WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Formulation and Evaluation of Fast Dissolving Tablets of Rizatriptan Benzoate

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ABSTRACT

The aim of the present study was to formulate and evaluate fast dissolving tablets of Rizatriptan Benzoate by direct compression technique. F1 was carried out using Spray dried Lactose and Pearlitol 200 SD in the ratio of 30:70 as diluent, Crosspovidone XL (5%) as superdisintegrant and Magnesium stearate (1.25%) as lubricant. In this trial the friablity of the tablets was very high which resulted in failure of structure of the tablet.The F2 trial was performed by using Avicel pH 102 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. It was observed that the hardness was higher and the disintegration time was more in both the tablets. The formulation F3 was performed by using Avicel pH102 and Pearlitol 200 SD in theratio of 70: 30 and the tablets were compressed as both 5 mg and 10 mg tablets. The disintegration time of the tablets was satisfactory, 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 F4 was carried out by taking Avicel pH 102 and Pearlitol 200 SD in the ratio of 30:70 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.

Key words: Rizatriptan Benzoate Lactose Spray Dried, Avicel ph 102, Pearlitol SD 200, Crosspovidone XL, Cross carmellose sodium, Sodium Starch Glycolate

Introduction

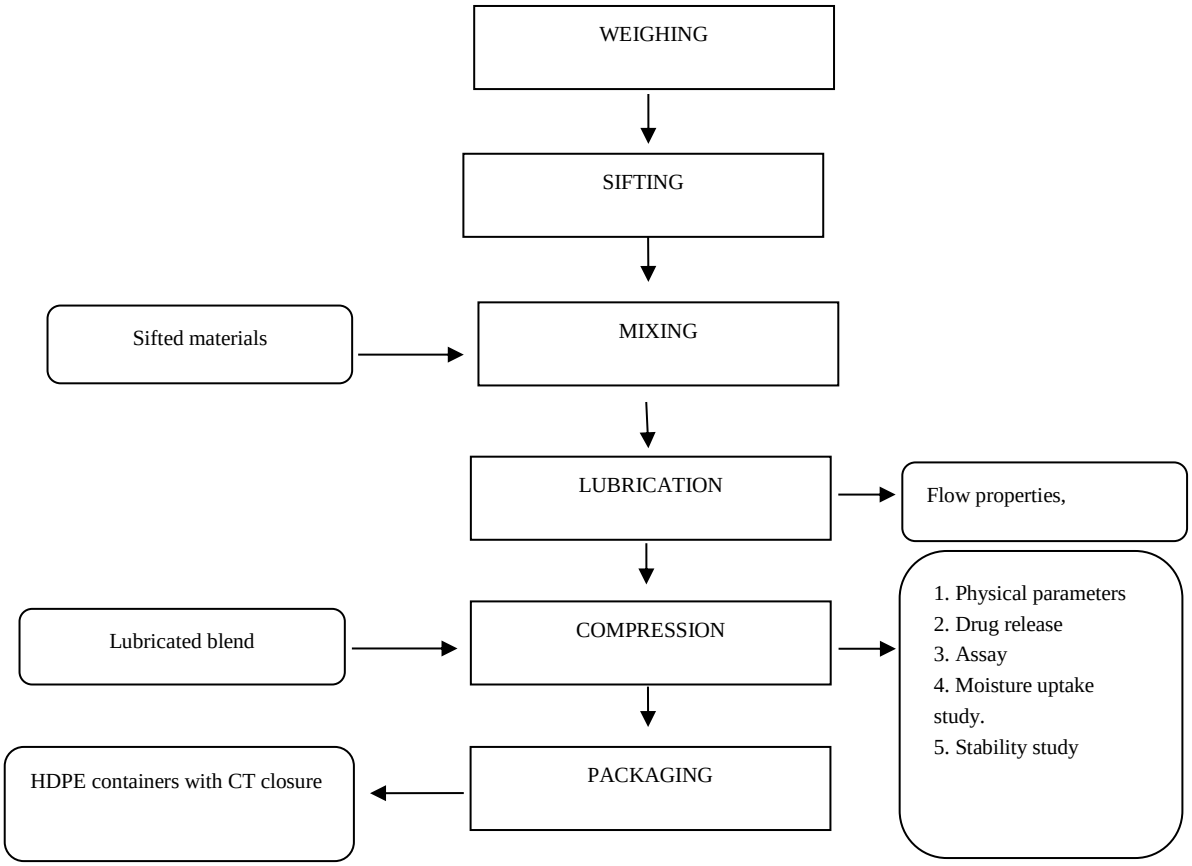
Rizatriptan Benzoate is an Anti migraine drug that is white to off white crystalline solid. Migraine[1-4]is a specific and common form of headache that has been known since antiquity. It is traditionally called as vascular headache due to the belief that it is due to abnormal changes in the blood vessel tone. The symptoms of a migraine may include throbbing or dull aching pain on one or both sides of the head nausea, vomiting, diarrhea, blurred vision or blind spots, , anxious or restlessness, light headedness, tender scalp, cold hands and feet. The therapeutic activity of Rizatriptan in migraine can most likely be attributed to agonist effects at 5-HT1B/1D receptors on the extra cerebral, intracranial blood vessels that become dilated during a migraine attack and on nerve terminals in the trigeminal system thus causing vaso constriction and inhibition of neuropeptide release and reduced transmission in trigeminal pain pathways and thus subsequent relief of migraine headache is seen.

