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Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF NIMODIPINE AND METOPROLOL BI-LAYERED TABLETS

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ABSTRACT:
The current study aimed to develop and assess an antihypertensive bilayer tablet combining Nimodipine and Metoprolol. Nimodipine's quick release layer was created utilizing several super disintegrants, with the optimal formula (F8) including sodium starch glycolate as a super disintegrant. The sustained release layer of Metoprolol was created utilizing several release retarding agents, with the optimum formula (F8) using a mix of HPMC and Xanthan gum as release retardants. Drug excipient compatibility tests employing FTIR revealed no interactions between medicines and excipients. The pre- and post-compression experiments were within approved guidelines. In vitro release investigations revealed that the Nimodipine immediate release layer in the bilayer tablet was 97.43% within 30 minutes, while the Metoprolol sustained release layer was 97.22% after 12 hours. The release kinetics were linear, and stability experiments demonstrated no changes in physical features or drug release after three months under accelerated circumstances.
Keyword: Nimodipine, Metoprolol, Bilayer tablet.

INTRODUCTION

- ✓ Bi-layer tablets can release two medications sequentially, segregate incompatible compounds, and provide prolonged or regulated release. In a bilayer tablet, the first layer provides quick release as the initial or loading dosage, while the second layer serves as the maintenance dose.[1]
- ✓ Hypertension, often known as high blood pressure, is caused by increased cardiac output that puts pressure on the artery wall. The Conventional dosage forms for hypertension therapy do not provide long-term therapeutic effects, leading to increased dose fluctuations and missed doses.[2]Fixed dosage combination treatment aims to improve blood pressure management by combining two antihypertensive medications with different modes of action. It also improves compliance by requiring only one daily tablet. [3]
- ✓ Nimodipine is 1, 4-dihydropyridine derivative L-type calcium channel blocker proposed in the prevention of ischemic neurological deficits following aneurysmal subarachnoid hemorrhage from ruptured congenital aneurysms.[4] It acts as an antihypertensive agent, a calcium channel blocker, a vasodilator agent, and a cardiovascular drug.
- ✓ 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. [5]

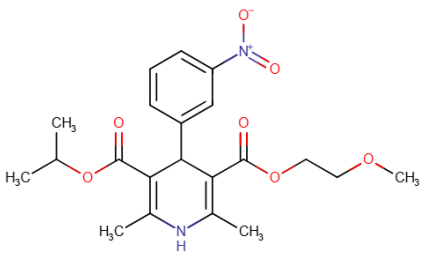

Figure.1 Structure of Nimodipine

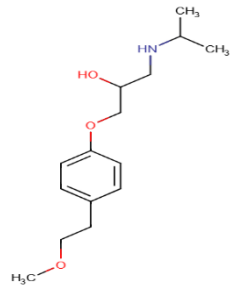

Figure.2 Structure of Metoprolol

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METHODOLOGY:

Characterization of IR/SR Granules

Solubility studies of the drugs were carried out in various aqueous solutions and buffers. Drug excipient compatibility studies were done using FTIR. The granules of both the layers of IR/SR were evaluated for various pre compression parameters. The angle of repose was measured by fixed funnel method. Bulk and tapped densities were determined by tapped density apparatus from which compressibility index and Hausner's ratio values were calculated and from the values obtained flow property of granules.

Drug-Excipient Compatibility Studies by FT-IR

The compatibility of drugs with their respective excipients was studied by FT-IR spectroscopy (Model number 02437, Shimadzu, India). The scanning was performed 20 times at scanning speed 2 mm/sec with resolution of 4 cm−1 over the region 4000–400 cm−1. The scans were evaluated for presence of principle peaks of drug, shifting and masking of drug peaks, and appearance of new peaks due to polymer interaction.

Analytical Method Development Construction of Calibration Curve

Standard dilutions were prepared in the range of 2–10 μg/mL using 0.1 N HCl for Nimodipine and absorbancewas determined at λmax (282 nm) in UV spectrophotometer (UV-1700, Shimadzu, India). Similarly standard dilutions were prepared in the range of 2–10 μg/mL using 0.01 N HCl with 0.5% w/v SLS for metoprolol and absorbance was determined at λmax (210 nm) in UV spectrophotometer. From the values obtained, standard graph can be plotted between concentration and absorbance values.[6]

Procurement of drug

Nimodipine and Metoprolol Succinate have been obtained/procured from IPCA Mumbai.

Preparation of Immediate Release layer of Nimodipine

Immediate release layer of Nimodipine (F1-F9) was prepared by direct compression method. Nimodipine and other excipients like microcrystalline cellulose, Crospovidone, Croscarmellose sodium, and sodium starch glycolate and sodium lauryl sulfate were accurately weighed and sifted through sieve #40 and mixed in a polybag and these formulations are given in Table 1. The sifted powders were thoroughly mixed for approximately 5 min and again passed through sieve #40 to get uniform particle size. Magnesium stearate was added into the powder mixture for lubrication after passing through sieve #40 and 0.125% w/w of iron oxide red previously sifted to sieve #100 was added to the above mixture and blended thoroughly to ensure uniform color.[7]

