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Research Article

Formulation and Evaluation of Floating Egalet System for Atenolol

NH ALOORKAR, MB SHINDE*, SH SHIRKE, VU SABLE

Department of Pharmaceutics, Satara College of Pharmacy, Degaon, Satara (India) 415004

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ABSTRACT

Egalet technology is one of the oral platform technologies. In the present investigation this approach coupled with floating and chronotherapy was utilized. The entire system was developed for the treatment of early morning massive hypertensive heart attacks. The objective of this study was to develop and evaluate floating Egalet drug delivery system. Floating of the dosage form was achieved by incorporating two erodible plugs and drug containing plug in the capsule and keeping the air spaces between each plug. The erodible Plugs were composed of HPMC E5 LV polymer and prepared by using direct compression method. Drug containing plugs were prepared by using wet granulation method. Assembling of the dosage form was done by placing two identical outer section plugs enclosing an internal plug of active drug in middle of the capsule. The whole system except the both ends after filling the tablets in capsule was coated with cellulose acetate phthalate to achieve drug release only from both the ends. Atenolol was chosen as s a candidate drug for this drug delivery system. *In vitro* dissolution study revealed that the drug release took place only after lag time of 6 h. The drug release was found to be dependent on the binder composition and concentration in the formulation. Thus the developed system offers a novel technique for chronotherapeutic release of atenolol in upper part of GIT to treat hypertension in a very effective way i.e. making drug availability at required time.

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INTRODUCTION

During recent years, modified release drug delivery systems have shown a tremendous potential for their ever-increase role in health care. Modified release drug delivery systems have gained increased importance, because of using formulation based approaches [1]. Egalet technology is one of the modified release platform technologies of oral drug delivery system[2]. Egalet system consists of a drug containing core surrounded by impermeable shell, so drug release takes place from both the ends of system [3]. Egalet system is of two types, matrix system and delayed release system. In matrix system drug is incorporated in polymer matrix [4] and this matrix is surrounded with impermeable shell i.e. matrix in cylinder system[5]. With the help of matrix system we can achieve the zero order drug release [2].

Author for Correspondence:
Email: manojshinde2489@gmail.com

In delayed release Egalet system, delayed release of the drug is achieved by placing two identical outer sections, called "plugs" enclosing an internal plug of active drug in the middle [6].

The lag plugs are prepared by using suitable polymers [2, 3]

The present research work was aimed to develop a floating Egalet system for chronotherapeutic drug delivery of atenolol. The floating Egalet system floats in stomach because of hard gelatin capsule and the air spaces present between the plugs [7]. One can achieve delayed release up to 6 h by using erodible outer section plugs [8] and after that drug release occurs as a pulse. So this system is very helpful in the treatment of chronotherapeutic diseases mainly for preventing cardiovascular attacks which frequently occur early in the morning. In most of the cases these attacks frequently occur early in the morning, so the patients should be provided with the adequate dose of the drug at that particular time. It is not possible to give the drug to the patients every day in the morning. Hence in the present investigation it was thought of

preparing floating Egalet chronotherapeutic drug delivery system of atenolol, which would release the drug after 6 h and thus patients need for the adequate amount of drug would be sufficed which in turn might result into increased patient compliance

MATERIALS AND METHODS

Atenolol was obtained as a gift sample from Ajanta Pharma, Mumbai, India; hydroxypropyl methylcellulose (K100M, K15M, K4M, E5LV, E3LV) and spray dried lactose were obtained from Watson Pharma, Mumbai, India; '0' size empty hard gelatin capsules were obtained as gift sample from Associated capsule Pvt. Ltd., Shirval, India. Lactose, PVP-K30, starch, acetone, methanol, dibutyl phthalate, cellulose acetate phthalate, talc, magnesium stearate, hydrochloric acid were obtained from Research Lab, Mumbai, India. All the other ingredients used were of analytical grade and were used as procured.

METHODS

Preparation of Granules

Atenolol, lactose and starch were passed through the 40 # sieve and added in a blender and mixed for 20 min. This mixture was wetted with binder solution (PVP-K30 and/or Starch paste). The wet mass was passed through 20 # sieve to obtain granules. Granules were dried in an oven at 55^0C for 45 min. The prepared granules were mixed with required quantity of magnesium stearate and talc which were previously passed through 80 # sieve. The granules were stored in air tight container and were used for further study.

Preformulation Study

Granules prepared by wet granulation method were characterized by determining bulk density, tapped density, Carr's index, Hausener's ratio and angle of repose to check flow property and compressibility.

Compatibility Study between Drug and Excipients

FTIR and DSC studies were carried out for the determination of the possible interactions between the drug and the excipients in the formulation.

