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FORMULATION AND EVALUATION OF SUBLINGUAL TABLETS OF SUMATRIPTAN

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ABSTRACT

Sumatriptan benzoate is a potent and selective 5-HTIB/ID receptor agonist and is effective for the treatment of acute migraine. Sublingual formulation has the advantage of offering fast relief from migraine due to faster drug delivery. The present study involves the formulation and evaluation of fast disintegrating sublingual tablets of Sumatriptan benzoate to produce intended effects. The sublingual Sumatriptan benzoate tablets were prepared by the method of direct compression. The superdisintegrants used were cross carmellose sodium and cross povidone. The powder flow properties of all formulations were evaluated for diameter, thickness, weight variation, hardness, friability, wetting time, water absorption ratio, drug content, in vitro and in vivo disintegration time as well as in vitro release and were found to be satisfactory. The optimized formulation containing cross povidone disintegrated very fast and in vitro drug release was very high.

Keywords: Sumatriptan, sublingual tablets, cross carmellose sodium, cross povidone.

INTRODUCTION

Fast-dissolving drug-delivery systems were first developed in the late 1970's as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience difficulties swallowing traditional oral solid-dosage forms. The novel technology of oral fast-dispersing dosage forms is known as fast dissolve, rapid dissolve, rapid melt and quick disintegrating tablets. However, the function and concept of all these dosage forms are similar. By definition, a solid dosage form that dissolves or disintegrates quickly in the oral cavity, resulting in solution or suspension without the need for the administration of water, is known as an oral fast-dispersing dosage form. Difficulty in swallowing (dysphagia) is common among all age groups, especially in elderly, and is also seen in swallowing conventional tablets and capsules [1]. Dysphagia is associated with many medical conditions, including stroke, Parkinson's, AIDS, thyroidectomy, head and neck radiation therapy, and other neurological disorders, including cerebral palsy [2]. The most common complaint was tablet size, followed by surface, form and taste. The problem of swallowing tablets was more evident in geriatric and pediatrics patients, as well as travelling patients who may not have ready access to water [3,4].

A headache [5] or cephalalgia is pain anywhere in the region of the head or neck. It can be a symptom of a number of different conditions of the head and neck. The most common way to relieve a headache is to look upside down for 3 minutes. A migraine [6,7] is a common type of headache that may occur with symptoms such as nausea, vomiting, or sensitivity to light. In many people, a throbbing pain is felt only on one side of the head. Sumatriptan [8] is 5HT1D agonist, which serves to inhibit both dual vasodilatation and inflammation. Absorption is more rapid followed by oral administration. Bioavailability is 45%. Food has no effect on the bioavailability of Sumatriptan. However, administering Sumatriptan with food will delay by 1 hour the time to reach peak plasma concentration. The rate of absorption is not affected by the presence of a migraine attack.

MATERIALS AND METHODS

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Sumatriptan is obtained from a gift sample from pharmatrain laboratories, Hyderabad. The polymers Crospovidone, Croscamellose sodium, Mannitol, Aspartame, Magnesium Stearate were purchased from Elite chemicals, Guntur.

Formulation of Sublingual Tablets

Sublingual tablets of Sumatriptan can be prepared by direct compression method. All the ingredients are passed through mesh #60 and mixed in a motor pestle for 5 min. The mixed blends of excipients are directly compressed by using 12 station tablet punching machine.

RESULTS AND DISCUSSIONS

Drug –Polymer compatibility studies by FTIR

The FTIR spectra of Sumatriptan, Crospovidone, Croscamellose Sodium and the combination of drug and polymers were shows no significant interaction between drug and polymer. The FTIR spectra's of Sumatriptan, Crospovidone, L-HPC, Croscamellose Sodium and mixture of drug along with polymers are shown in figure No.1, 2 & 3

Thickness

The thickness of the formulated Sumatriptan fast disintegrating sublingual tablets was measured by using digital vernier calipers. The mean thickness is reproduced in the Table No.2.

