DESIGN AND *IN VITRO* CHARACTERIZATION OF GASTRO-RETENTIVE BILAYER FLOATING TABLET OF METOPROLOL TARTRATE

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ABSTRACT

The purpose of the study is to develop a bilayer floating tablet of Metoprolol Tartrate by direct compression method and compare the effect of synthetic and natural polymers alone as well in combination on drug release. The dosage form deliver the drug in two phases i.e., immediate release and sustained release. Metoprolol tartrate is an anti-hypertensive agent act on β_1-adrenergic receptors (blockade effect) having half life 3-4hrs, which necessitates the administration twice a day in 25/50 mg. The polymers used are HPMC K4M, K15M, Ethyl cellulose and Xanthan gum, Guar gum, as gel forming agents and sodium bicarbonate and citric acid as effervescent base. The prepared tablets were characterized by hardness, drug content, floating lag time, total floating time, swelling index, *in vitro* drug release(0.1N HCl), stability studies and FT-IR. The best formulation F-7 formulated using HPMC K15M and Xanthan gum exhibited satisfactory physical parameters and good *in vitro* buoyancy. If this dosage form is retained in the stomach for about ~20hrs maximum absorption of Metoprolol Tartrate can be achieved. The FT-IR studies showed good compatibility of the ingredients and the short term stability studies conducted at 45±1ºC and 75RH over a period of three months indicate the difference in spectrum shift as negligible.

Keywords: Metoprolol Tartrate, HPMC K4M, K15M, EC, Xanthan gum, Guar

INTRODUCTION

The oral route represents the predominant and most preferable route for drug delivery. Oral drug delivery systems (DDS) are divided into immediate release and modified release systems. Immediate release DDS are intended to disintegrate rapidly, and exhibit instant drug release. They are associated with a fast increase and decrease, and hence fluctuations in drug plasma levels, which leads to reduction or loss in drug effectiveness or increased incidence of side effects. Administration of the DDS several times per day is therefore necessary to compensate the decrease in drug plasma concentration due to metabolism and excretion.

Modified release systems, on the other hand, have been developed to improve the pharmacokinetic profiles of active pharmaceutical ingredients (APIs) and patient compliance, as well as reducing side effects (Eisen et al., 1990; Getsios et al., 2004; Sansom, 1999). Oral modified release delivery systems are most commonly used for 1) delayed release (e.g., by using an enteric coating); 2) extended release (e.g., zero-order, first-order, biphasic release, etc.); 3) programmed release (e.g., pulsatile, triggered, etc.) and 4) site specific or timed release (e.g., for colonic delivery or gastric retention). Extended, sustained or prolonged release drug delivery systems are terms used synonymously to describe this group of controlled drug delivery devices, with predictability and reproducibility in the drug release kinetics (Longer and Robinson, 1990).

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One of the novel approaches in the area of oral sustained release drug delivery is gastroretentive drug delivery system (GRDDS). Drugs those are having a narrow absorption window and having more solubility in gastric region are suitable candidates for GRDDS. GRDDS prolongs the retention time of dosage forms in the stomach or upper gastrointestinal tract, as to improve solubility, bioavailability and the therapeutic efficacy of the drugs.

Several techniques have been proposed to increases the gastric residence time of dosage forms such as buoyancy or floating system3, hydrodynamically balanced system4, expanding or swelling system, bio/mucoadhesive system5, sedimentation or high density system, geometry or modified shape system may also use to increase gastric residence time. The biphasic system is used mostly when maximum relief needs to be achieved quickly followed by a sustained release phase. It also avoids repeated administration of drug. Coronary vasodilator, antihypertensive, antihistaminic, analgesic, antipyretics and antiallergenic agents are mainly used for this system. The biphasic system may contain one or two drugs for immediate release and sustained release layer.

Metoprolol tartrate (MT) is a β1-selective adrenergic blocking agent. When MT conventional tablets are administered with food rather than on an empty stomach, peak plasma concentrations are higher and the extent of absorption of the drug is increased. The maintenance of a constant plasma level of a cardiovascular drug is important in ensuring the desired therapeutic response. Since the half-life of MT is ~3 to 4 hours, multiple doses are needed to maintain a constant plasma concentration for a good therapeutic response and improved patient compliance.

