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## “Formulation, Evaluation and Validation of Orally Disintegrating Rizatriptan Benzoate Tablet”

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### ABSTRACT

The Current investigation deals with safety, efficacy and quick onset of action of existing drug molecule through novel concepts of drug delivery. Orally disintegrating tablets of Rizatriptan benzoate were prepared by direct compression method to provide faster relief from pain to migraine sufferers. About eight formulations for the present study were carried out based on  $3^2$  factorial design technique for each set of superdisintegrants. *Psyllium mucilage*, *Musa paradisiaca* were used as superdisintegrants, while microcrystalline cellulose was used as diluent. The prepared batches of tablets were evaluated for weight variation, hardness, friability, wetting time, *invitro* dispersion time, drug content and *invitro* dissolution studies. The formulation containing combination of *Psyllium mucilage*, *Musa paradisiaca* showed rapid *invitro* dispersion time as compared to other synthetic & natural formulations.

A simple, sensitive, rapid, precise, cost effective and reproducible UV spectrophotometric method has been developed for estimation of Rizatriptan Benzoate tablet dosage form. Rizatriptan benzoate shows maximum absorbance at 225 nm with molar absorptivity of  $1.619 \text{ A}^\circ$ . Beer's law was obeyed in the concentration range of 1-10  $\mu\text{g/ml}$ . Results of analysis were validated by statistical analysis and by recovery studies. The method was validated with respect to linearity, precision, LOD, LOQ, Sandell's sensitivity and specificity. The proposed method was found to be accurate and precise for routine estimation of Rizatriptan Benzoate in bulk and tablet dosage forms. The optimized formulation dispersed in 15-30 seconds. It also showed a higher water absorption ratio and 99.60% of drug is released within 2 min. & 15 second.

**KEYWORDS :** Orally disintegrating tablets, Superdisintegrants, Rizatriptan benzoate, Factorial design technique, Direct Compression, UV spectrophotometer.

### INTRODUCTION

Tablets may be defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared either by compression or molding methods. Tablets remain popular as a dosage form because of the advantages, afforded both to the manufacturer [eg. simplicity & economy of preparation, stability and convenience in packing, shipping, and dispensing] and the patient [eg. accuracy of dosage, compactness, poor stability, blendness of taste and ease of administration].<sup>[1]</sup> Although tablets are more frequently discoid in shape, they also may be round, oval, oblong, cylindrical or triangular. They may differ greatly in size and weight depending on the amount of drug substance present and the intended method of administration.<sup>[1]</sup>

### **ORALLY DISINTEGRATING TABLETS :-**

Most of the oral pharmaceutical dosage forms like conventional tablets and capsules are formulated to be swallowed or chewed. As a result children, bedridden patients and elderly patients have difficulty in swallowing these dosage forms. To overcome this drawback novel drug delivery systems like orally disintegrating tablets have been developed which disintegrate/dissolve/ disperse in saliva within few seconds without water. United States of America Food and Drug Administration (USFDA) define ODT as “A solid dosage form containing medicinal substances or active ingredient which disintegrates rapidly usually within a matter of seconds when

placed upon a tongue".<sup>[2]</sup> Many patients have difficulty in swallowing tablets and hard gelatin capsules and they do not take medications as prescribed, and 50% of the population is affected by this problem, which results in noncompliance and ineffective therapy. The demand for solid dosage forms that can be dissolved and suspended in water, chewed, or rapidly dissolved in the mouth is strong in the pediatric and geriatric markets, with further application to other patients who prefer the convenience of a readily administered dosage form. Because of the increase in the average human life span and the decline in swallowing ability with age, oral tablet administration to patients is a significant problem and has become the object of public attention.<sup>[3]</sup> The problem can be resolved by the creation of Orally Disintegrating Tablets (ODTs). ODTs rapidly disintegrate in the mouth without chewing upon and without the need for water, unlike other oral drug delivery systems. The dosage forms are placed in the mouth, allowed to dissolve in the saliva, and then swallowed in the normal way. Less frequently, they are designed to be absorbed through the buccal and esophageal mucosa as the saliva passes into the stomach. In the latter case, the bioavailability of a drug from fast dispersing formulations may be even greater than that observed for standard dosage forms. Furthermore, side effects may be reduced if they are caused by first pass metabolites.<sup>[4]</sup> The natural superdisintegrants involve various natural substances like gums, mucilages, and other substances of natural origin which are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. Some natural substances like gum karaya, modified starch and agar have been used in the formulation of ODT's and dispersible tablets.<sup>[5]</sup> The major **advantage** of the ODT formulation is that it combines the advantages of both liquid and conventional tablet formulations. It provides the convenience of a tablet formulation, and also allowing the ease of swallowing provided by the liquid formulation. The various technologies used to prepare ODT's include direct compression, sublimation, tablet moulding, spray drying, freeze drying and mass extrusion.<sup>[6-8]</sup> The new generation anti-migraine drug, **Rizatriptan benzoate** is a potent and selective 5- hydroxy tryptamine<sub>1B/1D</sub> receptor agonist and is considered more effective than the traditional triptans for the treatment of acute migraine attack.<sup>[9]</sup> Chemically it is 3-[2-(dimethyl amino) ethyl]-5-(1H- 1, 2,4-triazol-1-ylmethyl) indole monobenzoate. A 10mg dose of Rizatriptan benzoate is equipotent to a 100 mg of Sumatriptan, the traditional antimigraine drug. The bioavailability of Rizatriptan benzoate is about 45% which is superior to a poor 14-17% of Sumatriptan.<sup>[10]</sup> Migraine is a

