Research Article **ISSN: 2349 – 7106**

Asian Journal of Research in Chemistry and Pharmaceutical Sciences

Journal home page: www.ajrcps.com

FORMULATION AND CHARACTERIZATION OF ENALAPRIL MALEATE FAST DISSOLVING TABLETS

Satya Prakash Singh*[1] and Navneet Kumar Verma[2]

[1*]Kailash Institute of Pharmacy and Management, Gorakhpur, Uttar Pradesh, India.
[2]Department of Pharmaceutics, Buddha Institute of Pharmacy, Gorakhpur, Uttar Pradesh, India.

ABSTRACT

Fast dissolving tablets of Enalapril maleate has been prepared by direct compression method using the different super disintegrates: croscarmellose and sodium starch glycolate and Excipients: lactose, sucrose magnesium stearate, sodium lauryl sulphate. The prepared tablets were characterized for the pre-compression parameter UV Spectroscopy, post compression parameter such as thickness, hardness, friability, drugs contents, weight variation, water absorbance ratio, *in-vitro* disintegrating time, *in-vitro* dissolution studies. There were no chemical interaction between drugs and Excipients were confirmed by FTIR study. Fast dissolving tablets are prepared by direct compression method, 9 formulations as the F9 to be best as its shows in F9 87.10% (direct compression method) maximum drug release respectively. The prepared tablets stability tested at 40ºC having 75% relativity humidity for 1month and found to be stable. Prepared fast dissolving tablets of Enalapril maleate 5mg was found to be under fasting fed condition.

KEYWORDS

Enalapril maleate, Fast dissolving tablets and Superdisintragrants.

Author for Correspondence:

Satya Prakash Singh,

Kailash Institute of Pharmacy and Management,

Gorakhpur, Uttar Pradesh, India.

Email: satyap211@gmail.com

INTRODUCTON

The pill is that the most generally used dose type existing nowadays thanks to its convenience in terms of self-administration, compactness and ease in producing. However, geriatric, paediatric and insane patients experiences issue in swallowing standard tablets that ends up in poor patient compliance. To overcome these issues, scientists have developed innovative drug delivery system called mouth dissolving/disintegrating tablets (MDTs). These are novel sorts of tablets that dissolve/ disintegrate/ disperse in secretion inside

few seconds while not water. According to European collection, these MDTs ought to dissolve/disintegrate in but 3 minutes. The formulation is additional helpful for the bed-ridden and patients WHO have the swallowing drawback. The benefits of MDTs is to boost patients compliance, fast onset of action, increased bioavailability and good stability which make these tablets popular as a dosage form of choice in the current market[1-3]. Enalapril, once reaction to enalaprilate, inhibits angiotensin-converting protein (ACE) in human subjects and animals. ACE could be a peptidyl dipeptidase that catalyzes the conversion of angiotensin to the agent substance, angiotonin. Angiotensin II conjointly stimulates mineralocorticoid secretion by the endocrine. The helpful effects of Vasotec in cardiovascular disease and failure seem to result primarily from suppression of the renin-angiotensin-aldosterone system. Inhibition of ACE ends up in small plasma angiotonin that ends up in small vasoconstrictor activity and to decrease mineralocorticoid secretion. Although the latter decrease is small, it results in small increases of serum potassium[4].

MATERIAL AND METHODS

Enalapril maleate obtained as gift sample from Aristro Pharma Pvt. Ltd. (Chandigarh, India). Cross carmellose and sodium starch glycolate and other excipient were obtained from locally and use.

Method

Preformulation Study

Excipients Compatibility Study by IR spectroscopy

The IR spectra were recorded using IR spectrophotometer. The samples were prepared by mixing the drug and the excipient in 1:1 ratio and the mixtures were stored in closed containers for one week. IR spectrum of the samples was taken using KBr pellet method. The physical mixtures of Enalapril maleate and Excipients were scanned in the wavelength region between 4000 and 400 cm^{-1} and compared to check compatibility of drug with Excipients[5,6].

UV Spectroscopy

ʎmax for pure Enalapril maleate in water

The 1µg/ml sample was prepared and scanned between 200-400nm. The drug showed maximum absorption at 208nm. So the $ʎ_{max}$ of enalapril maleate was found to be 208nm.

