Formulation and Evaluation of Fast Disintegrating Tablets Contaning Anti Migrain Drug

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ABSTRACT

Sumatriptan succinateis used to treat migraines. It helps to relieve headaches, pain and other symptoms of migraines, including sensitivity to light/sound, nausea, and vomiting. Prompt treatment allows to get back to normal routine and may decrease need for other pain medications. Fast dissolving drug delivery systemoffers a solution for those patients having difficulty in swallowing, attempt has been made to prepare fast dissolving tablets of Sumatriptan succinate using super disintegrants like cros povidone, Crosscarmellose sodium and the prepared granules were subjected D.C method. The granules thus prepared were evaluated for hardness, friability, weightvariation, in vitro disintegration time and in vitro dissolution study. The hardness of the tablet was in range 2.5±0.98-2.9±0.98kg/cm2 .The percentage friability of the tablet was less than 1% , drug content uniformity study results showed that uniform dispersion of the drug throughout the formulation were in between 88.78±0.14%-98.83±0.02% .Weight variation test results showed that tablets were deviating from the average weight within the permissible limit of ± 7.5% .Finally in vitro drug release studies were carried out for 60 minutes that tablets prepared with SSG F2 formulation showed the release 99.98% in 0.1N HCl.

Keywords: *Superdisintegrates, fast disintegrating tablets and Sumatriptan succinate***.**

INTRODUCTION:

Fast-dissolving tablets are becoming popular as novel delivery systems for drug administration. They are more convenient for children, elderly patients, patients with swallowing difficulties, and in the absence of potable liquids.It is one of the most desirable formulation for the elderly as it is easy to swallow easy to handle. Taking these requirements into consideration, attempts have been made to develop a fast-disintegrating tablet. Since such a tablet can disintegrate in only a small amount of water in the oral cavity.

MATERIALS AND METHODOLOGY:

Sumatriptan succinate was obtained from AurbindoPharma Crosscarmellose sodium Crospovidone microcrystal line cellulose, Dibasic calcium phosphate and mannitol was obtained from the labtorary.

Preparation of the tablet formulations by direct compression method:

Each tablet (weight 200mg) consisted of Sumatriptan succinate, superdisintegrants such as crospovidone, Crosscarmellose sodium, mannitol /dibasic calcium phosphate, aspartame, talc and magnesium stearate, were prepared by direct compression method. The drug, diluent, superdisintegrantand sweeteners, were passed through the sieve no. 40. All the ingredients were mixed well for 15 min in the motor. Then mixed with lubricant (4 mg)

for 3 min in a motor. The mixer was compressed by using 10mm concave punches on sixteen station rotary tablet compression machine.

Table1: General composition of formulation prepared by direct compression method

Formula	Drug	CMS	CP	MCC	DITAB	Mannitol	Aspartame	Magnesium stearate	Talc
F1	50mg	4mg	-	36mg	-	94mg	4mg	4mg	8 mg
F2	50mg	6mg	-	54mg	-	74mg	4mg	4mg	8 mg
F3	50mg	8mg	-	72mg	-	54mg	4mg	4mg	8 mg
F4	50mg	-	4mg	36mg	-	94mg	4mg	4mg	8 mg
F5	50mg	-	6mg	54mg	-	74mg	4mg	4mg	8 mg
F6	50mg	-	8mg	72mg	-	54mg	4mg	4mg	8 mg
F7	50mg	-	4mg	36mg	94mg	-	4mg	4mg	8 mg
F8	50mg	-	6mg	54mg	74mg	-	4mg	4mg	8 mg
F9	50mg	-	8mg	72mg	54mg	-	4mg	4mg	8 mg

EVALUATION PARAMETERS:

Preparation of standard graph of Sumatriptan succinate in 0.1N HCl:

Accurately weighed amount (100 mg) of the drug was dissolved in 0.1N HCl in 100 ml volumetric flask and the volume was made up to 100ml. from this stock solution 10ml is withdrawn in to volumetric flask, made the volume up to 100ml with 0.1N HCl. From this 2nd stock solution (100mcg/ml), concentrations of 5, 10, 15, 20, 25, 30, µg/ml solutions were prepared and the corresponding absorbance was measured at 227 nm in a UV/Visible spectrophotometer.

