ISSN: 2279 - 0594

Journal of Biomedical and Pharmaceutical Research

Available Online at www.jbpr.in

CODEN: - JBPRAU (Source: - American Chemical Society)

Index Copernicus Value: 72.80

PubMed (National Library of Medicine): ID: (101671502)

Volume 7, Issue 2: March-April: 2018, 01-19

Research Article

Formulation and In-vitro Evaluation of Fast Disintegrating Tablet of Eprosartan Mesylate

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Received 18Jan. 2018; Accepted 26Feb. 2018

ABSTRACT

In the present work, fast dissolving tablets of Eprosartan Melysate were prepared by direct compression method with a view to enhance patient compliance. One super-disintegrants, viz., crospovidone use in different ratios with microcrystalline cellulose along with directly compressible mannitol to enhance mouth feel. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water absorption ratio and *in vitro* dispersion time. Based on *in vitro* dispersion time (approximately 13s), nine formulations batches were tested for the *in vitro* drug release pattern (in pH 6.8 phosphate buffer), short-term stability (at 40°/75% relative humidity for 6 month) and drug-excipient interaction (IR spectroscopy). Among the nine promising formulations, the formulation prepared by using 10% w/w of crospovidone and 35% w/w of microcrystalline cellulose emerged as the overall best formulation ($t_{50\%}$ 1.8 min) based on the *in vitro* drug release characteristics compared to conventional commercial tablet formulation ($t_{50\%}$ 16.4 min). Short-term stability studies on the formulations indicated that there were no significant changes in drug content and *in vitro* dispersion time.

Keywords: Fast dissolving tablets, Eprosartan melysate , Crospovidone, Microcrystaline cellulose

INTRODUCTION:

Many patients express difficulty in swallowing tablets and hard gelatin capsules, resulting in non-compliance and ineffective therapy. Recent advances in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach led to development of fast dissolving tablets. Advantages of this drug delivery system include administration without water, convenience of administration and accurate dosing as compared to liquids, easy portability, ability to provide advantages of liquid medication in the form of solid preparation, ideal for pediatric and geriatric patients and rapid dissolution/absorption of the drug, which may produce rapid onset of action. Some drugs are absorbed from mouth, pharynx and esophagus as the saliva passes down into the stomach and in such cases bioavailability of the drug is increased: pre-gastric absorption can result in improved bioavailability and as result of reduced dosage, improved clinical performance through a reduction of unwanted effects. Clonazepam is a benzodiazepine derivative with marked antiepileptic properties. It may be used in the treatment of all types of epilepsy and seizures. It is also indicated in mycoclonus and associated abnormal movements, and for the treatment of panic disorders[5]. It was selected as drug candidate, since it is not available in such dosage form. Aim of the present study was to develop fast dissolving tablets of clonazepam by simple and cost effective direct compression technique.

MATERIALS AND METHODS:

Materials:

Eprosartan melysate was obtained as a gift sample from Mylan Pharmaceuticals Ltd. Mumbai. Crosspovidone were obtained as a gift sample Cipla Pharmaceuticals Ltd. Panvel and remaining reagents were used are laboratory grade.

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Methods for preparation Tablet:

Direct compression

The materials required were first sifted through stainless steel sieve no. 40 mesh. The powders were then dry mixed by spatulation. Tablets were prepared by direct compression method with 12 mm stainless steel punch using rotary press (Karnavati Minitab, India). Compression force for all the tablets was adjusted to get tablets of hardness 4-6 kg/cm^2. Hardness was measured by Monsanto type hardness tester (Coslab). Weight of were adjusted to 450 mg of all compress tablets.

A) Flavour identification and flavour-excipients compatibility study

1. Organoleptic Property and Solubility

The sample of eprosartan mesylate was studied for organoleptic characteristics such as colour, odour and appearance. The solubility of eprosartan mesylate was checked in different solvents like like Methanol, 0.1 N Hydrochloric acids, 0.1 N NaOH and Phosphate buffer pH 6.8 etc.

2. Uv Specroscopy:

Determination of maximum absorbance in methanol : (235nm)

Stock solutions (100µg/ml) of Eprosartan Mesylate were prepared in methanol.These Solutions were diluted with methanol to obtain suitable concentrations of each. The UV spectrums were recorded in the range 200-450 nm by using UV-Visible double beam spectrophotometer (Shimadzu 2450). The wavelength of maximum absorption (λ_{max}) was determined .

Standard Calibration Curve of Eprosartan Mesylate in NaOH

Ten milligram was Eprosartan Mesylate accurately weighed and transferred to 100 ml volumetric flask. The volume was made up to 100 ml with NaOH produce stock solution of 100 µg/ml. Working standard solutions of strengths 10,20,30,40,50 µg/ml were made from the stock solution by appropriate dilutions. The above solutions were analyzed by UV spectrophotometer at λ_{max} 235nm. Methanol was used as blank during spectrophotometric analysis. The standard calibration curve was obtained by plotting absorbance vs. concentration. The concentration range over which the drug obeyed Beer- Lambert's law was chosen as the analytical concentration range.

Calibration Curve of Eprosartan Mesylate in 0.1 N HCl

Ten milligram Eprosartan Mesylate was accurately weighed and transferred to 100 ml volumetric flask. It was then dissolved in 0.1% HCL and sonicated for 10 min. The volume was made up to 100 ml with 0.1 N HCl to produce a stock solution of 100 µg/ml. Working standard solutions of strengths 2, 4, 6, 8 and 10 µg/ml were made from the stock solution by appropriate dilutions. The above solutions were analyzed by UV spectrophotometer at λ_{max}235nm. 0.1 N HCl used as blank during spectrophotometric analysis. The standard calibration curve was obtained by plotting absorbance vs. concentration.

Calibration Curve of Eprosartan Mesylate in Phosphate Buffer pH 6.8

Ten milligram Eprosartan Mesylate was accurately weighed and transferred to 100 ml volumetric flask. It was then dissolved in 10 ml methanol and sonicated for 10 min. The volume was made up to 100 ml with Phosphate Buffer pH 6.8 to produce a stock solution of 100 µg/ml. Working standard solutions of strengths 2,4,6,8,10 µg/ml were made from the stock solution by appropriate dilutions. The above solutions were analyzed by UV spectrophotometer at λ_{max} 235 nm. Phosphate Buffer pH 6.8 used as blank during spectrophotometric analysis. The standard calibration curve was obtained by plotting absorbance vs. concentration.