Preparation of Calibration curve in water for Enalapril maleate

10mg of Enalapril Maleate pure drug was accurately weighed and transferred into a 10ml volumetric flask, dissolved in little quantities of distilled water, then made up to 10ml with water (1000µg/ml). From this solution, 1ml of solution was withdrawn into a 10ml volumetric flask and made up to 10ml with distilled water to get a concentration of 100µg/ml. From this, again pipette out 1ml of solution and diluted to 10ml with distilled water to get a concentration of 10µg/ml. Absorbance of this was measured at 208 nm using UV/VIS spectrophotometer against blank (distilled water)[6].

Preparation of Calibration curve in phosphate buffer pH 6.8

Preparation of phosphate buffer pH 6.8

Dissolve 28.80g of disodium hydrogen phosphate and 11.45g of potassium dihydrogen phosphate in sufficient water to produced 1000ml[7].

Preparation of Calibration curve

10mg of Enalapril Maleate pure drug was accurately weighed and transferred into a 10ml volumetric flask, dissolved in little quantities of phosphate buffer 6.8, then made up to 10ml with phosphate buffer 6.8 (1000µg/ml). From this solution, 1ml of solution was withdrawn into a 10ml volumetric flask and made up to 10ml with 6.8phosphate buffer to get a concentration of 100µg/ml. From this, again pipette out 1ml of solution and diluted to 10ml with 6.8 phosphate buffer to get a concentration of 10µg/ml. Absorbance of this was measured at 212nm using UV/VIS spectrophotometer against blank (6.8phosphate buffer)[7].

Formulation Development

The critical parameters to formulate a fast dissolving tablet are choice of superdisintegrants and optimization of concentration of

superdisintegrants. The main criteria for quick dissolving tablets is to disintegrate or dissolve apace in rimaoris in 15-60 seconds, without need of water and should have pleasant mouth feel. The super disintegrate (croscarmellose, and Sodium Starch Glycolate) were used to formulate the tablets. All the ingredients as shown in Table No.1 were co-ground in a pestle and motor and then lactose and magnesium stearate were added and mixed for 10 minutes. All the ingredients were undergone # 60-mesh on an individual basis. The mixed blend of drug-excipient was compressed using a single punch tablet machine[7,8].

Characterization of the fast dissolving tablets

Quality control tests for FDTs of all formulations were performed, and the average values were calculated. All the tablets were evaluated for different parameters as weight variation, hardness, friability, drug content, wetting time, water absorption ratio, disintegration time and *in vitro* dissolution study.

Tablet thickness

The thickness of three tablets from each batch was determined using a Vernier caliper. The thickness was measured in centimeters.

Weight Variation

Twenty tablets were selected randomly from each batch and weighed individually on electronic balance (Shimadzu). The individual weighed is then compared with average weight for the weight variations.

Hardness

The strength of tablet is expressed as tensile strength (kg/cm2). The tablet crushing load, which is the force required to break a tablet into pieces by compression. It was measured using a tablet hardness tester (Monsanto hardness tester). Three tablets from each formulation batch were tested randomly and the average readings were noted.

Friability

Friability of the tablets was determined using Roche Friabilator. This device consists of a plastic chamber that is set to revolve around 25rpm for 4 min dropping the tablets at a distance of 6 inches with each revolution. Pre weighed sample of 20 tablets was placed in the Friabilator and were subjected to 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F %) is given by the formula,

% Friability = (Initial weight - Loss in weight) / Initial weight*100

Friability below 1% was considered as acceptable.

Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 10mg of Enalapril maleate was dissolved in 100 ml of phosphate buffer solution, pH 6.8., filtered, diluted suitably and analyzed for drug content at 212nm using UV-Visible spectrophotometer (Shimadzu1700, Tokyo, Japan).

Wetting time and water absorption ratio

A piece of tissue paper folded twice was placed in a small Petri dish (internal diameter = 6.5cm) containing 6 ml of phosphate buffer solution, pH 6.8. A tablet was placed on the paper and time required for complete wetting was measured using a stop watch. The wetted tablet was then weighed. Water absorption ratio (R) was determined using following equation,

$$R = \frac{Wa - Wb \times 100}{Wa}$$

Wa = Weight of tablet after water absorption,

Wb = Weight of tablet before water absorption

Wetting time

***In vitro* disintegration time**

10ml of phosphate buffer solution, pH 6.8 was placed in a petridish of 10cm diameter. The tablet was then carefully positioned in the center of the petridish and the time required for the tablet to completely disintegrate into fine particles was noted.

