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FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF ATENOLOL HYDROCHLORIDE

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ABSTRACT

The main objective of the present work was to develop sustained release matrix tablets of Atenolol HCl. To reduce the frequency of administration and to improve the patient compliance, a once daily sustained release formulation of Atenolol is desirable. So sustained release Matrix Tablet Of Atenolol HCl was designed by using different polymers viz. Hydroxy Propyl Methyl Cellulose (HPMC), Sodium Carboxy Methyl Cellulose (NaCMC) and Guar Gum Varying ratios of drug and polymer were selected for the study. After fixing the ratio of drug and polymer for control the release of drug up to desired time, the release rates were modulated by Single polymer, combination of two different rates controlling material and triple mixture of Polymer. The IR study revealed that there was no chemical interaction between drug and excipients. The granules were prepared by wet granulation method. Precompressional parameters i.e. angle of repose, percent compressibility, and Hausner's ratios were studied. These results indicate that granules are good flowing characteristics. After evaluation of physical properties like Weight variation, Hardness, Thickness, Friability of tablet, the different formulations checked for the Percentage Drug content which having good uniformity. The in vitro release study was performed in phosphate buffer pH 7.4 up to 12 hrs. The effect of polymer concentration were studied. 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 could 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 HCl, Hydroxy Propyl Methyl Cellulose, Sodium Carboxy Methyl Cellulose, Guar Gum.

INTRODUCTION

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. First and foremost, the drug concentration should be sufficiently high at the site of action in order to have a therapeutic effect, but at the same time it should not be too high, since this may result in side effects. For a safe and efficient therapy, the drug concentration should preferably lie essentially constant within this ''therapeutic window'' over the time of action. The goal of a constant drug concentration within the therapeutic window at the site of action over a suitable therapeutic time puts requirements not only on the drug but also on the drug formulation. 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.

Sustained release drug delivery system

The basic goal of Sustained release drug delivery system is to achieve a steady state drug in blood level for an extended periods of time. The design of proper dosage regimens is an important element in accomplishing this goal. Sustained release, sustained action, prolonged action, controlled release. Extended action, timed release depot and repository dosage forms are terms used to identify drug delivery system than are designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose. In the case of injectable dosage forms, this period may vary from day

to months. In the case of orallyadministered dosage forms. This period is measured in hours and critically depends on the residence time of the dosage form in the gastrointestinal tract. Products of this type have been formulated for oral injectable and topical use and inserts for placement in the body cavities. Sustained release preparations are not new but several new modifications are being introduced. They are also referred to as "long acting" or "delayed release" when compared to "rapid" or "conventional" release preparations. The term sometimes overlaps with "controlled release," which implies more sophisticated control of release and not just confined to the time dimension. Controlled release implies consistency, but release of drug in sustain Release preparations may not be consistent. Controlled-release drug administration means not only prolonged duration of drug delivery as in sustained release, but also implies the predictability and reproducibility of drug release kinetics. Optimal therapy of a disease requires the efficient delivery of active drugs to the tissue or organs that need treatment. In recent years considerable attention has been stressed on the development of controlled drug delivery system for convenience and patient compliance. By definition, sustained release formulations differ pharmaceutically and pharmacokinetically from the innovator drug. The excipients and particle sizes (usually larger) of the formulation are designed to dissolve more slowly and are almost always drugs for chronic diseases. Sustained release systems exhibiting zero-order release. These systems are suitable for diseases that have marked diurnal rhythms, where the therapeuticconcentrations should vary during the day. Drug levels should be highest when the symptoms are most severe. The therapeutic effect of drugs that have a short biological half-life may be enhanced by formulating them as extended- or sustained-release dosage forms. Extended- and sustained-release dosage forms prolong the time that systemic drug levels are within the therapeutic range and, thus, reduce the number of doses the patient must take to maintain a therapeutic effect, thereby increasing compliance. Drugs with a narrow therapeutic index are also suitable for incorporation into an extended release dosage form.

Advantages of Sustained Release products

- Improved patient convenience and compliance due to less frequent drug administration.
- Reduction in fluctuation in steady-state levels and therefore –

i) Better control of disease condition, and
ii) Reduced intensity of local or systemic side-effects.