Uniformity of weight

20 tablets were selected and were weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet weight was then compared with average weight to ascertain whether it was within permissible limits or not. Not more than two of the individual weights deviated from the average weight by more than 7.5% for 200mg tablets and none by more than double that percentage. These results are reproduced in Table No.2

Hardness test

Hardness of the tablet was determined using the Pfizer hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by turning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force. The results are reproduced in Table No.2

Friability test

20 previously weighed tablets were placed in the apparatus, which was given 100 revolutions and the tablets were reweighed. The percentage friability was calculated by using the following formula. The results are reproduced in Table No.2

Percentage friability = [(Initial weight-Average weight) / (Initial weight)] X 100

Disintegration test

Tablet disintegration study was performed in disintegration apparatus. One tablet in each of the six tubes in the basket were placed and the basket rack was positioned in a one litre beaker of water, at 37°C±2°C. The machine was operated until the tablets were completely disintegrated. Results were shown in Table No.3.

Drug content

For the content uniformity test, 10 tablets were weighed and pulverized to a fine powder, a quantity of powder equivalent to 5mg of Sumatriptan was transferred into a 10ml standard flask and the volume was made with mobile phase. Further 10ml of the above solution was diluted to 10ml with mobile phase. Results were shown in Table No.3.

Wetting time

The tablet wetting time was measured by procedure that is the tablet was placed at the center of two layers of absorbent paper fitted into a dish. After the paper was thoroughly wetted with pH 6.8 phosphate buffer, excess buffer was completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stop watch. The results were shown in Table No.3. and Figure No.4.

Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small petri dish containing 6ml of buffer pH 6.8. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighed. Water absorption ratio, R was determined using following equation. The results are presented in Table No.3. and Figure No.5.

$$R = 100 \times W_a - W_b / W_a$$

Where , W_a = Weight of tablet after water absorption

W_b = Weight of tablet before water absorption

***In-vitro* dissolution studies**

900ml of phosphate buffer (pH6.8) was used as a media, and was maintained at 37 ± 0.5^0c while the Type II USP (paddle type) was set at 50 rpm. 5ml of the sample were taken every 2 minutes and the same amount was replaced with fresh buffer. The withdrawn samples were filtered and analyzed by using a U.V Spectrophotometer at a wavelength of 224nm. The results obtained for all the formulations are tabulated in the table No.4 and represented in Figure No.6.

Table 1. Formulation Composition of Sumatriptan fast disintegrating sublingual tablets

Ingredients	Quantity for tablet(mg)					
	F1	F2	F3	F4	F5	F6
Sumatriptan	5	5	5	5	5	5
Crospovidone	3	4	5	-	-	-
Croscamellose sodium	-	-	-	3	4	5
Mannitol	89	88	87	89	88	87
Aspartame	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium Stearate	0.5	0.5	0.5	0.5	0.5	0.5

Table 2. Evaluation of Sublingual Tablets of Sumatriptan

Formulation Code	Thickness (mm)	Average weight (mg)	Hardness (kg/cm^2)	Friability (%)
F1	2.8±0.2	101.4	2.8	0.25
F2	2.79±0.2	101.67	2.7	0.21
F3	2.84±0.1	100.13	2.8	0.26
F4	2.91±0.1	101.9	2.9	0.22
F5	2.84±0.2	101.7	2.7	0.24
F6	2.67±0.2	101.6	2.5	0.23

Table 3. Evaluation of Sublingual Tablets of Sumatriptan

Formulation Code	Disintegration Time (Sec)	Drug Content (%)	Wetting Time (Sec)	Water Absorption Ratio(%)
F1	15	99.91	12.3	27.18
F2	14	99.20	11.4	31.24
F3	12	99.54	9.3	34.17
F4	17	98.34	15.1	32.14
F5	14	101.11	12.5	29.38
F6	13	99.5	10.4	34.37

Table 4. Dissolution Profiles for all Formulations in 0.1N HCl as Dissolution media

Time in mins	% Drug Release					
	F1	F2	F3	F4	F5	F6
2	56.18	61.27	68.32	52.78	57.26	65.37
4	62.24	69.46	74.43	59.24	62.47	72.14
6	69.72	74.34	82.69	65.46	69.43	79.42
8	74.47	81.12	89.42	77.18	76.27	88.65
10	81.96	90.46	98.79	78.34	87.38	95.9

