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FORMULATION DEVELOPMENT AND EVALUATION OF RIZATRIPTAN BENZOATE ORAL DISINTEGRATING TABLETS

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ABSTRACT

To formulate and evaluate Rizatriptan benzoate oral disintegrating tablets to prepared the various formulations and perform the pre-compression parameter and post compression parameters. Direct compression method was used for the preparation of oral disintegrating tablets of Rizatriptan. prepared drug parameters compared with standard drug MAXALT MLT parameters. based on the preliminary studies various formulation trials (f1-f11) were carried out with different concentrations of superdisintegrants and diluents. from the various formulations it was concluded that the formulation f11, the reproducibility batch of f5 was finalized as the optimized formula. formulation f11 showed satisfactory results with various physicochemical evaluation parameters like hardness, percentage weight loss, disintegration time, dissolution profile when compared with the marketed product.

KEYWORDS: Direct compressiom method, cross povidone polyme, Rizatriptan Benzoate, Phosphate buffers.

INTRODUCTION

Benzoate is white to off white crystalline solid that is insoluble in water. **:** N, N-dimethyl-5-(1H-1, 2, 4-triazol-1-yl methyl)-1H-Indole-3 ethanamine Mono benzoate.[1] **Rizatriptan** (trade name **Maxalt**) is a 5-HT_1 receptor agonist of the triptan class of drugs developed by Merck & Co. for the treatment of migraine headaches.[2] Rizatriptan belongs to a class of drugs known as triptans. It affects a certain natural substance (serotonin) that causes narrowing of blood vessels in the brain. It may also relieve pain by affecting certain nerves in the brain. Rizatriptan is a headache medicine that narrows the blood vessels around the

brain. Rizatriptan also reduces substances in the body that can trigger headache pain, nausea[3,4,5,6,7], sensitivity to light and sound, and other migraine symptoms. Rizatriptan is used to treat migraine headaches. Rizatriptan will only treat a headache that has already begun. It will not prevent headaches or reduce the number of attacks. Rizatriptan should not be used to treat a common tension headache[8], a headache that causes loss of movement on one side of your body, or any headache that seems to be different from your usual migraine headaches. Use this medicine only if your condition has been confirmed by a doctor as migraine headaches.[9]

MATERIALS AND METHODS

Materials

Rizatriptan benzoate obtained from the Natco pharma ltd kothur telangana India cross povidone iodine, Avicel pH102, Pearlitol 200 SD, Pearlitol 200 SD, Cross carmellose sodium were purchased from SD fine chemical private Ltd, Mumbi, Maharastra.

Method[10]

Formulation of oral disintegrating tablets of Rizatriptan 5 mg were carried out by direct compression technique.

Rizatriptan, Pearlitol 200 SD were weighed and sifted individually through #30 mesh and then blended in a polybag for 5 minutes. Crosspovidone XL was weighed and sifted through #30 mesh and added to the above mixture and mixed for 5 minutes. Aspartame and Mint flavor were weighed and passed through #30 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 lubricant Magnesium stearate was weighed and sifted through #30 and added to the above mixture and blended with the mixture for 1 minute. The final blend was mixed thoroughly for 5-10 minutes in the poly bag and tablets were compressed using 6.4 mm round flat punches.

S.NO	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
1	Rizatriptan Benzoate	7.26	7.26	7.26	7.26	7.26	7.26	7.26	7.26	7.26	7.26	7.26
2	Spray dried Lactose	_	_	41.99	_	_	_	_	_	_	_	_
3	Avicel pH102	_	_	_	41.99	33.59	33.59	33.59	33.59	33.59	33.59	33.59
4	Pearlitol 200 SD	83.99	83.99	41.99	41.99	50.38	50.38	50.38	50.38	50.38	50.38	50.38
5	Cross povidone	5	5	5	5	5	_	_	2	_	_	5
6	Cross carmellose sodium	_	_	_	_	_	5	_	_	2	_	_
7	Sodium starch glycollate	_	_	_	_	_	_	5	_	_	2	_
8	Aspartame	2	2	2	2	2	2	2	2	2	2	2

