International Journal of Current Research and Applied Studies, (IJCRAS)

ISSN: 2583-6781

available at https://ijcras.com/

Volume 4 Issue 1 Jan-Feb 2025, Page 111-128

To cite this article: Munija Pancheddula, Shabnam sajida, Fatima sultana, Sandya Rani Deekonda (2025). FORMULATION AND INVITRO EVALUATION OF ENALAPRIL MALEATE SUSTAINED RELEASE TABLETS BY USING VARIOUS POLYMERS, International Journal of Current Research and Applied Studies (IJCRAS) 4 (1): Article No. 113, Sub Id 188

FORMULATION AND INVITRO EVALUATION OF ENALAPRIL MALEATE SUSTAINED RELEASE TABLETS BY USING VARIOUS POLYMERS

Munija Pancheddula[1], Shabnam sajida[2], Fatima sultana[3], Sandya Rani Deekonda*

*Assistant Professor, Department of Pharmaceutics, Vision College of Pharmaceutical Sciences and Research, Boduppal, Hyderabad.

[1]Vice Principal, Vision College of Pharmaceutical Sciences and Research, Boduppal, Hyderabad

[2,3]Student, Pharm D III Year, Vision College of Pharmaceutical Sciences and Research, Boduppal, Hyderabad.

DOI : https://doi.org/10.61646/IJCRAS.vol.4.issue1.113

ABSTRACT

The primary objective of this study was to formulate and assess sustained-release tablets of Enalapril maleate utilizing various polymers, specifically Xanthan gum, Karaya gum, and HPMC K100M, employing the wet granulation method. Compatibility studies between the drug and excipients revealed no significant alterations. Fourier-transform infrared (FT-IR) retained, affirming the absence of interactions between the drug and excipients. The blend of formulations exhibited favourable flow properties, angle of repose, bulk density, and tapped density. Post-compression assessments of the prepared tablets met quality control criteria outlined in the Indian Pharmacopoeia (I.P) limits. In vitro drug release studies, conducted in simulated gastric fluid (0.1 N HCL) for the initial 2 hours and in phosphate buffer (pH 6.8) for the subsequent hours using USP apparatus II paddle method, revealed that the EM4 formulation achieved a notable drug release of 99.75% over 12 hours. Pre formulation studies were done initially and the results were found within the limits.

Keywords: Enalapril maleate, Hydroxy propyl Methyl cellulose

1. INTRODUCTION

The pharmaceutical products formulated for systemic delivery through the oral route of administration without considering the mode of delivery and the design of dosage forms, must be developed within the intrinsic characteristics. Administering a single dose of a drug that desire to maintain a near-constant level of a drug often translates into better patient compliance, as well as enhanced clinical efficacy of the drug3. Because of increased complication and expense involved in marketing of new drug, has focused greater attention on development of sustained release or controlled release drug delivery systems. Matrix system is widely used for the purpose of sustained release.

The product so formulated are designated as sustained action, sustain release, delayed action, depot, respiratory, retarded release and time release medications. Many drugs, to achieve a steady state blood level that is therapeutically effective and non-toxic for an extended period of time. Sustained release, sustained action, prolonged action, controlled release extended action, timed release and depot dosage form are designed to achieve prolonged therapeutic effect. Conventional drug therapeutic agents. These agents are formulated to produce maximum stability, activity and bioavailability.

2. MATERIALS AND METHODOLOGY:

Enalapril maleate, Xanthan gum, Karaya gum, Hydroxy propyl Methyl cellulose (HPMC) K100M, Talc, Magnesium stearate, Lactose. (Procured from Ranbaxy Labs, Provided by SURA LABS, Dilsukhagar, and Hyderabad.

2.1. Drug – Excipient compatibility studies Fourier Transform Infrared (FTIR) spectroscopy:

Drug excipient interaction studies is a successful formulation of every dosage form. (FTIR) Spectroscopy studies used for the assessment of physicochemical compatibility and interactions, which helps in the prediction of interaction between drug and excipients. In the current study 1:1 ratio was used for preparation of physical mixtures and for analysing of compatibility studies. FT-IR studies was carried out with a Bruker, ATR FTIR facility using direct sample technique.

2.2. Formulation development of Sustained release Tablets:

The tablets were prepared as per the procedure given below and aim is to prolong the release of Enalapril maleate.