3. Fourier Transform Infra-Red Spectra (FTIR)

The infrared absorption spectrum of Eprosartan Mesylate was recorded with a KBr disc over the wave number 4000 to 400 cm^{-1} by using Fourier transform infrared spectrophotometer (FTIR) (Shimadzu 8400s).

4. Compatibility Study [41]

7.2.1 Fourier Transform Infra Red spectroscopy: [46,47]

Compatibility study was carried out by using Fourier transform infrared spectrophotometer (Shimadzu 8400s). FTIR study was carried on pure drug and Physical mixture of drug and polymers

were prepared and samples kept for 1 month at 40^0C. The infrared absorption spectrums of Eprosartan Mesylate and physical mixture of drug and polymers was recorded using KBr disc over the wave number 4000 to 400 cm^{-1}.

B) FORMULATION AND EVALUTION:

Composition of formulation of tablet

C) Evaluationof Tablet

7.3.1 Pre-compression parameters:

a)Bulk density:

The bulk density was obtained by dividing the mass of powder by the bulk volume. The sample equivalent to 5 g was accurately weighed and fill in a 100 ml graduated cylinder and the powder was leveled and the unsettled volume, (V_0) was noted. The bulk density was calculated by the formulaWhere, ρ_0 = Bulk density,

M = Mass of powder taken and

V_0 = Apparent unsettled volume.

b) Tapped density:[40]

The tapped density was determined by mechanically tapping the measuring cylinder or by using the digital bulk density tester and the tapped volume was noted. The tapped density was calculated by the formula

Where, ρ_0 = tapped density,

M = weight of powder and

V_t= tapped volume of powder in cm^3.

c) Hausner's ratio:

Hausner's ratio gives an idea regarding the flow of the blend. It is the ratio of tapped density to the apparent density. Hausners ratio was calculated as

Table 1: Relationship between Hausner's ratio and flow property

Sr. No.	Hausners Ratio	Flow property
1	1 – 1.11	Excellent
2	1.12 - 1.18	Good
3	1.26 – 1.34	Poor

d) Compressibility index:

The compressibility index measures of the propensity of powder to be compressed. The packing ability of drug was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping (USP, 2008). It is indicated as Carr's compressibility index (CI) and can be calculated as follows:

Table 2: Relationship between % compressibility and flow property

Sr. No.	% Compressibility	Flow property
1	5-15	Excellent
2	12-16	Good
3	18-21	Fairly acceptable
4	23-35	Poor
5	33-38	Very poor
6	< 40	Extremely poor

e) Angle of repose:[40]

Funnel method: Funnel with a sound stem of 20 to 30 mm diameter was attached to theburette stand the height of which was adjusted such that its tip just touches the apex of powder. The graph paper sheet was placed below the funnel. The powder was allowed to flow through the funnel freely onto the surface of the graph paper sheet. Circle was marked around the heap covering approximately 90% of total powder bed. Procedure was repeated thrice to obtain the average reading & average diameter. Where h = height if the powder pile and r = radius of heap.[10,11,12,]

Table 3: Relationship between angle of repose (θ) and flow

Sr. No.	Flow character	Angle of Repose(0^0)
1	Excellent	25-30
2	Good	31-35
3	Fair	36-40
5	Passable	41-45
6	Poor	46-55
7	Very poor	56-65
8	Very, very poor	>66

7.3.2 Post-compression parameters:[40]

a) Hardness test:[40]

Although hardness test is not an official test, tablet should have sufficient handling qualities during packing and transportation. Hardness of tablet was measured using Monsanto hardness tester. It is the pressure required to fracture diametrically placed tablets by applying force. The hardness of randomly selected 6 tablets, from each batch was determined and means hardness was taken into account, which was expressed in kg/cm^2.

b) Thickness:[40]

All tablets were subjected for thickness measurement by using digital vernier caliper. All the measurements were made in triplicate.

c) Friability Test:[40]

As weight of tablet was less than 650 mg so tablets corresponding to 6.5 gm were taken for the test. All tablets were dedusted carefully and weighing accurately the required number of tablets were placed in the drum and rotated about 100 times. Tablets were removed from the drum and loose dust was removed from the tablets, weighed accurately. The percentage weight loss should not be more than 1% of the total weight.

d) Uniformity of weight:[40]

20 units were selected at random and were weighed individually, and average weight was calculated. Not more than 2 of the individual weight of tablets should deviate from the average weight by more than 5%.

e) Disintegration Test:[40]

Disintegration test determines whether dosage forms such as tablets disintegrates within prescribed time when placed in a liquid medium under prescribed experimental conditions. Disintegration is defined as that state in which no residue of the unit under test remains on the screen of the apparatus or, if a residue remains, it consist of fragment of disintegrated parts of tablet component part such as insoluble coating of the tablets is soft mass with no palpable core.

f) Drug content (Assay):[40]

Ten tablets were weighed and powdered. An amount of powder equivalent to 8 mg of Eprosartan Mesylate was dissolved in 100 ml of phosphate buffer [pH 6.8]. It was shaken by mechanical means for 1 hr. Then it was filtered through a whatsman filter paper. From this resulted solution 1ml was taken, diluted to 100 ml with phosphate buffer of pH 6.8 and absorbance

was measured against blank at 234 nm using UV-Visible spectrophotometer. From the absorbance values, amount of drug present in the given tablet was calculated using calibration curve. Procedure was repeated by using two or more tablets from the same formulation and the average value of all three tablets were calculated.

g) Dissolution Test:[39,41]

The test is designed to determine compliance with the dissolution requirement for solid dosage forms administered orally.

Apparatus: Paddle

Medium: 900 ml 6.8 PBH

Speed and time: 50 rpm and 2 minutes.

Temperature: 37^0c.

