Design And Invitro Characteristics of Sustained Release Sumatriptan Succinate Tablets

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Abstract: The goal of the present study is to create a sustained release tablet dosage form for the anti-migraine medication Sumatriptan Succinate, which agonistically acts on 5-HT receptors. The wet granulation method was used to prepare the tablets, and different concentrations amounts of polymers, including HPMC K4M, ethyl cellulose, and Eudragit RSPO. In order to ensure flow characteristics during punching of tablets, the formulated sustained release tablets were assessed for precompression parameters like bulk & tapped densities, Hausners ratio, Carrs index and Angle of repose. The tablets were assessed for physicochemical characteristics, including stability studies, weight fluctuation, thickness uniformity, and hardness. When compared to other formulations, the findings from in vitro release experiments demonstrated that formulation SSF7, which contained 50 mg of each of HPMC K4M, ethyl cellulose, and eudragit RSPO, demonstrated an acceptable outcome and optimal 95% of drug release after 12 hours. All formulations meet the Higuchi model, according to the drug release kinetic data. To analyze the drug's release mechanism from the polymeric system, the findings of in-vitro drug release data were fitted to Korsmeyer Peppa's model, which showed that the drug release followed a Fickian release mechanism. By bypassing first-pass metabolism, Sumatriptan Succinate has a longer therapeutic impact and improves patient compliance.

Keywords: Sumatriptan Succinate, HPMC K4M, Ethyl cellulose, Eudragit

I. INTRODUCTION

Drugs or dosage form modifications that provide a longer but not always consistent release of the medication are known as sustained release dosage forms. Maintaining therapeutic blood or tissue levels of the medication for a long time is the aim of a sustained release dosage form. Usually, this is achieved by trying to get the dose form to release zero-order. Zero-order release constitutes the drug release from the dosage form that is independent of the amount of drug in the delivery system[1,2]. Drugs with a limited therapeutic range of blood concentration or those that eliminate quickly can benefit from sustained release systems for oral dosing. The initial dose portion of sustained release products is intended to raise a drug's blood level to therapeutic concentrations right away, and the maintenance portion is meant to keep the level there for a predetermined amount of time[3]. Both consumers and doctors choose tablets, which are the most widely used oral solid formulations on the market. Many medicinal substances undergo extensive presystemic elimination when taken orally due to gastrointestinal breakdown and/or first-pass hepatic metabolism. This results in a low systemic bioavailability, a shorter duration of therapeutic activity, and the production of toxic or inactive metabolites. Because they improve patient compliance, maintain consistent drug levels, lower dosage and adverse effects, and boost the safety margin for high-potency medications, sustained release tablet formulations are recommended for this type of therapy[4].

MIGRAINE: Although neurotologic symptoms are frequently associated with migraine, little is known regarding their pathogenesis. Approximately two-thirds of migraine sufferers have motion sensitivity and episodes of motion nausea. About one-fourth of patients experience vertigo episodes, and for others, vertigo is the only symptom (the so-called "migraine equivalent"). Although phonophobia is the most prevalent auditory symptom, a tiny percentage of people have acute irreversible hearing loss and

fluctuating hearing loss. Meniere's illness can be mistaken for migraine, and migraine is typically linked to "vestibular Meniere's disease." A potential cause for neurotologic symptoms in people with more frequent types of migraine is suggested by the recent identification of a mutation in a brain calcium-channel gene in families with episodic vertigo and ataxia as well as in families with hemiplegic migraine[5].1-[3-(2-dimethylaminoethyl)-1H-indol-5-yl]-N-methylmethane sulphonamide succinate is the chemical form of sumatriptan succinate. It is an agonist of the 5-HT1 receptor that is used to treat migraines. Despite being unaffected by concurrent meal consumption, sumatriptan has a limited bioavailability upon oral administration (about 15%) and significant interindividual variation. The presence of food and an intense migraine episode cause a minor delay in Tmax, which is attained at around two hours. Except for the rate of absorption[6,7,8] Sumatriptans pharmacokinetics are linear for the dosage range of 25–200 mg.

Mechanism of Action: 5-HT1B and 5-HT1D are agonists of sumatriptan.This agonism prevents the production of pro-inflammatory neuropeptides and causes the cerebral blood vessels to contract. Sumatriptan increases blood flow velocity in the middle cerebral artery and internal carotid artery while decreasing carotid arterial blood flow.

