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"FORMULATION DEVELOPMENT & EVALUATION OF FAST DISSOLVING TABLET OF RIZATRIPTAN BENZOATE"

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ABSTRACT

The purpose of this investigation was to to develop fast dissolving tablet of Rizatriptan Benzoate using various concentration of disintegrants and superdisintegrants along with directly compressible excipients. Rizatriptan benzoate use to treat migraines. Fast dissolving tablet of Rizatriptan benzoate containing crospovidone-xl, croscarmellose sodium, avicel PH-102, aspartame, magnesium Stearate, Aerosil, menthol, pearlitol SD-200 The formulation were evaluated for disintegration time, in vitro dissolution, hardness, friability, weight variation and thickness, water absorption ratio.

KEYWORD: superdisintegrant, Fast dissolving Tablet, Migraine, Rizatriptan benzoate.

INTRODUCTION

Now a day more research carried on patient compliance dosage forms. The fast dissolving tablet is one of the very popular patient compliance dosage forms.[1] The tablet is widely used dosage form due to its self administration, compactness, and ease of manufacturing.[2] Oral dispersible tablet (ODT) are oral solid dosage forms that disintegrate in the oral cavity in easy swallow residue.[3,4] oral dispersible tablet also known as mouth dissolving tablets. Fast dissolving dosage forms, are a relatively novel technology mainly include rapid disintegration or dissolution of the dosage form.[5] the tablet disintegrate immediately after coming contact with saliva pH 6.8 completely disintegrate with in 90 sec (1.30 min) and then active moiety absorbed through the gastrointestinal epithelium to reach the target area an give their action.[6]

Advantage of fast dissolving Drug delivery system.[2,4,6]

- it is easy to administration without Water.
- rapid disintegration produce rapid dissolution ultimately fast onset of action is occurs.
- pregastric bioavailability increase bioavailabity of drug.
- chewing is not required.
- useful in cases like motion sickness, allergic attack and coughing.

Characterization of drug

❖ **I.R. spectrum of drug**

IR spectrum of drug was measured in the solid state as potassium bromide dispersion. FTIR spectra of a drug were obtained using a FTIR spectrometer (8400S, Shimadzu, Japan). The sample was previously ground and mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:100 (sample: KBr) ratio, respectively. The pellets were prepared by compressing the powders, under force of 12 tones for 5 min in a hydraulic pressed and IR was taken.

❖ **DSC**

Melting point of drug was determined using DSC. Thermo grams for a drug were obtained using DSC (METLLER DSC 1 STAR SYSTEM, Zürich, Switzerland).

Compatibility

❖ **Fourier Transform Infrared (FTIR) Spectroscopy**

Infrared spectroscopy was used to predict possible drug – excipients interaction. IR spectrum of drug was measured in the solid state as potassium bromide dispersion. For that drug, polymers and physical mixture were filled in prewashed and dried ampoules and sealed with aluminum paper. The sealed ampoules were kept at 37 °C±0.5 °C for 28 days in stability chamber. After one month stability period ampoules were taken from the stability cabinet and test samples were subjected to FTIR by preparing transparent pellets with potassium bromide (KBr) in ratio of 1:100 test samples to KBr.

MATERIAL AND METHOD

Rizatriptan benzoate was received from gen pharma pune MCC-102, Aspartame, Aerosil, Magnesium stearate, Pearlitol SD-200, ac-di-sol, Menthol, crospovidone-XL and Croscarmellose sodium purchased from Himedia.

❖ **Method**

oral dispersible tablet ware prepared by direct compression method. Weigh all ingredients except magnesium Stearate and pass through sieve #40. Blend for 10 min. then add magnesium Stearate (#60) and compress on compression machine. Compress tablet evaluated further.

Formulation Development Trial

Table 1: Formulation development batches

Tablet ingredient	Formulation Batches (mg)						
	P0	**F1**	**F2**	**F3**	**T4**	**T5**	**T6**
Rizatriptan benzoate	10	10	10	10	10	10	10
Crospovidone-XL+ Croscarmellose sodium	-	6	6	6	6	6	6
Avicel PH-102	30	30	30	30	30	30	30
Aspartame	3	3	3	3	3	3	3
Aerosil	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Pearlitol SD-200	102	96	96	96	96	96	96
Menthol	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Magnesium stearate	2	2	2	2	2	2	2
Total Weight	150	150	150	150	150	150	150

Po = without superdisintegrants

F1= 1:1 superdisintegrants

F2 = 1:2 superdisintegrants

F3 = 1:3 superdisintegrants

T4 = 1:1 co-processed superdisintegrants

T5 = 1:2 co-processed superdisintegrants

T6 = 1:3 co-processed superdisintegrants

Evaluation

❖ **Physical Parameter of Blend**

In this section carried out the bulk density, tapped density, carrs index, hausner's ratio of powder blend.

