Journal of Medical and Pharmaceutical Innovation
ISSN : 2347 - 8136

Research Article

Formulation and Evaluation of Floating Microspheres of Atenolol

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ABSTRACT

The objective of the present investigation was to prepare floating microsphere of atenolol to improve the bioavailability by increasing residence time in stomach. The microspheres of atenolol were prepared ed formulations were subjected to evaluation as FTIR, particle size, size distribution, % yield, drug content, buoyancy study, entrapment efficiency and in vitro dissolution. The FTIR spectra revealed that, there was no interaction between polymer and atenolol. The polymers used were compatible with atenolol. As the drug tby solvent evaporation technique using ethyl cellulose as polymer at different concentration. The preparo polymer ratio was increased, mean particle size of atenolol floating microspheres was also increased. Atenolol floating microspheres with normal frequency distribution were obtained.

Entrapment efficiency increased with increase in polymer concentration. From the results it can be inferred that there was the proper distribution of atenolol in the microspheres. On the basis of release data and graphical analysis formulation F-3 shows good controlled release profile with maximum entrapment efficiency because of high polymer concentration.

Keywords: Floating microspheres, atenolol, solvent evaporation, FT-IR

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Conflict of Interest: None declared

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(Received 11 September 2015; Accepted 11 October 2015; 1 November 2015) ISSN: 2347-8136 ©2014 JMPI

INTRODUCTION

Floating microspheres are gastro-retentive drug delivery systems based on non-effervescent approach. Hollow microspheres are in strict sense, spherical empty particles without core. These microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers. Solid biodegradable microspheres incorporating a drug dispersed or dissolved throughout particle matrix have the potential for controlled release of drugs. Floating microspheres have emerged as an efficient means of enhancing the bioavailability and controlled delivery of many drugs the increasing sophistication of delivery technology will ensure the development of increasing number of gastro-retentive drug delivery systems to optimize the delivery of molecules that exhibit absorption window, low bioavailability, and extensive first pass metabolism.[1]

Atenolol is a non-selective beta-blocker mainly used in the treatment of hypertension and arrhythmia. The plasma half-life of atenolol is short hence requiring taking thrice a day and it is decompose at alkaline pH3. The recommended adult oral dosage of atenolol is 10 mg 2 to 3 times in day. Gastro retentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastric retention will provide advantages such as the delivery of drugs with narrow absorption windows in the small intestinal region. Also, longer residence time in the stomach could be advantageous for local

action in the upper part of the small intestine, for example treatment of hypertension and arrhythmia.[2]

Materials and Methods

Atenolol was obtained as gift sample from Lupin Ltd. Aurangabad. Ethyl cellulose was purchased from Research fine lab and all other chemicals were of analytical grade.

Preparation of microspheres

Formulation design for atenolol floating microsphere using different ratios of drug and polymers.

Ingredients	F-1	F-2	F-3	F-4
Atenolol (mg)	100	100	100	100
Ethyl Cellulose (mg)	100	200	300	400
DCM (ml)	15	15	15	15
Ethanol (ml)	15	15	15	15
Tween 80%	1	1	1	1

Table 1: Formulation design for atenolol floating microspheres

Emulsification solvent evaporation method was employed for preparation of microspheres of atenolol. The drug & polymer (1:1, 1:2,1:3) this mixture was dissolved in ethanol & dichloromethane (15ml) containing 0.01% of tween 80, The solution was stirred for 1 hr at 700rpm. The formed microsphere were filtered & washed with water & dried at room temperature.

DISCUSSION

Evaluation of Atenolol Floating Microsphere

Frequency Distribution Analysis

Determinations of average particle size ofatenololfloating microsphere were carried out by optical microscopy in which stage micrometer was employed. A minute quantity of atenolol floating microsphere was spread on a clean glass slide and average size of 300 atenolol microsphere was determine in each batch. In order to be able to define frequency distribution or compare the characteristics of particles with many different diameters, the frequency distribution can be broken down into different size ranges, which can be presented in the form of a histogram. Histogram presents an interpretation of a frequency distribution and enables the percentage of particle having a given equivalent diameter to be determined.