Table.1. Formulation of Sustained release tablets

Ingredients	EM1	EM2	EM3	EM4	EM5	EM6	EM7	EM8	EM9
Enalapril maleate	5	5	5	5	5	5	5	5	5
Xanthan gum	10	20	30	-	-	-	-	-	-
Karaya gum	-	-	-	10	20	30	-	-	-
HPMC K100M	-	-	-	-	-	-	10	20	30
Talc	5	5	5	5	5	5	5	5	5
Mg Stearate	5	5	5	5	5	5	5	5	5
Lactose	75	65	55	75	65	55	75	65	55
Total weight	100	100	100	100	100	100	100	100	100

Procedure:

1) Enalapril maleate or ingredients were passed through 40 mesh except Mg Stearate and Talc.
2) Required quantity of drug (Enalapril maleate) polymer were mixed thoroughly than add sufficient quantity of the binder solution mix slowly up to 15 min.
3) Dry the above granules at 65-70ºC by using dryer
4) After drying the granules is passed through sieve no ≠ 22.
5) mg stearate was added as lubricant.
6) Finally subjected to compression

2.3. Evaluation parameters:

2.3.1 Pre compression parameters: Preformulation parameters are done by standard procedures.

Bulk density (D_B)

Bulk density is the ratio between a given mass of the powder and its bulk volume. **Bulk density = Mass of powder / Bulk volume of the powder**

Bulk density (D_B) = W/V_0

Procedure: An accurately weighed quantity of granules (w) (which was previously passed through sieve NO: 40) was carefully transferred into 250ml measuring cylinder and measure the bulk volume.

Tapped Density (D_T)

Tapped density is the ratio between a given mass of powder (or) granules and the constant (or) fixed volume of powder or granules after tapping.

Tapped density = mass of the powder / tapped volume

Procedure: An accurately weighed quantity of granules(w) (which was previously passed through sieve No:40) was carefully transferred into 250ml measuring cylinder and the cylinder was tapped on a wooden surface from the height of 2.5cm at two second intervals. The tapping was continued until no further change in the volume (until a constant volume) was obtained (V_f). The tapped density was calculated by using the formula **Tapped density (D_T) = W/V_f**

Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow and was calculated by the formula,

Hausner's ratio = D_T/D_B

Where, D_T is the tapped density

D_B is the bulk density

Compressibility index

Compressibility index (CI) [61] was determined by measuring the initial volume (V_0) and final volume (V_f) after hundred tapping's of a sample in a measuring cylinder. It indicates the powder flow properties and expressed in term of percentage and given in table and calculated by using the formula

% Compressibility index = $V_0 – V/V_0$ x 100

Angle of repose

Angle of repose[62] was measured by fixed funnel method. It determines flow property of the powder. It is defined as maximum angle formed between the surface of the pile of powder and the horizontal plane.

The powder was allowed to flow through the funnel fixed to stand at definite height (h). By measuring the height and radius of the heap of powder formed (r), angle of repose was calculated by using formula given below and the calculated values obtained was shown in table.

$\theta = \tan^{-1} (h/r)$

Where, **θ** is the angle of repose

h is the height in cm

r is the radius in cm

Table No.2. The flow property of powder blend

Flow property	Angle of repose	Compressibility index (%)	Hausner's ratio
Excellent	25-30	<10	1.00-1.11
Good	31-35	11-15	1.12-1.18
Fair	36-40	16-20	1.19-1.25
Passable	41-45	21-25	1.26-1.34
Poor	46-55	26-31	1.35-1.45
Very poor	56-65	32-37	1.46-1.59

Very very poor	>66	>38	>1.60

2.3.2. Post compression parameters15:

Weight variation test

Twenty tablets were randomly selected and weighed, to estimate the average weight and that were compared with individual tablet weight. The percentage weight variation was calculated as per Indian pharmacopeial specification.

Friability test

Twenty tablets were weighed and subjected to drum of friability test apparatus. The drum rotated at a speed 25 rpm. The friabilator was operated for 4 minutes and reweighed the tablets % loss (F) was calculated by the following formula

$F = 100(W0-W)/W0$

Where W0 = Initial weight, W= Final weight

Hardness test

The hardness of tablets was measured by using Monsanto hardness specification.

Thickness test

The rule of physical dimension of the tablets such as sizes and thickness are necessary for consumer acceptance and maintain tablet uniformity. The dimensional specifications were measured by using screw gauge.

