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FORMULATION AND EVALUATION OF CONTROLLED RELEASE TABLETS OFPERINDOPRIL ERBUMINE

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Abstract:

Perindopril Erbumine (PE) is an ACE inhibitor. It is effective in the treatment of Hypertension and Blood pressure, has a half-life 0.8-1 h and oral bioavailability is < 60 %. The objectives of the present research work are to formulate and evaluate controlled matrix tablets containing Perindopril Erbumine (PE) as a drug using different ratios of polymers to avoid hepatic first pass metabolism and to increase bioavailability of the drug. Different matrix carriers' hydroxy methyl cellulose (HPMC) K100M, Xanthan gum, Micro Crystalline Cellulose, Poly Vinyl Pyrrolidone like were used to develop matrix tablets. Various pre-compression characteristics of the powder bed like bulk density, tapped density, compressibility index, and repose angle were evaluated and studied. Matrix tablets were compressed and were all assessed for weight variation, hardness, thickness, friability, swelling index, in vitro release of the drug. The conditions were simulated and sink conditions were maintained. Further stability studies of the Perindopril Erbumine formulation F9 conducted according to ICH guidelines at 40 ±20 °C and 75 ±5% RH for a period of 90 days.

Keywords: *Perindopril Erbumine, Hypertension, Matrix carriers, Stability studies.*

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INTRODUCTION:

Although various novel and advanced drug delivery systems have been introduced for therapeutic use, the popularity of oral dosage forms, particularly tablets have not been eclipsed, because tablets still have numerous advantages, besides others an economical production [1]. However, one important drawback of tablets as a dosage form is the need to swallow. Dysphasia or general difficulties in swallowing of tablets may be a problem for geriatric, paediatric, or travelling patients, if the latter do not have access to water [2]. Dysphasia is also pertinent with the number of medical conditions including strokes, Parkinson's disease, AIDS, thyroidectomy, head and neck radiation therapy and other neurological disorders including cerebral palsy hence resulting in higher incidence of non-compliance and ineffective therapy. Thus, the orally disintegrating drug delivery system (DDS) is fast dissolving / dispersing, and dissolves in the patient's mouth within a matter of seconds without need of water or chewing. It may therefore be the best solution for patient suffering from dysphasia [3,4].

Perindopril ter-butyl amine belongs to a group called Angiotensin Converting Enzyme (ACE) inhibitors [5]. Inhibition of ACE results in decreased plasma Angiotensin II, leading to decreased vasoconstriction, increased plasma rennin activity and decreased aldosterone secretion. The overall effect of this is a drop in blood pressure and a decrease in the workload of the heart. Perindopril tert-butyl amine is a pro-drug that is hydrolyzed by esterases to the active metabolite Perindoprilat. Perindopril is rapidly absorbed, reaching peak plasma concentration about 1 hour after a single oral dose. Perindoprilat reaches peak plasma concentrations in 2 to 6 hours [6]. The bioavailability of Perindopril is about 70%. The presence of food does not affect the rate and extent of absorption of Perindopril; however, food reduces the conversion of Perindopril to Perindoprilat. [7]

Therefore, the purpose of the present study was to develop control release matrix tablet of Perindopril Erbumine by direct compression.

MATERIALS AND METHODS:

Materials:

Perindopril Erbumine was obtained from Aurobindo Pharma Limited, Hyd. Xanthan gum, HPMCK100M was obtained from Sigma Aldrich. Micro Crystalline Cellulose, Poly Vinyl Pyrrolidone was obtained from S.D. Fine chemicals limited, Mumbai.

Methods

Pre-Formulation Studies

Solubility studies

The drug's solubility was quantified by making a saturated solution of it in a predetermined capacity of various solvents. After that, these were kept for 24 hours while being periodically shaken [8].

Melting point

The capillary method was used to regulate the melting point of perindopril erbumine and compared to standards.

Loss on drying

The sample was placed in a bottle with a lid on top. It was possible to weigh the filled bottle precisely. Through gentle, side-to-side shaking, the sample was equally dispersed to a deepness of approximately 5 mm. In the drying chamber, the laden bottle was put. The sample was desiccated at the predetermined temperature until it attained a consistent weight [9]. The bottle was quickly closed when the compartment was unlocked, brought to room temperature in desiccators, and then weighed.

$$\% LOD = \frac{w_2 - w_3}{w_2 - w_1} X100$$

Were,

W_1 = Mass of unfilled weighed bottle

W_2 = Mass of balanced bottle + sample

W_3 = Mass of weighed bottle + desiccated sample

Pre-Compression charcateristics

Angle of repose:

The surface of the funnel was left open so that the precisely weighed blend could travel easily through. The powder cone's tallness and width were measured, and the following equation was used to determine the angle of repose [10].

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

Bulk density:

A predetermined amount was moved to a measure and mechanically tapped until a constant volume was obtained, either manually or by some tapping apparatus. The vacuum space between the powder particles and the true volume of the powder are both included in this volume, which is called the bulk volume (v). There are air voids between the particles of a particular powder peak [12]. It is also known as void volume or void space.