Preparation of Sustained Release Metprolol Succinate

Sustained release layer of Metprolol Succinate (F1-F9) was prepared by wet granulation technique by adding 5% concentration of PVP K 30 dissolved in isopropyl alcohol as a binding agent and these formulations are represented in the Table 2. Required quantities of and other excipients like HPMC E15, Guar gum, Xanthan gum, ethyl cellulose, mannitol, and microcrystalline cellulose were weighed accurately and were sifted through sieve #40 and were mixed thoroughly and a sufficient volume of binding agent was added slowly to get cohesive mass. Then mass was passed through sieve #20 to obtain the granules. Next the granules were dried at 50◦ C in a hot air oven until dry the dried granules were lubricated uniformly with magnesium stearate; then talc was added and mixed properly. The above granules were compressed into tablets by 10-station tablet compression machine using 9 mm punch. In batches N1 to N3, HPMC E15 was used as the sustained release polymer and in batches N4 to N7 Guar gum was used, and in N8 Xanthan gum, in N9 combination of HPMC E15 and Guar gum, and in N10 to N12 combination of Guar gum and ethyl cellulose, and finally in N13 combination of Guar gum and Xanthan gum was used as sustained release polymer. [8]

Preparation of Bilayer Tablets

In order to prepare bilayer tablets, the dissolution test was conducted for both layers of IR/SR separately with the aim of selecting the best formulations. Based on dissolution behavior, formulations NBL-8 and N-9 were selected for bilayer tablet. First, sustained release layer was placed in the die cavity and punched with low compression force. Then the immediate release layer was placed in the die cavity and allowed for punching with optimum hardness of 6–8 kg/cm2 to form bilayer tablets. Compression was made by using 10 mm punches. The total weight of each bilayer tablet was adjusted to 450 mg, in fast-release layer and in sustained release layer. Prepared bilayer tablets were evaluated for various post compression parameters and in vitro dissolution studies.[9]

Table.1 Composition of immediate release Layer

Batch Code	Ingredients in mg / tablet							
	Nimodipine	MCC	CP	CCS	SSG	Mg. Stearate	SLS	Fe_2O_3
F1	10	131	7.5	-	-	1.5	-	Qs
F2	10	123.5	15	-	-	1.5	-	Qs
F3	10	131	-	7.5	-	1.5	-	Qs
F4	10	123.5	-	15	-	1.5	-	Qs
F5	10	131	-	-	7.5	1.5	-	Qs
F6	10	123.5	-	-	15	1.5	-	Qs
F7	10	119.5	-	-	18.75	1.5	-	Qs
F8	10	131	-	-	7.5	1.5	0.3	Qs
F9	10	123.5	-	-	15	1.5	3.0	Qs

Table.2 Composition of sustained release layer

Ingredients	NI	N2	N3	N4	N5	N6	N7	N8	N9
Metoprolol Succinate	60	60	60	60	60	60	60	60	60
HPMC	30	45	60	-	-	-	-	-	45
Guar gum	-	-	-	30	45	60	75	-	-
X - gum	-	-	-	-	-	-	-	75	45
EC	-	-	-	-	-	-	-	-	-
Mannitol	-	-	-	-	-	-	-	-	-
MCC	180	165	150	180	165	150	135	135	120
PVP	15	15	15	15	15	15	15	15	15
Mg . stearate	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Talc	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Total wt	300	300	300	300	300	300	300	300	300

Evaluation of IR/SR Tablets [10]

The prepared tablets were subjected to various evaluation tests like thickness, hardness, weight variation, friability, and drug content. Thickness of the tablets was determined by using vernier calipers. Randomly 10 tablets were selected and used for determination of thickness. Hardness is termed as the tablet crushing strength and it is the force required to break a tablet diametrically. Hardness of tablets was measured by selecting 6 tablets randomly and the hardness of each tablet was measured with Monsanto hardness tester. The hardness was noted. The hardness is usually measured in terms of kg/cm2 . For weight variation test individual weight of 20 tablets was taken; then their average weight and their mean and standard deviation were calculated and compared with the standards. The weight of the tablet being made is measured to ensure that it contains predetermined amount of drug. The tablet friability is a measure of loss due to abrasion. The preweighed tablets were exposed to repeated shocks in Roche friabilator in which they are initially weighed ($W0$) and kept in a tumbling and rotating apparatus drum and were subjected to fall from 6 inches height. After completion of 100 rotations, the tablets were reweighed (W) and the percent loss in weight or friability (f) was calculated by the formula given below:

$$\%\text{Friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100. \quad (1)$$

Drug Content

Twenty tablets were selected randomly and average weight was calculated. The tablets were crushed in a mortar and accurately weighed amount of average tablet weight was taken from the crushed blend and transferred in to a 100 mL volumetric flask. To this little amount of methanol was added to dissolve the drug and volume was made up to the mark with concerned medium. The content was shaken periodically and kept for 1 hour to allow the drug to dissolve completely. Then it was filtered and appropriate dilutions were made. Finally dilutions were observed using spectrophotometer to determine % drug content.The drug content should be within the range between 90 and 110% of standard amount [11]

Disintegrating Time

The disintegration test is carried out in an apparatus (Electro lab, Mumbai) containing a basket rack assembly with six glass tubes of 7.75 cm in length and 2.15 mm in diameter, the bottom of which consists of a #10 mesh

sieve. The basket is raised and lowered 28–32 times per minute in a medium of 900 mL water which is maintained at 37 ± 2∘ C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the mesh (#10) was considered as the disintegration time of the tablet.[12]