- Increased safety margin of high potency drugs due to better control of plasma levels.
- Maximum utilization of drug enabling reduction in total amount of dose administered.
- Reduction in health care costs through –

✓ Improved therapy
✓ Shorter treatment period

- Lower frequency of dosing.
- Reduction in personnel time to dispense, administer and monitor patients.

MATERIALS AND METHOD

Atenolol hydrochloride (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); Dicalsium Phosphate (ACTO Lab., Warangal); Talc (Loba Chemicals, Mumbai) Sodium ortho phosphate (SD Fine Chemicals, Boisar); Sodium Hydroxide (SD Fine Chemicals, Boisar) Potassium dihydrogen orthophosphate (LR) (SD Fine Chemicals, Boisar); Methanol (LR))SD Fine Chemicals, Boisar).

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).

Preparation Of Matrices By Wet Granulation[6,63]

The batch size prepared for each formulation was of 20 tablets.

1. Preparation of sustained release matrix tablets of Atenolol HCl with HPMC as retarding material

- Accurately weighed quantity of Atenolol HCl,HPMC,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 50^0C 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 HCl.
- The drug matrix ratio was varied to obtain the matrix tablets of varying polymer concentration.

2. Preparation of sustained release matrix tablets of Atenolol HCl with Sodium CMC as retarding material

- Accurately weighed quantity of Atenolol HCl, 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 500C 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 HCl.

- The drug matrix ratio was varied to obtain the matrix tablets of varying polymer concentration.

3. Preparation of sustained release matrix tablets of Atenolol HCl with Guar Gum as retarding material

- Accurately weighed quantity of Atenolol HCl, Guar Gum, 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 500C 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 hydrochloride. The drug matrix ratio was varied to obtain the matrix tablets of varying polymer concentration.

Table 1: Formulation design of Sustained Release Matrix tablets by wet granulation method using Single Polymer.

Ingredient	H1	H2	H3	C1	C2	C3	G1	G2	G3
Atenolol HCl	50	50	50	50	50	50	50	50	50
HPMC 15 cps	35	70	105	-	-	-	-	-	-
Na-CMC	-	-	-	35	70	105	-	-	-
Guar Gum	-	-	-	-	-	-	35	70	105
Mg.-Stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Lactose	258	223	188	258	223	188	258	223	188
Talc	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Total	350	350	350	350	350	350	350	350	350

Table 2: Formulation design of Sustained Release Matrix tablets by wet granulation method using Combination of Two Polymer.

Ingredient	HC1	HC2	HC3	CG1	CG2	CG3	HG1	HG2	HG3
Atenolol HCl	50	50	50	50	50	50	50	50	50
HPMC 15cps	35	55	75	-	-	-	40	30	20
Na – CMC	70	50	30	25	30	35	-	-	-
Guar Gum	-	-	-	45	40	35	30	40	50
Mg.-Stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Lactose	188	188	188	223	223	223	223	223	223
Talc	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Total	350	350	350	350	350	350	350	350	350

Table 3: Formulation design of Sustained Release Matrix tablets by wet granulation method using Combination of Three Polymer.

Ingredient	HCG1	HCG2	HCG3
Atenolol HCl	50	50	50
HPMC 15cps	45	30	30
Na – CMC	30	45	30
Guar Gum	30	30	45
Mg.-Stearate	3.5	3.5	3.5
Lactose	188	188	188
Talc	3.5	3.5	3.5
Total	350	350	350

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 q = 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 the packing.

3. Compressibility Index

The compressibility of the granules was determined by Carr'sCompressibilityIndex.

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:

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

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.16 and 17.

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 HCl was accurately weighed and transferred to 100 ml volumetric flask containing 50 ml of 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 HCl 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:

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

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

7. In Vitro Release Studies

In vitro drug release 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 Hydrochloride by a UV-spectrophotometer for determining its cumulative % drug release or amount present in the sample.

