ISSN: 0976-4607
Research Article

International Journal of Innovative Pharmaceutical Research

Journal homepage: www.ijipr.com

Preparation and Evaluation of Atenolol Floating Beads as a Controlled Drug Delivery System

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ABSTRACT

Floating microspheres have been utilized to obtain prolonged and uniform release of drug in the stomach for development of once-daily formulation. A controlled-release system designed to increase the residence time in the stomach without contact with the mucosa. Atenolol is an anti -hypertensive drug having low water solublility and only 50% of oral bioavailability. Atenolol floating microspheres were prepared by the ionotropic gelation technique using hydroxyl propyl methyl cellulose and sodium alginate as polymers at different ratios. The 30ml of sodium alginate and hydroxyl propyl methyl cellulose solution in 9:1 ratio was prepared using 1%, 2% and 3% concentrations of polymers. The prepared formulations were characterized for their particle size, entrapment efficiency, drug content, and *in-vitro* drug release using 0.1N Hcl of pH 1.2. The microspheres were found to be regular in shape and highly porous. Amongst 3 formulations prepared (F1-F3), F3 showed prolonged drug release and remain buoyant for more than 8 hours and suggested that increased polymer concentration gives slower release of drug and more duration of drug release in the stomach.

Key words: Atenolol, Gastro retentive drug delivery, Microspheres.

INTRODUCTION

Atenolol is an anti- hypertensive drug which is a low water soluble drug and having only 50% of oral bio availability. The low water solubility of atenolol leads to poor bio availability. In order to increase the bioavailability of drug, it was formulated with the polymers like hydroxyl propyl methyl cellulose and sodium alginate which gives the property of floating in the stomach (Chun MK *et al*., 2011). When they come in contact with water, they swell and float on the water and gives buoyancy to the microspheres and gives slow and constant release of drug. Drug release based up on the time of buoyancy (Nagai T *et al*., 1985). These are known as hydrodynamically balanced systems. The density should be less than 1gm/cm^3.

MATERIALS REQUIRED

Atenolol (A to Z Pharma Pvt. Ltd. Chennai), Sodium alginate (Merck Pvt. Ltd. Mumbai), Hydroxyl propyl methyl cellulose (Merck Pvt. Ltd. Mumbai), sodium bicarbonate (Merck Pvt. Ltd. Mumbai), Glacial acetic acid (A to Z Pharma Pvt. Ltd. Chennai), Calcium chloride (A to Z Pharma Pvt. Ltd. Chennai)

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Method of preparation

The atenolol loaded sodium alginate-Hydroxyl propyl methyl cellulose microspheres were prepared by Ionotropic gelation method. 30ml of sodium alginate and hydroxyl propyl methyl cellulose solution in 9:1 ratio was prepared. Different polymer concentrations were taken (1%, 2% and 3%). The drug and sodium bi carbonates were dispersed in the alginate-hydroxyl propyl methyl cellulose solution. This process was done under magnetic stirring. Then above solution was added drop wise into 1% calcium chloride solution of 90 ml and 10 ml of 10% w/v acetic acid .Then beads were collected and washed with water and dried in an oven.

Evaluation of microspheres

Percentage practical yield

The prepared microspheres were weighed accurately and it was taken as practical yeild. Then the percentage practical yield was calculated by using the formula as follows:

$$\text{Percentage of practical yield} = \frac{Practical\ yeild}{Theoritical\ yeild} \times 100$$

Drug content

Percentage of drug content was estimated by single point drug analysis method. Equivalent weight of microspheres containing 1mg drug was weighed accurately and transferred in 10ml standard flask with buffer. Leave the microspheres for 24 hrs. Take 1ml from above the solution in 10ml standard flasks and volume made up to 10ml with buffer. The solution was filtered and analyzed for their drug content spectrophotometrically by measuring absorbance at 224nm.

Percentage of drug content was calculated by following formula:

$$\% \text{ of Drug Content} = \frac{\text{Observed value}}{\text{Actual Value}} \times 100$$

***In-Vitro* Dissolution studies**

The release of atenolol from microspheres was determined using USP type II (paddle type) dissolution apparatus. The dissolution test was performed using 0.1 N Hcl (pH 1.2) buffer as dissolution media at 37 ± 0.5^0C with 75 rpm for 7 hours. A sample of each preparation equivalent to 10 mg of drug was added to dissolution medium. A 5ml of aliquot was withdrawn at different time intervals (1, 2, 3, 4, 5, 6 and 7 hrs) and filtered and each sample was replaced with 5 ml of fresh dissolution medium. The filtered solutions were suitably diluted to 10ml with dissolution media. Samples were analyzed for its drug content spectrophotometrically by measuring the absorbance against blank at 224 nm (Indian Pharmacopoeia 1996, appendix-7, A-80-84). Percent of atenolol dissolved at various time intervals was calculated and plotted against time.