9	**Peppermint flavour**	**0.5**	**0.5**	**0.5**	**0.5**	**0.5**	**0.5**	**0.5**	**0.5**	**0.5**	**0.5**	**0.5**
10	**Magnesium stearate**	**1.25**	**1.25**	**1.25**	**1.25**	**1.25**	**1.25**	**1.25**	**1.25**	**1.25**	**1.25**	**1.25**
	Total weight(mg)	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Precompression parameters of Rizatriptan benzoate 5mg tablet

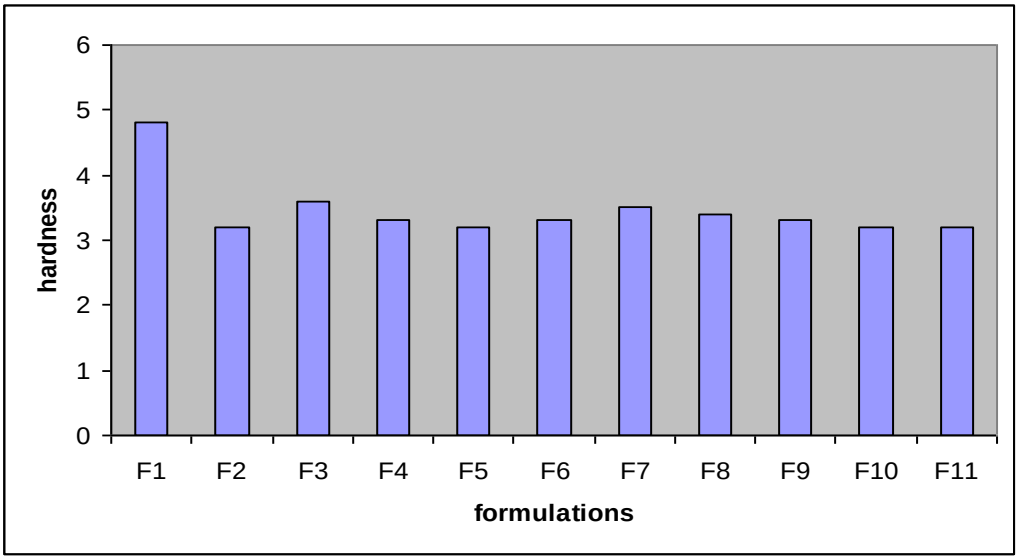
TEST	RESULT	SPECIFICATION
Description	Crystalline white powder.	Crystalline white to off white powder.
Solubility	Complies to the test	to be soluble in water and methanol
Bulk density (g/ml)	0.243	0.38-0.69
tapped density (g/ml)	0.465	0.74-0.93
Loss on drying (%)	0.12	NMT 0.5
Assay (%)	99.8	NLT 99.0 & NMT 101.0
Residue on ignition (%w/w)	0.03	NMT 0.1
Benzoic acid (chemical)(%)	31.3	NLT 30.8 & NMT 31.5
Particle size(microns)	30.4	NLT 50
Melting point(^{0}C)	178	NLT 178 & NMT 180

S.NO	Formulation Code	Bulk density (g/ml)	Tapped density (g/ml)	Carr'sindex	Hausners ratio	Angle of repose (θ)
1	F1	0.56	0.69	18.84	1.23	28
2	F2	0.61	0.72	15.2	1.18	26
3	F3	0.65	0.80	18.7	1.23	27
4	F4	0.63	0.72	12.5	1.14	24
5	F5	0.59	0.65	13.9	1.12	22
6	F6	0.57	0.69	17.3	1.21	24
7	F7	0.59	0.69	14.4	1.16	23
8	F8	0.64	0.75	14.6	1.17	25
9	F9	0.62	0.75	17.3	1.20	26
10	F10	0.59	0.71	16.9	1.20	24
11	F11	0.60	0.66	15.8	1.1	23