Formulation Design

Preparation of Impermeable Capsules

Capsules (size 0) were made impermeable to 0.1 N HCl by dip coating method. The entire capsule except at both the ends was coated with 8% w/w cellulose acetate phthalate (CAP) in acetone to prevent dissolution of capsules in gastric fluid. Dibutyl phthalate (DBP) (4%) was used as a plasticizer. Prepared impermeable capsules were air dried.

Preparation of the Erodible Plugs

Direct compression method was used to prepare the erodible tablet plugs. Various grades of HPMC like HPMC K100M, HPMC K15M, HPMC K4M, HPMC E5LV and HPMC E3LV were used and HPMC E5LV was selected for study. The erodible plugs contained 85% HPMC E5LV, 14% spray dried lactose and 1% magnesium stearate. These ingredients were compressed by using 7 mm flat faced punches on a tablet compression machine (Rimek II, Karnavati Engineering Ltd., Ahmedabad, India.)

Preparation of Atenolol Tablets

Atenolol tablets were prepared by wet granulation method according to the formulae given in table 1. All the ingredients were passed through # 60 mesh separately. All the ingredients were weighed accurately. Atenolol, lactose and starch were mixed in blender for 20 min. Then this mixture was wetted with binder solution. The wet mass was passed through 20 # sieve. Then wet granules were obtained, these wet granules were dried in an oven at 55^0C for 45 min. The prepared granules were mixed with magnesium stearate and talc.

Compression of Tablets

Prepared granules were compressed to tablets using 7 mm flat faced punches (Rimek II, Karnavati Engineering Ltd., Ahmedabad, India). Total eight formulations were prepared by keeping dose of the drug constant and changing the concentration of binder used in formulation.

Assembling of the Dosage Form

In the empty hard gelatin capsule body, one rate controlling plug was filled at the bottom, followed by tablet containing API at the middle and the second rate controlling plug at the top. Finally the assembled capsule body was sealed with gelatin cap.

Coating to the Assembled Capsule

The entire capsule except at both ends was coated with cellulose acetate phthalate. Both the ends of the capsules were left uncoated by covering with gelatin caps. The coating was done by using deep coating method. After coating, capsules were air dried and finally the covering caps were removed.

Table1: Composition of atenolol tablets

Sl.No.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
1	Atenolol	25	25	25	25	25	25	25	25
2	Lactose	156.5	154	151.5	149	154	149	144	139
3	Starch	10	10	10	10	10	10	10	10
4	PVP-K30	2.5	5	7.5	10	--	--	--	--
5	Starch (Paste)	--	--	--	--	5	10	15	20
5	Talc	3	3	3	3	3	3	3	3
6	Magnesium stearate	3	3	3	3	3	3	3	3
	Total	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

*All quantities are expressed in mg. Formula for one tablet is shown in table.

Table 2: Precompression parameters of prepared granules

Batch	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Angle of Repose (θ^0)	Carr's Compressibility Index (%)	Hausner's ratio
F1	0.434 ± 0.01	0.476 ± 0.01	25.86 ± 0.60	8.82 ± 0.5	1.09 ± 0.021
F2	0.416 ± 0.03	0.476 ± 0.06	26.83 ± 0.29	12.60 ± 1.18	1.14 ± 0.019
F3	0.370 ± 0.01	0.434 ± 0.02	26.42 ± 0.74	14.74 ± 0.5	1.17 ± 0.031
F4	0.384 ± 0.05	0.434 ± 0.02	27.31 ± 0.50	11.52 ± 1.21	1.13 ± 0.015
F5	0.421 ± 0.09	0.502 ± 0.02	27.08 ± 0.55	14.28 ± 1.03	1.23 ± 0.014
F6	0.400 ± 0.005	0.454 ± 0.01	26.74 ± 1.17	11.89 ± 0.50	1.13 ± 0.030
F7	0.370 ± 0.08	0.416 ± 0.05	28.02 ± 0.32	11.05 ± 1.23	1.12 ± 0.012
F8	0.384 ± 0.05	0.454 ± 0.01	26.42 ± 0.50	15.41 ± 1.10	1.18 ± 0.020

All values are expressed as mean ± SD, n=3

Table 3: Evaluation of impermeable capsules

Inner Diameter (mm)		Outer Diameter (mm)		Weight Variation (mg)		Weight Gain (mg)
Before coating	**After coating**	**Before coating**	**After coating**	**Before coating**	**After coating**	
6.988 ±0.12	6.993 ± 0.04	7.05 ± 0.05	7.1 ± 0.21	90.76 ± 0.04	94.7± 1.16	3.94 ± 0.12

