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Formulation and *In-vitro* Evaluation of Taste Masking Tablets of Rizatriptan Benzoate Using Tulsion

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A B S T R A C T

The main objective of this study was to formulate and evaluate the rapidly disintegrating technology makes tablets to disintegrate in the mouth without chewing and additional water intakes have drawn a great deal of attention. Rizatriptan benzoate is a potent anti-migraine drug with a bitter taste. Thus the taste has to be masked in order to reduce its bitterness, to increase its palatability and also to improve patient compliance. Therefore, attempts were undertaken to mask the bitter taste by using ion exchange resin Tulsion 339 and to formulate into RDT by adopting direct compression method by incorporating superdisintegrants Indion 234, CCS and SSG in various concentrations. The loading process was optimized for resin solubility, concentration, swelling, stirring and pH of loading solution and drug: resin ratio. The powder complex was evaluated for bulk density, angle of repose, drug release and drug-polymer complex's interactions. Precompressional studies revealed good micromeritic properties of powder blend for direct compression. The hardness (2.8 to 3.6 kg/cm2), friability (0.42 to 0.66), weight variation (0.94 - 1.28%), drug content (98.32 to 99.82 %) and disintegration time (21-39 sec) were found uniform and reproducible for all formulations. The process variables played a vital role resulting in maximum drug loading. Tulsion 339 complex (1:1) with 40 min swelling time at pH 3, stirred for 150 min showed maximum drug loading. Optimized formulation (R4) containing Indion 234 exhibited quicker disintegration than CCS, SSG and were also found to be superior to marketed tablet with respect to disintegration and dissolution. Release was proportional to superdisintegrant concentration irrespective of polymer complex. Selected tablets were found stable and followed diffusion controlled first order kinetics. The results revealed that Rizatriptan benzoate was successfully taste masked and formulated into a RDT as an alternative method to conventional tablets.

Keywords: Tulsion, Indion, Rapid-disintegrating tablets, Rizatriptan benzoate, Superdisintegrants

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1. Introduction

The new generation anti-migraine drug, Rizatriptan benzoate is a potent and selective 5- hydroxy tryptamine 1B/1D receptor agonist and is considered more effective than the traditional triptans for the treatment of acute migraine attack. Chemically it is 3-[2-(dimethyl amino) ethyl]-5-(1H-1, 2,4-triazol-1-ylmethyl) indole onobenzoate. 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[1]. Orally disintegrating tablets (ODTs) have received increasing attention during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. Upon introduction into the mouth, these tablets dissolve or disintegrate in the absence of additional water allowing the easy administration of active pharmaceutical ingredients. Such dosage forms are useful and convenient for children, older persons, and others who are unable to swallow conventional tablets and capsules. Masking the unpleasant taste of therapeutic agents is an important consideration in the formulation of ODTs and it can be achieved by minimizing direct contact between the active species and the taste receptors in the buccal cavity of the patient [2].

The unpleasant taste of the active drug can also be overcome by adding flavoring ingredients and sweeteners to improve taste and palatability. However, where the active drug possesses a particularly strong or bitter taste, such as is the case with many antibiotics, the mere addition of such flavoring ingredients and sweeteners is insufficient to improve taste and palatability. Accordingly, various taste-masked coating compositions have been used in the formulation of liquid suspensions and fast disintegrating tablet dosage forms. 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 [3, 4]. Therefore, the purpose of the present study was to develop a Orally disintegrating tablet of Rizatriptan benzoate by direct compression and to mask the bitter taste of Rizatriptan. Such tablet should disintegrate rapidly in the saliva without need of water and release the drug instantly for immediate therapeutic effect, and be of acceptable taste.

2. Materials and Methods

Rizatriptan benzoate was generously gifted by Aurobindo Pharmaceuticals Ltd; Hyderabad, Tulsion 339 was gifted by Thermx Ltd; Pune. Spray dried and mannitol were procured from Indchem International; Mumbai. Indion 234 was procured from Ion exchange Ltd; Mumbai. Cross carmellose sodium and SSG were obtained from S.Zaveri Pharmaken Ltd; Mumbai. All other chemicals used were of analytical grade.