Bulk Density = Bulk Mass / Bulk Volume

Tapped density:
It is the amount of the powder's whole mass to its tapped Density.

Tapped Density =m/V_f

Where, m = preliminary mass of solid in gm,

Vf = volume of solid after tapping.

Compressibility
The Hausner's ratio and compressibility index are indicators of a powder's susceptibility to be crushed.

Compressibility index: $=\frac{V_0-V_f}{V_0}100$

Where,

V_f = ultimate tapped capacity,

V_0 = preliminary untapped capacity.

Hausner's ratio = $\frac{V_0}{Vf}$

Drug-Excipient Compatability Studies by FTIR
A dry air purge was used to operate the device, scans were taken across the area 4000-400 cm-1. The scans were examined for the existence of the main drug peaks as a result of interactions with polymers [13].

Preparation of controlled release matrix tablets by direct compression technique
The required amount of medicine was placed and blended with the aid of a pestle after the precisely balanced amounts of polymers and MCC in a mortar and m blended geometrically. Magnesium stearate and talc were then combined for roughly three minutes, lubricating the powder mixture and compressed into a tablet with 6 mm round-shaped, flat punch sets [14].

Table 1. Construction of Perindopril Erbumine controlled release matrix tablet

Constituents (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Perindopril Erbumine	5	5	5	5	5	5	5	5	5
HPMC K100M	25	30	35	-	-	-	10	18	25
Xanthan gum	-	-	-	25	30	35	15	12	10
PVP	5	5	5	5	5	5	5	5	5
MCC	55	50	45	55	50	45	55	50	45
Talc	5	5	5	5	5	5	5	5	5
Mg. stearate	5	5	5	5	5	5	5	5	5
Total wt (mg)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Evaluation:
Tablet thickness and diameter
The consistency of tablet size was mostly dependent on the thickness and width of the tablets. Vernier callipers were used to measure the diameter and thickness [15].
Hardness
Six tablets were chosen at arbitrary for this study, and the solidity of each tablet was assessed using a Monsanto hardness tester.
Friability
The test was conducted in order to quickly measure the rigidity and constancy in Roche Friabilator. Twenty pills were placed in a revolving equipment drum after being initially weighed (Wo). They are then forced to drop from an elevation of 6 inches [16]. The tablets were once more weighed (w) following the completion of 100 revolutions, or 25 rpm for 4 minutes.

Weight variation
Randomly select a sample, weighing 20 pills, and calculating the mean weight. The average weight is not diverged by > 2 distinct weights, and no one are strayed by more than twice the proportion.
Content uniformity
In order to conduct this test, 20 powdered, weighed pills were chosen at random. 0.1 N HCL is dissolved in a 100 ml volumetric flask with an amount of crushed tablets equal to 100 mg of perindopril Erbumine [17]. The absorbance was determined at 216 nm and the sample's concentration was noted.

$$\% \text{ Medication content} = \frac{\text{Drug content}}{\text{Label claim}} \times 100$$

***In vitro* dissolution studies**

Utilising the USP type II (paddle) dissolving equipment, research on dissolution were conducted. 50 rpm was the stirring speed. The temperature was kept at 37 ± 0.5 ^{0}C. At determined intermissions, 5 ml samples were taken out, filtered, and substituted with 5 ml of new dissolving medium. When necessary, the collected samples were appropriately diluted with dissolving fluid before being examined at 216 nm by means of a UV spectrophotometer [18].

Release kinetic study [19]

Zero order calculation

$$Q = Q_0 - K_0 t$$

Q is the quantity of medicine residual undissolved at time t,
Q_0 is the quantity of drug undissolved at t = 0
K_0 is the conforming release rate constant.

First order release equation

$$\ln Q = \ln Q_0 - K1t$$

Where
M is the quantity of medication undissolved at time t,
K1 is the corresponding release rate constant.

Higuchi Square Root Law equation

$$Q = K2t0.5$$

Where Q (Q = 100 - M) is the quantity of drug softened at time t and K2 isthe diffusion constant.

The Korsmeyer - peppas equation

$$Mt / M_\infty = K\,tn$$

Where
Mt / M_∞ is the portion of medication released at time t,
K is the Korsmeyer release rate constant and
n - the mechanism of medication release from preparations during diffusion procedure.

Stability procedure

Accelerated storage conditions (40°C±2°C, /75%±5% RH) were used for stability studies. Every month for three months, the samples were examined for weight fluctuation, hardness, friability, drug content, and an in vitro dissolution study [20].

RESULTS AND DISCUSSION:

PRE-FORMULATION STUDIES

Solubility:

Only very slightly soluble in ether, chloroform, solvable in water, methanol, ethanol, acetic acid, and ethyl acetate.

