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Research Article

Formulation and Evaluation of Sustained Release Bilayer Tablets of Ramipril-7.5mg

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ABSTRACT

The objective of this study was to design Ramipril sustain release bi layer tablets containing immediate release layer and sustain release layer. Tablets were prepared by wet granulation technique using various polymers such as Hydroxy propyl methyl cellulose (HPMC K 100), Sod.CMC, Xanthum gum and Guar gum as release rate retardant and tablets were evaluated for hardness, friability, weight variation, thickness and drug content uniformity. *In vitro* release studies were performed using USP type II apparatus (paddle method) in 900 mL of pH 6.8 at 50 rpm for 8 hours and compared with USP specification. *In vitro* release studies revealed that the release rate decreased with increase of polymer loading. The maximum drug release was found to be 98.9% over a period of 8 hours in Xanthum gum based tablets (F11). Drug release was analyzed using zero-order, first order, Higuchi and Korsmeyer-Peppas equations to explore and explain the mechanism of drug release from the bi layer matrix tablets. Mathematical analysis of the release kinetics indicated that release from the matrix tablets followed diffusion. So the bi-layer tablets could be a potential dosage form for delivering Ramipril.

INTRODUCTION

Oral route is the most commonly employed route of drug administration. Although different route of administration are used for the delivery of drugs, oral route remain the preferred mode. The popularity of the oral route is attributed patient acceptance, ease of administration, accurate dosing, cost effective manufacturing method and generally improved shelf-life of the product. Even for sustained release systems the oral route of administration has been investigated the most, because of flexibility in dosage forms design that the oral route offers [1]. With many drugs, the basic goal of therapy is to achieve a steady-state blood level or tissue level that is therapeutically effective and non toxic for an extended period of time [2]. To achieve better therapeutic action various types of drug delivery systems are available, out of which sustained release systems are gaining much importance because of their wide advantages over others like ease of administration, convenience and noninvasiveness.

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Tablets are solid unit dosage forms containing medicament or mixture of Medicaments and excipients compressed or molded into solid cylindrical shape having either flat or convex surfaces.

Sustained Release Drug Delivery Systems [3- 6]

Sustained release drug delivery systems can be defined as any dosage form that prolongs the therapeutic activity of the drug by continuously releasing medication over an extended period of time. In absence of suitable clinical evidence of this therapeutic effect it can be defined as any dosage forms that give prolongation of the drug levels in the blood. The major advantage of this category is that, in addition to the convenience of reduced frequency administration, it provides levels that are devoid of the peak and valley effect. By providing smooth plasma level of drug over longer period of time, sustained -release drug delivery technology can minimize side effects, improve efficacy and by enabling once daily dosing- maximize patient compliance. The aim of this investigation is to Formulate and Evaluate the Sustain release Bilayer tablets of Ramipril for treatment of hypertension. The

concept of Bilayer tablet technology is utilized to develop sustains release and immediate formulation for a single drug or combination of drugs. Bilayer tablets are preferred in some cases because they maintain uniform drug levels, reduce dose, side effects, increase the safety margin for high-potency drugs and thus offer better patient compliance.

The Main Objective

1. To formulate and evaluate the Bilayered tablets of Ramipril.
2. To carry out the drug - excipients compatibility studies by IR spectral analysis.
3. To carry out the Precompressional parameters for the powder blend of IR layer of Bilayered tablets.
4. To carry out the Precompressional and Postcompressional parameters for Bilayered tablets.
5. To study the release kinetics and transport mechanism of drug from the formulations.

MATERIALS [6]

All the materials are listed in Table: 1 and 2.

Table 1: List of Ingredients

S. No	Ingredients	Supplier
1	Ramipril	Hetero labs,Hyderabad.
2	HPMC K100	Oxford laboratory reagent, Mumbai.
3	Sod.CMC	
4	Xanthum gum	Loba Chemicals, Mumbai.
5	Guar gum	
6	Ethyl cellulose	Shreeji Chemicals, Mumbai.
7	PEG-4000	SDFine Chemicals limited, Mumbai.
8	Lactose	
9	Talc	
10	Sodium hydroxide pellets	
11	Potassium di hydrogen phosphate	
12	Methanol	Merk specialities Pvt limited, Mumbai

EXPERIMENTAL SESSION [7-20]

Drug –Excipient Compatibility Studies

A Compatibility study focuses on a binary mixture of drug substance and some selected excipients in a fixed ratio with or without added moisture. The mixture stored at elevated temperatures as 40oc 75%RH, 55OC 60%RH in capped vials. The result of the interaction between the active drug and excipients is determined by FTIR.

