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FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF ATENOLOL

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ABSTRACT

The main objective of the present work was to develop sustained release matrix tablets of Atenolol. To improve the patient compliance & reduce the frequency of administration sustained release formulation of Atenolol is desirable. So sustained release Matrix Tablet of Atenolol was designed by using polymers such as Hydroxy Propyl Methyl Cellulose, Sodium Carboxy Methyl Cellulose and Guar Gum different ratio of drug and polymer were selected for the study. The IR study revealed that there was no chemical interaction between drug and excipients. The granules were prepared by wet granulation method. Precompressional parameters such as angle of repose, percent compressibility, and Hausner‟s ratios were studied. These results indicate that granules are having good flow property. After evaluation of physical properties like Weight variation, Hardness, Thickness, Friability of tablet, the formulations checked for the Percentage Drug content which have good uniformity. The in vitro release study was performed in phosphate buffer pH 7.4 up to 12 hrs. Dissolution data was analyzed by Percentage cumulative drug release. Matrix tablets studied for the different polymer ratios and performance checked for different concentration ratios. The results of drug dissolution studies showed improved drug release, retardation effects of the polymers and achieve better performance. It was observed that matrix tablets contained polymer blend of HPMC & Sodium CMC were successfully sustained the release of drug upto 12 hrs. Swelling Index of different formulations were studied. Stability studies (40±2ºC/75±5% RH) for 3 months indicated that Atenolol was stable in the matrix tablets.

KEYWORDS: Atenolol, Precompression, frequency of administration, Drug content, retardation effect.

INTRODUCTION

Oral route is one of the most popular routes of drug delivery due to its ease of administration, patient compliance and flexible design of dosage form.[1] Over 90% of the formulations manufactured today are ingested orally. This shows that this class of formulation in the most popular worldwide and the major attention of the researcher in toward this direction. With advancement in technology and increase awareness towards modification in standard tablets is done to achieve better acceptability as well as bioavailability because of which newer and more efficient tablet dosage forms are being developed. The main reasons behind formulation of different type of the tablets are to create a delivery system that is relatively simple, inexpensive & provide the dosage form that is convenient for patient's use. Tablet ingested orally are meant to be swallowed intact along with sufficient quantity of the potable water. First and foremost, the drug concentration should be sufficiently high at the site of action to achieve a therapeutic effect, but at the same time it should not be too high, it may cause side effects. For a safe and efficient therapy, the drug concentration should preferably lie essentially constant within this therapeutic concentration range over the time. The goal of a constant drug concentration within the therapeutic range at the site of action over a suitable therapeutic time puts requirements not only on the drug but also on the drug formulation. Exceptions are chewable tablet and oral dispersible tablets. Standard compressed tablets this class includes tablets like, multiple compressed tablets, compression coated tablets, layered tablets, modified released tablets etc.[9-12]

In the present work, Atenolol used with polymer SCMC and HPMC to formulate tablets for the treatment of hypertension. Atenolol has low bioavailability as is evident from the available literature although it is freely soluble in water, because it is a BCS class III drug which is known for their high solubility but low permeability and hence low bioavailability. Polymer used is known for its permeability enhancement through mucosal membrane and will enhance drug absorption. For decades an acute disease or chronic illness is being clinically treated through of drug to the patient in the form of some pharmaceutical dosage forms like tablets, capsules, pills, creams, liquids, ointment, aerosols, injectables and suppositories. A successful drug delivery requires consideration of numerous aspects. Depending on the route of administration, the properties of the drug, and many other aspects, various strategies have to be developed. Without doubt the most generically important aspects of any therapy is its efficacy and safety. The drug delivery system should preferably be designed such that a preferential accumulation of the drug is reached at the site of action, whereas the drug concentration elsewhere in the body should be as low as possible. This in

turn will reduce the dose size and dosing frequency and subsequently will result in result in efficient drug therapy and patient compliance.[13-20]

Sustained release drug delivery system

The goal of drug delivery system is to provide a therapeutic amount of the drug to the proper site in the body to achieve promptly and then maintain, the desired drug concentration that is the drug delivery system should deliver drug at a rate dictated by the needs of the body over the period of treatment.[38]

The idealized objective points to the two aspects most important to the drug, delivery, namely, spatial placement and temporal delivery of the drug. Spatial placement related to targeting a drug to a specific organ or tissue, while temporal delivery refer to the controlling the rate of the drug delivery to the tissue. An approximately designed sustained release drug delivery system can be a major advance toward solving these two problems. It is for this reasons the science and technology responsible for development of sustained release pharmaceuticals have been and continued to be the focus of great deal of attention in both industrial and academic laboratories.[24]

1. The bulk of research has been directed at oral dosage forms that satisfy the temporal aspect of drug delivery but many of the newer approaches under investigation.
2. Improved patient convenience and compliance dueto less frequent drug administration.
3. Reduction in fluctuation in steady-state levels.
4. Better control of disease condition.
5. Reduced intensity of local or systemic side-effects.
6. Increased safety margin of high potency drugs due to better control of plasma levels. Maximum utilization of drug enabling reduction intotal amount of dose administered.
7. Reduction in health care costs.
8. Improved therapy.
9. Shorter treatment period.
10. Lower frequency of dosing.
11. Reduction in personnel time to dispense, administer and monitor patients.

