ISSN: 2230-7346

Seetha Devi. A et al / JGTPS / 6(1)-(2015) 2456 – 2467

(Research Article)

Journal of Global Trends in Pharmaceutical Sciences

Journal home page: www.jgtps.com

FORMULATION AND EVALUATION OF TASTE MASKED ORODISPERSIBLE TABLETS OF SUMATRIPTAN SUCCINATE

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ABSTRACT

In the present work Sumatriptan succinate, an antimigraine drug having bitter taste is masked and orally disintegrating tablets were formulated. The bitter taste is masked by forming complex between drug and weak cation exchange resins, Indion 204 and Indion 234. Ratio of 1:2 drug:resin complex masked almost complete bitterness of Sumatriptan succinate. Formation of complex was confirmed by IR spectroscopy. Effect of pH, stirring time, swelling time, temperature on the drug loading was studied. Effect of superdisintegrants like sodium starch glycolate, carmellose sodium, crosspovidone (4%) was used. Six formulations were prepared by direct compression method using 10 station rotary tablet machine (Rimek, India) with 7mm round flat shaped punches. Tablet blend was subjected to pre-compression parameters. The prepared tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water absorption ratio, *in vitro* disintegration time and *in vitro* dispersion time. *In vitro* dissolution studies were performed in pH 6.8 phosphate buffer. Among all the formulations, FS4 showed about 98.48% of drug release within 30 minutes. Taste evaluation was done in human volunteers. Short term stability studies were performed for best formulation which indicated no significant change in the drug content.

Keywords: Orodispersible tablet, Sumatriptan succinate, Indion 204, Indion 234, sodium starch glycolate, carmellose sodium, crospovidone, direct compression, pH 6.8 phosphate

INTRODUCTION

Advances in medical care and drug therapy leads to improved treatment, patient compliance and quality of life[1]. In more recent years, increasing attention has been paid in formulating not only fast dissolving and/or disintegrating tablets, that are swallowed, but also orally disintegrating tablets that are intended to dissolve and/or disintegrate rapidly in the mouth[2,3].ODT's also known as mouth dissolving tablet, fast disintegrating/dissolving tablet, rapid dissolving tablet, quick disintegrating tablet are useful in patients[4] such as pediatric, geriatric, bedridden or developmentally disabled, who may face difficulty in swallowing conventional tablets or capsules and liquid orals[5,6].

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Advantages of ODT's are administration without water, suitable for the mentally ill, who do not have easy access to water. The benefits in terms of patient compliance, rapid onset of action, increased bioavailability and good stability make these tablets popular as a dosage form of choice in current market[7, 8]. The various technologies used to prepare ODT's include freeze drying, cotton candy, moulding, mass extrusion, phase transition, spray drying, sublimation, direct compression[9]. Migraine is a common disorder characterized by a unilateral headache that is often associated with nausea, vomiting, gastrointestinal disturbance and extreme sensitivity to light and sound.[10,11] Sumatriptan succinate is the first member of a new class of antimigraine compounds that acts as a specific and selective 5-hydroxytryptamine –I receptor agonist.It is highly water soluble and intensely bitter drug.[12]

Ion exchange resins have been used as drug carriers in pharmaceutical dosage forms for taste masking[13]. Ion exchange resins are water insoluble, cross-linked polymers containing salt forming groups in repeating positions on the

polymer chain. Drugs can be loaded into an ion exchange resin by an exchanging reaction and hence a drug-resin complex is formed[14]. Drug is released from resinate by exchanging with ions in the gastro-intestinal fluid, followed by drug diffusion[15]. It can be used in the drug formulations to stabilize the sensitive components, sustain release of drug, disintegrate tablets and mask taste[16]. The resin form insoluble adsorbates or resonates through weak ionic bonding with oppositely charged drugs so that dissociation of drug resin complex does not occur under the salivary pH conditions. Bitter cationic drugs can get adsorbed onto the weak cation exchange resin of carboxylic acid functionality to form the complex which is non bitter[17]. Indion 204 is high purity pharmaceutical grade weak acid cation exchange resin based on a cross-linked acrylic-copolymer, divinyl benzene matrix containing carboxylic acid functional groups, supplied in hydrogen form as free powder[18]. Indion 234 is high purity pharmaceutical grade weak acid cation exchange resin based on crosslinked polyacrylic acid, divinyl benzene matrix containing carboxylic acid functional groups; supplied as a dry powder in potassium form. It is insoluble in all common solvents, having excellent physical and chemical stability and operating characteristics[19] Thus in the present study an attempt has been made to mask the taste of Sumatriptan succinate and formulate orodispersible tablets with good mouth feel so as to prepare a "patient friendly dosage form."[20].

