WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 16, 863-881. Research Article ISSN 2277–7105

DEVELOPMENT AND IN-VITRO EVALUATION OF HYDROGEL POLYSACCHARIDE BEAD CONTAINING ATENOLOL FOR CONTROLLED DELIVERY

Umesh Kumar Chaurasiya*, Ishak Khan and Vijay Nigam

Daksh Institute of Pharmaceutical Science Chhatarpur M.P.

Article Received on
30 June 2024,

Revised on 20 July 2024,
Accepted on 10 August 2024

DOI: 10.20959/wjpr202416-33546

***Corresponding Author**
Prof. Umesh Kumar Chaurasiya
Daksh Institute of Pharmaceutical Science Chhatarpur M.P.

1. ABSTRACT

Atenolol, a β-blocker, is prescribed widely in diverse cardiovascular diseases, eg, hypertension, angina pectoris, arrhythmias, and myocardial infarction. The drug is also frequently indicated in the prophylactic treatment of migraine. Atenolol is a polar cardioselective β-blocker, widely used alone or in combination with other drugs for treatment of various cardiovascular conditions. It is slightly soluble in water with reported half-life of 6-7 hours. It is considered a drug with low jejunal permeability and a low extent of absorption, therefore it has an oral bioavailability of about 46-62%. Administration of conventional tablets of atenolol has been reported to exhibit fluctuations in the plasma drug levels, resulting either in manifestation of side effects or reduction in drug concentration at the receptor site. Accordingly, studies have been reported on regulation of drug release by formulating its diverse CR systems such as hydrophilic matrices,9 osmotic pumps, and transdermal drug delivery systems.

In the recent times, polysaccharide based bead for controlled delivery are gaining importance in the design of oral controlled drug delivery systems. Carrageenan has been used increasingly in pharmaceutical formulation studies, for example, microcapsules for sustained delivery, crosslinked spheres for controlled release. Carrageenans are naturally occurring high molecular weight polysaccharides extracted from red seaweed. They are made up of alternating copolymers of 1,3- linked ß-d-galactose and 1,4-linked 3,6-anhydro-α-d-galactose. Carrageenan forms a gel with potassium ions, but also shows gelation under salt-free conditions. However, gels prepared in the presence of metallic ions were substantially

stronger than those obtained under salt-free conditions. The gelling and melting temperatures of kapp-carrageenan are dependent almost solely on the concentration of potassium ions. When a polyelectrolyte (like carrageenan) is combined with a uni/multivalent ion of the opposite charge, it may form a physical hydrogel known as an 'ionotropic' hydrogel. Ionotropic hydrogel, which may degrade and eventually disintegrate and dissolve, are held together by molecular entanglements, and/or secondary forces including ionic, H-bonding or hydrophobic forces. All of these interactions are reversible, and can be disrupted by changes in physical conditions such as ionic strength, pH, temperature, application of stress, or addition of specific solutes that compete with the polymeric ligand for the affinity site on the protein. From these characteristics, kappa-carrageenan is used as an entrapment matrix for drug and enzymes as well as for pharmaceuticals and food adjuvants. In the past, conventional crosslinked potassium- kappa-carrageenan beads have been investigated for the development of a multiple unit drug delivery system. The purpose of this study was to prepare and evaluate the carrageenan gel beads as a new controlled drug release system for atenolol. Another purpose is to investigate the conditions in which the polymer bead is formed, and hence the dependence of the drug release on bead formation.

2. KEYWORD: Controlled, hydrogel, polysaccharide, crosslinking, microspheres.

3. INTRODUCTION

The ideal drug delivery system should be inert, biocompatible, mechanically strong, comfortable for the patient, capable of achieving high drug loading, safe from accidental release, simple to administer and remove, and easy to fabricate and sterilize. The goal of many of the original controlled-release systems was to achieve a delivery profile that would yield a high blood level of the drug over a long period of time. With traditional drug delivery systems, the drug level in the blood follows the in which the level rises after each administration of the drug and then decreases until the next administration. The key point with traditional drug administration is that the blood level of the agent should remain between a maximum value, which may represent a toxic level, and a minimum value, below which the drug is no longer effective. Controlled drug delivery systems can include the maintenance of drug levels within a desired range, the need for fewer administrations, optimal use of the drug in question, and increased patient compliance. While these advantages can be significant, the potential disadvantages cannot be ignored like the possible toxicity or non-biocompatibility of the materials used, undesirable by-products of degradation, any surgery required to implant

or remove the system, the chance of patient discomfort from the delivery device, and the higher cost of controlled-release systems compared with traditional pharmaceutical formulations. The United States Pharmacopoeia (USP) defines1 the modified-release (MR) dosage form as "the one for which the drug release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosage forms". One class of MR dosage form is an extended-release (ER) dosage form and is defined as the one that allows at least a 2-fold reduction in dosing frequency or significant increase in patient compliance or therapeutic.