Stability Studies

The selected formulation (HC2 &HC3) was tested for 3 Months at the storageconditions at room temperature and 40^0 C at 75 % RH, were analyzed for their drug content. The residual drug contents of formulations were found to be within the permissible limits as shown in the Table. The tablets showed satisfactory physicalstability at room temperature and 40^0 C at 75 % 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

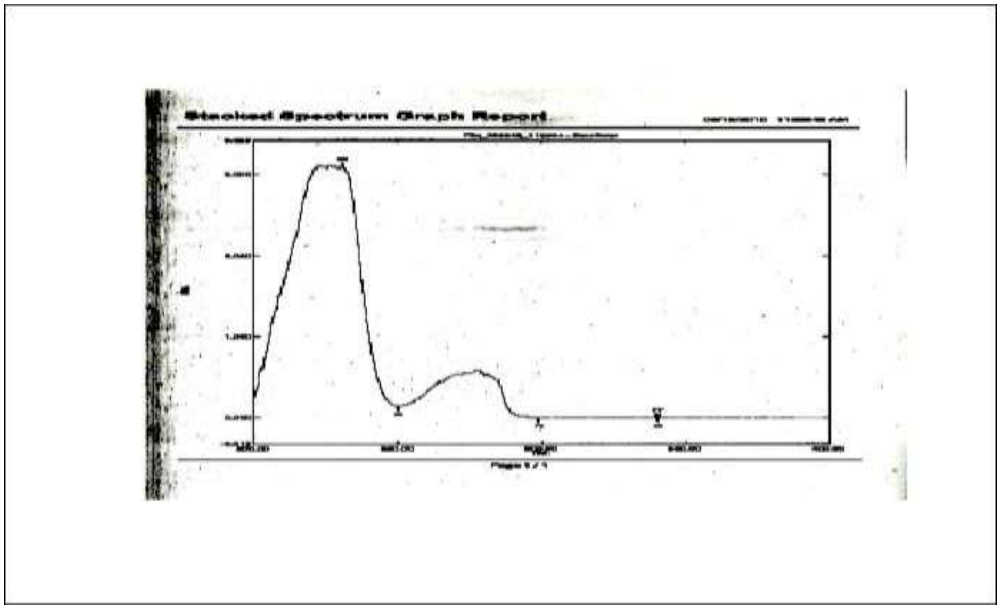

Fig. 1: UV Spectrum of Atenolol Hydrochloride.

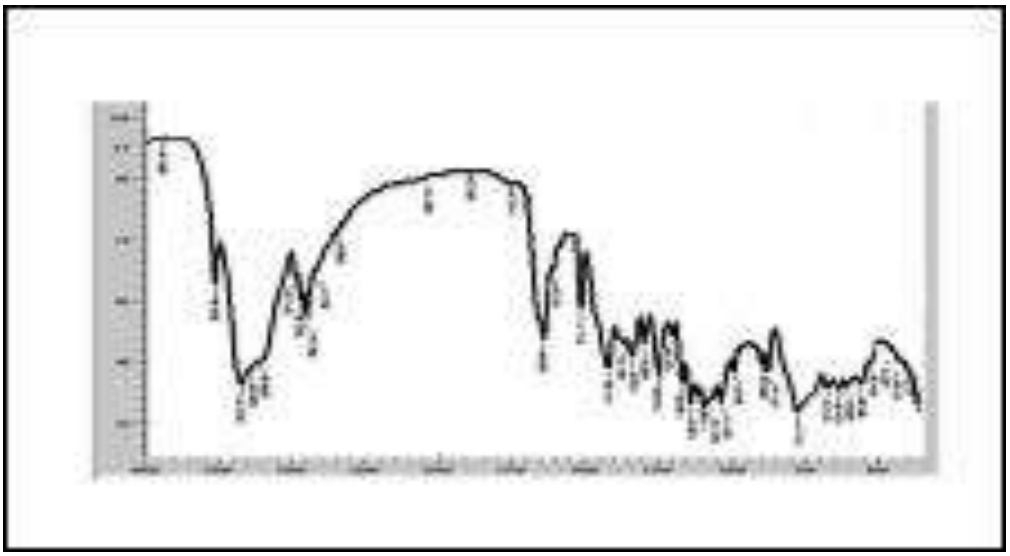

Figure. 2: Infrared Spectrum of Atenolol Hydrochloride.