Table 2: List of Equipments

S.NO	Equipments	Model And Manufacturer
1	Digital balance	Infrainstrumentspvt.LTD, Chennai.
2	Tablet dissolution test apparatus	Labindia DS 8000 Mumbai.
3	UV-Visible spectrophotometer	Elico Ltd., SL 150, Hyderabad
4	Compression machine.	Cadmach Machinery , Kolkata
5	Roche Friabilator	Campbell Electronics, Mumbai.
6	Monsanto Hardness Tester	Cadmach, Ahmedabad, India.
7	Disintegration apparatus	ThermonicCampbellelectronics,
8	Digital pH meter	Digisum Electronics, Hyderabad.

Preparation of Bilayer Tablets

In this present investigation Bilayered tablets of Ramipril were formulated by both Direct Compression and Wet Granulation Method using different polymers viz. HPMC Sod.CMC, Xanthum gum, and guar gum.

Formulation of Immediate Release Layer

Direct Compression Method

Immediate Release Layer of Ramipril was prepared by Direct Compression method. Lactose, Polyethyleneglycol-4000 and Session ingredient were mixed homogenously. Talc was added and mixed thoroughly before compression. The Final weight of IR layer was fixed to 28 mg.

Formulation of Sustained Release Layer

Wet Granulation Method

Ramipril and excipients: Lactose, HPMC K100, Sod.CMC, Xanthum gum, Guar gum were sifted through sieve no. 40, blended uniformly and granulated with PEG-4000 using water as granulating vehicle. The wet mass was first passed through sieve no #12 and the granules were dried in hot air oven at 50oC.The granules were passed through sieve no #16 . Talc was added and mixed thoroughly before compression of granules. Final weight of SR layer was fixed to 70 mg. Ethyl cellulose (2 mg) was added between two layers.

Preformulation Studies

Table 3: Compatibility studies of Ramipril with different excipients

Ingredients	ratio	Initial Colour	After one week	After two weeks	After three weeks	After four weeks
			40 ^{0}C 75%RH	40 ^{0}C 75%RH	40 ^{0}C 75%RH	40 ^{0}C 75%RH
Ramipril+xanthum gum	1:1	Cream or white	Cream or white	Cream or white	Cream or white	Cream or white
Ramipril+HPMCK100	1:1	White powder	White powder	White powder	White Powder	White powder
Ramipril+Sod.cmc	1:1	White powder	White powder	White powder	White Powder	White powder
Ramipril+Guar gum	1:1	White powder	White powder	White powder	White Powder	White powder
Ramipril+PEG- 4000	1:1	White powder	White powder	White powder	White Powder	White powder
Ramipril+Lactose	1:1	White powder	White powder	White powder	White Powder	White powder
Ramipril+Talc	1:1	White powder	White powder	White powder	White Powder	White powder
Ramipril+xanthum gum	1:1	Cream or white	Cream or white	Cream or white	Cream or White	Cream or white
Ramipril+HPMCK100	1:1	White powder	White powder	White powder	White Powder	White powder
Ramipril+Sod.cmc	1:1	White powder	White powder	White powder	White Powder	White powder

Table 4: Composition for SR layer of Bilayered Tablets prepared by Wet Granulation technique

S.No	Ingredients (mg/tab)	Formulation of different batches										
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
1	**Ramipril**	5	5	5	5	5	5	5	5	5	5	5
2	**HPMC K100**	30	-	-	-	40	-	-	-	50	-	-
3	**Sod.CMC**	-	30	-	-	-	40	-	-	-	50	-
4	**Xanthum gum**	-	-	30	-	-	-	40	-	-	-	50
5	**Guar gum**	-	-	-	30	-	-	-	40	-	-	-
6	**Talc**	1	1	1	1	1	1	1	1	1	1	1
7	**PEG-4000**	14	14	14	14	14	14	14	14	14	14	14
8	**Lactose**	20	20	20	20	10	10	10	10	-	-	-
9	**Water**	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
TOTAL WEIGHT		**70**										

Table 5: Direct Compression

S.No	Ingredients (mg/tab)	Formulation
1	Ramipril	2.5
2	Lactose	8.5
3	Talc	1
4	PEG-4000	16
	TOTAL WEIGHT	28
	Ethyl cellulose	2

