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Der Pharmacia Lettre, 2014, 6 (6):403-414
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Formulation and evaluation of bilayerd floating tablet containing carvedilol and atenelol

M. Harikrishna[1*], Rajesh Akki[1], Munagala Gayatri Ramya[2], P. V. A. Neelima[1] and V. Vasu Naik[1]

[1]Department of Pharmaceutics, Hindu College of Pharmacy, Amaravathi Road, Guntur, India
[2]Departmnet of Pharmaceutics, University College of Pharmaceutical Sciences, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur

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ABSTRACT

The present study was to develop a bilayer floating tablet for Atenelol and Carvedilol using direct compression method. Bilayer floating tablets were designed to prolong gastric retention time and increase the bioavailability of the drug. Bilayer floating tablets made up of two layers, immediate release layer and controlled release layer. Immediate release layer contains sodium starch glycolate as a super disintegrating agent and controlled layer contains carbapol934p grade polymers and Ethyl cellulose as controlled release polymers .Sodium bicarbonate is used as a gas generating agent. The tablets were evaluated for physico-chemical properties such as bulk density, tap density, hausners ratio, hardness, thickness, friability, drug content, floating lag time, floating duration in vitro drug release by dissolution studies and stability studies . FT-IR studies revealed that there was no interaction between the drug and polymer used in the study. The optimized tablets B12 showed controlled and complete drug released 99.95% over a period of 24 hrs. And it follows zero order release and non-Fickian diffusion.

Key words: Atenelol and Carvedilol, carbapol934p, Ethyl cellulose, sodium starch glycolate, bilayer floating tablets, Buoyancy, *in vitro* drug release.

INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that has been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms[1].

Gastro retentive system can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of therapeutic agents. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment .gastro retention helps to provide better availability of new products with new therapeutic possibilities and strong substantial benefits for patients[2].

Floating drug delivery system have a bulk density lower than gastric fluids thus remain buoyant in the stomach for a prolonged period of time ,without affecting the gastric emptying rate .while the system is floating on the gastric contents, the drug is released slowly and almost completely at a desired rate form the system. After the release of the drug, the residual system becomes liable to be emptied from the stomach .this results in an increase in the gastro retentive time, bioavailability and a better control of fluctuations in the plasma drug concentrations. Thus floating drug delivery system is a safe and efficient technology for drug delivery.

Bilayer floating tablets are composed of two layers of granulation compressed together. They have appearance of a sandwich because the edges of each layer are exposed. Bilayer tablets are prepared with one layer of drug for immediate release with second layer design to release drug later, either as second dose or in a sustained release maner[3].

To get sustained release of the drug is aimed to decrease the dose dumping frequency and so its side effects. Sustained –release formulations may be administered once or twice daily. The multilayered tablet concept has been long utilized to develop sustained release formulations. Such a tablet has a fast releasing layer and may contain bi or triple layers to sustain the drug release. The pharmacokinetic advantage relies on the fact that drug release from fast releasing granules leads to a sudden rise in the blood concentration .However; the blood level is maintained at steady state as the drug is released from the sustaining granules. Among the different polymers, Ethyl cellulose and Carbapol934p have been used successfully to obtain appropriate sustained release matrix formulations[4].

Atenelol is an antihypertensive agent, atenelol compacts with sympathomimetic neurotransmitters such as catecholamine's for binding at beta (1)-adrenergic receptors in the heart and vascular smooth muscle, inhibiting sympathetic stimulation. This results in a reduction in resting heart rate, cardiac output, systolic and diastolic blood pressure, and reflex orthostatic hypotension. The drug also has relatively half life of 6-7 hours. So SR products are needed for Atenelol to prolong its duration of action and improve patient compliance[5].

Carvedilol is a beta-adrenergic receptor blocking ability decreases the heart rate, myocardial contractility, and myocardial oxygen demand. Carvedilol also decreases systemic vascular resistance via its alpha adrenergic receptor blocking properties. Therefore, Carvedilol and its metabolites may be beneficial in chronic heart failure by preventing free radical damage. Antihypertensive agent, Vasodilator Agent, Carvedilol is indicated in the management of congestive heart failure. An elimination half life of 6-10hrs.So IR products is needed for Carvedilol[6, 7].

MATERIALS AND METHODS

Carvedilol and Atenelol were provided as gift sample AD Life sciences, Hyd, India. Carbapol934P, PVP-K 30, Citric acid, Cross povidone, micro crystalline cellulose of analytical grade were purchased from Lobachemie Pvt Ltd, Mumbai. Magnesium stearate, hydroxyl propyl methyl cellulose, xanthum gum, Guar gum, Cross carmillose sodium. Of analytical grade were purchases from S.D Fine chemical, Mumbai. Ethyl cellulose were purchased from S.P Chemicals, Mumbai.