Tablet was placed in jar containing 900ml of PHB 6.8for 12 Minutes and samples at different time interval 5 ml of aliquots were removed and filtered through whatman filter paper no.52 at time interval specified (2, 4, 6, 8, 10, & 12 min) and analyzed by UV-Visible spectroscopy at 231 nm using methanol as blank..

Table 4: Ranges of independent variables used in factorial design

Batch	Formulation code	CP	MCC
1	F1	25	25
2	F2	25	50
3	F3	25	75
4	F4	18	25
5	F5	18	50
6	F6	18	75
7	F7	10	25
8	F8	10	50
9	F9	10	75

Table 5: Composition of various tablets prepared for Eprosartan Mesylate Fast disintegrating tablet

Ingredients (mg)	S1	S2	S3	S4	S5	S6	S7	S8	S9
Eprosartan Mesylate	300	300	300	300	300	300	300	300	300
Crospovidon	25	25	25	18	18	18	10	10	10
MCC	25	50	75	25	50	75	25	50	75
Magnesium stearate	25	25	25	25	25	25	25	25	25
Talc	5	5	5	5	5	5	5	5	5
Starch	15	15	15	15	15	15	15	15	15
Citric Acid	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Mannitol	104.9	79.9	54.9	111.9	86.9	61.9	119.9	94.9	69.9
Total	**500**	**500**	**500**	**500**	**500**	**500**	**500**	**500**	**500**

(All quantities are in mg)

The independent variables in formulations are CP and MCC are used as superdisintegrants

Independent variables:-

X1 – CP(%w/w)

X2 - MCC(%w/w)

Dependent variables:-

Y1 - In-vitro drug release (%)

Stability studies:

Stability study of optimized bilayer tablet formulation was carried out to point out any visual physical or chemical changes made in the formulation after storing it at elevated temperature and humidity conditions. Chemical and physical stability of reproducible bilayer tablet formulation was assessed at 40±2 ^{0}c/ 75±5% RH as per ICH Guidelines in the stability chamber tempo instrument pvt.ltd. TI-710. Tablets of 500mg of Eprosartan Mesylate FDT were packed with aluminium strips and stored for 3 months. Samples were analyzed at 0, 30, 60, & 90 days for physical appearance, drug content, and disintegration time and invitro dissolution profile.[41,48,49,50]

RESULT AND DISCUSSION:

Organoleptic Property and Solubility: It is a white solidand odorless. The solubility of EprosartanMesylate was checked in solvents like Methanol,0.1 N NaoH ,0.1 N Hydrochloric Acid (HCl), Phosphate buffer pH 6.8 etc.

2. UV spectroscopy:

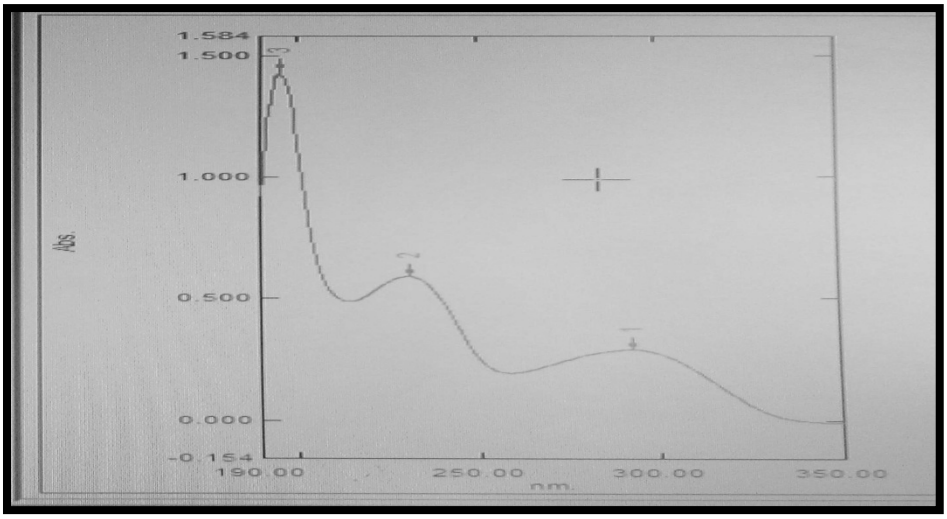


Figure 1: λ_{max} of EprosartanMesylate

λ_{MAX} of EprosartanMesylate

Name of drug	λ_{max}(nm)
EpropsartanMesylate	235

Wavelength of maximum absorption was found to be 235 nm for EprosartanMesylate in methanol. The drug content of formulation was determined at the same wavelength in Sodium Hydroxide.

8.2.2 Determination of Beers-Lambert's plot

Figure 9: Calibration Curve of EprosartanMesylate in Methanol

Methanolic solution of drug was very clear and readily analyzed by UV spectrophotometer. The data of absorbance vs. concentration were plotted on graph and the values of R^2 were determined. A linear relationship was obtained in between concentration (10-50µg/ml) and absorbance of EprosartaMesylate in Methanol with R^2 value of 0.998 at 237.6 nm.

8.2.3 Calibration Curve of EprosartanMesylatein Phosphate buffer pH 6.8

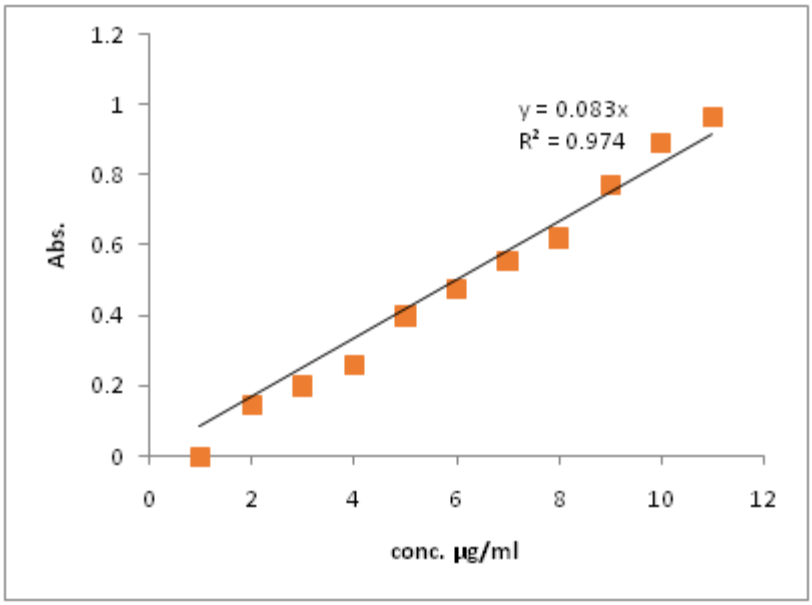


Figure 2: Calibration Curve of EprosartanMesylate in Phosphate buffer pH 6.8

Calibration curve of EprosartanMesylate was performed in phosphate buffer pH 6.8 since dissolution studies were carried out in these media. A linear relationship was obtained in between concentration (2-10µg/ml) and absorbance of EprosartanMesylate in Phosphate buffer pH 6.8 with R^2 value of 0.994.