Compression of Bilayer Tablets

The bilayer tablet compression was made using 6mm punch in a l6 station rotary tablet machine. In this, sustained release Ramipril granules (70 mg) were introduced first in to the die cavity and a slight precompression was made so that the layer was uniformly distributed. Over this precompressed layer Ethyl cellulose (2 mg) was added for separation of two layers, after that immediate release layer of Ramipril (28 mg) were added and a final compression was made .After final compression, total weight of bilayer tablet was 100mg.Repoeted in table no:-4,5

Evaluation of Bilayer Tablets [21-25]

Weight variation
Hardness
Thickness
Friability
Drug content uniformity
Disintegration test
In vitro dissolution studies

Weight Variation Test

Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation was allowed in

the weight of a tablet according to U.S.pharmacopiea. The following percentage deviation in weight variation was allowed. Standard values are listed in Table no:-6

$$\% \text{ Weight Variation} = \frac{\text{Average weight - Individual weight}}{\text{Average weight Hardness test}} \times 100$$

Table 6: Standard Values of Weight Variation Test

Average weight of tablet	Percentage deviation
130 mg or less	10
>130 mg and < 324 mg	7.5
324 mg or more	5

Table 7: Mechanism of Drug Release

Diffusion exponent (n)	Overall solute diffusion mechanism
0.45	Fickian diffusion
0.45 < n < 0.89	Anomalous (non-fickian) diffusion
0.89	Case-II transport
n > 0.89	Super case-II transport

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2.Five tablets were randomly picked and hardness of the tablets was determined.

Limits for Hardness are 4-6kg/sq.cm. All the results are reported in the table no: 9

Thickness

The thickness of the tablets was measured using Calibrated Vernier caliper. It is expressed in mm. five tablets of each formulation were picked randomly and thickness was measured individually.

Standard value- + 5 mm

All the results are reported in the table no: 9

Friability

The friability of tablets was determined by using Roche friabilator .It is expressed in percentage (%).Twenty tablets are initially weighed (w_i) and transferred into friabilator. The Friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets are again (w_f).The % friability was then calculated by-

$$F = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

% Friability of tablets less than 1% is considered acceptable.

All the results are repoted in the table no: 9

Drug Content

Equivalent to 10mg of Ramipril was accurately weighed from powdered Bilayered tablets and it was dissolved in methanol and distilled water respectively to form a clear solution. Later it was made up to volume with methanol and distilled water respectively.

One ml of the sample was withdrawn, suitably diluted with pH 6.8 phosphate buffers respectively and analyzed spectrophotometrically at 210 nm respectively.

All the results are reported in the table no: 9

Disintegration Test

The disintegration test was carried out as per pharmacopoeia procedure. One tablet was placed in each of the six tubes of the basket and the disc was added to each tube. The test was carried out by using water as medium. The temperature was maintained at 37 °C + 2°C.The apparatus was operated and disintegration time was noted.

All the results are reported in the table no: 9

In vitro Dissolution Studies

An *in vitro* drug release study from the prepared Bilayered tablets, was determined using the USP eight station Dissolution Rate Test Apparatus (Labindia DS 8000) employing a paddle stirrer. With 900 ml of phosphate buffer pH 6.8 was used as dissolution media and maintained at 37±0.5oC at a rotational speed of 50 rpm, for 8 hrs respectively. Test sample (5 ml) was withdrawn at particular time interval and replaced with fresh dissolution media maintained at the same temperature and the concentration of dissolved drug was determined using UV spectrophotometer at λmax 210 nm.

All the results are reported in the table no: 10

Drug Release Kinetics

To analyse the mechanism of the drug release rate kinetics of the dosage form, the data were plotted as:

Zero order release rate kinetics:-

To study the Zero order release kinetics the release rate data were fitted to the following equation.

$$\mathbf{F = K\,t}$$

Where, 'F' is the fraction of drug release,

'K' is the release rate constant, and't' is the release time.

When the data is plotted as Cumulative percent drug released versus time, if the plot is linear

then the data obeys Zero order release kinetics, The results are given in table. with slope equal to K.

Table 8: Compatibility Studies of Ramipril with Different Excipients for One Month

Ingredients	ratio	Initial Colour	After one week	After two weeks	After three weeks	After four weeks
			40 ^{0}C 75%RH	40 ^{0}C 75%RH	40 ^{0}C 75%RH	40 ^{0}C 75%RH
Ramipril+xanthum gum	1:1	Cream or white	No change	No change	No change	No change
Ramipril+HPMCK100	1:1	White powder	No change	No change	No change	No change
Ramipril+Sod.cmc	1:1	White powder	No change	No change	No change	No change
Ramipril+Guar gum	1:1	White powder	No change	No change	No change	No change
Ramipril+PEG- 4000	1:1	White powder	No change	No change	No change	No change
Ramipril+Lactose	1:1	White powder	No change	No change	No change	No change
Ramipril+Talc	1:1	White powder	No change	No change	No change	No change
Ramipril+xanthum gum	1:1	Cream or white	No change	No change	No change	No change
Ramipril+HPMCK100	1:1	White powder	No change	No change	No change	No change
Ramipril+Sod.cmc	1:1	White powder	No change	No change	No change	No change

The above data will explains that there is no any type of drug –Excipient incompatibility.