MATERIALS AND METHODS

Atenolol (Emcure Pharmaceutical, Pune), Hydroxypropylmethyl Cellulose 15 cps (SD Fine Chemicals, Boisar), Sodium Carboxy Methyl Cellulose (SD Fine Chemicals, Boisar), Guar

Gum (Warkem industries, Mumbai), Lactose (Loba Chemicals, Mumbai), Mg – stearate (SD Fine Chemicals, Boisar), Talc (Loba Chemicals, Mumbai), Dissolution test apparatus (Electrolab, USP XXIV), UV Visible spectrophotometer (U.V.– 1800, Shimadzu), Hot air Oven (M.C. Dalal and Co., Chennai), Digital Balance (Citizen), Vernier Caliper (Mitutoyo, Japan), Monsanto Hardness tester (Cadmach), Roche Friability Tester (Lab Hosp)(Electrolab, USP EF2), Sieve 14 mesh (Indicot India), pH meter (Elico pH Meter, Hyderabad), Tablet Punching Machine (Pilo+Press 10 Station) (Chamunda Pharma, Ahmadabad).

MEHODS

Preparation of matrices by wet granulation[6]

Accurately weighed quantity of Atenolol, Sodium CMC, Lactose were taken in mortar and mixed. Starch paste 6 % was added to the dry blend gradually with constant kneading to ensure a homogenous mass. The dough mass was passed through a #14 mesh sieve. Then granules were dried at 50·C and dried granules were lubricated with talc and magnesium stearate and compressed into tablets using 10 mm punches. Each tablet contains 50 mg of Atenolol. The drug matrix ratio was varied to obtain the matrix tablets of varying polymer concentration.

Evaluation of granules

1. Angle of repose

The angles of repose of the major components of the tablet formulations. The angle of repose of granules was determined by the funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the granules. The granules were allowed to flow through funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

Tan ϑ= h / r

Hence, $q = \tan^{-1} h / r$

Where, q = angle of repose; h = height of the cone**;** r =radius of the cone base

2. Bulk density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of 2 g of powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the

height of 2.5 cm at 2-second intervals. The tapping was continued was until no further change in volume was noted. LBD and TBD were calculated using the following formulas:

LBD = Weight of the powder/ Volume of the packing

TBD = Weight of the powder/ Tapped volume of thepacking.

3. Compressibility index

The compressibility of the granules was determined byCarr‟s Compressibility Index.

Carr‟s compressibility index (%) = [(TBD-LBD) X 100]/ TBD

Or it can be expressed as Carr‟s Index relates the poured density of the material to the tapped density and was calculated by using the following relationship:

$$\text{Carr's Index} = \frac{\text{Tapped density} - \text{Poured density}}{\text{Tapped density}} \times 100$$

Carr‟s Index values for pure drug, guar gum and granules were determined by measuring the initial volume (*V*p) and final volume (*V*t) of a known weight (*W*) of material after subjecting to 100 tappings in a graduated measuring cylinder. From thesevolumes, the poured density (*W*/*V*p) and the tapped density (*W*/*V*t) values were calculated and were substituted in the above equation to determine Carr‟s Index.

Evaluation of tablets

1. Thickness

Thickness of tablets was determined using Vernier caliper. Five tablets from each batch were used, and average values were calculated. The result is shown in Table No. 12.

2. Weight variation test

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (AW-220, Shimadzu), and the test was performed according to the official method.

3. Drug content

Four tablets were finely powdered; quantity equivalent to 50 mg of Atenolol was accurately weighed and transferred to 100 ml volumetric flask containing 50 mlof methanol. This was allowed to stand for 6 h to ensure complete solubility of the drug. Solutions were made up to volume, filtered, suitably diluted, and estimated for Atenolol contents at 275 nm, using a UV–visible spectrophotometer using methanol as blank.

4. Hardness

For each formulation, the hardness of 6 tablets were determined using the Monsanto hardness tester (Cadmach). The tablet was held along its oblong axis inbetween the two jaws of the tester. At this point, reading should be zero kg/cm^2 Then constant force was applied by rotating the knob until the tablet fractured.