Preparation of taste-Masked Granules of Rizatriptan benzoate using Tulsion 339 by complexation technique

Activation of Resin:

Ion exchange resins Tulsion-339 was swelled with deionised water for an hour and then washed with 1N HCl and 1N NaOH in order to remove impurities (alkali and acidic impurities). The treated resin was washed several times with freshly prepared deionized water to remove the traces of acid or alkali. This treated resin was kept in oven for 12h at 50^0C. The dried activated resin was kept in desiccator until further use [5].

Preparation of Drug-Resin complexes (DRC):

Drug was mixed separately with the resins in a drug: resin ratio of 1:1, 1:2 and 1:3. Two hundred ml of distilled water was added to the mixtures and stirred continuously on magnetic stirrer, for 24 hrs until the equilibrium was attained. Aliquots from the reaction mixture were withdrawn and filtered through Whatman filter paper no. 41 after every hr and were analyzed after appropriate dilution at 280 nm by UV/VIS spectrophotometer. The process was continued till the concentration values of two consecutive aliquots were almost constant [6]. The readings were taken in triplicate. The resultant complex was filtered through Whatman filter paper no. 41, washed with water to remove the unreacted drug and oven dried at 50°C for 1 hr and stored in air tight glass vial till the further use. Unbound drug in filtrate was estimated spectrophotometrically at 280 nm against blank and drug-loading efficiency was calculated. The results are shown in table: 1.

Optimization of Rizatriptan benzoate-Tulsion 339 Complexation for drug loading

The drug loading on to resin was optimized by considering various parameters such as concentration of resin, swelling time, stirring time, temperature and pH of resin solution. These parameters were studied and optimized for the maximum amount of drug loading.

Optimization of resin concentration:

The various concentration of resin with a fixed concentration of drug (1:1, 1:2, 1:3, 1:4 and 1:5) were optimized for amount of drug loading [7]. The resins were first washed with distilled water for neutralization and complexation was carried out by adopting batch method. In this method, drug solution of concentration 1 mg/mL was prepared in deionized water. The required quantity of resin was placed in drug solution and was stirred till the attainment of equilibrium. Time for attainment of equilibrium was decided to be 6 hr from preliminary experimentation. The slurry was filtered, and amount of drug remaining in the filtrate was determined spectrophotometrically. The amount of drug adsorbed was

determined by the difference between amount of drug present in stock solution and amount remaining in filtrate at the end of equilibrium. The ratio at which maximum drug loading occurs was considered as optimized concentration of resin. Among all ratios, the complex with 1:1 ratio was selected for further study. Results are shown in table: 2, 3 and 4.

FT-IR Studies

Compatbility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients. The samples were taken for FT-IR study.

DSC studies

The optimized complexes were subjected to differential scanning calorimeter equipped with an intracooler (Mettler-Toledo, Switzerland). Indium/Zinc standards were used to calibrate the DSC temperature and enthalpy scale. The samples (pure Rizatriptan benzoate and drug-polymer complex) were sealed in aluminum pans and heated at a constant rate of 200C/ min over a temperature range of 20-2500 C. Inert atmosphere was maintained by purging nitrogen gas at a flow rate of 50 ml/min.

Formulation of [bitterless] RDT of drug: Resin granules by adding superdisintegrant:

Preparation of RDT using Rizatriptan benzoate - Tulsion 339 complexes:

Tablets containing Drug-Tulsion 339 complex equivalent to approximately 10 mg of Rizatriptan benzoate were prepared by direct compression method The ingredients were mixed homogenously and co-grounded in a glass mortar and pestle (except talc and magnesium stearate) and were passed through sieve no.40. Finally talc and magnesium stearate sifted through #60 and were added and mixed for 5 min [8]. Finally these granules were compressed on tablet compression machine using 4 mm standard punches to give tablet weight of 200 mg. Various formulae (R1-R12) used in the study and ingredient utilized are depicted in Table 5.

Pre-compressional parameters [9]

Angle of repose (θ): Angle of repose is defined as the maximum angle possible between the surface of a pile of the Powder and horizontal plane. The frictional force in a loose powder or granules can be measured by angle of repose.

$\tan \theta = h / r$

$\theta = \tan^{-1}(h/r)$

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

Bulk density: Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another.

LBD=Weight of the powder --------- (a)
Volume of the packing

TBD=Weight of the powder ---------- (b)
Tapped volume of packing

Carr's compressibility index: The compressibility index of the granules was determined by Carr's compressibility index.