Methods

Preparation of bilayerd tablet; Bilayerd tablet of Atenelol and Carvedilol was developed in three different stages. Sustained release layer of Atenelol was prepared Carbapol934p, ethyl cellulose by direct compression technique. Immediate release layer of Carvedilol was prepared sodium starch gylcolate by direct compression technique[8,9].

Pre Compression Parameters:

Bulk density (D_b):

It is the ratio of mass of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder was carefully poured into graduated measuring cylinder through large funnel and volume was measured which is called initial bulk volume. Bulk density is expressed in gm/cc and is given by,

$$\mathbf{D_b = M / V_o}$$

Where, D_b = Bulk density (gm/cc)
M is the mass of powder (g)
V_o is the bulk volume of powder (cc)

Tapped density (D_t):

Ten grams of powder was introduced into a clean, dry 100ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and tapped volume was read. It is expressed in gm/cc and is given by,

$$\mathbf{D_t = M / V_t}$$

Where, D_t is the tapped density (gm/cc)
M is the mass of powder (g)
V_t is the tapped volume of powder (cc)

Compressibility index:
The compressibility of the powder was determined by the Carrs compressibility index.

Carrs index (%) = $[(D_b - D_t) \times 100]/D_t$

Angle of repose (θ)
It is defined as the maximum angle possible between the surface of pile of the powder and the horizontal plane. Fixed funnel method was used. A funnel was fixed with its tip at a given height (h), above a flat horizontal surface on which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of funnel.The angle of repose was then calculated using the formula,

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

Where, θ = angle of repose
h = height of pile,
r = radius of the base of the pile.

Post Compression Parameters:
Thickness and Diameter:
Control of physical dimension of the tablet such as thickness and diameter is essential for consumer acceptance and tablet uniformity. The thickness and diameter of the tablet was measured using Vernier calipers. It is measured in mm.

Hardness:
The Monsanto hardness tester was used to determine the tablet hardness. The tablet was held between a fixed and moving jaw. Scale was adjusted to zero; load was gradually increased until the tablet fractured. The value of the load at that point gives a measure of hardness of the tablet. Hardness was expressed in Kg/cm^2.

Friability (F):
Tablet strength was tested by Roche friabilator. Pre weighed tablets were allowed for 100 revolutions (4min), taken out and were deducted. The percentage weight loss was calculated by rewriting the tablets. The % friability was then calculated by,

$$F = \frac{(W_{initial}) - (W_{final})}{(W_{intial})} \times 100$$

Weight variation:
Randomly selected twenty tablets were weighed individually and together in a single pan balance. The average weight was noted and standard deviation calculated. The tablet passes the test if not more than two tablets fall outside the percentage limit and none of the tablet differs by more than double the percentage limit.

$$PD = \frac{(W_{avg}) - (W_{initial})}{(W_{avg})} \times 100$$

Where, PD = Percentage deviation, W_{avg} = Average weight of tablet, $W_{initial}$ = individual weight of tablet.

Disintegration time of Upper layer:
The disintegration time of upper layer was carried out by using disintegration test apparatus, using pH 1.2 Buffer

solutions as disintegration media, when all the upper layer of six tablets was completely disintegrated, the time was noted.

Swelling Index:
Swelling index of sustained release layer of the bilayer tablet is conducted by using USP dissolution apparatus-II in 900 ml of 0.1N HCl which is maintained at 37±0.5°C, rotated at 50 rpm. At selected regular intervals, the tablet is withdrawn the excess water was blotted with tissue paper. This procedure was repeated until the tablet reaches constant weight. The swelling index was calculated using following formula

% Swelling Index = {(W_t) – (Wo)/ (W_0)} x 100

Where
Wt is the weight of the swollen tablet, and
Wo is the initial weight of the tablet.

Buoyancy Studies:
The *in vitro* floating behavior of the tablets was studied by placing them in 900ml glass beaker filled with 900 ml of 0.1 N HCl (pH 1.2). The floating lag time (time period between placing the tablet in the medium and tablet floating) and floating duration of the tablets were determined by visual observation

Uniformity of drug content
A. Stock Solution: The assay for the drug content was carried out by weighing five tablets and calculated the average weight. Then the tablets were triturated to get a fine powder. From the resulting triturate weighed accurately powder which is equivalent to 100 mg of Carvedilol and Atenelol HCl in 100 ml of volumetric flask containing few ml of 0.1 N HCl and shake for some time and make Volume up to 100 ml with0.1 N HCl.