❖ **Weight variation test**[7]

20 tablet ware randomly selected and weighed to determine the average weight and ware compared with individual tablet weight. The percentage weight variation was calculated. As per Indian pharmacopoia specification tablet with an average weight between 80-250 mg, the

percentage deviation should not more than ± 7.5 % and tablet with an average weight more than 250 mg should not be more than ± 10 %.

$$\% \text{ Deviation} = \frac{\text{Tablet weight - Average weight}}{\text{Tablet weight}} \times 100$$

- **Hardness[7]:** The hardness ware measured on the dr. schleuniger hardness tester.
- **Thickness[7]:** Thickness of the tablet is important for uniformity of tablet size. Thickness of tablet was determined by using vernier caliper (Mitutoyo).
- **Friability[7]:** The friability of tablet was measured by using electro lab fraibilator. The limit of friability 0.5-1 % according to I.P. at 25 RPM per min for 4 min.

$$\% \text{ Friability} = \frac{\text{(Initial weight – Final Weight)}}{\text{Initial Weight}} \times 100$$

- **Water absorption ratio[8]**

water absorption ratio, which is criteria for understanding the capacity of disintegrates to swell in the presence of little amount of water. Weight of the tablet after and before test was taken. Water absorption ratio (R) is calculated using following formulae.

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

W_a = weights of the tablets after water absorption test.

W_b= Weights of the tablet before water absorption test.

- **Disintegration time[9]:** Disintegration test carried out at 37± 2 ^{0}c in 900 ml of distilled water, six tablets were taken for the test.
- ***In vitro* Dissolution[10]:** The dissolution test was carried out with following parameter

Table 2: *In vitro* Dissolution parameter

Apparatus	**USP Type II**
Speed of rotation	50 RPM
No. Of Tablet	6 tab
Temperature	37± 2^{0}c
Time	30 min
Test Medium	6.8 PH buffer
Volume of test medium	900 ml
ƛ max	225 nm

Content uniformity[8, 9]: The amount of active ingredient(s) is determined by the method described in assay and amount of active ingredient is calculated. New method was used for determination of drug content given below. Twenty tablets from each batch were weighed accurately and powdered powder equivalent to 10 mg Rizatriptan Benzoate was shaken with 100ml of pH 6.8 Phosphate buffer in 100 ml amber colored volumetric flask and from this 10 ml was pipette out and then dilute up to 100 ml. From standard solution again 10 ml pipette out and diluted up to 100 ml in 100 ml amber colored volumetric flask. Resulting solution was filtered and assayed at 225 nm, using a UV- visible beam spectrophotometer (UV-1700 Shimadzu) and content of Rizatriptan Benzoate was calculated.

Preparation of co-processed superdisintegrants[11]

The co-processed superdisintegrants were prepared by solvent evaporation method. A blend of polyplasdone-XL and Crosscarmellose sodium in the ratio (1:1, 1:2, 1:3) was added to 10 ml of ethanol. The content of beaker (250 ml capacity) were mixed thoroughly and stirring was continued till most of ethanol evaporated. The wet coherent mass was granulated through # 44mesh sieve. The wet granules were dried in a hot air oven at 60^0 c for 20 min. the dried granules were sifted through # 44 mesh sieve and stored in airtight container till further use.