syndrome that affects a significant fraction of the world population, with a higher prevalence in women (15%) than in men (6%).<sup>[11]</sup> Migraine is characterised by an intense and throbbing unilateral headache associated with anorexia, nausea, vomiting, photophobia, phonophobia and/or diarrhoea (common migraine). Sometimes the headache may be preceded by a focal neurological phenomenon ("aura") followed by headache (classical migraine); this aura consists of certain motor (weakness or paralysis) and/or focal neurological (scintillating scotoma) symptoms.<sup>[12]</sup>

On the basis of these considerations, in the present study it was proposed to formulate an oral delivery device, in the form of rapidly disintegrating tablets by using direct compression technology, with the aim of rapid disintegration and a complete drug release in a short period of time. In this study, effort has been made to prepare different formulations based on 3<sup>2</sup> full factorial design for each set of superdisintegrants at their two levels viz., higher and lower concentrations. The main effect and the interactions of disintegrants on dispersion time and drug release were studied.

## **MATERIALS AND METHODS:**

Rizatriptan Benzoate was obtained as a gift sample from Matrix laboratories Ltd, hyd. Crospovidone, Magnesium-stearate, Avicel-PH102(MCC), Talc, Aspartame were obtained as a gift sample from M/s. Alka Scientific Company, Nagpur. & *Psyllium mucilage*, *Musa paradisiaca* were Prepared at the laboratory. All other chemicals used were of analytical grade.

## **METHODOLOGY OF ISOLATION :**

### **2. Isolation Of *Plantago ovata* Mucilage<sup>[13]</sup> :-**

#### **Biological source :-**

Psyllium mucilage is obtained from the seed of the *Plantago ovate* plant belongs to the family of Plantaginaceae.

**Method :-** For the isolation of mucilage, seeds of *Plantago ovata* were used. They were soaked in distilled water for 48 hrs. then boiled for 1 h for complete release of mucilage into water. The material was filtered by squeezing in a muslin cloth to remove marc. Then equal volume of acetone was added to filtrate to precipitate the mucilage. The mucilage was separated and dried in oven at a temperature less than 60 °C, powdered (#60 mesh) weighed and stored in desicator until further use.

**Uses:-** Natural Superdisintegrating Agent

## 2. Isolation Of *Musa paradisiaca* powder <sup>[14]</sup> :-

### Biological source :-

Banana scientifically is known as *Musa paradisiaca* belonging to family Musaceae.

### Method :-

Collect the raw bananas and wash them thoroughly to remove organic matter if any.

Allow them to ripe in the laboratory in an incubator at 180-200 °C and a RH of 68-75% till the fruit becomes soft. The fruits are then peeled and pulp was then cut into small pieces with a stainless steel knife. The macerated pulp is then dried at 60 °C under 58 cm of vacuum. After 9 hours the dried product is pulverized and passed through a 60# mesh sieve and the powder is stored in air tight polythene bags in air tight containers. Spray drying of banana pulp yielded banana powder which is a hygroscopic material needing special care for preventing infection.

**Uses:-** Natural Superdisintegrating Agent & flavoring agent, binder.

## Formulation Designing

### Formulation designing :-

3<sup>2</sup> factorial design technique was employed to study the effect of independent variables (superdisintegrants) i.e.:- *Psyllium mucilage*(X<sub>1</sub>), *Musa paradisiaca*(X<sub>2</sub>), & crospovidone(X<sub>3</sub>) on dependent variables i.e.:- disintegration time (sec.) (Y<sub>1</sub>), & % CDR (Y<sub>2</sub>).

Each formulation was composed of drug and excipients in various proportions as shown in table(1).

**Table(1) : formulation designing:-**

Formulation no.	<i>Psyllium mucilage</i>	<i>Musa paradisiaca</i>	Crospovidone
1	-	-	-
2	+	-	-
3	-	+	-
4	+	+	-
5	-	-	+
6	+	-	+
7	-	+	+
8	+	+	+

**Table (2) : Dependent Variables**

Code	Dependent Variables	Unit
Y <sub>1</sub>	Disintegration Time	Second
Y <sub>2</sub>	CDR	%

**Table (3) : level used and actual values of independent variables**

Independent Variables	Level Used	
	-	+
X <sub>1</sub> , <i>Psyllium mucilage</i>	8	12
X <sub>2</sub> , <i>Musa paradisiaca</i>	15	25
X <sub>3</sub> , Crospovidone	4	8

Here, “-” Sign Indicates Lower Concentration & “+” Sign Indicates Higher Concentrations.

