Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2011, 3 (6):125-130
(http://scholarsresearchlibrary.com/archive.html)

Scholars Research Library
ISSN 0974-248X
USA CODEN: DPLEB4

Formulation and evaluation of rizatriptan benzoate orodispersible tablets

T. Satyanarayana*, J. Murali Krishna, P. Suresh Kumar, S. Navaneetha Krishnan and G. Shaji

Browns College of Pharmacy, Khammam, Andhra Pradesh, India

ABSTRACT

Oral disintegrating tablets have emerged as an alternative to the conventional oral dosage forms to improve the patient compliance. Due to problem in swallowing ability with age, the paediatric and geriatric patients complain of difficulty to take conventional solid dosage forms. The ODT's are solid dosage forms that dissolve or disintegrate rapidly in the oral cavity. This results in solution or suspension without the need of water. The main objective of this work is to formulate and evaluate Rizatriptan Benzoate ODT's using different concentration of super disintegrating agents like croscarmellose , Sodium Starch Glycolate (SSG),Crospovidone.Tablets were prepared by direct compression method and evaluated for hardness, thickness, friability, disintegration time, and percentage of drug release.. The results indicated that formulation prepared with Crospovidone was found to be optimised which provides maximum drug release (100%) and minimum disintegration time (less than 10 second).

Key words: Rizatriptan Benzoate, Oral disintegrating tablets, superdisintegrant, croscarmellose , Sodium Starch Glycolate, Crospovidone.

INTRODUCTION

In recent years, considerable attention has been focused on the development of novel drug delivery systems (NDDS). The reason for this paradigm shift may be due to relatively low development cost and time required for introducing a NDDS ($ 20-50 million and 3-4 years respectively) as compared to a new chemical entity (approximately $500 million and 10-12 years, respectively). In the form of NDDS, an exist ing drug molecule can get a 'new life', thereby increasing its market value, competitiveness, and patent life [1]. In addition to this, in clinical conditions like nausea and vomiting, administration of conventional dosage form with water is quite difficult [2]

Tablet is most popular among all dosage forms existing today because of convenience of self administration, compactness and easy manufacturing. However, patients especially elderly find it difficulty in swallowing tablets, capsules, fluids and thus do not comply with prescription which results in high incidence of noncompliance and ineffective therapy[3] .Patient convenience and compliance oriented research has resulted in bringing out many safer and newer drug delivery

systems. Mouth Fast disintegration or dissolving tablets are of such examples, for the reason of rapid disintegration or dissolution in mouth with little amount of water or even with saliva [4]. Significance of this drug delivery system includes administration without water, accuracy of dosage forms, ease of portability, alternative to liquid dosage forms, ideal for pediatric and geriatric patients and rapid onset of action.

Usually superdisintegrants are added to a drug formulation to facilitate the break-up or disintegration of tablet into smaller particles that can dissolve more rapidly than in absence of Disintegrants [5]. Elimination of bitterness is an important criterion in product formulation of mouth dissolving tablets [6]

Rizatriptan Benzoate is used for the treatment of migraine headaches, it is a selective 5-hydroxytryptamine 1 receptor subtype agonist .The aim of the study was to formulate an oral disintegrating tablet of Rizatriptan Benzoate using two superdisintegrants separately (crosscarmellose ,Crospovidone and sodium starch glycolate), and to select the best among the two based on the disintegration time and other tableting properties.

MATERIALS AND METHODS

Materials

Rizatriptan Benzoate was obtained as gift sample from Dr. Reddys laboratory, Hyderabad. Croscarmellose,Crospovidone and Sodium Starch Glycolate (SSG) where gift samples obtained from Madras Pharmaceuticals, Chennai. All chemicals used were of analytical grade.