8.2.4 Calibration Curve of EprosartanMesylate in NAOH

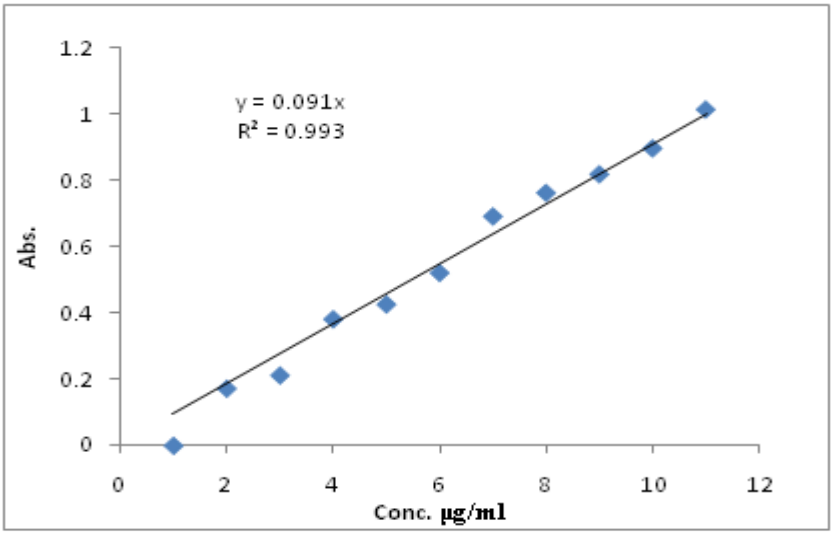


Figure 3:

Calibration curve of EprosartanMesylate was performed in NAOH. A linear relationship was obtained in between concentration (2-10µg/ml) and absorbance of EprosartanMesylate in NAOH with R^2 value of 0.993.

8.3 Infra-Red Spectrum:

A) EprosartanMesylate:

Infra- red spectrum of EprosartanMesylate was shown in figure no.8.1. The major peaks observed and corresponding functional groups are given table no 8.3. Infra-red spectrum shows peak characteristic of structure of EprosartanMesylate.

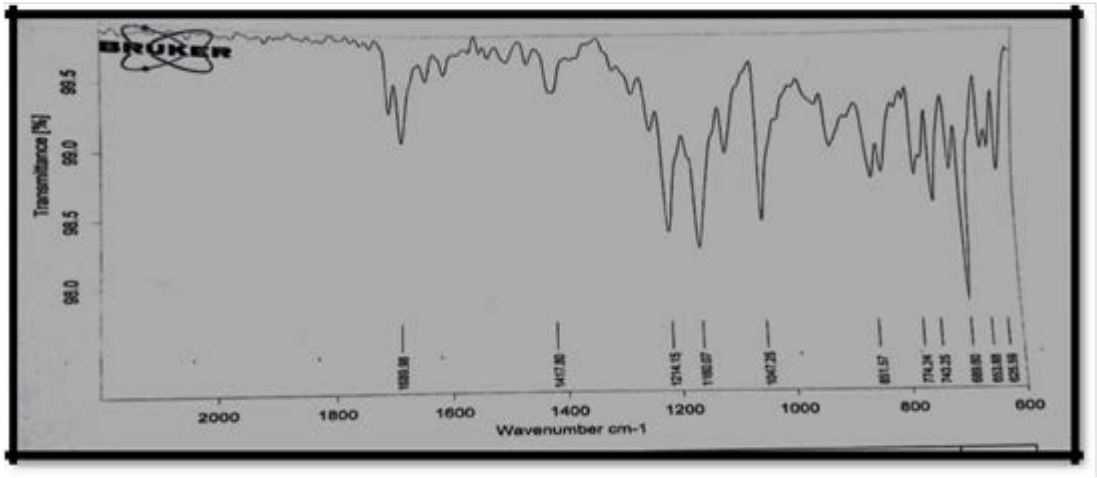


Figure 4: FTIR spectrum of EprosartanMesylate

8.4 Optimization by 3^2Factorial Design:

The application of mathematical optimization in the pharmaceutical field was first reported by Fonner et al (1970), using the Lagrangian method as a constrained optimization technique. A factorial design is used to evaluate two or more factors simultaneously. The treatments are the combinations of levels of the factors. The advantages of factorial design over one factor at a time experiment are that they are more effective and allow interactions to be detected. Interventionstudies with two or more categorical explanatory variables leading to a numerical outcome variable are called as factorial design. A factor is simply a categorical variable with two or more values referred to as levels. A study in which there are two factors with three levels is called as 3^2 factorial designs. For present work 3^2 factorial designs was selected. In this design, two factors were evaluated each at three levels and experimental trials were performed at all 9 possible combinations as reflected in table no.7.4.2 different formulation codes were assigned to all batches containing Crospovidon and Microcrystalline cellulose.