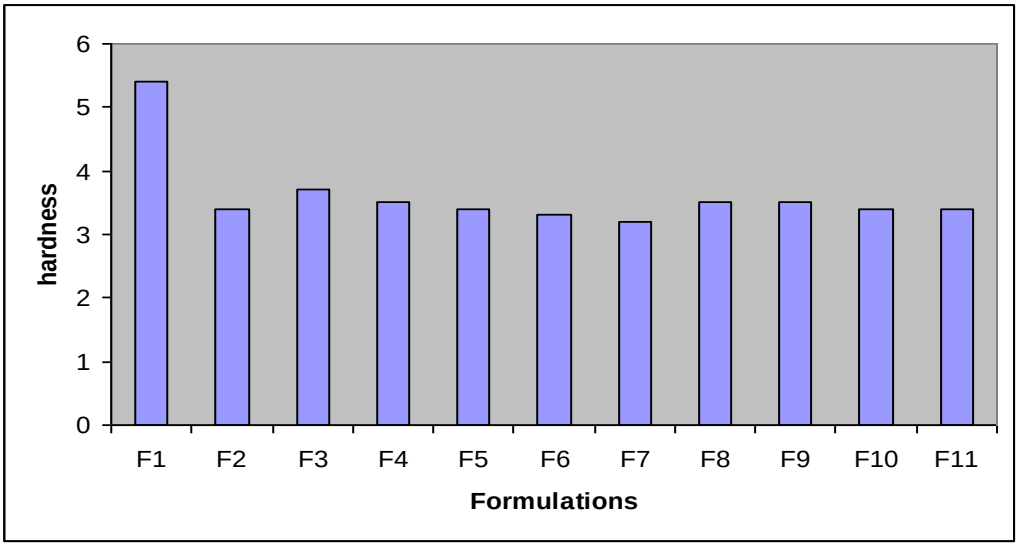
Post Compression Parameters of 5 mg Tablets

Formulation Code	Average weight (mg)	Thickness (mm)	Hardness (kp)	Percentage Friability (%)	Disintegration Time (sec)
F1	100.1	2.78	4.8	0.33	19
F2	100.2	3.12	3.2	0.37	11
F3	100.0	2.97	3.6	0.38	14
F4	100.0	2.89	3.3	0.45	10
F5	99.8	3.01	3.2	0.40	9
F6	100.1	2.88	3.3	0.39	10
F7	100.3	2.68	3.5	0.42	13
F8	100.0	2.79	3.4	0.43	13
F9	99.7	2.75	3.3	0.45	15
F10	99.9	2.81	3.2	0.41	18
F11	99.9	2.97	3.2	0.38	9

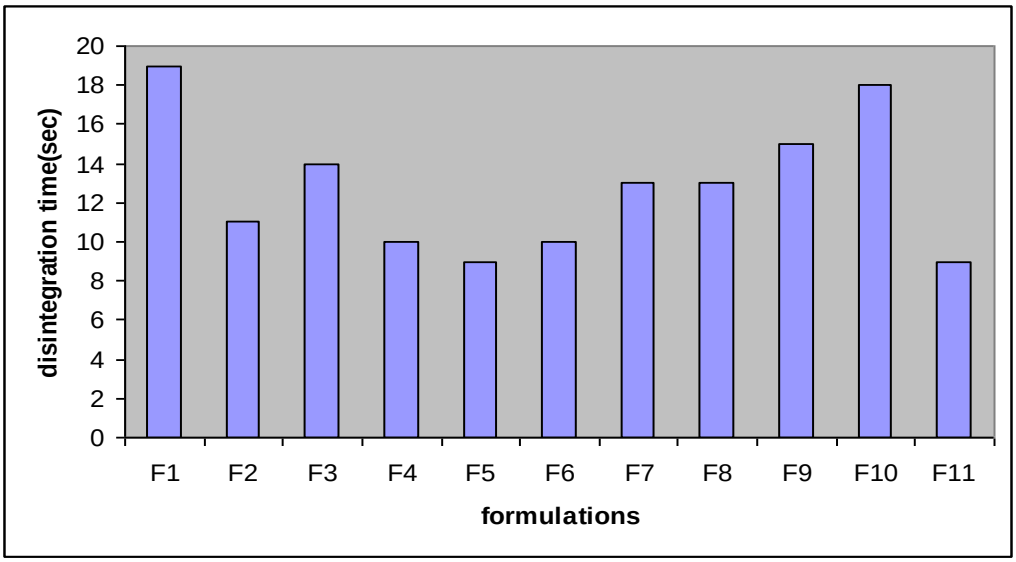
Comparision of Hardness of Different Formulations



