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FORMULATION AND EVALUATION FAST DISSOLVING TABLETS OF SUMATRIPTAN USING SUPER DISINTEGRANTS

B.Ranjith Kumar*, D.Saritha, B.Rajkamal

Department of Pharmaceutics, K.V.K College of Pharmacy, JNTU Hyderabad, India.

Keywords:

Sumatriptan, Fast Dissolving Tablets, Superdisintegrants, Dissolution Profile

For Correspondence:

B. Ranjith Kumar

Department of Pharmaceutics, K.V.K College of Pharmacy, JNTU Hyderabad India

E-mail:

bandameedi.ramu@gmail.com

ABSTRACT

Sumatriptan succinate is used for acute oral migraine therapy. In the present study an attempt was made to prepare oral fast dissolving tablets of Sumatriptan succinate with the dose of 25 mg in order to improve the quick on set of action and patient compliance fast dissolving tablets of Sumatriptan were prepared by using cross caremellose sodium, sodium starch glycollate cross povidone by direct compression method.study of the preformulation charcteristics and FTIR studies indicate that there was o interaction between Sumatriptan and excipients used in the formulation .out of different formulae from (F1 – F12) F3 found to be optimized which showed a faster rate of drug release .stability studies were conducted for the optimized formulae found to be satisfactory. These findings suggest that the fast dissolving tablets of Sumatriptan is considered to be potentially useful for treatment of migraine where quicker onset of action is desirable.

Introduction

FAST-DISSOLVING TABLETS

Fast-disintegrating and 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. The most desirable formulation for use by the elderly is one that 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, it is easy to take for any age patient, regardless of time or place. For example, it can be taken anywhere at any time by anyone who do not have easy access to water. It is also easy to dose the aged, bed-ridden patients, or infants who have problems swallowing tablets and capsules. Recently, many companies have researched and developed various types of fast-disintegrating dosage forms [1,2].

Sumatriptan succinateis used for acute oral migraine therapy. The drug is a selective agonist of 5-hydroxytryptamine1 (5-HT1) receptors, so it used in treatment of migraine attack and as well as in nausea, vomiting and headache. In the present study an attempt was made to prepare oral fast dissolving tablets of sumatriptan succinatewith the dose of 25 mgin order to improve the quick on set of action and patient compliance [3].

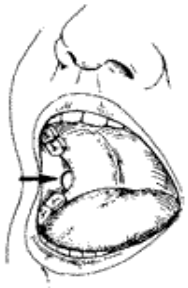

Fig 1 : Fast dissolving tablets (4)

2. METHODOLOGY

MATERIALS Sumtriptan pure drug was obtained as gift sample from hetero labs,cross povidone,cross caremellose sodium,sodium starch glycollate,magnesium sterate,low substituted hydroxyl propyl cellulose all of the analytical grade obtained from merck specialities pvt ltd,Mumbai,india. The fast dissolving tablets containing Sumatriptan were prepared with a total tablet weight of 200mg as shown in table 1.

Table no 1 FORMULATION OF SUMATRIPTAN FAST DISSOLVING TABLETS

Ingredients mg	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Sumtriptan	25	25	25	25	25	25	25	25	25	25	25	25
LHPC 21	5	10	15	-	-	-	-	-	-	-	-	-
CP	-	-	-	5	10	15	-	-	-	-	-	-
CCS	-	-	-	-	-	-	5	10	15	-	-	-
SSG	-	-	-	-	-	-	-	-	-	5	10	15
Mg.stearate (%)	1	1	1	1	1	1	1	1	1	1	1	1
Aerosil (%)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
MCC	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total	200	200	200	200	200	200	200	200	200	200	200	200

DRUG-EXCEPIENTS COMPATIBILITY STUDIES BY FTIR [5]

Excipients are integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients, which are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation.

Analytical methods for the estimation of Sumatriptan

Determination of λ max for Sumatriptan: On the basis of preliminary identification test, it was concluded that the drug complied the preliminary identification. From the scanning of drug, it was concluded that the drug had λ max of 231 nm.