***In- vitro* disintegration time**

In-vitro disintegration times for Fast dissolving tablets of Enalapril maleate were determined using USP disintegration test apparatus with 900ml of phosphate buffer solution, pH 6.8 as medium maintained at a temperature of 37°C. The time in seconds taken for complete disintegration of the tablets with no palpable mass remaining in the apparatus was measured.

***In-vitro* Dissolution Study**

The release rates of Enalapril maleate from fast dissolving tablets were determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900ml of phosphate buffer 6.8, at 37±0.5°C and 50rpm. A sample (5ml) of the solution was withdrawn from the dissolution apparatus at regular intervals of 1 min for 30mins. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through a Whitman filter. Absorbance of these solutions was measured at 212nm using UV Spectrophotometer. Cumulative percentage of drug release was then calculated.

Stability studies

In order to determine the change in *In-vitro* release profile on storage, stability studies of optimized batch i.e., F9 was carried out at 40°C in a humidity chamber having 75% RH. Samples were withdrawn at regular intervals of 15 days during the study of 30 days. Formulation is evaluated for change in *In-vitro* drug release pattern, hardness, wetting time, weight variation, percent drug content[9-11].

RESULTS AND DISCUSSION

Preformulation study

In Preformulation studies various characteristic of drug such as identification analytical method, micromeritics, solubitities study, loss on drying and partition coefficients were evaluated. The results for these studies are shown in Table No.5.

Enalapril maleate fast dissolving tablet were prepared by direct compression method was carried out by using superdisintegrants (crosscarmelose and sodium starch glycolate), excipient like lactose, sucrose, magnesium stearate, sodium lauryl sulphate. Preformulation studies such as bulk density, tapped density, angle of repose, compressibility index, Hausner ratio. All the Preformulation studies were found the prescribed limits and indicated good flow properties. The FTIR also revealed there is no interaction between the pure drugs and Excipients use for the formulation. The data obtained from physicochemical parameter such as hardness, friability, weight variation, drugs content, wetting time, disintegration time, *In-vitro* dissolution studies. Out of all formulation in direct compression method, F9 direct compression was found satisfactory. The angle of repose was ranged between 25.74º±1.8071 to 35.34º±0.4503. The compressibility index value were found to be in the range of 6.41 %to 80.34% the Hausner's ratio were found to be in the range of 1.07 to 1.20. The hardness was between 3.09±0.10 to 3.83±0.61. Thickness of all nine formulation varied from 4.5±0.039mm to 5.01±0.049mm. The loss of total weight of tablets due friability was in range of 0.19±0.18 to 0.68±0.10. The dugs content for all nine formulation was in the range of 69.97±0.38 to 99.69±0.63 %. The wetting for all nine formulation was in the range of 35.11±0.22sec to 40.22±0.25sec. Disintegration time the value of this test range from 69.60±0.63sec to 98.16±0.61sec. This was one test to be considered to selects one best formulation from nine formulation according to this test F9 is best formulation as it shown lowest time for disintegration (69.60±0.63). Dissolution test was carried out 50rpm using phosphate buffer P^H 6.8. Stability study was carried out for the best formulation of F9 formulation (sublimation method)at 40ºC and 75% RH for one month, 15 days interval the formulation was examined for physical appearance, hardness, friability, thickness, drugs contents, disintegration time, dissolution study, wetting time revealing excellent of the formulated formulation.