Performance when compared with that presented as a conventional dosage form (a solution or a prompt drug-releasing dosage form). The terms "controlled release (CR)", "prolonged release", "sustained or slow release (SR)" and "long-acting (LA)" have been used synonymously with "extended release".

A controlled release drug delivery system is capable of achieving the following benefits over conventional dosage forms

- Total dose is low.
- Reduced GI side effects and other toxic effects.
- Reduced dosing frequency.
- Better patient acceptance and compliance.
- Less fluctuation in plasma drug levels.
- More uniform drug effect.
- Better stability of drug.

Nearly all of the currently marketed monolithic oral ER dosage forms fall into one of the following two technologies

- Hydrophilic, hydrophobic or inert matrix systems: These consist of a rate controlling
- Polymer matrix through which the drug is dissolved or dispersed.
- Reservoir (coated) systems where drug containing core is enclosed within a polymer coating. Depending on the polymer used, two types of reservoir systems are considered.

(a) Simple Diffusion/Erosion systems where a drug-containing core is enclosed within hydrophilic and/or water-insoluble polymer coatings. Drug release is achieved by diffusion of the drug through the coating or after the erosion of the polymer coating.

(b) Osmotic systems where the drug core is contained within a semi-permeable polymer membrane with a mechanical/laser drilled hole for drug delivery. Drug release is achieved by osmotic pressure generated within the tablet core.

4. MATERIALS AND METHODS

Table 1: Equipment used.

S. No.	Instruments	Manufacturer
1	UV/VIS Spectrophotometer	Lab india
2	Weighing balance	Sartorius
3	Microscope	Kyowa Getnar
4	pH Meter	Electorlab
5	Centrifuge Machine	Osworld, Mumbai

Table 2: Excipients used.

S. No.	Materials	Manufacturer
1	Atenolol	Intas pharma
2	Kappa carrageenan	FMC biopolymer, Mumbai
3	Potassium chloride	LobaCheim Pvt. Ltd., Mumbai.
4	Methanol	Finar
5	Sodium chloride	Finar
6	Disodium hydrogen phosphate	Finar
7	Potassium dihydrogen phosphate	Finar

5. Preformulation study

5.1 Melting point

The most significant reason to figure out the melting point is to figure out how pure a medicine is. To determine the melting range, the material was dried first. The capillary fusion method was used to acquire this result, which was obtained using a digital capillary melting point device. One end of a capillary was sealed after bringing it close to the burner flame. The open end of the capillary tube was placed into a small heap of drug, resulting in a little plug of powder being collected in the open end, which was then gently tapped to settle the collected drug. This procedure was carried out several times more. The capillary tube was then placed in the melting point determination device, and the temperature at which the sample changed was noted. The experiment was performed in triplicate. The temperature at which starts to melt was noted with the help of thermometer compared with the earlier reported value.[122]

5.1.1 Preparation of calibration curve of atenolol in methanol

Absorption maxima (λ max) of drug were determined by UV spectrophotometer. Standard solution: Atenolol (10 mg) was accurately weighed and diluted in 100 mL methanol. A stock solution was made from the standard solution to yield a concentration of 100µg/ml in methanol, and aliquots of the standard solution were pipette out into a 10 ml volumetric flask. Methanol was used to get the volume up to the required level result in a concentration range 2 µg/ml to 18µg/ml. The absorbance of the prepared solution of Atenolol in methanol was measured at 224 nm using a UV/Vis double beam spectrophotometer against an adequate blank at these dilutions gives 2 µg/ml to 18µg/ml concentration of atenolol.[122]

5.1.2 Solubility Studies 130

Excess medication was placed in thoroughly cleaned test tubes with 5.0 ml of various solvents (Water, Methanol, 6.8 pH Phosphate buffer, 0.1NHcl,) and test tubes were tightly closed for quantitative solubility studies. These test tubes were shaken for 24 hours at room temperature using a water bath shaker. Each sample was centrifuged at 10,000 rpm for 24 hours and the supernatant was removed. After that, the supernatant was filtered, and the filtrate was diluted appropriately before being spectrophotometrically measured.[122]

5.1.3 Partition coefficient of drug

Before executing the trials, both solvents were mutually saturated in a 1:1 ration. In aqueous solutions, saturated solutions of a medication of unknown concentration were created.