In Vitro Dissolution Studies

The release of drug from different batches of prepared tablets was studied using USP dissolution apparatus type II. The dissolution medium used was 500 mL of 0.1 N HCl for first 30 minutes for immediate release layer and then 900 mL of 0.01 N HCl with 0.5% w/v SLS was used up to 12 hours for sustained release layer. The temperature was maintained at 37 ± 0.5∘ C and the stirring rate was 50 rpm. The samples were withdrawn at regular intervals and this withdrawn volume was replaced with fresh medium. The collected samples were filtered using Whatman filter paper and observed using spectrophotometer at respective λmax against a blank (respective medium).[13]

Evaluation of Bilayer Tablet

Evaluation parameters of bilayer tablet were performed according to I.P. specifications. Parameters such as weight variation were performed by taking average weight of 20 tablets and hardness test was performed by Monsanto hardness tester. Thickness of the tablet was measured using vernier caliper. Friability test was performed by taking 6 tablets in Roche friabilator and % friability was calculated.In vitro drug release studies of bilayer tablets were carried out uvusing USP dissolution apparatus type II in 500 mL of 0.1 N HCl for first 30 minutes and in 900 mL of 0.01 N HCl with 0.5% SLS up to 12 hours. Samples were collected at regular intervals of time and filtered. The medium in bowl was discarded after 30 minutes and replaced with another medium which was preferred for dissolution of sustain release layer. The collected samples were filtered and observed in UV spectrophotometer. The results were calculated using simultaneous equation method as given below:

$$Cx = \frac{A_2 a y_1 - A_1 a y_2}{a x_2 a y_1 - a x_1 a y_2},$$

$$Cy = \frac{A_1 a x_1 - A_2 a x_2}{a x_2 a y_1 - a x_1 a y_2},$$

where Cx and Cy are concentrations of Nimodipine and metoprolol, $A1$ is absorbance value at wavelength $\lambda 1$, $A2$ is absorbance value at wavelength $\lambda 2$[14]

Kinetic Data Analysis

The drug release kinetic studies were carried out for bilayer tablets were evaluated using the linear regression method:

- Zero order kinetic model—cumulative % of drug released versus T;
- First order kinetic model—log cumulative percent drug remaining versus T;
- Higuchi's model—cumulative percent drug released versus square root of T;
- Korsmeyer equation/Peppa's model—log cumulative percent drug released versus log T.[15]

Stability Studies

The purpose of stability testing is to provide evidence on how the quality of drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light. The optimized bilayer tablets were subjected to stability studies (as per ICH guidelines) at 40∘ C ± 2∘ C/75% ± 5% RH in a humidity chamber. The products were evaluated for their physical characteristics and in vitro drug release profiles over a period of 3 months.[16]

RESULTS AND DISCUSSION:

Solubility studies

Table.3 Solubility study data of Nimodipine and metoprolol in various solvents and buffers

Name of solvent / buffer	Nimodipine (mg / mL)	Metoprolol (mg / mL)
Water	0.0017	0.001
HCl buffer pH 1.2	1.2234	0.105
Phosphate buffer pH 6.8	0.0012	0.021
PEG	0.9102	-
DMSO	0.4567	0.574
Methanol	0.0814	0.342

Drug-Excipient Compatibility Studies by FT-IR

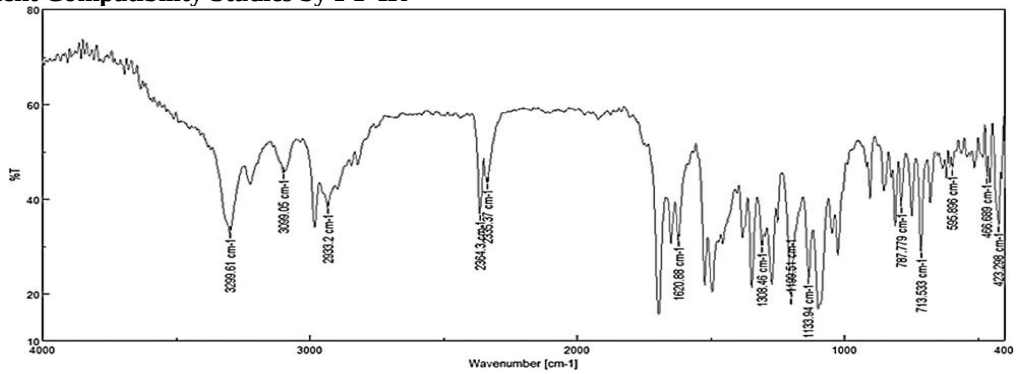


Figure.3 FT-IR (Nimodipine pure drug)

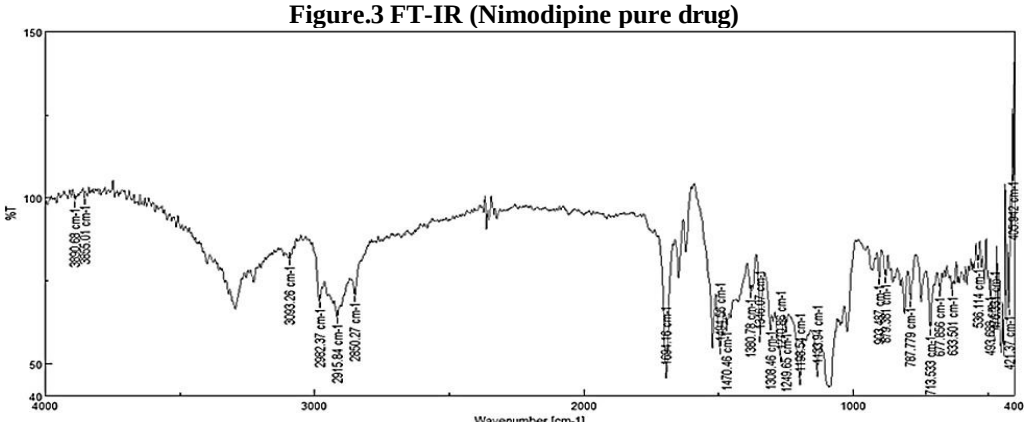


Figure.4 FT-IR (Nimodipine optimized formula)