Comparision of % Friability of Different Formulations



Comparision of Disintegration Time of Different Formulations



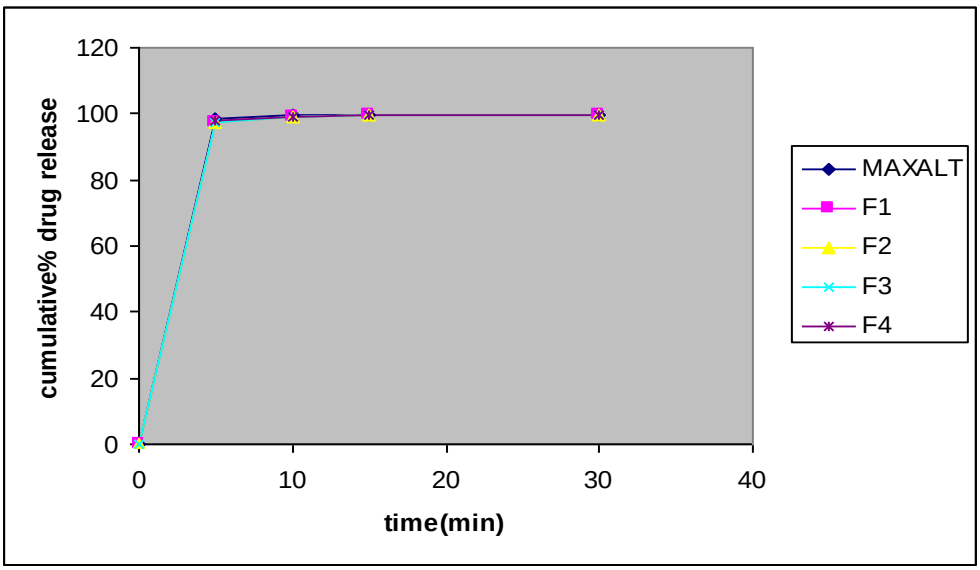
Dissolution Studies for Rizatriptan ODT

% drug release of 5 mg tablets

S.NO	TIME(min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
1	0	0	0	0	0	0	0	0	0	0	0	0
2	5	97.5	97.6	97.4	97.8	98.2	97.0	93.3	93.6	92.4	89.9	98.3
3	10	99.2	99.1	98.9	99.3	99.5	98.6	96.8	96.5	95.8	93.3	99.5
4	15	99.6	99.5	99.6	99.8	100.1	99.3	98.4	99.0	97.9	95.9	100.0
5	30	99.8	99.8	99.9	99.9	100.0	99.7	99.2	99.4	99.1	98.4	100.0

Comparison of % drug release of all formulations with reference product

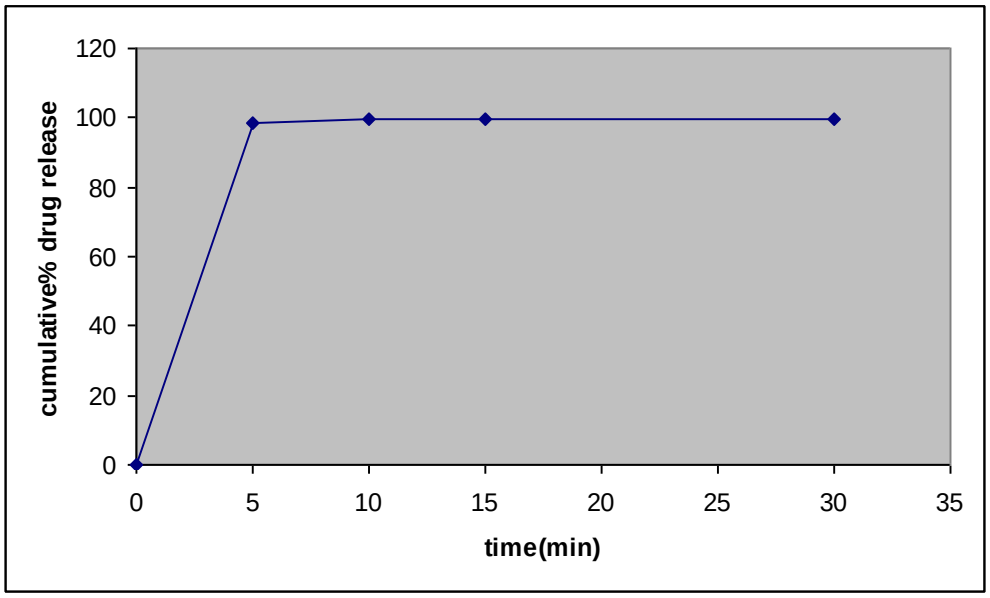
Comparision of Dissolution Studies of 5 mg ODT