Table: 1 Formulation development trial (mg/tablet)

Ingredients	F1	F2	F3	F4	F5	F6
Dizatriptan Benzoate	10(14.53)	10(14.53)	10(14.53)	10(14.53)	10(14.53)	10(14.53)
Lactose	50.47	_	_	_	_	_
Avicel PH 102	_	70	90	50.47	50.47	50.47
Mannitol	90	70	50.47	90	90	90
Crospovidone XL	10	10	10	—	—	10
Croscarmellose	_	_	_	10	_	_
Sodium starch glycolate	_	_	_	_	10	_
Glycine	23	23.47	23	23	23	23
Sodium Chloride	5	5	5	5	5	5
Aspartame	4	4	4	4	4	4
Mint flavour	1	1	1	1	1	1
Magnesium stearate	2	2	2	2	2	2
Total weight (mg)	200	200	200	200	200	200

Preparation of orally disintegrating tablet

Rizatriptan Benzoate was weighed accurately and sifted through #40 mesh. Micro crystalline cellulose and Mannitol were weighed accurately sifted through #40 mesh separately and added individually to the above and mixed for 5 minutes.Sodium chloride, Glycine, Aspartame and Mint were weighed accurately and passed through #60 mesh separately and added to the above mixture one after the other and for each addition the mixture was blended thoroughly for 5 minutes.The Super disintegrant Crospovidone was weighed and sifted through #40 and added to the above mixture and blended for 5 minutes.Magnesium sterate was weighed accurately and sifted through #40 and added to the above blend.The final blend was mixed thoroughly for 2-3 minutes in the poly bag and tablets were compressed using 7 mm round flat shaped punches.[Table 1]

Evaluation of blends [7]
Prior to the compression of both granules into tablets, the granules were evaluated for properties like Angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio.

Evaluation of tablets [8, 9, 10, 11]
Thickness
Thickness was determined for twenty pre-weighed tablets of each batch using a digital vernier scale (Mitutoyo- Digi) and the average thickness was determined in mm**.** The tablet thickness should be controlled within a ± 5% variation of a standard.

Hardness
Hardness or crushing strength is the force required to break a tablet in diametric compression.

Hardness of the tablets is determined by Monsanto hardness tester which consists of a barrel with a compressible spring. The pointer moving along the gauze in the barrel at which the tablet fractures indicates the hardness of the tablet. Six tablets from each batch were taken randomly and their hardness was determined.

Friability
This test is performed to evaluate the ability of a tablet to withstand abrasion in packing, handling and transporting purpose. Twenty sample tablets were rotated at 25rpm for 4 minutes by a USP-type Roche friabilator, then reweighed after removal of fines and the percentage weight loss was calculated according to the following formula. The tablets were found to pass the friability test, if the percentage weight loss was found to be less than 1%.

$$\% \text{ Friability} = (W0-W)/W0 \times 100$$

Where W0=initial weight of twenty tablets
W= weight of 20 tablets after 100 revolutions

Disintegrating Time
The disintegration test is carried out in an apparatus (Electro lab, Mumbai) containing a basket rack assembly with six glass tubes of 7.75 cm 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 times per minute in a medium of 900 ml which is maintained at 37±2 °C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh (#10) was considered as the disintegration time of the tablet. The disintegration time that patients can experience for oral disintegrating tablets ranges from 5 to 30 sec.

Dissolution study
Dissolution study was carried out by using USP Type II dissolution apparatus. The dissolution was carried out in pH 7.2 buffer solution as dissolution medium. 5ml sample where collected at 5, 10, 15,20,25,30 and 45 minutes time intervals and after proper dilution they were analysed at 280nm against the blank pH 7.2 buffer solutions using an Eli co UV Double beam Spectrophotometer.

Stability studies[10]
The optimized formulation was subjected for stability studies at accelerated conditions of a temperature 40^0 C and a relative humidity of 75% and at 0,10,20 and 30 days for their physical appearance,hardness,disintegration time, drug content,friability,thickness and %drug release.

RESULTS AND DISCUSSION

Oral disintegrating tablets Rizatriptan Benzoate,were prepared by direct compression method using Croscarmellose ,Crospovidone and Sodium Starch Glycolate (SSG) as super disintegrants in different concentration. Six formulations were prepared.

The powder blend of six formulations F1 to F6 was evaluated for Angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio, which showed the pre-compressed blend, has good flow property. The results are shown in [Table 2].