Percentage Yield

Percentage practical yield of atenolol floating microspheres is calculated to as certain efficiency method of production. As per equation:

$$\text{Percentage Yield} = \frac{\text{wt of microsphere}}{\text{Sum of wt of solid excipients}} \times 100$$

Buoyancy Percentage

One hundred milligram of microspheres was placed in 0.1M HCL, 100ml containing 0.02%w/v Tween 80. The mixture was stirred at 100rpm in magnetic stirrer. After 12 hr the layer of buoyant microsphere was pipette and separated by filtration. Particles in the sinking particulate layer were separated by filtration. Particles of both type were dried in desiccators until constant weight. Both the fractions of microsphere were weighed and buoyancy was determined by the weight ratios of floating particles to the sum of floating and sinking particles.[3]

$$\text{Buyancy}(\%) = \frac{Wf}{Wf + Ws} \times 100$$

Where, W f and Ws are the weights of a floating and settled microsphere respectively

Determination of Percentage Drug Entrapment

Efficiency of drug entrapment for each batch was calculated in terms of percentage drug entrapment as per formula:

$$PED = \frac{\text{Practicaldrugloading}}{\text{Theoreticaldrugloading}} \times 100$$

Theoretical Drug Content

Theoretical drug content was determined by calculation assuming that entire atenolol present in the polymer solution used gets entrapped in atenolol floating microsphere, and no loss occurs at any stage of preparation of atenolol floating microsphere.

Practical Drug Content

Procedure- Practical Drug Content was analyzed by using following procedure, weighed amount of atenolol floating microspheres equivalent to 10mg of atenolol floating microspheres was dissolved in 100ml of 0.1N HCL. This solution was kept overnight for the complete dissolution of the atenolol floating microspheres in 0.1N HCL. This solution was filtered and suitably diluted. The absorbance was measured at 226.6nm against 0.1N HCL solution as blank and calculated for percentage of drug present in the sample.[4]

In-Vitro Dissolution Studies

Procedure for in-vitro dissolution studies

The release rate of atenolol floating microspheres was determined by employing USP XXIII

apparatus by rotating paddle method. The dissolution rate was performed using 900ml 0.1N HCL, in 37± 0.5ºC at 50 rpm. Atenolol floating microspheres equivalent to 10mg were placed in paddle to avoid floating of microspheres. A sample (5ml) of the solution was withdrawn from the dissolution apparatus hourly for 12 hr, and the sample were replaced with fresh dissolution medium. The samples were passed through whatman filter paper and the absorbance of these solutions was measured at 226.6nm. Dissolution profiles of the formulation were analyzed by plotting drug release verses time plot.

Stability Studies

The stability study of the optimized F-3 formulation was carried out according to ICH guidelines at RT and 40° C temperature by storing the samples in stability chamber.[5]

Results and discussion

The Average particle size of atenolol floating microspheres is given in table 2

Sr. No	Formulation Code	Average particle size (µm)
1	F-1	50
2	F-2	70
3	F-3	100
4	F-4	125

Table 2: Average particle size of Atenolol floating microsphere

Frequency Distribution Analysis

As the atenolol to polymer ratio was increased, the mean particle size of atenolol microsphere was also increased (table 3). The significant increase may be because of the increase in viscosity of the droplets (may be due to the increase in the polymer concentration.). Atenolol floating microspheres having the size range of 10-150µm (table 3) with normal frequency distribution was obtained.

Size range	**Number of particles**			
(µm)	**F-1**	**F-2**	**F-3**	**F-4**
0-30	45	53	42	15
30-60	73	80	65	59
60-90	79	94	83	92
90-120	40	49	61	53
120-150	25	32	48	47
150-180	-	-	31	37

Table 3: Particle Size Distribution of Atenolol floating microsphere

Buoyancy Percentage

The microsphere floated for prolonged time over the surface of the dissolution medium. As the polymer concentration increases the buoyancy time increases. Percentage buoyancy of the microspheres was in the range 50% to 77% after 12hrs. The results obtained are given in table 4

Sr.No	Formulation Code	% Buoyancy
1	F-1	50
2	F-2	60
3	F-3	85
4	F-4	77

Table 4: Buoyancy Percentage of Atenolol floating microsphere

Percentage yield

The percentage yield for atenolol floating microspheres were 50.95%, 66.80%, 95.75%, 73% for formulation F-1, F-2, F-3, F-4 respectively are given in table 5.

