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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET OF RIZATRIPTAN BENZOATE WITH NATURAL SUPERDISINTEGRANT

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ABSTRACT

Fast dissolving tablets are dissolved or disintegrated without water within few second to few minutes. Rizatriptan Benzoate is an antimigraine agent used in treatment of migraine associated with severe one-sided throbbing. In the present, study, fast dissolving tablets of Rizatriptan Benzoate was prepared by direct-compression method after incorporating superdisintegrants sodium starch glycolate (SSG), Crospovidone and yellow potato starch in different concentrations. Six formulations having superdisintegrants with different concentration levels were prepared to assess their efficiency and critical concentration level. Yellow potato starch could be an effective tablet disintegrates. All the formulations were evaluated for hardness, friability, wetting time, disintegration time and in-vitro dissolution study. Formulation containing yellow potato starch shows the fast disintegration of tablet as compared to other superdisintegrants. It was concluded that Yellow potato starch is to be good superdisintegrant.

KEYWORDS : *fast dissolving tablets, Rizatriptan Benzoate, Sodium Starch Glycolate, Crospovidone, Yellow potato starch.*

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INTRODUCTION

Fast disintegrating tablets (FDTs) have received ever-increasing demand during the last decades and the field has become a rapidly growing area in the Pharmaceutical industry. These tablets dissolve or disintegrate in the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. Such tablets readily dissolve or disintegrate in the saliva generally within <60 seconds. Fast or mouth dissolving tablets have been formulated for pediatric, geriatric, bedridden patients and for active patients who are busy and travelling and may not have access to water. Such formulations provide an opportunity for product line extension in the many elderly persons will have difficulties in taking

conventional oral dosage forms (viz., solutions, suspensions, tablets, and capsules) [1].Rizatriptan Benzoate is an antimigraine agent used in treatment of migraine associated with severe one-sided throbbing headache, which is followed by intense pain. Hence to provide quick action there was a need to develop fast dissolving tablets with Natural superdisintegrants. It is a 5-Hydroxy Tryptamine (1B/1D) [5HT (1B/1D)] receptor agonist used in fast dissolving tablet providing quick action[2] Rizatriptan Benzoate is incompletely absorbed from the gastrointestinal tract and has an oral Bioavailability of only 45 %. This is because of its poor absorption in lower gastrointestinal tract. It undergoes hepatic first pass metabolism and its elimination half-life is 2 to 3 hours. In the present study, an attempt was made to develop fast dissolving tablets of Rizatriptan benzoate and to improve its bioavailability.[3, 4, 5] The fast disintegrating tablets prepared by direct compression method, in general, are based on the action established by super disintegrates such as sodium starch glycolate, crospovidone and yellow sweet potato starch. The objective of the present work is to develop fast dispersible Rizatriptan Benzoate tablets and to study the effect of functionality differences of superdisintegrant on the tablet properties.

MATERIALS AND METHOD

Rizatriptan Benzoate was obtained as a gift sample from Cipla Ltd. Mumbai, sodium starch glycolate, crospovidone, microcrystalline cellulose, talc, magnesium stearate, saccharine sodium were purchased from S.D. Fine chemicals Mumbai, All reagents and solvents used were of analytical grade Yellow sweet potato starch were extracted in lab.

STARCH EXTRACTION [6]

Yellow starch was extracted from yellow sweet potato (*Ipomoea batatas*) yellow sweet potato starch were sliced and dried at 45ºC. for 24h. Dried yellow sweet potato powder was subsequently dispersed in 0.05% Sodium Hydroxide. After 12h, the supernatant layer was removed. The solvent was rinsed off with purified water and let stand for 12h. The suspension was filtered and the powder was dried at 45ºC for 24h.

PREPRATION OF RIZATRIPTAN BENZOATE FAST DISSOLVING TABLET

Rizatriptan Benzoate and all other ingredients were passed through sieve no. 60. Rizatriptan Benzoate, excipient and superdisintegrant were mixed in mortar and mixed it well by pestle. Talc was added and triturated to get uniform mixture. The tablets were prepared by direct compression on a rotary tablet press, fitted with concave punches of 6 mm diameter. The turret was rotated at a fixed speed of 30 rpm. The compositions of various batches are shown in Table 1.

Table No. 1. Composition of Rizatriptan Benzoate fast dissolving tablet.

