Research Article

Formulation and Evaluation of Bilayer Tablet of Amlodipine and Metoprolol in the Treatment of Hypertension

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ABSTRACT

The current work focuses on the development and evaluation of bilayer tablet of Amlodipine & Metoprolol in the treatment of hypertension. The release of Amlodipine and Metoprolol was controlled by formulating it into a immediate and sustained release layer respectively. The formulae was developed using various individual concentrations of crospovidone and various individual concentrations and viscosity grades of HPMC polymers for both immediate and sustained release layers respectively . The compatibility of polymers and excipients along with pure drugs was evaluated using FTIR studies. The tablets were prepared and Pre- and Post-compression parameters, In-vitro dissolution testing, release rate kinetics and stability studies were evaluated. The FT-IR spectra's confirms the absence of chemical interaction between drug and polymers. All the Pre and post-compression parameters were found to be in limits. From the results of dissolution testing it was found that the batches IRL-4 and SRL-12 were found to be best of all the immediate and sustained release layer batches respectively. Thus they both were compressed to get a novel bilayer tablet formulation. The data for stability studies revealed that no considerable differences in drug content and dissolution rates for a period of 6 months as per ICH guidelines. Thus, a novel bilayer tablet formulation of Amlodipine and Metoprolol were successfully developed by combining both immediate and sustained release layers.

Keywords: Amlodipine, Crospovidone, HPMC polymers, Hypertension, Metoprolol.

INTRODUCTION

Hypertension or high blood pressure occurs when the high cardiac output exerts pressure on the arterial wall as the blood flow increases. The present available conventional dosage form used in the treatment of hypertension cannot produce the desired therapeutic effect for prolonged period of time and thus dose fluctuation and missing of dose chances are more.[1] The rationale for using fixed dose combination therapy is to obtain increased blood pressure control by employing two antihypertensive drugs with different mode of action and enhance the compliance by using single tablet that is taken once a day.[2]

Bi-layer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release or controlled release. In bilayer tablet one layer is immediate release as initial dose or loading dose and second layer is maintaining dose.[3] Amlodipine is a long-acting 1, 4-dihydropyridine type calcium channel blocker. It is used to lower blood pressure and to treat angina chest pain.[4,5] Whereas, Metoprolol is a cardio selective β1-adrenergic blocking agent used for acute myocardial infarction (MI), heart failure, angina pectoris and mild to moderate hypertension.[6] Both Amlodipine & Metoprolol in combination is used for the treatment of hypertension. In the present study a bilayer tablet formulation of Amlodipine as immediate release & Metoprolol as sustained release was developed and evaluated to treat hypertension by decreasing the dosing frequency of drug.

MATERIALS AND METHODS

Materials

Amlodipine, Metoprolol, Crospovidone, HPMC K 4M, HPMC K 15M, HPMC K 100M, PVP K30, Microcrystalline Cellulose, Mannitol, Aerosil, Magnesium Stearate, Quinoline yellow were received from Pharma Tech lab, Hyderabad and all the other chemicals were of analytical grade.

Methods

Pre-compression Parameters

Drug Excipients compatibility studies: The compatibility studies were performed by using FTIR analysis. The FTIR was performed on a Shimadzu electronic system. The samples of pure drug and its combination with excipients were mixed required quantity of potassium bromide (KBr) sealed in an aluminum pan and heated at a constant rate 100c/minute, over a temperature range 250 ^{0}C to 4000 ^{0}C. The FTIR studies performed to standard Amlodipine, Metoprolol and Excipients.

The powder blend was evaluated for bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose.