FTIR Studies:

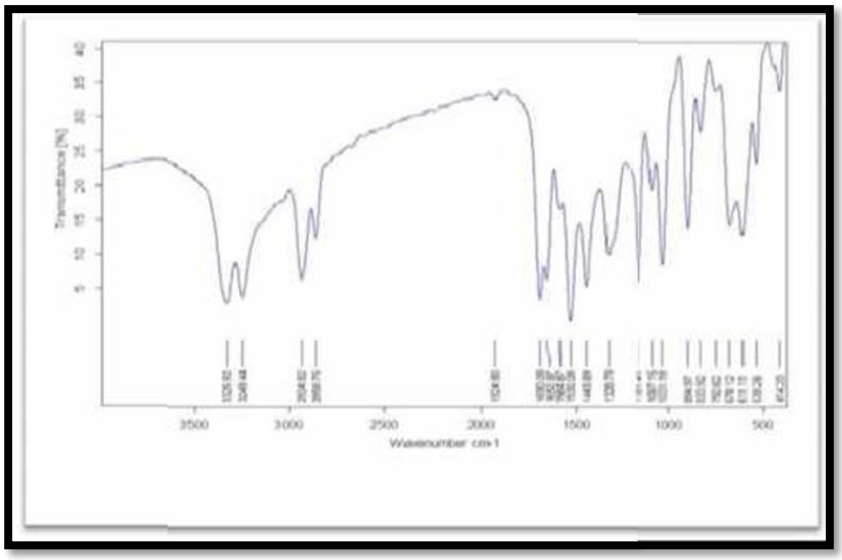

Figure No 1: FTIR spectra of Perindopril Erbumine

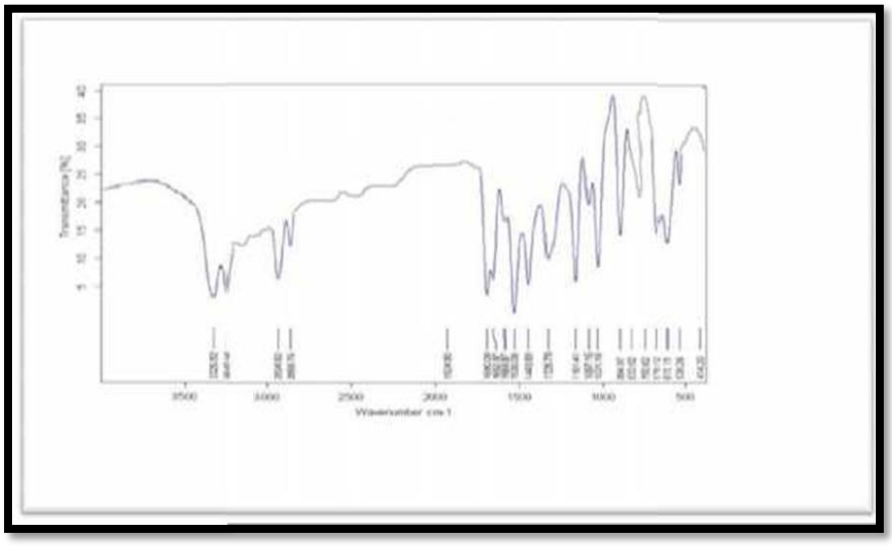

Figure No 2: FTIR spectra of Drug with excipients

Table No 2: FT-IR spectra of various compounds

Functional groups (Stretching)	Pure drug (cm^{-1})	Physical mixture (cm^{-1})
C-N	1150.2	1151.4
C-NH_2	1305.3	1306.4
C=O	1800.6	1800.7
C-CH_3	2983.7	2984.1
N-H	3304.8	3305.6

In optimized formulations, above stretching resulted in the preservation of these peaks as well as the appearance of additional peaks that are related to the excipients utilized in the preparation. This proved there was no drug-excipient interaction.

Assessment of pre compression parameters

Table No 3: Powder representation of formulation

Formulation code	Angle of repose (± SD)	BD (gm/ml) (± SD)	TD (gm/ml) (± SD)	Carr's index (%)(± SD)	Hausner's ratio (± SD)
F-1	22.98±0.06	0.408±0.03	0.468±0.05	15.04±0.06	1.22±0.08
F-2	21.08±0.03	0.398±0.05	0.492±0.06	15.0±0.09	1.22±0.06
F-3	21.0±0.06	0.406±0.08	0.475±0.03	14.01±0.05	1.18±0.03
F-4	22.96±0.02	0.389±0.06	0.488±0.01	14.68±0.06	1.22±0.08
F-5	20.02±0.11	0.401±0.05	0.478±0.02	12.98±0.05	1.2±0.05
F-6	22.12±0.05	0.404±0.03	0.492±0.05	14.3±0.05	1.2±0.06
F-7	22.04±0.09	0.410±0.05	0.468±0.03	13.48±0.05	1.09±0.06
F-8	22.12±0.08	0.399±0.06	0.488±0.05	13.02±0.06	1.2±0.02
F-9	23.98±0.05	0.409±0.03	0.489±0.05	15.10±0.08	1.19±0.05

(n=3±S.D)

The angle of repose for the powder blend of all the formed batches was discovered to be between 19° and 24°, indicating excellent flow qualities. For all batches, Hausner's ratio was < 1.20, signifying good flow characteristics.