Table No.1: Standard calibration curve in water

S.No	Concentration	Absorbance
1	0	0
2	0.1	0.126
3	0.2	0.235
4	0.3	0.329
5	0.4	0.429
6	0.5	0.528
7	0.6	0.621

Table No.2: Standard calibration curve in phosphate buffer

S.No	Concentration(µg/ml)	Absorbance
1	0.0	0.0
2	0.1	0.050
3	0.2	0.102
4	0.3	0.150
5	0.4	0.199
6	0.5	0.244
7	0.6	0.292

Table No.3: Pre-compression parameter of powder blend (direct compression method)

Formulation code	Bulk density (gm/ml) ± SD	Tapped density (gm/ml) ± SD	Angle of repose (◦) ±SD	Carr index (%) ± SD	Hausner's ratio ± SD
F1	0.38±0.0057	0.41±0.0020	27.88±1.29	12.9±1.12	1.15±0.02
F2	0.39±0.0059	0.44±0.0017	30.00±1.66	14.93±1.34	1.18±0.03
F3	0.36±0.0041	0.38±0.0037	27.75±1.03	6.41±1.21	1.07±0.04
F4	0.37±0.0042	0.43±0.0019	33.57±0.38	12.23±1.41	1.14±0.04
F5	0.42±0.0032	0.51±0.0042	35.34±0.45	16.31±1.61	1.19±0.02
F6	0.48±0.0076	0.62±0.0039	28.60±3.88	16.7±1.53	1.20±0.03
F7	0.41±0.0063	0.48±0.0046	25.74±1.80	16.94±1.58	1.20±0.04
F8	0.42±0.0033	0.54±0.0042	27.95±2.26	15.00±2.23	1.18±0.04
F9	0.42±0.0067	0.49±0.0061	32.85±1.45	18.34±2.02	1.22±0.02

Table No.4: Formulation of Enalapril maleate fast dissolving tablet (Direct compression method)

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	ENM	5	5	5	5	5	5	5	5	5
2	Crosscarmellose	10	15	20	25	28	30	35	38	40
3	SSG	40	38	35	30	28	26	25	22	20
4	Mg. stearate	100	100	100	100	100	100	100	100	100
5	Lactose	50	50	50	50	50	50	50	50	50
6	Sucrose	120	120	120	120	120	120	120	120	120
7	SLS	30	30	30	30	30	30	30	30	30
8	Starch (20%conc)	q.s	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Table No.5: Preformultion study

S.No	Organoleptic properties	
1	State	White crystalline powder
2	Color	White
3	Odor	Odorless
4	Taste	Bitter
Identification		
5	UV absorption maxima	208, 212
6	TLC	R_f =0.56
7	Melting point	143-144^oC
8	Infra-red spectra	No change spectra
Assay of Drugs		
9	98.5 to101.5% (Standard as per IP)	
Calibration Curve		
10	In water	λmax y =1.069x
11	In phosphate buffer P^H 6.8	λmax y =0.491x
Micromeritics		
12	Bulk density	0.38±0.03 gm/ml
13	Tapped density	0.56±0.06 gm/ml
14	Carr' s index	13.77±6.64 (flow property- poor)
15	Angle of repose	38.35±0.895 (flow property -fair)
Solubility		
16	Methanol, ethanol, distilled water, dimethyl formide	
Partition Cofficients		
17	2.45±0.011(lipophilic in nature)	

Table No.6: Evaluation of fast dissolving tablet of Enalapril maleate (Direct compression method)

Evaluation parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness(mm)±SD	4.68±0.040	4.57±0.039	4.56±0.05	4.88±0.045	5.03±0.049	4.88±0.042	4.85±0.042	4.49±0.050	4.48±0.044
Hardness (kg/cm^2)±SD	3.86±0.12	3.76±0.31	3.55±0.25	3.58±013	3.52±0.23	3.39±0.37	3.33±0.34	3.19±0.06	3.05±0.10
%Friability ±SD	0.51±0.18	0.59±0.14	0.63±0.19	0.55±0.11	0.60±0.16	0.61±0.14	0.67±0.10	0.69±0.10	0.21±0.18
Disintragration time (sec) ± SD	98.16±0.61	96.11`0.42	90.51±0.23	88.20±0.23	87.86±0.82	86.52±0.41	78.52±0.84	71.69±0.76	69.60±0.63
Wetting (sec)±SD	40.22±0.25	38.90±0.11	37.45±0.20	36.65±0.24	36.75±0.35	36.25±0.53	35.90±0.47	35.78±0.58	35.11±0.22
Water absorption ratio	141.68±0.56	149.27±0.78	156.34±0.81	150.65±0.45	148.36±0.78	155.28±0.91	180.91±0.78	193.69±0.54	209.65±0.89
Content uniformity(%)±SD	99.27±0.63	96.99±0.55	99.81±0.35	98.85±0.20	97.81±0.44	98.92±0.87	69.97±0.38	98.64±0.29	99.69±0.63