Table 9: Evaluation of Bilayer Tablets of Ramipril

Formulation code	Wt. variation (mg)	Thickness (mm)	Hardness kg/cm2	% Friability	Drug Content %	*In vitro* disintegration time (mins)
F1	100.75±1.44	2.23±0.05	4.29±0.05	0.23±0.05	99.45±0.21	3 ± 0.2
F2	100.70±1.38	2.25±0.05	4.33±0.05	0.21±0.06	98.15±0.28	5 ± 0.3
F3	100.60±1.35	2.28±0.03	4.25±0.05	0.20±0.05	101.23±0.25	5.5 ± 0.5
F4	100.50±1.43	2.23±0.08	4.33±0.05	0.17±0.04	100.57±0.15	4.5 ± 0.2
F5	99.80.±1.43	2.23±0.06	4.33±0.05	0.19±0.03	99.56±0.52	3.5 ± 0.3
F6	100.70±1.49	2.34±0.03	4.31±0.05	0.20±0.08	101.62±0.47	5.5±0.4
F7	98.55±1.39	2.25±0.05	4.29±0.05	0.23±0.05	99.34±0.31	6 ± 0.2
F8	99.90±1.41	2.27±0.05	4.33±0.05	0.21±0.06	100.25±0.23	2.5 ± 0.4
F9	100.75±1.44	2.23±0.07	4.33±0.05	0.20±0.05	101.29±1.21	3.5 ± 0.5
F10	99.80±1.43	2.25±0.04	4.25±0.05	0.17±0.04	99.68±0.27	4± 0.2
F11	99.32±1.43	2.25±0.05	4.29±0.05	0.19±0.03	98.15±0.28	5±0.2
F12	100.50±1.43	2.28±0.03	4.31±0.05	0.21±0.06	99.45±0.21	6±0.5

Table 10: Cumulative Percent Drug Release Data for Bilayer Tablet

Time (hrs)	Cumulative % Drug Release											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
0	0	0	0	0	0	0	0	0	0	0	0	0
1	40	42.6	39.3	37.6	39.7	39.3	40.6	41.6	36.6	37.7	34.4	35.2
2	60	62.6	58.6	58.9	50.6	56.6	54.9	60.5	40.4	59.3	41.4	40.1
3	90.6	92.6	83.3	90.4	78.6	78.5	68.8	71.3	68.2	73.3	59.8	60.8
4	98.5	98.9	96.6	98.2	92	91.8	83.7	90.5	82	80	71.3	75.3
5	-	-	99	99.7	96	99.7	91.3	94.9	88.5	85.7	79.6	91.7
6	-	-	99.2	-	99.1	-	96.4	97.2	98.9	99.5	88.8	96.2
7	-	-	-	-	-	-	97.2	98.6	-	-	93.2	99.4
8	-	-	-	-	-	-	-	-	-	-	98.9	-

Table 11: Mathematical Modeling and Drug Release Kinetics of F1-F12 Formulation

Formulation Code	Drug release kinetic Regression values (R)				Release Exponential (n)
	Zero order	First order	Higuchi	Peppas	
F1	0.9582	0.9091	0.9493	0.4991	2.1539
F2	0.9475	0.9123	0.9543	0.4861	2.1380
F3	0.8672	0.9578	0.9574	0.5178	1.6374
F4	0.9093	0.9347	0.9446	0.525	1.8791
F5	0.8962	0.9521	0.9634	0.5213	1.6293
F6	0.9424	0.8127	0.9815	0.5129	1.8316
F7	0.8751	0.9794	0.9852	0.5083	1.4404
F8	0.8436	0.9843	0.9741	0.500	1.4413
F9	0.9426	0.8412	0.9632	0.5432	1.6299
F10	0.8972	0.7508	0.9825	0.5079	1.5870
F11	0.9276	0.8832	0.9891	0.5562	1.3626
F12	0.9423	0.888	0.9741	0.5622	1.5015
F1	0.9582	0.9091	0.9493	0.4991	2.1539
F2	0.9475	0.9123	0.9543	0.4861	2.1380
F3	0.8672	0.9578	0.9574	0.5178	1.6374
F4	0.9093	0.9347	0.9446	0.525	1.8791
F5	0.8962	0.9521	0.9634	0.5213	1.6293
F6	0.9424	0.8127	0.9815	0.5129	1.8316
F7	0.8751	0.9794	0.9852	0.5083	1.4404
F8	0.8436	0.9843	0.9741	0.500	1.4413
F9	0.9426	0.8412	0.9632	0.5432	1.6299