All values are expressed as mean ± SD (n = 3)

Table 6(a): Evaluation studies for atenolol tablets

Batch	Weight Variation (mg) €	Hardness (Kg/cm^2)	Thickness (mm)	Diameter (mm)
F1	197.02 ± 3.19	3.75 ± 0.27	3.04 ± 0.005	6.96 ± 0.05
F2	197.01 ± 3.89	4.16 ± 0.51	3.03 ± 0.005	7.00 ± 0.00
F3	196.87 ± 3.06	4.00 ± 0.44	3.03 ± 0.010	6.93 ± 0.06
F4	195.87 ± 3.23	4.08 ± 0.58	3.02 ± 0.005	6.96 ± 0.05
F5	196.71 ± 3.52	3.83 ± 0.51	3.03 ± 0.01	6.95 ± 0.08
F6	197.84 ± 3.41	3.83 ± 0.25	3.03 ± 0.005	7.00 ± 0.00
F7	196.79 ± 2.80	3.91 ± 0.49	3.02 ± 0.017	7 ± 0
F8	195.78 ± 3.69	4.25 ± 0.52	3.03 ± 0.005	6.93 ± 0.05

All values are expressed as mean ± SD

Evaluation of Prepared Formulation

Evaluation of Impermeable Capsules

1. Capsule Dimensions

3 capsules were selected and evaluated for inner and outer diameter using vernier caliper before and after coating [9].

2. Weight Variation

20 capsules were weighed individually before and after coating and average weight was calculated. Not more than two individual weights of capsules should deviate from the average weight. 10% deviation is allowed in average weight of capsule as per IP specification [11].

3. Uniformity of Coating

20 capsules were weighed before and after coating and average weight were calculated. The uniformity of coating was determined by calculating the difference in weight before and after coating of capsules. If the calculated difference is same for each batch, it confirms uniform coating [9].

4. Impermeability Test

Impermeability test was performed to check impermeability character of prepared impermeable capsules. Six capsules were selected. Each capsule contained two erodible plugs, placed at the either ends of the capsule and dry color powder (food color) was placed between two plugs. The entire capsule except at both the ends was coated with cellulose acetate phthalate and placed in vessels containing 900 ml of 0.1 N HCl of USP XXIII type II tablet dissolution apparatus with stirring rate of 50 rpm. No leaching of color in 0.1 N HCl is indicative of impermeability of capsule body [8].

Evaluation Test for Erodible Plug

1. Plug Dimensions

3 plugs were selected and evaluated for thickness and diameter study using vernier caliper [9].

2. Weight Variation

20 plugs were weighed and the average weight was calculated. Not more than two of the individual weights of plugs should deviate from the average weight by more than 7.5% deviation as per IP 2007 specification.

3. Hardness

3 plugs were selected and evaluated for hardness. Monsanto hardness tester was used to determine hardness of erodible plugs. It is expressed in kg/cm^2. The mean hardness of each formulation was determined.

4. Swelling Studies

The swelling properties of HPMC erodible plug were determined by placing the plug in the dissolution test apparatus USPXXIII type I in 900 ml of 0.1 N HCl. The plugs were removed periodically from dissolution medium. After draining free water by blotting, the plugs were measured for weight gain on electronic balance. Swelling characteristics were expressed in terms of percentage water uptake (wu %). The equation, given below, shows relationship between swelling index and time [8].

$$\text{Swelling index} = \frac{\text{Swollen wt. of plug} - \text{Initial wt. of plug}}{\text{Initial wt. of plug}} \times 100 \quad \text{---------Eq. (1)}$$

Evaluation Parameters of Tablets

1. Hardness Test

The hardness of 3 tablets of each formulation was determined by using Monsanto hardness tester. It is expressed in kg/cm^2.

2. Friability Test

Twenty tablets were weighed and placed in the Roche friabilator and apparatus was rotated at 25 rpm for 4 min. After 100 revolutions the tablets were dedusted and weighed again. Percentage friability was calculated as per the method described I.P.

3. Thickness and Diameter

3 tablets from each formulation were selected and evaluated for thickness and diameter study using vernier caliper.

4. Weight Variation Test

20 tablets of each formulation were weighed individually by using an electronic balance and mean weight was calculated. Not more than 2 tablets should deviate from the average weight of the tablets, as per the specifications given in I.P. [10].

5. Disintegration Test

Randomly three tablets were selected from each batch for disintegration test. Disintegration test was performed in 0.1N HCl using USP disintegration test apparatus. The mean ± SD of 3 tablets was calculated [10].