Table 6: Ranges of independent variables used in factorial design

Batch	Formulation Code	CP	MCC
1	*F1*	25	25
2	*F2*	25	50
3	*F3*	25	75
4	*F4*	18	25
5	*F5*	18	50
6	*F6*	18	75
7	*F7*	10	25
8	*F8*	10	50
9	*F9*	10	75

Table 7: Method of preparation and evaluation of powder blend

Formulation batches	Physical properties*				
	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose (^{0}C)	Compressibility Index (%)	Hausner Ratio
F1	0.3303±0.018	0.3825±0.01	29.79±1.94	22.4±1.38	1.15±0.01
F2	0.3277±0.04	0.3729±0.01	30.73±1.83	15.9±4.69	1.13±0.02
F3	0.3338±0.06	0.3798±0.005	28.84±1.01	27.3±3.52	1.13±0.017
F4	0.3290±0.03	0.3781±0.008	28.25±1.9	18±6.36	1.14±0.025
F5	0.3310±0.01	0.3813±0.01	30.44±1.28	22.7±5.36	1.15±0.025
F6	0.3290±0.05	0.3751±0.05	30.24±1.09	16.9±9.08	1.13±0.013
F7	0.3290±0.07	0.3835±0.02	28.64±1.86	21.4±1.98	1.16±0.022
F8	0.3249±0.01	0.3835±0.02	30.28±0.73	17.8±2.43	1.16±0.027
F9	0.3284±0.06	0.3801±0.014	30.57±1.25	22±4.41	1.15±0.038

8.5 Formulation fast dissolving tablet by direct compression method

The present work undertaken to formulate and evaluated fast dissolvingtabletofEprosartanMesylate by direct compression method.Superdisintegrats at different concentrationwere included to assist fast disintegration.

8.6Evaluation of tablets

All batches of prepared tablets were evaluated for the different parameters.

TABLE 8: EvaluationofeprosartanMesylate Fast Dissolvingtablets

Formulation batches	Parameters			
	Thickness(mm) (±SD)	Hardness (Kg/cm^2) (± SD)	Drug content (%) (± SD)	Friability (%) (± SD)
F1	3.83 ± 0.01	3.66±0.05	99.40±1.78	0.48±0.01
F2	3.93±0.01	3.43±0.32	98.77± 2.61	0.49±0.02
F3	3.84±0.02	3.76±0.14	101.09 ±1.43	0.340±0.023
F4	3.92±0.04	4.3±0.89	102.53 ±1.79	0.421±0.0
F5	3.93±0.01	4.1±0.06	98.87 ±2.58	0.44±0.012
F6	3.94±0.04	4.1±0.06	101.27± 2.41	0.48±0.01
F7	4.08± 0.012	4.86±0.056	99.72 ± 3.37	0.49±0.02
F8	4.04± 0.12	4.85±0.005	98.31 ± 3.27	0.41±0.004
F9	3.44± 0.58	3.86±0.17	98.67+/-3.24	0.43±0.04

Table 9: EvaluationofEprosartanMesylate Fast Dissolving Tablets

Formulation batches	Parameters			
	Weight variation (mg) (± SD)	Wetting time (sec.) (± SD)	Water absorption Ratio (%) (± SD)	Disintegration Time (sec.) (± SD)
F1	499.9 ± 1.30	18.6 ± 0.66	60.6± 2.63	22.5± 2.07
F2	500 ± 1.75	26.6 ± 0.66	57.6±1.6	33.33± 2.12
F3	499.7± 1.39	27.3 ± 2.51	51± 1.6	26.1± 5.02
F4	500.15± 2.27	30 ± 2	55± 1.8	21±2.56
F5	500.3± 1.56	24 ± 3.46	65± 1.02	37.6± 9.15
F6	501.05± 1.92	22 ± 1.73	69.3 ±1.67	28± 4.19
F7	500.5± 1.43	22 ± 4.5	73.3 ±1.47	25.3± 2
F8	500±1.58	26 ± 1.73	63.3±1.48	23.8± 1.72
F9	500± 1.93	30.6 ± 1.5	56.6 ±1.66	35.66± 4.60

Wetting time of all formulation (F1-F9) was found in between the 61 to70 sec.

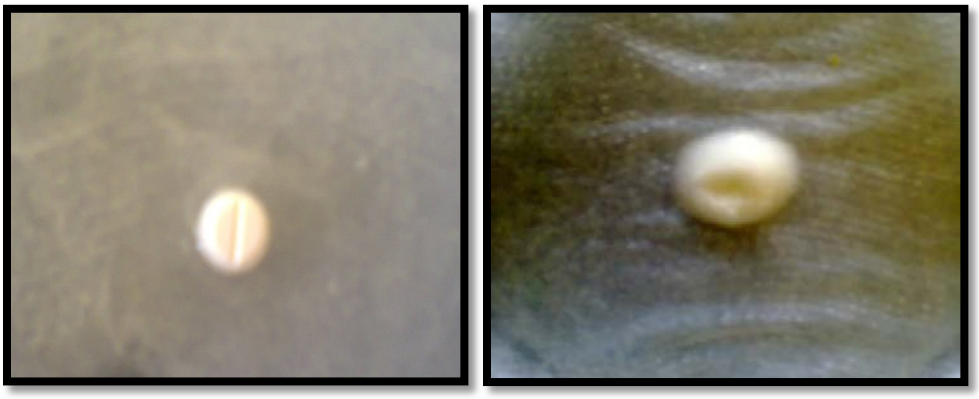


Fig. 5: Tablet before Wetting Fig.10: Tablet After Wetting

Water absorption ratio was found in ranging from 53.39 % to 78.49%

8.6.3 Disintegration time

Fast dissolving Tablets should disintegrate within three minute. Three Tablets of each formulation were taken and placed in 6 tubes of disintegration apparatus. The time taken for complete disintegration was noted.The disintegration time for formulation F1-F9 was found to be in the range of 61to 73sec

8.6.4 *In-vitro* drug Release Study of Eprosartan Mesylate FDT

TABLE 10: Cumulative drug release of Formulation (F1-F9)