Evaluation of Perindopril Erbumine tablets

Table No 4: Post-Compression characteristics

Formulation code	Weight difference (mg)	Hardness (kg/cm^2)	Thickness(mm)	Drug content (mg)	Friability %
F1	100.5±1.18	4.88±0.18	3.010±0.03	94.05±0.20	0.29
F2	100.8±1.58	4.21±0.28	3.008±0.03	97.98±0.32	0.38
F3	100.5±1.48	3.68±0.09	3.006±0.03	90.15±0.38	0.15
F4	100.4±1.32	3.88±0.18	3.008±0.03	98.02±0.25	0.39
F5	100.7±1.21	4.08±0.21	3.009±0.04	94.06±0.18	0.58
F6	100.1±1.35	4.3±0.35	3.006±0.05	94.98±0.22	0.59
F7	100.6±1.12	4.1±0.3	3.010±0.04	94.805±0.24	0.49
F8	100.7±1.32	3.48±0.08	3.006±0.03	90.12±0.30	0.52
F9	100.4±1.06	4.06±0.21	3.008±0.04	97.90±0.22	0.56

(n=3±S.D)

All of the prepared formulations' physical properties, including hardness, thickness, weight fluctuation, and friability, were examined, and they were all determined to be within pharmacopeial limits.

Invitro drug release study:
The dissolving work of formulations were performed with a pH of 1.2 for two hours and in 6.8 for the remaining 22 hours as the dissolution medium.

Table No 5: Cumulative % medication release of formulations withHPMC K100M (F_1-F_3)

Time(hr)	Cumulative % medicine release		
	F_1	F_2	F_3
0	0.00	0.00	0.00
1	4.88	3.72	3.22
2	7.92	7.02	6.38
4	15.52	14.02	13.05
6	24.22	22.92	19.72
8	36.52	33.82	31.22
10	49.05	47.42	42.36
12	60.38	58.02	52.72
14	74.52	70.42	64.98
16	83.84	79.08	74.54
18	90.20	86.68	82.18
20	96.68	91.24	86.36
22	99.18	94.82	89.58
24	-	97.32	90.72

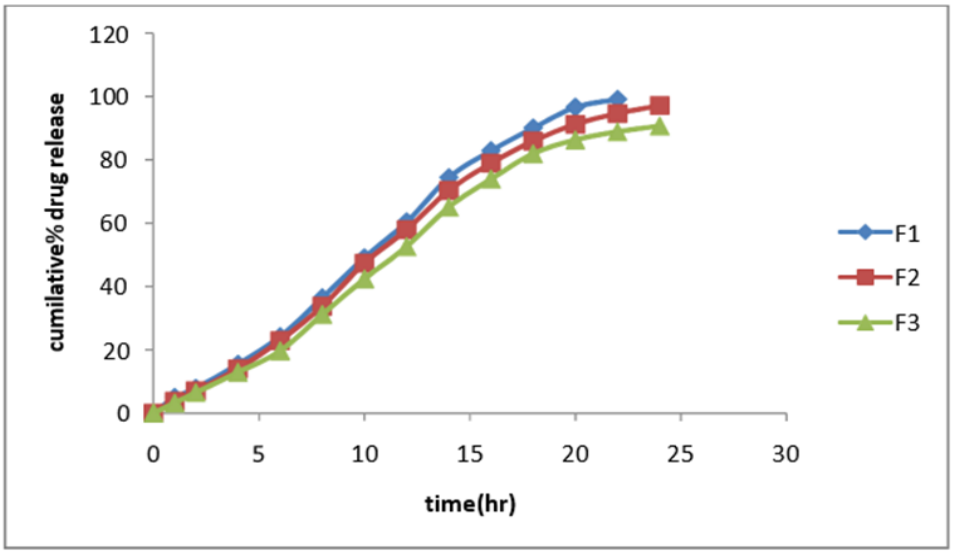

Figure 3: Cumulative % drug release of preparations containingHPMC K100 M
The presence of varying polymer concentrations was the cause of the differences in the medication release profiles of the various formulations.