**Table (4):** Formulation of Rizatriptan Benzoate Orally Disintegrating Tablets By Direct Compression Method

Sr.no.	Ingredients	F <sub>1</sub>	F <sub>2</sub>	F <sub>3</sub>	F <sub>4</sub>	F <sub>5</sub>	F <sub>6</sub>	F <sub>7</sub>	F <sub>8</sub>
1	Rizatriptan benzoate	10	10	10	10	10	10	10	10
2	<i>Psyllium mucilage</i>	8	12	8	12	8	12	8	12
3	<i>Musa paradisiaca</i>	15	15	25	25	15	15	25	25
4	Crospovidone	4	4	4	4	8	8	8	8
5	Magnesium stearate	3	3	3	3	3	3	3	3
6	Talc	4	4	4	4	4	4	4	4
7	Aspartame	3	3	3	3	3	3	3	3
8	Avicel PH-102 (MCC)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Tablet Wt.(mg)		150	150	150	150	150	150	150	150

## PREPARATION OF TABLET

### Preparation of orally disintegrating tablets<sup>[15]</sup> :-

Orally disintegrating tablet of Rizatriptan was prepared by **direct compression method**:-

All the ingredients were passed through 60# mesh sieve separately. The Rizatriptan benzoate, Crospovidone, *Psyllium mucilage*, *Musa paradisiaca*, Avicel PH-102, and mannitol were mixed up using a mortar and pestle. The blends were lubricated with 1% magnesium stearate and 1% Talc. The blends ready for compression were converted into tablets. Tablets were compressed at 3 mm size flat round punch to get tablet.

The compositions of experimental factorial design were shown in **Table 4**.

## EVALUATION PARAMETERS

### 1. Bulk density<sup>[16]</sup> :-

a) **Loose bulk density**:- 2 gm of powder blend was transferred in 10 ml graduated cylinder. Without compaction the unsettled apparent volume was read. The apparent bulk density was calculated in gm/cm<sup>3</sup> by the following formula.

Bulk density = Weight of powder / Bulk volume

b) **Tapped bulk density**<sup>[16]</sup>:- After the initial volume was observed, the cylinder was placed into the tap density tester and the machine was set to a fixed rpm. The reading of tapping was continued until no further change in volume was noted. The tapped bulk density was calculated in gm/cm<sup>3</sup> by the following formula.

Tapped density = Weight of powder / Tapped volume

2. **Hausner's Ratio**<sup>[16]</sup>:- It is a number that is correlated to the flow-ability of a powder. Hausner's Ratio = TD / BD

3. **Carr's Index**<sup>[16]</sup>:- Compressibility index of the powder blend was determined by Carr's index. The formula for Carr's index is as below: Carr's index (%) = [(TBD – LBD) X 100] / TBD

4. **Angle of Repose**<sup>[16]</sup> :- The angle of repose of powder blend was determined by the funnel method. Accurately weighed powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder blend. Powder blend was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation. Angle of repose,  $\theta = \tan^{-1} (h/r)$

Where, h and r are the height and radius of the powder cone.

### 5. Weight variation test<sup>[16]</sup> :-

The U.S.P. weight variation test is run by weighing 20 tablets individually, calculating the average weight,

and comparing the individual tablet weights to the average. The tablets meet the USP test if

“Not more than 2 tablets are outside the percentage limit and if No tablet differs by more than 2 times the percentage limit.”

### 7. Tablet Hardness<sup>[17]</sup>

A tablet is taken between the 2nd and 3rd finger and pressing it with the thumb as fulcrum. If the tablet breaks with a “sharp snap”, yet, it does not break when it falls on the floor – is said to possess proper hardness. **7. Tablet thickness**<sup>[18]</sup>

The thickness was measured by placing tablet between two arms of the Vernier calipers. 5 tablets were taken and their thickness was measured.

### 8. Tablet friability<sup>[18]</sup>

The friability of the 10 tablets was measured in a Roche friabilator. Tablets of a known weight are dedusted in a drum for a fixed time (100 revolutions) and weighed again. Percentage friability was calculated from the loss in weight as given in equation as below.

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

The weight loss should not be more than 1 %. Determination was made in triplicate.

### 9. Wetting time<sup>[19]</sup> :-

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water- containing Eosin, a water soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

### 10. Water absorption ratio (%)<sup>[20]</sup> :-

A piece of tissue paper folded twice was placed in a small petridish (Internal Diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was determined using the following equation.

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

Where,

W<sub>b</sub> is the weight of the tablet before water absorption  
W<sub>a</sub> is the weight of the tablet after water absorption.

### 11. In Vitro Disintegration Test<sup>[17]</sup> :-

The test was carried out on 6 tablets using Tablet disintegration tester. Distilled water at 37°C ± 2°C was used as a disintegration media and the time in seconds taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured.

### 12. *In vitro* dispersion time<sup>[21]</sup> :-

Tablet was added to 10 ml of phosphate buffer solution (pH 6.8) at  $37 \pm 0.5^\circ\text{C}$ . Time required for complete dispersion of a tablet was measured.

### 13. *In-vitro* dissolution study<sup>[22]</sup> :-

The release rate of Rizatriptan benzoate from orally disintegrating tablets was determined using Indian Pharmacopoeia (IP) dissolution testing apparatus I (paddle method).

