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Journal of Nanomedicine Research

Preparation and Characterization of Atenolol Laden Nanoparticles

Abstract

In the present study, an attempt was made to develop nanoparticles of Atenolol for effective treatment of Glaucoma. By developing the nanoparticulated delivery the required action of drug at the target site i.e. at eye can be provided. The nanoparticles were prepared by nano precipitation method. The formulation was subjected to different evaluation parameters like particle size, zeta potential, drug content uniformity, entrapment efficiency, in-vitro drug release study.

The particle size range of nanoparticles was found to be 100-256 nm. The zeta potential of nanoparticles was found to be 55.87 to 64.87 mV. The drug content of different formulations F1 to F8 was calculated and the content was found to be in range of 95.98 TO 102.14 %. The entrapment efficiency was found to be in range of 45.76 to 72.98%. From the in-vitro drug release studies, it was found that the cumulative percent drug release for optimised formulation F5 found to be between 12.56 to 88.15 % respectively.

Research Article

Volume 4 Issue 2 - 2016

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Received: July 25, 2016 | **Published:** October 18, 2016

Introduction

Glaucoma is a disease that damages eye's optic nerve. It usually happens when fluid builds up in the front part of eye. That extra fluid increases the pressure in eye, damaging the optic nerve. Glaucoma is a leading cause of blindness for people over 60 years old. When glaucoma occurs, usually early there are no early symptoms and the disease progress slowly. If glaucoma is not diagnosed and treated, it can progress to loss of central vision and blindness [1-3].

There are two types of glaucoma.

a) Primary open-angle glaucoma (POAG)

b) Angle-closure glaucoma (also called "closed-angle glaucoma" or "narrow-angle glaucoma")

Nanotechnology based ophthalmic formulations are one of the approaches which is currently used for both anterior, as well as posterior segment drug delivery. Nanoparticulates are designed to ensure low irritation, adequate bioavailability, and ocular tissue compatibility. Several nanocarriers, such as nanoparticles, nanosuspensions, liposomes, nanomicelles and dendrimers have been developed for ocular drug delivery [4-6].

Nanoparticles can be defined as the colloidal particles having size ranging from 10 to 1000 nm. The nanotechnology can be used to effectively deliver the drug in eyes [7]. A large number of drugs can be delivered using nanoparticulates carrier via a large number of routes. These include many hydrophilic drugs, hydrophobic drugs as well as for proteins, vaccines, biological macromolecules, etc. They can be formulated for targeted delivery to the lymphatic system, brain, arterial walls, lungs, liver, spleen, or made for long -term systemic circulation [8].

Experimental Methods

Materials

Atenolol was a gift sample from Mepromax Life sciences Pvt. Ltd Dehradun, Eudragit RS -100, Eudragit S-100, poloxamer -188 were purchased from Central Drug House Ltd, New Delhi. All the reagents and solvents used were of analytical grade satisfying Pharmacopeia standards (Table 1).

The nanoparticles were prepared with the different ratios of drug and eudragit RS-100 and eudragit S-100 polymer using the nano precipitation method. The drug and the polymer were dissolved in acetone at room temperature. The resultant solution was added into 50 ml aqueous phase containing 0.5% and 1 % (w/v) of poloxamer-188. The mixture was homogenized, at constant agitation speeds of 20,000 rpm. The suspension was centrifuged 20,000 rpm and collected.

Characterization of Nanoparticles

Shape and Size

The morphology of nanoparticles was determined by Scanning electron microscopy (SEM).

(Zeiss, Evo 40, India) and size was determined by Zetasizer Nano ZS-90 (Malvern Instruments Ltd, UK).

Drug entrapment efficiency

The 10 mg/ml portion of the freshly prepared nanoparticle was prepared and centrifuged at 14,000g for 2 hrs at 40˚C temperature. The amount of unincorporated drug was measured by at 274 nm using double beam UV spectrophotometer (Elico SL 210, India) against blank.

Table 1: Formulation plan for Atenolol nanoparticles.