It has also been reported that MT absorption in the duodenum and jejunum is directly proportional to the dose availability. The objective is to study the influence of different synthetic and natural polymers on drug release kinetics and buoyancy of floating tablets containing different model drugs. Developing oral controlled release tablet for highly water-soluble drugs with constant release rate has always been a challenge to the pharmaceutical technologist. Most of these highly water soluble drugs, if not formulated properly, may readily release the drug at a faster rate and are likely to produce the toxic concentrations, when administered.

MATERIALS AND METHODS:
Materials:

MT obtained from SD fine chemicals, Mumbai, HPMC K4M, HPMC K15M from Cadila Pharma, Ahmadabad, Xanthan gum, Guar gum, Micro crystalline cellulose (Direct compressible grade) from Ozone international, Mumbai, Sodium bicarbonate from Moly chem, Mumbai, Crospovidone from SD fine chemicals, Lactose from Signet chemicals, Mumbai, Magnesium stearate, Talc from Lobachemie, Mumbai.

METHODS:
Formulation of bilayer floating (BLF) tablet of MT:

Bilayer floating tablets contain two layers i.e. immediate release layer and floating sustained release layer.

Optimization of immediate release (IR) layer:

The immediate release layer prepared by blending the drug with different concentrations of super- disintegrating agent as (Crospovidone 4, 5, 6%) and other excipients lactose, micro crystalline cellulose, magnesium stearate and talc. The physical mixture then compressed by direct compression method for preliminary studies to optimize the immediate release formulation using 8mm die in 12 station Cemach tablet compression machine. Three formulas were made in order to achieve desired disintegration time and drug release.

Formulation of floating sustained release (SR) layer:

The floating SR layer prepared by weighing required quantities of drug, polymer(HPMC K4M,

HPMC K15M, Ethyl cellulose, Xanthan gum, Guar gum), effervescent base (sodium bicarbonate, citric acid) and passing through #40 mesh and mixing in a poly bag for about 5-10 min and taken into a mortar.

To that mixture micro crystalline cellulose, Magnesium stearate, talc were added and mixed thoroughly. Formulation composition of all batches given in the table no.1.

Ingredients	Formulation code									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
IR3	100	100	100	100	100	100	100	100	100	100
MT	40	40	40	40	40	40	40	40	40	40
HPMC K4M	110	150	---	---	---	---	---	---	---	---
HPMC K15M	---	---	110	150	---	---	98	12	98	12
Xanthan gum	---	---	---	---	110	---	12	98	---	---
Guar gum	---	---	---	---	---	110	---	---	12	98
Ethyl cellulose	10	10	10	10	10	10	10	10	10	10
NaHCO$_3$	30	30	30	30	30	30	30	30	30	30
Citric acid	5	5	5	5	5	5	5	5	5	5
MCC	45	5	45	5	45	45	45	5	45	5
Magnesium stearate	5	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5	5
Total	350	350	350	350	350	350	350	350	350	350

Table 1: Formulation composition of all batches of Metoprolol tartrate (MT)

BLF tablets were prepared by direct compression method using 9mm flat faced punch of 12 station Cemach compression machine. First the mixture of floating SR layer was poured into the die cavity and compressed. Then the upper punch lifted and punches are drawn back to the feed place and contents of immediate release layer were placed in the die cavity over the floating layer tablet and compressed with optimum compression strength to produce bilayer floating tablets.

Drug - Excipients compatibility study:

Sample Preparation

Each excipients used in the formulations was blended with the drug level that are realistic with respect to the final dosage form. Each excipient was thoroughly blended with drug to increase drug-excipient molecular contacts to accelerate the reactions known mass of blends on a mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the drug in the cylinder and this minimum volume, the tapped density may be computed.

Tapped Density= weight of the blends/Tapped Volume of blend

If possible each drug excipients blend was taken separately into vials and kept for one month and two months study at 40°C. After that, each blend was tested for stability by physical observation.

I.R Spectroscopy:

Metoprolol tartrate discs were prepared by pressing the MT with potassium bromide and the spectra between 4000^{-1}cm 400^{-1}cm was obtained under the operational conditions. The absorption maxima in spectrum obtained with the substance being examined correspond in position and relative intensity to those in the reference spectrum represented

EVALUATION OF BLF TABLETS

Hardness test:

The crushing strength (Kg/cm^2) tablets were determined by using Monsanto hardness tester. In all the cases, means of six replicate determinations were taken. The results are given in table 4.