The thickness of the tablet is mostly
related to the tablet hardness can be used as initial parameter.

Table3: Standards of uniformity of weight

S. No.	Average weight of tablet	% of deviation
1	≤ 80 mg	10
2	> 80 mg to <250 mg	7.5
3	≥ 250 mg	5

Drug content

The amount of drug is to be monitor from tablet to tablet, or batch to batch is to evaluate for efficacy of tablets. For this, taken ten tablets from each batch were weighed and powdered.

Weighed equivalent to the average weight of the tablet powder and transferred into a 100 ml volumetric flask and dissolved in a suitable quantity. The solution was mixed properly.

Then filter it and the filtrate sample was analysed by UV spectrophotometer.

***In vitro* drug release studies**

Apparatus--USP-II, Paddle Method

Dissolution Medium -- 0.1N HCL,

P H 6.8 Phosphate buffer

RPM -50

Sampling intervals[hrs]-- 1,2,3,4,5,6,7,8,9,10,11,12

Temperature--37º c ± 0.5º

Procedure:

900ml of 0.1 N HCL was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The media was allowed to equilibrate to temp of 37ºc± 0.5ºc. Tablet was placed in the vessel and apparatus was operated for 2 hours. Then 0.1 N HCL was replaced with pH 6.8 phosphate buffer and process was continued up to 24hrs at 50rpm. At specific time intervals, with drawn 5 ml of sample and again 5ml media was added to maintain the sink condition. Withdrawn samples were analysed at 226 nm wavelength of drug using UV- spectrophotometer.

Application of Release Rate Kinetics to Dissolution Data

Various types of models were tested for explaining the kinetics of drug release. To analyse the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer -Pep-pas release model.

Zero order release rate kinetics:

To study the zero-order release kinetics the release rate data are fitted to the following equation.

$$F = K_0 t$$

Where, 'F' is the drug release at time 't', and 'K_0' **is** the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation. A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

$$\text{Log (100-F)} = kt$$

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation[9].

F=k t1/2

Where, 'k' is the Higuchi constant.

In Higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus long time according to Korsmeyer-Pappas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight line.

$$M_t/M_\infty = K\ t^n$$

3. RESULT AND DISCUSSION

The present work was designed to develop sustained tablets of Enalapril maleate using various polymers.

3.1 Drug and Excipient Compatibility Studies

3.1.1 FTIR study

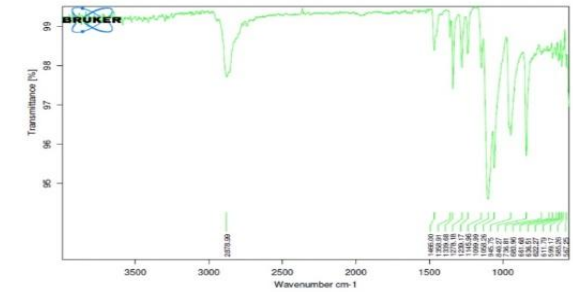

Fig.1Ftir Graph Of Pure Drug

Fig .1 FTIR graph of pure drug

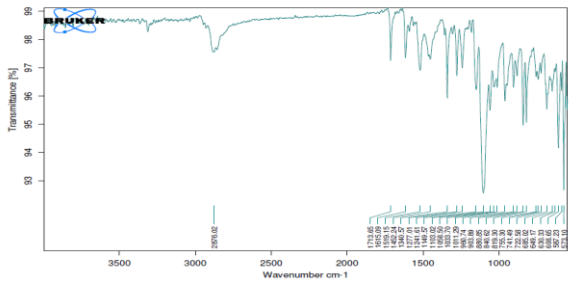

Fig.2: FTIR graph of optimized Formulation

There is no change in the peak from the FTIR data was evident that the drug and excipient does not have any interactions. Hence, they were compatible.