Ingredients	Formulation Code							
	F1	F2	F3	F4	F5	F6	F7	F8
Atenolol(mg)	100	100	100	100	100	100	100	100
Eudragit RS -100(%)	1	2	3	4	-	-	-	-
Eudragit S- 100(%)	-	-	-	-	1	2	3	4
Poloxamer 188(%)	0.5	1	0.5	1	0.5	1	0.5	1

Drug content

10 mg of nanoparticles was taken into 10ml volumetric flask and volume was made up with methanol. It was solicited for 5 min in sonicator. The solution was filtered through Whatman filter paper (0.45 µ) and filtrate was analyzed at 274 nm using double beam UV spectrophotometer.

Zeta potential

The zeta potential was determined using zeta potential analyzer.

In- Vitro drug release study

The dialysis membrane (Himedia) was used to determine the in-vitro release of the nanoparticles using diffusion cell. Nanoparticles corresponding to 100 mg of drug was placed in the donor compartment whereas 50 ml of phosphate buffer saline pH 7.4 was used as receptor medium. The entire system was kept at 37° ± 1 °C with continuous magnetic stirring. Sample of 5 ml were withdrawn at predetermined time and same amount of medium was supplemented. The amount of drug released was determined at different time intervals (1, 2,3, 4, 5, 6, 7, 8, 24 h) at b maximum wavelength of 274 nm using double beam UV spectrophotometer and cumulative percentage drug release was calculated.

Kinetic modelling

The data obtained from in vitro release studies of the optimized batch was placed to various models in order to understand the release mechanism of drug. The kinetic models used were zero order, first order, Higuchi, and Peppas equation.

Results and Discussion

Shape and Size

The SEM of photomicrographs was shown in Figure 1. The mean particle sizes of the prepared nanoparticles as measured by Zeta Sizer were in size range of 100 to 256 nm. This size of nanoparticles are suitable for the ocular delivery and also does not cause any irritation in the eye. The variability in poly dispersity index was due to various variables like polymer type and concentration, surfactant concentration, homogenization speed and evaporation time.

The surface morphology was determined using scanning electron microscopy. The SEM image of nanoparticles revealed spherical shape with smooth surface but also have slight aggregation.

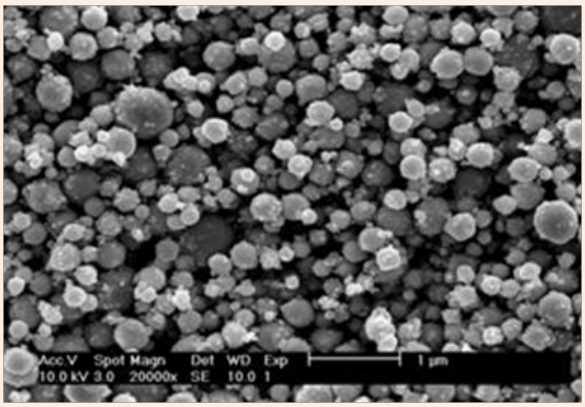

Figure 1: Scanning Electron Microscopy of Atenolol laden Nanoparticles (F5).

Drug entrapment efficiency

The entrapment efficiency of nanoparticles is influenced by the characteristics of the polymer, drug, surfactant etc. the entrapment efficiency was found to be in range 45% to 72%. The high entrapment efficiency results from the more affinity of the drug and polymer to the same solvents. In the present study the drug entrapment efficiency were affected by the polymer and drug ratio in the formulations. The increased entrapment efficiency was due to the greater proportion of polymer in the formulation.

Drug content

The drug content was found to be in the range of 95-102 % indicating that the Atenolol was uniformly distributed in Nanoparticles and there was no loss of the material during the preparation. The result was shown in Table 3.

Zeta potential

The zeta potential of the formulated nanoparticles has positive values of +55.87 to + 64.87 mV (Table 3). The effect of zeta potential on stability of the colloid is shown in Table 2. The value of zeta potential shows excellent stability in solvent (Figure 2).

In-Vitro release study

In-vitro drug release of Atenolol loaded nanoparticles was studied using modified dialysis method. The results are tabulated in Table 4. All batches showed the initial rapid drug release of around 10- 20% within two hours followed by sustained drug

release of the remaining 80-90% up to 24 h. The initial rapid drug release may be attributed to the diffusion of dissolved drug initially deposited inside the pores of the nanoparticles, presence of free drug in the external phase and on the surface of the nanoparticles.