Drugto polymer compatibility study's:

IR spectrum ofsumatriptan succinate and other excipients were recorded using FTIR spectrophotometry.

Pre-compression parameters:

Angle of Repose:

The angle of repose is the constant,three-dimension angle (relative to horizontal base) assumed by a cone like pile of material formed by any of several different methods. When the angle of repose exceeds 50degrees, the flow is rarely accepted for manufacturing purpose.

Bulk Density:

The bulk density was determined by transferring the accurately weighed sample of powder to the graduate cylinder. The initial volume and weight were noted. Ratio of weight of the sample was calculated by using the following formula.

Bulk Density =Mass /Bulk volume.

Tapped Density:

Weighed powder sample was transferring to a graduated cylinder and was placed on the tap density apparatus, was operated for fixed number of taps (100). The tapped density was determined by the following formula.

Tapped Density =Mass/Tapped volume.

Percentagecompressibility:
Based on the apparent bulk density and tapped density, the percentage compressibility of the bulk drug was determined by the following formula
% Compressibility=Tapped Density-Bulk density×100/ Tapped density.

Hauser's Ratio:
It is measured by the tapped density to bulk density.
Hauser's Ratio= Tapped density/Bulk density

POST COMPRESSION PARAMETERS:

Tablet thickness:
Randomly 5 tablets were taken from each formulation trial batch and their thickness was determined by using screw gauge.

Weight variation test:
20 tablets were randomly selected from each formulation trial batch and their average weight was calculated using digital balance. Individual weight of each tablet was also calculated using the same and compared with the average weight.

Measurement of tablet hardness:
Hardness of 10 tablets was found using Monsanto hardness tester, mean and standard deviation were computed and reported. It is expressed in kg/cm ^{2}

Friability:
10 tablets were weighed and placed in Roche friabilator where the tablets were exposed to rolling and repeated shocks resulting from free falls within the apparatus. The Friabilator was operated at 25 rpm for 4 mins. After 100 revolutions, tablets are removed, deducted and weighed again. The friability was determined as the percentage loss in weight of the tablets.

Disintegration Time:
The test is carried out on the 3 tablets using the apparatus specified in USP distilled water at 37 ^{0} C ± 2 ^{0} C was used as a disintegration media and the time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

Wetting time:
A sample of the final tablet was placed in a petri dish (10 cm in diameter) containing 10 ml water at room temperature. The wetting time is that necessary for the complete wetting of the tablet is noted.

In vitro dissolution:
Freshly prepared 0.1N HCl of 900 ml was placed in each dissolution vessels of dissolution test apparatus (USP, II paddle method). The tablets were placed in the dissolution medium. The temperature of the dissolution medium was maintained at 37± 0.5^{0}C and the paddle was rotated at 50 rpm. 5 ml samples were withdrawn. The sample volume was immediately replaced with the same volume of fresh media as when a sample was taken. The samples withdrawn were filtered, diluted and estimated spectrophotometrically at 227 nm.

Water absorption ratio:
A small cultureof petri dish was taken containing 6ml of water and a piece of tissue paper folded twice is placed. A tablet is placed gently on it and the time for complete wetting is measured. The wetted tablet is reweighed.

Content uniformity:

From each batch of prepared tablets, ten tablets were collected randomly and powdered. A quantity of powder equivalent to weight of one tablet was transferred in to a 100 ml volumetric flask, to this 50 ml of 0.1N HCl was added and then the solution was subjected to sonication for about 2 hrs. The solution was made up to the mark with 0.1N HCl. The solution was filtered and suitable dilutions were prepared with 0.1N HCl. Same concentration of the standard solution was also prepared.