Bulk density (D_b): It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve # 20) into a measuring cylinder and the initial volume was noted. This initial volume is called the bulk volume. From this, the bulk density is calculated according to the

formula mentioned below. It expressed in g/cc and is given by:

$$D_b = \frac{M}{V_0}$$

Where, M is the mass of powder, V_0 is the bulk volume of the powder

Tapped density (D_t): It is the ratio of total mass of powder to the tapped volume of powder. The volume was measured by tapping the powder for 500 times. Then the tapping was done for 750 times and the tapped volume was noted (the difference between these two volumes should be less than 2 %). If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. It is expressed in g/cc and is given by:

$$D_t = \frac{M}{V_1}$$

Where, M is the mass of powder, V_t is the tapped volume of the powder

Carr's index (%): The bulk density is the measurement of weight to the volume of the sample. Tapped density is determined as the measurement of weight of the sample to the volume after tapping the measuring cylinder for 500 times from a height of 2 inches. The percentage compressibility (Carr's index) was calculated as 100 times the ratio of the difference between tapped density and bulk density to the tapped density.

$$\text{Carr's index} = 100 \times \frac{\text{Tapped density - Bulk density}}{\text{Tapped density}}$$

Hausner's ratio: Hausner's ratio is the ratio of tapped density to bulk density. Lower the value of Hausner's ratio better is the flow property.

$$\text{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Angle of repose (θ): It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.

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

Where,

θ is the angle of repose

h is the height in cm

r is the radius in cm

Method: The powder mixture was allowed to flow through the funnel with its tip fixed to stand at a definite height (h) from a graph paper placed on a horizontal surface. The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. A value for angle of repose $\geq 40^o$ suggests a poorly flowing material.[7]

Preparation of Immediate release layer (IRL) of Amlodipine

The Amlodipine layer was prepared by using direct compression method. All the ingredients except magnesium Stearate and Aerosil were passed through sieve No: 40, weighed and mixed for 15 mints and finally blended well in ascending order of their weights. Magnesium Stearate and Aerosil were passed through sieve No: 60 and mixed it to the above blend. Finally colorant was added and blended uniformly and compressed in a 16 station automatic punching machine with a punch size of 6 mm.

Table 1: Composition of Immediate Release layer of Amlodipine

Ingredients (mg/tab)	F1	F2	F3	F4
Amlodipine	10	10	10	10
Crospovidone	2.5	5	7.5	10
PVP K 30	5	5	5	5
Mannitol	80	77.5	75	72.5
Aerosil	1.2	1.2	1.2	1.2
Magnesium Stearate	1.2	1.2	1.2	1.2
Colorant	QS	QS	QS	QS
Total	100	100	100	100

Note: IRL= Immediate release layer

Preparation of Sustained release layer (SRL) of Metoprolol

The Metoprolol layer was prepared by using direct compression method. All the ingredients except magnesium Stearate and Aerosil were passed through sieve No: 40 weighed and mixed for 15 mints and finally blended well in ascending order of their weights. Magnesium Stearate and Aerosil were passed through sieve No: 60 and mixed it to the above blend and compressed in a 16 station automatic punching machine with a punch size of 6 mm.

Post compression Parameters

Weight uniformity

Twenty tablets from each batch at random were taken and weighted. The average weight was calculated, then each tablet was weighed individually and weights of each tablets was noted. The weights of individual tablets were then compared with the average weight that was already calculated. The deviation if any in the weight of individual tablets from the average weight was checked. This test highly describes that all the tablets of a particular batch should be uniform in weight. If any weight variation is there, that should be within IP limits. The test was considered correct if not more than two tablets fall outside the IP limits out of twenty tablets taken for the test.

Table 2: Composition of Sustained Release layer of Metoprolol

Ingredients (mg/tab)	Batches											
	SRL-1	SRL-2	SRL-3	SRL-4	SRL-5	SRL-6	SRL-7	SRL-8	SRL-9	SRL-10	SRL-11	SRL-12
Metoprolol	100	100	100	100	100	100	100	100	100	100	100	100
HPMC K 4M	25	50	75	100	--	--	--	--	--	--	--	--
HPMC K 15M	--	--	--	--	25	50	75	100	--	--	--	--
HPMC K 100M	--	--	--	--	--	--	--	--	25	50	75	100
PVP K 30	5	5	5	5	5	5	5	5	5	5	5	5
Micro Crystalline Cellulose	116	91	66	41	116	91	66	41	116	91	66	41
Aerosil	2	2	2	2	2	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2	2	2
Total weight (mg)	250	250	250	250	250	250	250	250	250	250	250	250