Table No 6: % drug release of formulations withXanthan gum (F_4-F_6)

Time(hr)	Cumulative % drug release		
	F_4	F_5	F_6
0	0.00	0.00	0.00
1	4.02	3.68	3.42
2	10.28	9.36	8.05
4	19.22	17.42	16.70
6	28.82	27.70	25.36
8	39.42	36.88	34.32
10	51.60	47.36	43.92
12	63.84	58.82	54.48
14	75.62	70.58	65.36
16	84.72	80.66	75.22
18	92.32	87.65	82.32
20	97.25	92.68	87.32
22	99.86	96.35	90.82
24	-	98.22	92.70

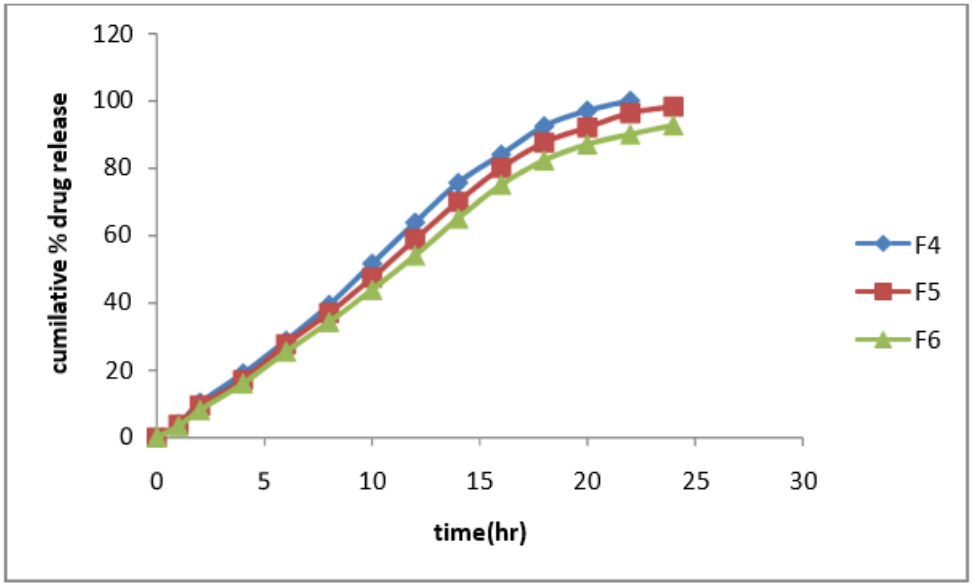

Figure No 4: Cumulative % medication release of preparations comprisingXanthan gum (F_4-F_6)

In a 24-hour period, 99.98%, 98.15%, and 92.64% of the medication was released from formulations F4, F5, and F6, respectively. distinct polymer concentrations were present, which caused a variance in the drug release profiles of distinct formulations.

Table No 7: Cumulative Percentage drug release withcombination of polymers (F_7-F_9)

Time(hr)	Cumulative % drug release		
	F_7	F_8	F_9
0	0.00	0.00	0.00
1	4.48	3.78	3.56
2	9.02	7.85	7.02
4	18.35	17.24	16.96
6	26.56	23.52	24.25
8	39.42	36.48	35.18
10	50.36	46.24	44.72
12	62.32	55.52	52.36
14	74.35	68.25	65.96
16	89.45	84.72	80.08
18	93.72	90.30	86.04
20	99.99	94.85	89.48
22	-	99.82	93.52
24	-	-	99.82

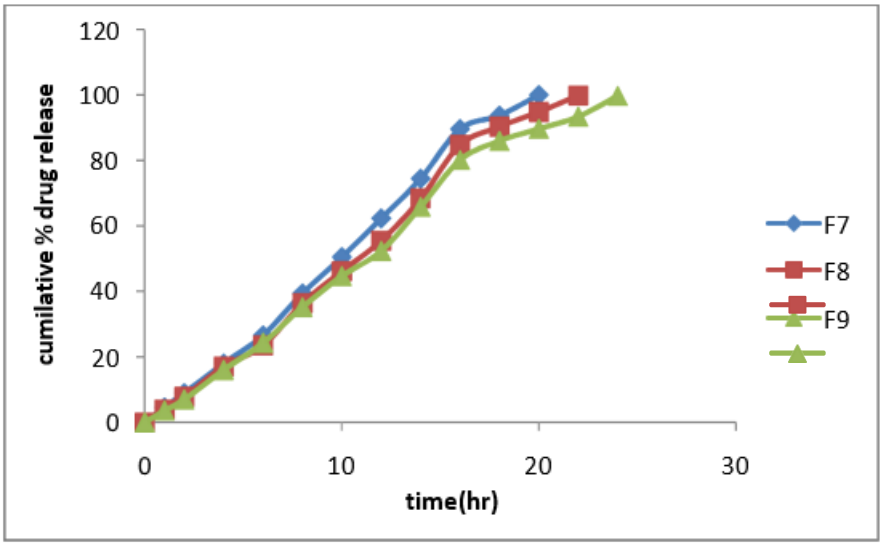

Figure 5: % Drug release of preparations comprising combination of polymers (F_6-F_9)

In a 24-hour period, 99.98%, 99.79%, and 99.74% of the medication was released from formulations F7, F8, and F9, respectively. These are the polymer-based formulations that have been created. In terms of drug release over 24 hours, the formulations F2, F3, F5, F6, and F9 showed respective percentages of 97.27%, 90.81%, 98.15%, 92.64%, and 99.74%.

Formulation F9, which regulated the medication release for the essential period (24 hours), was regarded as the finest formulation among all formulations.