RESULT AND DISSCUSSION:

Fig.No.1: FTIR spectra of pure drug Sumatriptan succinate:

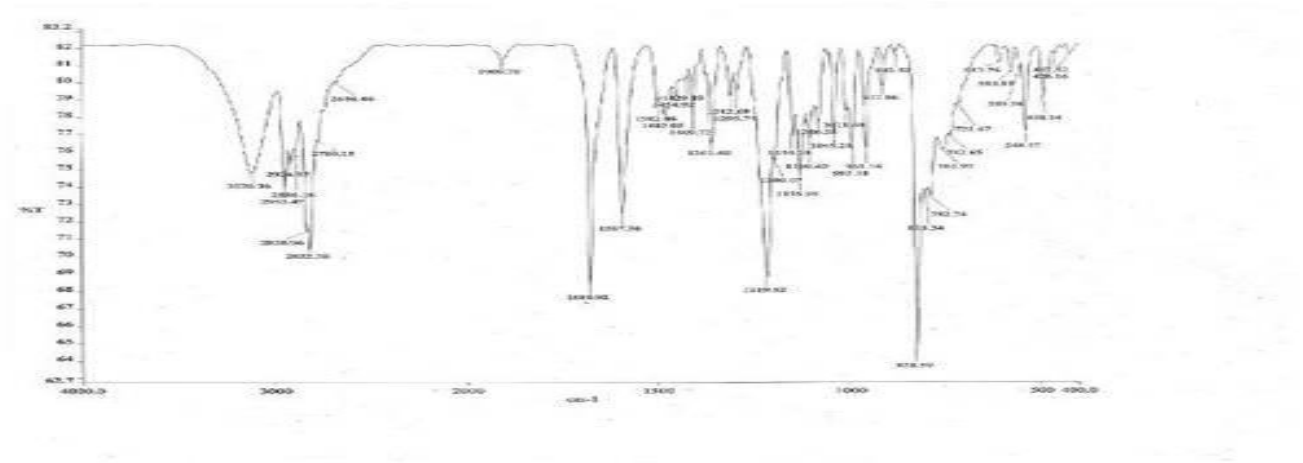

Fig.No.2: FTIR spectra of drug and excipients.