Then, in glass flasks, 1.0 mL of octanol was added to 1.0 mL of the aqueous chemical solution. After that, the mixes were shaken for an hour in a mechanical shaker. The samples were kept at room temperature for 24 hours in a separating funnel. After that, the aqueous phases were separated, and the drug concentrations were measured by measuring UV absorbances as reported earlier. The partition coefficients were computed using the following equation. At least three times, all partitioning experiments were carried out. Drugs with P values substantially higher than one are classed as as lipophilic, where as those with values much less than 1 are indicative of a hydrophilic drug.[122]

5.1.4 FT-IR Analysis

For the identification of that particular component, Fourier transform infrared spectroscopy of other compounds was used. The final improved formulation was tested using KBr pellets and FT-IR spectroscopy of the pure medication. The identification of various groups in the

structure of the pure medication and improved formulations was done using FT-IR peaks. Any physicochemical interactions between distinct components can also be investigated and predicted using FT-IR Spectroscopy.[122]

5.2 Preparations of beads

The Ionotropic gelation method was used to create microbead formulations of atenolol. Heat a dispersion of the powder to 70°C to produce a homogeneous solution and cool to 40°C to get a concentrated solution of k-carrageenan in 50ml pure water. 50mg atenolol was weighed and dissolved in a tiny amount of water before being mixed with the final k-carrageenan solution. The final k-carrageenan concentration was set between 2.5 and 3.5 percent w/v. The beads were made by dumping a k-carrageenan solution containing atenolol from a syringe into a magnetically agitated potassium chloride solution (100 mL) using an 18Gx12" flat-tip hypodermic needle and allowing it to solidify. Decanting the potassium chloride solution collected the beads, which were then rinsed in deionized water and dried to a constant weight in a vacuum desiccator at room temperature for 48 h.[123]

Table 3: Composition of different beads formulations.

Formulation	Atenolol (mg)	κ-Carrageenan (%w/v)	KCl Concentration (M)
A1	50	0.5	0.2
A2	50	1	0.2
A3	50	1.5	0.2
A4	50	2	0.2
A5	50	2.5	0.2
A6	50	2	0.4
A7	50	2	0.6
A8	50	2	0.8

5.3 Evaluation of beads

5.3.1 Visual appearance: All the batches of beads were studied for color and physical appearance.[123]

5.3.2 Percentage yield

We gathered and weighed the prepared beads. The total weight of all excipients and medication was divided by the measured weight. The percent yield was estimated using the formula below.[123]

% yield = Total powder weight/Total weight of all excipients drug

5.3.3 Determination of entrapment efficiency

The percentage of atenolol entrapment in the beads was quantified by heating a 100ml aqueous solution containing a bead equivalent to 100mg of atenolol for 10 minutes and then cooling the solution to room temperature. The supernatant was diluted with methanol after centrifugation at 10000rpm for 10 minutes. UV-Vis spectrophotometry was used to assess the proportion of free medication on the surface of the beads. The following equation was used to compute the encapsulation efficiency (EE). All of the experiments were carried out in triplicate.[124]

$$Percentage\ drug\ entrapment = \frac{\textbf{drug in supernatent}}{\textbf{Initial Amount of drug}} \times \mathbf{100}$$

5.3.4 Bead size

Particle size of the prepared beads was determined using an optical microscope fitted with the stage and an ocular micrometer. Twenty dried beads were measured for calculating the mean diameter of beads. The result is expressed as the mean diameter (mm)±standard deviation.

5.3.5 In-Vitro drug release study

Using a dissolution device 1, in vitro drug release tests were performed on the beads (USP). The capsule containing 50mg of atenolol was placed in a basket and dipped in a dissolution tank containing 900 ml of pH 1.2 0.1NHcl for 2 hours, then pH 7.4 phosphate buffer until the completion of the study at 37°C and 100 rpm speed. 5 ml aliquots were extracted, filtered, and the amount of drug released was measured spectrophotometrically at predetermined times. A fresh buffer solution was used to replace the same amount of medium. To determine which mathematical model best fits the obtained release profile, the release data were fitted to multiple mathematical models.[125]

5.3.6 Drug release kinetics

Different mathematical functions that characterise the release profile are used in model-dependent techniques. The release profiles are evaluated based on the obtained model parameters once a suitable function has been chosen.[126] The data from the in vitro dissolution investigation was plotted in various data treatment models as follows:

- Zero Order model
- First Order model
- Higuchi's Model
- Korsmeyer-Peppas model

5.3.6.1 Zero order kinetics

It can be used to explain the dissolving of medications in a variety of modified release pharmaceutical dosage forms, including as transdermal systems, matrix tablets with low soluble drugs in coated forms, osmotic systems, and so on. Zero order release can be written as

Q0 - Qt = K0t in its simplest form.

Where Qt is the amount of drug dissolved in time t, Q0 denotes the initial amount of drug in the solution (most of the time, Q0 = 0), and K0 denotes the zero order release constant expressed in concentration/time units. Data from in vitro drug permeation tests were shown as cumulative amount of drug released vs time to evaluate release kinetics.

5.3.6.2 First order kinetics

It's a term that describes how pharmaceuticals dissolve in pharmaceutical dosage forms such porous matrices containing water-soluble medications. The equation log C = log C0 – K.t / 2.303 can be used to explain the release of a medication that followed first order kinetics.