The data obtained from the drug release of optimized batch of Atenolol loaded nanoparticles was fitted to different kinetic models to understand the drug release mechanism and kinetics. When the data was fitted to Higuchi model (Figure 3), R2 value was found to be between 0.922 to 0.989. This indicated that the release followed Higuchi diffusion. The release was fitted to both the zero order and first order models (Figure 4 & 5). R2 values for zero order and first order models were found to be between 0.963-0.983 and 0.948-0.976 respectively, indicating that the release followed zero order release kinetics. The drug release data was fitted to Korsmeyer-Peppas model to determine the value of diffusion exponent (n) (Figure 6). The value of n for a spherical system is < 0.5 for Fickian release; 0.5 < n < 1 indicates non-Fickian release; n > 1 indicates super case II release. The n value for was greater than 0.85 therefore the release mechanism is said to follow Case -II transport diffusion kinetics. It can be concluded that the release of Atenolol from the nanoparticles follows zero order kinetics and mechanism of drug release is Case II transport.

Among the different nanoparticles formulations, the formulation F5 was selected as the ideal formulation after considering its optimum particle size, zeta potential, drug content, entrapment efficiency and also drug release at controlled manner up to 24 hrs (Table 5).

Table 2: Effect of Zeta Potential on stability of the colloid.

S No	Zeta Potential [mV]	Stability Behavior of the Colloid
1	From 0 to ±5	Rapid coagulation or flocculation
2	From ±10 to ±30	Incipient instability
3	From ±30 to ±40	Moderate stability
4	From ±40 to ±60	Good stability
5	More than ±61	Excellent stability

Table 3: Evaluation Parameters of different formulations (F1-F8).

Formulation Code	Particle Size± SD (n = 3)	Poly Disparity Index ± SD	% Entrapment Efficiency	Drug Content (%)	Zeta Potential (mV)
F1	100 ± 0.89	0.88 ±0.85	45.76±0.16	95.98 ±1.98	60.23±0.98
F2	130 ± 0.98	0.54 ±0.92	55.76±0.24	97.45±0.98	55.87±0.76
F3	159±0.99	0.39 ±0.65	58.14±0.74	96.65±0.99	59.09±0.83
F4	190 ±0 .84	0.86 ±0.89	60.5±0.76	98.78±0.94	63.85±0.99
F5	200±1.25	0.78 ±0.93	71.12±0.89	102.14±1.09	64.87±1.04
F6	216±1.42	0.82 ±1.09	69.45±0.46	99.0±1.85	62.09±0.75
F7	248±0.98	0.67 ±1.01	72.98±0.55	100.1±1.03	60.98±1.06
F8	256±1.19	0.91 ±0.99	67.89±0.87	100.8±1.58	61.55±1.55

Table 4: *In -vitro* drug Release data of different formulations (F1-F8).

Time(hrs)	Cumulative % Drug Release							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	16.48	15.23	14.54	13.98	12.56	10.98	10.97	9.99
2	18.05	17.32	16.78	15.89	14.89	12.87	12.45	11.67
3	19.9	18.67	18.45	17.69	15.76	13.32	13.89	12.67
4	21.57	20.09	19.89	18.98	18.78	15.78	15.76	14.98
5	25.76	26.8	23.78	24.31	21.46	22.83	19.87	21.01
6	32.67	34.56	31.98	32.98	30.98	29.75	27.13	25.96
7	40.89	38.98	36.98	35.87	33.56	33.1	29.61	27.12
8	46.67	42.87	42.14	40.09	36.86	38.09	33.14	30.98
24	98.78	96.75	94.73	91..91	88.15	85.09	82.13	80.01

Table 5: Model fitting release profile of Formulations F1-F8.