5. Friability

It is measure of tablet strength. It is related to tablet ability to withstand both shock and abrasion without crumbling during the handling of manufacture, packing, shipment and consumer use.

6. Determination of swelling index

The swelling indices of tablets were determined in Phophate Buffer (pH 7.4) at room temperature up to 8 h. The swollen weight of the tablet was determined atpredefined time intervals. The swelling index was calculated using following equation:

$$\% \text{ water uptake or polymerswelling} = \frac{(W_s - W_i)}{W_i} \times 100$$

Where W_s is the weight of the swollen matrix at time t, W is the initial weight of the matrix.

7. In vitro release studies

In vitro dissolution study for the prepared matrix tablets were conducted for period of 10-12 hours using a six station USP type II (paddle) apparatus at 37^0C ± 0.5^0C and 50 rpm speed. The dissolution studies were carried out in triplicate for 8 hours in phosphate buffer of pH 7.4 under sink condition. At first half an hour and then every 1- hour interval samples of 5 ml were withdrawn from dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solution was analyzed at 275 nm for Atenolol by a UV- spectrophotometer for determining its cumulative % drug release or amount present in the sample.

Stability studies

The selected formulation F2 was tested for 3 Months at the storage conditions at room temperature and 25^0 C at 45 % RH, were analyzed for their drug content. The residual drug contents of formulations were found to be within the permissible limit. The tablets showed satisfactory physical stability at room temperature and 25^0 C at 45 % RH. No appreciable changes were found in any of the formulations. The tablets were also subjected to IR studies to determine compatible the drug with the excipients used in the tablets. The IR studies showed that there are no interactions between the drug and polymers.

RESULT AND DISCUSSION

Preformulation studies

Organoleptic properties of Atenolol

Table no. 1: Description of the drug (Atenolol).

S. no.	Description	Atenolol drug
1	State	Solid
2	Colour	White or yellowish
3	Odour	Odourless
4	Texture	Amorphous powder

Determination of melting point

Table no. 2: Melting point of drug.

Drug	Specification	Observation
Atenolol	146-148^{o}C	147-149^{o}C

Solubility study: An excess quantity of Atenolol was taken separately and add in 10 ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the table no.3

Table no. 3: Solubility profile of atenolol in different solvents.

S no.	Solvents	Solubility
1	Water	Freely soluble
2	Methanol	Soluble
3	Acetone	Insoluble
4	Alcohol	Sparingly soluble
5	Methylene chloride	Practically insoluble

Loss on drying studies

About 1g of the powder was weighted and kept for checking the loss on drying on a moisture sensitive balance at 105°C for 3 minute % loss of moisture was 8%.

pH of the solution

The pH study was done for the drug by dissolving it in their water as solvent and determining the pH while the help of pH meter. The pH value of drug has been shown in table no. 4.

Table no. 4: pH of drug solution.

Drug	Specification	Observation
Atenolol	5.5-7.5	6.8

Determination of Wavelegnth of Maximum Absorbance (λ_{max})

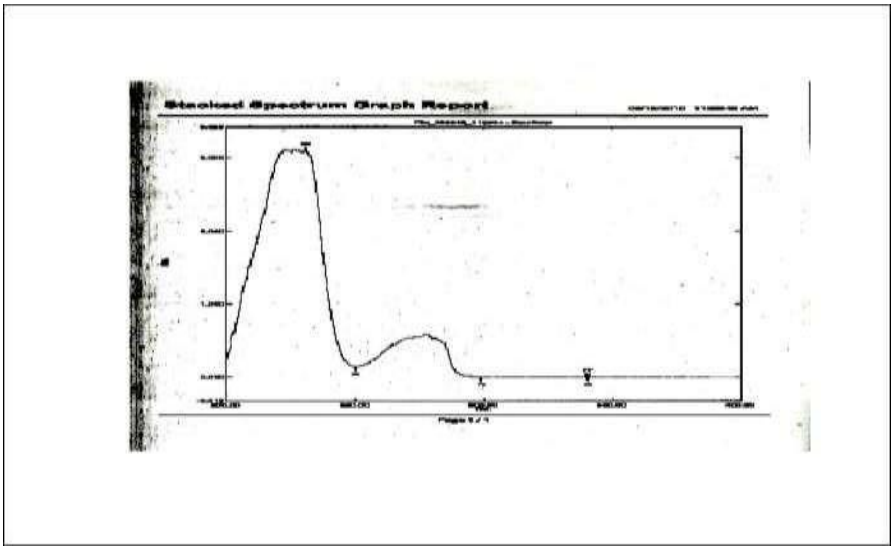


Figure no. 1: Scanning of wavelenth of atenolol.

Table no. 5: Wavelength of maximum absorbance (λ_{max}).