II. MATERIALS AND METHODS

A gift sample of Sumatriptan Succinate was obtained from Dr Reddy's Laboratories, Hyderabad, HPMC from Otto Chemie Pvt. Ltd, Mumbai and all other chemicals & reagents were of SD fine chemicals provided by the college.

Preparation of Tablets by Wet granulation method[4]: Drug and polymers and diluent were mixed in a poly bag and the mixture was made to pass by a mesh No. 60. Granulation carried out with a granulating agent. The mass passed by through mesh No. 12. The wet obtained granules were dried at 60º for about 4 hours. The dry granules sized by a mesh No. 18 and added with magnesium stearate and talc. Granules thus obtained weighing equivalent to require weight were compressed into tablets.

Table 1: Compositions of Sustained release Sumatriptan succinate tablets

Ingredients (mg/tab)	SSF1	SSF2	SSF3	SSF4	SSF5	SSF6	SSF7
Sumatriptan succinate	200	200	200	200	200	200	200
HPMC K4M	50	100	-	-	-	-	50
Ethyl cellulose	-	-	50	100	-	-	50
Eudragit RS PO	-	-	-	-	50	100	50
Lactose	200	150	200	150	200	150	100
Microcrystalline cellulose	30	30	30	30	30	30	30
Magnesium Stearate	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10
Total weight in mg	500	500	500	500	500	500	500

III. RESULTS & DISCUSSION

Precompressional Parameters: The tablet powder blend was subjected to a number of preformulation parameters; the bulk density of all formulations was found to be between 0.25±0.02 and 0.31±0.05 (gm/cm3), the tapped density of all formulations was found to be between 0.30±0.04 and 0.36±0.02, the Hausner's ratio was found to be between 1.23±0.29 and 1.28±0.18, the Carr's index of all formulations was found to be between 21.00±0.85 and 22.90±0.42, and the angle of repose was found to be between 230.10'±0.79 and 280.99'±0.55. All of these values indicate that the powder blend has good flow properties.

Table 2: Precompressional Properties of all the formulation

Formulation Code	Bulk density (gm/cm3)	Tapped density (gm/cm3)	Hausner ratio (HR)	Carr's index (CI)	Angle of repose (θ)
SSF1	0.25±0.07	0.32±0.02	1.25±0.12	22.90±0.42	25^0.80'±0.27
SSF2	0.30±0.05	0.30±0.04	1.24±0.56	21.00±0.85	26^0.14'±0.16
SSF3	0.30±0.06	0.32±0.02	1.23±0.29	21.70±0.97	28^0.99'±0.55
SSF4	0.25±0.03	0.31±0.06	1.27±0.30	21.98±0.54	23^0.56'±0.80

SSF5	0.25±0.03	0.32±0.07	1.27±0.19	21.90±0.49	23^0.10'±0.79
SSF6	0.31±0.05	0.35±0.03	1.28±0.18	22.10±0.76	24^0.90'±1.12
SSF7	0.27±0.04	0.36±0.02	1.24±0.36	22.00±0.63	25^0.40'±0.96

Post Compression parameters:

Each batch's tablets were tested for thickness, hardness, friability, weight fluctuation, and drug content. For every tablet, the weight difference and percentage deviation were computed. The acceptable limit is ± 5% (more than 500 mg) since the average weight of the tablet is roughly between 498±0.86 and 502±0.67. The weights of the tablets met pharmacopoeial requirements. A Monsanto hardness tester was used to measure the hardness of the three tablets in each batch. The findings indicated that the tablets' hardness ranged between 5.3 and 6 kg/cm^2. This suggests that the tablets were strong. All of the formulations' percentage friability ranged from 0.47 to 0.69%. This suggested that the manufactured tablets had good handling qualities. Specifications for thickness and diameter can be established for each product separately. Too much variance in tablet thickness and diameter can lead to issues with both patient acceptability and packing. It was between 7.1 and 7.3 mm in thickness. It was discovered that the formulation's drug content ranged from 99.18±0.86 to 101.02±0.10 % w/w, falling within the IP-specified range of 90–110% w/w.

It was found that every characteristic, including weight fluctuation, friability, hardness, thickness, and drug content, was within acceptable bounds.