EXPERIMENTAL

Materials:

Sumatriptan succinate was obtained as a gift sample from Reddy's laboratories, Hyderabad. Resin Indion 204 and Indion 234 were obtained as gift sample from Ion Exchange (India) Ltd., Mumbai. Other chemicals used were of analytical grade.

Methods:

Preparation of standard calibration curve in pH 6.8phosphate buffer:

Stock solution was prepared by dissolving 100mg of sumatriptan in 100mL of pH 6.8 buffer, so as to get a solution of 1mg/1mL concentration. 10 mL of stock solution was diluted to 100mL with pH 6.8 phosphate buffer thus giving a concentration of 100 µg/mL.10mL of prepared solution(100 µg/mL) diluted to 100mL with pH 6.8 buffer thus giving a concentration of 10µg/mL. From the standard drug solution (10µg/mL) aliquot quantities 1,2,3,4 and 5mL were transferred into 10ml volumetric flasks and were diluted upto the mark with pH 6.8 buffer, thus the final concentration ranges from 1-5µg/mL respectively. Absorbance of each solution was measured at 228nm against pH 6.8 buffer as the blank. A graph of concentration of drug versus absorbance was plotted. (Table no.2 & Fig. no.1)

Preparation of drug resin complex[21]

An accurately weighed amount (200mg) of resin particles (Indion 204 and Indion 234) were suspended in deionised water for 15 min to allow uniform swelling of polymer. Sumatriptan succinate (100mg) was added and slurry was stirred with the help of magnetic stirrer at 500 rpm for 45 min to allow maximum adsorption of drug on the resin. Resinate thus formed was filtered, dried at 40^0C and the drug content was determined spectrometrically at 228nm

Assessment of the bitter taste of the Sumatriptan succinate (Bitterness threshold):

The bitter taste threshold value of Sumatriptan succinate was determined based on the bitter taste recognized by ten volunteers (five females and five males). A series of Sumatriptan succinate resinate were prepared with Indion 204, 234 in different ratios i.e. 1:1, 1:2 & 1:3 respectively. Small amount of resinate was placed on the centre of the tongue, it was retained in the mouth for 30 seconds, and then the mouth was thoroughly rinsed with distilled water. The ratio was correspondingly selected which had lowest bitter taste.

Optimization of swelling time on drug loading:

200 mg of Indion 204 and 234 were individually soaked in 25mL of deionised water for 10, 20, 30, 40, 50 &60 min. 100mg of Sumatriptan succinate was added to it and stirred on magnetic stirrer at 500rpm. The amount of drug loaded at the end of 45min was determined indirectly by estimating the amount remaining to be loaded in solution spectrophotometrically at 228nm.(Table no. 3)

Optimization of stirring time on drug loading:

For optimization of stirring time on drug loading, accurately weighed, 100mg of drug was added to 200mg of resin (Indion 204, 234) individually and slurred in deionised water. Stirring time of 30, 60, 120, 180 & 260 min was processed using magnetic stirrer at 500rpm. Amount of maximum bound drug was estimated spectrophotometrically at 228nm. (Table no. 4)

Optimization of pH on maximum drug loading:

The study was carried out at pH 1.2, 2, 3, 4 &5. The pH of solution was adjusted by prepared standard solutions of hydrochloric acid and potassium hydroxide maintained at 25^0C. Solution of 100mg drug was stirred with 100mg of resin using magnetic stirrer. The amount of drug loaded at the end of 45 min was determined indirectly by estimating the amount to be loaded in solution spectrophotometrically at 228nm. (Table no. 5)

Optimization of temperature on maximum drug loading:

The study was carried out at 25^0C, 30^0C, 40^0C, 50^0C &60^0C. In each case, 100mg of sumatriptan succinate was stirred with 100mg of resin (Indion 204, 234) individually using temperature-controlled magnetic stirrer at 500rpm. The amount of drug loaded at the end of 45min was determined indirectly by estimating the amount remaining to be loaded in solution spectrophotometrically at 228 nm. (Table no. 6)

Formulation of orodispersible tablets:

Mouth dissolving tablets each containing Sumatriptan succcinate equivalent to 25 mg of sumatriptan were prepared according to the formula given in Table 1.Six formulations were prepared by direct compression and the total weight of single tablet is 200mg. All the ingredients were passed through 60 mesh sieve separately and collected. Except magnesium stearate all the ingredients were weighed as per the formulae and triturated for 10min. Finally to this blend magnesium stearate was added and mixed further for 5min. The tablet mixture was then compressed using 10 station rotary tablet machine (Rimek, India) with 7mm round flat shaped punches. Before tablet preparation, the mixture blend of all the formulations were subjected to pre-compression parameters like angle of compression, bulk density, tapped density, compressibility index and Hausner's ratio. (Table no.7)

Evaluation of blend for orodispersible tablets:

Blend was evaluated for the following flow properties[22, 23].

