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(RESEARCH ARTICLE)

Development and evaluation of sustained release microparticles of atenolol of gastrointestinal delivery

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Abstract

The aim of the present study is to development and evaluation of sustained release micro particulates of atenolol prepared by solvent evaporation technique. In this method Eudragit RS-100 was dissolved in Acetone and suitable solvent was mixed well with the pure Atenolol drug with different ratios and filtered it. Add magnesium stearate and it was dispersed in solution by ultra sonification. This solution keep it on a side and take another fresh beaker contain 100 ml of liquid paraffin and add 20 ml of n-hexane. Both liquid paraffin and n-hexane stirred continuously by using mechanical stirrer. In this solution add previous ultra sonification solution in the form of drops with the help of syringe until acetone evaporated. By this process microparticles were formed and they dried at room temperature. The drug product percentage yield, drug entrapment efficiency, particles size parameters are in desired manner. The *in-vitro* drug release studies Shows that the percentage of drug release is in standard level. Among all formulations F3 and F5 formulations with drug, polymer was found to be satisfactory in terms of excellent micromeritic properties, percent yield (92.12%), Drug entrapment efficiency (77.79%), Percent buoyancy (80%) and highest *in-vitro* drug release of 85.60% in sustained manner over an extended period of time for 12 hrs.

Keywords: Atenolol; Microparticles; Eudragit RL 100; Magnesium stearate

1. Introduction

The Micro particulate Drug Delivery System (MDDS) is one of the processes to provide the Sustained Controlled Delivery (SDD) of drug is taken to long period of time. Micro particles are small particles of Solids (or) Small droplets of liquids surrounded by the walls of the natural & synthetic polymer films of different types of thickness and degree of permeability its acting as a release rate of controlling substance and have a diameter up to range from 0.1µm to 200µm [1].

Atenolol, a competitive beta (1)-selective adrenergic antagonist, has the lowest lipid solubility of this drug class. Although it is similar to metoprolol, atenolol differs from pindolol and propranolol in that it does not have intrinsic sympathomimetic properties or membrane-stabilizing activity. Atenolol is used alone or with chlorthalidone in the management of hypertension and edema [2].

Micro particles is widely used in the pharmaceutical and other sciences to mask tastes or odors, impart stability to drug molecules, improve bioavailability, and as multi-particulate dosage forms to produce controlled or targeted drug delivery. It is therefore a rapidly expanding technology for achieving sustained-release dosage forms. the micro particles being produced by the solvent evaporation method.

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The main objective of this work was to investigate the possibility of obtaining a sustained release formulation of atenolol micro particles by using Eudragit RS100 and Magnesium stearate in various drugs, polymer ratios. The various physicochemical characteristics and the in-vitro release rates from these microspheres were thus examined.

2. Material and methods

2.1. Preformulation studies

Preformulation studies investigated the physicochemical properties of drug and other excipients.

2.1.1. Selection of drugs and other ingredients

Atenolol was selected as physicochemical and biological properties and also based on its suitability for sustained release drug delivery. Eudragit RL 100 was selected as matrix forming polymers. Magnesium stearate was selected as lubricant in the production of pharmaceutical and cosmetic products.

2.1.2. Preparation of standard solution

Stock solution-I: 100 mg of atenolol was dissolved in small quantity of methanol and make up to 100 ml 0.1 N HCL to give a concentration of 1 mg/ml.

Stock solution-II: Solution II was prepared by taken 10 ml from the stock solution-I and dissolved in 100 ml of 0.1 N HCL, so as to get a solution of 0.1 mg/ml.

2.1.3. Atenolol standard graph [3]

From the stock solution-II 0.1mg/ml was prepared and UV scan was taken between 200 to 400 nm. The absorption maximum was found to be 275 nm and was used for the further analytical studies.

2.2. Formulation studies

2.2.1. Development of microparticles

Sustained drug delivery was prepared by solvent evaporation method [4]. The microparticles were prepared according to the formula shown in table-1. Eudragit RS-100 was weighed requisite ratio and then dissolved in Acetone and suitable solvent was mixed well with the pure Atenolol drug with different ratios and filtered drug solution, add magnesium stearate and it was dispersed in solution by ultrasonification. This solution keep it on a side and take another fresh beaker contain 100 ml of liquid paraffin and add 20 ml of n-hexane. Both liquid paraffin and n-hexane stirred continuously by using mechanical stirrer at 400 RPM at room temperature for 1.30 hrs. In this solution add previous ultrasonification solution in the form of drops with the help of syringe until acetone evaporated. The microparticles were formed and washed 4-5 times in 40ml n-hexane. Finally dried at room temperature in desiccator for 24 hrs.

Table 1 Formulation design of atenolol microparticles

Ingredients(mg)	F1	F2	F3	F4	F5
Atenolol	100	100	100	100	100
Eudragit RS100	100		200	-	200
Magnesium stearate	-	100	-	200	200
n-Hexane	15	15	15	15	15
Liquid paraffin	20	20	20	20	20
Acetone	20	20	20	20	20

3. Results

3.1. Spectroscopic studies [3]

A solution of 0.1mg/ml Atenolol was prepared and UV scan was taken between 200 to 400 nm. The absorption maximum was found to be 275 nm in simulated gastric fluid pH 1.4 and had good reproducibility and standard curve graph was shown in figure-1.