Sr.no	Ingredients	F1	F2	F3	F4	F5	F6
1	Rizatriptan benzoate	10	10	10	10	10	10
2	Yellow sweet potato starch	5	10	--	--	--	--
3	Sodium starch glycolate	--	--	5	10	--	--
4	Crospovidone	--	--	--	--	5	10
5	Micro crystalline cellulose	40	35	40	35	40	35
6	Talc	2	2	2	2	2	2
7	Lactose	38	38	38	38	38	38
7	Saccharine sodium	2	2	2	2	2	2
8	Magnesium stearate	3	3	3	3	3	3
9	Total weight	100	100	100	100	100	100

Pre compression parameters:

Bulk density[7, 8, 9]

Granular powder weighing 10 g was placed in 100ml measuring cylinder. Volume occupied by the powder was noted without disturbing the cylinder and bulk density was calculated by the following equation.

Bulk density = weight of sample / Volume of packed

The experiment was repeated for three times.

Tapped Density[7, 8, 9]

Granular powder weighing 10g was placed in 100ml measuring cylinder. The cylinder was then subjected for the fixed number of taps (≈100) until the powder bed has reached the minimum. The final volume was recorded and the tap density was calculated by the following equation.

True density = Mass of bulk sample / Volume of bulk drug on tapping

The experiment was repeated for three times

Carr's Index[7, 8, 9]

Carr's percent compressibility was calculated for granules prepared by using the equation

[δ tap- δ bul / δ tap] × 100

Where,

δ tap= Tapped density or True density

δ bul = Bulk density.

Hausner ratio

Tapped density and bulk density were determined and the Hausner ratio was calculated by the following formula,

Hausner ratio = δ tap / δ bul

Where, δ tap= Tapped density or True density

δ bul = Bulk density.

Angle of Repose[7.9,10]

It is the maximum angle that can be obtained between the free standing surface of the granule heap and the horizontal plane. The angle of repose can be calculated by the following formula,

tanθ = h / r OR θ

= tan- h/r

Where,

θ = Angle of repose

h = height of the pile

r = radius of plane surface occupy by the powder.

Post compression parameters:

Thickness and Diameter

Tablet thickness and diameter were measured using Vernier Caliper. The limit specified was average thickness ± 5% deviation.

Crushing strength[11]

The crushing strength of six tablets at each compression force level was determined using Erweka hardness tester. Hardness and friability tests were carried out according to EP IV for uncoated tablets

Friability

Twenty tablets were weighed and placed in the Roche friabilator and apparatus was rotated at 25 rpm for 4 minutes. After completion of revolutions the tablets were dedusted and weighed again. The percentage friability was measured using the formula

% F = {1- (wt/w)} X 100

Where,

% F = friability in percentage

W = Initial weight of tablet

Wt = Weight of tablets after revolution

Weight variation[15, 16]

Weight variation of sustained release tablet was carried out using 10 tablets. The maximum percentage deviation allowed was ± 10 % of the average weight of tablet. 10 tablets were weighed individually. The Average weight and standard deviation calculated.

Wetting time[11, 16]

A piece of tissue paper folded twice was placed in Petri dish. A sample of final tablet was placed in Petri dish (10cm in diameter) containing 10ml simulated saliva pH (Phosphate buffer pH 6.8) at room temperature. The tablet was put on the paper and time required for the complete wetting of tablet was measured. The wetting time is that necessary for the complete wetting of the tablet.

De-aggregation time[12,13]

De-aggregation time is the time required to transform a tablet in to small fragments when immersed in water at room temperature without stirring. The de-aggregation test was performed according to the methods described in EP IV Ed. *In vitro* de-aggregation time was performed using

Phosphate buffer pH6.8, 900ml was used as a deaggregating medium and temperature was maintained at 37 ± 2°C and time in seconds was noted for the complete deaggregation of the tablet with no population of mass remaining in the apparatus.

***In vitro* Dissolution test**[14, 15]

In vitro dissolution test was performed at 37 ^{0} C using USP XXVIII rotating paddle method at 50 rpm with 900ml phosphate buffer (pH 6.8) as a dissolution medium which maintained at 37 ±0.50 C. Aliquot of dissolution medium (10ml) was withdrawn at specific time interval (Initially 2.5 & then after 5min.) and was filtered. The amount of drug dissolved was determined by UV Spectrophotometer (Shimadzu 1800, Japan.); by measuring the absorbance of sample at 227.5 nm. From this results the % drug release was calculated and recorded.