#### Dissolution test parameters :-

Medium:- 900 ml water

Temperature:-  $37^\circ\text{C} (\pm 0.5^\circ\text{C})$

RPM:- 50

Timing :- 30 minutes.

Sampling volume:- 5 ml

A sample (5ml) of the solution was withdrawn from the dissolution apparatus at 1, 2, 3, 4, 5, 10, 20 and 30 min.

The samples were filtered through a 0.45 membrane filter. Absorbance of these solutions was measured at 280 nm using a Shimadzu UV-1700 UV/VIS spectrophotometer.

Cumulative percentage of drug release (table 18) was calculated using an equation obtained from a standard curve fig.(3).

## **VALIDATION STUDY ON ORALLY DISINTEGRATING TABLETS**

### **(SPECTROPHOTOMETRIC ESTIMATION OF RIZATRIPTAN BENZOATE)**

Analysis is an important aspect of formulation development of any drug molecule. A suitable and validated method has to be available for the analysis of drug in the bulk, in drug delivery systems, for release dissolution studies and estimation of drug in biological samples.<sup>[23]</sup>

The **objective** of the study was :-

- To develop a simple, sensitive, rapid, precise, cost effective and reproducible UV method for estimation of Rizatriptan benzoate in 0.1 N HCl, as per ICH guidelines.<sup>6</sup>
- To demonstrate that the procedure, when correctly applied, produces results that are fit for purpose.

#### **Preparation of standard stock solution<sup>[23]</sup>:-**

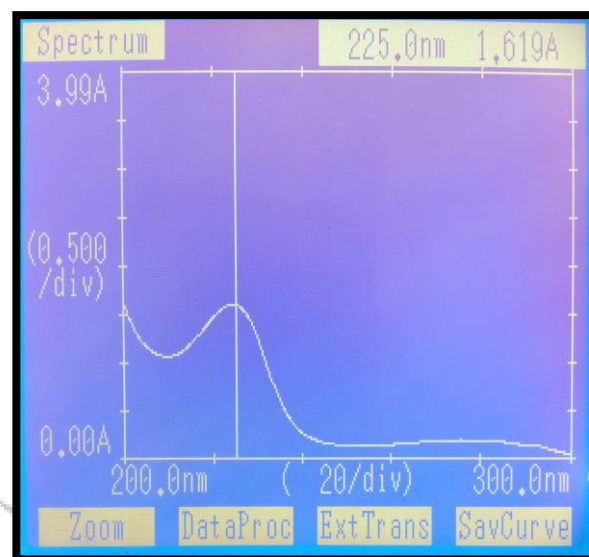
Standard solution of drug (100  $\mu\text{g/ml}$ ) was prepared by dissolving 10mg Rizatriptan benzoate in 0.1 N HCl, ultrasonicing the solution for 10 min.

#### **Preparation of calibration curve<sup>[23]</sup>:-**

Aliquots of 0.1 to 1 ml portions of the standard solution were transferred to a series of calibrated 10 ml volumetric flasks, and volume was adjusted with 0.1 N HCl. Solutions were scanned in the range of 200-400 nm against blank 0.1N HCl. The absorption maxima of solutions was found to be at 225 nm the absorbance

of solutions was measured at 225nm against blank (Table 6) and calibration curve was constructed (Figure 2). The optical characteristics were summarized in (Table 12).

**Preparation of sample solution<sup>[23]</sup>:-** The proposed method was applied to marketed Rizatriptan benzoate tablet. Ten tablets of Rizatriptan benzoate were weighed and powdered in glass mortar. Powder equivalent to 10 mg of the drug was weighed accurately and transferred to 100 ml volumetric flask, dissolved in about 20ml of 0.1 N HCl with frequent shaking and made up the volume to the mark with 0.1 N HCl to obtain the concentration of 100  $\mu\text{g/ml}$ . The solution was filtered through Whatmann filter paper No.41. The filtrate was diluted suitably with 0.1 N HCl to get the concentration of 5 $\mu\text{g/ml}$ . The absorbance of sample solution was measured at 225 nm and the amount of Rizatriptan benzoate present in tablet formulation was determined by extrapolating from the calibration curve. The results are shown in (Table 13).



## **RESULTS AND DISCUSSION**

### **A. Preformulation Study**

#### **a. Characterization of Rizatriptan Benzoate**

##### **1. Organoleptic properties:**

The prepared tablets of Rizatriptan benzoate was found to be :-

Colour : white to off-white crystalline solid.

Odour : odourless

Taste: sweet

##### **2. Melting point:**

The melting point of Rizatriptan benzoate was found to be in the range of  $179^\circ$  to  $181^\circ\text{C}$ .

##### **3. Determination of saturation solubility:**

The solubility of Rizatriptan benzoate as observed in 0.1 N HCL, deaerated water, and buffer pH 6.8 presented in Table 5. Solubility of drug is highest in deaerated water as compared to 0.1 N HCl and buffer pH 6.8.