Table No.7: % Drug release profile of fast dissolving tablets Enalapril maleate

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	14.73	19.13	16.71	23.42	17.48	20.01	23.42	13.52	28.15
2	19.57	23.53	25.4	37.5	26.94	28.48	34.52	28.15	37.14
3	26.5	26.5	35.63	42.56	38.16	37.5	39.37	42.34	46.52
4	31.56	34.31	40.63	47.52	45.31	43.66	45.31	47.51	54.65
5	35.3	41.24	47.4	43.78	47.84	45.31	52.35	57.29	58.39
10	47.73	47.71	53.56	57.29	54.76	54.76	58.72	64.55	61.8
15	53.56	50.15	58.39	61.36	58.39	58.39	65.76	68.29	64.99
20	56.41	57.25	63.12	67.3	65.65	63.67	69.72	69.72	76.1
25	65.65	62.79	69.5	73.9	72.14	74.56	74.67	78.3	83.8
30	67.52	68.62	74.23	75.54	76.76	77.2	78.3	86.33	87.1

Table No.8: Accelerated stability study of optimized formulation MD6 at 40°C/75% RH for one month

S.No	Period	Hardness (kg/cm^2)	Disintegration time (sec)	Wetting time (sec)	Drug content (%)	%drugs release
1	0Day	3.09±0.10	69.60±0.65	35.11±0.18	99.69±0.03	86.33
2	15 day	3.07±0.09	68.58±0.56	33.12±0.12	99.57±0.04	85.95
3	30 day	3.02±0.4	67.48±0.47	31.15±0.10	98.97±0.09	85.31