Thickness:

Thickness of the tablet was measured by using Vernier calipers in mm. Thickness of fabricated tablets is presented in table 4.

Weight variation:

The weight (mg) of each of 20 individual tablets was determined by dusting each tablet off and placing

it in an electronic balance. The weight data from the tablets were analyzed for sample mean and percent deviation. The results are summarized in table 4.

Friability test:

This was determined by weighing 10 tablets after dusting, placing them in the friabilator and rotating the plastic cylinder vertically at 25 rpm for 4 min. After dusting, the total remaining weight of the tablets was recorded and the percent friability was calculated according to:

Percentage Friability = (W1 – W2)/W1 * 100

Uniformity of drug content:

The test for uniformity of content should be carried only after the content of active ingredient in a pooled sample of tablets has been shown to be within accepted limits of the stated content. 5 tablets were taken and their content was determined by UV spectrophotometry.

$$Drug\ content = \frac{Amount\ in\ test}{Amount\ in\ standard} \times 100$$

Buoyancy determination:

In practice floating time and buoyancy lag time was determined by using beaker containing 100 ml of 0.1N HCl, which was maintained at 37ºC. The time required for the tablet to rise to the surface of the medium was determined as Buoyancy Lag time and the duration of which the tablet floats on the surface of the medium was noted as the Buoyancy floating time. Results presented graphically in Table 5.

Swelling Index:

The individual tablets were weighted accurately and kept in 50 ml of water. Tablets were taken out carefully after 60 minutes, blotted with filter paper to remove the water present on the surface and weighed accurately. Percentage swelling (swelling index) was calculated by using the formula: The results are shown in table 6.

$$Swelling\ index = \frac{Wet\ weight - Dry\ weight}{Dry\ weight} \times 100$$

In vitro dissolution studies:

In vitro dissolution studies were carried out in USPXXIII tablet dissolution test apparatus-II (Electrolab), employing a paddle stirrer at 50 rpm using 900ml of 0.1N HCl at 37±0.5ºC as dissolution medium. One tablet was used in each test. At predetermined time intervals 5ml of the samples were withdrawn by means of a syringe fitted with a pre filter. The volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium maintained at 37±0.5°C. The samples were analyzed for drug release by measuring the absorbance at 275 nm using UV-Visible spectrophotometer after suitable dilutions. All the studies were conducted in triplicate.

Model dependent approach:

The results of in vitro release profiles obtained for all the BLF tablet formulations were fitted into four models of data treatment as follows:

1. Cumulative percent drug released versus time (zero-order kinetic model). $Q = Q_0 - K_0 t$

2. Log cumulative percent drug remaining versus time (First-order kinetic model). $\ln Q = \ln Q_0 - K_0 t$

3. Cumulative percent drug released versus square root of time (Higuchi's model).

$$Q = \left[\frac{D\varepsilon}{\tau} (2A - \varepsilon C_s) C_s t \right]^{1/2}$$

4. Log cumulative percent drug released versus log time (Korsmeyer-Peppas equation). $Q = K2t^{1/2}$

Model independent approach:

According to US FDA guidance for dissolution data equivalence, model independent approach is recommended. This involves the use of similarity (f_2) and dissimilarity factor (f_1) which provides simple means to compare the dissolution data summarized in the table 10.

Drug polymer interaction studies:

There is always a possibility of drug polymer interaction in any formulation due to their intimate contact. The technique employed in the present study for this purpose is IR spectroscopy. IR spectroscopy is one of the most powerful analytical techniques, which

offers the possibility of chemical identification. The IR spectrum of MT and formulation were obtained by KBr pellet method employing Perkin-Elmer FTIR 1516 series.

Stability studies:

Short-term stability studies were performed at a temperature of 45°±1℃ over a period of three months on the promising BLF tablet formulation BLF7. At the end of three months period, dissolution test and *in vitro* floating studies were performed to determine the drug release profiles, *in vitro* floating lag time and floating time. The FT-IR studies were also conducted on the optimized formulation.