**Table (5): Solubility Data of Rizatriptan Benzoate**

Solvent	Solubility (mg/mL)
0.1 N HCl	43.42
Deaerated water	219.98
Buffer pH 6.8	50.12

**4. UV spectroscopy (Determination of  $\lambda$  max):-**

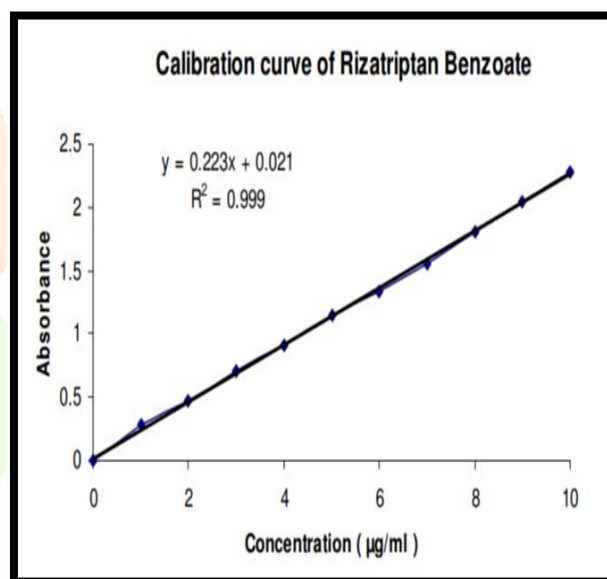
Wavelength of maximum absorbance ( $\lambda$  max) of Rizatriptan benzoate was found to be 225 nm in deaerated water (Figure 1).

**Figure (1) :** UV Spectra of Rizatriptan Benzoate( $\lambda$  max.).

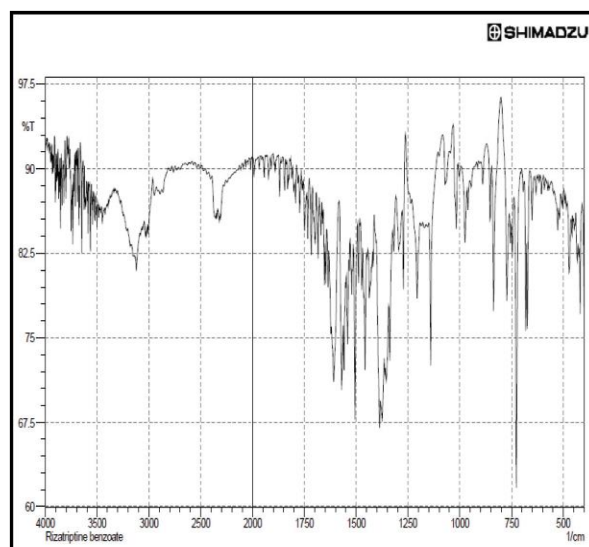
**b. Calibration Curve for Rizatriptan Benzoate:-** The calibration curve for Rizatriptan benzoate in deaerated water is shown in Figure 3 and Table 14. The graph of absorbance vs. concentration for Rizatriptan benzoate was found to be linear in the concentration range of 1-10  $\mu\text{g/ml}$  at 225 nm. The  $R^2$  of the calibration curve was found to be 0.999, indicating that it follows the Beers Lambert law within this concentration range.

**Table (6) :- Calibration curve of Rizatriptan Benzoate**

Sr. no.	Concentration ( $\mu\text{g/ml}$ )	Absorbance at 225nm
1	0	0
2	1	0.2763
3	2	0.4676
4	3	0.7083
5	4	0.9149
6	5	1.1441
7	6	1.3439
8	7	1.5565
9	8	1.8086
10	9	2.0412
11	10	2.2827

**Figure (2) :** Calibration curve of Rizatriptan Benzoate.**5. FTIR Spectroscopy:-**

The FTIR spectrum of pure Rizatriptan benzoate is shown in Figure 4 and interpretation of FTIR spectra is given in Table 7. FTIR spectrum of Rizatriptan benzoate showed all the peaks corresponding to the functional groups present in the structure of Rizatriptan benzoate.



**Table (7):- Interpretation of FTIR Spectrum of Rizatriptan Benzoate**

Peak observed (cm <sup>-1</sup> )	Interpretation
3446	-NH stretching
2947	-CH <sub>3</sub> stretching
2893	-CH <sub>2</sub> stretching
1608	-C=C stretching

1506	-C=N stretching
1570	-NH bending
1458	-CH <sub>2</sub> bending
1375	-CH <sub>3</sub> bending
1296	-C-N stretching
1140	
1016	

**Figure (3) : FTIR Spectra of Rizatriptan Benzoate.****EVALUATION OF TABLETS :-**

Tablets were prepared by **direct compression** technique.