6. Determination of Drug Content

Drug content from the tablets was determined by taking tablets from each formulation. Twenty tablets from each formulation were accurately weighed and powdered. Powder equivalent to 0.2 gm of the drug was weighed and transferred to a volumetric flask and added to it 300 ml of methanol. The resultant solution was heated at 60^{0}C and shaken for 30 min. Then the solution was cooled and a portion of solution was filtered through sintered glass funnel. A suitable volume of filtrate was diluted with a sufficient quantity of methanol to produce a solution containing 0.01% w/v of atenolol. The absorbance was then measured at 273.5 nm. The content of atenolol was calculated by taking 53.7 as a value of A at λ_{max} of 273.5 [10].

Table 7(a): Percent drug release profile of F1 to F4 formulations

Time (min)	F1	F2	F3	F4
0	0	0	0	0
120	0	0	0	0
240	0	0	0	0
360	0	0	0	0
365	9.96 ± 1.13	6.09 ± 1.35	3.06 ± 2.01	2.22 ± 0.98
370	20.49 ± 2.95	16.83 ± 1.73	10.62 ± 2.02	5.52 ± 2.43
375	34.11 ± 2.12	28.41 ± 3.67	16.20 ± 1.73	15.99 ± 1.90
380	48.75 ± 2.85	40.74 ± 2.05	30.36 ± 0.30	29.28 ± 2.43
385	66.87 ± 1.71	51.15 ± 1.82	40.71 ± 2.01	40.68 ± 3.50
390	84.66 ± 2.18	63.96 ± 1.35	52.11 ± 2.35	48.99 ± 1.33
395	101.1 ± 1.87	78.57 ± 1.58	67.47 ± 2.79	59.10 ± 3.49
400	-	91.20 ± 2.54	80.34 ± 0.83	73.47 ± 1.85
405	-	100.2 ± 1.94	91.65 ± 2.51	83.22 ± 2.63

All values are expressed as mean ± SD, (n = 3).

Table 7(b): Percent drug release profile of F5 to F8 formulations

Time (min)	F5	F6	F7	F8
0	0	0	0	0
120	0	0	0	0
240	0	0	0	0
360	0	0	0	0
365	5.10 ± 0.95	3.54 ± 1.19	2.25 ± 1.06	0.33 ± 0.57
370	12.42 ± 3.45	9.81 ± 1.94	9.06 ± 0.59	3.81 ± 2.06
375	20.67 ± 1.04	17.52 ± 4.37	14.94 ± 2.18	10.53 ± 2.48
380	33.57 ± 1.62	33.24 ± 4.08	25.71 ± 2.57	17.25 ± 3.21
385	48.81 ± 3.30	43.50 ± 1.62	38.28 ± 1.22	25.05 ± 1.53
390	60.81 ± 1.59	54.18 ± 1.27	47.61 ± 2.71	37.38 ± 2.25
395	71.04 ± 1.55	65.13 ± 2.17	57.63 ± 2.02	51.63 ± 2.71
400	81.06 ± 0.90	77.10 ± 3.32	69.15 ± 3.40	61.80 ± 3.12
405	95.49 ± 1.32	89.16 ± 3.17	80.49 ± 1.71	72.69 ± 2.52

All values are expressed as mean ± SD, (n = 3).