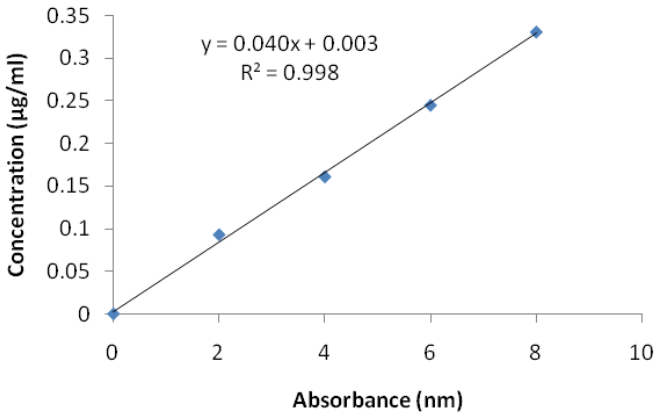

Figure 1 Standard curve of atenelol

3.2. Percentage yield [5]

It was observed that as the polymer ratio in the formulation increases, the microparticles product yield also increased. The low percentage yield in some formulations may be due to blocking of needle and wastage of the drug polymer solution, adhesion of polymer solution to magnetic bead and microparticles lost during the washing process. The microparticles percentage yield was recorded in table-2.

3.3. Buoyancy studies [6]

The *in-vitro* buoyancy was determined by floating lag time, and total floating time. The percentage buoyancy study of the prepared microparticles was recorded in table-2.

3.4. Drug entrapment efficiency [7, 8]

Percentage of Drug entrapment efficiency of atenelol arranged from 62.58 to 69% for microparticles containing various polymers and other Chemicals. The Drug entrapment efficiency of the prepared microparticles increased progressively with an increase in proportion of the dispersed phase. Increases the viscosity of particle size. Increased viscosity of the polymer solution at the Increases the polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in increased entrapment efficiency. The percentage Drug entrapment efficiency of the prepared microparticles was recorded in table-2.

Table 2 The percentage yield, buoyancy and drug entrapment efficiency of all atenelol formulations

Formulations	% Yield	% Buoyancy	% Drug entrapment Efficiency
F1	87.2	64	62.58
F2	89.62	68	69.72
F3	92.12	72	77.79
F4	90.56	77	66.58
F5	88.52	74	69.08

3.5. Particle size [9]

Particle sizes was determined by using microscope and calculate average of particle size. The results were shown in in figure 2

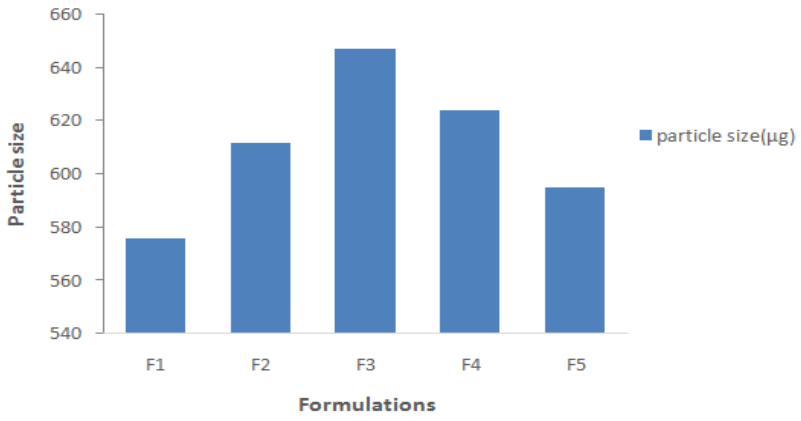

Figure 2 Graph of particle size of different atenolol formulations

3.6. *In-vitro* drug release studies [10, 11]

In-vitro drug release studies of all formulations were carried out using dissolution apparatus USP Type-I. The dissolution studies were conducted by using dissolution media, pH 1.4. The results of the *in-vitro* dissolution studies of formulation F1 to F5 are shown in table 3.

Table 3 Percentage of cumulative drug release for all formulations

Time (hrs)	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	21	20	22	21	25
2	29	28.1	31.8	28	31
3	36	36	42.7	39.1	40.2
4	48.2	49.1	51.8	48.8	49.5
5	56.6	58.2	62	59.9	58.6
6	72.1	69.9	71.8	70.8	69.8
7	82.5	77.8	76.9	75.6	73.9
8		83.2	81.2	82.4	76.2
10			85.9	84.3	80
12					85.6

4. Conclusion

The prepared formulations were characterized for their percentage yield, micromeritic properties, morphology, buoyancy studies, drug entrapment and drug release studies. Percentage drug entrapment efficiency ranges from 62.58 to 77.79% for microspheres containing Eudragit RL 100 and Magnesium stearate solid as the formulations showed fairly acceptable values for all the parameters evaluated. Among all formulations F3 and F5 formulations with drug; polymer was found to be satisfactory in terms of excellent micromeritic properties, percent yield (92.12%), Drug entrapment efficiency (77.79%), Percent buoyancy (80%) and highest in-vitro drug release of 85.60% in sustained manner over an extended period of time for 12 hrs.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

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