Note: SRL= Sustained release layer

Table 3: Pre-compression Parameters of immediate and sustained release layers

Formulation	Angle of Repose	Bulk Density	Tapped Density	C. Index (%)	Hausner's Ratio
IRL-1	22.62±0.45	0.46±0.10	0.54±0.12	14.81±0.22	1.17±0.02
IRL-2	24.19±0.73	0.59±0.12	0.68±0.20	13.04±0.18	1.15±0.03
IRL-3	23.72±0.17	0.48±0.14	0.53±0.15	9.43±0.29	1.10±0.04
IRL-4	24.61±0.12	0.48±0.09	0.56±0.14	14.28±0.15	1.16±0.02
SRL-1	24.74±0.28	0.44±0.06	0.50±0.14	12.00±0.18	1.13±0.01
SRL-2	24.28±0.31	0.48±0.16	0.53±0.14	9.43±0.25	1.10±0.03
SRL-3	24.06±0.63	0.47±0.15	0.53±0.12	11.32±0.11	1.12±0.03
SRL-4	23.40±0.16	0.46±0.09	0.52±0.13	11.53±0.20	1.13±0.02
SRL-5	24.72±0.48	0.46±0.05	0.53±0.17	13.20±0.17	1.15±0.01
SRL-6	22.65±0.53	0.45±0.12	0.52±0.12	13.46±0.12	1.15±0.04
SRL-7	24.17±0.29	0.50±0.14	0.57±0.15	12.28±0.21	1.14±0.02
SRL-8	23.24±0.22	0.52±0.06	0.57±0.15	9.25±0.18	1.09±0.03
SRL-9	22.42±0.30	0.45±0.16	0.51±0.14	11.76±0.14	1.13±0.01
SRL-10	24.24±0.21	0.53±0.16	0.59±0.14	10.16±0.19	1.11±0.02
SRL-11	23.94±0.40	0.41±0.15	0.47±0.13	12.76±0.11	1.14±0.04
SRL-12	24.48±0.11	0.39±0.10	0.44±0.12	13.63±0.28	1.12±0.03

* All the values are expressed in MEAN±SD (N=3)

Hardness

Hardness of the tablets determined by using Monsanto hardness tester (Tab machines, Mumbai). The tablet to be tested held fixed and moving jaw and reading of the indicator adjusted to zero. Then force to the edge of the tablets was gradually increased by moving the screw knob forward until the tablets breaks. The reading was noted from the scale which indicates the pressure required in kg to break the tablet. The hardness of tablets depends on the weight of the material used, space between the upper and lower punches at the time of compression and pressure applied during compression.

Friability

Friability test was performed by using Roche friabilator (Remi equipments, Mumbai). Twenty tablets of a batch were weighted and placed in a friabilator chamber and it was allowed to rotate for 100 revolutions. During each revolution these tablets fall from a distance of six inches to undergo shock. After completion of 100 revolutions, tablets were again weighed and the loss in weight indicated the friability. The acceptable limits of weight loss should not be more than 0.8%. This test was performed to evaluate the ability of the tablets to with stand abrasion during packing, handling and transporting.[8]

Content uniformity test

Ten immediate and sustained release layers were weighed and powdered, a quantity of powder equivalent to 10 mg of Amlodipine and 100 mg of Metoprolol was taken. The Amlodipine and Metoprolol content was estimated by HPLC method at 239 nm and 297 nm respectively after appropriate dilutions. The mean percent drug content was calculated as an average of three determinations.