Carr's Index (%)=TBD – LBD/TBD x 100 ----- (c)

Hausner's ratio: It is determined by comparing tapped density to the bulk density by using following equation

Hausners ratio=TBD / LBD.

The results of the powder flow properties determination are summarised in Table 6.

Evaluation of rapidly disintegrating Tablets [10]

a) Thickness:

The thickness of the tablets was determined using a vernier calipers. Five tablets from each batch were used, and average values were calculated.

b) Weight variation test:

Weight variation test was carried out as per IP. Twenty tablets were randomly selected and individually weighed. The average weight and standard deviation was calculated.

c) Hardness:

The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring. It is expressed in Kg / cm2. Results are shown in Table: 7.

d) Friability:

Friability of the tablets was determined using Roche friability (Electrolab, Mumbai). This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions [11]. Tablets were dedusted using a soft muslin cloth and reweighed. Results are shown in Table: 7. The friability (f) is given by the formula.

$f = (1 - W0 / W) \times 100$

Where,

W0 is weight of the tablets before the test and

W is the weight of the tablet after the test

e) In vitro disintegration time:

The disintegration time of the tablet was measured in water (37±2°C) according to disintegration test apparatus with disk [12]. The time in seconds taken for the complete disintegration of the tablet with no palpable mass in the apparatus was measured in seconds. Three tablets from each batch (formulation) were tested for the disintegration time calculations. Results are shown in Table: 8.

f) In vitro dispersion time:

In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH of 6.8 at 37±0.5°C. Time required for complete dispersion of a tablet was measured. Three tablets from each formulation were randomly selected and in vitro dispersion time was performed [13].

g) Wetting time:

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 Petri dish with a 10 cm diameter. Ten millimeters of water containing Eosin, a water soluble dye, is added to Petri dish. A tablet is carefully placed on the surface of the tissue paper [14, 15]. The time required for

water to reach upper surface of the tablet is noted as a wetting time. Results are shown in Table 8.

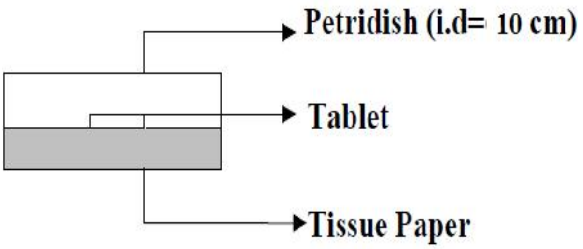

Fig 1: Determination of wetting

h) Water absorption ratio:

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured [16]. The wetted tablet was then weighed. Results are shown in Table 8. Water absorption ratio (R) is calculated by using the equation.

$$R = \frac{10 \times Wa - Wb}{Wb}$$

Where,

Wa is the weight of the tablets before the test and

Wb is the weight of the tablet after water absorption.

i) In vitro dissolution profile:

In-vitro drug release study was performed at 37±0.5°C using eight station USP type-II apparatus with paddle rotating at 50 rpm. The drug release study was carried out in 0.1N HCl by taking about 900ml of the dissolution medium [17].

The drug release study was performed in 0.1N HCl to demonstrate the availability of Rizatriptan benzoate in gastric pH. About 5 ml of sample was withdrawn at specified time intervals from the dissolution medium and replaced with equal volume of fresh medium. Samples were filtered through whattmann filter paper and analyzed using UV spectrophotometer (UV-1700, Shimadzu Corporation, Japan) at 280 nm. Results are shown in Fig. 2-5.

j) Stability studies:

The tablet formulations were packed in aluminum foil and were exposed to 40°C ± 2°C / 75% ± 5% RH in humidity control oven as per ICH guidelines118 Q1C: "Stability testing of new dosage forms." Sampling was done at predetermined time intervals [18] of initial and 30 days. Results are shown in Table: 9.