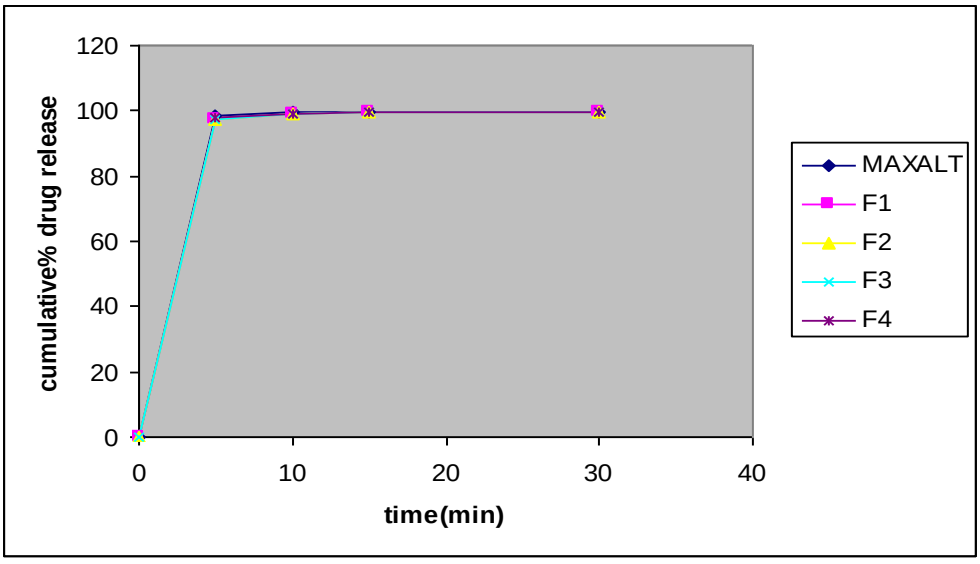


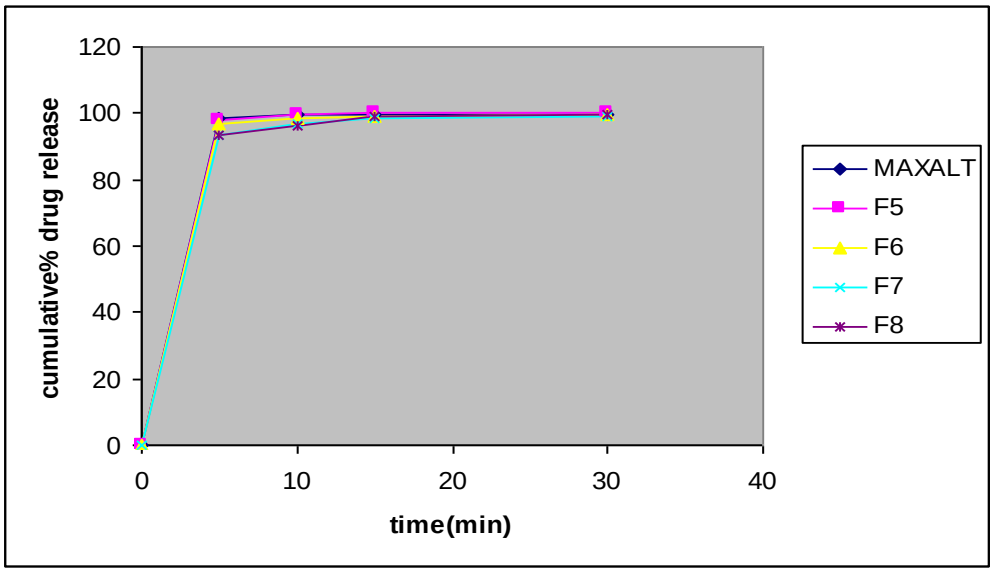
Dissolution studies of reference product MAXALT-MLT 5 mg tablets