3.2. Analytical Method

3.2.1 Standard graph of Enalapril maleate in 0.1N HCL:

The scanning of the 10µg/ml solution of Enalapril maleate the ultraviolet range (200-400nm) against 0.1 N HCL the maximum peak observed at λ_{max} as 226nm.The standard concentration of Enalapril maleate (5-25 µg/ml) was prepared in 0.1N HCL

Table 4: Standard curve of Enalapril maleate 0.1N HCL

Concentration (µg/ mL)	Absorbance
0	0
5	0.149
10	0.309
15	0.472
20	0.649
25	0.816

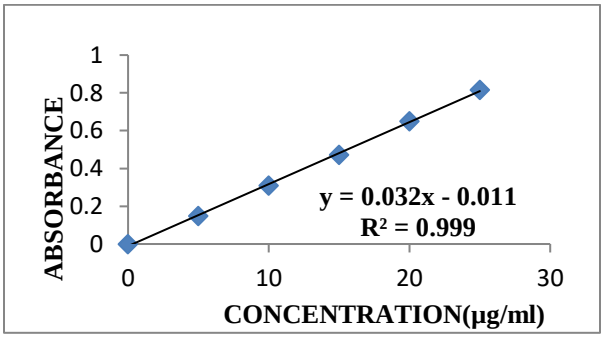

Fig 3: Calibration curve of Enalapril maleate 0.1N HC1 at 226 nm

3.2.2 Standard Curve of Enalapril maleate Phosphate buffer pH 6.8

The scanning of Enalapril maleate the ultraviolet range (200-400nm) against 6.8pH phosphate the maximum peak observed at the λ_{max} as 230nm. The standard concentrations of Enalapril maleate prepared in 6.8 pH phosphate buffer showed good linearity with R^2 value of 0.999

Table 5: Standard curve of Enalapril maleate Phosphate buffer pH

Concentration (µg / ml)	Absorbance
0	0
5	0.158
10	0.343
15	0.535
20	0.722
25	0.914

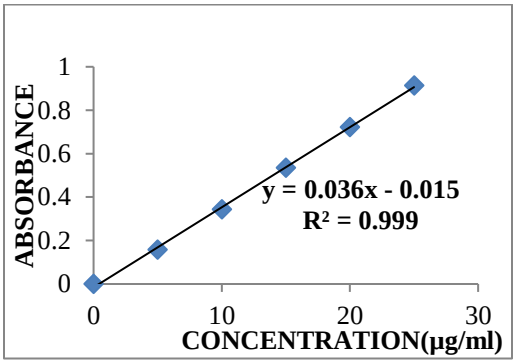

Fig.4 Calibration of Enalapril maleate Phosphate buffer pH 6.8

3.3: Evaluation parameters:

3.3.1 Pre-compression parameters:

Table:6 Pre-compression parameters of powder blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
EM1	25.01	0. 59	0.57	14.03	1.16
EM2	26.8	0. 46	0.67	16.41	1.19
EM3	27.7	0. 32	0. 54	18.75	1.23
EM4	25.33	0.54	0.64	15.62	1.18
EM5	25.24	0.52	0.65	18.46	1.22

EM6	28.12	0. 46	0. 56	15.15	1.17
EM7	27.08	0.58	0.69	15.94	1.18
EM8	25.12	0.48	0.67	15.78	1.18
EM9	26.45	0.54	0.65	16.92	1.25

The angle of repose values was showed from 25.01 to 28.12. The bulk density of all the formulations was found to be in the range of 0. 32 to 0.59 (gm/cm3). The tapped density of all the formulations was found to be in the range of 0.54 to 0.69 The compressibility index of all the formulations was found to ranging from 14.03 to 18.75.

3.3.2 Post Compression Parameters For tablets

Formulation codes	**Average Weight (mg)**	**Hardness (kg/cm2)**	**Friability (%loss)**	**Thickness (mm)**	**Drug content (%)**
EM1	98.37	5.67±0.84	0.37	3.25±0.22	98.72
EM2	99.91	5.51±0.47	0.56	3.68±0.18	97.88
EM3	97.88	5.62±0.55	0.48	3.75±0.47	99.62
EM4	100.05	5.48±0.38	0.44	3.98±0.71	100.02
EM5	96.53	5.66±0.22	0.58	3.55±0.38	98.96
EM6	99.78	5.58±0.49	0.42	3.62±0.26	99.57
EM7	97.62	5.45±0.96	0.61	3.48±0.55	97.34
EM8	98.58	5.61±0.44	0.54	3.71±0.48	98.87
EM9	96.86	5.58±0.82	0.39	3.48±0.66	99.66

Table 7: Post compression parameters of tables

TIME (hr.)	**CUMULATIVE PERCENTAGE DRUG RELEASED**								
	EM 1	**EM 2**	**EM3**	**EM4**	**EM5**	**EM6**	**EM7**	**EM8**	**EM9**
0	0	0	0	0	0	0	0	0	0