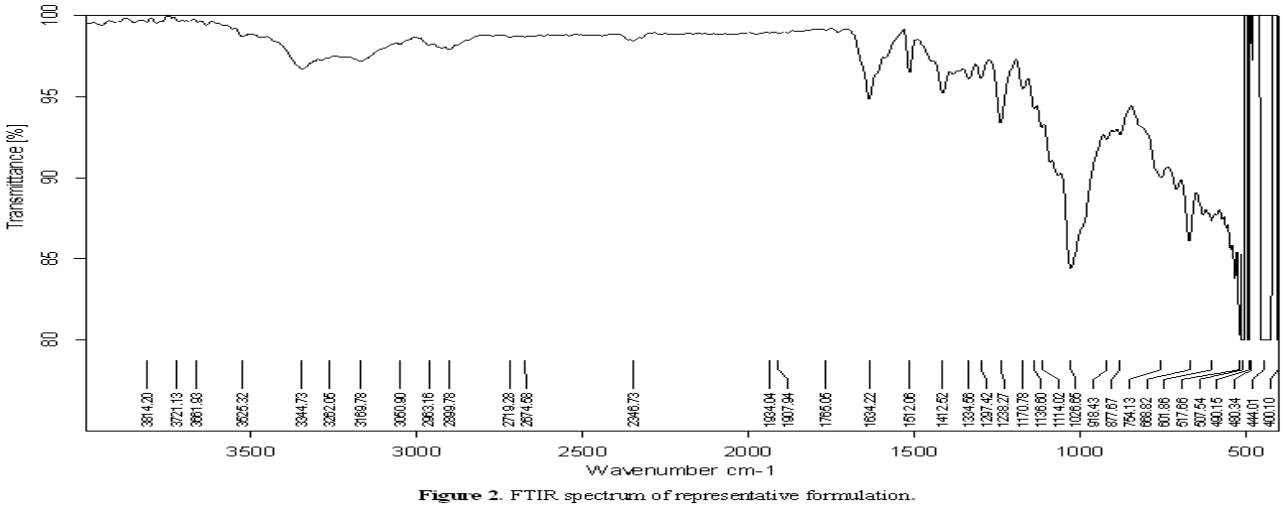

Figure 2. FTIR spectrum of representative formulation.

Figure 1: FTIR spectrum of atenolol

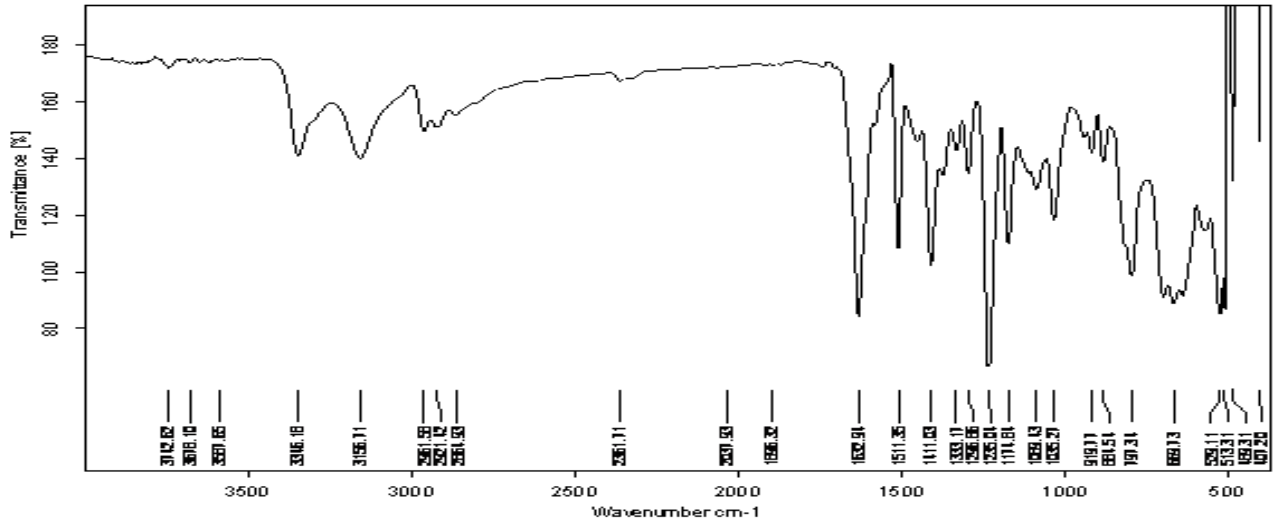

Figure 1. FTIR spectrum of atenolol.

Figure 2: FTIR spectrum of representative formulation

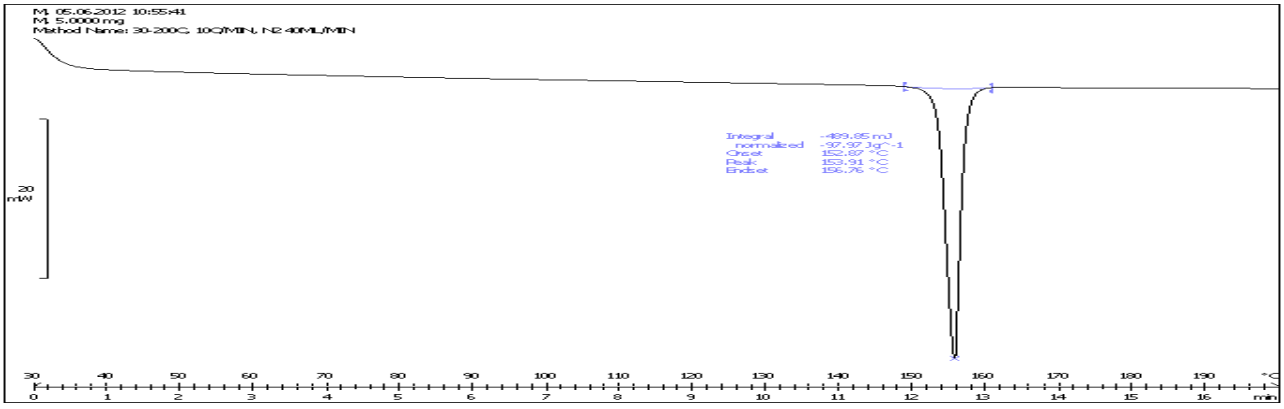

Figure 3. DSC thermogram of atenolol.