Table 4: Infrared spectral assignments for Atenolol Hydrochloride.

Frequency(cm^{-1})	Assignments
3600-2300	-OH, Aliphatic
3400	-NH Stretching.
1690	Carbonyl Group
1300-1600	Aromatic Ring
1242	Aromatic Ether
1180	Isopropyl Group
1110	Aliphatic Ether, Secondary Alcohol
2800	Aromatic –CH

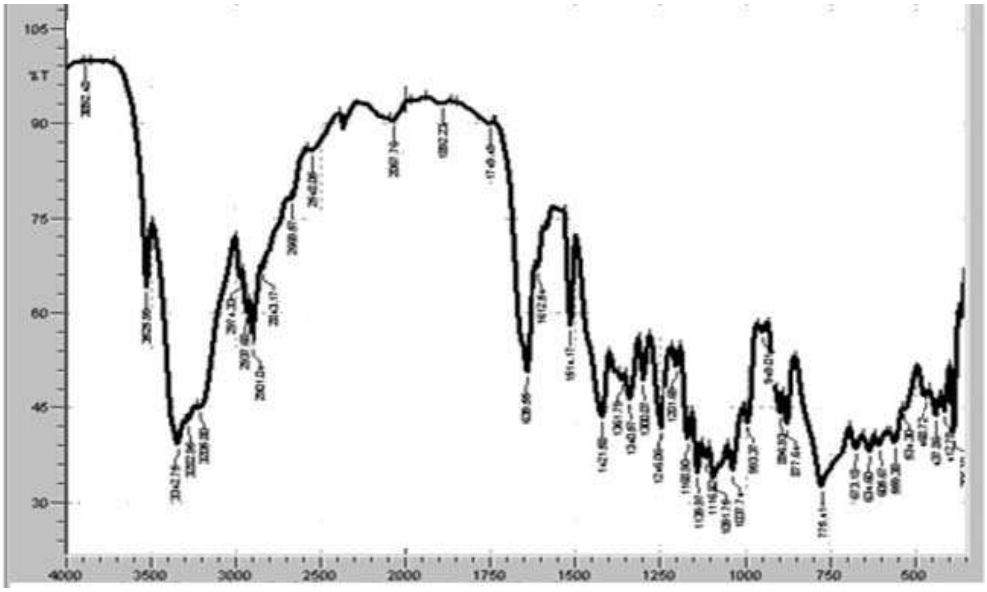

Figure 3: Infrared spectrum of Combination of Atenolol HCl +HPMC+Sodium CMC.