Conc. (µg/mL)	Scanning range (nm)	Peaks Observed (nm)	Selected λ_{max}
10	200-400	275	**275**

Preparation of the calibration curves of atenolol

Table no. 6: Linearity of atenolol 7.4 pH buffer.

Conc. (µg/ml)	0	10	20	30	40	50
Absorbance	0	0.132	0.251	0.348	0.471	0.529

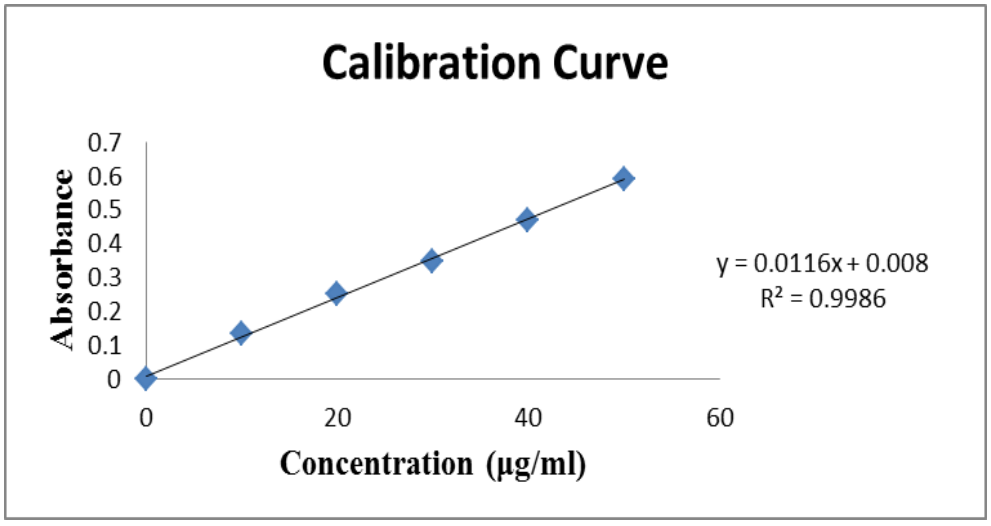


Fig. no. 2: Calibration curve of atenolol in 7.4 pH buffer.

Compatibility study

Physical compatibility study

Table no. 7: Physical compatibility study.

S. no.	Drug-excpients	Storage at room temperature	Final
1	Atenolol+HPMC (1:1)	White colour	White colour
2	Atenolol+ Sod.-CMC (1:1)	Off white colour	Off white colour
3	Atenolol+ Guar gum (1:1)	White colour	White colour
4	Atenolol+Lactose (1:1)	Off white colour	Off white colour
5	Atenolol+mg stearate (1:1)	Off white colour	Off white colour
6	Atenolol+ Talc (1:1)	Off white colour	Off white colour

Table no. 8: Physical compatibility study at different temperature.

S. No.	Drug-excipients	Storage at room temperature	Storage at 45^0C -50^0C	Storage at 2^0C -8^0C
1	Atenolol (pure drug)	Stable	Stable	Stable
2	Atenolol+HPMC (1:1)	Stable	Stable	Stable
3	Atenolol+ Sod-CMC (1:1)	Stable	Stable	Stable
4	Atenolol+ Guar gum (1:1)	Stable	Stable	Stable
5	Atenolol+Lactose (1:1)	Stable	Stable	Stable
6	Atenolol+mg-stearate (1:1)	Stable	Stable	Stable
7	Atenolol+ Talc (1:1)	Stable	Stable	Stable

Chemical compatibility Study by FT-IR

Table no. 9: FT-IR peaks of atenolol.

S. No	Functional Group	Actual Values (cm^{-1})	Values Obtained (cm^{-1})
1	-NH Stretching	3500-3100	3174
2	-OH Stretching	3650-3600	3356
3	-OH Bending, 2° –OH	1060-1100	1091
4	C=O Stretching	1680-1630	1637
5	C-O Stretching	1310-1010	1301
6	O=C-NH_2 Stretching	1690-1630	1637
7	C-H Stretching	3000-2850	2964
8	C=C, Aromatic	1680-1620	1637
9	C-CH3 Stretching	2960-3000	2964
10	C=CH_2 Bending	≈ 900	885