**Table (8): Data of Pre-formulation Study :-**

Formulation	Bulk density (gm/cm <sup>3</sup> )	Tapped density (gm/cm <sup>3</sup> )	Hausner's ratio	Carr's index (%)	Angle of repose
F1	0.40	0.41	1.10	10.05	31.54
F2	0.35	0.38	1.07	07.94	27.71
F3	0.36	0.35	1.06	09.11	25.60
F4	0.40	0.33	1.11	14.75	26.47
F5	0.33	0.40	1.08	09.53	28.90
F6	0.37	0.34	1.08	09.53	28.92
F7	0.36	0.32	1.07	10.54	26.43
F8	0.38	0.34	1.10	09.34	26.72

As the material was free flowing, tablets of all formulations were obtained of uniform weight due to uniform die fill, complied with pharmacopoeia limits. Hardness of tablets of formulations is kept within 3-4 kg

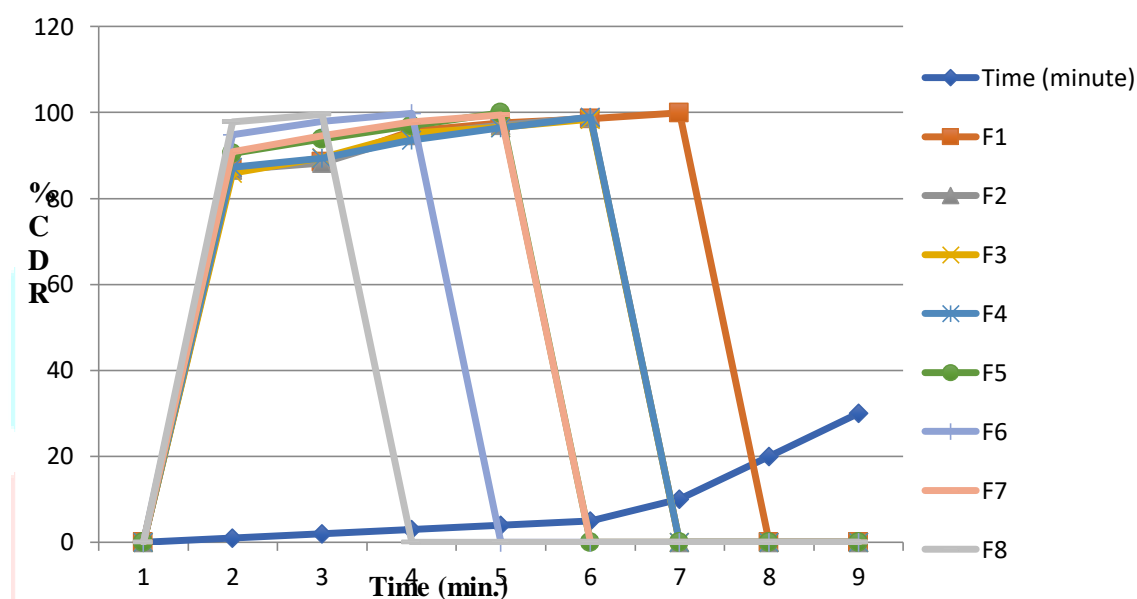
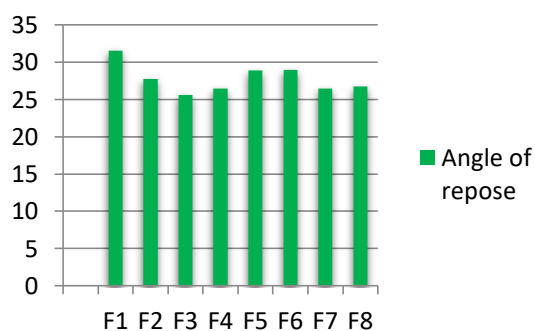
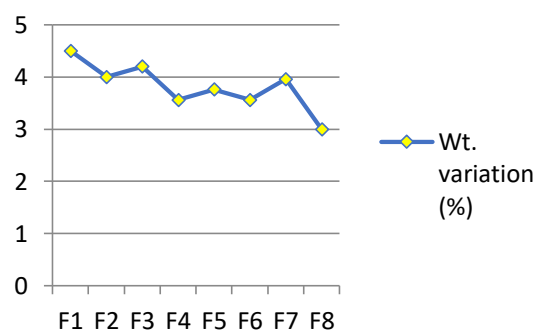
/cm<sup>2</sup>. Friability of the formulations were below 1.0% was an indication of good mechanical resistance of tablets. When assayed Drug content was found to be 95-105% which is within acceptable limit.

**Table (9) :- Evaluation of directly compressible orally disintegrating tablets:-**

Formulation	Wt. variation (%)	Hardness (kg/cm <sup>2</sup> )	Friability (%)	Thickness (mm)	Wetting time (s)	Water absorption ratio (%)	Disintegration time (s)	in-vitro dispersion time (s)	Assay (%)
F1	4.50	4.2	0.82	3.20	32	79.90	58±1.2	52±1.0	97.70
F2	4.00	3.6	0.85	3.14	22	82.25	56±1.2	48±1.2	98.22
F3	4.20	3.9	0.74	3.23	19	83.34	46±1.4	42±1.0	96.40
F4	3.56	3.2	0.45	3.15	18	85.76	43±1.3	40±1.3	98.42
F5	3.76	3.4	0.35	3.20	16	88.57	40±1.2	32±1.1	97.50
F6	3.56	3.2	0.36	3.22	16	92.72	36±1.6	31±1.2	97.40
F7	3.96	3.8	0.42	3.14	14	93.20	32±1.2	28±1.2	98.33
F8	3.00	3.2	0.42	3.10	13	99.00	20±1.4	15±1.2	99.40