RESULTS AND DISCUSSION

Preformulation studies:

In the present study direct compression method was adopted for tabletting. Hence the physical mixture of drug and excipients should possess good flow and compaction properties. Plain MT exhibited angle of repose 36.02±0.15º indicating poor flow property. It was further supported by high compressibility index value 23.1±0.19% and Hausner's ratio 1.30±0.05. The drug mixed with flow promoters diluents and lubricants to improve flow property. The blend in which MCC used in higher concentrations, angle of repose found between 30-33º, indicates passable flowability. This property may be attributed due to the presence of filamentous particles of MCC. The Carr's index and Hausner's ratio were in the range of 10-20% and 1.12-1.23 respectively, indicates good flowability. The values tabulated in the table no.2

Formulation code	Bulk density	Tapped Density	Carr's index (%)	Hausners Ratio	Angle of Repose(˚)
MT	0.53±0.24	0.69±0.04	23.1±0.19	1.30±0.05	36.02±0.15
F1	0.35±0.09	0.44±0.61	20.6±0.3	1.14±0.12	30.8±0.25
F2	0.37±0.49	0.43±0.07	13.9±0.11	1.16±0.09	28.1±0.08
F3	0.32±0.14	0.39±0.17	17.9±0.41	1.22±0.3	31.6±0.09
F4	0.37±0.07	0.42±0.13	11.9±0.05	1.13±0.11	27.9±0.12
F5	0.34±0.16	0.41±0.44	17.01±0.23	1.21±0.07	31.2±0.16
F6	0.35±0.1	0.43±0.45	18.6±0.42	1.23±0.31	30.9±0.08
F7	0.38±0.46	0.46±0.34	17.39±0.22	1.21±0.15	31.1±0.02
F8	0.36±0.7	0.43±0.14	16.3±0.1	1.19±0.1	29.9±0.18
F9	0.39±0.42	0.48±0.19	18.75±0.01	1.23±0.14	30.8±0.04
F10	0.33±0.51	0.39±0.15	15.4±0.23	1.18±0.19	30.9±0.08

Physico- chemical evaluation of bilayer floating tablets:

The prepared tablets were evaluated for their various physico chemical properties. The tablets were white, circular in shape and were found to be uniform with respect to hardness (4.5-5.2 kg/cm²) and thickness (4.02-4.16mm). The weight variation (1.08-3.12%) and friability (0.1-0.27%) of different batch of tablets were found within acceptable limits. Drug content (99.08-100.04%) was found uniform within the batches of different tablets. The results of physico-chemical evaluation of tablets are given in table no.3

Formulation code	Hardness (kg/cm²)	Thickness (mm)	Weight variation (%)	Friability (%)	Drug content (%)	Floating lag time (sec)	Total floating time (hr)
F1	4.5±0.24	4.12±0.05	2.55	0.3	99.32	35	~24
F2	5.1±0.18	4.08±0.54	1.08	0.19	99.97	45	~24
F3	5.0±0.54	4.16±0.02	3.06	0.26	99.12	39	~24
F4	5.2±0.05	4.02±0.42	2.85	0.12	99.94	47	~24
F5	5.1±0.15	4.09±0.15	2.45	0.1	99.08	110	~18
F6	4.9±0.64	4.15±0.18	1.76	0.27	99.43	125	~18
F7	5.1±0.14	4.15±0.05	2.42	0.16	100.92	48	~20
F8	5.1±0.05	4.09±0.12	3.12	0.19	99.03	75	~20
F9	5.0±0.15	4.11±0.06	2.73	0.24	100.04	79	~20
F10	5.1±0.08	4.15±0.15	1.83	0.14	99.07	98	~20

BUOYANCY DETERMINATION:

The *in vitro* buoyancy studies in SGF pH 1.2, revealed good buoyancy for all formulations (Table 4. Citric acid and sodium bicarbonate combination used as the effervescent base upon contact with the acidic medium, the fluid permeated into the tablet, causing neutralization reaction to occur, which generates CO_2. The swelling polymer traps the CO_2 generated and thus provides continued buoyancy. Preliminary studies were done to estimate the ideal amount of the effervescent base needed to obtain short floating lag time together with prolonged buoyancy. This revealed that citric acid and sodium bicarbonate in the amount 5mg and 30 mg were optimum for the desired formulation to provide good buoyancy with floating lag time less than 2min. All the tablets floated in the buffer solution for more than 12hr. The gas generating base decreases the lag time by accelerating the hydration of the swelling polymer, thus allowing a higher floating duration because of constant generation and subsequent trapping of CO_2. Citric acid was used to accelerate the CO_2 generation and also it permits the generation of CO_2 even if the gastric pH is abnormally high.