Angle of repose: The frictional force in a loose powder can be measured by the angle of repose. Angle of Repose (θ) is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by fixed funnel method and is the measure of the flow ability of powder/granules. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully poured through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The studies were done in triplicate. The angle of repose (θ) was calculated using the following formula: $\theta = \tan^{-1}h/r$

Where 'h' is the height of pile; 'r' is radius of the base of the pile; 'θ' is the angle of repose.

Bulk density: It is the mass of powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density (gm/cc) was determined by pouring gently 25 gm of sample (w) through a glass funnel into a 100mL graduate cylinder. After pouring the powder bed was made uniform without disturbing. The volume measured was called as the bulk volume and the studies were done in triplicate. Bulk density was calculated by following formula:

Bulk density (ρ_b) = weight of the powder (w) / Bulk volume (v_b)

Tapped density: It is the ratio of total mass of powder to tapped volume of powder. Tapped density was determined by USP method II. The powder sample was screened through sieve No. 18 and 10 g of tablet blend was filled in 100 mL graduated cylinder of tap density tester (Electrolab, ETD 1020). The mechanical tapping of the cylinder was carried out using tapped density tester at a nominal rate of 250 drops per minute for 500 times initially and the initially tapped volume was noted. Tapping was proceeded further for additional 750 times and the volume was noted. The difference between two tapping volumes was calculated. Tapping was continued for additional 1250 times if the difference is more than 2%. This was continued in increments of 1250 taps until difference between volumes of subsequent tapings was less than 2 %. This volume was noted as final tapped volume. Tapped density was calculated using following formula: Tapped density (ρ_t) = Weight of the powder (w) / Tapped volume (v_t)

Compressibility index*:* Compressibility is the ability of the powder to decrease in the volume under pressure. Compressibility is a measure that is obtained from density determinations. It is indirectly related to the relative flow rate, cohesiveness and particle size. It is also one of the simple methods to evaluate flow property of powder by comparing the bulk density and tapped density. High density powders tend to possess free flowing properties. Compressibility index can be calculated by the following formula:

Carr's index= (Tapped density- Bulk density/ Tapped density) ×100

Hausner's ratio: Hausner's ratio provides an indication of the degree of the densification which could result from vibration of the feed hopper. A lower value of Hasuners' ratio indicates better flow and vice versa.

Hausner's Ratio = Tapped density /Bulk density.

EVALUATION OF TABLETS:

The prepared orodispersible tablets were subjected to post-compression parameters like weight variation, hardness, friability, thickness, wetting time & water absorption ratio, *in vitro*

disintegration time, *in vitro* dispersion time, content uniformity, *in vitro* dissolution studies and taste evaluation. (Table no. 8 and Table no 9)

Weight variation: Weight variation was calculated as per the method describe in USP. Twenty tablets were weighed individually and the average weight is calculated. The percent weight variation was calculated by using the following formula.

% weight variation = Average weight-Individual weight /Average weight ×100

Hardness: Five tablets from each batch were selected and hardness was measured using Monsanto hardness tester to find the average tablet hardness or crushing strength. The hardness was measured in terms of kg/cm^2.

Friability: Twenty tablets from each batch were selected randomly and weighed. These pre weighed tablets were subjected to friability testing using Roche Friabilator for 100 revolutions. The tablets in the friabliator are subjected to both abrasion and shock in a plastic chamber revolving at 25rpm, dropping the tablet at a height of 6 inches in each revolution. Tablets were removed, dusted and weighed again. Following formula was used to calculate the friability = Initial – Final weight/ Initial weight × 100

Thickness: Tablet thickness was measured by vernier calipers.Tablet thickness should be controlled within a ± 5% of a standard value[24, 25].

Wetting time and water absorption ratio[26]: Five circular tissue papers of 12.5cm diameter were placed in petridish. Ten milliliters of water was added to petridish. Tablet was carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as the wetting time. For measuring water absorption ratio the weight of the tablet before keeping in the petridish is noted (W_b). The wetted tablet from the petridish is taken and reweighed (W_a). The water absorption ratio, R can be determined by the following equation:

$$R = \frac{W_a - W_b}{W_b} \times 100 \times 100$$

Where, W_b and W_a are weights before and after absorption respectively.

***In vitro* disintegration time[27]:** Disintegration time is the time taken by the tablet to breakup into smaller particles. The tablet containing a basket rack assembly with two glass tubes of 7.75cm in length and 2.15 mm in diameter, the bottom of which consists of a #10 mesh sieve. The basket is raised and lowered 28-32 minutes per minute in a medium of 900mL which is maintained at 37±2^{0}C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh was considered as the disintegration time of the tablet.