3. Results and Discussion

The blends of different formulations were evaluated for angle of repose, LBD, TBD, compressibility index, and hausners ratio (Table 6). The results of angle of repose and compressibility index (%) ranged from 20.38 ± 0.23 to 23.56 ± 0.70, and 7.40 ± 0.26 to 10.88 ±1.98, respectively. The results of LBD and TBD ranged from 0.40 ± 0.06 to 0.58 ± 0.16 and 0.47 ± 0.11 to 0.58 ± 0.16, respectively. The results of hausners ratio ranged from 1.06 ± 0.31 to 1.12 ± 0.48. The results of angle of repose (<30) indicate good flow properties of the blend. This was further supported by lower compressibility index values. Generally, compressibility index values up to 15% result in good to excellent flow properties and Hausner's ratio below 1.25 which indicated good compressibility and flowability.

Orally disintegrating tablets were prepared by direct compression method. A total of twelve formulations were prepared using different superdisintegrants described above. All the formulations passed weight variation test. The hardness of all the tablets containing superdisintegrants was found in the range of 2.8-3.5 kg/cm2. Friability was found to be below 1% which was an indication of good resistance of tablets. The results of these evaluation are shown in table 7.

Wetting time:

Wetting time was determined for all the formulations were observed that all formulations showed less wetting time. It was also observed that the batch R4 showed the wetting time of 16.78 ± 0.31 seconds which was less as compared to other batches. It was also observed that the batches containing CCS showed better wetting time as compared to tablets containing SSG. The results were shown in table 8.

Water absorption ratio:

Water absorption ratio for the three different superdisintegrants used was in the order: Indion 234 R4 (85.76 ± 1.34) > Croscarmellose sodium R8 (83.81 ± 1.86) > SSG R12 (81.81 ± 1.43) as shown in Table 8. It was observed that with increase in water absorption ration the disintegration of tablets was faster as compared to the tablets with low water absorption ratio.

In-vitro disintegration Test:

Disintegration time is a significant parameter of importance in the formulation of RDTs. The disintegration time was found to be in the range of 21.16 ± 0.25 to 37.16 ± 0.25 sec for the tablets containing different superdisintegrants in the order Indion 234 < CCS < SSG. It was also observed that the tablets with the least wetting time also showed minimum disintegration time respectively shown in Table 8. It shows a strong correlation between wetting time and disintegration time.

In vitro drug release Study:

The in-vitro dissolution was studied in 0.1N HCl of pH 1.2. The In-Vitro drug release data for each of the formulation is shown below: In vitro dissolution study of formulations R1, R2, R3 and R4, R5, R6 batches showed drug release, 99.468, 99.171, 99.243 and 99.519, 99.468 and 99.284 within 5 min, in this R4 batch show good dissolution property (Figure 6-9). Among these formulations, the release rate was increased in the following polymer order: Indion 234 > CCS > SSG.

In vitro dissolution study of formulations R7 batch drug release within 5 min 98.532, with in 5 min R8 batch drug release 98.268, with in 5 min R9 batch release the drug 98.106, with in 5 min R10 batch drug release is 97.884, with in 5 min R11 batch release the drug 97.748, with in 5 min R12 batch release the drug release 97.487. From above results comparison of different formulation from R1 to R12, from the above results the formulation R4 has shown good dissolution profile.

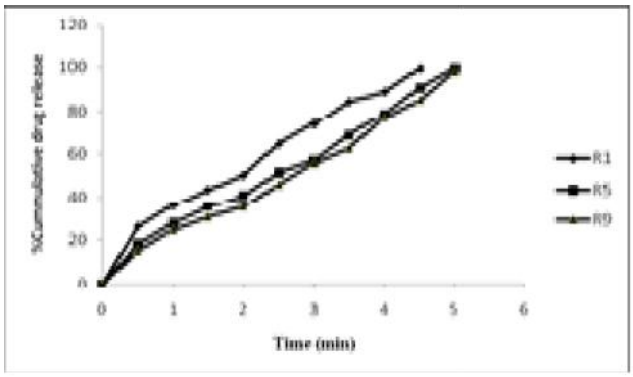

Fig 2: In-vitro release of Rizatriptan benzoate from RDT containing 1% Indion 234 (R1) CCS (R5) and SSG (R9)