Oral Disintegrating Tablets (ODTs)[5-9] are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue. The marketed drug of Rizatriptan is available under the brand name Maxalt-MLT[25] in 5 mg and 10 mg strengths. Maxalt-MLT is prepared using freeze drying technique which is very cumbersome process and costly. Further the product obtained is very brittle which requires special attention during packing and removal from the pack. So, the aim of the present study is to develop better formulation of Rizatriptan that is having good stablity using a cost effective process [10-13].

MATERIALS AND METHODS

Rizatriptan Benzoate were obtained from Natco Pharma Ltd., Hyderabad Lactose Spray Dried, Avicel ph 102, Pearlitol SD 200, Crosspovidone XL, Cross carmellose sodium, Sodium Starch Glycolate were obtained from Signet chemical corporation Mumbai.

FORMULATION DEVELOPMENT



Flow chart for formulation of tablets by direct compression method

FORMULATION DEVELOPMENT FOR 5mg TABLETS

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	25.19	_	_	_	_	_	_	_	_	_	_
3	Avicel pH102	_	41.99	58.79	25.19	25.19	25.19	25.49	24.89	25.38	25.01	33.59
4	Pearlitol 200 SD	58.79	41.99	25.19	58.79	58.79	58.79	59.49	58.09	59.23	58.35	50.38
5	Cross povidone	5	5	5	5	_	_	4	6	5	5	5
6	Cross carmellose sodium	_	_	_	_	5	_	_	_	_	_	_
7	Sodium starch glycollate	_	_	_	_	_	5	_	_	_	_	_
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	0.62	1.87	1.25
	Total weight(mg)	100	100	100	100	100	100	100	100	100	100	100

POST COMPRESSION PARAMETERS OF 5 mg TABLETS

Formulation Code	Average weight (mg)	Thickness (mm)	Hardness (kp)	Percentage Friability (%)	Disintegration Time (sec)	Wetting time(sec)
F1	100.1	2.78	1.09	1.32	18	12
F2	100.2	3.12	2.01	0.19	19	11
F3	100.0	2.97	1.75	0.35	10	8
F4	100.0	2.83	1.73	0.38	9	6
F5	99.8	3.01	1.75	0.37	14	10
F6	100.1	2.88	1.76	0.36	18	11
F7	100.3	2.68	1.73	0.37	12	8
F8	100.0	2.79	1.73	0.38	9	6
F9	99.7	2.75	1.71	0.42	10	7
F10	99.9	2.81	1.76	0.34	11	7
F11	99.9	2.81	1.74	0.38	9	6

POST COMPRESSION PARAMETERS OF 10 mg TABLETS

Formulation Code	Average weight (mg)	Thickness (mm)	Hardness (kp)	Percentage Friability (%)	Disintegration Time (sec)	Wetting time(sec)
F1	199.23	2.97	1.12	1.29	22	14
F2	200.01	3.01	2.08	0.21	21	13
F3	200.03	2.89	1.77	0.36	12	9
F4	199.89	2.94	1.75	0.38	11	7
F5	200.01	3.01	1.78	0.43	15	12
F6	200.12	2.99	1.80	0.42	20	14
F7	199.98	3.03	1.76	0.40	14	9
F8	200.00	3.00	1.75	0.39	10	7
F9	200.02	3.01	1.74	0.39	12	7
F10	200.00	2.98	1.79	0.35	11	8
F11	200.00	2.95	1.74	0.34	11	7

DISCUSSION

Formulation 1

F1 was carried out using Spray dried Lactose and Pearlitol 200 SD in the ratio of 30:70 as diluent, Crosspovidone XL (5%) as superdisintegrant and Magnesium stearate (1.25%) as lubricant. In this trial the friablity of the tablets was very high which resulted in failure of structure of the tablet.