Where C0 represents the drug's initial concentration, k represents the first order rate constant, and t represents the period. The data is presented as a straight line with a slope of K/2.303 when plotted as log cumulative percentage of medicine remaining vs. time.

5.3.6.3 Higuchi's model

The goal of this model was to predict drug release from a matrix system. It was first used to describe planar systems, but it was later expanded to include other geometrics and porous systems. This model is based on the assumptions that I initial drug concentration in the matrix is much higher than drug solubility; (ii) drug diffusion occurs only in one dimension (edge effect must be negligible); (iii) drug particles are much smaller than system thickness; (iv) matrix swelling and dissolution are negligible; (v) drug diffusivity is constant; and (vi) perfect sink conditions are always achieved in the release environment.

Higuchi was the first to calculate the square root of a time-dependent process based on Fickian diffusion to describe the release of a drug from an insoluble matrix. Simplified Higuchi equation is following

$Q_t = K_H (t)^{0.5}$

Where, Qt is the amount of drug released in time t and K_H is the release rate constant for the Higuchi model. When the data is plotted as cumulative drug released versus square root of time, it yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to 'K_H'.

5.3.6.4 Korsmeyer-Peppas model

Korsmeyer derived a simple relationship which described drug release from a polymeric system.

The release rates from controlled release polymeric matrices can be described by the equation proposed by Korsmeyer et al.

$Q = K.t^n$

Where, Q is the percentage of drug released at time't' K is a kinetic constant incorporating structural and geometric characteristics of the tablets and 'n' is the diffusional exponent indicative of the release mechanism.

For Fickian release, n=0.45 while for anomalous (Non-Fickian) transport, n ranges between 0.45 and 0.89 and for zero order release, n = 0.89. The Korsmeyer-Peppas model was plotted between log cumulative % drug releases versus log time.

Table 5: Interpretation of diffusional release mechanisms.

Release exponent (n)	Drug transport mechanism	Rate as a function of time
0.5	Fickian diffusion	$t^{-0.5}$
0.45 < n = 0.89	Non-Fickian transport	t^{n-1}
0.89	Case II transport	Zero order release
Higher than 0.89	Super case II transport	t^{n-1}

6. RESULT AND DISCUSSION

6.1 Preformulation study of drug

6.1.1 Organoleptic properties

The medicine atenolol organoleptic qualities were found to be in accordance with the I.P. monograph. The following table 4 lists the organoleptic features of atenolol.

Table 4: Organoleptic Properties of atenolol.

Sr. no.	Properties	Inferences[127]
1	Colour	White
2	Odour	Odourless
3	Taste	Slighty bitter

6.1.2 Melting point

Melting point of atenolol shown in table 5.

Table 5: Melting point of atenolol.

Drug	Reference M.P.[127]	Observed M.P.
Atenolol	158-160°C	158.34±0.58 to 159.34±1.53°C

The melting point of pure atenolol was determined to be between 158.34±0.58 to 159.34±1.53°C. As a result, the medicine sample was free of any contaminants.

6.1.3 Preparation of standard calibration curve of atenolol in methanol

The absorption maxima of atenolol were found to be at 224 nm, which is consistent with previous findings. Table 6-7 shows the standard calibration curve of atenolol in methanol at various concentrations.[127]

Table 6: Standard Calibration curve of atenolol in methanol (λ_{max} = 224 nm).

Con. (µg/ml)	Absorbance at 224 nm	STD
0	0.000	0.000
2	0.092	0.003
4	0.187	0.003
6	0.272	0.002
8	0.375	0.004
10	0.465	0.003
12	0.574	0.004
14	0.670	0.004
16	0.773	0.004
18	0.849	0.003

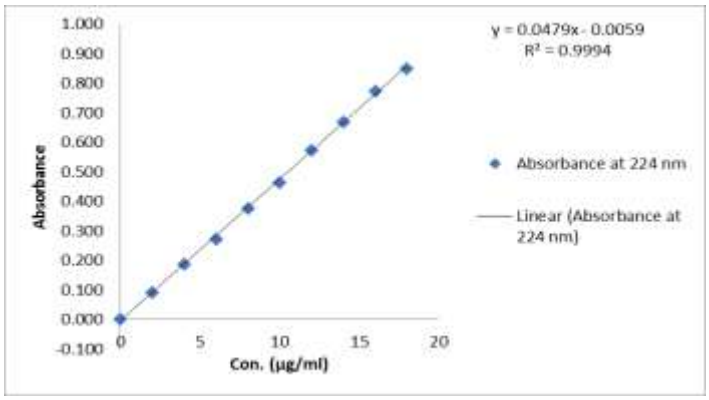

Figure 4: Graph of standard calibration curve of atenolol in methanol (λ_{max} = 224nm).

Table 7: Result of regression analysis of UV method for estimation of atenolol in methanol (λ_{max} = 224 nm).