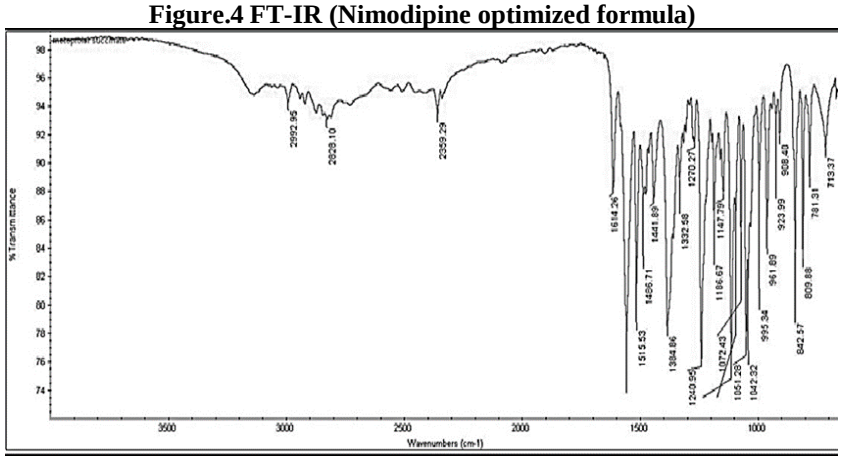


Figure.5 FT-IR (Metoprolol pure drug)

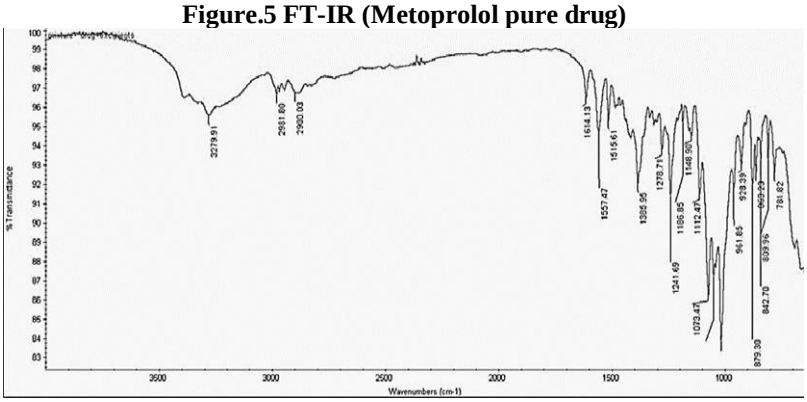


Figure.6 FT-IR (Metoprolol optimized formula)

Analytical Method Development

Calibration curves were plotted for both Nimodipine and Metoprolol based on the data obtained in UV spectrophotometer and these curves showed regression coefficient of 0.9999 and 0.9996 for the respective drugs.

Construction of Calibration Curve

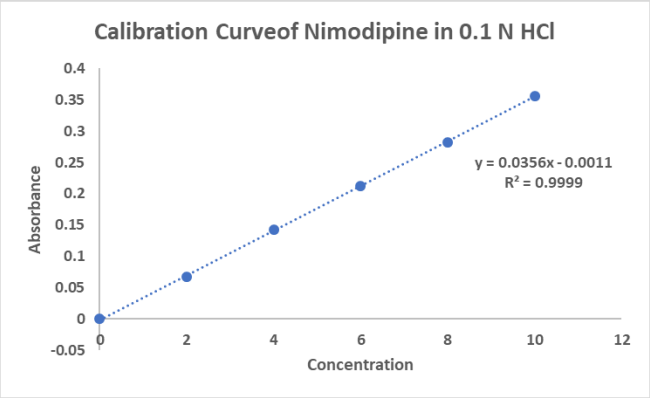


Figure.7 Calibration Curve

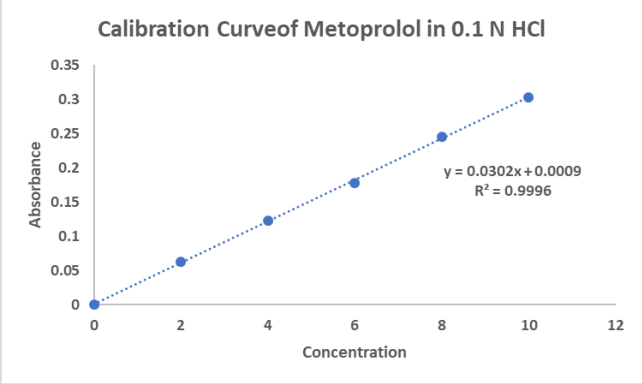


Figure.8 Calibration Curve

Discussion: There was no significant shift in the positions of wave numbers when compared to that of the pure drugs. As there is no interaction observed between the drugs and excipients of the formulations, these excipients were chosen for the formulations.