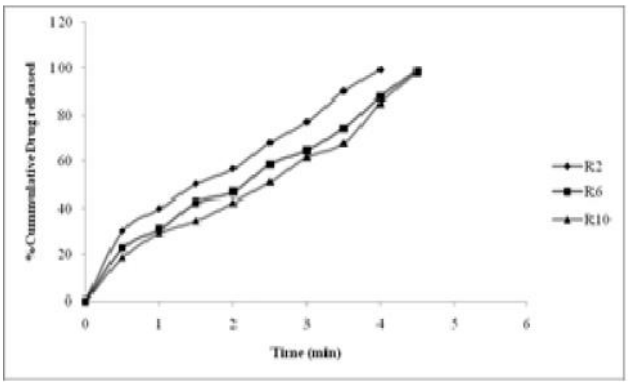

Fig 3: In-vitro release of Rizatriptan benzoate from RDT containing 2% Indion 234 (R2) CCS (R6) and SSG (R10)

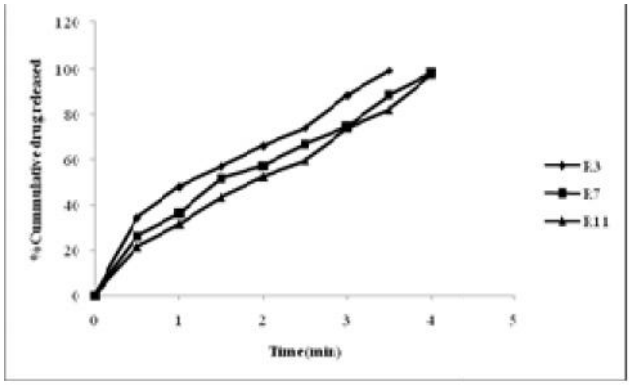

Fig 4: In-vitro release of Rizatriptan benzoate from RDT containing 3% Indion 234 (R3) CCS (R7) and SSG (R11)

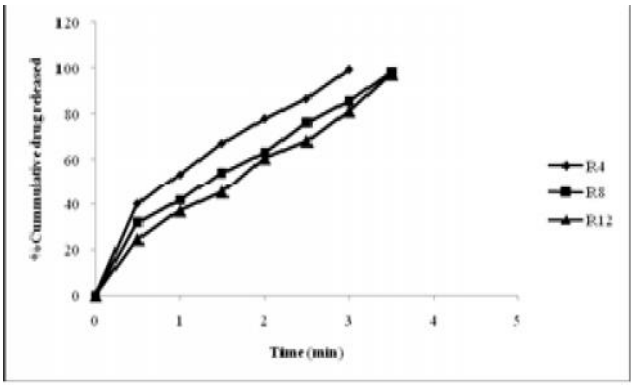

Fig 5:4 In-vitro release of Rizatriptan benzoate from RDT containing 4% Indion 234 (R4) CCS (R8) and SSG (R12)

FTIR studies:

FT-IR studies are carried out to investigate if there is any chemical interaction between polymer, added excipients and Rizatriptan benzoate in the formulated product, the FT-IR of pure drug of Rizatriptan benzoate, and Optimized formulation. The pure rizatriptan benzoate exhibited characteristic peaks at 3120 cm–1 (aromatic secondary amine N-H stretching), 2974 cm–1 (aromatic C-H stretching), 1608 cm–1 (C=O five member cyclic stretching) and 1270 cm–1 (C-N aliphatic amine stretching). It was observed however, that the entire characteristic peak observed for both pure drug and excipients remained unchanged, and no significant shift or reduction in the intensity of peak of rizatriptan benzoate. FT-IR spectroscopic studies indicate that drug is compatible with polymer. Results are shown in Figure: 5 and 6.