***In vitro* dispersion time[26]:** *In vitro* dispersion time of orally disintegrating tablets was determined by placing 10 mL of water in a petridish of 12.5 cm diameter. The tablet was then carefully placed in the center of the petridish and the time required for the tablet to break into fine particles was noted.

Content uniformity: Five tablets were selected randomly and powdered. A quantity of this powder equivalent to 25mg of Sumatriptan succinate was dissolved in 100 mL of pH 6.8 phosphate buffer stirred for 60 min and the solution was filtered and diluted suitably with pH 6.8 phosphate buffer. Absorbance of this solution was measured at 228nm using pH 6.8 phosphate buffer as blank and content of Sumatriptan succinate was estimated.

Dissolution studies*:* The *in vitro* dissolution studies were carried out using USP apparatus type II at 50 rpm. The dissolution medium used was 900ml pH 6.8 phosphate buffer maintained at 37± 0.5^0 C. At appropriate intervals (5, 10, 15, 20, 25, 30 minutes) 5mL of each sample was taken. The dissolution medium was then replaced by 5mL of fresh dissolution fluid to maintain constant volume. The samples were analyzed spectrophotometrically by UV-Visible spectrophotometer (Elico SL 244) at 228nm. The percentage drug release was calculated using calibration curve of the drug in buffer. The dissolution experiments were conducted in triplicate. (Table no. 10)

Release kinetics[28]: Data of *in vitro* release was fitted into different equations to explain the release kinetics. The kinetic equations used were zero order and first order equations. R^2 valves suggest that the release from the formulations may either follow zero order release kinetic model or first order release kinetic model. (Fig. no 5 & Table no.11)

Taste evaluation: Taste evaluation of drug-resin complex was performed in human volunteers in the age of 18 to 25 years by using time intensity method. The study protocol was explained and written consent was obtained from volunteers. Resinate of small amount was held in the mouth for 30seconds by each volunteer. Bitterness levels were recorded instantly and then after 30 to 150sec. The bitterness level was recorded against pure drug using numerical scale (3-strongly bitter, 2-moderately bitter, 1- slight bitter, X-threshold bitter, 0- No bitter. (Table no. 12, 13, 14)

Characterization of drug in orodispersible tablets: FT-IR studies were conducted for characterization of drug in tablet. The IR spectra's were recorded using Fourier Transform Infrared spectrophotometer. The IR spectrum of pure drug and best formulation were taken, interpreted and compared with each other (Fig.no.4)

Stability studies: Short term stability studies were conducted for best formulation of Sumatriptan succinate tablets at 4^0 C and at room temperature for 8 weeks. After 8 weeks, the % drug content of the formulations was estimated and compared. (Table no.15)

RESULTS:

Table 1: Composition of Sumatriptan succinate tablets

Name of the ingredients	FS1 (mg)	FS2 (mg)	FS3 (mg)	FS4 (mg)	FS5 (mg)	FS6 (mg)
Sumatriptan succinate	35	35	35	35	35	35
Crospovidone	8	-	-	8	-	-
Carmellose sodium	-	8	-	-	8	-
S.S.G	-	-	8	-	-	8
Indion 204	70	70	70	-	-	-
Indion 234	-	-	-	70	70	70
MCC	63	63	63	63	63	63
Mg.stearate	2	2	2	2	2	2
Mannitol	20	20	20	20	20	20
Talc	2	2	2	2	2	2
Total (mg)	200	200	200	200	200	200

Table 2: Calibration curve of Sumatriptan succinate in pH 6.8 phosphate buffer

Concentration µg/mL	Absorbance (at 228 nm)
0	0.0000
1	0.1125 ± 0.0002
2	0.2276 ± 0.0001
3	0.3512 ± 0.0003
4	0.4873 ± 0.0005
5	0.5975 ± 0.0002

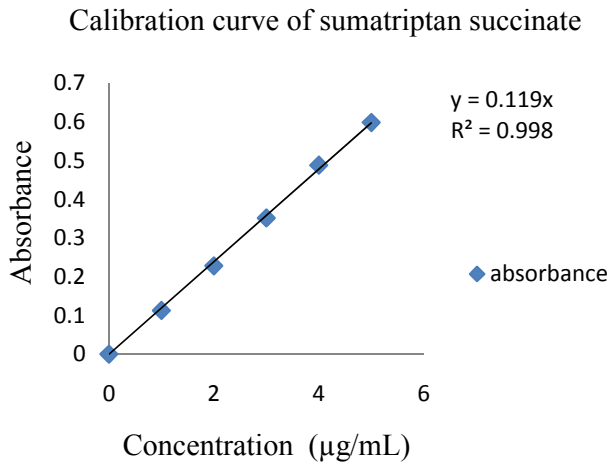

Table 3: Effect of swelling time on drug loading

s.no	Swelling time (min)	% drug bound to resin	
		Indion 204	Indion 234
1	10	89.34±0.06	89.33±0.09
2	20	93.54±0.14	90.23±0.11
3	30	96.41±0.17	95.86±013
4	40	96.40±0.11	95.83±0.11
5	50	96.40±0.05	95.82±0.11
6	60	96.40±0.22	95.83±0.21