Micromeritics Studies

Table.4 Flow properties of Nimodipine immediate release layer

Batch code	Angle of repose	Bulk density (g /cm³)	Tapped density (g /cm³)	Carr's index (%)	Hausner's ratio
F1	30.17	0.34	0.40	15.00	1.17
F2	34.70	0.35	0.47	25.53	1.34
F3	26.10	0.34	0.41	17.07	1.20
F4	29.12	0.34	0.40	15.00	1.17
F5	28.47	0.34	0.39	12.82	1.14
F6	26.96	0.35	0.43	18.60	1.22
F7	26.10	0.36	0.41	12.19	1.13
F8	27.92	0.35	0.42	16.66	1.20
F9	28.01	0.35	0.40	12.50	1.14

Table.5 Flow properties of Metoprolol sustained release layer

Batch code	Angle of repose	Bulk density (gm / cm³)	Tapped density (gm / cm³)	Carr's index (%)	Hausner's
F1	35.12	0.32	0.37	13.50	1.
F2	32.15	0.31	0.40	22.50	1.29
F3	31.18	0.34	0.38	10.52	1.
F4	32.20	0.38	0.44	13.63	1.15
F5	34.80	0.30	0.35	14.28	1.16
F6	33.15	0.36	0.42	14.28	1.16
F7	30.00	0.29	0.33	12.12	1.
F8	28.55	0.30	0.35	14.28	1.
F9	27.50	0.31	0.35	11.42	1.13

Evaluation of IR/SR Tablets

Table.6 Evaluation parameters of Nimodipine immediate release tablets.

Batch code	Weight variation (%)	Hardness (kg / cm²)	Thickness (mm)	Friability (%)	Drug content (%)	Disintegration time (min)
F1	0.53	4.3	2.83	0.13	95.56	3.40
F2	1.19	4.5	3.29	0.15	97.20	2.55
F3	2.51	4.0	3.18	0.14	96.45	4.10
F4	1.19	5.0	3.30	0.13	90.84	3.28
F5	1.25	3.5	2.85	0.16	103.01	3.56
F6	3.18	4.3	2.91	0.12	97.62	2.45
F7	0.53	4.2	3.10	0.15	100.94	1.50
F8	1.25	4.5	3.05	0.18	98.19	3.45
F9	0.53	4.5	3.20	0.16	99.42	2.40

Table.7 Evaluation parameters of Metoprolol sustained release tablets.

Batch code	Weight variation(%)	Hardness (kg / cm²)	Thickness (mm)	Friability (%)	Drug content (%)
F1	0.22	7.0	3.97	0.59	96.12
F2	0.89	5.8	3.95	0.62	97.45
F3	0.55	7.2	3.99	0.60	98.10
F4	1.55	6.8	3.85	0.54	95.53
F5	1.20	6.2	3.57	0.70	98.63
F6	0.89	5.5	3.84	0.69	98.84
F7	0.22	6.5	3.73	0.72	97.14
F8	0.22	5.5	3.69	0.54	101.15
F9	0.55	6.8	3.89	0.52	98.68

Table.8 In vitro drug release data of Nimodipine immediate release tablets

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	11±3.12	16±3.26	14±3.11	19±3.80	16±3.57	19±3.85	19±2.4	25±3.96	27±3.68
10	21±3.45	28±3.40	25±4.25	28±3.54	29±4.20	32±3.15	31±3.20	43±3.56	41±3.24
15	35±3.08	36±4.05	34±4.50	38±3.69	42±4.22	46±4.12	48±4.01	50±3.94	58±3.80
20	49±4.15	50±4.91	47±3.75	52±4.52	58±3.75	59±3.46	60±4.23	66±4.25	73±4.31
25	55±3.89	61 ±3.89	53±3.90	59±3.96	64±3.58	66±4.29	70±3.99	80±3.98	88±3.78
30	64±4.52	69 ±3.68	65±4.82	68±4.95	74±4.52	80±4.42	84±4.58	96±3.80	97±3.94