The tablets were found to float up to 24 hrs. The incorporation of the natural gums such as Xanthan gum and guar gum reduced the total floating time of the tablet. The floating lag time was varied for different batches depending on the polymer used. The lag time for batches F5 & F6 was high due to the high density of the natural gums.

Swelling index:

Investigation of polymer swelling is a valuable exercise to better understand the mechanism of release and relative importance of participating parameters. Swelling ratio describes the amount of water that is contained within the hydrogel at equilibrium and is a function of network structure, hydrophilicity and ionization of functional group. Swelling study was performed on all the batches for about 24hrs. It was concluded that as the viscosity of hydrophilic polymer increased the water uptake of

tablets was increased which results in increasing of swelling index. At the same time concentration of HPMC also having similar impact on the swelling property of the formulation i.e, as the concentration of HPMC increased the swelling index was increased accordingly.

Formulation code	Swelling index (n=3) (%)
F1	82±2.6
F2	98±6.9
F3	91±4.6
F4	109±3.2
F5	79±2.5
F6	76±1.6
F7	80±4.5
F8	95±3.6
F9	90±1.2
F10	105±5.1

In vitro disintegration studies:

The most important parameter that is needed to optimize during the development of immediate release tablet is disintegration time. Disintegration time is very important for an IR tablet which is desired to be less than 60sec. in the present study three formulations IR1-IR3 containing crospovidone disintegrated in 30, 26 and 21sec respectively. Crospovidone when it comes in contact with water quickly wicks water into the tablet through capillary action to create internal pressure that disintegrates tablet. The results are tabulated in the table 7.

Formulation code	Disintegration time (sec)
IR1	30
IR2	26
IR3	21

Table no.5: *In vitro* disintegration time of MT IR tablets

In vitro dissolution studies:

The *in-vitro* dissolution study of formulations F1, F2, F3 & F4 were done in 0.1N HCl and the percent of drug release from formulations found to be 99.7, 97.24, 97.34 & 93.48 respectively. Various grades of **HPMC i.e, K4M & K15M** were used, because the HPMC fail to retard the release of drug through the matrix due to its solubility in stomach pH; so Ethyl

cellulose was incorporated in the formulations to maintain the integrity of the tablet matrix and to reduce the floating lag time. Different viscosity grades show good floatability due to the low density, so the viscosity grades were chosen arbitrarily.

It is clear from the figures that the formulations showed biphasic release of MT. In the first phase, the first fraction of the dose (immediate release layer) was released in less than 30 min, because of prompt disintegration of the immediate release layer and the enhanced rate of dissolution of MT from the system. This behavior was identical for all the formulations. The formulation F1 was unable to sustain the drug release for a desired period of time; may be due to the low viscosity of K4M. But the formulation F2 was able to retain the drug release up to 12hr; since the concentration of the polymer is high this cannot be chosen as optimized one. The formulations F3 & F4 was able to retard the drug release for the desired period of time. As the percent drug release from the formulation F3 is more satisfactory than the F4; it was chosen as the optimized formulation.

The present work is focused on the Comparision of drug release from combination of synthetic and natural polymers, for the comparative study the drug release from the natural polymers alone is performed by formulating F5 & F6 using **Xanthan gum & Guar gum** respectively. The polymer to drug ratio was chosen based on the formulation F3. The cumulative percent drug release from the BLF tablets of the formulations F5 & F6 was found to be 93.37 & 89.91 respectively. When used alone the natural polymers due to the high density were not able to float rapidly so, the formulations were further modified and prepared in combination with the low density polymer HPMC K15M.

The formulations F7, F8, F9 & F10 formulated in **combination of HPMC K15M and natural gums (Xanthan gum & Guar gum)**. The cumulative drug release from these formulations was reported as 94.01, 93.45, 92.04 & 90.04 respectively.