Drug release of Reference product

S.NO	TIME(min)	% DRUG RELEASE (5 mg)
1	0	0
2	5	98.4
3	10	99.6
4	15	99.6
5	30	99.7






120
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cumulative% drug release
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time(min)
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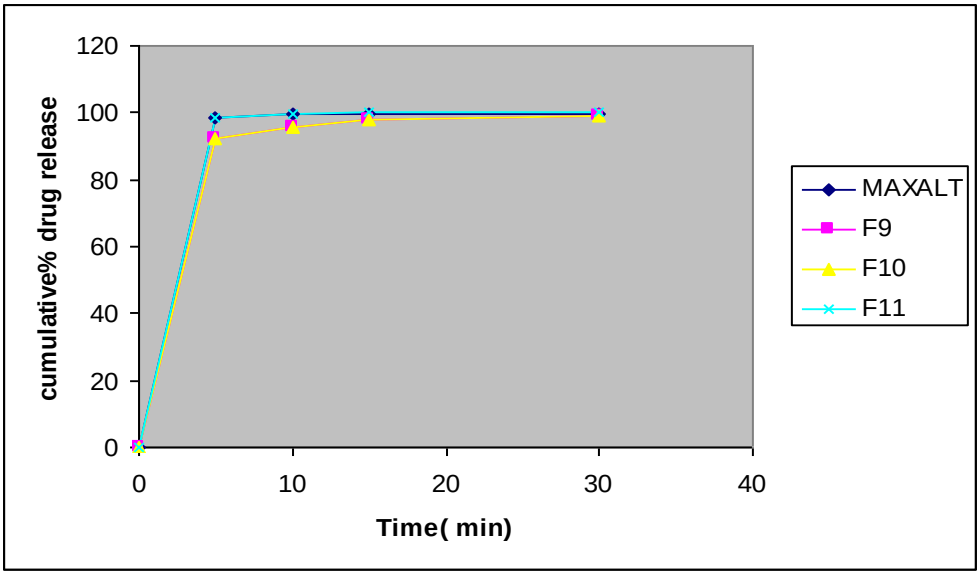
F6
F7
F8


120
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cumulative% drug release
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Time(min)
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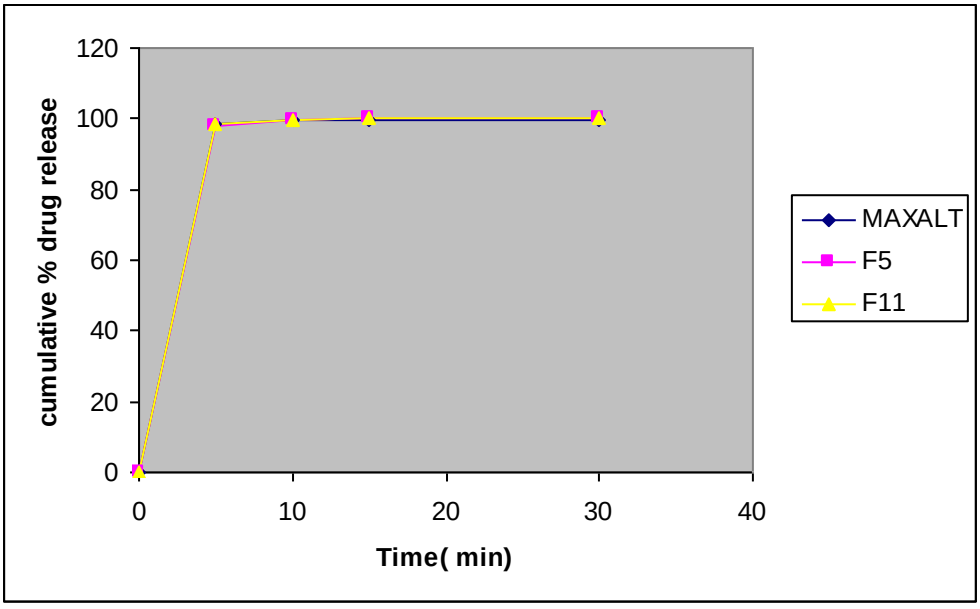
F10
F11


120
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cumulative % drug release
0
10
20
30
40
Time(min)
MAXALT
F5
F11

RESULTS AND DISCUSSION

F1 was carried out using Pearlitol 200 SD as diluent, Crosspovidone XL (5%) as super disintegrant and Magnesium stearate (1.25%) as lubricant. In this trial the hardness of the tablets was very high which resulted in failure of disintegration (19 sec for 5 mg tablets) Also the tablets were bitter in taste.