Formulation Code % CDR	Time (Min)					
	2	4	6	8	10	12
F1 %CDR	38.66±0.18	48.01±0.32	47.85±0.50	49.49±0.51	66.87±1.01	85.09±1.01
F2 %CDR	39.4±0.17	45.59±0.26	48.55±0.21	49.77± 0.2	69.59±0.66	88.82±1.19
F3%CDR	39.38±0.42	48.81±0.17	47.42±0.15	49.86±0.59	68.86±0.36	92.2± 0.91
F4 %CDR	39.23±0.28	49.31±0.10	48.52±0.60	50.70±0.08	68.82±0.30	87.07±0.77
F5 %CDR	39.57±0.22	47.7±0.38	49.13±0.44	50.67±0.02	69.01±0.37	89.07±2.44
F6 %CDR	39.95±0.18	48.64±0.91	50.33±0.29	51.37±0.19	71.27±0.10	90.37±0.19
F7 %CDR	40.39 ± 0.4	48.71 ± 0.6	50.19±0.28	51.19±0.30	68.21±0.28	88.95±0.18
F8 %CDR	40.8± 0.23	48.46±0.36	50.86±0.54	51.47±0.67	69.09±0.93	87.21±0.21

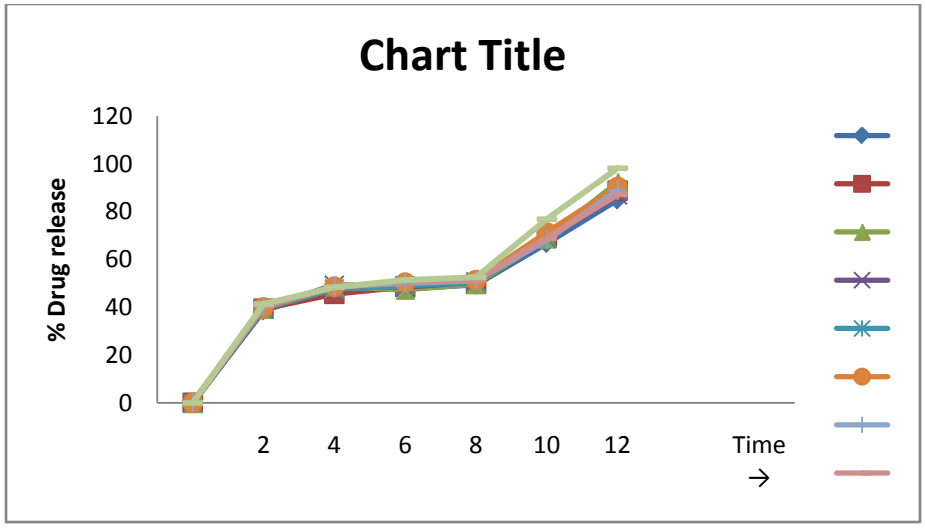


Figure 6: Dissolution profile of Formulation batches (F1-F9)

Table 11: ANOVA for % drug release (Y1)

Source	Squares	df	Square	Value	Prob> F	
Model	75.86	2	37.93	5.78	0.0399	significant
A-crosspovidone	*11.37*	*1*	*11.37*	*1.73*	*0.2360*	
B-MCC	*64.48*	*1*	*64.48*	*9.83*	*0.0202*	
Residual	39.36	6	6.56			
Cor Total	115.21	8				

The Model F-value of 5.78 implies the model is significant. There is only a 3.99% chance that an F-value noise. Values of "Prob> F" less than 0.0500 indicate model terms are significant.

In this case B is a significant model term. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

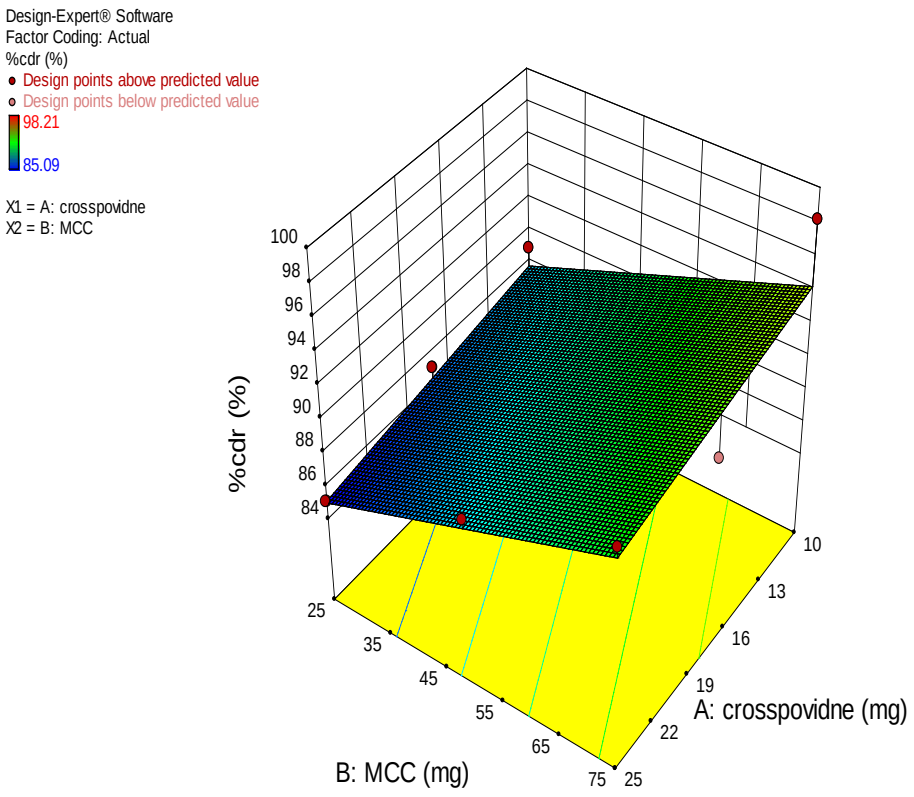
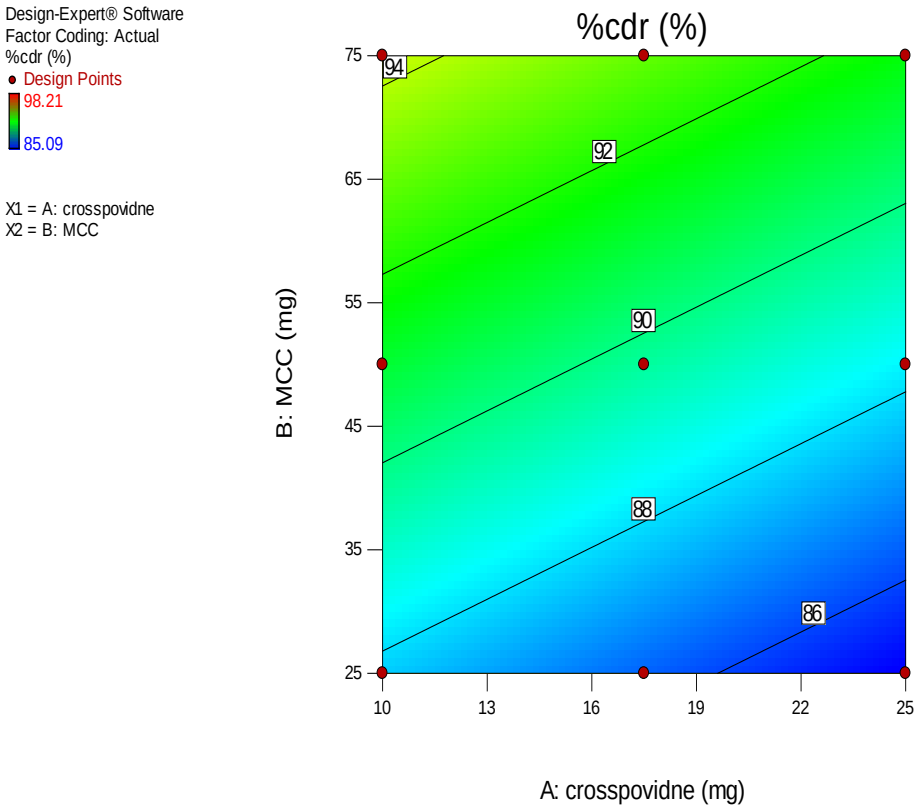