Identification of Drug by IR

The IR spectrum of the pure Rizatriptan Benzoate sample recorded by FTIR spectrum is shown in Figure No.1. This was compared with standard functional group frequencies of Rizatriptan Benzoate as shown in Table No.2

Fig. No.1. IR Spectra of Rizatriptan Benzoate

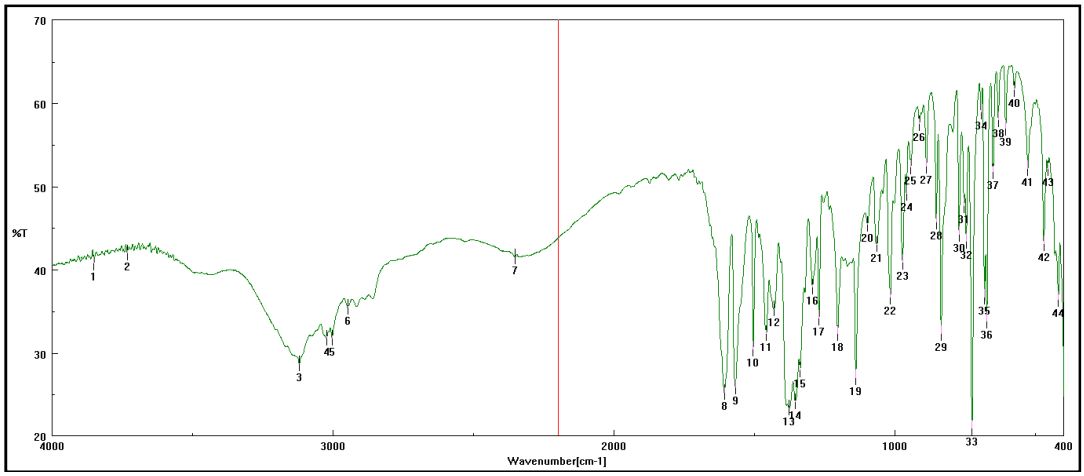


Table No. 2 Reported and observed IR frequencies of Rizatriptan Benzoate

Functional group	Reported Frequencies	Observed Frequencies
C- N	1360-1250	1300
C- H	3020-3000	3010
OH	3400-3300	3350
C-O	1260-1000	1200
C=C	1600	1500
N-H	3500-3300	3170

Table no.2 showed that, functional group frequencies of Rizatriptan Benzoate were in reported range which indicates that the obtained sample was of Rizatriptan Benzoate and pure

RESULT AND DISCUSSION

In present study, Rizatriptan Benzoate fast dissolving tablet were prepared by using various excipients specifically by using super disintegrants, e.g. Yellow sweet potato starch, MCC, Cross povidone. Total six lots of tablets, F1-F6 were assessed by direct compression technique. Results of the pre compression parameter evaluated were within prescribed limits and indicated good free flowing property which is described in table no.3.

Table no. 3. Results of pre compression parameter.

Formulation	F1	F2	F3	F4	F5	F6
Residual humidity (%RH)	2.5	2.7	3.1	2.7	2.6	2.9
Bulk density	0.43	0.48	0.54	0.48	0.45	0.50
True density	0.56	0.53	0.59	0.53	0.52	0.58
Carr's Index (%±0.05)	10.87	12.08	11.97	15.95	8.98	9.53
Hausner ratio	1.222	1.023	1.101	1.652	1.076	1.023
Angle of repose	30^0	31^0	28^0	30^0	30^0	29^0

The data obtained from all the post compression parameter evaluated are such as thickness, diameter, crushing strength, friability, weight variation, wetting time, and de-aggregation time are shown in table no.4

The hardness was found in the range of 3-4kg/cm^2.in all the formulation indicating good mechanical strength having a capability to withstand physical and mechanical stress condition while handling and transportation.

All of the 6 formulations were having friability values less than one which meets with the IP [Indian Pharmacopoeia] limits. All the tablets passed weight variation test as the % weight variation was within Pharmacopeial limit. The values of weight variation indicate efficient mixing of all the excipients with the drug. The result of *in vitro* wetting time and de aggregation time of the entire tablet were found to be within prescribed limit and safety criteria of Rizatriptan Benzoate fast dissolving tablets.