Table: 2 Evaluation of Directly Compressible Blend

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Carr's Index	Hausner Ratio	Angle of repose(θ)
F1	0.378	0.477	20-26	1.25	33.92
F2	0.407	0.528	16.91	1.31	31.25
F3	0.419	0.555	18.50	1.32	32.61
F4	0.461	0.596	17.97	1.26	30.61
F5	0.467	0.529	15.76	1.19	28.42
F6	0.438	0.513	14.61	1.17	26.25

The values of different physical tests are given in [Table 3]. The tablets obtained had drug contents in the range of 98 to 100%. This is within the acceptable limit. Hardness of tablet was found in the range of 3.10 to 3.45 kg/cm^2. Friability was found to be below 1% which indicates good mechanical strength of the tablets.. All the formulations found to have much faster wetting time when compared to the control with significant increase in the water absorption capacity. The disintegration time (DT) for the formulation prepared with Sodium Starch glycolate,Croscarmellose and crospovidone was found to be in the range of 10-14 second.. Among all the formulations F_6 were showing promising results as the DT was 10 second.

Table: 3 Evaluations of Compressed Formulations

Formulation code	Average weight(mg)	Thickness (mm)	Hardness (Kp)	Percentage friability (%)	Disintegration time (sec)
F1	203.0	3.21	1.09	1.56	13
F2	197.6	3.10	1.30	0.69	14
F3	200.0	3.41	2.86	0.16	12
F4	198.4	3.45	1.75	0.35	11
F5	198.0	3.37	2.21	0.17	13
F6	200.2	3.16	2.92	0.12	10

In-vitro drug release studies were performed with all formulations. The results are accordingly tabulated in [Table 4] [Fig 1,2]. The percentage drug release for the formulation F_6 was found 100% respectively at the end of 15 minutes. Formulation F_6 prepared with crospovidone was found to be the optimised formulation.

Table: 4 Cumulative percentage drug release of Rizatriptan Benzoate

Time (min)	F 1	F 2	F 3	F4	F5	F6	Marketed product
0	0	0	0	0	0	0	0
5	85.3	84.4	85.2	85.5	87.6	88.5	90.4
10	89.1	92.4	94.6	90.6	92.9	98.71	97.6
15	93.2	95.5	98.6	96.3	98.0	101.4	100.9

.

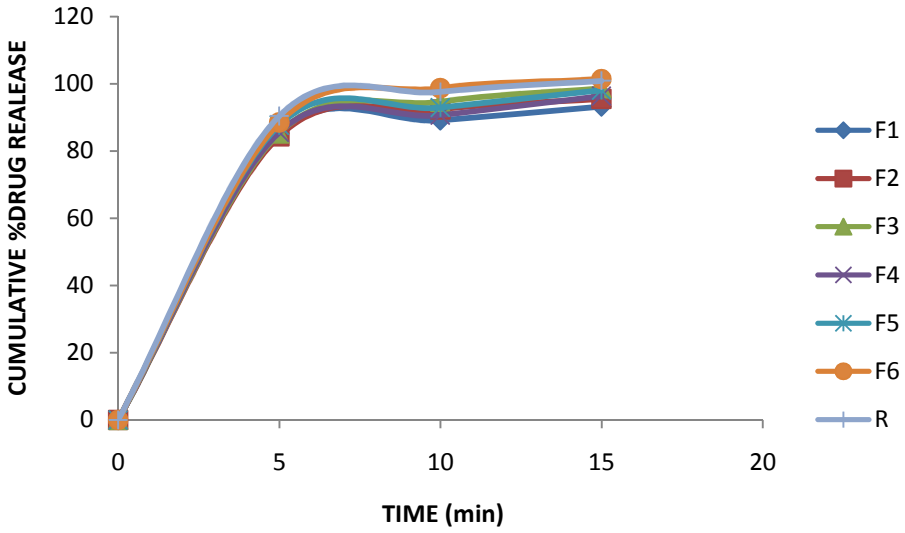

Figure: 1 Dissolution profile (F1-f6) along with marketed product (R)