Figure 7: Surface response plot showing effect of Crossprovidne and MCC on % CDR.



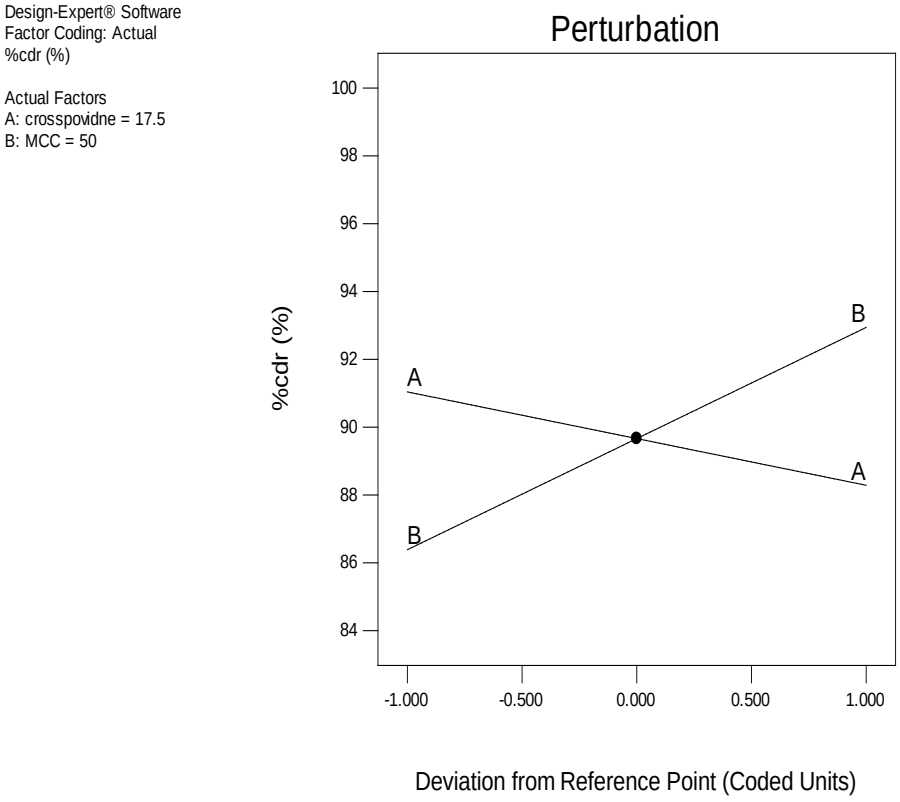


Figure 8: Perturbation plot

TABLE 12: EVALUATION PARAMETERS OF F9 OPTIMIZED BATCH

Sr. No.	Parameters	Results*
1	Weight variation (mg)	500±1.58
2	Thickness (mm)	3.44±0.58
3	Hardness (kg/cm2)	3.86±0.17
4	Friability (%)	0.43±0.04
5	Disintegration time (sec)	35.66±4.60
6	Uniformity of content (%)	96±0.17

TABLE 13: Cumulutive drug release

Sr. No.	Time (min)	% Cumulative drug release*
1	0	0
2	2	41.37± 0.25
3	4	48.38 ± 0.3
4	6	51.36± 0.13
5	8	56 ± 0.52
6	10	76.90 ± 0.48
7	12	98.21 ± 0.64

*mean of three values **±** SD)