**Dissolution profile :-****Table (10) :-** Cumulative drug release (%) [CDR] of all formulation

Sr.no.	Time (minute)	F1	F2	F3	F4	F5	F6	F7	F8
1	0	0	0	0	0	0	0	0	0
2	1	86.85	86.65	85.86	87.30	90.46	94.89	90.87	97.85
3	2	88.49	88.20	89.49	89.40	93.89	97.93	94.60	99.60
4	3	95.71	94.71	95.24	93.60	96.98	99.78	97.86	--
5	4	97.52	97.04	96.52	96.46	99.87	--	99.43	--
6	5	98.52	98.85	98.40	98.97	--	--	--	--
7	10	99.98	--	--	--	--	--	--	--
8	20	--	--	--	--	--	--	--	--
9	30	--	--	--	--	--	--	--	--

**Fig. (4) :** Cumulative drug release(%[CDR] of all formulation.**Angle of repose****Fig. (5):** Comparison of Angle of repose**Wt. variation (%)****Fig. (6):** Comparison of wt. variation

### Friability (%)

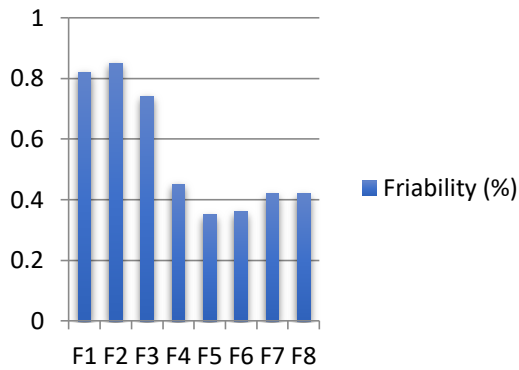


Fig.: (7) : Comparison of Friability (%)

### Disintegration time (s)

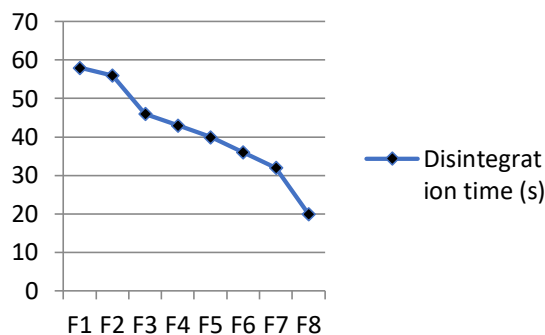


Fig.: (8) : Comparison of wetting time(s)

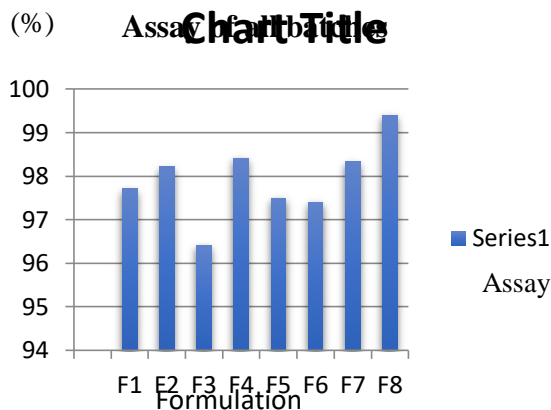


Fig.: (9): Comparison of water absorption ratio (%)

### Water absorption ratio (%)

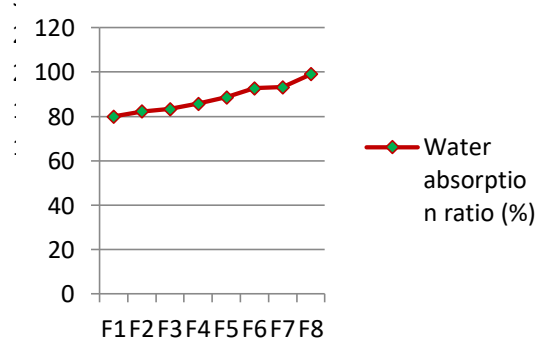


Fig.: (10) : Comparison of disintegration time

### in-vitro dispersion time (s)

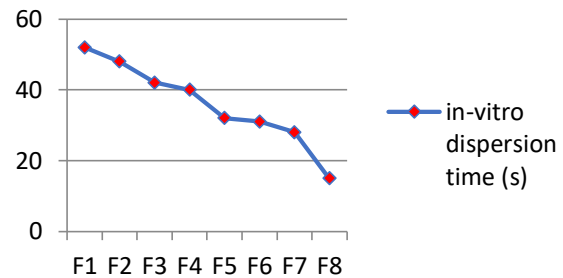


Fig.: (11): Comparison of in-vitro dispersion time

Fig.: (12): comparison of Assay of all batches.

### VALIDATION PARAMETERS :-

**Accuracy (Recovery Test):** In order to ascertain the suitability and reproducibility of the proposed method, recovery studies were carried out by adding known quantities of standard Rizatriptan benzoate (80,100,120%) to the tablet and the mixtures were analyzed by the proposed method. Three samples were prepared for each recovery level. The percentage recovery of Rizatriptan benzoate was found to be  $99.7169 \pm 0.7532\%$  (Table 13) indicating that there is no interference by the excipients in the method.