First Order Kinetics

A First order release would be predicated by the following equation.

$$\text{Log C} = \text{Log Co} - \frac{\text{Kt}}{2.303}$$

Where = Amount of drug remained at time't'
Co = initial amount of drug
K = First order rate constant (hr-1)
When the data is plotted as Cumulative percent drug remaining versus time yields a straight line, Indicating that the release follows First order kinetics .The constant 'K' can be obtained by multiplying 2.303 with slope value.

Higuchi Release Model

To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = K\, t^{\frac{1}{2}}$$

Where,'F' is the amount of drug release
'K' is the release rate constant, and
't' is the release time.

When the data is plotted as Cumulative drug released Versus Square root of time, yields a straight line, indicating that the drug was released by diffusion mechanism .The slope is equal to 'K'.

Korsmeyer and peppas release model: - The release rate data were fitted to the following equation.

$$Mt/M_{\infty} = K\, t^{n}$$

Where, Mt / M_{∞} is the fraction of the drug release,
'K' is the release rate constant,
't' is the release time, and
'n' is the diffusional exponent for the drug release that is dependent on the shape of the matrix dosage form. When the data is plotted as Log of drug released Versus log time, yields a straight line with a slope equal to 'n' and the, 'K' can be obtained from Y-intercept.
All the results are reported in the table no: 11

RESULTS AND DISCUSSION

Evaluation of Bilayer Tablets

Bilayer tablets are weight variation, hardness; friability, percent drug content and disintegration time were found to be within the limits.