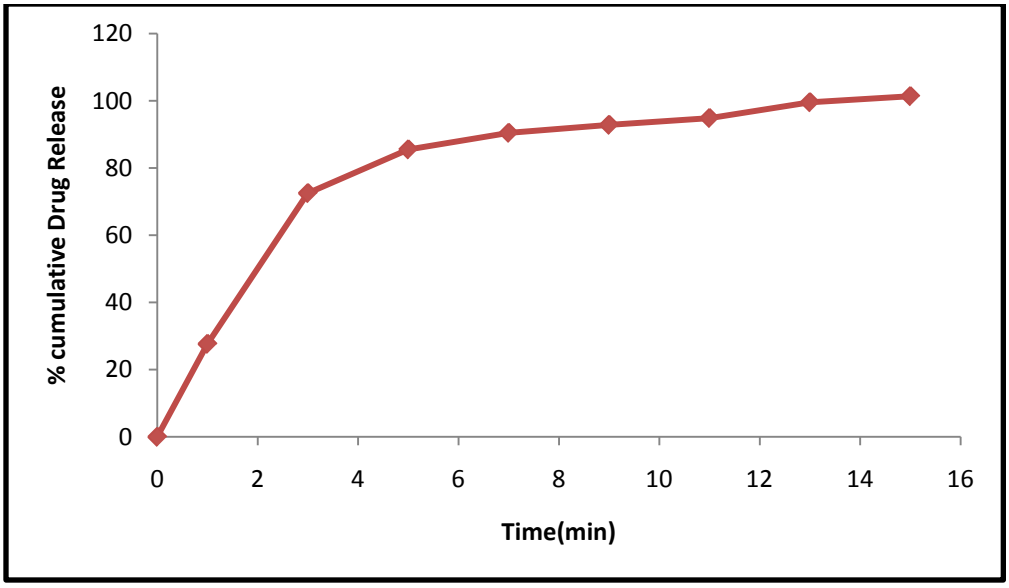


Figure 9: Graphical presentation of dissolution profile of optimized batch

The accelerated stability studies (carried out 3 month due to lack of time), at temperature of 40ºC ± 2º C and % RH 75% ± 5 % RH indicated that the developed floating tablet was unaffected after 3 month storage under the accelerated condition as slightly change was observed in flavor content, Flavor release no sign of distinguishable change was observed in the appearance, texture color of the formulation. The data of flavor content before the study and after the study show change with limit.

8.11 Stability Study

The accelerated stability study was carried out on optimized formulation F9. The tablets were wrapped in aluminium foil and stored at 40 ± 2^0C &75 ± 5 % RH for three months. After three months samples were withdrawn and tested for physical parameters, thickness, hardness, percent friability, content uniformity, disintegration time, wetting time, Water absorption ratio (%) and *in-vitro* drug release studies. Table No.26 showed that there was no considerable change in thickness, hardness, percent friability, content uniformity, disintegration time, wetting time and Water absorption ratio (%)of formulation F9 before and after accelerated stability study. Also formulation F6 showed whitecolor after stability studies. Table No. 26 showed that there was hardly any difference between dissolution profile of formulation F9 before and after stability study. Hence FDT prepared was found to be stable.

TABLE 14: DISSOLUTION STUDY OF FORMULATION [F9] BEFORE AND AFTER STABILITY STUDY.

Parameters	Before stability study	After stability study
Colour	White	White
Thickness (mm)	3.87 ± 0.05	3.67 ±0.20
Hardness (kg/cm^2)	2.17 ± 0.28	2.67 ± 0.28
Content uniformity (%)	98.46 ± 1	97.66 ± 1.15
Weight variation(mg)	99.73 ± 1.90	99.73 ± 1.90
friability (%)	0.72± 0.05	0.74±0.5
Disintegration time (sec.)	61.66 ±2.51	62.33 ±2.08
Wetting time (sec.)	68 ± 2	66.67 ± 1.52
Water absorption ratio (%)	58.27 ± 6.26	57.54± 6.21

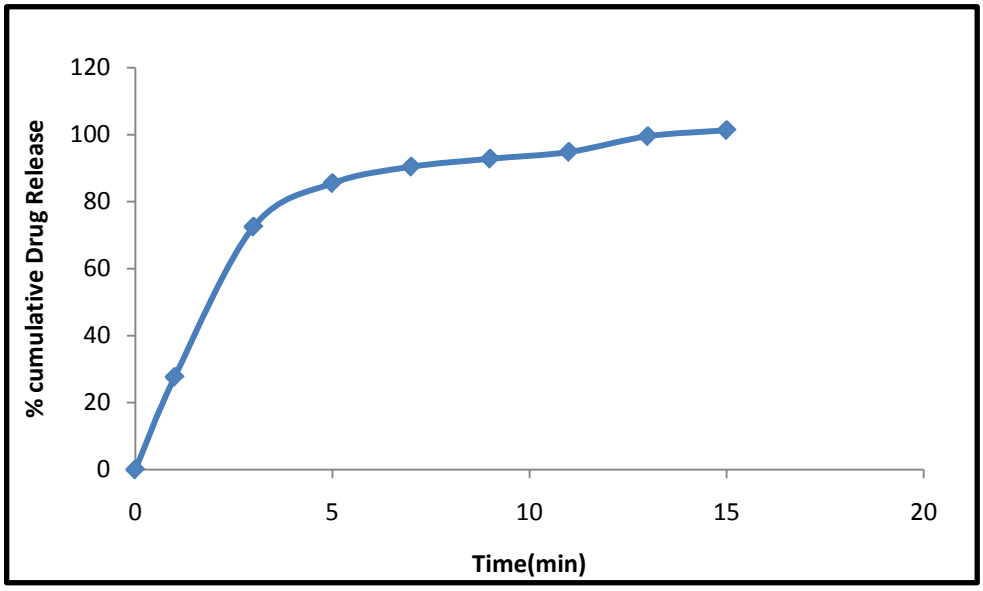


Figure 10: Dissolution profile of formulation F9 before and after stability study

CONCLUSION:

The present study was aimed to formulate and evaluate the mouth dissolving tablet of Eprosartan Mesylate Preliminary investigation of the drug was carried out with different parameters ,drug shows sharp M.P. at 148-150^{0}c ,determination of solubility shows that drug was soluble in methanol, ethanol and phosphate buffer6.8. UV spectroscopy was carried out for the

determination of λ max of the drug with various solvents like methanol and ethanol and phosphate buffer 6.8. Calibration curve of Eprosartan Mesylate was carried out with different dilutions on above wavelength. Compatibility of drug was confirmed with FTIR study Fast disintegrating tablet was prepared by direct compression method .The nine preliminary batches were prepared by using 3^2 factorial design lead to the final optimization concentration of the factor. Dissolution profile was taken as the response for study which was found to be with in the expected range. The optimized concentration of crosprovidone and mannitol obtained by applying 3^2 factorial design were 34 and 85 mg mannitol. The drug loaded tablet of all batches were evaluated for weight variation and thickness showed satisfactory result.

Acknowledgements

Thanks to Mylan Pharmaceuticals Pvt. Ltd.Mumbai for providing a gift sample of drug. The authors also thankful to prof. D.M. Shinkar R.G. Sapkal College of Pharmacy Anjneri Nashik for their valuable suggestion to carrying research work.

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