Table (11) :- Calibration curve of Rizatriptan Benzoate

Sr. no.	Concentration (µg/ml)	Absorbance	standard deviation
1	0	0	0
2	1	0.2763	$\pm 0.01695$
3	2	0.4676	$\pm 0.01364$
4	3	0.7083	$\pm 0.00825$
5	4	0.9149	$\pm 0.01014$
6	5	1.1441	$\pm 0.00699$
7	6	1.3439	$\pm 0.00416$
8	7	1.5565	$\pm 0.00654$
9	8	1.8086	$\pm 0.01402$
10	9	2.0412	$\pm 0.00121$
11	10	2.2827	$\pm 0.00195$

### Precision:

Intra-day precision was evaluated by analyzing six test samples of Rizatriptan benzoate. The intermediate precision (inter-day precision) of the method was determined by evaluating the samples of Rizatriptan benzoate on different days and by two different analysts in the same laboratory. The assay and relative standard deviation (RSD) values are 99.668%, 0.8554 and 98.563%, 1.0603 respectively (Table 14).

**Linearity :**

Rizatriptan benzoate exhibits its maximum absorption at 225 nm and obeyed Beer's law in the range of 1-10 µg/ml. Linear regression of absorbance Vs concentration yielded equation  $y = 0.223x + 0.021$  with a correlation coefficient of 0.999.

**Limit of Detection (LOD) and Limit of Quantification (LOQ) :-**

The LOD and LOQ of Rizatriptan benzoate were determined by using standard deviation of the response and slope approach as defined in International Conference on Harmonization (ICH) guidelines .7 The LOD and LOQ was found to be 0.31µg/ml and 0.94 µg/ml respectively. The proposed method of determination of Rizatriptan benzoate showed molar absorptivity of 1.619A° and Sandell's sensitivity 8 0.004305 µg/cm<sup>2</sup> /0.001 absorbance units.

**Table (12) :- Validation parameters**

Sr. no.	Parameter	Result
1	Absorption maxima (nm)	225
2	Linearity Range (µg/ml)	1-10
3	Standard Regression Equation	$y = 0.223x + 0.021$
4	Correlation Coefficient (r <sup>2</sup> )	$r^2 = 0.999$
5	Molar absorptivity	1.619 A°
6	A( 1% , 1cm )	233.13
7	Accuracy (% recovery ±SD)	99.7169 ± 0.7532%
8	Precision (%)	99.668, 98.563
9	Specificity	A 5µg/ml solution of drug in 0.1N HCl at UV detection lemnda of 225 nm shows an absorbance value of 1.1441± 0.00699
10	Sandell's Sensitivity <sup>8</sup> (ug/cm <sup>2</sup> /0.001 absorbance unit)	0.004305
11	LOD (µg/ml)	0.31
12	LOQ (µg/ml)	0.94

**Table (13) :- Determination of Accuracy by percentage recovery method**

Ingredients	Tablet amount (µg/ml)	Level of addition (%)	Amount added (µg/ml)	Amount recoverd (µg/ml)	% recovery	Average recovery %
Rizatriptan benzoate.	5	80	4	8.8967	98.8531	99.7169 + 0.7532%
	5	100	5	10.0236	100.2368	
	5	120	6	11.0067	100.0609	

**Table (14) :- Determination of Precision**

Sample number	Assay of rizatriptan benzoate as % of amount	
	Analyst-I (Intra-day precision)	Analyst-II (Inter-day precision)
1	99.842	97.360
2	98.190	97.124
3	100.323	99.493
4	100.559	99.431
5	99.860	98.732
6	99.239	99.239
Mean	99.668	98.563
Std. deviation	0.8554	1.0603

## SUMMARY AND CONCLUSION

The goal of the present investigation was to identify the optimum combination of superdisintegrants for the development of orally disintegrating tablets of Rizatriptan benzoate. FTIR study performed for identification and compatability study of drug and exepients, found no characteristic change in drug-exciipient powder mixture. Hence, the excipients were selected for the formulation development. Three superdisintegrants viz., *Psyllium mucilage*, *Musa paradisiacal* and crospovidone were tried. 3<sup>2</sup> factorial design technique was used for each set of superdisintegrants and totally eight formulations were made by direct compression method. Powder blends were evaluated for tests, such as bulk density, tapped density, compressibility index and Hausners ratio before being punched as tablets and also evaluated for friability and the key parameters like *invitro* dispersion time, wetting time and water absortion ratio.

Factorial design had facilitated the study and helped in understanding the interaction between superdisintegrants when used in combinations. *Psyllium mucilage*(12mg), *Musa paradisiacal*(25mg) and crospovidone(8mg) (F8) was identified as the optimum combination of super disintegrants based on *invitro* dispersion time, wetting time and water absorption ratio. The developed method was found to be simple, sensitive, accurate, precise, reproducible, and can be used for dissolution studies as well as routine quality control analysis of rizatriptan benzoate in bulk and tablet formulation.

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