B. Stock Solution: Pipette out 10 ml from the stock solution 1 into another100 ml of volumetric flask and make up the volume with 0.1 N HCl. (i.e. 100µg / ml).

Aliquots: From the above solution withdraw quantity (as per Beers range i.e. 2-20 µg/ml) and the volume was making up to 10 ml with 0.1 N HCl. The absorbance was measured at 242-282 nm by using 0.1 N HCl as blank.

In-Vitro Release Study:
In-vitro drug release studies were carried out using USP II dissolution apparatus type II (Electrolab, Mumbai, India) at 50 rpm. The dissolution medium consisted of 900 ml of pH 1.2 acidic buffers, maintained at 37 $\pm$ 0.5^0 c. The drug release at different time intervals was measured using an ultraviolet visible spectrophotometer (Labindia, Mumbai, India) at 242 and 282 nm.

Kinetic Analysis of In-Vitro Release Rates of Bilayler Floating Tablets of Carvedilol and Atenelol [10]
The results of in vitro release profile obtained for all the formulations were plotted in modes of data treatment as follows:-
1. Zero – order kinetic model – Cumulative % drug released versus time.
2. First – order kinetic model – Log cumulative percent drug remaining versus time.
3. Higuchis model – Cumulative percent drug released versus square root of time.
4. Korsmeyer equation / Pappas model – Log cumulative percent drug released versus log time.

Zero order kinetics:
Zero order release would be predicted by the following equation:-

$$\mathbf{A_t = A_0 - K_0 t}$$

Where,
A_t = Drug release at time t.
A_0 = Initial drug concentration
K_0 = Zero – order rate constant (hr^{-1}).

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys Zero – order release kinetics, with a slope equal to K_0.

First Order Kinetics:
2First – order release would be predicted by the following equation:-

$\text{Log } C = \log C_0 - Kt / 2.303$

Where,
C = Amount of drug remained at time t.
C_0 = Initial amount of drug.
K = First – order rate constant (hr^{-1}).

When the data is plotted as log cumulative percent drug remaining versus time yields a straight line, indicating that the release follow first order kinetics. The constant K can be obtained by multiplying 2.303 with the slope values.

Higuchis model:
Drug release from the matrix devices by diffusion has been described by following Higuchis classical diffusion equation.

$Q = [D / (2 A - Cs) Cst]^{1/2}$

Where,
Q = Amount of drug released at time t.
D = Diffusion coefficient of the drug in the matrix.
A = Total amount of drug in unit volume of matrix.
Cs = the solubility of the drug in the matrix.
Cst = Porosity of the matrix.
t = Time (hrs) at which q amount of drug is released.

Above equation may be simplified if one assumes that D, Cs, and A, are constant. Then equation becomes:

$Q = Kt^{1/2}$

When the data is plotted according to equation i.e. cumulative drug release versus square root of time yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to „K (Higuchis 1963)

Korsmeyer equation / Peppa's model:
To study the mechanism of drug release from the sustained – release floating matrix tablets of cefixime, the release data were also fitted to the well – known exponential equation (Korsmeyer equation / Peppas law equation), which is often used to describe the drug release behavior from polymeric systems.

$M_t / M_a = Kt^n$

Where,
M_t / M_a = the fraction of drug released at time t.
K = Constant incorporating the structural and geometrical characteristics of the drug / polymer system.
N = Diffusion exponent related to the mechanism of the release
Above equation can be simplified by applying log on both sides, and we get:

$\text{Log } M_t / M_a = \text{Log } K + n \text{ Log } t$

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. For Fickian release n = 0.45 while for anomalous (non – Fickian) transport n ranges between 0.45 and 0.98. The result of in -vitro drug release study of all the formulation as shown below.

FTIR study:
FTIR spectra of the selected formulation were taken and compared with the spectrum of pure drug. The characteristic peaks of drug were checked in the formulation spectra.

Stability Studies[11]
Stability studies of pharmaceutical products were done as per ICH guide lines. These studies are designed to increase the rate of chemical or physical degradation of the drug substance or product by using exaggerated storage conditions.Selected formulations were stored at different storage conditions at elevated temperatures such as 25^{o}C± 2^{0}C / 60% ± 5% RH, 30^{0}C ± 2^{0}C / 65% ±5% RH and 40^{0}C ± 2^{0} / 75% ± 5% RH for 90 days. The samples were withdrawn at intervals of 30 days and checked for physical changes, hardness, friability, drug content.