RESULT AND DISCUSSION

❖ **Characterization of API**

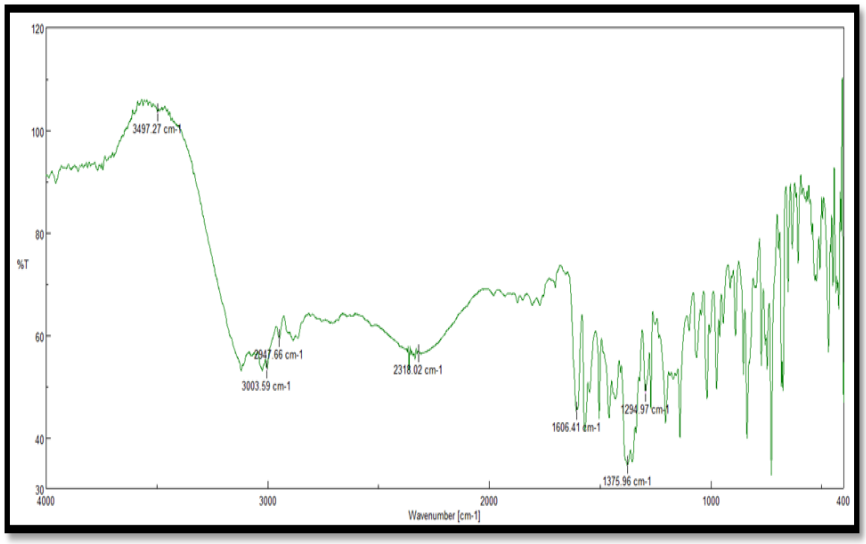

Figure 1: I.R. specrtrum of drug

❖ **DSC of API**

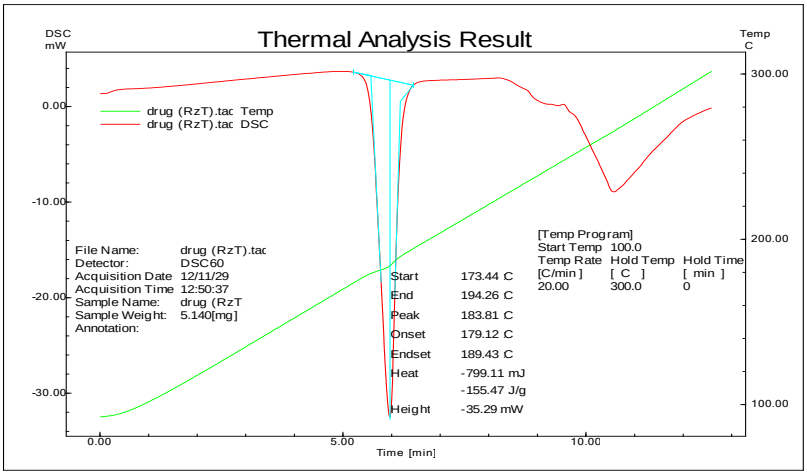

Figure 2: DSC of API

Compatibility

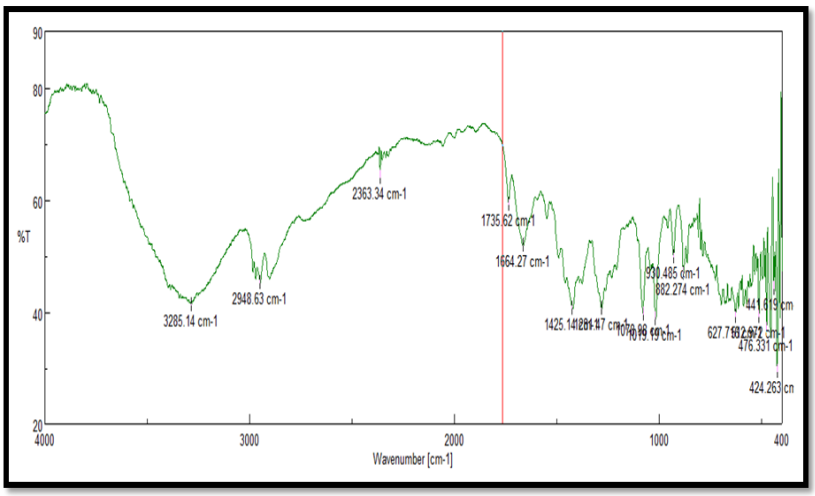

Figure 3: IR spectra of API + Excipient physical mixture

Physical Parameter of Blend

Table 3: Physical Parameter of Blend

Formulation batch	Evaluation Parameters					
	Angle of repose	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Compressibility Index (%)	Hausner's Ratio	Flowability
P0	29.53	0.5357	0.612	10.71	1.1200	Good
F1	25.11	0.4137	0.4615	10.35	1.1155	Good
F2	25.20	0.4081	0.4580	10.89	1.1222	Good
F3	27.29	0.4379	0.5042	13.14	1.1514	Good
T4	25.82	0.3797	0.4347	12.65	1.1450	Good
T5	27.68	0.4651	0.5357	13.17	1.1518	Good
T6	28.89	0.4166	0.4761	12.49	1.1430	Good

