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Formulation and evaluation of rapimelts of Eletriptan

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ABSTRACT

Eletriptan is a second generation triptan drug intended for treatment of migraine headaches. The prepared tablets were shown good compression parameters and they passed all the quality control evaluation parameters as per IP limits. All the formulations were prepared by direct compression method using 8mm punch on 8 station rotary tablet punching machine. The blend of all formulations showed good flow properties such as angle of repose, bulk density, tapped density. Twelve formulations F1-F12 were formulated and evaluated for various quality control parameters. All the formulations were passed the tests and the results were within limits. From the dissolution data it was evident that formulation F3 was found to be best formulation with maximum % drug release of 99.9 % in 6 minutes. Disintegration time of F3 was found to be 16.33 seconds.

Keywords: Eletriptan, Rapimelts, Disintegration time, Drug release.

INTRODUCTION

Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities [1]. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly [3]. Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance [2]. It is always the aim of a scientist or a dosage form designer to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in NDDS aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance. Mouth Dissolving Tablet (MDT) or rapimelts is one among such approaches [5, 6].

Improved patient compliance has achieved enormous demand. Consequently demand for their technologies is also increasing many folds [4]. To develop a chemical entity, a lot of money, hard work and time are required. So focus is rather being laid on the development of new drug delivery systems for already existing drugs, with enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects [7]. The oral route of administration is the most preferred route due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliance [11, 13]. Tablets and capsules are the most popular dosage forms [8].

But one important drawback of such dosage forms is Dysphasia or difficulty in swallowing [9]. This is seen to afflict nearly 35% of the general population. To solve these problems, pharmaceutical technologists have put in their best efforts to develop a Fast dissolving drug delivery, i.e. Mouth Dissolving Tablet that disintegrates and dissolves rapidly in the saliva, within a few sec without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 10 sec to 3 min. Most of the rapimelts include certain super disintegrants and taste masking agents [10].

MATERIALS AND METHODS

Table 1: List of materials

Materials
Eletriptan
Crospovidone
Cros carmellose sodium
Sodium starch glycolate
Magnesium stearate
Talc
Avicel pH 102

METHODOLOGY

Determination of UV Absorption maxima

Eletriptan solution was prepared in 0.1 N HCl and diluted suitably. The UV spectrum of the solution was taken on Lab India 3200 UV/Vis double beam Spectrophotometer [12]. The Solution exhibited UV maxima at 221 nm.

Preparation of Standard Calibration Curve of Eletriptan

100 mg of Eletriptan was accurately weighed and dissolved in little amount of Methanol and make up the final volume up to 100 ml with 0.1 N HCl (pH 1.2) to prepare stock solution. The 10 ml of stock solution was further diluted with 0.1 N HCl (pH 1.2) in 100ml to get 100µg/ml (working standard). Then 0.2,0.4,0.6,0.8 and 1 ml of working standard was taken in 10 ml standard volumetric flask and made up the volume with 0.1N HCl to prepare 2, 4, 6, 8, and 10µg/ml solutions. Then the absorbance was measured in a UV spectrophotometer at 221 nm against 0.1 N HCl (pH 1.2) as blank [13].

Tablet formulation

Formulation of Eletriptan Dispersible Tablet by Direct- Compression [14]

All the ingredients were weighed. Required quantity of drug and excipient mixed thoroughly in a polybag. The blend is compressed using rotary tablet punching machine, 8 station with 6mm flat punch.

Table 2: Formulation of Eletriptan rapimelts

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Eletriptan	40	40	40	40	40	40	40	40	40	40	40	40
CP	6	8	10	12	-	-	-		-	-	-	-
CCS	-	-	-	-	6	8	10	12	-	-	-	-
SSG	-	-	-	-	-	-	-	-	6	8	10	12
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Mg. Stearate	2	2	2	2	2	2	2	2	2	2	2	2
MCC	50	48	46	44	88	84	80	44	88	84	80	44
Total	100	100	100	100	100	100	100	100	100	100	100	100

Cros povidone = CP
Cros Carmellose Sodium = CCS
Sodium Starch Glycolate = SSG
All ingredients are expressed in mg only

Evaluation of tablets

Weight variation

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in table 3 [15].

Table 3: Weight Variation Specification as per IP

Average Weight of Tablets	%Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Hardness

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm^2.

Thickness

Three tablets were selected randomly from each batch and thickness was measured by using Vernier Caliper.

Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at the height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula [16].

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

In-Vitro drug release

Release of the drug *in vitro*, was determined by estimating the dissolution profile.

Dissolution test

USP II Paddle apparatus was used and paddle was allowed to rotate at 50 rpm, acid buffer 0.1N HCL (pH 1.2, 500 ml) was used as a dissolution medium.