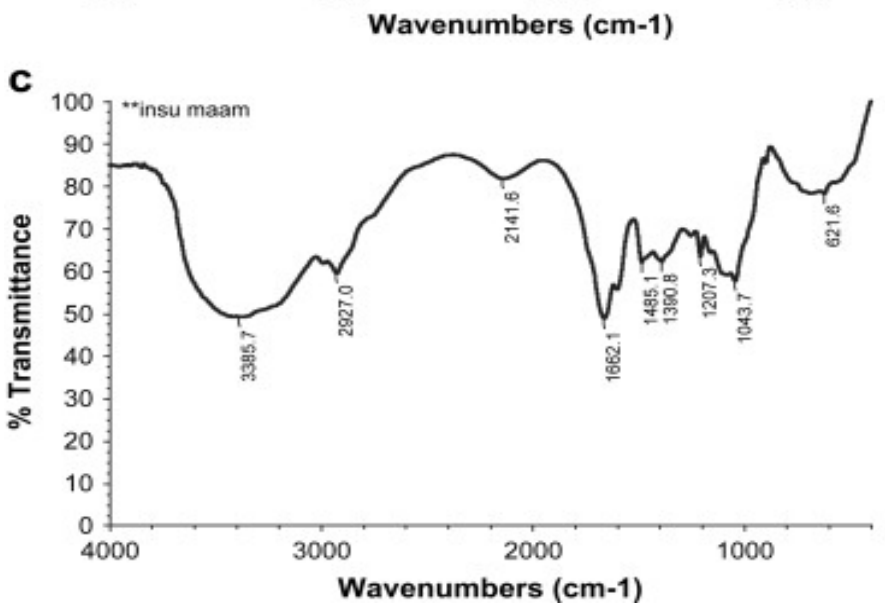
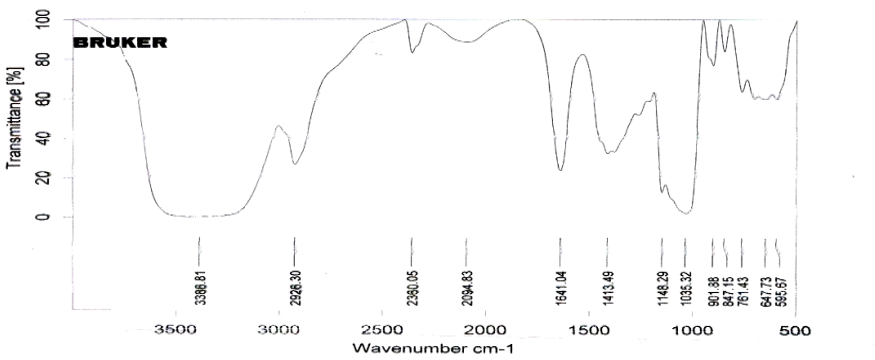


Figure no. 3: Standard IR spectrum of atenolol.



Wavenumber	Abs. intensity	Rel. intensity	Width	Found if threshold <	Shoulder
3386.8084	0.002	0.998	819.3735	99.516914	0
2926.3026	0.269	0.230	79.1725	19.379833	0
2360.0535	0.833	0.167	60.3735	16.650850	0
2094.8317	0.888	0.102	203.1533	9.518667	0
1641.0440	0.239	0.653	85.8945	58.850266	0
1413.4943	0.324	0.436	504.7881	31.091932	0
1148.2850	0.129	0.061	170.8220	4.061526	0
1035.3205	0.022	0.981	196.9900	97.669777	0
901.8749	0.770	0.233	49.4244	22.936014	0
847.1526	0.843	0.151	27.9472	13.850245	0
761.4299	0.637	0.116	1061.0450	6.295144	0
647.7276	0.599	0.069	119.7672	2.664022	0
595.6672	0.599	0.396	240.7933	39.267700	0

Figure no. 4: IR spectrum of atenolol.

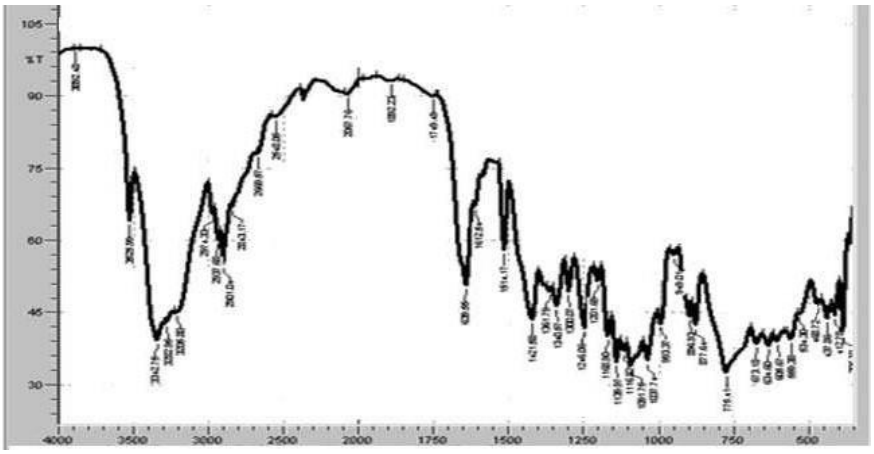


Figure no. 5: Infrared spectrum of combination of atenolol +HPMC+Sodium CMC.