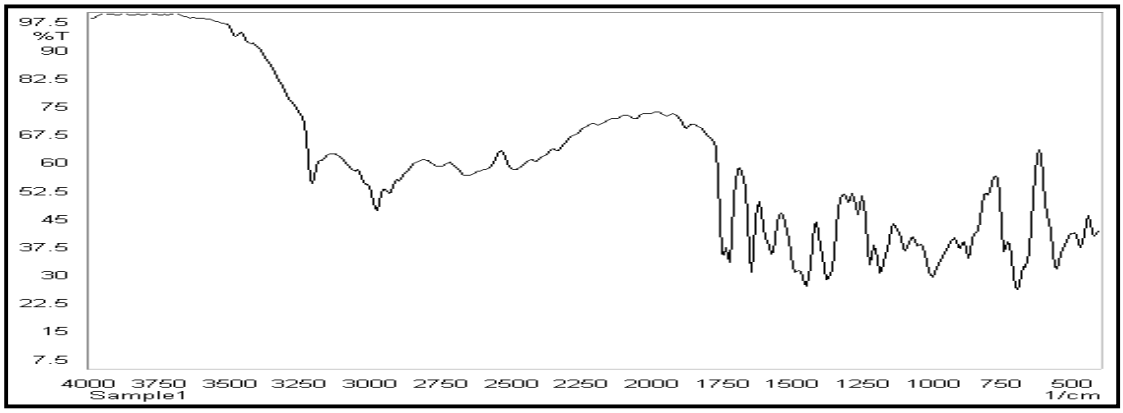

Figure No.1: FTIR of pure Enalapril maleate

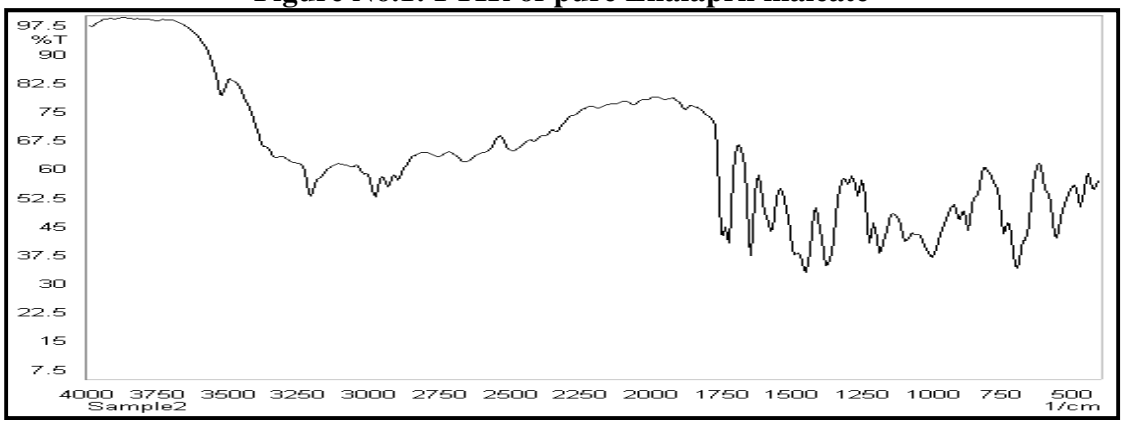

Figure No.2: FTIR of drugs + Excipients

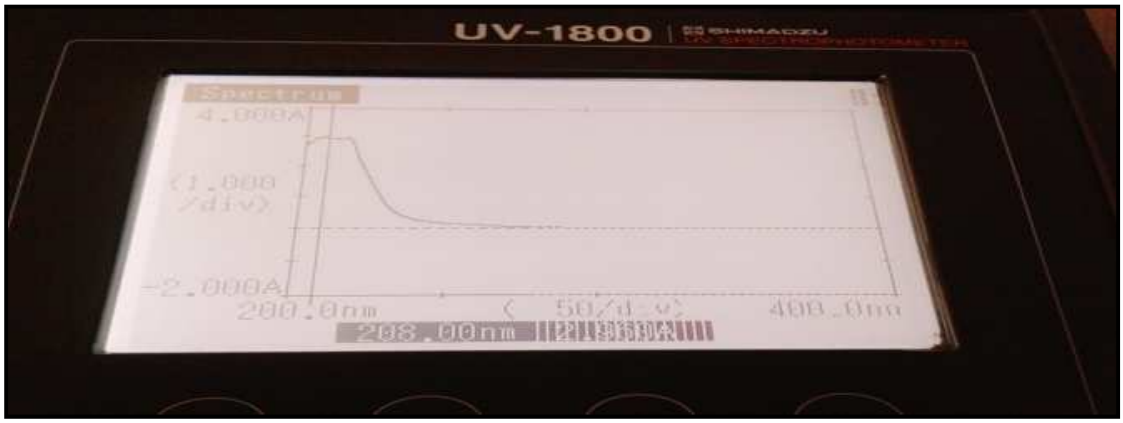

Figure No.3: Standard curve Enalapril maleate in water

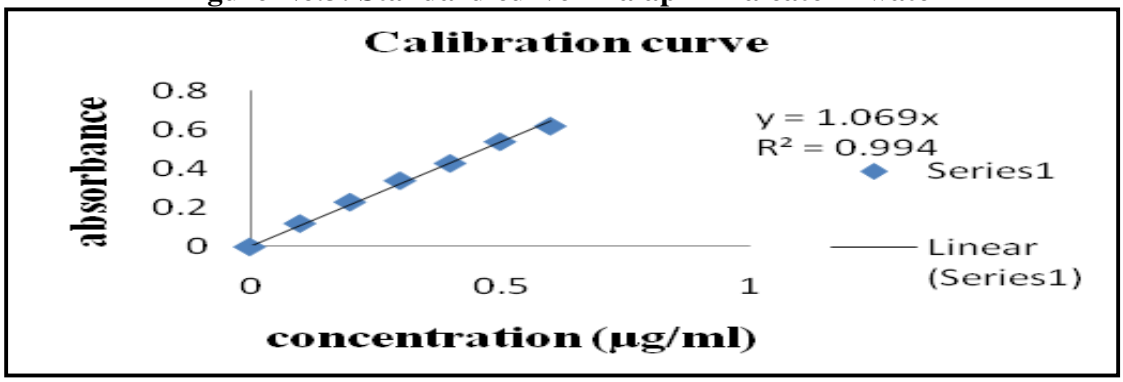

Figure No.4: Calibration graph of Enalapril maleate in water

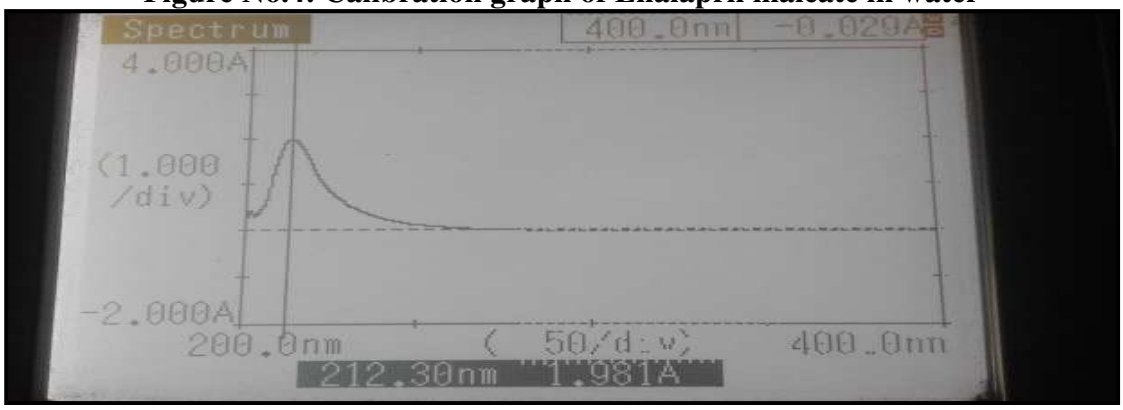

Figure No.5: Spectra of Enalapril Maleate in phosphate buffer

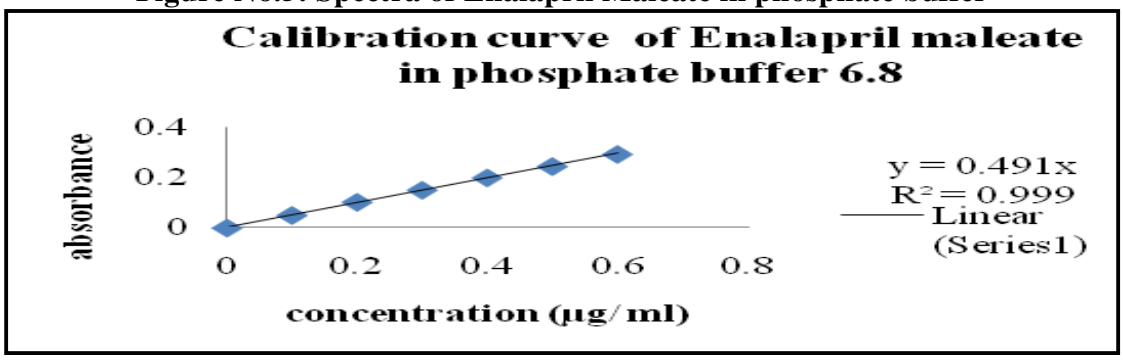

Figure No.6: Calibration graph of Enalapril maleate in phosphate buffer 6.8 pH

Figure No.7: Wetting time study

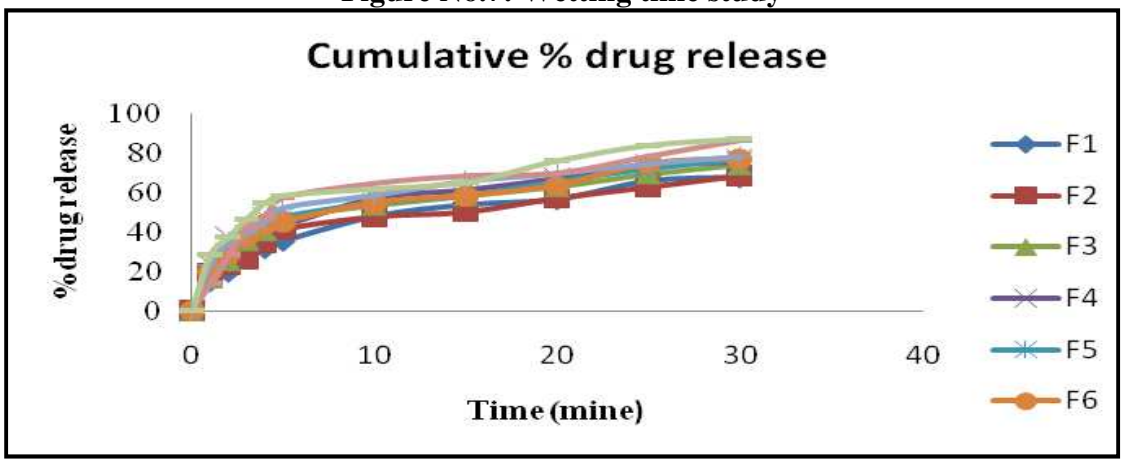

Figure No.8: *In-vitro* drug release profile of fast dissolving tablets Enalapril maleate

CONCLUSION

Fast dissolving tablets of Enalapril maleate can be successfully prepared by direct compression technique using selected superdisintegrants for the better patient compliance for effective therapy. The fast dissolving tablets prepared by using croscarmellose and sodium starch glycolate by direct compression is more efficient by the evaluation parameter (disintegration time, wetting time, dissolution profile) and result obtained.

ACKNOWLEDGEMENT