Table 3: Post compressional Properties of all the formulation

Formulation Code	Weight variation(mg)	Hardness (kg/cm2)	Friability (%)	Thickness (mm)	Drug content (%)
SSF1	501±0.23	5.3	0.69	7.2	99.23±0.55
SSF2	502±0.67	5.5	0.60	7.2	99.79±0.12
SSF3	500±0.75	5.8	0.69	7.2	100.2±0.10
SSF4	502±0.55	5.4	0.49	7.3	99.87±0.08
SSF5	499±0.05	5.8	0.47	7.1	99.18±0.86
SSF6	498±0.86	6	0.48	7.2	101.02±0.10
SSF7	500±0.98	6	0.51	7.3	99.98±0.91

IN-VITRO DRUG RELEASE STUDIES

Sustained release Sumatriptan Succinate tablets were released in a controlled manner in all formulations, according to the drug release results. However, formulation SSF7 demonstrated the maximum cumulative percentage of drug release of 95±1.02 at the end of 12 hours, which was the goal of the finalized formulation, while other formulations did not reach the time point of maximum release but continued to extend the release.

Table 4: Invitro drug release data of formulations SSF1-SSF7

Time in hrs	Cumulative % drug released						
	SSF1	SSF2	SSF3	SSF4	SSF5	SSF6	SSF7
1	39.11±0.82	32.67±0.18	28.33±0.78	30.50±0.43	30.12±0.89	29.86±0.57	21.50±0.65
2	48.35±0.67	37.71±0.74	37.47±1.01	42.21±0.56	35.17±1.24	37.98±0.18	26.76±0.87
3	57.66±0.35	46.34±0.84	44.65±0.86	46.89±0.75	43.70±0.45	42.67±1.24	39.16±0.41
4	62.10±0.79	54.30±0.63	50.76±0.68	51.45±0.27	51.31±0.65	51.86±0.68	53.87±0.94
5	67.87±0.76	58.41±0.11	56.78±0.67	58.81±0.67	60.50±0.82	58.44±0.56	62.54±0.78
6	71.34±0.65	61.54±0.36	61.11±1.08	62.32±0.84	69.87±0.57	64.90±0.84	71.77±0.43
7	78.55±1.24	68.12±0.92	70.54±0.34	71.48±0.86	71.33±0.34	77.76±0.48	77.34±0.98
8	83.80±0.68	77.34±0.48	77.58±0.98	76.14±0.97	77.10±0.77	83.90±0.64	80.97±1.06
9	86.24±0.77	86.10±0.98	84.44±0.79	85.26±0.31	84.40±1.42	89.80±0.84	82.85±0.74
10	-	-	89.90±0.06	90.00±0.53	90.23±0.67	91.40±0.18	84.90±0.43
11	-	-	-	-	-	-	90.97±0.56
12	-	-	-	-	-	-	95.90±1.02