1	7.26	8.17	9.32	10.18	8.15	9.52	8.26	10.26	8.98
2	14.11	17.02	16.12	18.69	15.37	17.01	14.11	15.22	19.66
3	22.73	25.26	23.52	25.78	29.88	27.91	25.73	20.75	24.35
4	31.47	32.52	30.54	39.91	34.25	33.36	38.47	33.15	37.28
5	39.06	43.57	38.65	42.27	46.71	41.58	44.06	45.73	41.63
6	48.25	49.31	45.25	48.13	56.19	51.11	55.25	54.69	45.26
7	56.09	52.25	55.05	56.96	63.47	58.23	64.09	62.05	56.96
8	61.29	59.25	58.77	65.33	72.59	68.88	71.29	67.32	60.19
9	68.36	63.01	66.95	72.67	75.28	73.43	78.36	74.77	68.24
10	72.28	69.19	72.18	77.89	78.76	82.57	81.28	79.67	75.58
11	80.47	76.63	83.22	86.17	87.08	86.72	85.47	81.65	79.44
12	88.96	85.28	92.52	99.75	90.39		97.21	88.12	83.97

Table 8: Dissolution data of Enalapril

Weight variation and thickness:

The average tablet weight of all the formulations was found to be between 96.53 to 100.05. The maximum allowed percentage weight variation for tablets weighing >100 mg is 5%. Thus, all the formulations were found to comply with the standards given in I.P.

Hardness and friability:

The average hardness for all the formulations was found to be between (5.45±0.96 to 5.67±0.84) kg/cm^2.

The average percentage friability for was between 0.37 and 0.61.

Drug content: The drug content values for all the formulations were found to in range of (97.88 to 100.02). The tablets must contain not less than 95% and not more than 105% of the stated amount of the drug.

The tablets dissolution study was carried out in paddle dissolution apparatus using 0.1 N HCL for 2 hr and 6.8 pH phosphate buffer for remaining hours as a dissolution medium

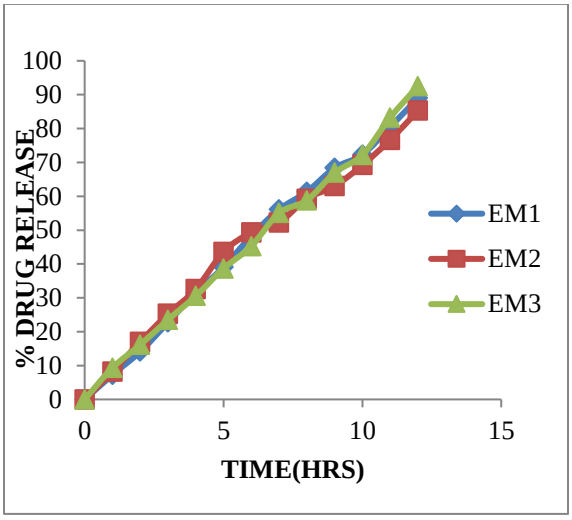

Figure 5: Dissolution study of Enalapril maleate Sustained Release tablets (F1 to F3)

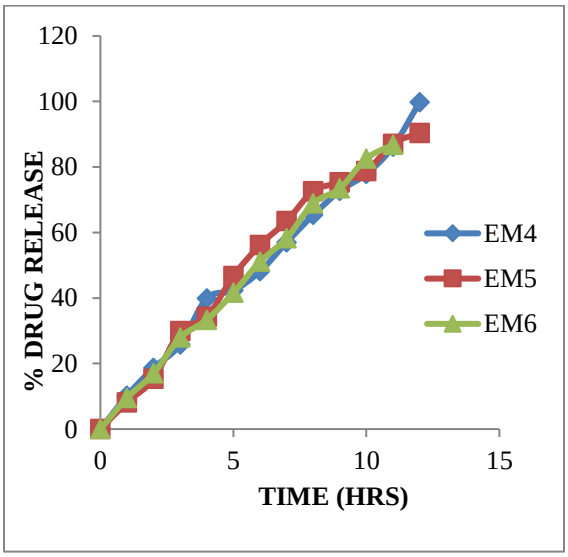

Figure 6: Dissolution study of Enalapril maleate tablets (F4 to F6)