Drug Release Studies for Immediate release layer

The *in vitro* dissolution of immediate release layer was determined using USP XXIII (basket method) dissolution apparatus. The basket was allowed to rotate at a speed of 100 rpm and temperature of 37 ± 0.5°C was maintained. The dissolution medium used was 900 ml of 0.1N HCl (pH 1.2) for 2 hours. Aliquots (5 ml) of sample were collected at predetermined time intervals (5, 10, 15, 20, 25 and 30min) from the dissolution apparatus and it was replaced with equal volume of fresh dissolution medium. The aliquots withdrawn were filtered through 0.45µm millipore filters. The concentration of Amlodipine in the dissolution media was estimated by HPLC method at 239 nm.

Drug Release Studies for sustained release layer

The *in vitro* dissolution of sustained release layer was determined using USP XXIII (basket method) dissolution apparatus. The basket was allowed to rotate at a speed of 100 rpm and temperature of 37 ± 0.5°C was maintained. The dissolution medium used was 900 ml of 0.1N HCl (pH 1.2) for the initial 2hours followed by study in simulated intestinal fluid Phosphate buffer solution (pH 6.8). Aliquots (5 ml) of sample were collected at predetermined time intervals (1, 2, 4, 6, 8, 10, 12, 16, 20, and 24 hrs) from the dissolution apparatus and it was replaced with equal volume of fresh dissolution medium. The aliquots withdrawn were filtered through 0.45µm millipore filters. The concentration of Metoprolol in the dissolution media was estimated by HPLC method at 297 nm.

Drug Release Studies for Bilayer Tablets

The *in vitro* dissolution of Amlodipine and Metoprolol bilayer tablets were determined using USP XXIII (basket method) dissolution apparatus. The basket was allowed to rotate at a speed of 100 rpm and temperature of 37 ± 0.5°C was maintained. The dissolution medium used was 900 ml of 0.1N HCl (pH 1.2) for the initial 2hours followed by study in simulated intestinal fluid Phosphate buffer solution (pH 6.8). Aliquots (5 ml) of sample were collected at predetermined time intervals (1, 2, 4, 6, 8, 10, 12, 16, 20, and 24 hrs) from the dissolution apparatus and it was replaced with equal volume of fresh dissolution medium. The aliquots withdrawn were filtered through 0.45µm millipore filters. The concentration of both the drugs in the dissolution media was estimated by HPLC method at 239 nm and 297 nm for Amlodipine and Metoprolol respectively.

Conditions used in HPLC

The parameters used in HPLC analysis are as follows;

Equipment : High performance liquid chromatography equipped with Auto Sampler and DAD detector (model no- Detector 2487 and Separation module 2695

Column : C8 (4.6 x 250mm, 5 m)

Flow rate : 1.0mL per min

Injection volume : 20 µl

Temperature : Ambient

Run time : 8.0 min

Mobile phase : Acetonitrile: Methanol (400:600)

Release kinetics studies

To study the release kinetics and mechanism of release in-vitro release data was applied to kinetic models such as zero order (Cumulative % drug release vs. time), first order (Log Mean % drug unreleased vs. time), Higuchi (Mean % cumulative drug release vs. square root of time) and Korsemeyer-Peppas (Log mean % cumulative drug release vs. Log time) using Microsoft Excel-2003 software and the regression values (R^2) were calculated.[8]

Stability studies

In the present study, stability studies were carried out for both at room temperature and accelerated stability conditions. The conditions for storing at room temperature were kept as 30±2 °C and 65±5% RH and for accelerated stability conditions were kept at 40±2°C and 75±5% RH in a humidity chamber. At regular intervals of time (0, 2, 4 and 6 months) samples were withdrawn and were evaluated for drug content and in-vitro release profile.[8]

RESULTS AND DISCUSSION

Drug excipients interaction studies

When the spectra's of pure drug and its combination with excipients were taken as shown in Figure 1 it was found that all the peaks corresponding to the constituents were found to be present in its higher spectra indicating that none of the functional groups of either drug or polymer have undergone any chemical reaction. All functional groups are intact. Hence, it is a confirmation that no chemical reactions have taken place amongst any of the constituents in the bilayer tablet formulation and thus it can be used for its desired purpose.