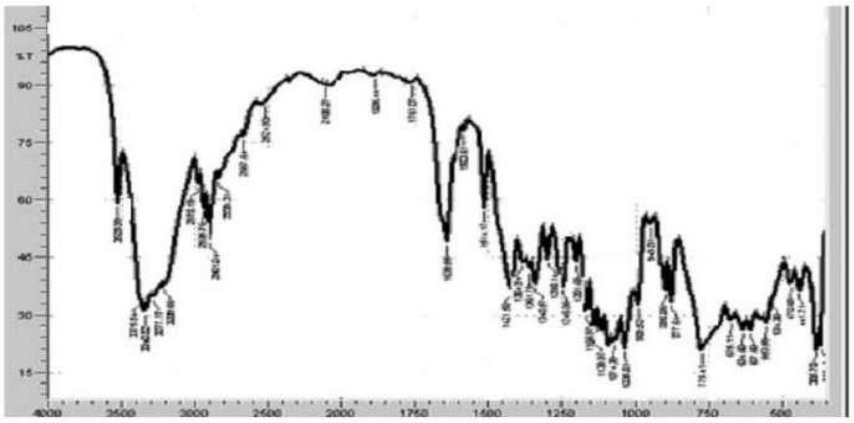


Figure 5: Infrared spectrum of Atenolol +HPMC+Guar Gum.

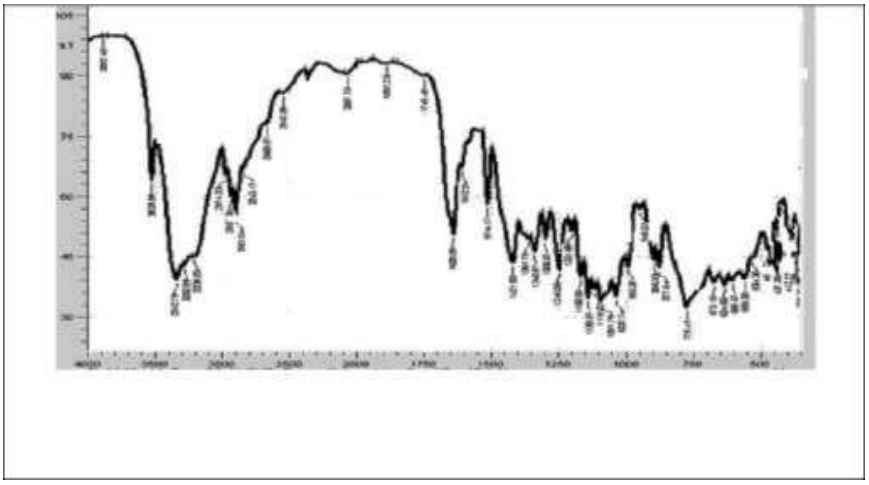


Figure 6: Infrared spectrum of Atenolol+HPMC+Sodium CMC+Guar Gum.

Formulation development

Table no. 10: Formulation design of sustained release matrix tablets by wet granulation method using combinationof two polymer.

Ingredient	F1	F2	F3	F4	F5
Atenolol HCl	50	50	50	50	50
HPMC 15cps	35	55	75	-	-
Sodium-CMC	70	50	30	25	30
Guar Gum	-	-	-	45	40
Mg.-Stearate	3.5	3.5	3.5	3.5	3.5
Lactose	188	188	188	223	223
Talc	3.5	3.5	3.5	3.5	3.5
Total	350	350	350	350	350

Pre compression parameter of formulation

Table no. 11: Result of precompression parameter.

Formulation Code	LBD* (g/ml)	TBD* (g/ml)	Carr's index*	Hausner's Ratio*	Angle of repose*
F_1	0.439	0.551	12.70	1.14	27.34
F_2	0.447	0.533	14.13	1.12	24.30
F_3	0.452	0.519	12.90	1.14	27.46
F4	0.461	0.527	12.52	1.14	28.18
F5	0.433	0.515	15.92	1.18	29.12

Post compression parameter of formulation

Table no. 12: Result of postcompression parameter.

F. Code	Thickness (mm)± SD	Weight variation (mg)	Hardness (kg/cm^2)	Friability(%)	Drug content(%)
F1	6.9	259.89	8.3	0.9	92.25
F2	4.0	252.88	7.0	0.58	99.8
F3	8.2	256.12	8.0	0.89	93.54
F4	7.9	258.81	8.5	0.91	96.67
F5	9.0	255.80	9.8	0.87	95.37
F6	6.8	257.92	9.1	0.79	94.97
F7	9.1	254.61	8.0	0.78	97.61

Invitro drug release study

Table no. 13: % Drug release of different formulation.