Statistical parameters	Results
λ max	224 nm
Regression equation: y=mx+C	Y= 0.0479x - 0.0059
Correlation coefficient (r^2)	0.999

6.1.4 Solubility studies

The solubility of medications in different solvents was tested in order to find the components that would be used in formulation creation. The medication was evaluated using a UV Spectrophotometer at 224nm.

Table 8: Solubility studies of atenolol for different solvents.

Name of solvent	Solubility (mg/ml)[127]
Water	63.142±0.276
Methanol	25.459±0.209
Phosphate Buffer 6.8pH	28.243±0.493
0.1NHcl	20.031±0.280

* Each value is average of three independent determinations

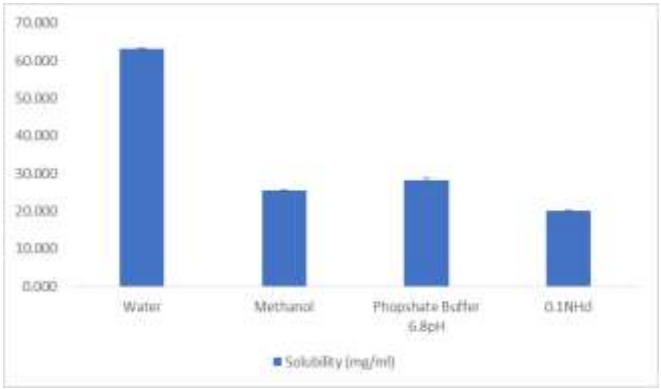

Figure 5: Solubility study of the atenolol in different solvents.

From the above data, it was clearly seen that atenolol is highly soluble in Water followed by 6.8 pH Phosphate buffer. (**Figure 10 and Table 8**)

6.1.5 Partition coefficient determination

Using n-octanol and water, the partition coefficient of atenolol was found. A log P greater than one implies that the drug is lipophilic in nature, whereas a log P less than one suggests that the drug is hydrophilic. This reflected the drug's lipophilicity and purity.

Table 9: Partition coefficient determination of atenolol.

Partition coefficient of drug	Solvent system	Log P Values
Atenolol	n-octanol:water	0.257±0.007

Discussion

The partition coefficient of atenolol in n- Octanol: Water was found to be 0.257±0.007 this indicating that the drug is hydrophilic in nature.

6.1.6 FTIR of Atenolol and Optimized formulation

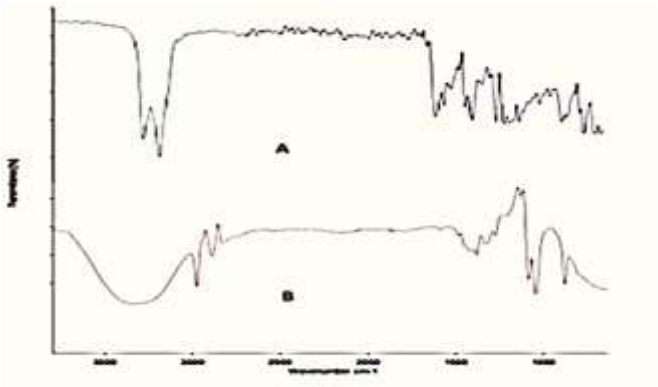

Figure 6: FTIR spectrum of A) Pure drug atenolol B) Optimized formulation A7.

FTIR spectrum of pure drug demonstrated the following peaks at 3348.42 cm^{-1} for N-H group. The band 2964.59 cm^{-1} may be caused by aromatic and aliphatic C-H bond stretching. The band at 1512.19 cm^{-1} is for aromatic C=C bond and 1236.37 cm^{-1} is for C = N stretching. The FTIR spectrum of optimized formulation displayed very less peaks of drug with reduced intensity that confirm the encapsulation of the drug in the polymeric bead.

6.2 Preparation of bead

Using k-carrageenan, a multiparticulate delivery method of atenolol capable of regulated release was developed in this study. The procedure for making beads was discovered to be easy and repeatable.

6.3 Evaluation of bead

6.3.1 Appearance of bead

Table 10: Appearance of different k-carrageenan based beads containing atenolol.

Formulation	Appearance
A1	Bead not formed
A2	Bead formed
A3	Bead formed
A4	Bead formed

A5	Bead formed
A6	Bead formed
A7	Bead formed
A8	Bead formed

All formulation was prepared as spherical beads as shown in a table 10. Except the formulation was A1. This formulation either was not formed or formed but in irregular shape and allow clump formation.

6.3.2 Percentage yield

The percentage yield of all prepared atenolol containing kappa-carrageenan bead was given in Table 11.

Table 11: Percentage yield of different k-carrageenan based bead containing atenolol.