Drug- excipient compatibility studies by FT-IR

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany(Alpha T).The potassium bromide pellets were prepared on KBr press by grounding the solid powder sample with 100 times the quantity of KBr in a mortarb[17]. The finely grounded powder was then introduced into a stainless steel die and was compressed between polished steel anvils at a pressure of about $8t/in^2$. The spectra were recorded over the wave number of 8000 to $400cm^{-1}$.

RESULTS AND DISCUSSION

Standard Calibration curve of Eletriptan

Table 4: Calibration curve of Eletriptan in 0.1 N hydrochloric acid buffer (pH 1.2)

Concentration (µg/ml)	Absorbance
0	0
2	0.124
4	0.269
6	0.399
8	0.557
10	0.709

It was found that the estimation of Eletriptan by UV spectrophotometric method at λ_{max} 243.0 nm in 0.1N Hydrochloric acid had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 2- 10µg/ml. The regression equation generated was y = 0.056x - 0.003.

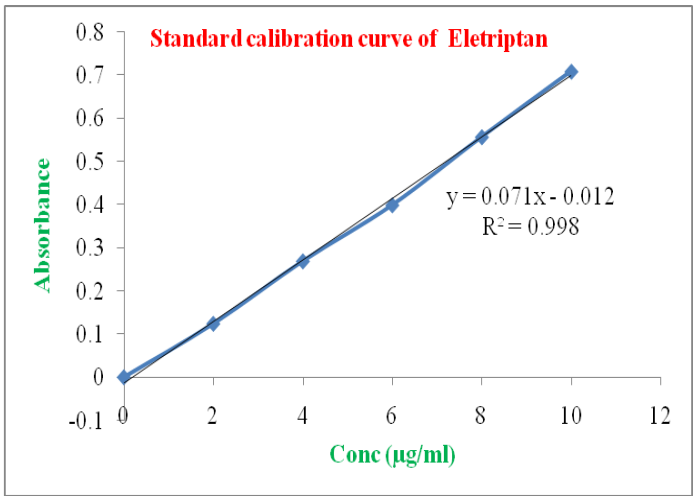

Fig 1: Standard graph of Eletriptan in 0.1 N HCl

Evaluation Parameters for Fast Dissolving Tablets of Eletriptan

Table 5: Pre-compression parameters

Formulations	Bulk Density (gm/cm^2)	Tap Density (gm/cm^2)	Carr's Index (%)	Hausner ratio	Angle of Repose(Θ)
F1	0.40	0.54	17.18	1.20	26.91
F2	0.50	0.56	15.54	1.18	28.23
F3	0.50	0.58	13.79	1.19	29.34
F4	0.46	0.56	16.36	1.19	26.71
F5	0.44	0.58	13.79	1.16	29.34
F6	0.48	0.56	14.54	1.17	28.23
F7	0.50	0.58	13.79	1.16	29.34
F8	0.42	0.50	18	1.20	26.78
F9	0.49	0.50	18	1.20	26.78
F10	0.47	0.49	14	1.17	28.45
F11	0.46	0.53	16	1.15	26.59
F12	0.43	0.49	16	1.19	28.87

Table 6: Post compression Parameters

F. No	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Assay (%)
F1	100	2.5	3.49	19.33	0.74	96.20
F2	100	2.6	3.44	17.66	0.80	97.15
F3	102	2.5	3.49	16.33	0.73	96.11
F4	109	2.6	3.48	12.00	0.81	99.24

F5	104	2.3	3.49	20.33	0.71	96.26
F6	101	2.7	3.44	21.66	0.64	96.25
F7	101	2.5	3.49	20.33	0.75	98.26
F8	104	2.6	3.46	27.00	0.79	97.23
F9	102	2.5	3.46	20.50	0.80	97.25
F10	105	2.6	3.45	22.59	0.73	96.34
F11	106	2.4	3.49	24.63	0.78	97.54
F12	102	2.5	3.48	25.76	0.79	98.21

Invitro Dissolution studies

Table 7: Invitro dissolution data

Time (Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
2	26.4	38.5	**83.9**	**81.9**	23.3	48.3	48.3	16.6	19.4	34.2	63.4	21.3
4	34.2	75.3	**96.4**	**91.4**	32.6	83.9	83.9	21.2	25.2	48.9	78.1	31.6
6	47.9	95.2	**99.9**	**97.9**	48.3	88.7	88.7	49.7	49.7	65.8	89.5	46.3
8	67.8	98.7		**99.7**	57.3	97.8	97.8	54.3	58.3	79.3	93.5	52.3
10	77.1				73.3			65.3	75.3	89.9	99.9	64.3
15	88.4				86.1			78.4	87.4	93.5		76.1
20	100.3				93.6			89.77	99.77			83.6
30					99.1			96.45				89.9

