference on formulation F4 and F5 (P-value was <0.01), means the guar gum and sodium starch glycolate playing a significant role for their formulation, but not significant on formulation F6 (P- value> 0.05). The dinette`s study was performed using Prism software version 3.0.

5. CONCLUSION

It is conclude that the fast dissolving tablet prepared by wet granulation method using guar gum and SSG showing all evaluation parameters such as weight variation, hardness, friability and D.T. within limit. The F3 batch is showing better onset of action and drug release than F6 batch. So, it is conclude that at the same concentration (8%) guar gum containing tablet showing good release of drug as compared to SSG containing tablet. It is also concluding that in future guar gum could be a better option of super disintegrating agent for fast dissolving tablet by its better swelling property.

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