Formulation code	Percentage yield
A2	79.16±0.44
A3	81.13±0.41
A4	89.32±0.40
A5	92.68±0.52
A6	92.42±0.27
A7	95.19±0.34
A8	96.17±0.32

As indicated in table 11, the percentage yield of all formulations were determined to be in the ranges of 79.16±0.44% to 96.17±0.32%. Formulation A8 had the highest percentage yield 96.17±0.32%., respectively.

6.3.3 Percentage drug entrapment

The percentage drug entrapment of all prepared atenolol containing kappa-carrageenan bead was given in Table 12.

Table 12: Percentage drug entrapment of different k-carrageenan based bead containing atenolol.

Formulation Code	Percentage drug entrapment
A2	47.57±0.31
A3	68.73±0.74
A4	74.78±0.80
A5	70.04±1.18
A6	89.22±0.69
A7	96.09±0.80
A8	93.48±0.95

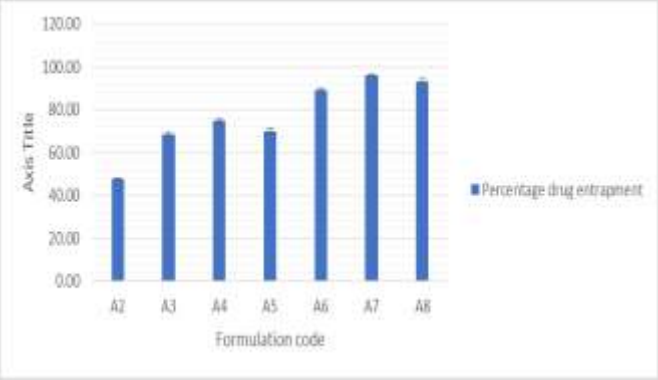

Figure 7: Percentage drug entrapment of all atenolol containing kappa carrageenan bead.

As indicated in table 12, the percentage drug entrapment of all formulations were determined to be in the ranges of 47.57±0.31% to 96.09±0.80%. Formulation A7 had the highest percentage yield 96.09±0.80%., respectively. When the concentration of bead forming polymer was increased, the % drug entrapment increased up to a specific concentration, but additional increases had no effect on the percentage drug entrapment.

6.3.4 Bead size analysis

Particle size of formulations was given in a Table 13.

Table 13: Size of different atenolol containing k-carrageenan bead.

Formulation Code	Bead size (mm)
A2	4.653±0.091
A3	6.267±0.095
A4	8.420±0.079
A5	12.580±0.636
A6	7.420±0.075
A7	5.687±0.085
A8	5.977±0.081

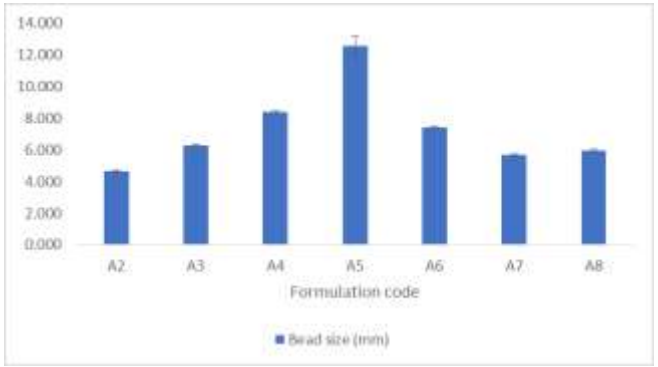

Figure 8: Size of atenolol loaded k-carrageenan bead.

All prepared atenolol beads were between 4.653±0.091mm to 12.580±0.636mm in size. The beads were suitably rigid and spherical in shape when they were created. The minimal bead size in the A7 formulation is 5.687±0.085mm.

6.3.5 In-vitro Drug release study

The comparison of in-vitro drug release of Formulation A7 and Pure drug was given in a Table 14.

Table 14: Comparison of Percentage drug release of Formulation A7 and Pure drug.

Time(min.)	Percentage Drug release of Pure drug	Percentage Drug release of formulation A7
0.0	0.000±0.00	0.000±0.0
0.5	22.694±0.106	6.309±0.113
1	34.174±0.239	14.126±0.038
2	85.453±0.797	32.088±0.099
4	98.793±0.531	46.184±0.752
6		73.616±1.127
8		79.754±0.574
10		91.904±1.320
24		96.914±1.127

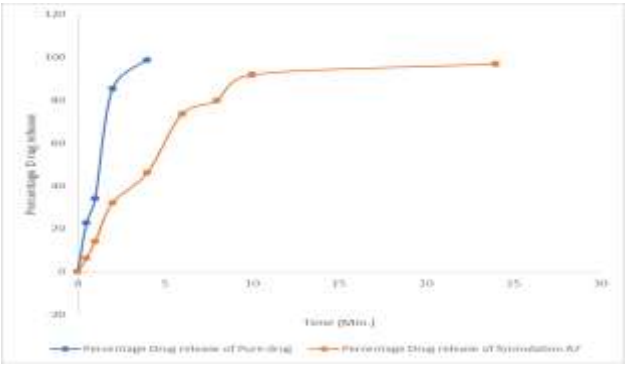

Figure 9: Comparison of In-Vitro Drug release of pure drug and atenolol loaded k-carrageenan bead.