Table 4: Effect of Stirring time on drug loading

s.no	Stirring time (min)	% drug bound to resin	
		Indion 204	Indion 234
1	30	83.36±0.08	90.33±0.07
2	60	93.44±0.17	90.23±0.14
3	120	95.79±0.13	94.76±011
4	180	95.76±0.12	94.13±0.07
5	240	95.78±0.05	94.05±0.19

Table 5: Effect of pH on drug loading

s.no	pH	% drug bound to resin	
		Indion 204	Indion 234
1	1.2	80.34±0.01	80.33±0.05
2	2	83.86±0.13	90.23±0.18
3	3	93.48±0.12	94.76±011
4	4	95.76±0.15	95.54.±0.04
5	5	95.45±0.08	95.24±0.20

Table 6: Effect of temperature on drug loading

s.no	Temperature (^{0}c)	% drug bound to resin	
		Indion 204	Indion 234
1	25	97.26±0.11	95.33±0.24
2	30	97.78±0.15	96.23±0.17
3	40	97.10±0.19	96.16±014
4	50	97.89±0.06	96.73±0.09
5	60	97.34±0.08	96.05±0.10

Table 7: Micromeritic properties of the physical mixtures of formulations of sumatriptan succinate

Formulation code	Angle of repose (^{0})*	Bulk density*(g/cc)	Tapped density (g/cc)*	Carr's index (%)*	Hausner's ratio *
FS1	26.811±0.03	0.475±0.047	0.569±0.048	16.52±0.370	1.26±0.043
FS2	25.115±0.07	0.490±0.122	0.588±0.035	16.89±0.268	1.19±0.049
FS3	25.22±0.143	0.487±0.053	0.580±0.067	16.03±0.28	1.12±0.183
FS4	28.159±0.07	0.453±0.042	0.570±0.133	15.76±0.09	1.22±0.06
FS5	29.357±0.05	0.455±0.134	0.478±0.01	16.11±0.278	1.111±0.08
FS6	26.465±0.05	0.455±0.122	0.478±0.111	15.03±0.332	1.195±0.07

Table 8: Post Compression Evaluation parameter

Formulation code	%Weight* Variation	Thickness* (mm)	Hardness* (Kg/cm^2)	Friability * (%)
FS1	0.28±0.24	2.26±0.03	3.0±0.13	0.81±0.022
FS2	0.34±0.36	2.28±0.02	3.3±0.15	0.84±0.011
FS3	0.33±0.27	2.32±0.01	3.2±0.20	0.82±0.023
FS4	0.34±0.16	2.31±0.03	3.1±0.10	0.83±0.019
FS5	0.36±0.18	2.32±0.02	3.3±0.11	0.81±0.011
FS6	0.30±0.26	2.28±0.03	3.2±0.22	0.80±0.026

Table 9: Post Compression Evaluation parameters

Formulation code	Wetting time* (sec)	Water absorption ratio	*In vitro* disintegration time* (sec)	*In vitro* dispersion time* (sec)	% Drug content*
FS1	26.89±1.44	140±1.56	29.23±0.44	30.11±0.67	99.86±0.083
FS2	26.54±0.90	134.61±0.84	28.57±0.36	29.09±0.24	100.19±0.063
FS3	27.90±1.31	135.00±0.46	28.03±0.11	29.00±0.63	99.48±0.012
FS4	25.81±0.61	143.07±0.75	27.19±0.32	28.99±0.41	100.16±0.032
FS5	29.45±1.23	142.49±0.98	30.00±0.37	30.16±0.33	99.38±0.082
FS6	29.57±0.40	128.56±0.38	30.45±0.11	30.88±0.12	99.58±0.058