Evaluation of powder blend

Powder blend ready for compression containing drug and various excipients were subjected for pre-compression parameters (Micromeritic properties) to study their flow

properties and to achieve uniformity of tablet weight. The results of all the pre-compression parameters are given Table 3. The angle of repose of all the batches was found to range between 22°.62' to 24°.74' which is lesser than 25 and thus the powder blend has excellent flow properties. For all the batches of powder blend, the LBD and TBD were found in range between 0.46±0.10 to 0.59±0.12 and 0.44±0.12 to 0.68±0.20 gm/cc respectively. This indicates good packing capacity of the powder blend. The results of Carr's consolidation index or compressibility index (%) for all the batches of the powder blend were found to range between 9.25±0.18 % and 14.81±0.22 % which is lesser than 15 %. Hausner's ratio of all batches were found to be in the range between 1.09±0.03 to 1.16±0.02 which is lesser than 1.25 and thus indicates better flow properties.

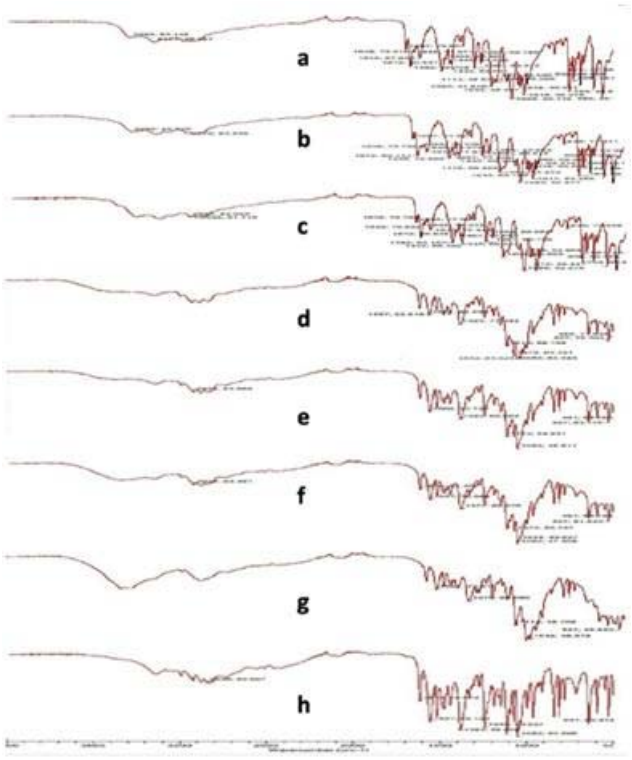

Figure 1: IR spectra's of a) Amlodipine b) Amlodipine & PVP c) Amlodipine & Mannitol d) Metoprolol e) Metoprolol & HPMC K4M f) Metoprolol & HPMC K15M g) Metoprolol & HPMC K100M h) Metoprolol & Mannitol.

Evaluation of post-compression parameters

The results of all the post-compression parameters are given Table 4. In the present study, the hardness of all the batches were found to range between 5.8±0.27 kg/cm^2 to 6.2±0.06 kg/cm^2 and 3.6±0.86 to 3.8±0.22 for all the immediate and sustained release layer batches respectively indicating that they possessed sufficient mechanical strength. The friability of all the batches was found to range between 0.12±0.07 to 0.19±0.08 and 0.21±0.09 to 0.41±0.08 for all the immediate and sustained release layer batches respectively. Conventional compressed tablets that loose less than 1 % of their weight are generally considered acceptable. In the present study, percent friability of all the batches was below 1 % limit as shown in the pharmacopoeia indicating that the friability is within the standard limit. It ensures that all the batches were mechanically stable. The weight variation test was performed according to the procedure given in the pharmacopoeia. The average percentage deviation were found to range between 99±0.10 to 102±0.18 and 247±0.25 to 254±0.21 mg for all the immediate and sustained release layer batches respectively and it was within the Pharmacopoeial limits. The percentage drug content were found to range between 98.52±0.12 to 99.97±0.08 and 98.98±0.22 to 99.98±0.10 % of Amlodipine and Metoprolol respectively indicating good content uniformity in all the batches. This indicates drug was uniformly distributed throughout the batches. Whereas the disintegration time of all the IRL batches was found to range between 12±0.14 to 19±0.05 sec which was also within the limit.