Figure 3: DSC thermogram of atenolol

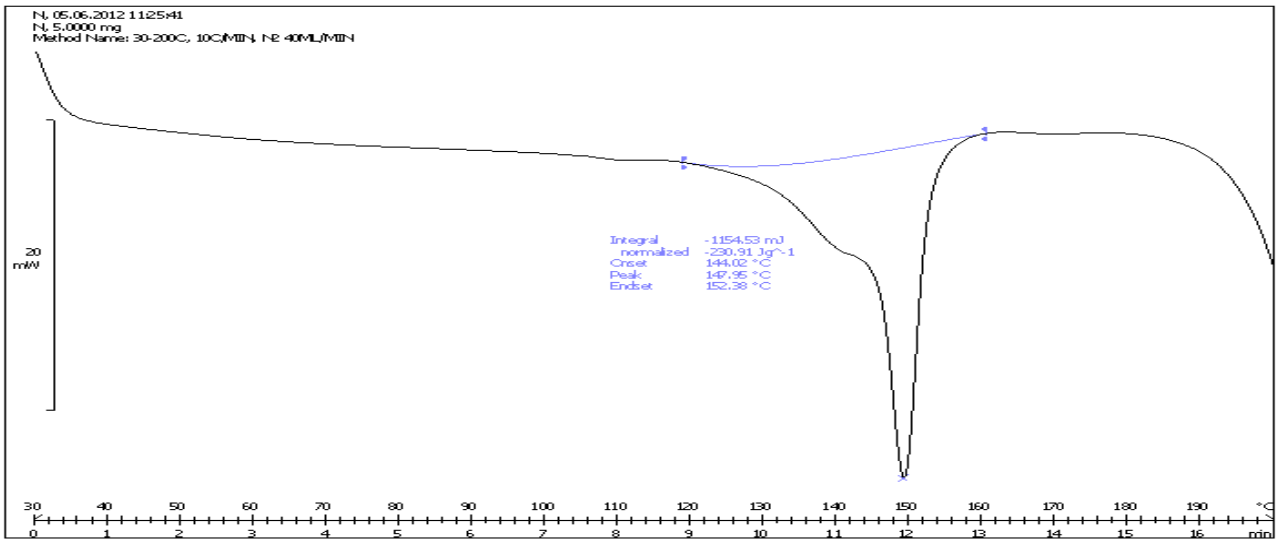

Figure 4. DSC thermogram of representative formulation.

Figure 4: DSC thermogram of representative formulation

In vitro Drug Release

In vitro dissolution tests were conducted in triplicate for all formulations in a USP XXIII type II tablet dissolution apparatus (TDT- 08L, Electrolab, India.) for 8 h under sink conditions. The dissolution medium used was 900 ml 0.1N HCl (pH 1.2) at 37±0.5^{0}C. The speed of rotation was maintained to 50 r.p.m. At a predetermined time intervals samples were withdrawn and absorbance was recorded. The samples were analyzed for drug release by measuring the absorbance at 273.5 nm using spectrophotometric method (Pharmaspec 1700, Schimadzu, Japan) [11].

Floating Behavior of Impermeable Capsules

The in vitro floating behavior of capsules was studied by placing them in USP XXIII dissolution apparatus type II containing 900 ml 0.1 N HCl at 37 ± 0.5^{o}C at 50 rpm. The Floating ability was determined by visual observation [8].

RESULTS AND DISCUSSION

Preformulation Study of Granules

The results of preformulation study of granules are as shown in Table 2. Bulk density of all the formulations was found to be in the range of 0.370 -0.420 g/ml, whereas tapped density of all the formulations was found to be in the range of 0.416 - 0.476 g/ml. Angle of repose was observed to be less than 30^o. Carr's index was found between 8.82 -15.41 which was well within the range of 8-16. All the formulations exhibited Hausner's ratio less than 1.25.

From these observations, it could be concluded that prepared granules were having good flow properties and good compressibility.

Compatibility Study between Drug and Excipients

FTIR Study

From the IR spectrum of pure drug (Fig. 1) and the representative formulation (Fig. 2), it was observed that all the important peaks that were found to be present in IR spectrum of drug were found to be present in IR spectrum of representative formulation. Neither any additional peak was observed in the IR spectrum of representative formulation nor was any important peak of the drug found to be missing. Thus, from the IR spectra of drug and the representative formulation, it could be concluded that both the drug and the excipients were compatible with each other.