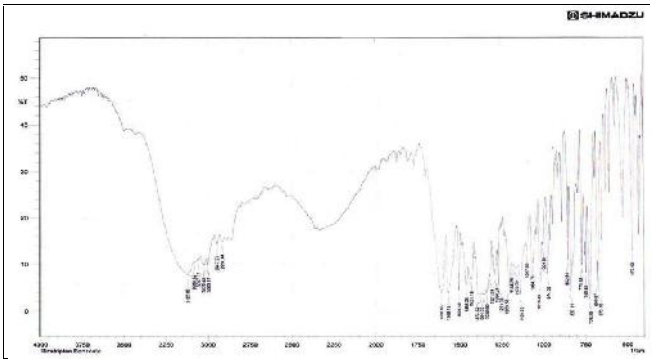

Fig 6:IR spectra of Rizatriptan benzoate pure drug

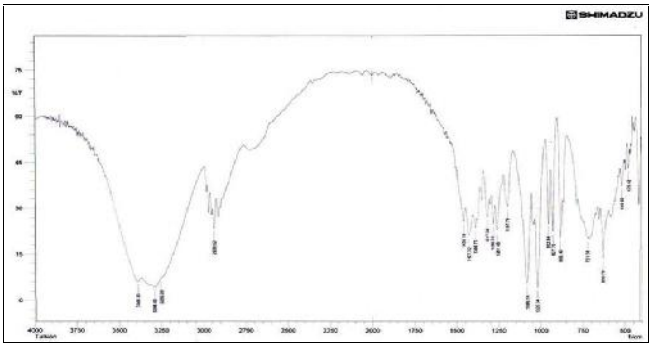

Fig 7:IR spectra of Optimized formulation containing Drug: Tulsion complex

DSC:

In order to check chemical interaction between drug and polymer, thermal analysis was carried out by using DSC. The melting point of drug was confirmed from the endothermic peak of Rizatriptan benzoate at 183°C in DSC analysis. DSC thermograms of Rizatriptan benzoate, Rizatriptan benzoate + excipients showed that there were no changes in the endotherms (Fig. 4 & 5). The drug exhibited a small melting endotherm in the drug polymer mixture. These slight changes in the melting endotherm of the drug may be attributed to the mixing process, which lowers the purity of each component in the mixture, thus resulting in slightly broader and lower melting points, but not truly representing any incompatibility. Results are shown in Fig. 8 and 9.

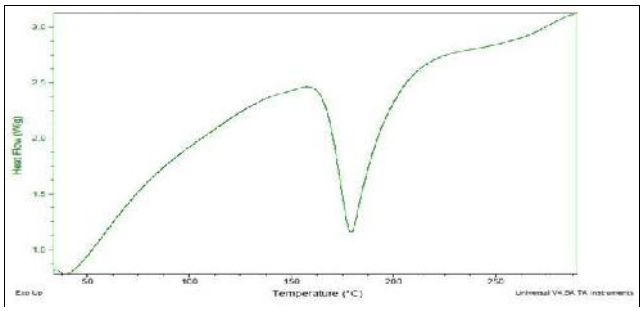

Fig 8:DSC thermograms of Rizatriptan benzoate pure drug

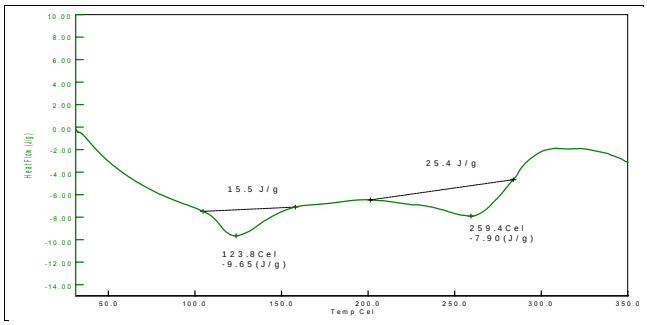

Fig 9:DSC thermograms of formulation containing Tulsion complex (R4)

Stability Study:

The best formulation of each batch was subjected for one month stability study by exposing the tablets to 40±2°C temperature and relative humidity 75±5% in programmable environmental test chamber. The stability studies revealed that there is not much considerable change in appearance, physical attributes, drug content, and in vitro drug release. The Rizatriptan benzoate rapid disintegrating tablets were found to be stable with respect to stability studies. Results are shown in Table 9.

4. Conclusion

In conclusion, the objective of formulating fast disintegrating tablets of Rizatriptan benzoate using the technique of complexation and super-disintegrant addition has been successfully achieved. Also, as a prerequisite, effective inhibition of the bitter taste of Rizatriptan benzoate was achieved by preparing taste-masked tablets which dissolve at salivary pH. The tablets with an acceptable taste and rapid disintegration in the mouth will be useful practical for both geriatric and pediatric patients and can be successfully produced commercially after a full stability evaluation.