Table No. 4. Result of post compression parameter study

Formulation	F1	F2	F3	F4	F5	F6
Thickness (mm)	4.2	4.2	4.2	4.2	4.2	4.2
Diameter	9.56	9.56	9.56	9.56	9.56	9.56
Crushing Strength (kg/cm^2)	3.15	3.20	3.00	3.50	3.50	3.00
Friability	0.46	0.60	0.58	0.97	0.98	0.76
Weight variation	100.2 ±0.123	100.8 ±0.326	100.6 ±0.287	100.0 ±0.643	100.4 ±0.123	100.0.2 34
Wetting time	33.34	35.45	34.99	110.23	119.98	99.08
De-aggregation time	32.34	37.98	35.43	105.97	110.86	97.87

Dissolution rate:

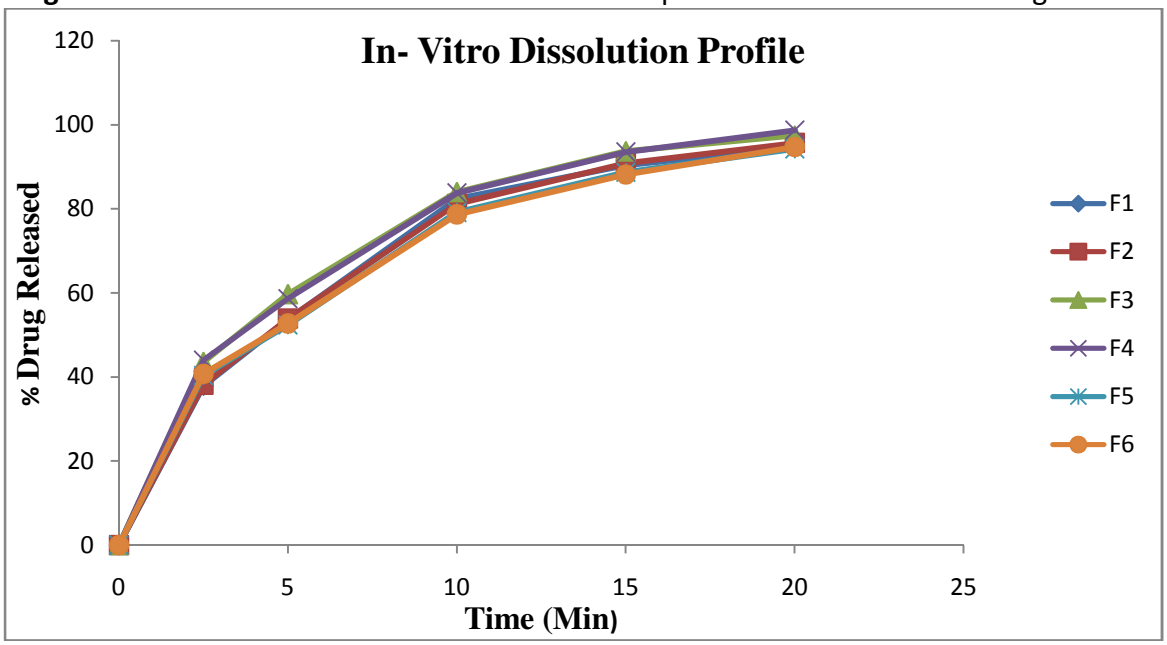
In condition simulating the buccal cavity the dissolution rate and solubility of Rizatriptan Benzoate was studied. In addition we found that the dissolution rate was good i.e. minimum 2.5 min and maximum 20 min only.

Table No. 5. In vitro dissolution profile data for F1 to F6 formulations

Time (Min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
2.5	37.88	38.16	43.54	43.54	40.32	40.69
5	53.68	53.87	59.68	58.68	52.34	52.69
10	82.35	81.14	83.97	83.97	79.12	78.65
15	90.35	90.88	93.65	93.65	88.69	88.16
20	94.57	95.64	97.41	98.68	94.21	94.67

Overall the Rizatriptan Benzoate formulations showed an average of 94-99% drug release range at the end of 20 min (table no. 4) which is as per IP specifications of 90-110% and in vitro drug release of all formulations showed in figure No 2. The IR Spectroscopy was used to confirm the structure of Rizatriptan Benzoate in the given dosage form.

Figure No. 2 : In vitro dissolution Profile of Rizatriptan Benzoate Fast Dissolving Tablet.



CONCLUSION

On the basis of evolutionary result of precompression and post compression studies of all the formulation, we conclude that all the technological / evolutionary parameters of mouth dissolving tablet of Rizatriptan Benzoate with various superdisintegrants. Among that the yellow potato starch is having the better disintegrating property, it is cheap and eassy for extraction hence it can be used as superdisintegrants.

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