Time (hrs)	Cumulative %drug release				
	F-1	F-2	F-3	F-4	F-5
0	0	0	0	0	0
1	14.14	18.49	19.77	17.12	18.45
2	29.33	39.44	39.02	34.23	36.99
4	51.69	60.57	67.61	57.2	67.25
6	66.76	78.57	87.82	75.97	87.1
8	75.5	88.34	88.99	84.83	89.71
10	81.23	93.79	90.9	94.39	92.82
12	85.23	99.78	93.28	96.12	95.36

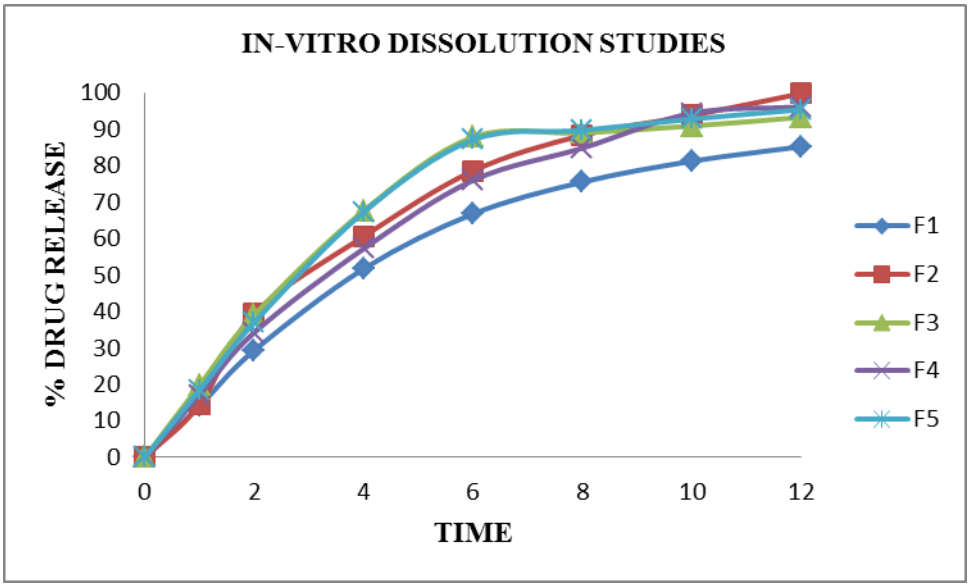


Figure no. 7: Comparative dissolution profile of the formulation F1 to F5.

Stability studies

Based on the results of *in-vitro* drug release best formulations F_2 was selected for three month stability studies at 25ºC/60% RH and at 45ºC/75% RH. The stability studies were conducted according to the method described in section four. The selected formulations were evaluated for physical appearance, hardness, friability, and drug content and *in-vitro* drug release. The results showed that there was no significant change in physical appearance, hardness, friability, drug content and drug release profile throughout the study period. Three months of stability studies revealed that; there was no any significant degradation of the drug. Thus prepared formulations were physically and chemically stable. The result of stability studies were tabulated in table no. 14

Table no. 14: Results of stability studies for formulation F_4 stored at 25ºC/60%

Storage Period	Stored at 25ºC/60% RH Formulation F_2		
	HardnessKg/cm^2	% friability	% CDR
Initial	7.0	0.58	99.78
After 1month	6.9	0.6	99.2
After 2 Month	6.8	0.62	98.6
After 3month	6.7	0.63	98.0

Table no. 15: Results of stability studies for formulation F_4 stored at 45°C/75% RH.

Storage Period	Stored at 40°C/75% RH Formulation F_2		
	HardnessKg/cm^2	% friability	% CDR
Initial	7.0	0.58	99.78
After 1month	6.8	0.61	99.0
After 2 month	6.6	0.64	98.3
After 3month	6.4	0.65	97.8

DISCUSSION

In the matrix tablet, HPMC and SCMC were used as retardant materials for sustained release action.

Preformulation of the drug was carried out with respect to different parameters. Drug was separately tested for their physicochemical characteristics. Melting point of Atenolol was found to be 146-148°C respectively. Similarly solubility studies were conducted for the drug in different solvents. It was found that the drug was freely soluble in water, soluble in methanol, insoluble in acetone, sparingly soluble in alcohol and practically insoluble in methylene chloride. Partition coefficient of the drug was calculated which was found to be -7.09 of Atenolol. The pH of the drug solution was found to be 6.8. UV spectroscopy of the drug was also performed and the drug was scanned on different wavelengths. λ_{max} of Atenolol was found to be 275 nm. All the values calculated were found to be concordant which that of the standard values reported in Standard Pharmacopoeial books. IR spectroscopy study was performed for the drug, the IR spectrum for the drug was found to be in agreement with that of the standard IR graph reported. Compatibility studies was performed by keeping the drug mixed with that of the different excipients which was kept for one month to three month and no change was observed with respect to physical properties of the drug which represents that the excipients are compatible with that of the drug. It was observed that there was no significant shift in the melting point of the drug when taken alone or in combination with that of polymer used. On the basis of the compatibility studies, it was found that drug is compatible with all other excipients selected for the study and hence can be used in combination for the preparation of the tablets.