Table 1: Effect of concentration of Tulsion 339 resin on drug loading

S. No	Drug : Resin ratio	Drug loading* (%)
1	1 : 1	92.18 ± 0.22
2	1 : 2	92.68 ± 0.12
3	1 : 3	92.71 ± 0.24

Table 2: Effect of swelling time on drug loading of Tulsion 339 complex (1:1)

S. No	Swelling time	Drug loading* (%)
1	10	65.36 ± 0.21
2	20	77.5 ± 0.22
3	30	85.23 ± 0.19
4	40	92.76 ± 0.25
5	50	92.77 ± 0.77

Table 3: Effect of stirring time on drug loading of Tulsion 339 complex (1:1)

S. No	Stirring time (min)	Drug loading* (%)
1	30	62.59 ± 0.22
2	60	70.12 ± 0.19
3	90	78.12 ± 0.21
4	120	86.30 ± 0.21
5	150	91.97 ± 0.24
6	240	92.11 ± 0.19

Table 4: Effect of pH on drug loading of Tulsion 339 complex (1:1)

S. No	pH	Drug loading* (%)
1	1.2	60.2 ± 0.32
2	2.0	75.88 ± 0.31
3	3.0	96.22 ± 0.25
4	4.0	93.46 ± 0.24
5	5.0	79.65 ± 0.24
6	6.0	63.24 ± 0.21

7	7.0	55.35 ± 0.3
8	8.0	49.24 ± 0.21

Table 5: Composition of Rizatriptan benzoate - Tulsion 339 complex (1:1) rapidly disintegrating tablets

Ingredients (mg/tablet)	**Formulation code**											
	R1	**R2**	**R3**	**R4**	**R5**	**R6**	**R7**	**R8**	**R9**	**R10**	**R11**	**R12**
Rizatriptan benzoate – Tulsion 339 Complex*	20	20	20	20	20	20	20	20	20	20	20	20
SDM	170	168	166	164	170	168	166	164	170	168	166	164
Indion 234	2	4	6	8	-	-	-	-	-	-	-	-
CCS	-	-	-	-	2	4	6	8	-	-	-	-
SSG	-	-	-	-	-	-	-	-	2	4	6	8
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Aerosil	2	2	2	2	2	2	2	2	2	2	2	2
Aspartame	2	2	2	2	2	2	2	2	2	2	2	2
Total weight	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

SDM: Spray Dried Mannitol, **CCS:** Cross Caramel lose Sodium, **SSG:** Sodium Starch Glycolate

Table 6: Micrometric properties of prepared blend

Formulation Code	**Bulk density g/cm^3**	**Tapped density g/cm^3**	**Angle of repose (Θ)**	**Carr's index %**	**Hausner's ratio**
R1	0.44 ± 0.22	0.49 ± 0.14	22.05 ± 0.17	9.20 ± 0.42	1.09 ± 0.02
R2	0.47 ± 0.15	0.52 ± 0.12	21.19 ± 0.21	8.60 ± 0.14	1.11 ± 0.02
R3	0.50 ± 0.21	0.54 ± 0.14	20.80 ± 0.23	7.40 ± 0.26	1.08 ± 0.02
R4	0.52 ± 0.15	0.52 ± 0.11	20.38 ± 0.23	8.09 ± 0.21	1.08 ± 0.02
R5	0.48 ± 0.15	0.56 ± 0.14	21.30 ± 0.13	9.47 ± 0.16	1.10 ± 0.02
R6	0.40 ± 0.06	0.47 ± 0.11	23.88 ± 0.77	8.93 ± 0.77	1.12 ± 0.55
R7	0.44 ± 0.04	0.49 ± 0.12	22.13 ± 0.78	9.54 ± 0.98	1.11 ± 0.45
R8	0.55 ± 0.02	0.59 ± 0.21	21.25 ± 0.81	7.88 ± 1.98	1.07 ± 0.43
R9	0.58 ± 0.16	0.62 ± 0.13	20.40 ± 0.45	10.88 ±1.98	1.06 ± 0.31
R10	0.57 ± 0.04	0.63 ± 0.09	21.94 ± 1.35	7.93± 0.98	1.10 ± 0.27
R11	0.55 ± 0.02	0.61 ± 0.18	23.56 ± 0.70	8.86 ± 1.42	1.11 ± 0.57
R12	0.55 ± 0.02	0.62 ± 0.12	21.45 ± 1.15	9.57 ± 1.13	1.12 ± 0.48