In-vitro buoyancy studies: In-vitro buoyancy studies were performed for the formulations as per the method described by Rosa et. The randomly selected tablets from each formulation were kept in a 100ml beaker containing simulated gastric fluid, PH 1.2 as per USP. The time taken for the tablet to the surface and float was taken as floating lag time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time (TLT).

Release rate study: The release rate of Atenelol from floating tablets was tablet was determined USP dissolution testing apparatus type 1 (Basket method) and that of Carvedilol in USP dissolution testing apparatus type II. The dissolution test was performed using 900 ml of 0.1N hydrochloric acid, at 37± 0.5^{0} C and 50rpm.A sample (5ml) of the solution was withdrawn from the dissolution apparatus hourly and the sample were replaced with fresh dissolution medium. The sample were filtered through a 0.45µ membrane filter and diluted to a suitable concentration with 0.1N hydrochloric acid Absorbance of these solutions was measured at 282nm(Atenelol) and 242nm (for Carvedilol) using a UV/Visible spectrophotometer. The percentage of drug release was plotted against time to determine the release profile

.RESULTS AND DISCUSSION

All the formulations given in table 1 and 3 were formulated. Once daily dosage form of sustained release Atenelol and immediate release Carvedilol tablets were formed they were evaluated for various physical properties individually and the values are shown in the table and 7 respectively. As swelling polymers are used to sustain the release swelling indexes were obtained for 24 hrs . Figure 1 and 2 shows the dissolution profile of Atenelol sustained release tablets and Carvedilol immediate release tablet.

Table: 1 Formulation table of Carvedilol immediate release layer CFI-CF6

CONTENTS(mg)	CF1	CF2	CF3	CF4	CF5	CF6
Carvedilol	3.125	3.125	3.125	3.125	3.125	3.125
SSG	10	_	_	15	_	_
CP	_	10	_	_	15	_
CCS	_	_	10	_	_	15
PVPK30	10	10	10	10	10	10
Mg Stearate	5	5	5	5	5	5
MCC	171.75	171.75	171.75	166.75	166.75	166.75
TOTAL	200	200	200	200	200	200

TABLE:2 Precompression parameters of powder blend

Formulation code	Bulk density (gm/mL)	Tapped density (gm/mL)	Compressibility index(%)	Hausner's ratio	Angle of repose (^{0})
CF1	0.376	0.422	1.15	13.20	20.51
CF2	0.382	0.412	1.18	15.38	19.71
CF3	0.324	0.410	1.23	18.75	22.45
CF4	0.385	0.421	1.19	16.07	23.44
CF5	0.425	0.561	1.73	14.81	20.14
CF6	0.377	0.424	1.14	12.62	24.65

TABLE3: Post-compression parameters for immediate formulation

Formulation Code	Weight Variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)
CF1	200 ±2.54	3.93 ±0.023	3.23± 0.022	0.31
CF2	198 ±2.63	3.94± 0.019	3.23 ±0.041	0.16
CF3	196.4 ± 2.41	3.25 ±0.031	3.34 ± 0.027	0.24
CF4	199± 2.64	3.83± 0.013	3.43± 0.012	0.26
CF5	197± 2.43	3.84 ± 0.029	3.33± 0.031	0.22
CF6	198.4± 2.71	3.85 ±0.021	3.44± 0.017	0.34

TABLE 4: In vitro % Cumulative drug release (CF1-CF6)

Time(min)	CF1	CF2	CF3	CF4	CF5	CF6
5	21.26	25.99	14.76	22.81	18.4	18.6
10	26.28	34.56	39.28	29.4	29.3	41.2
15	48.14	37.51	52.87	39.8	38.4	58.6
30	62.32	69.45	75.02	60.9	60.8	74.8
45	72.16	87.4	93.98	80.4	68.3	89.2
60	89.24	85.7	91.87	99.96	87.4	93.98