Formulation A7 was chosen for additional in-vitro drug release testing based on the results of the following criteria. In comparison to the immediate release of pure drug, formulation MB7 demonstrated a sustained release of 95.56±0.65 at 24 hours.

6.3.6 In-vitro drug release kinetic

In-vitro drug release kinetic study data of formulation A7 was given below.

6.3.6.1 Zero order

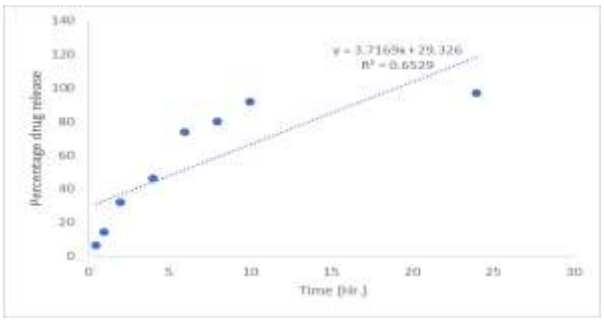

Figure 10: Zero order graph of formulation A7.

6.3.6.2 First order

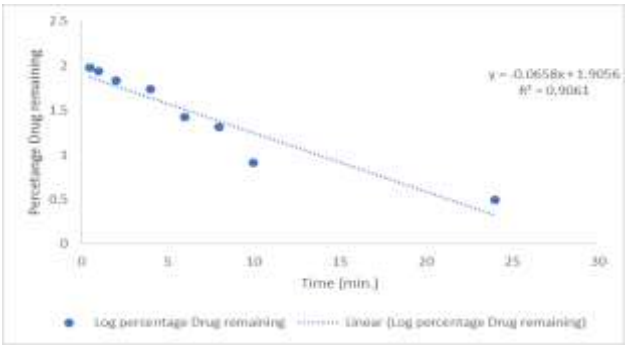

Figure 11: First order graph of formulation A7.

6.3.6.3 Higuchi

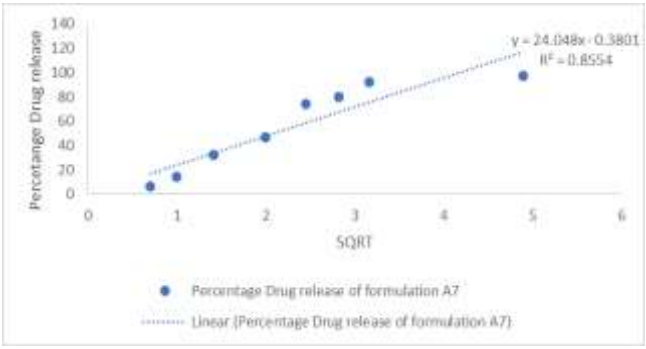

Figure 12: Higuchi order graph of formulation A7.

6.3.6.4 Korsmeyer peppas

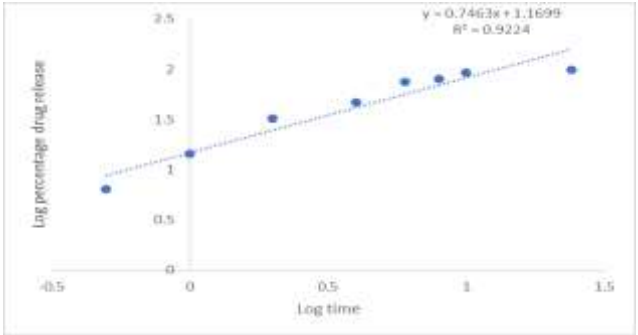

Figure 13: Korsmeyer peppas order graph of formulation A7.

The R^2 value was determined from the graph in each case. The Korsmeyer and Peppas Exponential Equation (R^2=0.9224) was found to best fit the release data when the determination coefficients were considered.