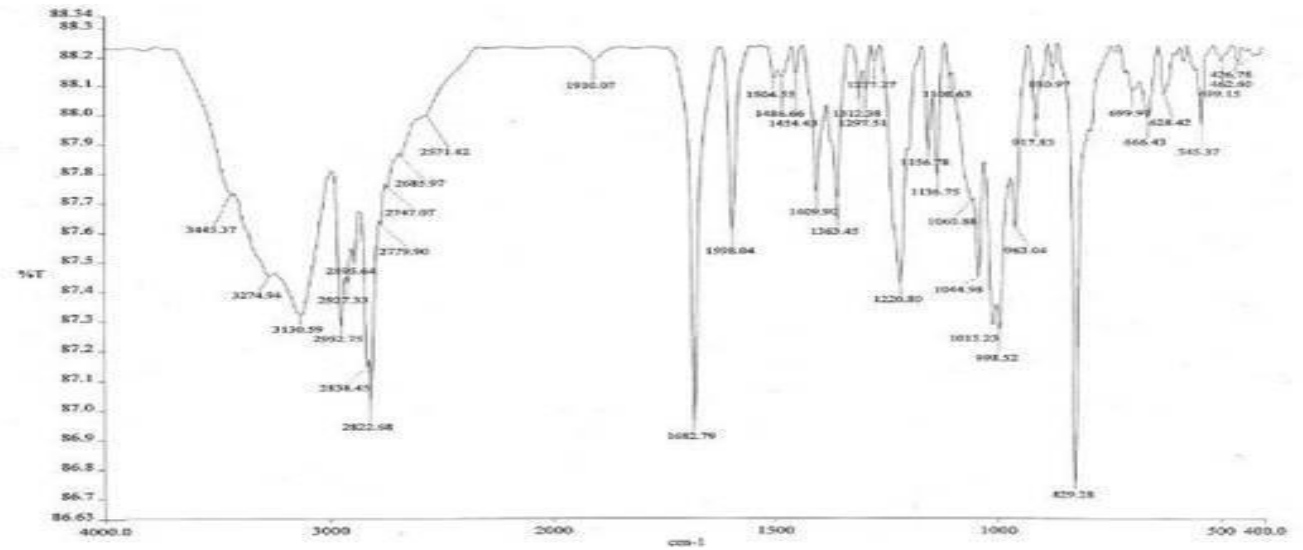

Table No.2 Data for pre-compression parameters

Formulations	Angle of repose Ɵ	Bulk Density (g/cc)	Tapped Density (g/cc)	% Compressibility	Hausner's Ratio %
F1	12.29± 0.270	0.225±1.295	0.362±0.915	14.68±1.759	1.197±0.656
F2	12.30±0.813	0.282±0.48	0.601±0.974	16.02±1.245	1.246±0.128
F3	13.29±0.270	0.225±1.295	0.492±0.915	14.68±1.759	1.257±0.956
F4	13.27±0.270	0.325±1.295	0.492±0.915	14.68±1.759	1.157±0.056
F5	11.28±0.257	0.258±0.421	0.576±0.730	15.920±1.350	1.237±0.164
F6	13.2±0.270	0.225±1.295	0.492±0.915	14.18±1.759	1.397±0.556
F7	12.2±0.270	0.245±1.275	0.592±0.912	13.68±1.759	1.231±0.520
F8	14.2±0.270	0.239±1.230	0.672±0.315	13.28±1.650	1.230±0.530
F9	11.2±0.270	0.259±1.394	0.622±0.615	16.68±1.732	1.297±0.556

Table No.3: Data for post -compression parameters

Formulation	Weight Variation (mg)	Hardness (Kg/cm^2)	Friability (%)	Thickness (mm)	Uniformity of Content (%)	Water absorption ratio(%)	Disintegration Time (seconds)
F1	198±1.35	2.5±0.98	0.64±0.89	2.25±0.23	88.78±0.14	88.91±0.96	40
F2	197±0.97	2.7±0.29	0.76±0.04	2.18±0.12	90.48±0.13	90.48±0.59	38
F3	199±0.43	2.7±0.16	0.82±1.2	2.35±0.54	95.62±0.23	92.58±0.45	39
F4	201±1.56	2.6±1.16	0.75±0.69	2.43±0.43	96.23±0.06	91.98±0.49	50
F5	198±1.25	2.8±0.26	0.66±0.48	2.24±0.13	97.57±0.01	93.32±0.48	51
F6	200±1.09	2.9±0.64	0.74±0.18	2.41±0.25	98.83±0.02	95.25±0.75	55
F7	199±1.22	2.7±0.9	0.72±0.8	2.28±0.23	89.52±0.05	89.62±0.98	70
F8	198±1.82	2.6±0.8	0.74±0.4	2.20±0.18	91.15±0.18	91.48±0.87	69
F9	197±2.4	2.8±0.9	0.77±0.6	2.36±0.16	96.42±0.24	94.58±0.84	69

Table 4 :Data for dissolution profile.

Time (min)	Cumulative %Drug released					
	FI	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	5.2	6.42	7	6.55	4.23	6.42
10	23.8	25.81	28.45	27.28	20.26	26.51
15	45.6	49.57	50.25	46.58	38.49	44.72
20	60.75	65.95	67.77	65.44	56.45	63.88
25	72.68	74.83	78.34	76.73	65.37	76.83
30	82.56	82.74	88.92	86.36	77.69	87.98
45	88.93	94.41	94.35	92.97	85.69	93.36
60	91.67	99.98	95.02	96.26	97.96	93.42