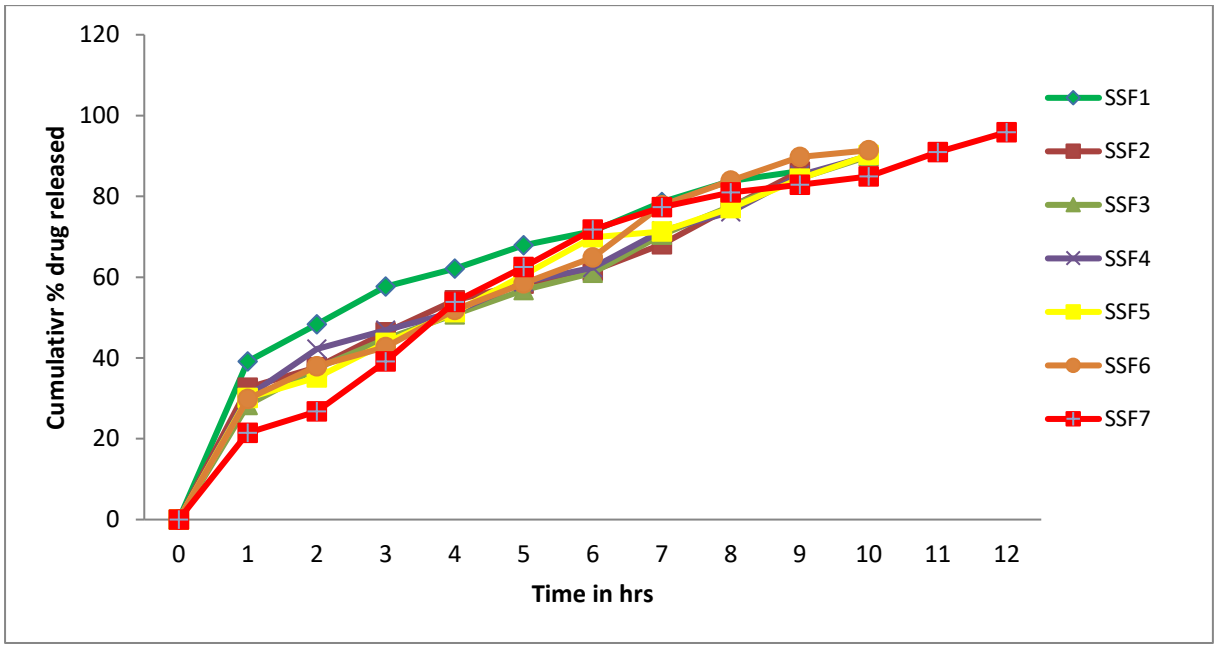

Fig 1: Invitro drug release curves of formulations SSF1-SSF7

Cumulative Drug Release at t50 % and t90 % : The cumulative drug release of Formulation SSF1 to SSF7 where t50 is time at which 50% drug was released and t90 is time at which 90% drug is released.

Table 5: Drug Release of t50% and t90% of formulations SSF1-SSF7

Formulation code	t50 (%) hrs	t90 (%) hrs
SSF1	2.1	-
SSF2	3.3	-
SSF3	4	10
SSF4	3.5	10
SSF5	3.5	10
SSF6	3.5	9
SSF7	3.4	11

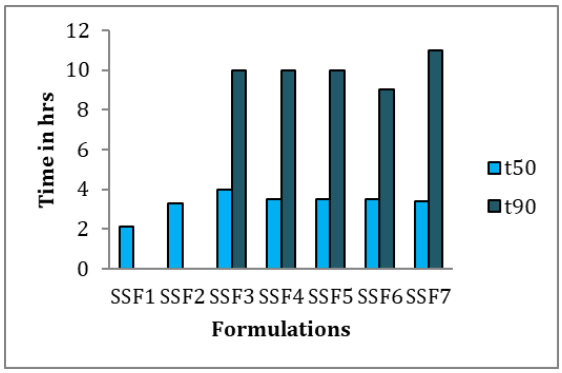

Fig 2: Bar graph of Drug Release of t50% and t90% of formulations SSF1-SSF7

Stability studies: Short term stability studies were performed for formulations SSF7 at 45^0C ± 1^0C for 4 weeks (30days).The sample were analyzed for percent drug content and invitro drug release studies. The results are given in table appreciable difference was observed for the above parameters.

Table 6: Stability Studies For Formulation SSF7

Time in Days	Physical Changes	Mean ±Sd (45^0 C)
01	----------	86.2±0.58
07	No changes	88.22±0.39
14	No changes	84.10±0.12
30	No changes	85.11±1.77

Table 7: Cumulative % Drug Release of Formulation SSF7

Time (Min)	Cumulative % Drug Release ±SD	
	45±1^0c	45±1^0c
	1^{st} Day	30^{th}day
01	19.44±0.12	18.54±0.81
02	28.65±1.90	27.10±0.32
03	34.88±1.03	33.10±0.34
04	48.01±0.26	46.19±0.50
05	60.11±0.61	58.00±0.03
06	66.78±1.15	64.19±0.90
07	72.13±0.89	70.14±0.84
08	88.11±0.73	87.10±0.15
09	89.15±0.54	88.23±0.10
09	91.54±0.31	90.18±1.17

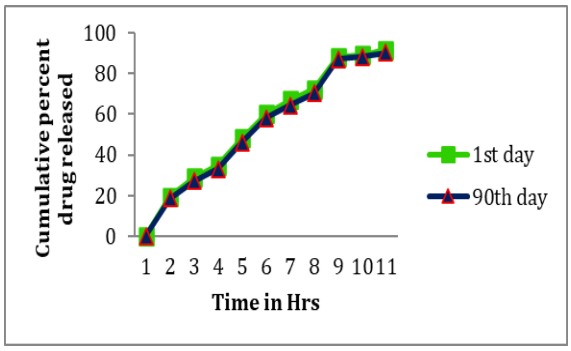

Fig 3: Cumulative % Drug Release curve of Formulation SSF7

IV. CONCLUSION

The current investigation found that the wet granulation process was used to prepare the sustained release tablets containing Sumatriptan Succinate. The prepared formulation SSF7 was shown to have the most promising in-vitro drug release experiments. It maintained a great release of 95.90% for up to 12 hours, extending the duration time. It exhibits the traits of persistent release. After Higuchi's model was released, the SSF1–SSF7 formulation was released. The drug release follows a Fickian mechanism, as indicated by the value of "n" being smaller than 0.500 when the results of the invitro release data were fitted to Korsmeyer Peppa's equation.

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