Table 10: Cumulative % drug released from Sumatriptan succinate

time (min)	cumulative % drug release					
	FS1	FS2	FS3	FS4	FS5	FS6
0	0	0	0	0	0	0
5	41.51±0.16	40.28±0.23	25.97±0.17	43.45±0.18	40.88±0.15	39.08±0.11
10	54.05±0.18	50.74±0.14	49.62±0.16	50.4±0.20	64.54±0.17	50.4±0.14
15	65.4±0.17	70.2±0.23	64.02±0.17	65.57±0.23	78.17±0.19	61.7±0.15
20	72.4±0.15	78.85±0.14	72.7±0.15	78.94±0.26	84.34±0.23	79.2±0.22
25	85.88±0.14	83.57±0.14	82.5±0.14	85.62±0.21	90±0.18	86.4±0.17
30	98.22±0.17	94.62±0.15	92±0.13	98.48±0.21	96.6±0.17	94.88±0.26

Fig 2: Cumulative percentage Drug Release profiles of Sumatriptan succinate orodispersible tablets (FS1-FS3)

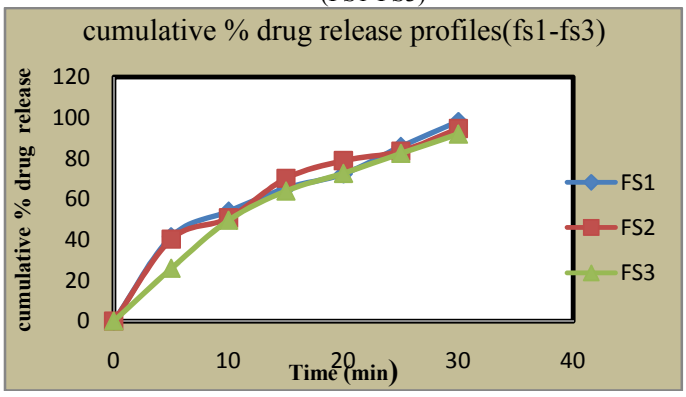

Fig 3: Cumulative percentage Drug Release profiles of Sumatriptan succinate orodispersible tablets (FS3-FS6)

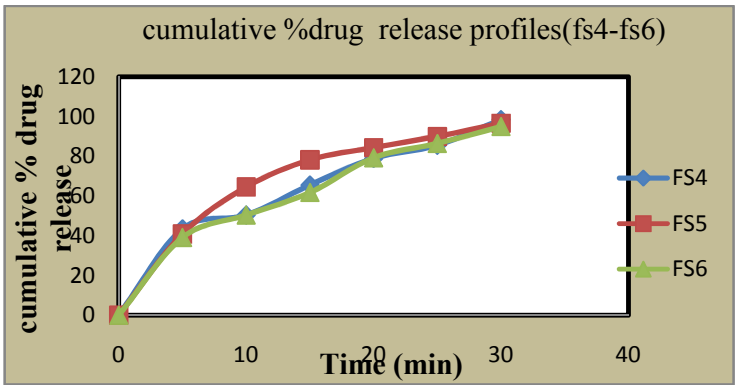

Fig 4: IR spectrum of Sumatriptan succinate

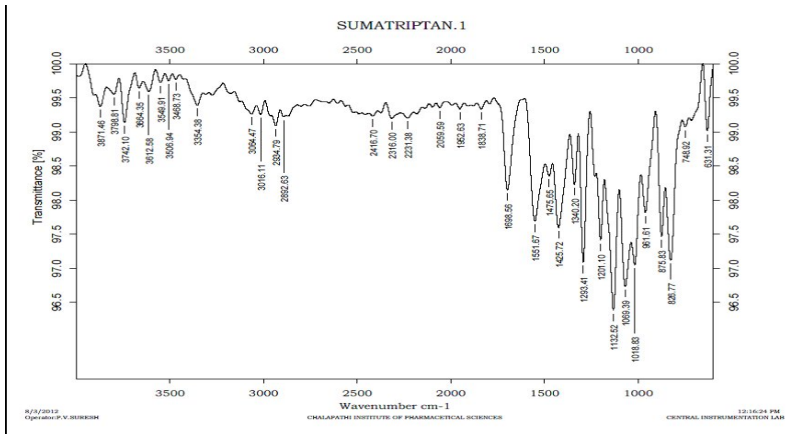

Fig 5: IR spectrum of FS4

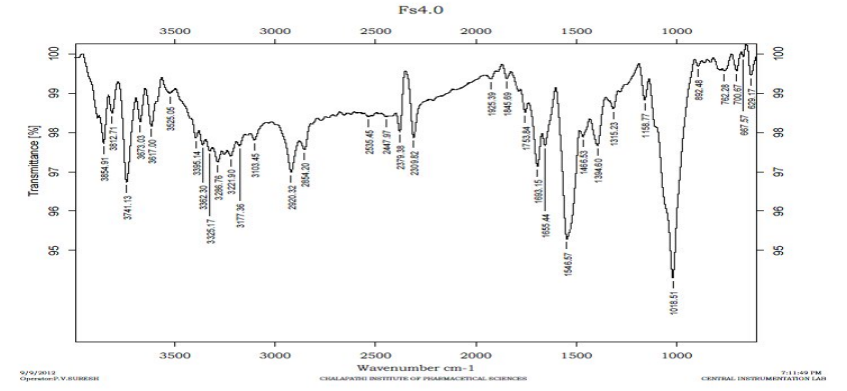

Fig 6: *In vitro* drug release profiles of Sumatriptan succinate (FS1-FS3)