Fig 1. FTIR spectrum of Sumatriptan

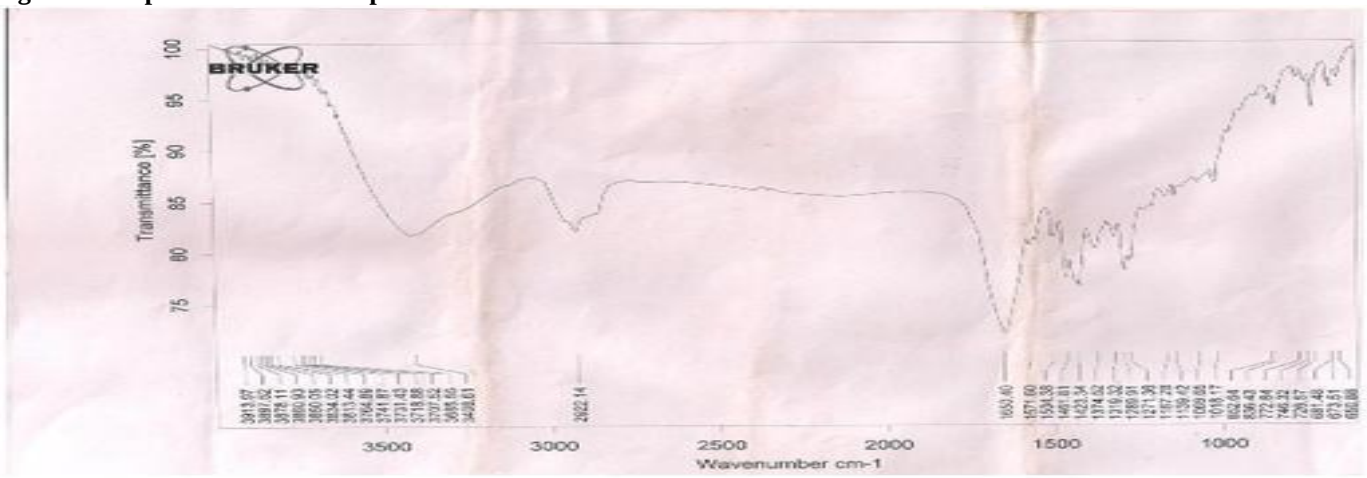


Fig 2. FTIR Spectrum of Sumatriptan+ Crospovidone

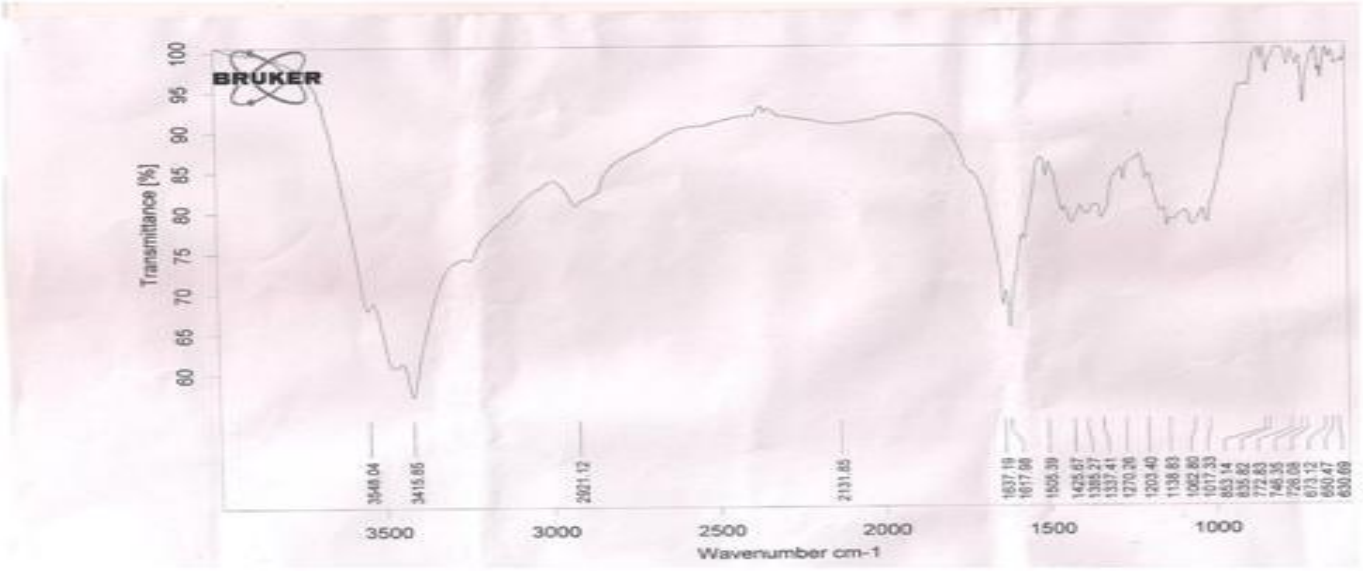


Fig 3. FTIR Spectrum of Sumatriptan + Croscamellose sodium

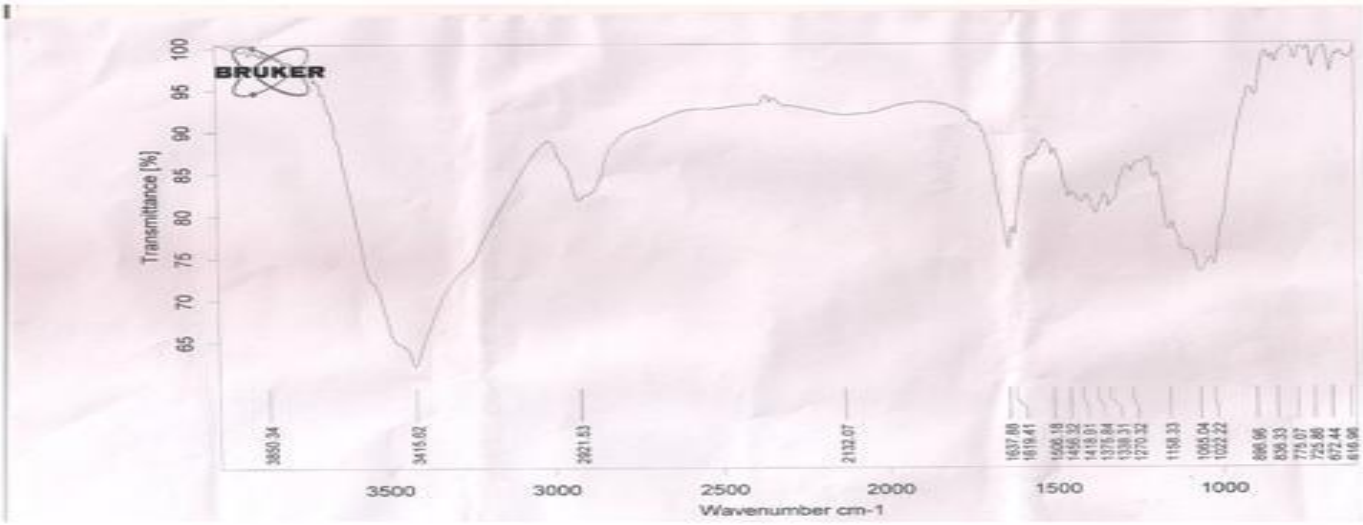


Fig 4. Wetting time profile of all formulations

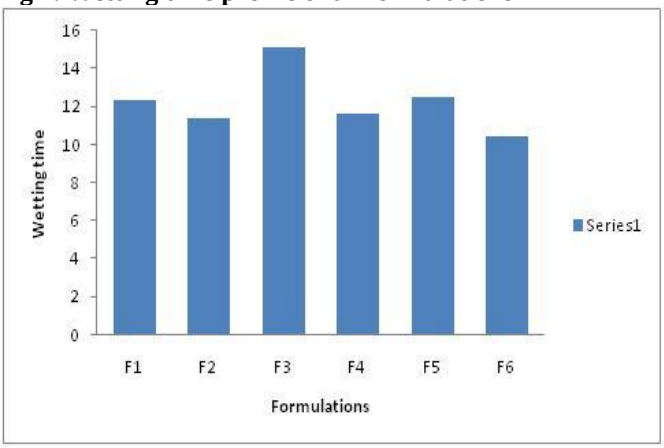


Fig 5. Water absorption profile of all formulations

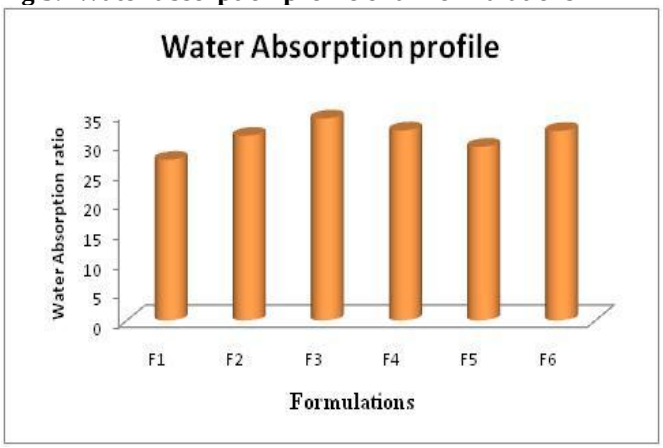
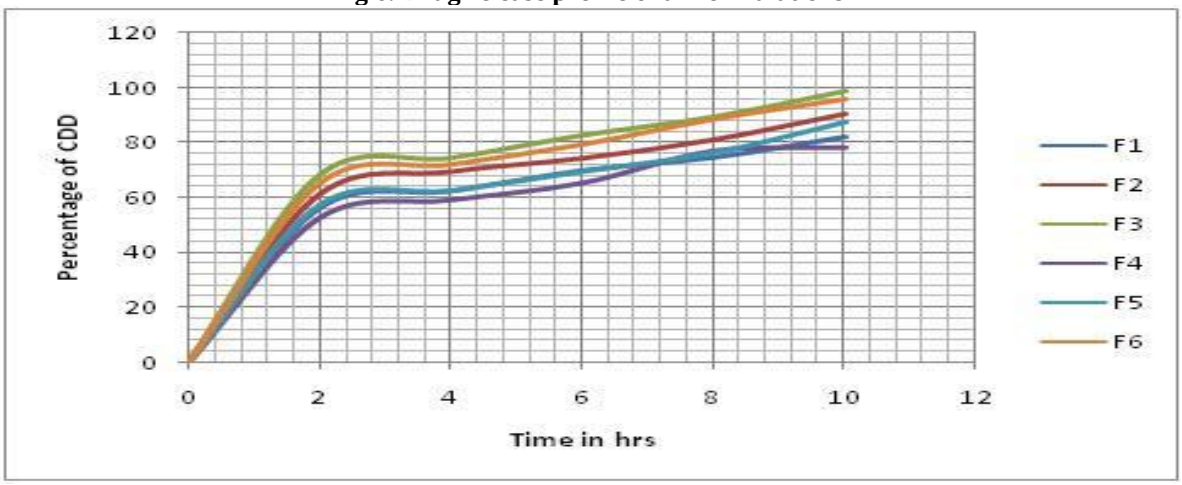


Fig 6. Drug release profile of all formulations



CONCLUSION

In the present study, fast disintegrating sublingual tablets of Sumatriptan 100mg were prepared by direct compression method by using Croscarmellose sodium and Crospovidone as super disintegrants at the concentration of 3%, 4% and 5% of each and compared the effect of each at different concentrations, and finished the optimum formulation. A total number of 6 formulations were prepared by using different super disintegrants at different concentrations. Among this, formulation F-3 was selected as best formulation because of its wonderful mouth feel which contains drug (5mg), crospovidone 5mg, mannitol (87mg), aspartame(2.5mg) and magnesium stearate(0.5mg) and it releases the drug 98.79% when compared to remaining formulations which were prepared by Crospovidone as a super disintegrates. Table 2 & Table 3 shows the data obtained from the evaluation of tablets. All batches of the tablets were preliminarily evaluated for various physical parameters such as hardness, friability, Average weight, disintegration, thickness, water absorption ratio, wetting time and drug content which were reported in Table no 2 & Table No.3. All above properties and value were near to boundary of standard limit. All the tablets maintained hardness in the range of 4.9 – 6.8kg/cm2. The loss in total weight of the tablets due to friability was in the range of0.18-0.6%. The drug content in different formulations was highly uniform and in the range of 98-100%. Various Physico-chemical parameters are tested for this formulation showed good results. From the release study and mathematical models it was concluded that the novel formulation can bypass the first pass metabolism and produced the quicker onset of action.

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