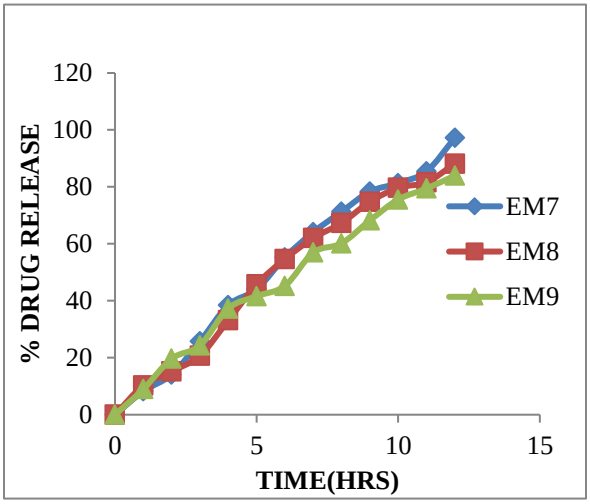

Figure 7: Dissolution study of Enalapril maleate tablets (F7-F9)

The drug release up to 12 hours and showed maximum of 99.75 % in 12 hours with good retardation. The formulations prepared with HPMC K100M were able to retard up to 12 hours. The EM4 formulation containing 1:1 ratio showed maximum % drug release. Hence based on dissolution data of 9 formulations, EM4 formulation showed better release up to 12 hours.

3.4. Application of Release Rate Kinetics to Dissolution Data

Data of in vitro release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Enalapril maleate release from sustained tablets. The results were shown in the below table

Table 9: Release kinetics data. (EMF4)

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM % RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000

10.18	1	1.000	1.008	0.000	1.953	10.180	0.0982	-0.992	89.82	4.642	4.478	0.163
18.69	2	1.414	1.272	0.301	1.910	9.345	0.0535	-0.728	81.31	4.642	4.332	0.309
25.78	3	1.732	1.411	0.477	1.871	8.593	0.0388	-0.589	74.22	4.642	4.202	0.439
39.91	4	2.000	1.601	0.602	1.779	9.978	0.0251	-0.399	60.09	4.642	3.917	0.725
42.27	5	2.236	1.626	0.699	1.761	8.454	0.0237	-0.374	57.73	4.642	3.865	0.777
48.13	6	2.449	1.682	0.778	1.715	8.022	0.0208	-0.318	51.87	4.642	3.729	0.912
56.96	7	2.646	1.756	0.845	1.634	8.137	0.0176	-0.244	43.04	4.642	3.504	1.137
65.33	8	2.828	1.815	0.903	1.540	8.166	0.0153	-0.185	34.67	4.642	3.261	1.381
72.67	9	3.000	1.861	0.954	1.437	8.074	0.0138	-0.139	27.33	4.642	3.012	1.629
77.89	10	3.162	1.891	1.000	1.345	7.789	0.0128	-0.109	22.11	4.642	2.807	1.835
86.17	11	3.317	1.935	1.041	1.141	7.834	0.0116	-0.065	13.83	4.642	2.400	2.241
99.75	12	3.464	1.999	1.079	-0.602	8.313	0.0100	-0.001	0.25	4.642	0.630	4.012