Atenolol sustained release matrix tables were prepared by wet granulation method, different formula were designed to formulate the tablets which have been mentioned in table no.9. In the matrix tablet, HPMC were selected as retardants material for the sustained released action

(more than 20% drug released in 1 hrs). 8%. Lactose was selected as a diluents with 17.6% and Magnesium stearate was selected as a lubrication and Talc was selected as a glidant. All different formulation containing different amount of HPMC, Lactose and Dicalciumphosphate were prepared to formulate the tablets. Angle of repose was found to be between 24.30°, where some of the blend fell between the specified limit of 24.30°-29.12° representing good flow. Bulk density was found to be between 0.433 – 0.461g/ml. Tapped density was found to be between 0.515 – 0.551g/ml. Carr's index (%) was found to be in the range of 12.70 – 15.92, all the powder blend are well within the specification limit. Hausner's ratio was found to be between 1.12-1.18. With this the powder blends were found to be free flowing material and showed suitability to be compressed as tablets of expected weight.

It was observed that hardness of the all sustained released tablets were measured by Monsanto hardness tester and were controlled between 5 to 10 kg/cm^2. The thickness of all SR matrix tablets was measured by vernier caliper and was ranged between 4.0-9.1. The loss in total weight of the tablets due to friability was less than 1 %, the high value of crushing strength and low friability indicated that the compressibility of Atenolol and adjuvant was good. on the basis of the parameters viz. weight variation, hardness and friability the best formula was selected. F-2 formulation was found to be the best formula and hence was taken as the optimized formula. Tablets prepared out of formula F-2 represented a weight variation of 252.88 mg, hardness of 7.0, friability of 0.58.

The tablets prepared out of the optimized formula was taken into consideration for further in vitro dissolution drug release study. In- vitro dissolution studies of the sustained release matrix tablets of Atenolol were performed using USP type II dissolution apparatus (paddle) at 50 rpm. The study was performed for 12 hours, and percentage drug release was calculated at 1 hours time intervals. The drug release profile were characterized by an initial burst effect (more than 14 drug release in 1 hrs) followed by a sustained release thereafter. The formulation F-2 contained SCMC which might have sustained the release since it is also known for its polymeric sustaining effect. The formulation F-2 gave 99.78 % of the drug release in 12 hrs of study. This is in fact true for the polymeric tablets since the surface drug gives a burst effect thereby releasing a amount of drug at once and since polymer like SCMC and HPMC are present which provide matrix to the tablet, the further release is sustained. The drug release indicates sustained drug release from the matrix tablets. This is again due to the presence of the polymer like SCMC and HPMC.

CONCLUSION

Matrix tablets are very easy to prepare. They are cost effective and exhibit predictable release behavior. So the ultimate aim of the present study was to prepare once daily sustained release matrix tablets of Atenolol for improved patient compliance, better therapeutic efficacy, less side effects and reduced dosage regimen with less toxicity for treatment of hypertension. The Sustained released matrix tablet of Atenolol was designed by using hydrophilic polymers like Hydroxypropylmethyl Cellulose (HPMC 15 cps), Sodium CMC and Guar gum with suitable granulating agents. Different ratios of drug and polymer were selected for the study and drug release rates were studied. Following conclusions have been drawn from the present study. The analytical method used in the present study was found to be suitable for the estimation of Atenolol in different dissolution media. IR study indicates that the drug is compatible with the polymers.

The wet granulation method, which employed 6% Starch as granulating agent, was found to produce granules of good quality. The good quality of granules was further confirmed with respect to flow properties, bulk density, Hausner's ratio, compressibility index, angle of repose.

The drug Atenolol was selected for the study, because of its proved activity and better clinical application. Sustained release matrix Tablet of Atenolol containing blend of HPMC and sodium CMC successfully sustains the release of Atenolol for the period of 12 hrs. and formulation containing only single polymer could not control the release of Atenolol asdesired.

The effect of drug to polymer ratio on the in-vitro drugrelease behavior was significant. Formulation F2 showed better sustained release when compared to other batches and this shows the ideal drug, polymer and excipients combination. From these formulations F2 was found to be better released than other formulation. Stability study indicates that there is insignificant change either in the physical appearance or in the drug content of the formulations.

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