The authors are sincerely thanks to the Kailash Institute of Pharmacy and Management, Gorakhpur, Uttar Pradesh, India for providing the facilities to complete this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBILIOGRAPHY

1. Cheng R, Guo X, Burusid B, Couch R. A review of fast dissolving tablets, *Pharm Tech, (North America),* 24, 2000, 52-58.
2. Bi Y, Sunada H, Yonezawa Y, Dayo K, Otsuka A, Iida K. Preparation and evaluation of compressed tablet rapidly disintegrating in oral cavity, *Chem Pharm Bull (Tokyo),* 44(11), 1996, 2121-2127.
3. Quick dissolving tablets, http:/www.biospace.com, 27 may, 2001.
4. British pharmacopeia, Department of health social service and public safety, *The Stationary Office Limited, London,* 1, 2001.

5. Lokesh B V S, Naidu S R. New dissolution method of enalapril maleate by uvspectroscopy, *JASA,* 2007, 31-35.
6. Kapil Kumar Goel, Nidhi Goel, and Asmita Gajbhiye. Development of new UV spectrophotometer method for the estimation of enalapril maleate in bulk and tablet dosage form, *Asian Journals of Experimental Chemistry,* 3(1-2), 2008, 92-93.
7. Indian Pharmacopeia 2007, *Published by the Indian Pharmacopeia Commission, Ghaziadad,* 1, 480.
8. Jain C P and naruka P S. Formulation and evaluation of fast dissolving table of valsartan, *International Journal of Pharmacy and Pharmaceutical Sciences,* 1(1), 2009, 219-226.