Preparation of standard calibration curve of Sumatriptan: The standard calibration curve for Sumatriptan was prepared using 6.8pHPhosphate buffer.

Standard solution: 25 mg of Sumatriptan was dissolved in 25 ml of 6.8pHPhosphate buffer to give a concentration of 1 mg/ ml (1000 µg/ml).

Flow Properties:

Angle of Repose:

The flow property was determined by measuring the Angle of Repose. In order to determine the flow property, the Angle of Repose was determined. It is the maximum angle that can be obtained between the free standing surface of a powder heap and the horizontal.

$$\text{Angle of repose} = \tan^{-1}(h/r)$$

Where, h = height of a pile (2 cm) r = radius of pile base.

Bulk density:

Bulk density is ratio of given mass of powder and its bulk volume. Bulk density was determined by measuring the volume of known mass of powder sample that has been passed through the screen in to graduated cylinder or through volume measuring apparatus in to cup.

$$\text{Bulk density} = M / V_0$$

Where M= mass of the powder;

V_0=bulk volume of the powder.

Tapped density:

A known quantity of powder was transferred to a graduated cylinder and volume V_0 was noted. The cylinder fixed to a density determination apparatus, tapped for 500 times then reading was Observed. The density is achieved by mechanically tapped by a measuring cylinder containing the powder sample. After observing the initial volume the cylinder is mechanically tapped and volume reading were taken until little further volume changes is observed.

$$\text{Tap density} = M / Vr$$

Where M = mass of the powder,

Vr = final tapping volume of the powder.

Compressibility index and Hausner ratio:

The compressibility index and hausner ratio may be calculated using measured values of bulk density and tapped density as follows:

Compressibility index = 100 × tapped density / bulk density

Hausner ratio = tapped density / bulk density

Flow properties and corresponding Angle of repose, Compressibility index and Hausner ratio:

EVALUATION OF TABLETS [6,7]

The quantitative evaluation and assessment of a tablets chemical, physical and bioavailability properties are important in the design of tablets and to monitor product quality. There are various standards that have been set in the various pharmacopoeias regarding the quality of pharmaceutical tablets. These include the diameter, size, shape, thickness, weight, hardness, disintegration and dissolution characters.

1. Physical Appearance:

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurement of size, shape, colour, presence or absence of odour, taste etc.

2.Size & Shape:

It can be dimensionally described & controlled. The thickness of a tablet is only variables. Tablet thickness can be measured by micro-meter or by other device. Tablet thickness should be controlled within a ± 5% variation of standard value.

3. Weight variation test:

This is an in process quality control test to ensure that the manufacturers control the variation in the weight of the compressed tablets, different pharmacopoeia specify these weight variation tests. These tests are primarily based on the comparison of the weight of the individual tablets of a sample of tablets with an upper and lower percentage limit of the observed sample average.

4. Content Uniformity:

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch. Due to increased awareness of physiological availability, the content uniformity test has been included in the monographs of all coated and uncoated tablets and all capsules intended for oral administration where the range of size of the dosage form available include 50mg or smaller sizes.

5. Thickness and diameter: The thickness and diameter of 10 tablets were recorded during the process of compression using vernier calipers.

6. Hardness:

The force required to break the tablet is measured in kilograms. The small and portable hardness tester measures the force required to break the tablet when the force generated by a coil spring is applied diametrically to the tablet.

7. Friability:

Friction and shock are the forces that most often cause tablets to chip, cap or break. The friability test is closely related to tablet hardness and designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping. It is usually measured by the use of the Roche friabilator.