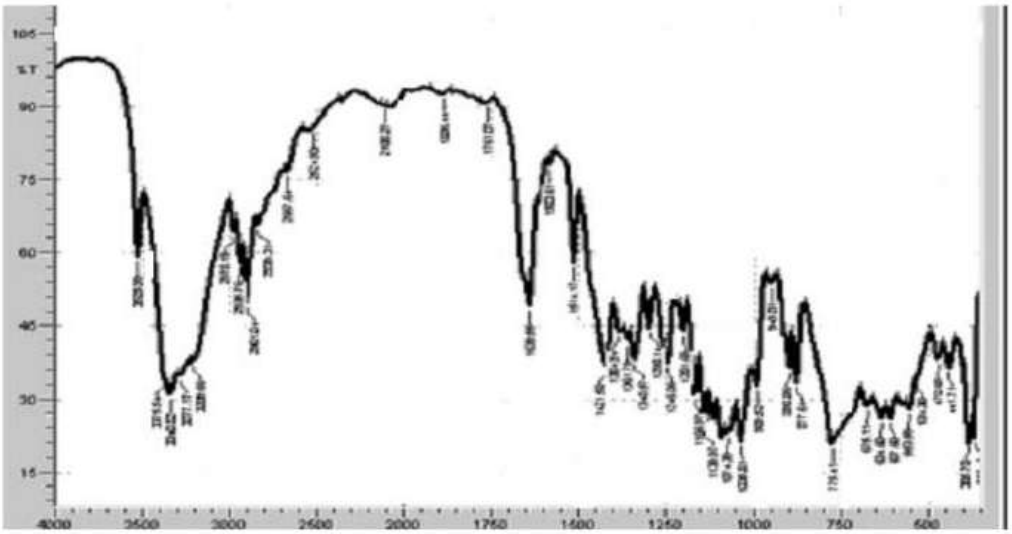

Figure 4: Infrared spectrum of Atenolol HCl +HPMC+Guar Gum.

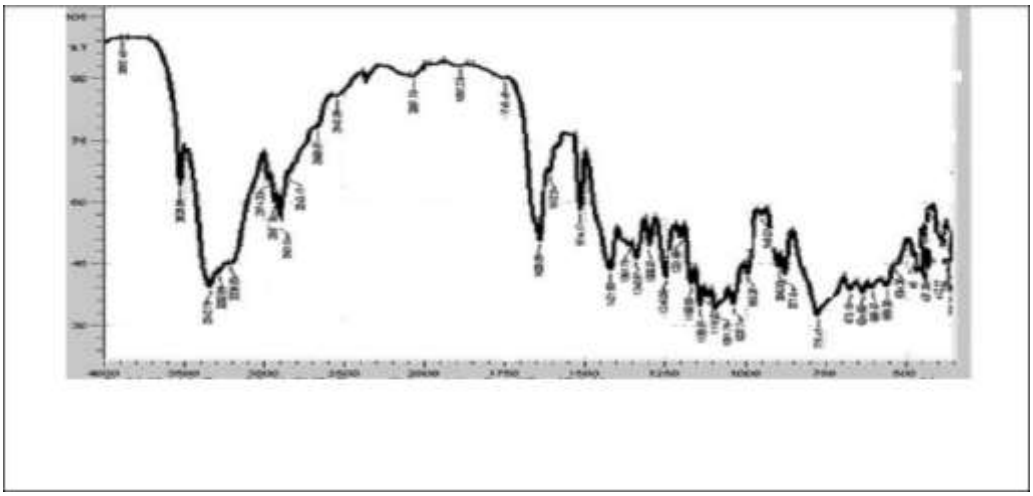

Figure 6: Infrared spectrum of Atenolol HCl +HPMC+Sodium CMC+Guar Gum.

Evaluation of Granules

Table 5: Evaluation of Granules properties of single polymer.

Formulation code	LBD* (g/ml)	TBD* (g/ml)	Carr's index*	Hausner's Ratio*	Angle of of repose*
H_1	0.458±0.04	0.514±0.04	10.89±0.01	1.22±0.02	25.49±0.03
H_2	0.454±0.02	0.519±0.04	12.52±0.04	1.14±0.01	25.13±0.02
H_3	0.428±0.04	0.528±0.06	12.68±0.04	1.14±0.05	25.71±0.03
C_1	0.433±0.04	0.504±0.02	15.06±0.02	1.17±0.06	27.00±0.04
C_2	0.462±0.02	0.514±0.05	15.75±0.03	1.18±0.05	25.11±0.08
C_3	0.478±0.04	0.504±0.02	8.33±0.03	1.09±0.04	27.18±0.04
$^{G}1$	0.439±0.02	0.517±0.04	7.54±0.07	1.08±0.05	27.78±0.02
G_2	0.429±0.09	0.524±0.05	16.22±0.02	1.19±0.11	25.16±0.05
G_3	0.481±0.03	0.537±0.02	20.11±0.08	1.25±0.04	26.14±0.05

Table 6: Evaluation of Granules properties of combination of polymers.