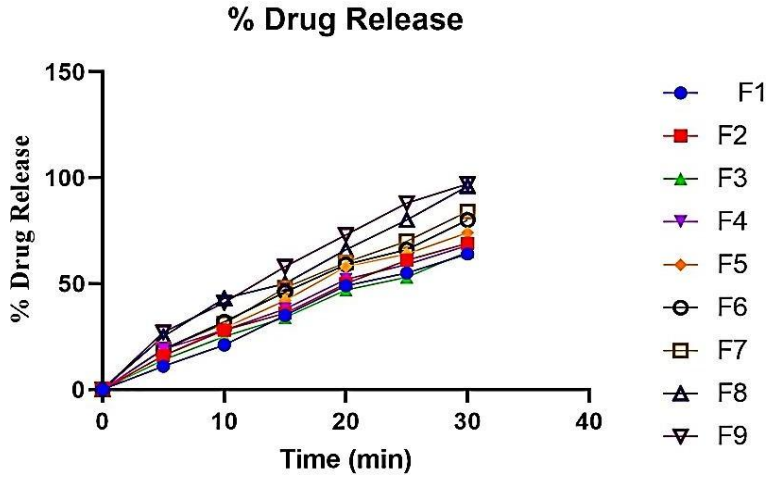


Figure.9 In vitro drug release data of Nimodipine immediate release tablets

Table.9 In vitro drug release data of Metoprolol sustained release tablets

Time(hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	18±3.99	14±3.45	16±3.51	29±3.68	19±4.03	16 ±4.02	15±3.38	10±3.37	9±3.90
2	40±3.46	38 ±4.14	28±4.07	38±3.72	39±3.72	32 ±3.61	20±3.64	18±3.99	15±3.68
3	56±3.14	59 ±3.78	49±3.54	54±3.58	48±3.80	41±3.94	31±437	26±3.42	26±3.42
4	78 ±4.44	72 ±3.45	61±3.92	79 ±4.45	61±4.19	59±4.55	42±4.11	37±3.98	32±4.20
5	85±3.83	83±4.42	75±3.96	94±3.83	80±3.27	73-±3.93	53±3.67	48±3.71	39±3.63
6	97 ±4.56	90±4.28	84±3.52		95±3.36	85±4.19	61±4.10	59±4.45	47±3.06
7		95±4.01	90±4.08			91±3.40	69±3.36	65±3.23	53±3.67
8			96±3.81			98±3.79	78±3.44	78±3.44	60±3.27
9							97±3.43	85±3.87	75±4.14
10								98±3.30	81±3.74
11									92±3.48
12									96±3.92

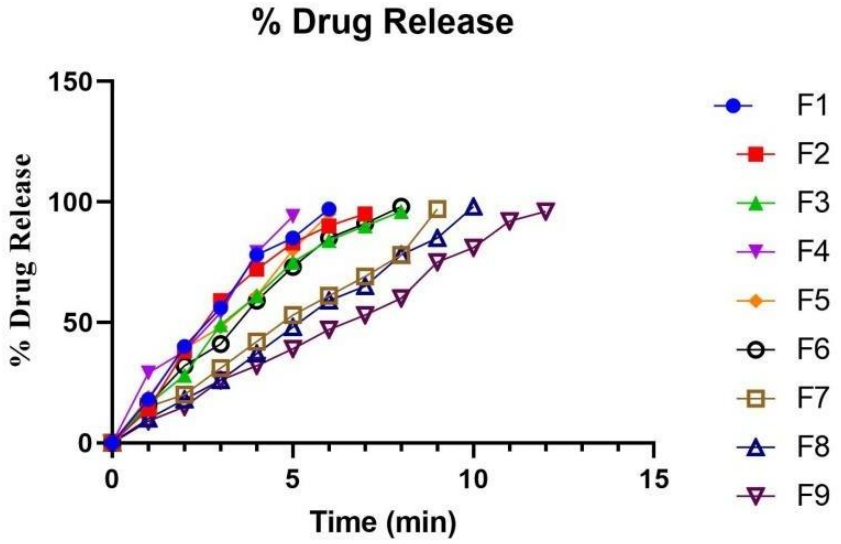
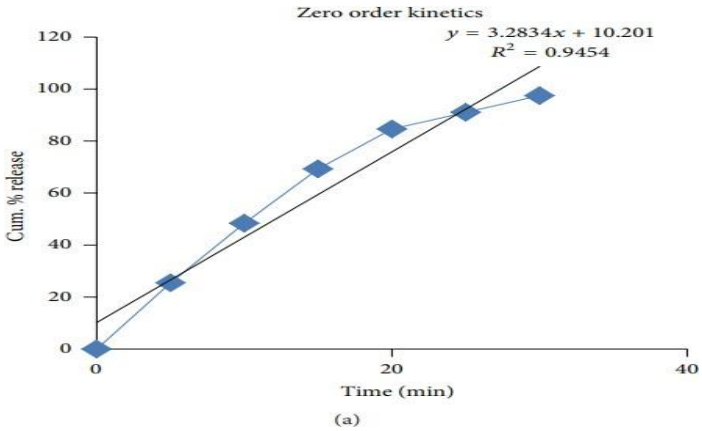


Figure.10 In vitro drug release data of Metoprolol sustained release tablets

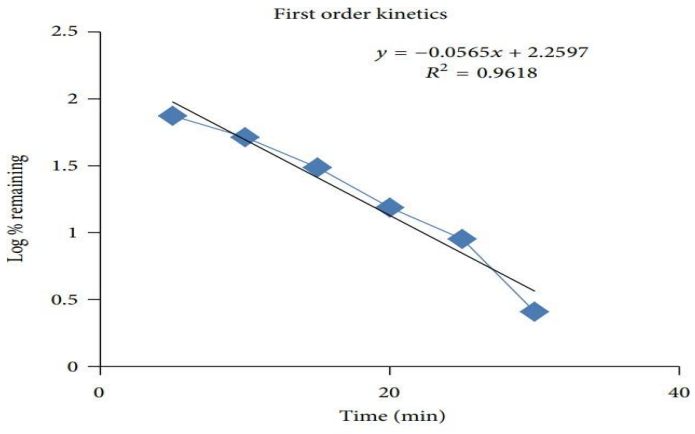
Evaluation of Bilayer Tablets

Bilayer tablets were prepared successfully after selecting the optimized formulation of immediate release layer (F8) and sustain release layer (F9) using 10 mm punches. The prepared bilayer tablets were evaluated for postcompression parameters and results were found to be within the limits mentioned in the above section and were shown in Table 9. In vitro drug release studies of bilayer tablets were carried out using USP dissolution apparatus type II in 500 mL of 0.1 N HCl for first 30 minutes and in 900 mL of 0.01 N HCl with 0.5% SLS up to 12 hours. From the results, drug release of Nimodipine immediate release layer was found to be 97.43% in 30 minutes and that of the Metoprolol sustain release layer was 97.22% at the end of 12 hours and % drug release of Metoprolol in first half hour was found to be 4.9%. It implies that the release of sustain release drug in the medium preferred for immediate release layer was found to be negligible and thus shows no irregularities in the drug release of bilayer tablet and values are represented.