Figure 1;-In-Vitro dissolution profile of formulation CF1-CF6

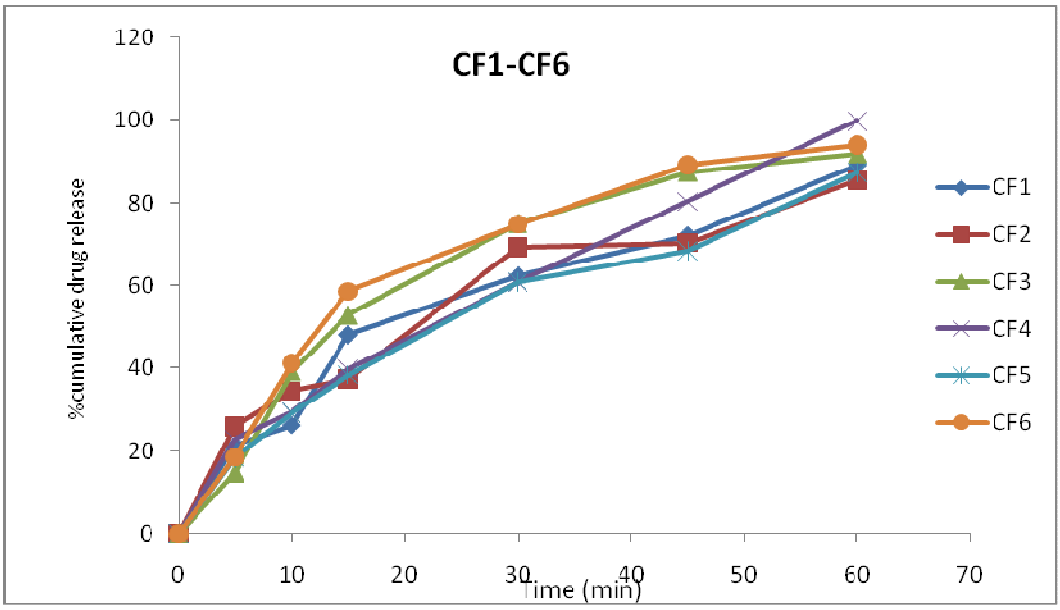


Table:5 Formulation table of Atenelol sustained release layer AF1-AF11

CONTENTS (mg)	AF1	AF2	AF3	AF4	AF5	AF6	AF7	AF8	AF9	AF10	AF11
Atenelol	50	50	50	50	50	50	50	50	50	50	50
HPMCK4M	60	_	_	65	_	_	75	_	_	90	_
Carbapol934	_	60	_	_	65	_	_	75	_	_	90
Guar gum	_	_	60	_	_	60	_	_	75	_	_
Ethyl cellulose	_	_	_	15	15	15	30	30	30	30	30
$NaHCO_3$	60	60	60	60	60	60	60	60	60	60	60
Mg stearate	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Citric acid	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Mcc	115	115	115	100	100	100	70	70	70	55	55
TOTAL	300	300	300	300	300	300	300	300	300	300	300

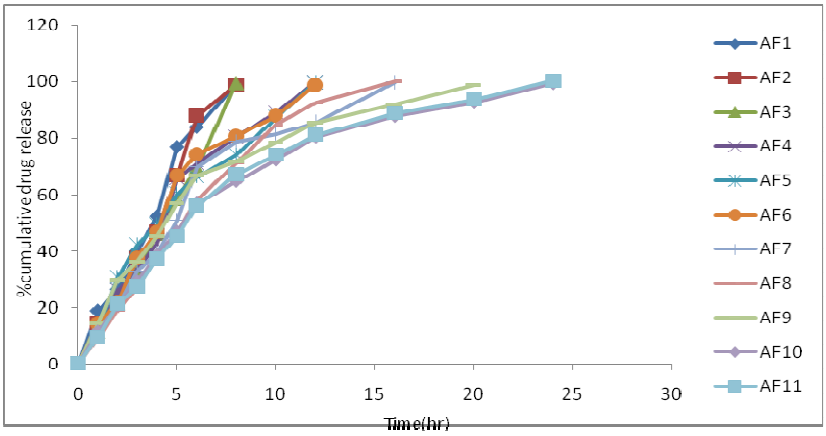
TABLE:6 Precompression parameters of powedr blend[8]

Formulation code	Bulk density	Tapped density	Compressibility index (%)	Hausner's ratio	Angle of repose
AF1	0.721±0.045	0.87± 0.01	17.126±0.6	1.206±0.06	26.62±0.21
AF2	0.710±0.043	0.873±0.04	19.714±0.7	1.251±0.04	27.46±0.11
AF3	0.41±0.045	0.483±0.5	15.113±0.8	1.178±0.08	28.32±0.31
AF4	0.45±0.045	0.52 ± 0.09	15.60±0.2	1.15±0.02	28.06±0.31
AF5	0.45±0.045	0.50 ± 0.07	12.23±0.6	1.11±0.04	27.58±0.15
AF6	0.44±0.044	0.50 ± 0.09	12.58±0.8	1.13±0.08	28.44±0.11
AF7	0.45±0.045	0.52 ± 0.09	15.60±0.2	1.15±0.02	28.06±0.31
AF8	0.41±0.04	0.42±0.05	15.1±0.8	1.1±0.08	28.3±0.31
AF9	0.37± 0.09	0.43± 0.4	12.65± 0.09	1.14±0.06	26.19±0.11
AF10	0.36± 0.04	0.42± 0.04	13.22± 0.09	1.15±0.04	25.49±0.12
AF11	0.33± 0.04	0.37± 0.2	12.40± 0.09	1.14±0.03	27.18±0.20