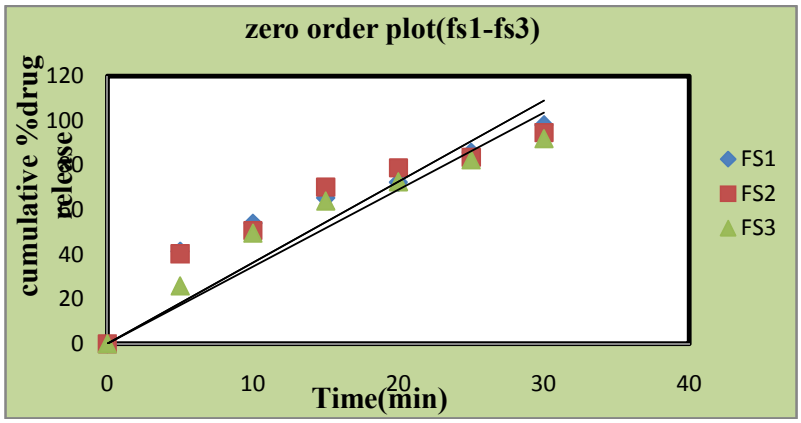

Fig 7: In vitro drug release profiles of Sumatriptan succinate (FS4-FS6)

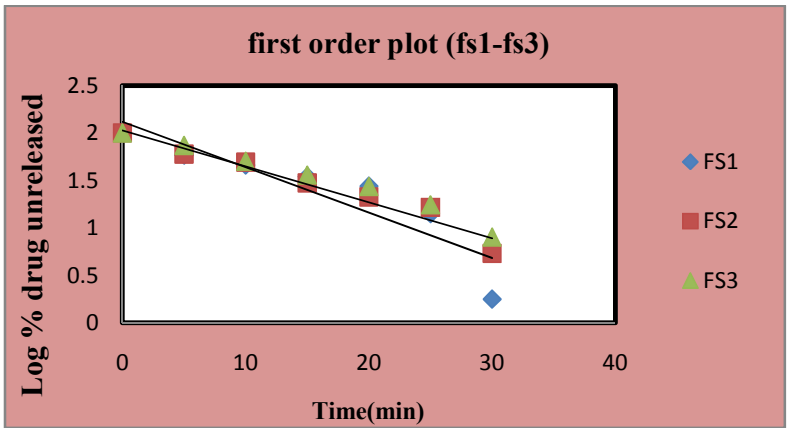

Table 11: Regression values of Sumatriptan succinate formulations

Formulation code	Zero Order (R^2)	First order (R^2)
FS1	0.822	0.841
FS2	0.802	0.949
FS3	0.904	0.971
FS4	0.827	0.834
FS5	0.712	0.974
FS6	0.852	0.948

Table 12: Taste Evaluation of Sumatriptan succinate (1:1)

Volunteers	**Bitterness level after**				
	10sec	30 sec	60sec	90sec	120 sec
1	X	0	0	0	0
2	0	0	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
5	0	0	0	0	0
6	X	X	0	0	0
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	0	0	0	0	0

Table 13: Taste Evaluation of Sumatriptan succinate (1:2)

Volunteers	Bitterness level after				
	10sec	30 sec	60sec	90sec	120 sec
1	X	0	0	0	0
2	0	0	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
5	0	0	0	0	0
6	X	X	0	0	0
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	0	0	0	0	0

Table 14: Taste Evaluation of Sumatriptan succinate (1:3)

Volunteers	Bitterness level after				
	10sec	30 sec	60sec	90sec	120 sec
1	X	0	0	0	0
2	0	0	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
5	0	0	0	0	0
6	X	X	0	0	0
7	0	0	0	0	0
8	0	0	0	0	0
9	0	0	0	0	0
10	0	0	0	0	0

Table 15: Short time stability studies of FS4 formulation

S.NO	Formulation code	Time (weeks)	% drug content		
			4^0C	Room Temperature	45^0 C
1	FS4	0	99.8±0.02	99.9±0.01	99.8±0.02
2	FS4	1	99.6±0.03	99.8±0.02	99.7±0.04
3	FS4	2	99.6±0.04	99.7±0.02	99.5±0.03
4	FS4	3	99.5±0.02	99.7±0.04	99.4±0.03
5	FS4	4	99.4±0.02	99.6±0.03	99.3±0.04
6	FS4	5	99.3±0.05	99.5±0.02	99.2±0.04
7	FS4	6	99.2±0.04	99.4±0.02	99.0±0.03
8	FS4	7	99.0±0.02	99.3±0.03	98.8±0.04
9	FS4	8	98.9±0.03	99.1±0.02	98.5±0.04