The percentage friability was determined by the formula:

$$\% \text{ Friability} = (W_1 - W_2) / W_1 \text{ X } 100$$

W_1 = Weight of tablets before test

W_2 = Weight of tablets after test

8. Disintegration test [7,8]:

For a drug to be absorbed from a solid dosage form after oral administration, it must first be in solution, and the first important step toward this condition is usually the break-up of the tablet; a process known as disintegration. The disintegration test is a measure of the time required under a given set of conditions for a group of tablets to disintegrate into particles which will pass through a 10 mesh screen. Generally, the test is useful as a quality assurance tool for conventional dosage forms.

Disintegration time: Uncoated tablet: 5-30 minutes.

9. Dissolution [9]:

Dissolution is the process by which a solid solute enters a solution. In the pharmaceutical industry, it may be defined as the amount of drug substance that goes into solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent composition. Dissolution is considered one of the most important quality control tests performed on pharmaceutical dosage forms and is now developing into a tool for predicting bioavailability.

Stability studies

Stability studies were carried out according to ICH guidelines by exposing the. Formulation F3 in their final packing mode to the temperature 40±2°C and relative humidity 75±5 % for a period of 3months. After three months samples were analyzed for change in drug content and in-vitro dissolution profile.

Results: In the present study an attempt has been to formulate and evaluate Fast dissolving tablets of Sumatriptan. The procured drug sample of Sumatriptan was tested for its identification by means of organoleptic properties, melting point, UV spectra and FTIR spectrum.

Drug Interaction Study [10]:

FTIR spectra of Sumatriptan and physical mixture of Sumatriptan and Excipients were taken. Spectra are shown in figure for drug& figure no. for physical mixture of drug and both polymer. All the characteristic peaks of pure drug were observed in the spectrum of mixture. This indicated that there was not any interaction between drug and polymer.