During the F2 batch trails were performed for optimizing the hardness of the tablets using three different trials T1, T2 and T3. Based on the readings obtained the hardness for the tablets in the further studies was fixed in the range of 3.0 to 3.5 kp.

The F3 trial was performed by using spray dried lactose and Pearlitol 200 SD in the ratio of 50 : 50 as the diluents, crosspovidone(5%) as the super disintegrant and magnesium stearate(1.25) as the lubricant. The bitter taste was reduced to some extent but it was observed that the hardness was somewhat high and the disintegration time is more than the F2 trail in both the tablets.

The formulation F4 was performed by replacing the spray dried lactose with Avicel PH102 and the tablets were compressed as both 5 mg and 10 mg tablets. The disintegration time of the tablets was reduced than the F3 trail, but the taste of the tablets was found to be very bitter. So, the concentration of Pearlitol 200 SD was increased in further trails.

Formulation F5 was carried out by taking AVICEL pH 102 and Pearlitol 200 SD in the ratio of 40: 60 respectively, crosspovidone (5%) as the superdisintegrant and Magnesium stearate (1.25) as the lubricant and the tablets were compressed. It was found that all the factors like disintegration friability, hardness and dissolution were satisfactory. This formulation was used as the final formulation and compressed for the reproducibility batches to conduct the stability studies.

F6 was performed by using AVICEL pH 102 and Pearlitol 200 SD in the ratio of 40: 60 respectively as the diluents, Cross carmellose sodium as superdisintegrant (5%) and magnesium (1.25%) as the lubricant. The disintegration time of the tablets was found to be more than that of the tablets formulated with cross povidone as the super disintegrant. All other parameters were found to be satisfactory.

F7 was performed by using AVICEL pH 102 and Pearlitol 200 SD in the ratio of 40: 60 respectively as the diluents, sodium starch glycollate (5%) as the super disintegrant and

magnesium (1.25%) as the lubricant. All the parameters were found to be satisfactory in this trial except the disintegration time which is higher than that of both cross povidone and cross carmellose sodium.

F8 was performed by using AVICEL pH 102 and Pearlitol 200 SD in the ratio of 40: 60 respectively as the diluents, cross povidone was taken in 2% concentration as the super disintegrant and magnesium (1.25%) as the lubricant. The disintegration time was found to be more than that of 5% concentration of all the super disintegrating agents.

F9 was performed with AVICEL pH 102 and Pearlitol 200 SD in the ratio of 40 : 60 respectively as the diluents, cross carmellose sodium(2%)as the super disintegrant and magnesium (1.25%) as the lubricant. The disintegration time was found to be more than that of the 2% cross povidone and all the 5% concentrations of all the super disintegrants.

F10 was performed with AVICEL pH 102 and Pearlitol 200 SD in the ratio of 40: 60 respectively as the diluents, sodium starch glycollate (2%) as the super disintegrant and magnesium (1.25%) as the lubricant. The disintegration time was found to be more than that of the 2% cross povidone and 2%.

CONCLUSION

Rizatriptan Benzoate is widely used as Anti migraine agent. They are formulated as oral disintegrating tablets which show better patient acceptability and compliance with improved efficacy when compared with conventional dosage forms. Based on various studies carried out we have arrived at the following conclusions. Direct compression was used for the preparation of oral disintegrating tablets of Rizatriptan. Based on the preliminary studies various formulation trials (F1-F11) were carried out with different concentrations of superdisintegrants and diluents. From the various formulations it was concluded that the formulation F11, the reproducibility batch of F5 was finalized as the optimized formula. Formulation F11 showed satisfactory results with various physicochemical evaluation parameters like Hardness, Percentage weight loss, Disintegration time, Dissolution profile when compared with the marketed product. cross carmellose sodium and all the 5% concentrations of the super disintegrants. Reproducibility batch for formulation F5 to study all the parameters for the stability studies. All the precompression and the post compression parameters showed good results and were comparable with the reference product.

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