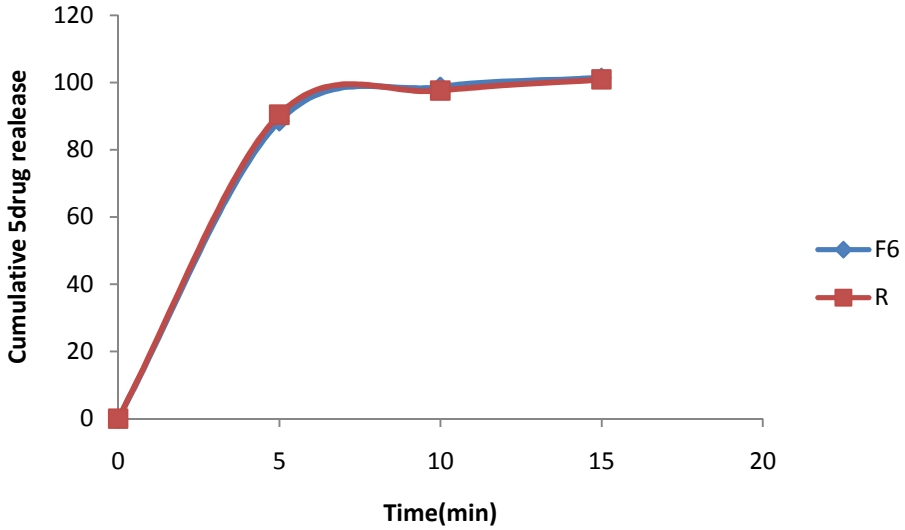

Figure: 2 Dissolution profile of F6 and Marketed product (R)

Table 5: Accelerated Stability studies of the optimized batch at 40°C/75%RH

S.No	Parameters	Initial	15 days	30 days
1	Average weight of Tablet (mg)	200.2	200.3	200.3
2	Thickness (mm)	3.35	3.35	3.35
3	Hardness (kp)	3.2	3.3	3.3
4	Friability (%)	0.38	0.37	0.38
5	Disintegration time	10	10	9
6	Drug content (%)	101	102	101
7	%Drug release(at 15 sec)	102.3	100	100.2

The optimized formulation F6 were selected for accelerated stability studies and the tablets possessed the same parameters even after the stressed conditions, indicates good stability properties of formulation [Table.5]

CONCLUSION

The prime objective of the study was to develop Rizatriptan Benzoate,ODT by using commonly available excipients and conventional technology. From the above study it was concluded that by employing commonly available excipients such as super disintegrants, hydrophilic excipients and proper filler an ODT's tablet of Rizatriptan Benzoate can be developed which can be commercialized.

Acknowledgement
The authors are thankful to Dr. Reddys laboratories for providing gift sample of Rizatriptan Benzoate, and also are thankful to Madras Pharmaceuticals, Chennai for providing gift samples of Croscarmellose ,Crospovidone and Sodium Starch Glycolate (SSG).

REFERENCES

[1] Tapan kumar Giri; Dulal krishna Tripathi; Rana Majumdar; *Int J Pharm Pharm Sci*, **2010**, 2, 38-42.
[2] Gaurav Sharma; Vivek Kumar Pawar; Garima Garg; Rajendra Awasthi;Giriraj T. Kulkarni; *Der Pharmacia Lettre*, **2010**, 2(3): 83-94.
[3]Chandrsekhar Patro;S Sreenivas patro;Bibhu Prasad Panda; *Der Pharmacia Lettre*,**2011**:3(4) 63-70.
[4]W Habib; R Khankari;J Hontz; *Drug Carrier*. *Systems* **2000**, 17(1*),* 61-72.
[5]C.P. Jain; P.S .Naruka; *Int J Pharm Pharm Sci*, **2009**, 1, 219-226.
[6] Ravikumar ;Sachin R Patil;MB Patil; Mahesh S Paschapur; Mahalaxmi R; *Der Pharmacia Lettre,* **2010**: 2 (1) 220-236.
[7]Manish kumar; Sharad Visth ; Sazid Ali; Shikha Agarwal,;Amit Bhola; *Int J Pharm Pharm Sci* 2010, 2,109-111.
[8] Rahman Z; Ali M; *Acta Pharm* **2006**, 56, 49-57.
[9]Chinam N.P; Kumar A.B; Pandit H.K; Singh S.P;Devi M.V;.*Acta Pharm* **2007**,57,479-489.
[10] Narendiran.C; Srinath M;S,Ganesh babu; *AAPS Pharm Scitech* **2006**,34, E1-E7.
[11] Siva Prasad Reddy S; Hindustan Abdul Ahad; Sreenivasulu R; Kishore Kumar ReddyB;Krishna Mahesh CH;Kranthi G;Chandrasekhar A; *Der Pharmacia Lettre*, **2011**, 3(1): 113-120