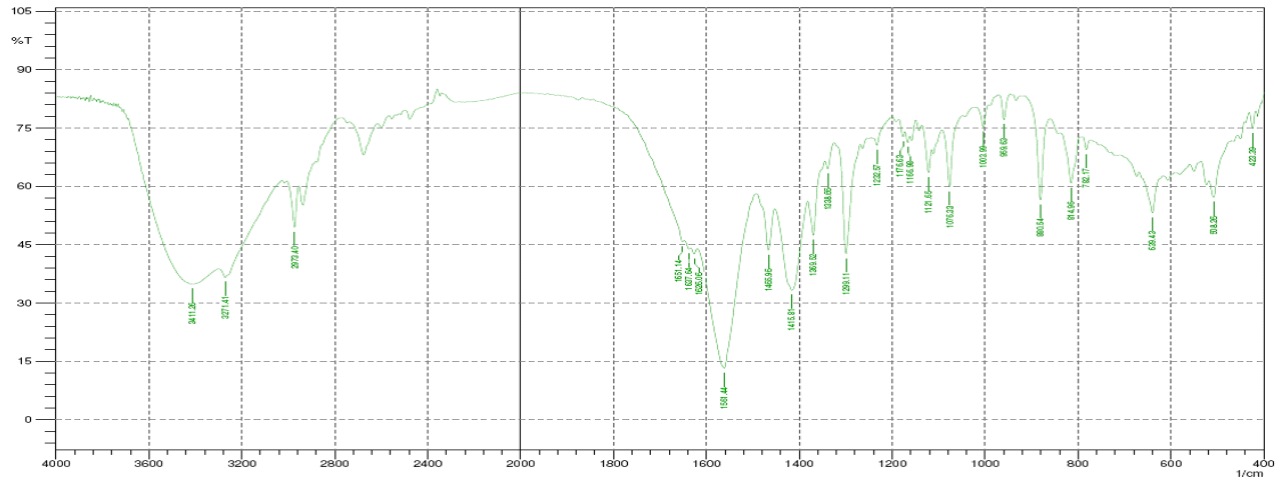

Fig no 2: FTIR Spectra of Sumatriptan pure drug

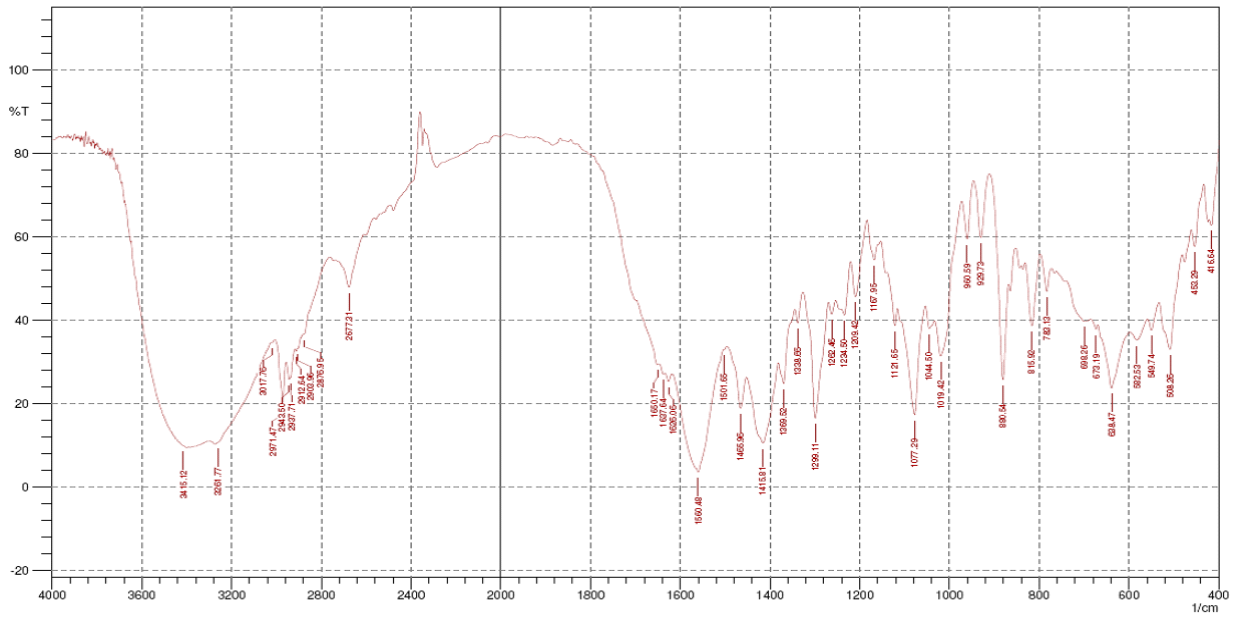

Fig no 3: FTIR Spectra of Sumatriptan optimized formulation

Physical characterization of Tablets of Sumatriptan:

Tablet thickness, hardness, weight variation, friability and drug content of formulated Tablets of batches from F1 to F12 are presented in Table 3.

Uniformity of weight:

All the prepared tablets of Sumatriptan were evaluated for weight variation. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits of ±7.5%.

Hardness and friability:

The hardness of the tablet formulations was found to be in the range of 4.3 to 6.5 kg/cm^2. The friability values were found to be in the range of 0.30 to 0.69 %.

Uniformity of drug content:

The low values of standard deviation indicates uniform drug content within the tablets The percent drug content of all the tablets was found to be in the range of 98.20 to 102.6 percent (which was within the acceptable limits of ±5%.).

Disintegration test:

The disintegration for all the formulation was to be satisfactory. The formulation F3 was found to have Disintegration time of 1 min 27sec.

3) Evaluation of Tablets:

Table 2: Post compression studies

Formulation code	Weight variation	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	Content uniformity	Disintegration Time (min)
F1	201	6.5	0.35	3.41mm	98.28	2min
F2	200	6.3	0.37	3.43mm	99.16	1 min 48sec
F3	202	5.0	0.48	3.45mm	100.1	1 min 27sec
F4	200	5.4	0.44	3.42mm	99.68	2min 20 sec
F5	197	6.1	0.44	3.44mm	99.41	1 min 44 sec
F6	199	5.0	0.45	3.42mm	99.28	1min 30 sec
F7	200	6.2	0.35	3.4mm	102.6	3min 15sec
F8	201	5.5	0.30	3.6mm	99.5	2 min18sec
F9	202	5.3	0.38	3.62mm	99.6	2 min 35sec
F10	204	5.0	0.69	3.60mm	100.4	3min 24sec
F11	200	4.3	0.55	3.66mm	98.3	2min
F12	198	5.6	0.45	3.64mm	99.4	1 min

4. In -vitro drug release study [11]

Paddle method Dissolution data of fast dissolving formulations of Sumatriptan by Paddle method (USP II) are reported in Table.