TABLE7: Post-compression parameters for immediate formulation

Formulation code	Avg. Weight (Mean± S.D) (n=20)	Hardness (kg/cm^2) (n=3)	Friability (Means) (n=20)	% Drug content (mg)	Buoyancy Lag time (min)	Total floating Time(hrs)
AF1	303±0.6	7.2±0.4	0.546	98±0.7	2	8hrs
AF2	300±0.9	7.5±0.4	0.612	99±0.5	2	8hrs
AF3	307±0.3	7.4±0.6	0.527	98±0.6	3	8hrs
AF4	301±0.8	7.3±0.1	0.511	99±0.6	1	>12hrs
AF5	306±0.8	7.6±0.6	0.525	99±0.6	30 sec	12hrs
AF6	304±0.8	7.3±0.4	0.555	98±0.5	3	12hrs
AF7	301±0.4	7.6±0.1	0.511	99±0.6	2	>16hrs
AF8	301±0.5	7.4±0.1	0.511	99±0.6	5	>16hrs
AF9	305±0.8	7.2±0.4	0.545	98±0.5	3	>20hrs
AF10	308±0.4	7.3±0.1	0.541	99±0.6	45sec	>24hrs
AF11	307±0.5	7.1±0.1	0.561	98±0.6	2	>24hrs

Figure :2-In-Vitro dissolution profile of formulation CF1-CF6



Compression of bilayer tablets:

For immediate layer of Carvedilol, we used sodium starch glycol ate as superdisintegrant. In above formulations CF1, CF2, CF3 Sodium starch glycolate was used in concentration of 5% and CF4, CF5, CF6 in concentration of 7.5% respectively. From it can be told formulation CF4 released 99.96% of drug with in 60min which is desirable. Hence Batch CF4 with 7.5% of sodium starch glycolate was selected.For sustained layer of Atenelol, we used polymers of carbapol934p (30%), Ethyl cellulose (10%) was used .Hence AF11 batch was selected.

Bi-layer tablets were prepared by direct compression method[12] the optimized formulations combining batch CF4-AF11 of immediate release layer with various formulations of controlled release layer. Batch CF4 showed disintegration time of 1min was selected for further studies. Sustained layer was compressed first followed by immediate release layer. The quantity of granules for sustained release layer was compressed lightly using 13 mm diameter die. Over this compression layer, required quantity of the immediate release layer was placed and compressed with a compressed force.

Table :8 - *In-Vitro* drug release profile of bilayerd tablet (B12)

TIME (hr)	B12
15mins	53.8
30mins	78.2
60mins	99.96
1	12.4
2	21.8
3	23.3
4	37.5
5	44.9
6	56.0
8	65.8
10	75.4
12	83.5
16	89.9
20	95.8
24	99.95

TABLE 9: All data of optimized batch

Parameters	**B12**
Friability (%)	0.56
Hardness(Kg/cm2)	6.23±0.05
Disintegration time (min)	1 min
Floating lag time(hrs)	90 sec
Total floating time (hrs)	24hrs
Swelling index (%)after 12hrs	142
Kinetics(values)	(0.956) Zero order
	(0.771) non-Fickian diffusion.
Drug release	
After 24 hrs	99.95

The drug release data of Atenelol and Carvedilol were fitted to models representing zero order, first order, higuchi's and koresmeyer's equation kinetics to know the the release mechanisms. The data were processed for regression analysis using MS EXCEL 2007statitical function [13, 14]

Table:10 Correlation coefficient (r2) of different kinetic model for formulation B12