9. Raviteja Penjarla, Muralidhar S, Ramesh R, Narayana T V, Vasantha Kumar P, Vijay Kumar G. Formulation and Evaluation of Valsartan Fast Disintegrating Tablets Using Solid Dispersion Technique, *International Journal of Innovative Pharmaceutical Research,* 4(1), 2013, 274-280.
10. Buddhadev Sheetal, Buddhadev Sandip. Formulation and evaluation of fast dissolving tablets of albendazole by sublimation method, *International Journal of Applied Pharmaceutical and Biological Research,* 2(4), 2017, 35-47.
11. Anie Vijetha K, Padmaja B, Sravan Kumar G, Hima Swethaj, Sravanthi P, Sravanthi D. Formulation and characterization of fast dissolving tablets of isradipine by using different technologies, *International Journal of Pharmaceutical Research and Biomedical Analysis,* 1(2), 2012, 1-10.
12. Sharma Shailesh, Gupta G D. Formulation and characterization of fast-dissolving tablet of promethazine theoclate, *Asian Journal of Pharmaceutics,* 2(1), 2008, 70-72.

Please cite this article in press as: Satya Prakash Singh and Navneet Kumar Verma. Formulation and characterization of Enalapril maleate fast dissolving tablets, *Asian Journal of Research in Chemistry and Pharmaceutical Sciences,* 7(4), 2019, 936-945.