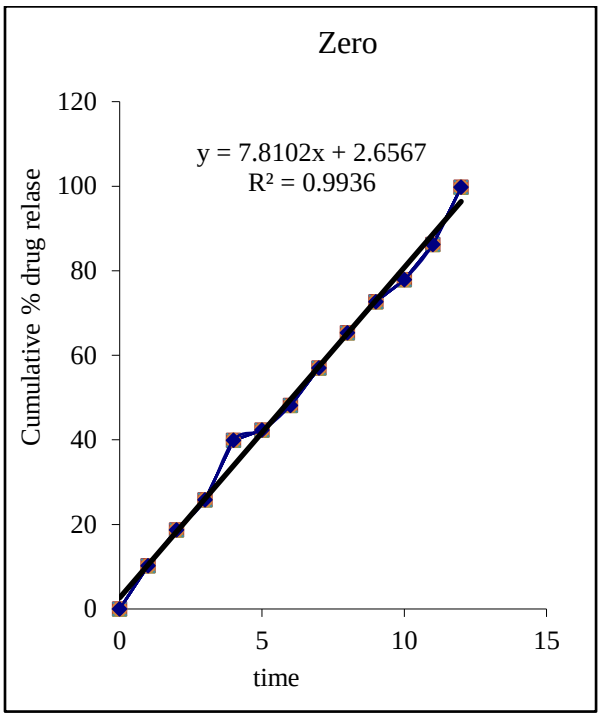

Figure 8: Graph of zero order kinetics

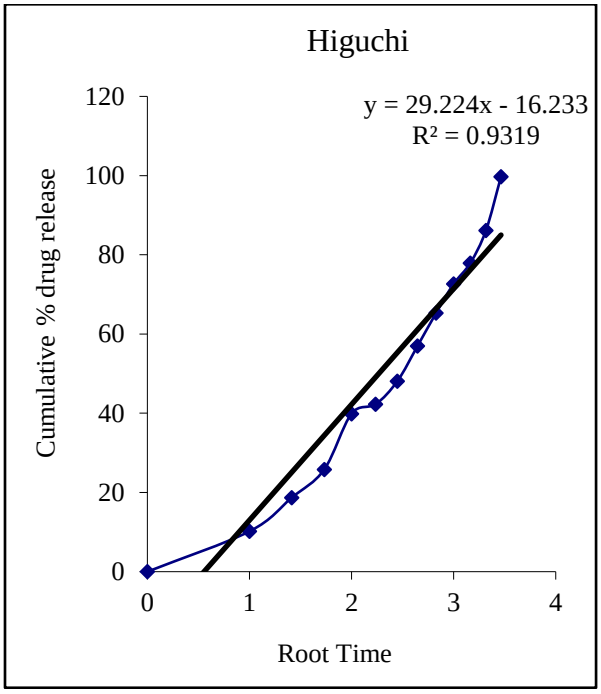

Figure 9: Graph of Higuchi release kinetics

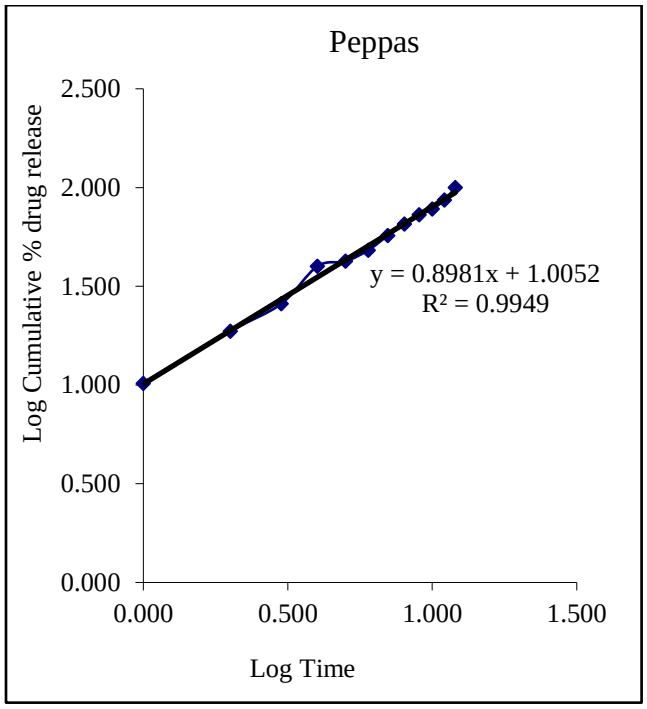

Figure 10: Graph of peppas release kinetics

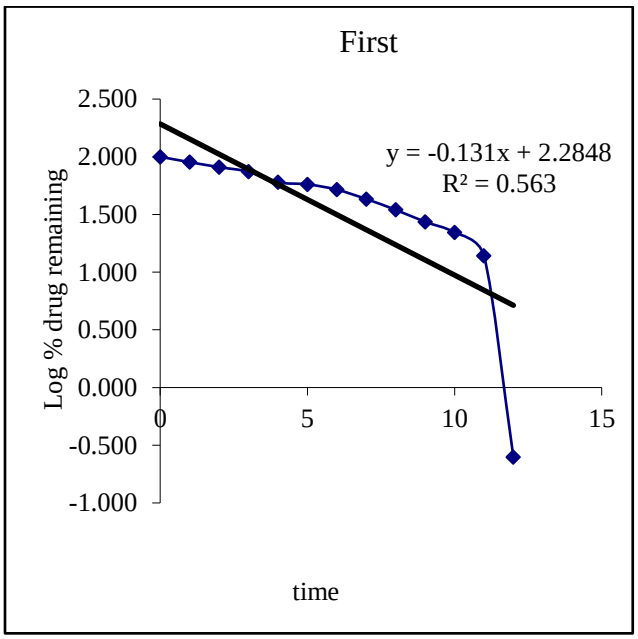

Figure 11: Graph of first order release kinetics

Based on the data above results the optimized formulation followed Kors mayer Peppas Release Kinetics.