Formulation code	LBD* (g/ml)	TBD* (g/ml)	Carr's index*	Hausner's Ratio*	Angle of of repose*
HC_1	0.439±0.04	0.551±0.03	12.70±0.08	1.14±0.02	27.34±0.02
HC_2	0.447±0.03	0.533±0.03	16.13±0.05	1.19±0.03	28.30±0.01
HC_3	0.452±0.07	0.519±0.04	12.90±0.06	1.14±0.10	27.46±0.02
HG_1	0.461±0.03	0.527±0.03	12.52±0.05	1.14±0.04	28.18±0.05
HG_2	0.433±0.04	0.515±0.07	15.92±0.06	1.18±0.08	29.12±0.03
HG_3	0.447±0.04	0.531±0.05	15.81±0.06	1.18±0.07	25.31±0.07
CG_1	0.439±0.05	0.547±0.03	19.74±0.02	1.24±0.08	27.15±0.02
CG_2	0.475±0.03	0.517±0.07	13.89±0.07	1.13±0.06	26.48±0.01
CG_3	0.463±0.07	0.541±0.08	11.97±0.05	1.13±0.06	24.14±0.08
HCG_1	0.452±0.04	0.526±0.05	12.57±0.05	1.14±0.03	28.16±0.06
HCG_2	0.457±0.09	0.517±0.05	13.28±0.05	1.15±0.09	27.51±0.06
HCG_3	0.458±0.03	0.527±0.02	12.92±0.03	1.14±0.04	28.38±0.07

DISCUSSION

Sustained release matrix tablets of Atenolol HCl were prepared using hydrophilic Polymers. Polymers used were HPMC , Sodium CMC and Guar gum. The hydrophilic matrices for Atenolol HCl containing a blend of one or more gel forming polymers. The compositions of the formulations are shown in Table No.3 and Table No.4 Lactose was used as filler.

Determination of Interaction Between Drug And Used Polymers

The IR spectra of all combinations containing drug and one or more polymers also shows the characteristic peaks same as that of the pure drug at Specific wave no. is shown in Table No .12 & 13 The IR spectrum of all the combinations containing drug and one or more polymer shows same or slightly shift in peak values when compared with the characteristic peak values of the pure drug.

Thus, from the above it is concluded that there is no interaction between the Atenolol HCl and used polymers.

Evaluation of Granules

The granules were prepared by wet granulation method using 6 % (w/w) starch paste as binder. Precompressional parameters i.e. angle of repose, percent compressibility, and Hausner's ratios are shown Table No.14 and Table No.15 These results indicate that granules are good flowing characteristics.

The results of angle of repose (<30) indicate good flow properties of the granules. This was further supported by lower Hausner's ratios, lower compressibility index values. Compressibility index values upto 20.11% result in good to excellent flow properties. And thus the granules were suitable for compression.

Evaluation of Tablets

All the formulations of Atenolol HCl Sustained Released Matrix Tablet showed uniform thickness. As in Table No.16 and Table No.17. In a weight variation test, the pharmacopoeial limit for percentage deviation for the tablets of more than 350 mg is ±5%.The average percentage deviation of all the tablet formulations was found to be within the above limit, and hence all the formulations passed the test for uniformity of weight as per the official requirements. Good uniformity in drug content was found among different batches of tablets, and percentage of drug content was more than 95%. All the formulations shows required hardness this could be due to presence of starch paste which is generally responsible for more hardness of the tablet.

Dissolution Study

In-vitro drug release study for the prepared matrix tablets were conducted for period of 10-12 hours using a USP XXIV type II (paddle) apparatus at $37^0C \pm 0.5^0C$ and 50 rpm speed. The dissolution studies were carried out in phosphate buffer of pH 7.4 under sink condition. 5 ml sample was withdrawn from dissolution medium andreplaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solution was analyzed at 275 nm for atenolol HCl by UV-spectrophotometer.

The drug release data for HPMC 15cps formulation were shown in Table No. -18 and drug release profiles shown in Fig No. –11. The formulation with HPMC 15cps 10 %, 20 %, 30% has released the drug 98.70 %, 98.43% and 97.24 % at the end of 8 hrs, 10 hrs and 11hrs respectively.

The drug release data for Sodium CMC containing formulation were shown in Table No. -19 and drug release profiles shown in Fig No. –12. The formulation with Sodium CMC 10 %, 20 %, 30% has released the drug 98.13 %, 95.98 % and 96.41 % at the end of 9hrs, 10 hrs and 11hrs respectively. The quick release from Sodium CMC containing system is due to high solubility of Sodium CMC at pH 7.4.