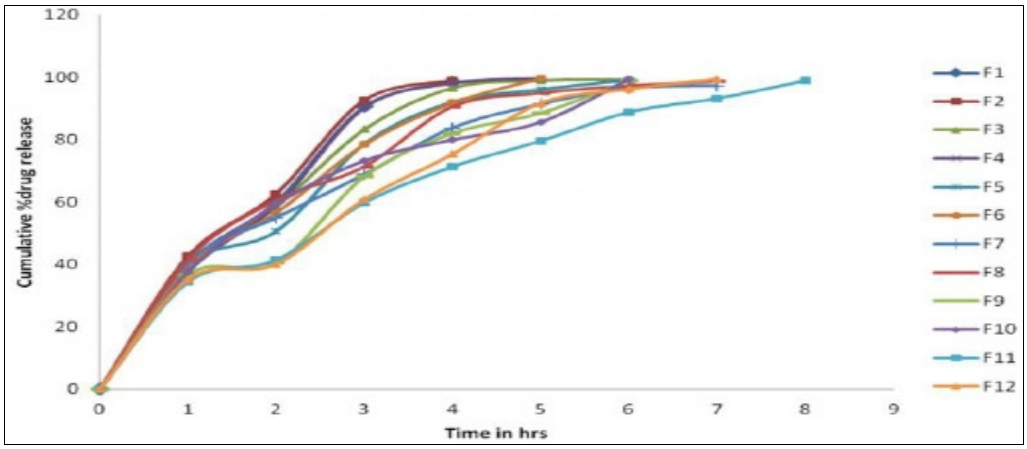

Figure 1: Cumulative Percent Drug Release profiles for formulations F1-F12**.**

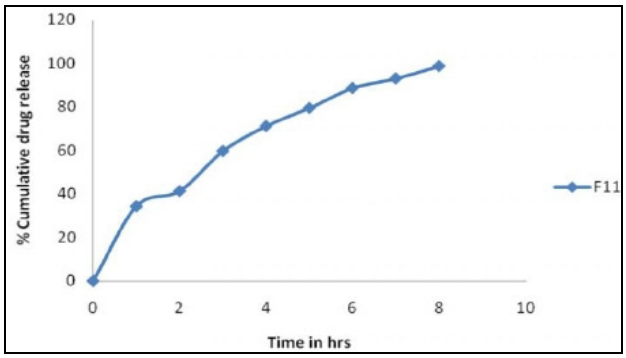

Figure 2: Cumulative Percent Drug Release profiles for optimized batch F11

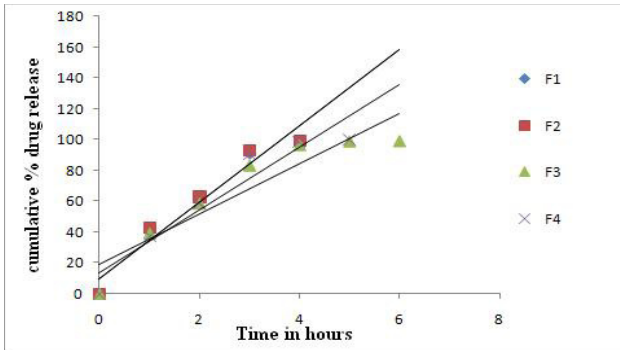

Figure 3: Zero Order Drug Release Kinetics Model of F1-F4.