DSC Study

As shown in the Fig. 3, the DSC thermo gram of atenolol showed an endothermic peak at 153.91^0 C which is close to the melting point of drug. As observed in DSC thermo gram of representative formulation, Fig. 4, no significant shift in the endothermic peak of drug was found (endothermic peak at 147.95^0 C). This indicated the absence of any interaction between drug and excipients. Hence from the DSC thermo grams, it could be concluded that there was compatibility between drug and excipients.

Evaluation of Capsules

Table 3 shows evaluation parameters of impermeable capsules. The prepared impermeable capsules exhibited negligible changes in diameter, weight variation and weight gain after coating.

Uniformity of Coating

Weight gain by impermeable capsules after coating was found to be 3.94 ± 0.12 (mg). From the obtained results it could be concluded that all the prepared impermeable capsules were having uniform coating (Table 3).

Impermeability Test

During the study it was found that dissolution fluid (0.1N HCl) had not penetrated through impermeable capsules. Dissolution fluid was remained colorless until the plug was eroded after 6 h. From this observation it could be concluded that prepared capsules passed the test for impermeability.

Evaluation of Erodible Plugs

Table 4 shows evaluation parameters of erodible plugs. Diameter and thickness of plugs were found to be 6.98 ± 0.07 (mm) and 4.03 ± 0.05 (mm) respectively. Uniform diameter and thickness indicates uniform die fill, good flow properties, uniform pressure and uniform punch movement. Hardness of erodible plugs was found to be 2.41 ± 0.20 Kg/cm^2. The plugs showed average weight of 179.81 ± 1.80 (mg) and none of the plugs were found to deviate from the average weight of plugs as per the specification given in IP 2007.

Table 4: Evaluation of erodible plugs

Diameter (mm)	Thickness (mm)	Hardness (Kg/cm^2)	Weight Variation(mg)
6.98 ± 0.07	4.03 ± 0.05	2.41 ± 0.20	179.81 ± 1.80

All values are expressed as mean ± SD (n = 3)

Table 5: Swelling study of plug

Time (h)	Swelling index (%)
0	0.00 ± 0.00
1	35.71 ± 0.53
2	54.69 ±0.79
3	76.87 ± 0.26
4	79.50 ± 0.26
5	75.85 ± 0.10
6	69.73 ± 0.79
7	65.78 ± 053

Swelling Study for Erodible Plugs

Table 5 shows the swelling index of erodible plugs. This indicated that initial swelling of the polymer due to water uptake and swelling up to 4 h followed by a platue which was observed up to 6 h and finally the erosion of the plug after 6 h. From the obtained results it could be concluded that the plug was remaining in the body of the capsule up to 6 h, was getting ejected from the body of the capsule after 6 h, and thus paving the way for drug release. In the present investigation various grades of HPMC were tried during optimization studies and based on the experimental results, HPMC E 5LV was chosen as the material for formulating the plug. It was selected based on the observation that it was able to prevent the drug release up to 6 h and the plug was getting ejected from the capsule at the end of 6 h, which was the lag time set for this study.

Evaluation of Tablets

Table 6a and 6b show evaluation parameters of eight different formulations of atenolol tablets. The thickness of tablets of all formulations was found to be in the range of 3.02 – 3.04 mm and diameter was found to be in the range of 6.93 – 7.00 mm. Hardness of tablets was found to be in the range of 3.75 to 4.25 kg/cm^2. Weight variation test revealed that the tablets were within the range of pharmacopoeial specifications and none of the tablet was found to deviate from the average weight of all the tablets. All the tablets had acceptable friability as none of the formulations had percentage loss in tablet weights more than 1%. Disintegration time was found to be varying from formulation to formulation because of the difference of the concentration of binder used in the formulation. The formulation having less concentration of binder exhibited less disintegration time and the formulation having greater concentration of binder exhibited more disintegration time. Drug content was observed in the range from 94.88 ± 0.58 to 99.54 ± 0.21 which was as per the IP (2007) specification (not less than 92.5% and not more than 107.5 %) (10). Thus all the formulations complied with the uniformity of active content test.