There is an increase in the percent drug release when used in combination with synthetic polymers than the natural polymers alone. The formulation F7 was chosen as optimized when compared to other three formulations because of its good flowability, floating lag time, total floating time. From the above results it was observed that as the concentration of the polymer increased, there is a decrease in the drug release rates due to the increased diffusion path (tortuosity). But there was no significant difference observed with the change of polymer grade.
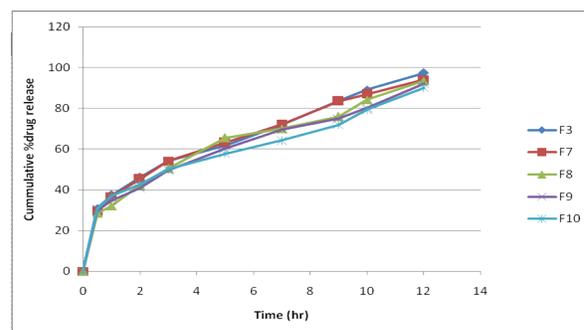

Figure no.1: Comparative dissolution profile of combination formulations (F7-F10) with F3

S. No.	Sampling time (hr)	F3	F7	F8	F9	F10
1	0.5	30.94	29.4	28.45	29.94	30.71
2	1	37.48	36.72	32.15	34.81	37.02
3	2	46.19	45.32	42.25	40.95	42.62
4	3	54.12	54.16	50.49	49.64	50.09
5	5	61.57	63.25	65.49	60.15	57.64
6	7	71.85	71.95	70.04	69.54	64.28
7	9	83.64	83.45	75.95	74.92	71.94
8	10	89.05	86.94	84.15	80.15	79.26
9	12	97.34	94.01	93.45	92.04	90.04

Table no.6: Comparison of Cumulative %drug release of MT floating bilayer tablets

Model dependent approach:

To investigate the mechanism of drug release from bilayer floating tablets, various kinetic models like zero order, first order, Higuchi, Korsmeyer- Peppas equations were applied to the *in vitro* release data obtained from different formulations. From the observations it was concluded that the optimized formulation (F7) was best explained by the Korsmeyer- Peppas equation, as the plots showed

highest linearity (R²=9941), followed by Higuchi (R²=0.9829), first order (R²=0.9748), Zero order (R²=0.8820). The drug release was proportional to the square root of time indicating that the drug release from all the formulations was diffusion controlled. The kinetic release data also suggest the diffusion mechanism to be Fickian diffusion since it indicates a good linearity (R²=0.9941) and the release exponent

(n) value was found to be 0.360. The results of kinetic study are shown in table 7.

Model independent approach:

The f_1 value of all the combination formulations were calculated and entered in the table 10. The difference factor of the formulation F7 with respect to F3 found to be 1.153, which is very near to 0 when compared with the other formulations. So, the formulation F7 considered as the optimized formulation.