Fig4 Dissolution profile of formulation F1-F6

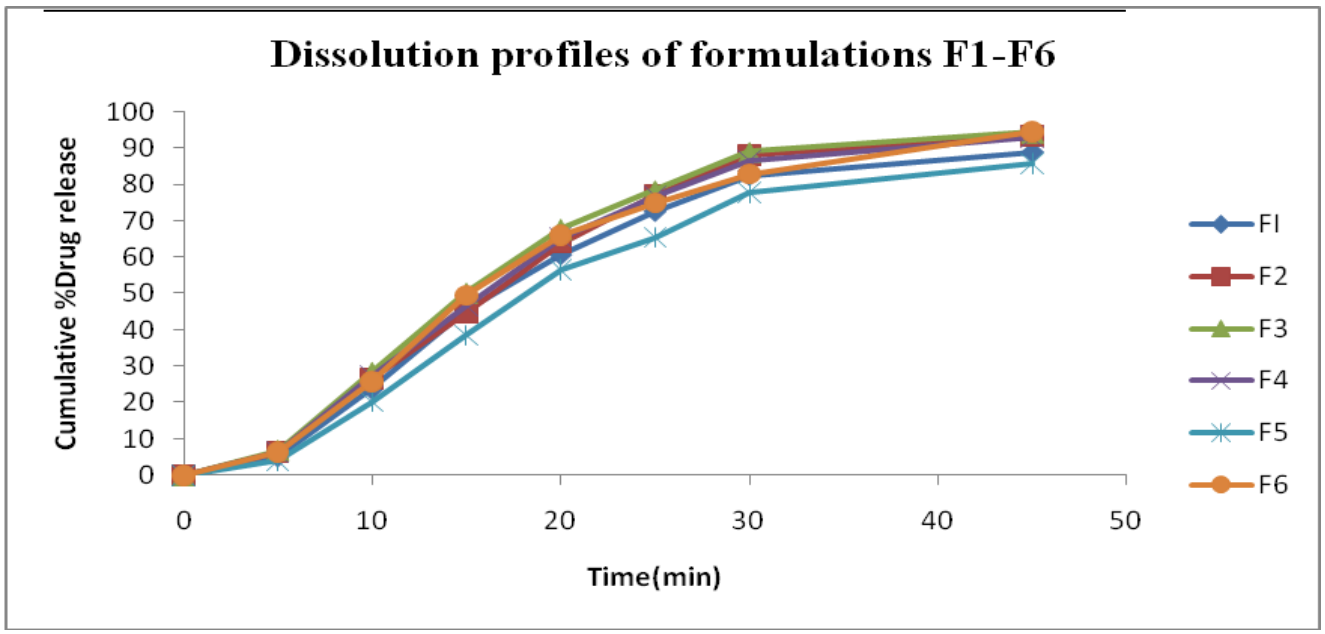

Table No.5: Data for dissolution profile F7-F9

Time(min)	Cumulative % drug released		
	F7	F8	F9
0	0	0	0
5	5.8	6.4	7.2
10	24.6	22.4	24.2
15	44.6	44.8	50.4
20	61.75	64.2	67.4
25	74.28	76.4	78.4
30	82.92	85.2	86.2
45	94.92	88.6	94.6
60	96.92	97.2	97.9

CONCULSION:

Oral disintegrating tablets of Smatriptan succinate were prepared by direct compression, it was achieved by using different super disintegrents. The angle of repose, bulkdensity, tappeddensity,% compressibility and Hausner's were all found to be within the limits (Table no 2) hence having good flow properties.Standard curve for Sumatriptan succinatewas prepared in 0.1N HCL absorbance was measured at 227 nm in a UV/Visible spectrophotometer with the $R^2 = 0.999$.The interaction between the drug and polymer was studied by FT-IR Spectrophotometer, it revealed that no interaction between them(Figure1and 2).Post compression data of weight variation showed the range between 197±0.97-201±1.56,Hardness of 2.5±0.98-2.9±0.9 kg/cm^2 ,Friability in range of 0.64±0.89-0.89±1.2%, Thickness in range 2.18±0.12 -2.36±0.1mm,Content uniformity in range of 88.78±0.14-98.83±0.02%,water absorption ratio in range 88.91±0.96-98.83±0.02%and disintegration time of 38-70sec. Disintegration result shows that the tablets containing Crospovidone took a longer time to disintegration with respect to concentration, where as Croscarmellose sodium containing tablets showed good disintegration ability with in the time limit .The formulations containing dibasic calcium phosphate the disintegration time was longer. Dissolution results indicates that tablets prepared with SSG F2 formulation showed the release 99.98% in 0.1N HCl in 60 minutes.

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