Release kinetics:

Table No 8: Kinetics of the optimum formulation

Time(hr)	√T	Log T	% medication dissolved	% medicine un dissolved	Log % drug dissolved	Log Cumulative % drug Undissolved
0	0.00	0.00	0.00	100	0.00	2.00
1	1	0.00	3.58	95.96	0.562	1.96
2	1.414	0.301	7.02	92.92	0.838	1.95
4	2.0	0.60	19.62	80.35	1.32	1.88
6	2.44	0.778	25.42	74.72	1.36	1.91
8	2.8	0.90	35.15	64.8	1.48	1.78
10	3.16	1.0	44.72	55.28	1.58	1.74
12	3.46	1.079	52.35	47.62	1.74	1.72
14	3.74	1.146	65.90	34.24	1.78	1.48
16	4.0	1.20	80.25	19.9	1.85	1.32
18	4.2	1.255	86.04	13.95	1.88	1.20
20	4.47	1.30	89.75	10.25	1.88	1.12
22	4.69	1.34	93.35	6.62	1.95	0.84
24	4.89	1.38	99.82	0.24	1.98	-0.575

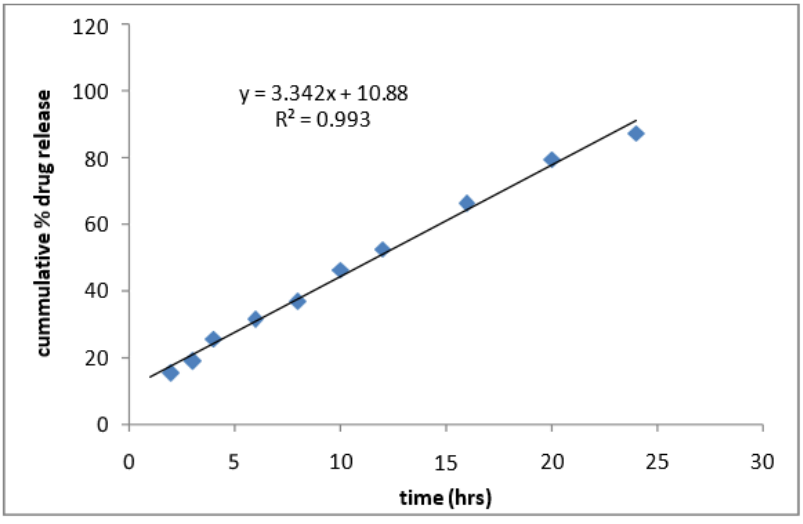

Figure No 6: Zero order design of F_9

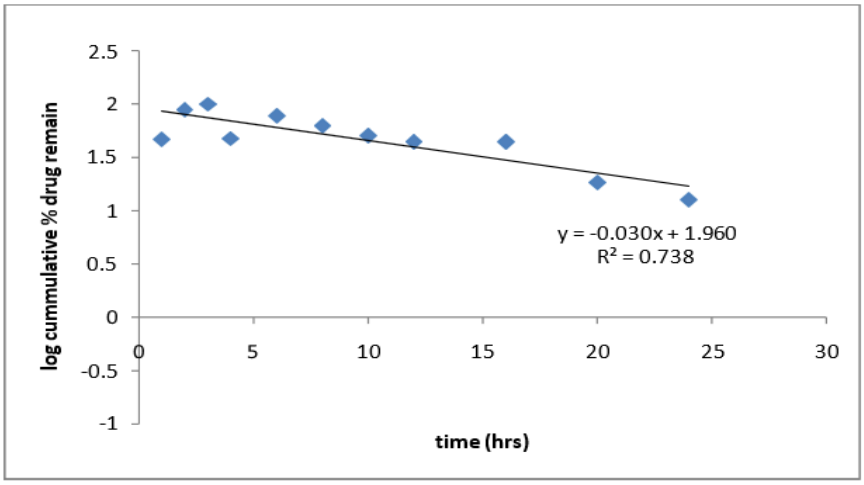

Figure No 7: First order plot of F9

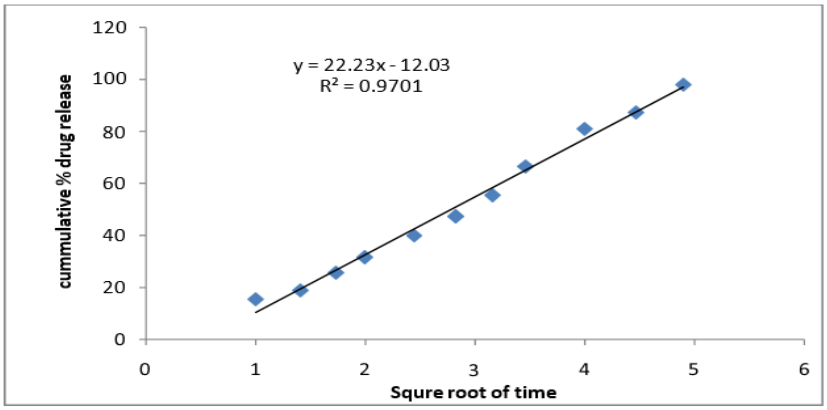

Figure No 8: Higuchi Plot for F9

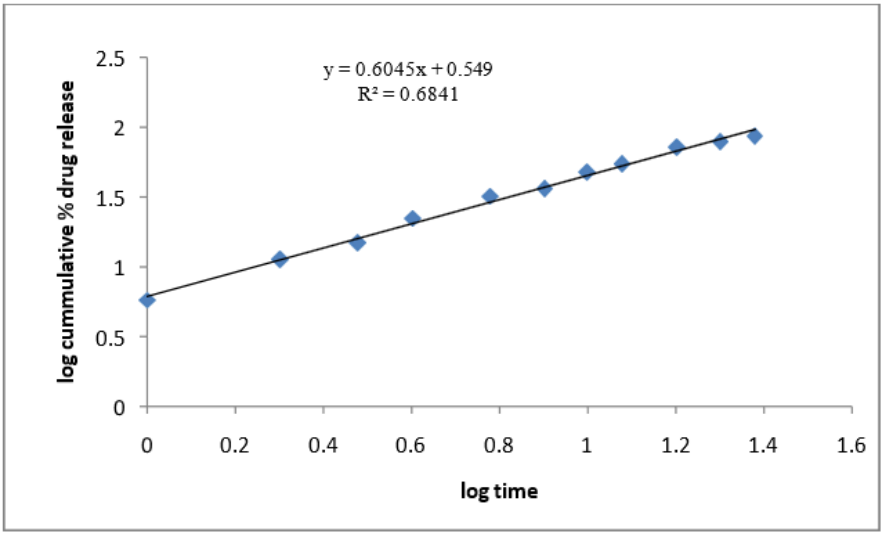

Figure No 9: Korsemeyer Peppas Model of F9

The F9 was selected as the optimal formulation since it is best fit for the Korsemeyer-Peppas (0.6841) and zero order (0.993) models.

Accelerated stability studies:

Stability tests on formulation F9 were done in the current study. The tablets were examined for their characteristics three months of storage at 40 ±20 °C and 75 ±5% RH.

Table No 10: Improved perindopril erbumine controlled release matrixtablet

	Drug content (%)	Hardness (kg/cm^2)	Friability (%)
1st Month	99.65±0.22	4.0±0.108	0.56
2nd Month	99.58±0.08	4.0±0.22	0.59
3rd Month	99.56±0.09	4.0±0.08	0.62

Table No 11: *In Vitro* Dissolution Studies

Time in hours	Cumulative % medication release			
	Initial	1st month	2nd month	3rd month
0	0.00	0.00	0.00	0.00
1	4.58	4.62	3.48	3.52
2	7.02	6.88	6.85	6.92
4	18.65	19.65	19.5	19.52
6	23.16	23.20	24.18	24.18
8	36.18	34.08	36.30	35.09
10	43.70	43.55	45.65	44.48
12	54.36	51.32	53.40	52.24
14	67.75	65.75	65.64	66.56
16	81.12	81.08	80.85	79.96
18	86.02	86.12	86.04	86.04
20	90.15	90.52	90.45	90.06
22	94.12	94.06	93.95	94.05
24	99.55	99.85	99.55	99.54

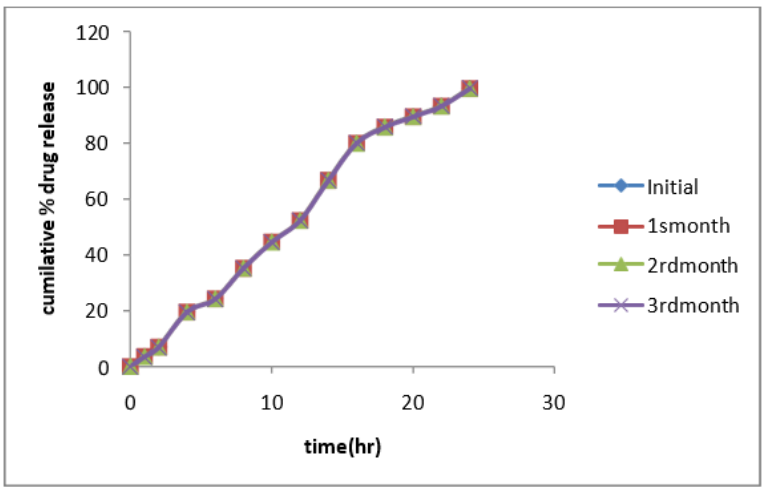

Figure 10: Stability plot of F_9

Three months of stability testing were conducted and after storage did not reveal any appreciable changes. The formulation F9 was stable since accelerated stability experiments showed little change.