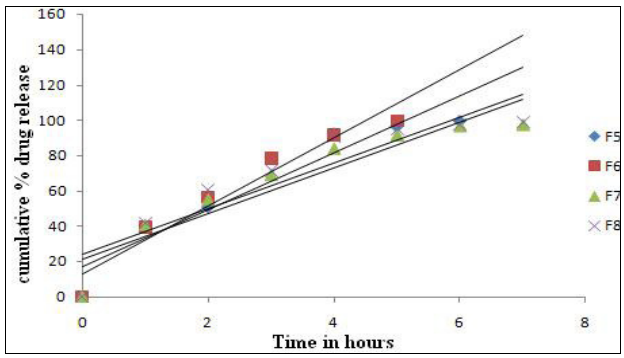

Figure 4: Zero Order Drug Release Kinetics Model of F5-F8

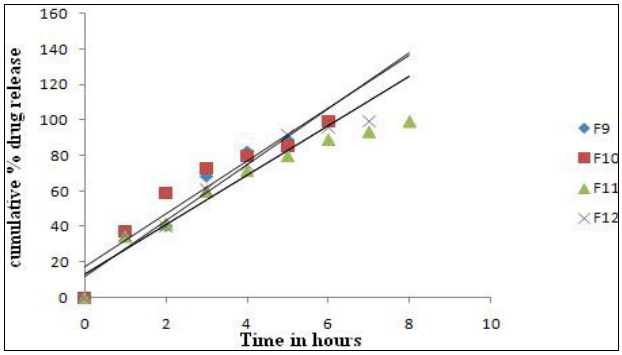

Figure 5: Zero Order Drug Release Kinetics Model of F9-F12

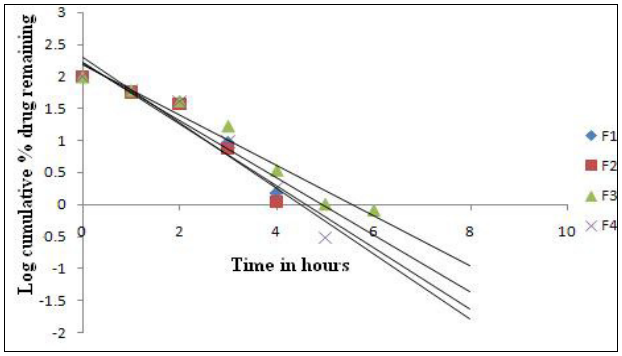

Figure 6: First Order Drug Release Kinetics Model of F1-F4

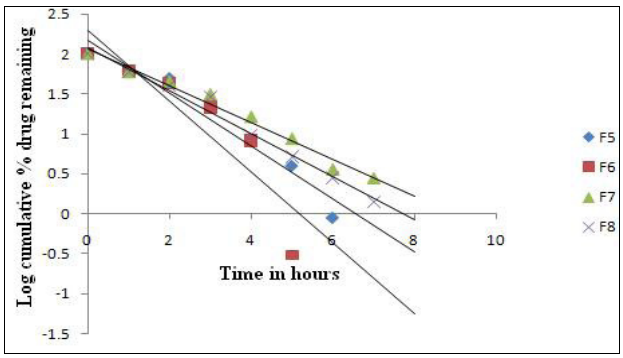

Figure 7: First Order Drug Release Kinetics Model of F5-F8

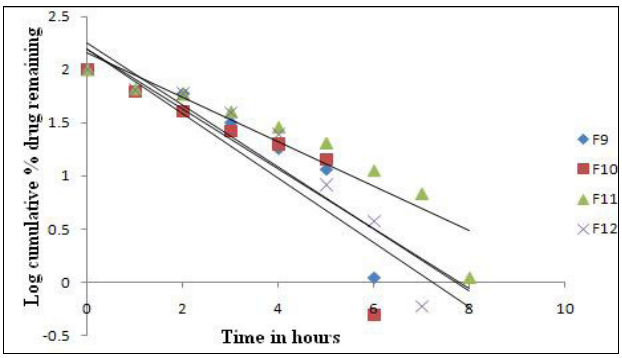

Figure 8: First Order Drug Release Kinetics Model of F9- F12

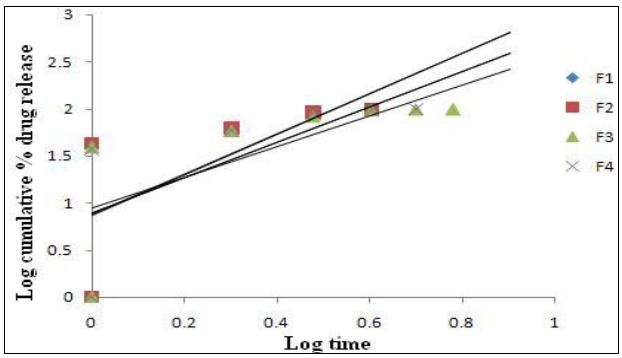

Figure 12: Korsemeyer Peppa's kinetics model of F1-F4.

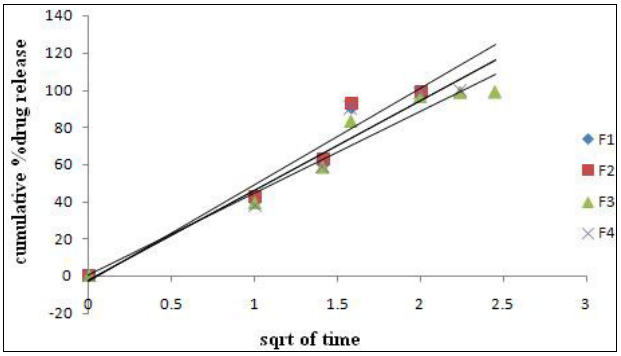

Figure 9: Higuchi's kinetics model of F1-F4.

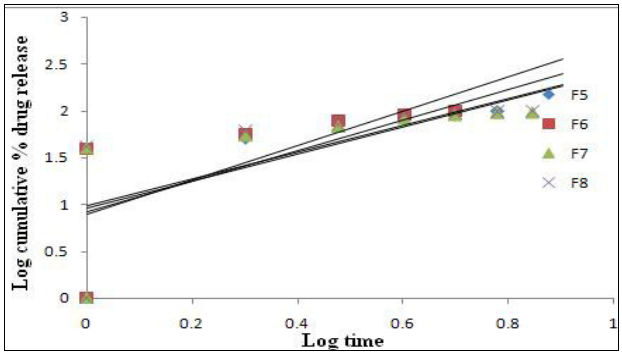

Figure 13: Korsemeyer Peppa's kinetics model of F5-F8.