This polymer characteristic gives to the matrix a quick gel erosion rate and a high erosion degree of the overall system. It Means matrices with only Sodium CMC release rate retardant were not able to control the release rate for Atenolol HCl for 12 hrs.

The control release above 12 hrs was seen with formulation containing combination of Sodium CMC / HPMC the slower release from this combination was due to interaction between Sodium CMC chain and HPMC chain. The capacity of Sodium CMC to form hydrogen bonds with the hydroxyl group of HPMC led to a synergistic effect on gel viscosity that explain the better control of these polymers on the release of Atenolol HCl.

The drug release data for combination of HPMC and Guar gum were shown in Table No.- 22 and drug release profiles shown in Fig No. – 15. The formulation HG1,HG2,HG3 has released the drug 78.52 %, 73.14% and 68.08 % respectively at the end of 11 hrs.

The dissolution data containing combination of Sodium CMC and Guar gum is shown in Table no.23 and dissolution profile of same is shown in Fig. no.16. The formulation CG1, CG2, CG3 has released the drug 73.33 %, 75.22 % and 78.40 % respectively atthe 11hrs.

In formulation when guar gum matrix tablet came in contact with dissolution medium it take up medium into the system which is responsible for dissolution of active constituent and then drug diffuse out of the system formulation but due to less guar gum less viscous gel layer is formed this gel layer becomes more viscous when guar gum content is more. Because of above reasons the difference in drug release pattern is seen in CG1, CG2 and CG3 formulations of Atenolol Hydrochloride matrix tablet.

All the polymers used in the study were used for the preparation of Atenolol HCl matrix tablet the dissolution data of these formulations is shown in Table No.24 anddissolution profile is shown in Fig. No.17. HCG1,HCG2,HCG3Formulation has released the drug 68.20 %, 66.18 % and 60.96 % respectively at the end of 11hrs.

Swelling Study

The swelling index of HC1, HC2, and HC3 is shown in Fig. No.18 The swelling behavior of various polymer blends was analyzed to compare their water uptake capacity. At the same time other soluble excipients or drug will also wet, dissolved and diffuse while increasing polymer level tends to decrease drug release. The most common explanation of the effect of increase in polymer level on drug release is that, it results in the increase in the thickness of gel layer, which retards drug diffusion out of the tablet.

Stability Study

Stability studies were conducted on the selected formulations of Atenolol HCl (HC2 and HC3) to assess their stability with respect to their physical appearance, drug content after storage at 40°C / 75 5% RH for 4 Weeks to assess their long term stability. Whenthe matrix tablets of Atenolol HCl (HC2 and HC3) were stored at 40°C / ambient RH for 3 weekss there was no appreciable change either in physical appearance or in drug content

The insignificant change either in the physical appearance, drug content of the selected formulations (HC2and HC3) after storage at 40°C / 75 5 % RH for 4 weeks indicate that the formations could provide a minimum shelf life of 2 years.

CONCLUSION

Matrix tablets are 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 HCl 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 HCl 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 HCl 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 HCl was selected for the study, because of its proved activity and better clinical application.

Sustained release matrix Tablet of Atenolol HCl containing blend of HPMC and sodium

CMC successfully sustains the release of Atenolol HCl for the period of 12 hrs. and formulation containing only single polymer could not control the release of Atenolol HClasdesired.

According to swelling study matrices containing a minimum Sodium CMC achieve higher Swelling Index.

The effect of drug to polymer ratio on the in vitro drug release behavior was significant.

Formulation HC2 and HC3 showed better sustained release when compared to other batches and this shows the ideal drug, polymer and excipients combination. From these formulations HC2 was found to be better released than HC3.

Stability study indicates that there is insignificant change either in the physical appearance or in the drug content of the formulations.

Future proposed works

Scale-up studies of the ideal formulation. Bioavailability studies.

Bioequivalence studies with marketed formulations.

Clinical trials if the earlier works yield encouraging results.

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