CONCLUSION:

FTIR spectra displayed that nearby was no contact among medication and polymer. The bulk of the batches' physical characteristics, including hardness, weight fluctuation, and friability, met Pharmacopoeia requirements. All tablets had a medication content

between 93% and 100%. All of the formulations performed in vitro dissolving testing in phosphate buffer pH 6.8 and acid buffer pH 1.2. For F9 formulation, a cumulative% drug release of 99.74 was seen. The kinetic study for F9 revealed that the medication release shadows zero order. For three months, the accelerated stability experiments for the F9 formulation were conducted. Data showed that there wasn't much of a difference.

REFERENCES:

1. Rahman Z, Siddiqui A, Khan MA. Orally disintegrating tablet of novel salt of antiepileptic drug: Formulation strategy and evaluation. Eur J Pharm Biopharm 2013;85:1300-9.
2. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential. J Control Release 2009;139:94-107.
3. Badar H, Yasmeen R, Ayeen FQ, Badar J. Method development and validation for the analysis of perindopril erbumine and amlodipine besylate by RP-HPLC in pure and pharmaceutical dosage form. Res J Pharm Technol 2020;13:2163-6.
4. Preis M, Woertz C, Kleinebudde P, Breitkreutz J. Oromucosal film preparations: Classification and characterization methods. Expert Opin Drug Deliv 2013;10:1303-17
5. Borges AF, Silva C, Coelho JF, Simões S. Outlining critical quality attributes (CQAs) as guidance for the development of orodispersible films. Pharm Dev Technol 2017;22:237-45.
6. Sakur AA, Balid B. Direct spectrophotometric determination of perindopril erbumine and enalapril maleate in pure and pharmaceutical dosage forms using bromocresol green. Res J Pharm Technol 2021;14:3276-2.
7. Peterson KL, Jacobs JP, Allender S, Alston LV, Nichols M. Characterising the extent of misreporting of high blood pressure, high cholesterol, and diabetes using the Australian health survey. BMC Public Health 2016;16:695.
8. Purnachandra reddy guntaka, Sriram N,Formulation And Evaluation Of Sustained Release Matrix Tablets Of Glimipride Using Natural Polymers Tamarind Seed Mucilage And Guar Gum Journal of Pharmaceutical Negative results,2013,19(3),5256 – 5267
9. Koland M, Sandeep VP, Charyulu NR. Fast dissolving sublingual films of ondansetron hydrochloride: Effect of additives on in vitro drug release and mucosal permeation. J Young Pharm 2010;2:216-22
10. Upasana K, Rathore KS, Saini S, Meenakshi B. Formulation and evaluation of ketorolac tromethamine using 32 factorial design. Res J Pharm Technol 2020;13:2556-62.
11. Gidwani B, Vyas A, Ahirwar K, Shukla SS, Pandey R, Kaur CD. Factorial design and a practical approach for gastro-retentive drug delivery system. Res J Pharm Technol 2016;9:641-9. 13. Semalty M, Semalty A, Kumar G. Formulation and characterization of mucoadhesive buccal films of glipizide. Indian J Pharm Sci 2008;70:43-8.
12. Shiledar RR, Tagalpallewar AA, Kokare CR. Formulation and in vitro evaluation of xanthan gum-based bilayered mucoadhesive buccal patches of zolmitriptan. Carbohydr Polym 2014;101:1234-42.
13. Yedurkar P, Dhiman MK, Petkar K, Sawant K. Biopolymeric mucoadhesive bilayer patch of pravastatin sodium for buccal delivery and treatment of patients with atherosclerosis. Drug Dev Ind Pharm 2013;39:670-80.
14. Kale SS, Bakal RL, Chandewar AV, Sakhare RS. Two wavelength method for estimation of indapamide and perindopril erbumine in combined tablet dosage form. Res J Pharm Technol 2011;4:545-8.
15. Guntaka, Purna Chandra Reddy; Lankalapalli, Srinivas,Design and development of spray dried Telaprevir for improving the dissolution from tablets. International Journal of Pharmaceutical, Chemical & Biological Sciences. 2017, 4(9), 430-438.
16. Jyothirmayi P, Devalarao G, Rao MV. Optimization of pulsatile compression coated floated tablets of tramadol HCL for chronopharmacotherapy of rheumatoid arthritic pain using 23 factorial design. Res J Pharm Technol 2020;13:5823-30.
17. Mounica PS, Kumar TH, Rao YS, Rao KV. Simultaneous spectrophotometric estimation of amlodipine besylate and perindopril erbumine in tablet formulation. Res J Pharm Technol 2019;12:6101-6.
18. Siddiqui MD, Garg G, Sharma PK. A short review on a novel approach in oral fast dissolving drug delivery system and their patents. Adv Biol Res 2011;5: 291-303.
19. Bhupendra RT, Bhushan RR, Nayan AG, Sunil RB, Pranav RT, Pawar SP. A short review on a novel approach in oral fast dissolving drug delivery system. Pharm Sci Monit 2012; 3: 3380-98.
20. Vinod KR, Reddy TR, Sandhya S, Banji D, Reddy BV. Critical review on mucoadhesive drug delivery systems. Hygeia JD Med 2012; 4:1-5.