Evaluation of Compressed tablets

Table 4: Evaluation of Compressed tablets

Evaluation Parameters	Formulation batches						
	PO	F1	F2	F3	T4	T5	T6
Weight Variation (Kg/cm^2)	149.33	150.33	150.66	149.66	150.66	149	149.25
Thickness(mm)	4.73	4.76	4.7	4.8	4.66	4.76	4.8
Hardness(Kg/cm2)	3.60	3.09	3.38	3.42	3.38	3.19	3.36
Friability(%)	0.47	0.62	0.53	0.50	0.59	0.67	0.56
Water Absorption Ratio (%)	53.64	93.33	86.00	83.89	71.14	76.51	78.66
D.T.(sec)	105	23	33	38	53	58	60
Drug Content(%)	99.36	99.65	99.45	98.06	98.55	98.06	99.75

Dissolution profile of formulation batches.

Table 5: Dissolution profile of formulation batches

Time (min)	Cumulative % drug release						
	P0	F1	F2	F3	T4	T5	T6
2	26.88	62.49	56.21	51.12	59.20	47.83	33.16
4	30.00	75.24	68.10	62.14	69.29	58.87	51.73
6	38.12	84.00	76.89	70.97	76.60	68.60	64.76
8	44.09	97.06	88.82	80.87	89.70	78.23	72.63
10	54.96	99.73	93.00	90.37	93.59	86.27	80.42
12	63.67		98.87	98.58	96.55	95.09	91.89
14	69.38				98.89	98.60	98.31
18	73.87						
22	78.59						
26	86.38						
30	94.07						

In present study, Fast dissolving tablet of Rizatriptan Benzoate were prepared by using novel co-processed superdisintegrants. The study was performed in two stages, In first stage the novel co-processed superdisintegrants prepare in different ratio by using solvent evaporation method and also physical mixture of superdisintegrant prepare in same ratio. While second stage involved formulation and evaluation of the fast dissolving tablet of Rizatriptan Benzoate by use of co-processed superdisintegrants. Formulation was developed with the aim to provide a convenient means, of taking the medication, for patients suffering from migraine.

- Preformulation studies were carried out during the stage of this work. It has found that Rizatriptan Benzoate is having maximum absorption at wavelength 225 nm.

- The drug-polymer compatibility study was carried out to determine the interactions between the drug and the polymers used in the study. The IR revealed that, polymers and excipients used were compatible with drug.

- The fast dissolving tablet were formulated using the co-processed and physical mixture of superdintegrants (Crospovidone-XL, and Croscarmellose sodium) by direct compression technique, disintegrant agent used as MCC pH-102 and Pearlitol SD-200.

- Amongst all the formulations, formulation containing 1:1 co-processed superdisintegrants and MCC pH-102 as disintegrating agent and perlitol SD-200 as diluents has shown excellent in vitro disintegration time and in vitro percent dissolution, compared to other formulations. Overall, formulations F1, F2, F3 and T4, T5, T6 containing co-processed and physical mixture of superdisintegrants respectively at 4% and consisting MCC pH 102 at 20% concentration, tablets disintegrated rapidly to release the drug.

- From above discussion co-processed supersintegrants consisting of crospovidone-XL croscarmellose sodium exhibited good flow and compression characteristics. Rizatriptan Benzoate tablets containing co-processed superdisintegrants exhibit quick disintegration and improved drug dissolution.

- It can be concluded from the present work that co-processed superdisintegrants of crospovidone-XL and croscarmellose are superior to physical mixture of crospovidone-XL and croscarmellose used in Rizatriptan Benzoate fast dissolving tablets and it may increase the bioavailability.

CONCLUSION

All tablets met the compendia limits in terms of physical parameters, disintegration and dissolution efficiency. From above discussion co-processed supers integrants consisting of Crospovidone-XL, Croscarmellose sodium exhibited good flow and compression characteristics. Rizatriptan Benzoate tablets containing co-processed superdisintegrants exhibit quick disintegration and improved drug dissolution. It can be concluded from the present work that co-processed superdisintegrants of crospovidone-XL and croscarmellose are superior to physical mixture of crospovidone-XL and croscarmellose used in Rizatriptan Benzoate fast dissolving tablets and it may increase the bioavailability.

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