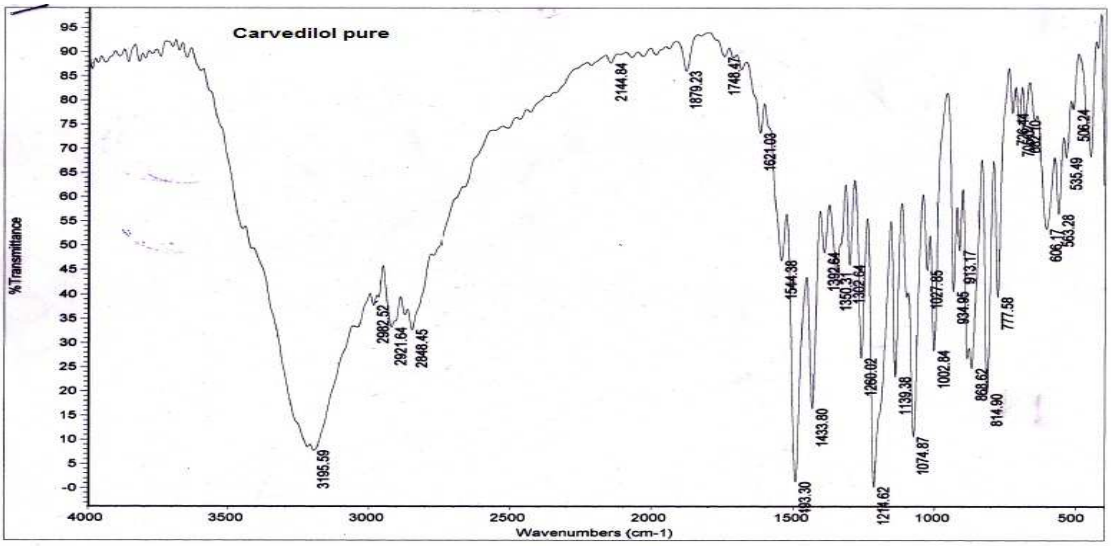
Formulation Cod	Zero order R^2	First order R^2	Higuchi R^2	Peppas	N
B12	0.956	0.731	0.932	0.756	0.771

Drug- excipients compatibility studies

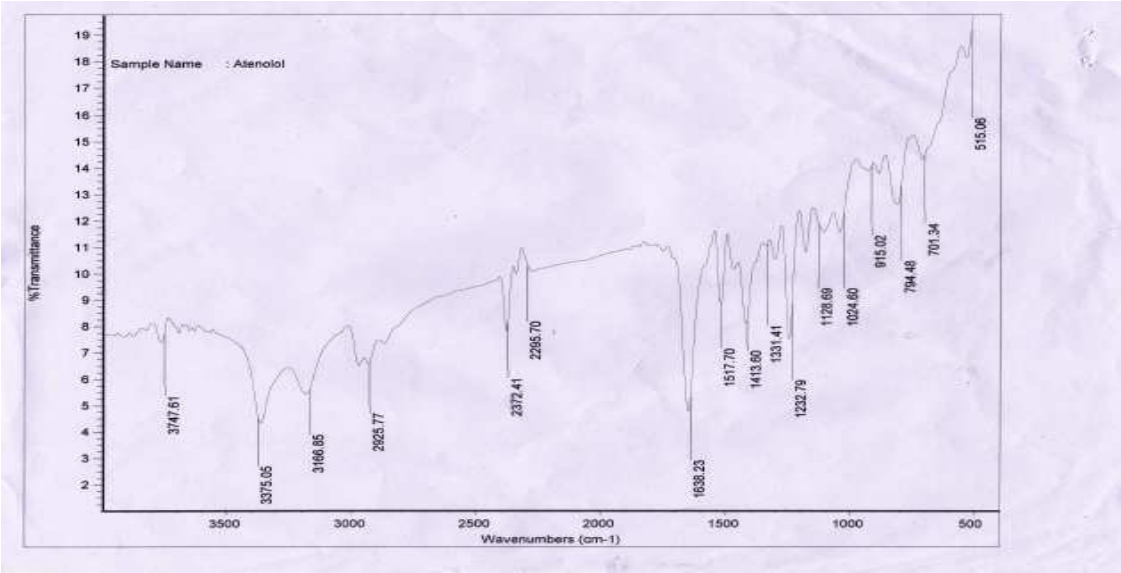
Carvedilol and Atenelol pure drug and the optimized tablet was subjected for FTIR spectroscopic analysis for compatibility studies and to ascertain whether there is any interaction between the drug and excipients used,

The FTIR spectra of the pure drug and formulation F indicated that characteristics peaks of Carvedilol and Atenelol were not altered including any change in their positions, no chemical interaction between the drug and carrier used.