***In - vitro* drug release study of immediate release layer of Amlodipine**

The release profile of Amlodipine from different batches of formulated tablets was represented in Figure 2a. Based on the results of in-vitro dissolution testing it was known that all the immediate release layer batches shown the drug release within 20-30 minutes. But the formulation F-4 shown maximum amount of drug release i.e. 99.96±0.95 % within 20 minutes in a immediate release manner and hence was considered as the best batch to get incorporated in bilayer tablet formulation. From the results of in-vitro drug release studies it was also found that as the concentration of crospovidone was increasing from 2.5 % to 10 % the release rate of Amlodipine was also increased. This is due to the reason that increased concentration of disintegrant lead to decreased disintegration time and thus increased release of Amlodipine.

***In - vitro* drug release study of Sustained release layer of Metoprolol**

The release profile of Metoprolol from different batches of formulated tablets was represented in **Figure 2b**. Based on the results of in-vitro dissolution testing it was known that all the sustained release layer batches shown the drug release within 10-24 hours. Among all the batches only the batch SRL-12 shown maximum amount of drug release i.e. 99.58±0.84 % at the end of 24 hours in a sustained release manner and hence was considered as the best batch to get incorporated in bilayer tablet formulation. From the results of in-vitro drug release studies it was also found that as the concentration or viscosity of hydroxy propyl methyl cellulose polymer was increasing the release of Metoprolol was also increased. This is due to the reason that increased concentration or viscosity of hydrophilic HPMC polymer leads to increased uptake of water which results in more swelling of tablet which in turn leads to decreased release rate of Metoprolol.

In - vitro drug release study of bilayer tablet formulation of Amlodipine and Metoprolol

The release profile of bilayer tablet formulation of Amlodipine and Metoprolol was represented in Figure 2c. The optimized immediate release layer (IRL) of Amlodipine and optimized sustained release layer (SRL) of Metoprolol was combined to obtain a novel bilayer tablet formulation. Based on the results of in-vitro dissolution testing it was known that both the IRL and SRL layers were released in immediate and sustained release manner. The IR layer released 99.67±0.37 % of Amlodipine at the end of 45 minutes whereas the SR layer released 99.38±0.88 % of Metoprolol at the end of 24 hours. Thus a novel bilayer tablet formulation was obtained.

Table 4: Post-compression Parameters of immediate and sustained release layers

Formulation	Average Wt. Variation (mg)	Hardness (Kg/Cm^2)	Friability (%)	Disintegration time (Sec)	Content Uniformity (%)
IRL-1	99±0.10	3.8±0.22	0.12±0.07	19±0.05	99.92±0.05
IRL-2	102±0.12	3.7±0.64	0.15±0.06	15±0.09	98.30±0.10
IRL-3	100±0.20	3.8±0.17	0.14±0.04	12±0.14	99.97±0.08
IRL-4	102±0.18	3.6±0.86	0.19±0.08	18±0.06	98.52±0.12
SRL-1	247±0.25	5.9±0.18	0.21±0.09	--	99.98±0.10
SRL-2	251±0.17	6.2±0.06	0.26±0.06	--	99.54±0.16
SRL-3	252±0.16	5.9±0.12	0.24±0.07	--	99.62±0.18
SRL-4	249±0.22	5.8±0.27	0.32±0.03	--	99.74±0.13
SRL-5	248±0.09	6.1±0.09	0.41±0.08	--	99.68±0.08
SRL-6	250±0.19	6.0±0.16	0.37±0.05	--	99.02±0.10
SRL-7	250±0.13	6.1±0.12	0.32±0.08	--	98.98±0.22
SRL-8	249±0.21	6.2±0.11	0.34±0.07	--	99.47±0.17
SRL-9	253±0.18	5.9±0.13	0.42±0.10	--	99.23±0.09
SRL-10	252±0.16	6.1±0.11	0.26±0.8	--	99.68±0.18
SRL-11	254±0.21	6.0±0.2	0.38±0.06	--	99.37±0.12
SRL-12	251±0.26	5.9±0.14	0.29±0.04	--	99.76±0.20