4. CONCLUSION:

Sustained release matrix tablets of Enalapril maleate were prepared by wet granulation Method. the tablet was formulated by using karya gum, xanthan gum and HPMC K100M polymers. Infrared spectra of the drug along polymers reveal that there is no significant interaction between drug and polymers. Pre formulation studies were done initially and the results were found within the limits. The evaluation tests results are found within the limits. The evaluation tests results found to be within the pharmacopeial specifications. Invitro drug release studies were carried out in stimulated gastric fluid and From in vitro dissolution study it was concluded that the formulation EM4 was showed the drug release 99.75. The results indicated graphs it was evident that the formulation EM4 was followed Pep-pas release kinetics mechanism.

5. ACKNOWLEDGEMENT:

We express our best gratitude to the management of vision college of pharmaceutical sciences and research for the support, guidance and valuable suggestions of my research work.

6. REFERENCE:

1.M.m. Gupta, ray brijesh. A Review On: Sustained Release Technology. International Journal of Therapeutic Applications, Volume 8, 2012, 18 – 23.
2. Altaf AS, Friend DR, MASRx and COSRx Sustained-Release Technology in Rathbone MJ, Hadgraft J, Robert MS, Modified Release Drug Delivery Technology, Marcell Dekker Inc., New York, 2003.
3. Jantez GM, Robinson JR. Sustained and controlled release drug delivery systems. In: Banker GS, Rhodes CT, editors. Modern pharmaceutics. 3rd edition. New York: marcel dekker inc; 1996.
4. Popli H, shrma SN. Trends in oral sustained release formulations-I The eastern pharmacist 1989; 32: p. 99-103.
5. Abhijeet Welankiwar. Review: Sustained Release Dosage Forms.
6. Chugh I, Seth N, Rana AC, Gupta S. Oral sustained release drug delivery system: anoverview. International research journal of pharmacy 2012; 3(5): 57-62.
7. Patel Chirag J., Satyanand T., Novel Sustained Release Drug Delivery: A Modern Review, International Journal of Applied Pharmaceutics 2014;1:115-119.
8. Wadher G., Satish B., Tukaram MK., Recent (Aspects) trend on Sustained drug delivery system, International Journal of Chemical and Pharmaceutical Sciences 2013;4:1-7.
9. Higuchi T., Mechanism of sustained action medication, theoretical analysis of rate of release of solid drugs dispersed in solid matrices, Journal of Pharmaceutical. Ciences 1963;1145-1149.
10. Gwen MJ. And Joseph R., Sustained and Controlled Release Drug Delivery System, Modern Pharmaceutics Journal of Applied Sciences 2002;507-510.
11 D. M. Patil, P. A. Pawar, R. Y. Pagar, R. S. Ghule, V. A. Bairagi. Formulation and development of sustained release Matrix tablets of lornoxicam. Journal of Drug Delivery & Therapeutics. 2018; 8(2):102-106.
12. Pavani Chowdary, T Sravani, MD Basheeruddin. Formulation And Evaluation of Sustained Release Tablets of Nateglinide by Using Natural Polymers. Vol 9, No 1 (2017).

13. Jamil QA, Masood MI, Jamil MN, Masood I, Iqbal SM. Formulation and in vitro evaluation of sustained release matrix tablets using cross-linked natural gum. Pak J Pharm Sci. 2017 Mar;30(2):355-362.
14. Vinod R. Formulation and Evaluation of Sustained Release Matrix Tablets Using Natural Gum Limonia acidissimaas Release Modifier. Asian Journal of Biomedical and Pharmaceutical Sciences; 3(23) 2013, 38-44.
15. P.R. Radhika; T.K. Pal; T. Sivakumar. Formulation and Evaluation of Sustained Release Matrix Tablets of Glipizide. Volume 5, Issue 4, Autumn 2009, Page 205-214.