Table.1 Preparation of microspheres

S.No	Formulation	Atenolol (mg)	Sodium Alginate (gm)	Hydroxypropyl methyl cellulose (gm)	Sodium bi carbonate (gm)	Calcium chloride (gm)	Acetic Acid (ml)
1	F 1	100	0.27	0.3	0.25	0.9	1
2	F 2	100	0.54	0.6	0.25	0.9	1
3	F 3	100	0.81	0.9	0.25	0.9	1

***In-Vitro* Buoyancy study**

The prepared beads showed excellent floating characters. The beads remained on top of 0.1 N Hcl (pH 1.2) for duration time over 7 hrs. Besides, buoyancy was not affected by the changes of the formulation variables during the overall study. Meanwhile, no change was observed on the whole integrity of floated beads concerning color and shape during the period of buoyancy test. The floating ability of the prepared beads is because of the use of low density materials which produced an inherently low density beads that float immediately following contact with 0.1 N Hcl (pH 1.2).

Buoyancy can be determined by the following formula:

$$\text{Buoyancy} = \frac{\text{Floated microspheres}}{\text{Taken amount}} \times 100$$

Particle size determination

The eye piece micrometer was calibrated by using a standardized stage micrometer at 45X. The powder sample was taken and suspension was prepared by using propylene glycol. The sample of suspension was placed on mechanical stage. The size of particles was estimated with the help of eye piece micrometer.

RESULTS AND DISCUSSION

Percentage practical yield

Table.2 % Practical yield of microspheres

S.NO	FORMULATION CODE	% PRACTICAL YIELD
1	F1	72.0%
2	F2	75.6%
3	F3	78.3%

Particle size determination

The average particle size of prepared microspheres was found to be 41.25µm. There is no significant change in particle size in three formulations.

Entrapment efficiency

Table.3 % Drug content of microspheres

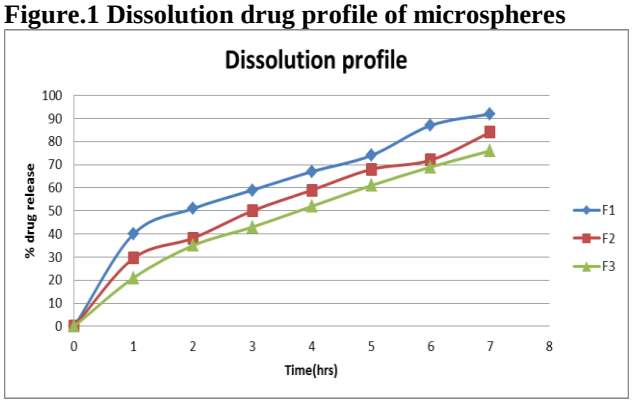
S.NO	FORMULATION CODE	% DRUG CONTENT
1	F1	53.2%
2	F2	62.1%
3	F3	70.20%

Dissolution studies

Table.4 Dissolution Profile of microspheres

S.NO	Time(hrs)	F1	F2	F3
1	1	40.3%	29.6%	21.4%
2	2	51.2%	38.4%	35.2%
3	3	59.5%	50.4%	43.3%
4	4	67.4%	59.3%	52.7%
5	5	74.4%	68.6%	61.2%
6	6	87.0%	72.4%	69.5%
7	7	92.2%	84.2%	76.3%

Figure.1 Dissolution drug profile of microspheres



CONCLUSION

Atenolol was successfully formulated as floating alginate-hydroxyl propyl methyl cellulose beads by Ionotropic gelation method. The drug and polymer mixture ratio, sodium alginate-hydroxyl propyl methyl cellulose polymers ratio are significant formulation factors which affected drug encapsulation efficiency and controlled release of drug from microspheres. The release profile of atenolol from the alginate hydroxy propyl methyl cellulose beads increased as a function of drug: polymer mixture ratio. It is possible to achieve slow atenolol release rates from the alginate – hydroxyl propyl methyl cellulose beads by increasing the amount of sodium alginate-hydroxy propyl methyl cellulose used in the polymeric mixture. In view of the prolonged buoyancy of beads in the acidic environment, accompanied by slow drug release, entrapment of atenolol in these beads may provide a satisfactory oral controlled release drug delivery system. From dissolution studies, it has been identified that 3% of polymeric mixture (sodium alginate and hydroxyl propyl methyl cellulose) gave prolonged release of 72% over a extended period of 7 hrs.

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