(a)

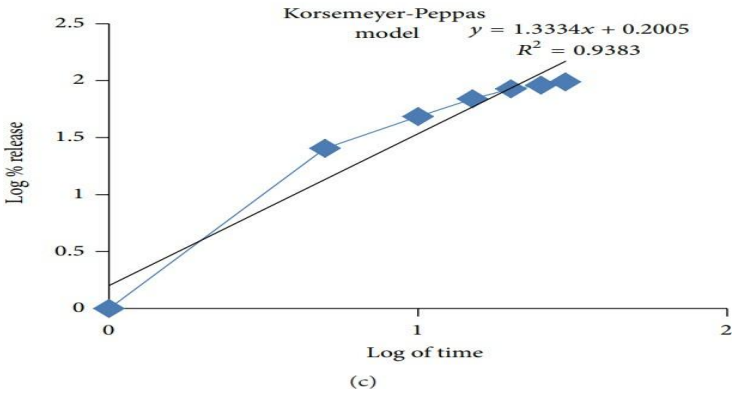
Figure.11 Zero order



(b)

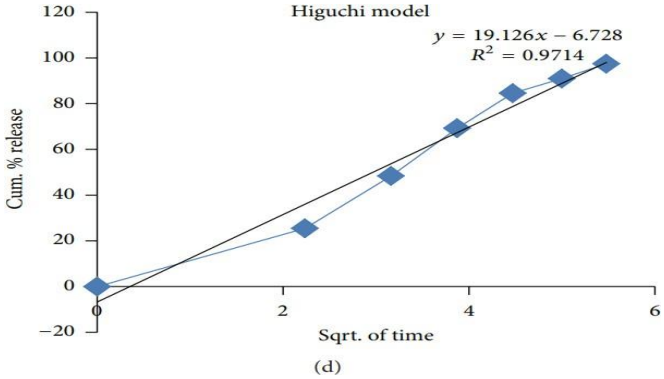
Figure.12 First order

(a)



(c)

Figure.13 Korsemeyer peppas model



(d)

Figure.14 Higuchi model

Table.10 Evaluation parameters of bilayer tablet

Name	Weight variation (%)	Hardness (kg/ cm²)	Thickness (mm)	Friability (%)
Bilayer tablet	0.54	6.5	5.36	0.48