Table no.7: Drug release kinetics

Formulation code	Zero order (R²)	First order (R²)	Higuchi (R²)	Korsmeyer Peppas(R²)	Peppas (n)
F1	0.9309	0.7811	0.9929	0.9920	0.344
F2	0.9680	0.9835	0.9981	0.9925	0.346
F3	0.8907	0.9780	0.9860	0.9608	0.347
F4	0.9062	0.9633	0.9801	0.9726	0.351
F5	0.7978	0.9343	0.9348	0.9871	0.294
F6	0.8254	0.9367	0.9516	0.9826	0.317
F7	0.8820	0.9748	0.9829	0.9941	0.360
F8	0.8893	0.9651	0.9821	0.9855	0.373
F9	0.8871	0.9697	0.9773	0.9835	0.338
F10	0.8681	0.9439	0.9597	0.9837	0.304
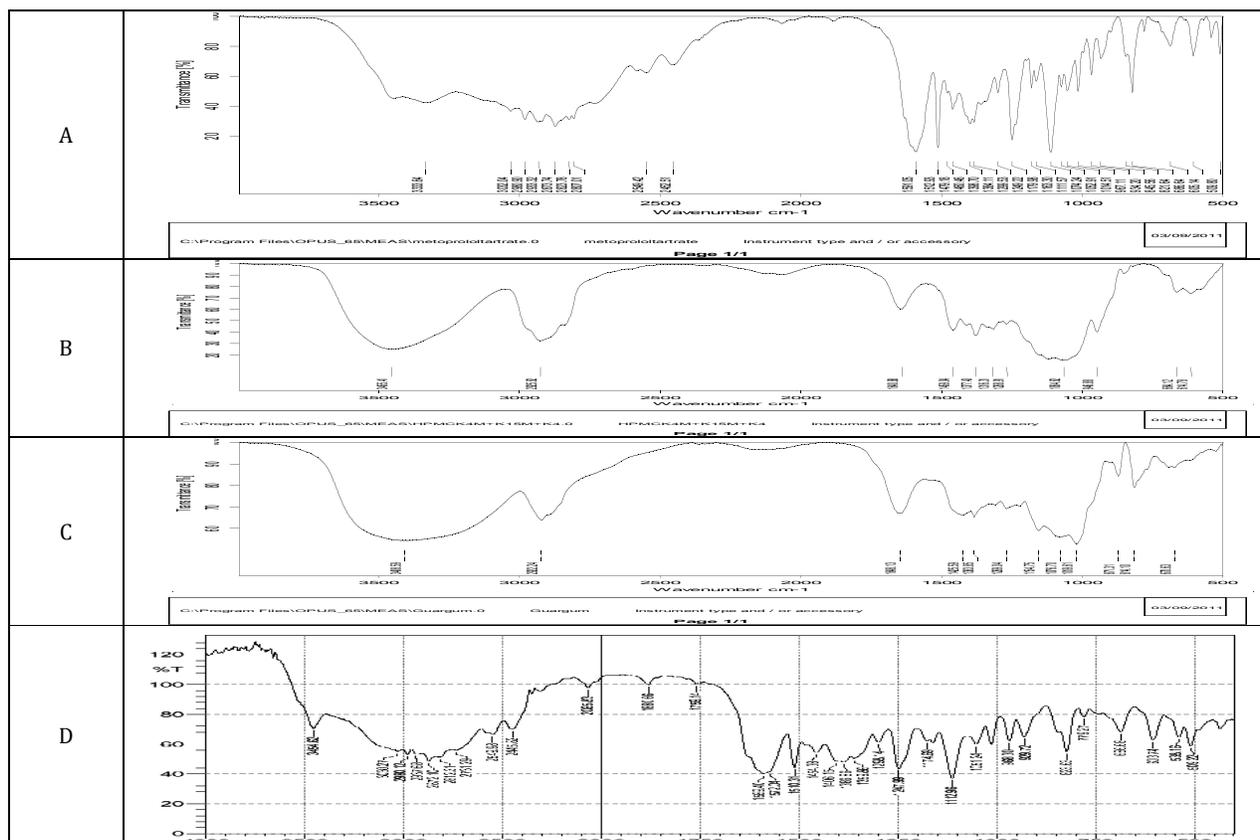
A) IR spectrum of the pure drug
B) IR spectrum of the pure drug +HPMC K4M+HPMC K15M+EC
C) IR spectrum of the pure drug + XG + GG
D) Stability study-FT-IR (formulation F7)
Figure no.2: Stability study-FT-IR (formulation F7)

Stability studies (FT-IR studies):

IR spectra of the drug and its formulations were used to establish the physical characterization. The drug and its formulations exhibited characteristic absorption bands in the corresponding IR regions. The difference in the values of characteristic absorption bands indicating the positions of functional groups and bonds present in the drug molecule negligible and is well within the permissible range. Thus it is clear from the FT-IR spectra that the drug and formulations are almost identical suggesting that the drug remains in the same normal form before and after its use in the preparation of formulation. From the above discussion it can be concluded that no interaction is observed between the drug and various types of polymers used in different formulations. The results are shown in the figure 2.

By comparing the initial values of drug content, % Cumulative Drug release, floating lag time, total floating time of formulation F7 with their respective values analyzed after 3 months of stability studies, a very minute difference have been found between those values. Hence with respect to these tests, the formulation is considered to be stable even after 3 months of stability testing. The FT-IR studies also indicate that the difference in the spectrum shift is negligible.

CONCLUSION

The present study concludes that the bilayer floating tablets of anti-hypertensive drug Metoprolol Tartrate can be formulated as an approach to increase gastric residence time thereby improve its bioavailability and to overcome the limitations of conventional approaches of gastric retention. The formulation F7 gave better controlled drug release in comparison to the other formulations. Among the polymers used to improve the gastric residence, HPMC K15M and Xanthan gum combination showed better control over drug release.

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