* All the values are expressed in MEAN±SD (N=3)

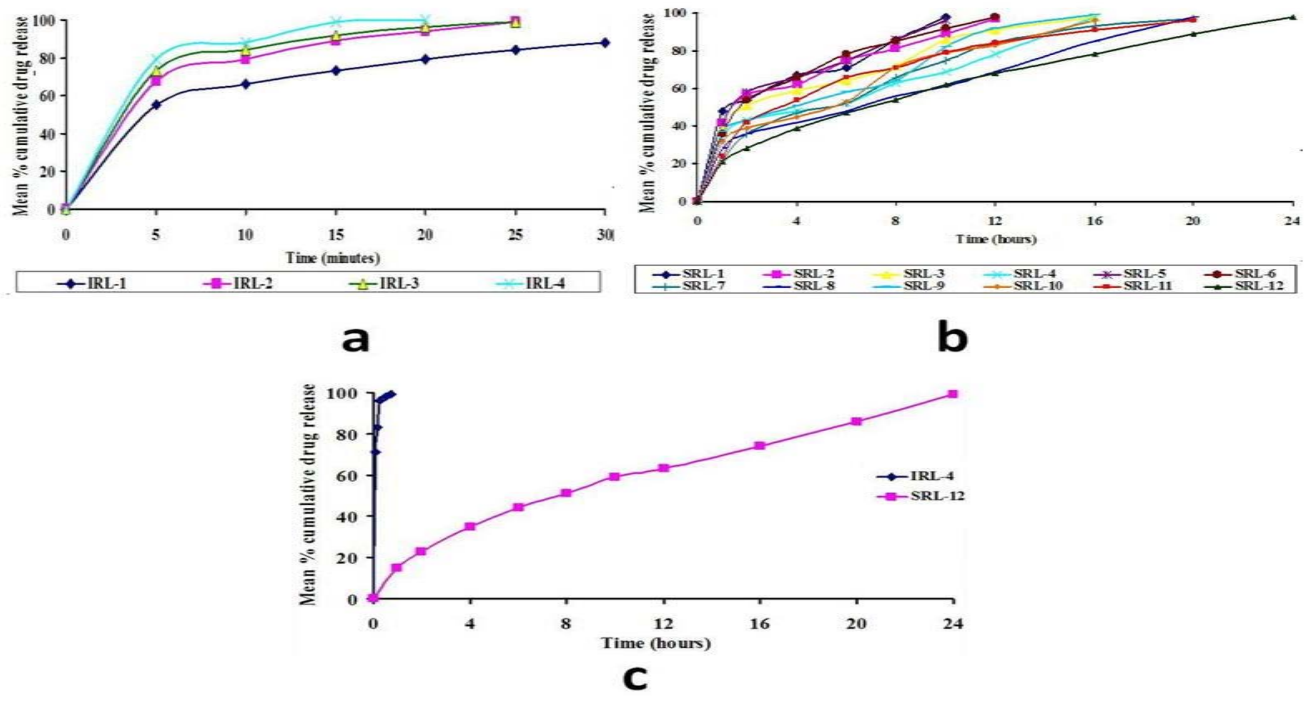

Figure 2: a) In-vitro release profile of immediate release layer of Amlodipine b) In-vitro release profile of sustained release layer of Metoprolol c) In-vitro release profile of bilayer tablet formulation of Amlodipine and Metoprolol

Drug release study

The kinetic data of all the formulations are shown in Table 5. When the data were plotted according to zero-order kinetics, the formulations showed correlation coefficient values (R^2) between 0.8071-0.9308. But when the data were plotted according to the first order kinetics, the formulations showed correlation coefficient values i.e. from 0.8317 to 0.9778. From the results it was found that only the formulations SRL-4, SRL-8, SRL-9 and SRL-12 follows zero-order kinetics whereas all the remaining formulations were found to release Metoprolol by first order kinetics.