Table 7: Physico-chemical evaluation of rapidly disintegrating tablets

Code	**Hardness$^+$ (kg/cm^2)**	**Friability† (%)**	**Weight variation* (%)**	**Thickness*** (mm)**	**Drug Content (%)***
R1	3.2 ± 0.33	0.66 ± 0.01	1.08 ± 0.34	5.19 ± 0.03	99.15 ± 0.16
R2	3.4 ± 0.25	0.50 ± 0.02	1.07 ± 0.19	5.22 ± 0.01	99.51 ± 0.10
R3	3.1 ± 0.64	0.65 ± 0.01	1.05 ± 0.37	5.23 ± 0.04	98.73 ± 0.29
R4	3.3 ± 0.30	0.66 ± 0.03	1.37 ± 0.48	5.27 ± 0.06	99.82 ± 0.04
R5	3.1 ± 0.28	0.48 ± 0.06	0.99 ± 0.65	5.30 ± 0.02	99.22 ± 0.09
R6	3.3 ± 0.35	0.58 ± 0.01	1.12 ± 0.16	5.38 ± 0.01	99.55 ± 0.16
R7	2.9 ± 0.40	0.47 ± 0.04	1.16 ± 0.75	5.34 ± 0.03	99.71 ± 0.10
R8	2.8 ± 0.46	0.58 ± 0.02	0.97 ± 0.35	5.12 ± 0.05	99.03 ± 0.29
R 9	3.5 ± 0.24	0.42 ± 0.03	0.94 ± 0.29	5.22 ± 0.04	99.82 ± 0.04
R10	3.1 ± 0.33	0.58 ± 0.01	0.97 ± 0.14	5.23 ± 0.01	99.22 ± 0.09
R11	3.3 ± 0.55	0.52 ± 0.02	1.10 ± 0.19	5.32 ± 0.01	99.51 ± 0.20
R12	2.9 ± 0.64	0.64 ± 0.01	1.07 ± 0.37	5.29 ± 0.04	99.41 ± 0.18

Table 8: Physico-chemical evaluation of rapidly disintegrating tablets

Formulation Code	Wetting time (sec)*	Water absorption ratio (%)*	Disintegration time (sec)*
R1	24.93 ± 0.12	78.81 ± 1.64	29.14 ± 0.17
R2	21.14 ± 0.27	80.13 ± 1.91	26.01 ± 0.13
R3	19.93 ± 0.18	83.81 ± 1.86	24.55 ± 0.21
R4	16.78 ± 0.31	85.76 ± 1.34	21.16 ± 0.25
R5	26.82 ± 0.26	78.83 ± 1.22	34.28 ± 0.12
R6	24.93 ± 0.12	80.91 ± 1.64	28.34 ± 0.17
R7	20.14 ± 0.27	81.13 ± 1.91	26.01 ± 0.13
R8	17.93 ± 0.18	83.81 ± 1.86	25.55 ± 0.21
R9	29.78 ± 0.31	74.76 ± 1.34	37.16 ± 0.25
R10	25.82 ± 0.26	78.83 ± 1.22	34.28 ± 0.12
R11	22.33 ± 0.17	80.16 ± 1.16	30.01 ± 0.43
R12	19.64 ± 0.45	81.81 ± 1.43	28.78 ± 0.68

Table 9: Physico-chemical data of selected RDT before and after stability study

Formulation code	Hardness test (kg/cm^2)		Friability (%)		Weight variation (%)		Thickness(mm)		Drug content (%)	
	Before	After	Before	After	Before	After	Before	After	Before	After
R4	3.3± 0.30	3.3± 0.12	0.65± 0.03	0.61± 0.03	1.37± 0.48	1.41± 0.01	5.14± 0.06	5.24± 0.46	99.82 ± 0.04	99.62 ±0.14
R8	2.8± 0.46	2.7± 0.98	0.58± 0.02	0.54± 0.02	0.94± 0.35	1.01± 0.29	5.53± 0.05	5.73± 0.45	99.03 ± 0.29	98.93 ±0.19
R12	2.9± 0.64	2.8± 0.84	0.64± 0.01	0.62± 0.01	1.07± 0.37	1.51± 0.49	5.79± 0.04	5.99± 0.14	99.41 ± 0.18	99.11 ±0.28

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