7. SUMMARY

- The melting point of pure atenolol was determined to be between 158.34±0.58 to 159.34±1.53°C. As a result, the medicine sample was free of any contaminants.
- The absorption maxima of atenolol were found to be at 224 nm with linear equation and regression coefficent Y= 0.0479x - 0.0059 and 0.999.
- The partition coefficient of atenolol in n- Octanol: Water was found to be 0.257±0.007 this indicating that the drug is hydrophilic in nature.
- All formulation was prepared as spherical beads as shown in a table 10. Except the formulation was A1.
- The percentage yield of all formulations were determined to be in the ranges of 79.16±0.44% to 96.17±0.32%. Formulation A8 had the highest percentage yield 96.17±0.32%., respectively.
- The percentage drug entrapment of all formulations were determined to be in the ranges of 47.57±0.31% to 96.09±0.80%. Formulation A7 had the highest percentage yield 96.09±0.80%., respectively.
- All prepared atenolol beads were between 4.653±0.091mm to 12.580±0.636mm in size. The beads were suitably rigid and spherical in shape when they were created. The minimal bead size in the A7 formulation is 5.687±0.085mm.
- Formulation A7 was chosen for additional in-vitro drug release testing based on the results of the following criteria. In comparison to the immediate release of pure drug, formulation MB7 demonstrated a sustained release of 95.56±0.65 at 24 hours.
- The Korsmeyer and Peppas Exponential Equation (R^2=0.9224) was found to best fit the release data when the determination coefficients were considered.

8. REFERENCES

1. Howard C, Ansel, NIcholos G. Popvich, lyold V. Allen, 1995; 78.
2. Shaji J, Chadawar V, Talwalkar P, The Indian Pharmacist, June, 2007; 6(60): 21-28.
3. John C, Morten C, The Science of Dosage Form Design, Aulton: Churchill Livingstone, 2002; 290-300.
4. Lee VHL, Marcel Dekker, Inc. New York, 1987; 2: 16-25.

5. Vyas SP, Khar RK, 2002; 156-189.
6. Chien YW, Novel drug delivery system, 50.
7. Allen LV, Popvich GN, Ansel HC, Ansel's, 2004; 260-263.
8. Patrick JS. Martin's, Varghese Publishing House. Bombay, 1991; 512-519.
9. Kar RK, Mohapatra S, Barik BB, Asian J Pharm Cli Res, 2009; 2: 54-6.
10. Lachaman L, Liberman HA, Kanig JL, Varghese publishing house, 1987.
11. Jain NK, Controlled and novel drug delivery, CBS publisher and distribution, 1997; 1-25.
12. Wichterle O, Lim D. Hydrophilic gels in biologic use, Nature, 1960; 185: 117.
13. Jensen, OM, Hansen, PF, Cement Concr. Res, 2002; 32: 973–978.
14. Karadag ED, Saraydin C¸ AldiranY, Guven, O, Polym. Adv. Technol, 2000; 11: 59–68.
15. Chen P, Zhang W, Luo W, Fang, Y, J. Appl. Polym. Sci, 2004; 93: 1748–1755.
16. Sun X, Zhang G, Shi Q, Tang B,Wu Z, J. Appl. Polym. Sci, 2002; 86: 3712–3717.
17. Chauhan, G.S. and Lal, H, Desalination, 2003; 159: 131–138.
18. Kulicket W, Kull AH, Kull W, Thielking, Engelhardt HJ, Pannek J. Polymer, 1996; 37: 2723–2730.
19. Chen J, Blevins WE, Park H, Park, K, J. Controlled Release, 2000; 64: 39–51.
20. Bucholz FL, Graham T, Modern Superabsorbent Polymer Technology. Wiley-VCH: New York, 1998; 1–154.
21. Tsukasa M, Yuuki T, Sachiko A, Takahiko I, Akie H, Keiko E, Polymer Volume, 2010; 23: 5539–5549.
22. Nguyen KT, West JL, Biomaterial, 2002; 23: 4307- 4314.
23. Peppas NA, Bures P, Leobandung W, Ichikawa H, Eur J Pharm Biopharm, 2000; 50: 27-46.
24. Sawhney AS, Pathak CP, van Rensburg JJ, Dunn RC, Hubbell JA, J Biomed Mat Res, 1994; 28: 831-838.
25. Kopecek J. Hydrogel, Biomaterials, 2007; 28(34): 5185–5192.
26. Lutolf MP, Nat Mater, 2009; 8(6): 451–453.
27. Chung HK, Park TG, Nano Today, 2009; 4(5): 429–437.
28. Oh JK, Can J Chem, 2010; 88(3): 173–184.
29. Ulijn RV, Bibi N, Jayawarna V, Mater Today, 2007; 10(4): 40–48.
30. Lee J, Cuddihy MJ, Kotov NA, Tissue Eng Part B, 2008; 14(1): 61–86.
31. Geckil H, Xu F, Zhang XH, Moon S, Demirici U, Nanomedicine, 2010; 5(3): 469–484.
32. Hunt NC, Grover LM, Biotechnol Lett, 2010; 32(6): 733–742.
33. Drury JL, Mooney DJ,Biomaterials, 2003; 24(24): 4337–4351.

34. Liu SQ, Tay R, Khan M, Ee PLR, Hedrick JL, Yang YY, Soft Matter, 2010; 6(1): 67–81.
35. Slaughter BV, Khurshid SS, Fisher OZ, Khademhosseini A, Peppas NA, Adv Mater, 2009; 21(32–33): 3307–3329.