To ascertain the drug release mechanism, the in-vitro data were also subjected to Higuchi diffusion. The 'R^2' values of Higuchi diffusion plot were found to range between 9603-9901 for batches SRL-1 to SRL-12. It suggests that the Higuchi diffusion plots of all the formulations were fairly linear because 'R^2' values were nearer to about 1 in all the cases. So it confirms the drug release by Higuchi diffusion mechanism.

The formulations were also subjected to Korsemeyer's peppas plots. When the slope value (n value) was calculated it was found in range between 0.81 to 1.13, indicating the drug was released by non-Fickian diffusion mechanism.

Table 5: Results of kinetic studies

FC	Zero order (R^2)	First order (R^2)	Higuchi's plot (R^2)	Korsemeyer's Peppa's (n)
SRL-1	0.8071	0.8476	0.9533	1.11
SRL-2	0.8044	0.9226	0.9603	1.03
SRL-3	0.8227	0.9376	0.9664	0.95
SRL-4	0.8823	0.7833	0.9585	0.81
SRL-5	0.8111	0.9283	0.9662	1.13
SRL-6	0.8923	0.9459	0.978	1.08
SRL-7	0.8893	0.9778	0.9901	0.97
SRL-8	0.9247	0.8317	0.9782	0.89
SRL-9	0.8818	0.8687	0.9688	0.96
SRL-10	0.9007	0.9348	0.9818	0.98
SRL-11	0.8136	0.9916	0.9732	0.94
SRL-12	0.9308	0.8915	0.9989	0.9

FC- Formulation code

Table 6: Results of Stability studies

Parameters		Storage conditions and time (months)				
		Initial results	Room temperature 30±2 °C and 65±5% RH		Accelerated stability 40±2 °C and 75±5% RH	
		0 Months	3 Months	6 Months	3 Months	6 Months
Drug content (assay) (%)	IRL-4	98.52±0.12 %	98.34±0.16 %	98.07±0.09 %	98.44±0.15 %	97.95±0.12 %
	SRL-12	99.76±0.20 %	99.28±0.11%	99.01±0.18 %	99.32±0.22 %	99.10±0.16 %
% Cumulative Drug Released at the end	IRL-4	99.67±0.37 %	99.19±0.25 %	98.92±0.18 %	99.44±0.34 %	99.10±023 %
	SRL-12	99.38±0.88 %	99.28±0.64 %	99.05±0.39 %	99.18±0.52 %	98.76±0.20 %

*All the values are expressed in MEAN±SD (N=3)

Stability studies

Formulation batches IRL-4 and SRL-12 was packed in 90 ml HDPE containers (30s count/container) and charged at both room temperature (30±2°C and 65±5% RH) and accelerated stability conditions (40±2°C and 75±5% RH) in a humidity chamber. The tablets were evaluated for assay and dissolution profile testing at 0, 3 and 6 months. The data for stability studies revealed that no considerable differences in drug content and dissolution rates were observed. The results of drug content and dissolution rate after 6 months are given in Table 6.

CONCLUSION

The study was undertaken with the aim to Formulation and evaluation of bilayer tablet formulation of Amlodipine and Metoprolol. Thus, from the results, it is concluded that the formulation of immediate release layer of Amlodipine using 10 % concentration of crospovidone and 40 % concentration of HPMC K 100M are considered as ideal for optimized bilayer tablet formulation. Thus, this optimized bilayer tablet formulation can be successfully used in the treatment of hypertension.

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