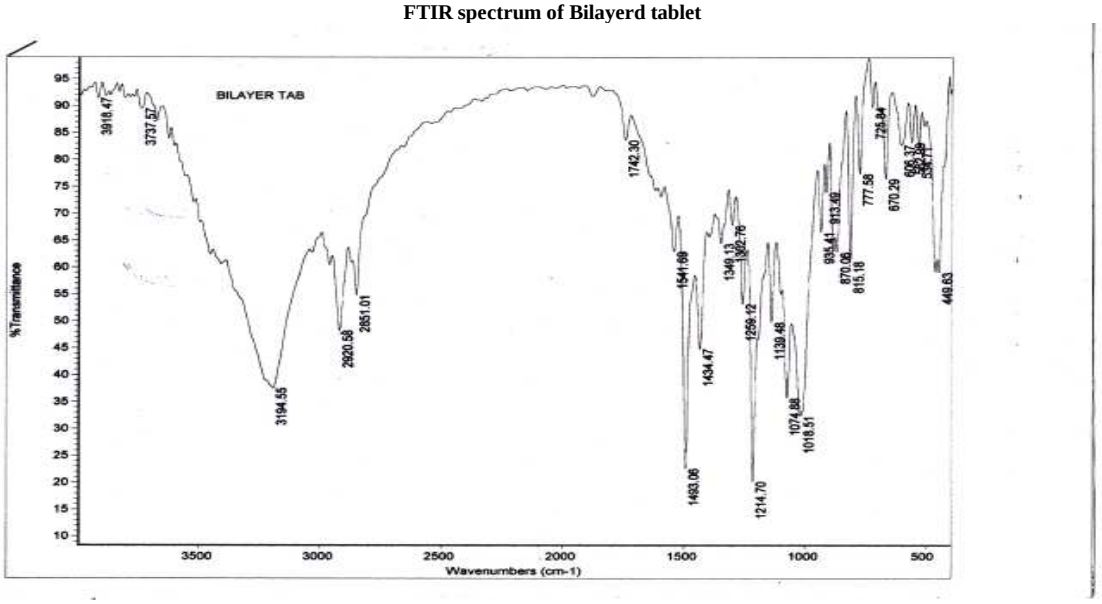
FTIR spectrum of Carvedilol pure drug



FTIR spectrum of Atenelol pure drug



FTIR spectrum of Bilayerd tablet



CONCLUSION

HPMCK4M, Guar gum and Carbapol934p were used as matrix polymer for the preparation of Atenelol sustained release layer which enabled drug release from 24hrs in different proportion of matrix polymers with near to zero order release profile. Carvedilol immediate release layer was prepared using sodium starch glycolate different proportion where 7.5% was found promising which disintetegtates completely with in 60mim .The core tablet of Atenelol in bilayerd tablet was prepared by direct compression and immediate release layer of Carvedilol was compression coated on it.

The optimized bilayerd tablet can be used as combination therapy for hypertension which reduces dosing frequency and improves patient compliance. Carvedilol release shows that the dissolution rate of Carvedilol can be enhanced considerably by using sodium starch glycolateas a super disintegrate.

SR fixed dose bilayer matrix tablets containing 50mg Atenelol as IR from one layer and 3.125mg Carvedilol as from another layer can be successfully formulated.

REFERENCES

[1] Deshpande A.A,shah N, H,Rhodes C T , Malick W, *Pharm.Res*.**1997**:14(6):815-819.
[2] Singh BM, Kim KH, *J,control. Rel*. (**2000**), 235-259.
[3] Aulton ME, Bilayer tablets in pharmaceutics,The science of dosage form design,Churchill livingstone,2nd edition ,(**2002**),414-418.
[4] Floating bi layer tablet technology:a review *Int. j.pharm.sci.Rev.Res*.,19(1)-**2003** :n0 112-122.
[5] DeLima Kharasch ED, Butler S (**1995**). *Anesthesiology* 83 (1): 204–207
[6] Metabolic and cardiovascular effects of Carvedilol and Atenelol hypertension Dario Glugliano ,MD Rita Acampora MD,Raffaela MD, Nicolete de Rosa MD,**1997**, 126(12) 955-959.
[7] Morgan T. *Clin Pharmacokinet*. **1994**; 26:335–46.
[8] Harikvaghasiya, niravsolanki,et., *Ph Tech Med* .vol-2,nov-dec **2013**.
[9] Prititagde, Nidhijain, A.K Pathak, *IJBAR*, **2012**
[10] Korsemeyer RW, PeppasNA. Macromolecular and modeling aspects of swelling – controlled Systems. In: Mansdrofsz, Roseman TJ, ad, Controlled Release Delivery systems. New – York, NY: Marcel Dekker; **1983**:77.
[11] ICH Q1A (R2) stability testing guidelines: stability testing of new drug substances and products. [Online]. **2003** [cited **2008** Nov10]; Available from: URLhttp://www.tga.health.gov.au/docs/pdf/euguide/inch/273699r2en.pdf.
[12] Fassihi RA, Ritschel WA, *J. Pharm sci*; **1993**; 82; 750-754.
[13] Peppas NA . *Pharm.ActaHeelv*.**1985**; 60; 110-111

[14] Korsmeyer RW,gurny R,Doelker E. *International journal of pharmaceutical sciences*.**1983**;15;25-35.