Percentage drug entrapment efficiency

Entrapment efficiency increases with increase in the polymer concentration. From the results it can be inferred that there is the proper distribution of atenolol in the microspheres and the deviation is within the acceptable limits.

The percent of drug content in the formulations was found to be in the range of 56% - 85%. The percentage drug entrapment was found to be 50% - 77%.The results obtained are given in table 5. A maximum of 85% drug entrapment efficiency was obtained in the atenolol floating microspheres. It was further observed that the drug entrapment was proportional to the atenolol: polymer ratio and size of floating microsphere. By increasing the polymer concentration, the encapsulation efficiency was increased.

Sr.No	**Formulation Code**	**Percentage yield**	**Drug Content (%)**	**Entrapment Efficiency (%)**
1	F-1	50.95	56	50
2	F-2	66.80	67	60
3	F-3	95.75	92	85
4	F-4	73	85	77

Table 5: Percentage drug entrapment efficiency of Atenolol floating microsphere

In-Vitro Dissolution Study

The In-Vitro performance of the atenolol floating microspheres showed prolonged and controlled release of atenolol. The result of the in-vitro dissolution studies shows controlled and predictable manner as the polymer concentration increases the drug release from the floating microsphere increase. The formulations are F-1 73.69 to F-3 98.13. The In-Vitro drug releases of the atenolol floating microspheres were given in figure 1, table 6.

Sr. No	Time (hr)	% Cumulative Drug Release			
		F-1	F-2	F-3	F-4
1	1	32.76	31.32	35.28	36.54
2	2	32.956	31.522	35.52	36.756
3	3	35.507	36.59	43.487	39.071
4	4	41.132	41.663	51.98	34.565
5	5	49.148	47.646	58.505	33.509
6	6	34.029	55.419	66.448	37.853
7	7	37.029	61.316	70.26	42.207
8	8	55.964	53.56	76.086	48.369
9	9	62.205	50.75	87.989	56.00
10	10	51.681	63.555	92.151	69.924
11	11	68.987	67.84	96.122	80.429
12	12	73.693	61.799	98.132	92.116

Table 6: In-Vitro drug release of the atenolol floating microspheres

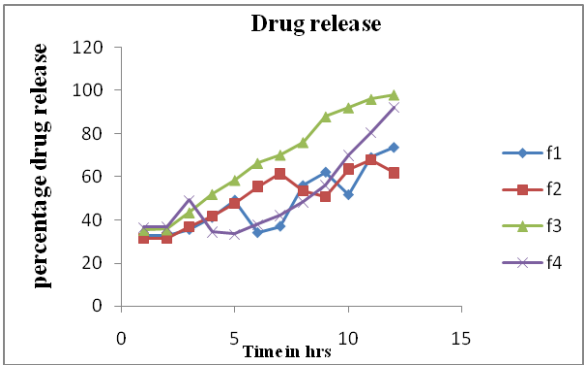

Figure 1: In-Vitro dissolution of the atenolol floating microspheres

Stability Studies

Atenolol microspheres (optimized batch F-3) were kept at different storage conditions. Test samples were kept at room temperature and at 40°C. Percent entrapment efficiency of the formulation was determined initially which was found to be 92.4%. The samples were withdrawn at different time intervals and the drug contents were determined. The percent drug remaining is reported in table 7. The controlled release atenolol microspheres were found to be stable at the different storage condition for one month period.

Condition	% Entrapment Efficiency After		
	7 days	15 days	30 days
Room Temperature	87.12	87.09	87.02
40° C	87.18	87.05	87.05

Table 7: Stability data of Atenolol microspheres

CONCLUSION

The floating microspheres of atenolol were prepared and evaluated by solvent evaporation technique using ethyl cellulose polymer. The prepared microspheres showed good entrapment efficiency, byoyancy and prolonged drug release. Formulating floating microsphere of atenolol will be a better, practical approach to achieve a prolonged therapeutic effect by continuously releasing the medication over the extended period of time in the stomach.

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