Improvisation of trial

- Replace spray dried lactose with Avicel Ph 102.
- Increase the compression force of the punches on the tablets.

Formulation 2

The F2 trial was performed by using Avicel pH 102 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. It was observed that the hardness was higher and the disintegration time was more in both the tablets.

Improvisation of trial

- Increase the concentration of Avicel PH102 to 70%.
- Decresae the compression force.

Formulation 3

The formulation F3 was performed by using Avicel pH102 and Pearlitol 200 SD in the

ratio of 70: 30 and the tablets were compressed as both 5 mg and 10 mg tablets. The disintegration time of the tablets was satisfactory, but the taste of the tablets was found to be very bitter. So, the concentration of Pearlitol 200 SD was increased in further trails.

Improvisation of trial

- Increase in the concentration of Pearlitol 200 SD.

Formulation 4

Formulation F4 was carried out by taking Avicel pH 102 and Pearlitol 200 SD in the ratio of 30:70 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.

Formulation 5

F5 was performed by using AVICEL pH 102 and Pearlitol 200 SD in the ratio of 30: 70 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.

Formulation 6

F6 was performed by using Avicel pH 102 and Pearlitol 200 SD in the ratio of 30: 70 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.

Formulation 7

F7 was performed by using Avicel pH 102 and Pearlitol 200 SD in the ratio of 30: 70 respectively as the diluents, Cross povidone was taken in 4% 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 Cross povidone.

Formulation 8

F8 was performed with Avicel pH 102 and Pearlitol 200 SD in the ratio of 30 : 70 respectively as the diluents, Cross povidone was taken in 6% concentration as the super disintegrant and magnesium (1.25%) as the lubricant. The disintegration time was found to be nearly equal to the 5% concentration of the Cross povidone.

Formulation 9

F9 was performed with Avicel pH 102 and Pearlitol 200 SD in the ratio of 30: 70 respectively as the diluents, Cross povidone was taken in 5% concentration as the super disintegrant and magnesium (0.62 %) as the lubricant. All the parameters were found to be satisfactory.The flow properties were found to be poor than the above batches (F1-F8).

Formulation 10

F10 was performed with Avicel pH 102 and Pearlitol 200 SD in the ratio of 30: 70 respectively as the diluents, Cross povidone was taken in 5% concentration as the super disintegrant and magnesium (1.87 %) as the lubricant. All the parameters were found to be satisfactory.The flow properties were found to be nearly equal to above formulation (F1-F8).

Formulation 11

Reproducibility batch for formulation F4to 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.

CONCLUSION

The purpose of the present study was to develop and characterize a generic product of RizatriptanOral disintegrating tablets of strength 5 mg and 10 mg; comparable to the brand product MAXALT-MLT(Merck. co. INC, USA).

To accomplish the objective, API characterization and reference product evaluation was carried out. The drug and excipients were subjected to preformulation studies which encompasses the "Drug-Excipient" compatibility.

Direct compression technique was choosen to develop a finished pharmaceutical product of the envisaged form. Various formulation trials (F1-F11) were taken. In these trials, Drug: Excipient ratio was varied and the effect of Diluent, Superdisintegrant and lubricant on the performance of both blend as well as tablets was studied.

Based on the results obtained it was concluded that the formulation F11, the reproducibility batch of F4 was finalized as the optimized formula.

The final trial F11 was reproduced from formulation F4 to check various tablet parameters like Thickness (2.8-3.2)mm; Hardness (1.5-1.80)kp; Percentage Friability (<1%) and Disintegration time (<30 seconds), which were within the specified limits. The Dissolution and Assay results of F4 and F11 were good when compared with the reference product.

Moisture uptake studies for the final batch F11 were performed at 43, 64 and 75% RH and there was a slight moisture uptake observed in tablets at 75% RH. The reproducibility batch F11 was loaded for long term and accelerated stability studies at 25 ± 2C/60±5% RH and 40±2C/75±5% RH respectively.. The results of stability data for 1st, 2nd month and 3rd months (40±2C/75±5% RH) were found to be good.

When subjected to accelerated stability studies the tablets were found to be stable. Thus, the work resulted in the development of a ODT of Rizatriptan comparable to inventors product.

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