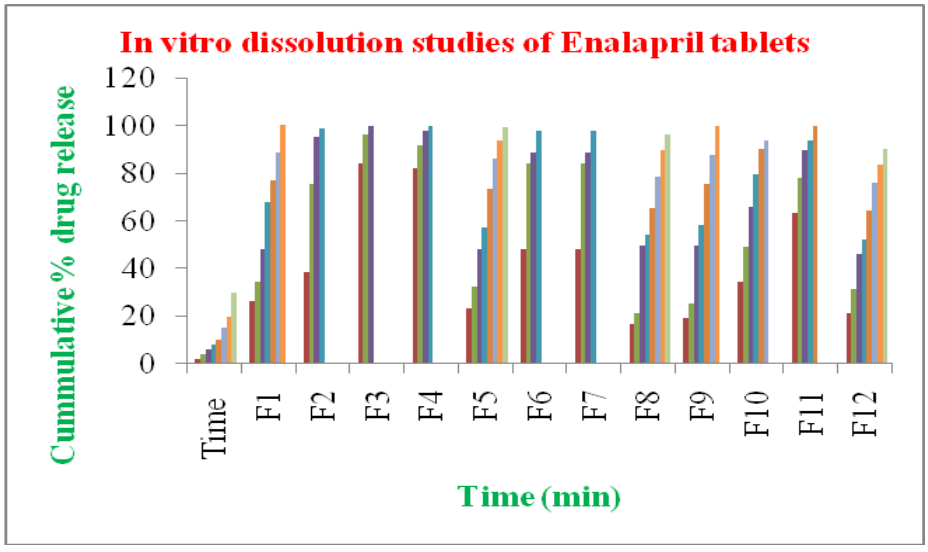

Fig 2: Dissolution profile of formulations F1-F12

Fourier Transform-Infrared Spectroscopy

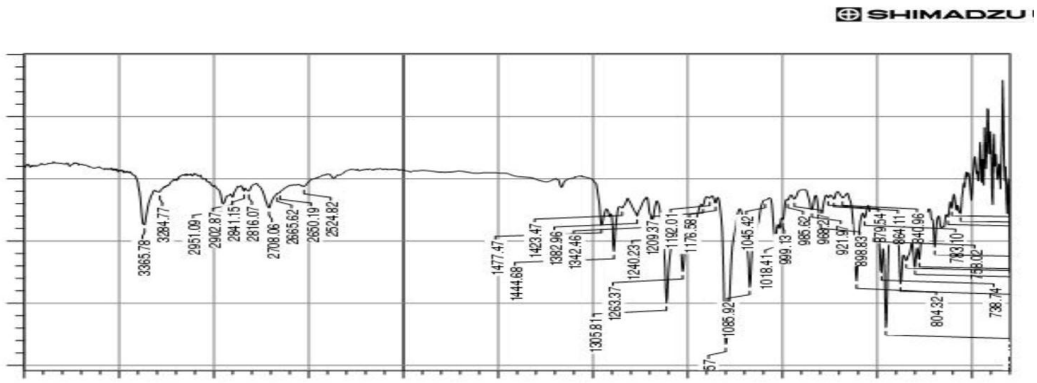

Figure 3: FT-TR Spectrum of Eletriptan pure drug

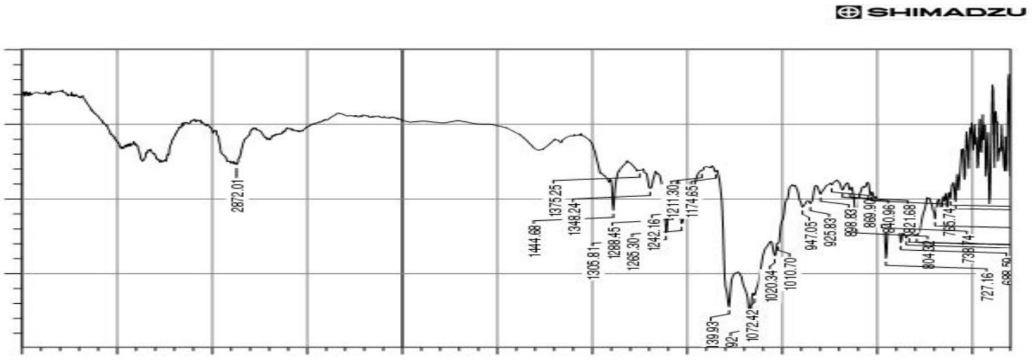

Figure 4: FT-IR Spectrum of Optimized Formulation

From the FTIR data it was evident that the drug and super disintegrates, other excipients doses not have any interactions**.** Hence they were compatible.

SUMMARY AND CONCLUSION

In the present work, an attempt has been made to develop fast disintegrating tablets of Eletriptan. New generation super disintegrants Cros povidone, Cros Carmellose Sodium, Sodium Starch Glycolate were selected as super disintegrates. All the formulations were prepared by direct compression method using 8mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed god flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F3formulation showed maximum % drug release i.e., 99.9 % in 6 minutes hence it is considered as optimized formulation. The F3 formulation contains crospovidone as super disintegrant in the ratio of 10 %. F3 formulation was considered as optimized formulation.

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