DISCUSSION

The bitterness threshold of Sumatriptan succinate was recognized by the human volunteers. From the majority of volunteers the threshold value of Sumatriptan succinate was found to be same for 1:2 and 1:3. Hence 1:2 was selected for further studies

Optimization:

The optimized percentage drug loading was found to 96.41±0.17 for Indion 204 and 95.86±013 for Indion 234 with swelling time 30 min. The equilibrium ion exchange in solution occurs stoichiometrically and hence affected by stirring time. The optimized percentage drug loading (w/w) was found to be 95.79±0.13 for Indion 204 and 94.76±011 for Indion 234 with stirring time 120 minutes. The optimized percentage drug loading (w/w) was found to be 95.76±0.15 for Indion 204 and 95.54.±0.04 for Indion 234 with pH 4. The optimized percentage drug loading (wt/wt) was found to be 97.89±0.06 for Indion 204 and 96.73±0.09 for Indion 234 at 50^0C.

Physical properties of tablet blend:

The tablet blend was evaluated for different derived properties. Angle of repose was found to be between 25^0-30^0 .Bulk density and tapped density was found to be between 0.453-

0.490g/cc and 0.478-0.588g/cc, which indicated good free flowing property. carr's index was found to be between 15.03%-16.89%. The results indicated that the flow ability of blend is significantly good. All the tablets passed weight variation test as the percent weight variation was within the pharmacopoeial limits. Hardness was shown in the range of 3.0-3.3 kg/cm^2. The results of friability indicate that the tablets withstand mechanical shocks during handling. The friability values of none of the formulations exceeded 1%. Thickness of all the tablets was between 2.261±0.03 – 2.32±0.02mm showing fairly uniform tablet. The wetting time of the formulations (FS1-FS6) was found to be between 25.81sec to 29.57sec, Water absorption ratio was found to be between 128.56% to 143.07%, *In vitro* disintegration time was found to be between 27.19 sec to 30.45 sec, *In vitro* dispersion time was found to 28.99 sec to 30.88 sec, % drug content was found to be between 99.38±0.082 to 100.19±0.063.The Prepared tablets were evaluated for *in vitro* drug release studies and maximum drug release was 98.48±0.21% in 30 minutes. The drug release from Orodispersible tablets containing superdisintegrants was found to be in order:

FS4>FS1>FS3>FS6>FS5>FS2; [Crospovidone (Indion 234) > Crospovidone (Indion 204) > Sodium starch glycolate (Indion 204) > Sodium starch glycolate (Indion 234) > carmellose Sodium (Indion 234) > Carmellose (Indion 204)]

The obtained drug release data was fitted in various kinetic models in-order to elucidate the mode of mechanism. The kinetics and release mechanism was estimated by the regression plots for zero order and first order. When R^2 values of regression plots for first order and zero order were considered it was found that R^2 values of first order were found to be more than the zero order. Hence it was confirmed that drug release from Sumatriptan succiante ODT's FS1-FS6 followed first order release and the release rate is dependent on concentration or amount of drug incorporated.

Taste evaluation:

Taste evaluation revelaed that Indion 204 and Indion 234 masked the bitter taste of the drug completely.

Characterization of drug in orodispersible tablets:

The best formulation selected was investigated for chemical interactions. IR analysis revealed that there was no known chemical interaction of drug with Ion exchange resins, superdisintegrants and other ingredients in prepared orodispersible tablets. The best formulation FS4 shows characteristic peak at 1541.97cm^{-1}. This indicated that there was no appreciable change in the position and intensity of peak with respect to the pure drug and resin spectrum

Short term stability studies:

Short term stability studies (FS4) were conducted for best formulation of Sumatriptan succinate tablets at 4^0 C, at room temperature for 8 weeks and it was found that there was no significant change in % drug content after 8 weeks.

CONCLUSION:

Pharmaceuticals complexed using ion exchange resin have shown improved organoleptic characteristics and better patient compliance.Indion 204 and Indion 234 weak cation exchange resin offers good taste masking of Sumatriptan succinate and its formulation into orodispersible tablet offers advantages over conventional tablet

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How to cite this article:
A. Seetha Devi*,Tabasum.Md ,, formulation and evaluation of taste masked orodispersible tablets of sumatriptan succinate, 6(1): 2456 - 2467. (2015)