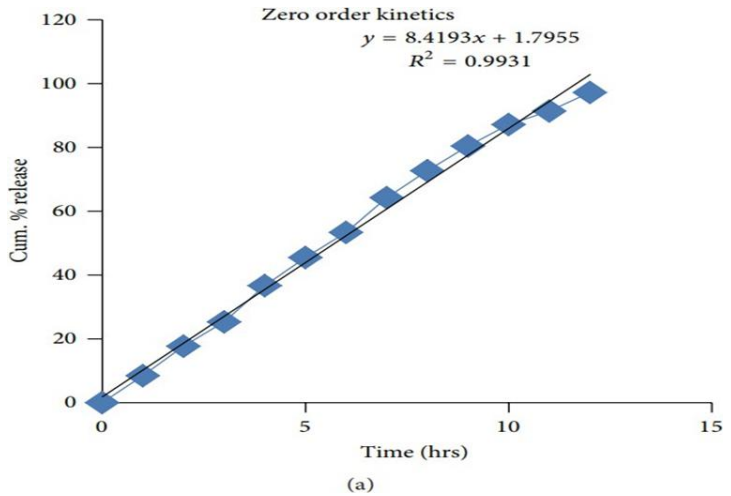


Figure.15 Zero order

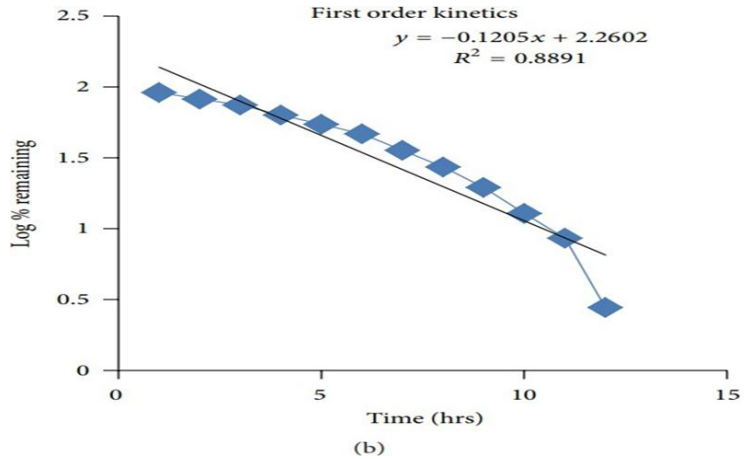


Figure.16 First order

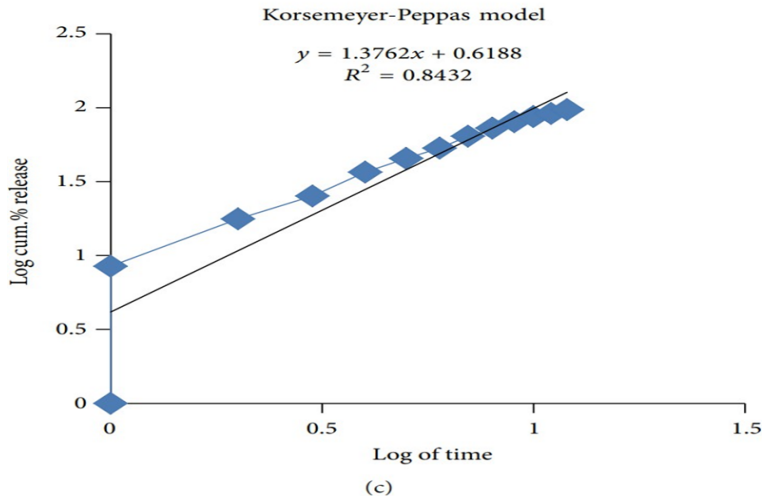
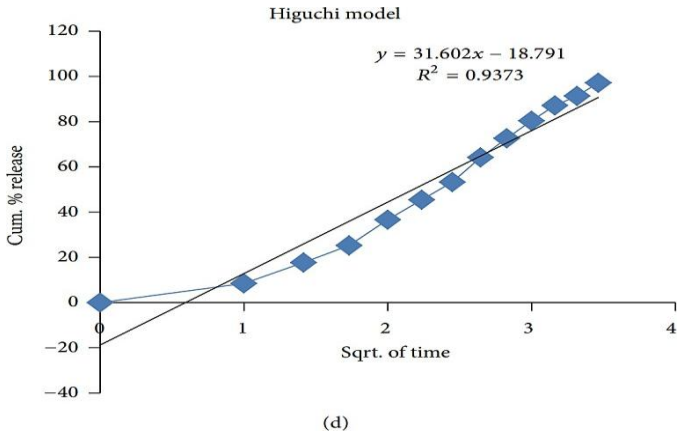


Figure.17 Korsemeyer-peppas model



(d)

Figure.18 Higuchi model

Kinetic Data Analysis

The drug release kinetic data of Nimodipine layer is shown in Table10 and graphs are represented.

From the graphical representation it can be understood that this layer is best fit in to Higuchi model which had shown a regression coefficient ($R2$) of 0.9714.The results of the in vitro release data of this layer were fitted to the Korsemeyer-Peppas equation given in Table 4 to analyze the release pattern of the drug from the polymeric system. The value of "n" was found to be more than 0.89, indicating the drug release follows super case-II transport. The drug release kinetic data of Metoprolol layer is shown in Table 19 and graphs are represented in Figure 11. From the graphical representation it can be understood that this layer is best fit in to zero order kinetics which had shown a regression coefficient ($R2$) of 0.9931. The results of the in vitro release data of this layer were fitted to the Korsemeyer- Peppas equation to analyze the release pattern of the drug from the polymeric system. The value of "n" was found to be more than 0.89, indicating the drug release follows super case-II transport.

Stability Studies

Table.11 Stability studies

S. number	Parameters	Initial 0 days	Conditions 40 ° C / 75 % RH		
			1 month	2 months	3 months
Bilayer tablet					
1	**Average weight (mg)**	450 ± 5.0	450 ± 5.0	450 ± 5.0	450 ± 5.0
2	**Hardness (kg / cm²)**	6.5 ± 0.5	6.5 ± 0.5	6.3 ± 0.5	6.0 ± 0.5
3	**Thickness (mm)**	5.36 ± 0.04	5.34 ± 0.05	5.34 ± 0.08	5.34 ± 0.08
Dissolution (Cumulative % drug release)					
4	**Nimodipine (30 min)**	97 ± 3.43	97 ± 3.15	96 ± 3.24	96 ± 3.65
	Metoprolol (12 hrs)	97 ± 3.22	97 ± 3.83	96 ± 3.67	96 3.48

Summary:

The present study aimed to formulate and evaluate an antihypertensive bilayer tablet containing Nimodipine and Metoprolol. The immediate release layer of Nimodipine was prepared using various super disintegrants, and the optimized formula (F8) contained sodium starch glycolate as a super disintegrant. The sustained release layer of Metoprolol was prepared using different release retarding agents, and the optimized formula (F8) contained a combination of HPMC and Xanthan gum as release retardants. The drug excipient compatibility studies using FTIR showed no interaction between drugs and excipients. Pre and post-compression studies were within official limits. In vitro release studies showed that Nimodipine immediate release layer in the bilayer tablet was 97.43% within 30 minutes, while Metoprolol sustained release layer was 97.22% at the end of 12 hours. Release kinetics showed good linearity, and stability studies revealed no changes in physical characteristics or drug release after exposing the tablets to accelerated conditions for three months. The study concludes that the prepared bilayer tablets achieve the research's objective in treating hypertension with the sequential release of two drugs. The tablets' twice-daily administration reduces the dosage frequency and is cost-effective, making them an alternative to conventional dosage forms that require more frequent administration.

Conclusion:

The study successfully formulated and evaluated an antihypertensive bilayer tablet containing Nimodipine and Metoprolol. The immediate release layer of Nimodipine and the sustained release layer of Metoprolol were prepared using different methods and optimized formulas. The drug excipient compatibility studies and pre and post-compression studies were within official limits. The in vitro release studies and release kinetics demonstrated good linearity. Stability studies showed no changes in physical characteristics or drug release after exposing the tablets to accelerated conditions for three months. The prepared bilayer tablets achieved the research objective in treating hypertension with the sequential release of two drugs. The tablets' twice-daily administration reduces the dosage frequency and is cost-effective, making them a potential alternative to conventional dosage forms that require more frequent administration.

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