Table 3: Dissolution Values

Time in min	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
3	29	41	48	22	26	31	21	23	25	20	23	25
6	45	55	70	35	42	46	31	35	37	32	35	38
9	57	71	83	51	55	64	51	56	58	47	45	49
12	75	80	91	60	66	81	61	75	72	50	61	65
15	86	90	98	81	83	87	87	85	89	79	83	86
18	95	96	102	88	92	94	92	89	92	83	89	92

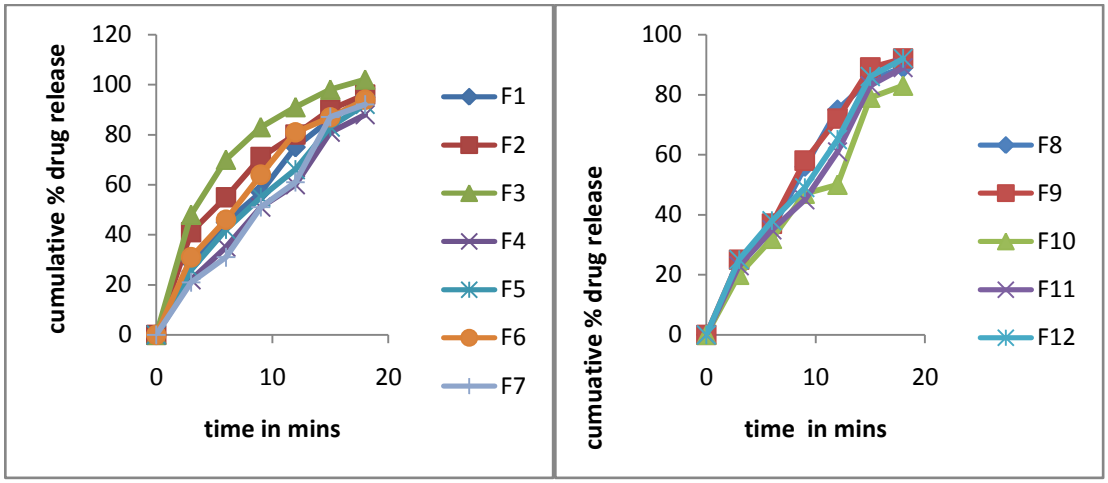

Figure 4: Cumulative % drug released for formulations F1-F7,F8-F12.

STABILITY DATA [12]

Storage Conditions: $40^0C \pm 2^0C$ at 75%±5%RH

Table .4 Stability Data of optimized F3 Sumatriptan fast dissolving tablet.

SNO	Tests	Initial 0 month	After 3 month
1.	Dissolution Profile (Cumulative % drug release)	3min- 48 9min - 83 18min - 102	3min- 45 9min - 80 18min – 99.6
2.	Assay	100.1%	98.5%

CONCLUSION

Sumatriptan tablets were formulated by using microcrystalline cellulose as filler, L Hydro propyl cellulose as super disintegrant and magnesium stearate as lubricant.The powdered blend were compressed into tablets and were analyzed for the parameters such as average weight, disintegration time, friability, thickness, weight variation, hardness and drug content. The F3

formulation found to be shown fast drug release compared to other batches. The dissolution profiles and drug content of the tablets were found to be satisfactory even after subjecting the tablets to stability studies at 40^{o}C and 75%RH for 1 month and 3 months respectively.

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