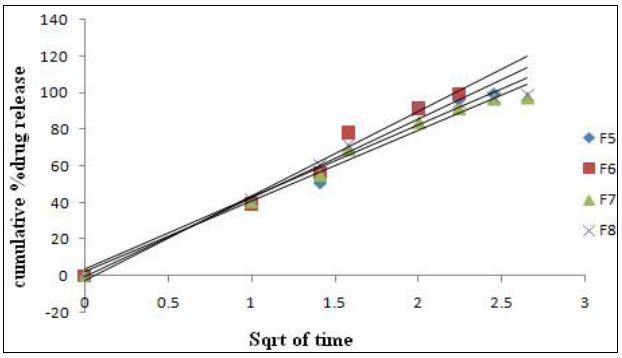

Figure 10: Higuchi's kinetics model of F5-F8

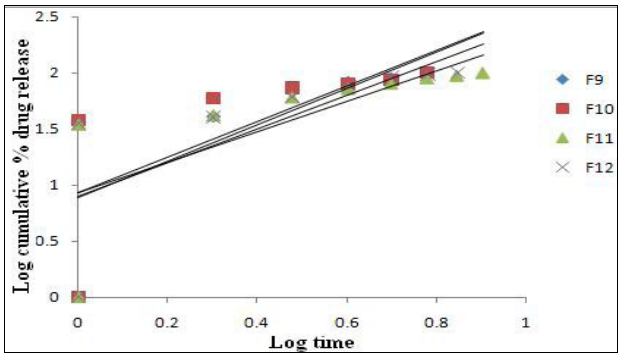

Figure 14: Korsemeyer Peppa's kinetics model of F9-F12

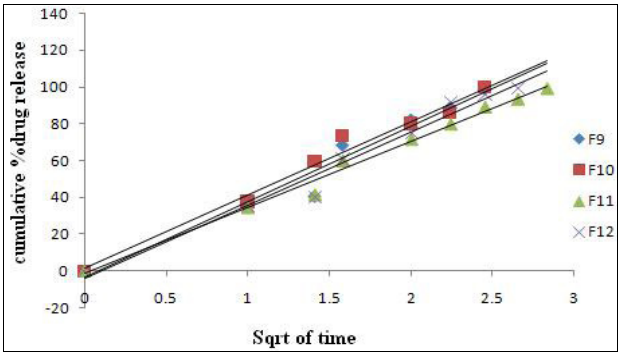

Figure 11: Higuchi's kinetics model of F9-F12.

In vitro Dissolution Studies

The Cumulative percentage drug release from formulations F1, F2 the polymer concentration 30% was 98.5% and 98.9 % at the end of 4 hr. The Cumulative percentage drug release from formulations F3, F4 the polymer concentration 30% was 99.2 % at the end of 6 hr and 99.7% at the end of 5 hr.

F1-F4 failed to sustain the drug release in 8 hrs due to in sufficient polymer concentration in the matrix system. It can be seen that polymer concentration was 30% are insufficient to produce adequate extended release of Ramipril.

The *in vitro* dissolution study also shows that an increase polymer concentration in the formulation resulted in a decreased drug release rate.

Cumulative Percent Drug Release Profiles

The Cumulative percentage drug release from formulations F5, F6 the polymer concentration 40% was 99.1% at the end of 6 hr and 99.7% at the end of 5 hr. The Cumulative percentage drugs release from formulations F7, F8 the polymer concentration 40% was 97.2 % and 98.6 % at the end of 7 hr.

F5-F8 failed to sustain the drug release in 8 hrs due to in sufficient polymer concentration in the matrix system. It can be seen that polymer concentration of 40% are insufficient to produce adequate extended release of Ramipril. The *in vitro* dissolution study also shows that an increase polymer concentration in the formulation resulted in a decreased drug release rate.

The Cumulative percentage drug release from formulations F9, F10 the polymer concentration 50% was 98.9% and 99.5% at the end of 6 hr. The Cumulative percentage drug release from formulations F11, F12 the polymer concentration 50% was 98.9% at the end of 8 hr and 99.4% at the end of 7 hr.

Optimised Batch F11

Optimized formulation F11 which is prepared with Xanthum gum at concentration 50% has show 98.9 % drug release in 8.hrs.It is mainly due to high swelling rate of Xanthum gum. From the *in vitro* results it was observed that increasing the amount of gum in the formulation, resulted in slower rate and decreased amount of drug release from the tablet was found to be more slowly compared to Guar gum based tablets. The slow release is because of the formulation of more thick gel like structure around the matrix, where hydration of individual Xanthum gum particles results in extensive swelling. Thus, maintain the integrity of tablet and retarding further penetration of dissolution medium, prolong the drug release.

Mathematical Modelling and Drug Release Kinetics

The rate and mechanism of release of Ramipril from the prepared bilayer tablets were analyzed by fitting the dissolution data into the zero order, First order, Higuchiand Korsmeyer-Peppas equation.

Formulations (F1, F2, F6, F9, F10, F11, and F12) followed Zero order release mechanism and r2 values were also linear. Formulations (F3, F4, F5, F7, and F8) followed first order release mechanism and r2 values were also linear. Higuchi plots for all these formulations showed good linearity (r2 = 0.9446 to 0.9891) indicating the drug release by diffusion .To explore the release pattern, results of the in-vitro dissolution data were fitted to the Korsmeyer-Peppas equation, which characterizes the transport mechanism. The value releases of release exponent (n) for all formulations were in between 1.36 to 2.15 indicates the super case-II transport.

The value of "n" in Korsmeyer-Peppas equation was found to be >0.89 in all cases (Table no: 11).These values indicated that drug release mechanism followed super case-II transport mechanism in all formulations which is mainly a relaxation release process. Relaxation release is the drug transport mechanism associated with stress and state transition in hydrophilic glassy polymers which swell in water .This process also involves polymer disentanglement and erosion.

CONCLUSION

The present study was carried out to develop Bilayered matrix tablets of Ramipril Immediate release layer by direct compression method and hydrophilic polymers for sustain release layer by wet granulation method. It can be concluded that the optimized batch F11 by adopting biphasic drug release pattern in a single dosage could improve patient compliance and give better disease management.

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