Table 6(b): Evaluation studies for atenolol tablets

Batch	Friability (%) €	Disintegration Time (min)	Drug content (%)
F1	0.46 ± 0.10	5.30 ± 0.82	99.54 ± 0.21
F2	0.27 ± 0.12	8.66 ± 1.41	99.12 ± 1.10
F3	0.32 ± 0.10	12.24 ± 1.23	98.00 ± 0.97
F4	0.36 ± 0.18	15.82 ± 1.12	97.80 ± 0.78
F5	0.41 ± 0.11	9.10 ± 1.98	98.21 ± 1.09
F6	0.57 ± 0.10	12.33 ± 1.15	98.18 ± 0.94
F7	0.52 ± 0.18	17.00 ± 0.95	94.88 ± 0.58
F8	0.39 ± 0.15	20.15 ± 1.20	97.91 ± 1.10

All values are expressed as mean ± SD, (n = 3, € - indicates n=20)

In vitro Drug Release

After exposing the impermeable capsule to the dissolution medium, uncoated ends of the capsule were found to be eroded within 5 to 10 minutes, after which plugs were exposed to the dissolution medium, 0.1 N HCl. Because of penetration of dissolution medium in to the plugs, it started swelling. During dissolution studies it was observed that the plugs were swelling for first 4 h and after which polymer started to erode slowly. It means that plugs placed at both the ends of the capsule ensured a good seal, preventing premature drug release and the lag time of the Egalet system was found to be uniform throughout the dissolution studies. At 6 h both the plugs got ejected completely and the actual drug release was started. Table 7a and 7b shows the percent drug release profile of all formulations. Formulations F1 to F4 consisted of PVP-K30 as a binder and the concentration of the binder was 1.25%, 2.5%, 3.75%, 5% respectively. From the dissolution studies it was found that the F1 exhibited faster drug release compared to F2 followed by F3 and F4.

Formulations F5 to F8 consisted of starch paste as a binder and the concentration of the binder was 2.5%, 5%, 7.5% and 10% respectively. From the dissolution studies it was found that F5 showed faster drug release compared to F6 followed by F7 and F8. It was also found that formulations containing PVP-K30 as a binder exhibited faster drug release as compared to

formulations containing starch paste as a binder. This may be due to more hydrophilicity of PVP-K30 as compared to starch which in turn might have contributed to increased capillary action and thus the earlier disintegration of the tablets and more amount of the drug release from the formulation at the end of the stipulated time. The same thing is evident from the in vitro disintegration and dissolution studies.

Figure 5: Morphological changes in the formulation during *in vitro* dissolution study

Fig. 5 shows the morphological changes in the system during the dissolution. Fig. 5a shows the photograph of a prepared dosage form kept in contact of dissolution medium. Within 5 to 10 minutes the uncoated ends got eroded and system behaved as a cylindrical one. In the cylindrical system drug core was placed at the centre of the cylinder and the lag plugs were placed at the ends of the cylinder to delay the drug release. After the opening of both ends of the capsule single surface of each plug was exposed to the dissolution medium So dissolution medium got penetrated in the plugs from the exposed surfaces and therefore plugs started to swell and as time was passed swelling of the plugs was increased. Fig. 5b shows the photograph of the system at 3 h. System exhibited swelling up to 4 h and after that it started to erode. At 6 h both the plugs were completely eroded and middle drug containing tablet was exposed to the dissolution medium. This drug containing tablet got dissolved from both the open ends. Fig. 5c shows system at 6 h. From this observation it was found that the actual drug release was started after 6 h. Fig. 5d shows system after total drug release. The hollow impermeable cylinder was remained undissolved and after gastric emptying this hollow cylinder may reach to the small intestine and may erode because it was coated with pH dependent polymer, cellulose acetate phthalate.

Floating Behavior

The system was found to be floating for more than 6 h on the surface of dissolution medium. During the dissolution study cylindrical portion of capsules were found to be intact up to 6 h. This indicated that the capsules were having good coating of acid resistant coating agent. The floating ability was determined by visual observations.

CONCLUSION

A novel floating Egalet drug delivery system for atenolol was formulated and evaluated. Floating behavior of the formulation was found to be good. All the formulations were found to be floating till the entire drug was released. Among all the grades of HPMC tried, HPMC E5 LV was found to be the suitable polymer that could resist the drug release up to 6 h after which it got eroded paving the way for drug release. The coating of the capsules was found to be intact except at both ends as it was proved by test for impermeability. All the formulations exhibited good results for pre formulation and post formulation studies. The formulations containing PVP-K30 as the binder were found to give earlier drug release as compared to formulation containing starch paste as a binder. This could probably due to more hydrophilic nature of PVP-K30 as compared to starch paste. All the formulation exhibited drug release only after 6 h indicating the chronotherapeutic pulsed drug release. Thus from the above discussion it was clear that a floating Egalet pulsatile drug delivery system could effectively be formulated for better and effective management of hypertension.

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