Formulation Code	Regression Coefficient (R^2)			Slope (n) Value
	Zero Order	First Order	Higuchi's	Korsmeyer- Peppas
F1	0.975	0.957	0.987	0.863
F2	0.964	0.948	0.989	0.872
F3	0.963	0.958	0.993	0.886
F4	0.965	0.956	0.992	0.892
F5	0.975	0.962	0.995	0.899
F6	0.979	0.96	0.997	0.912
F7	0.98	0.976	0.982	0.926
F8	0.983	0.972	0.922	0.954

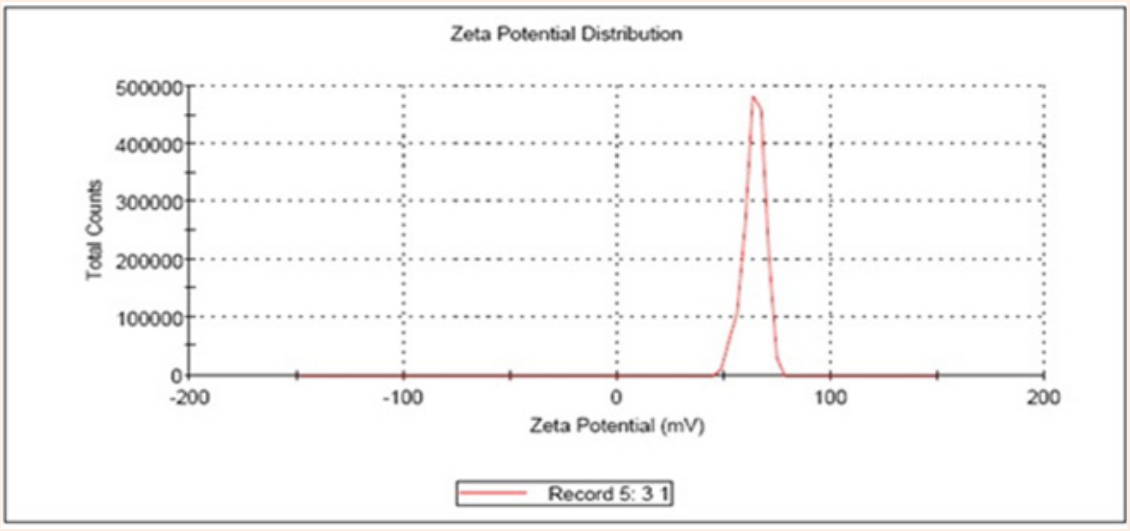

Figure 2: Zeta potential of Atenolol nanoparticles.

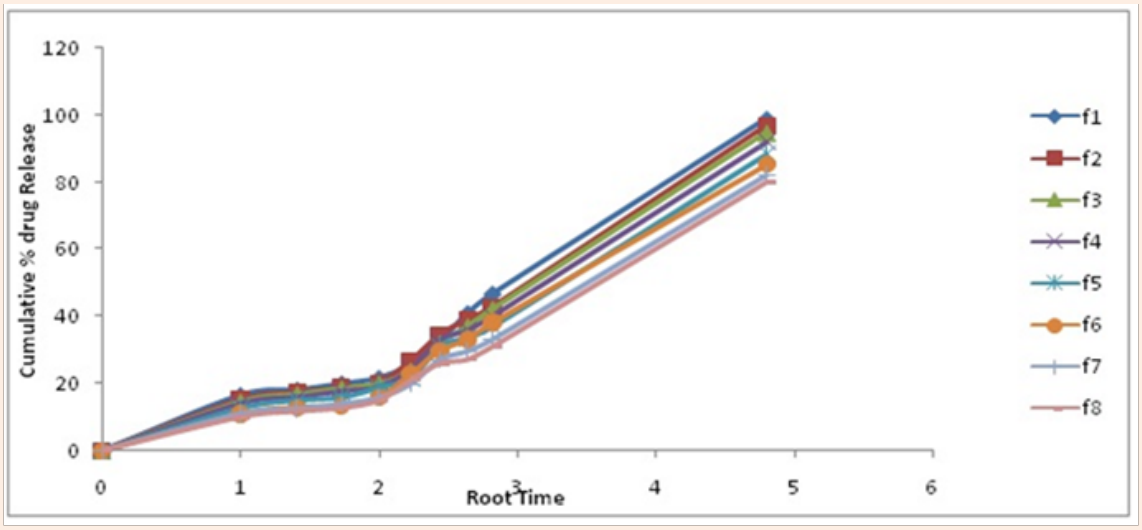

Figure 3: Higuchi plot of Atenolol nano particles.

Citation: Archana D, Divya J (2016) Preparation and Characterization of Atenolol Laden Nanoparticles. J Nanomed Res 4(2): 00084. DOI: 10.15406/jnmr.2016.04.00084

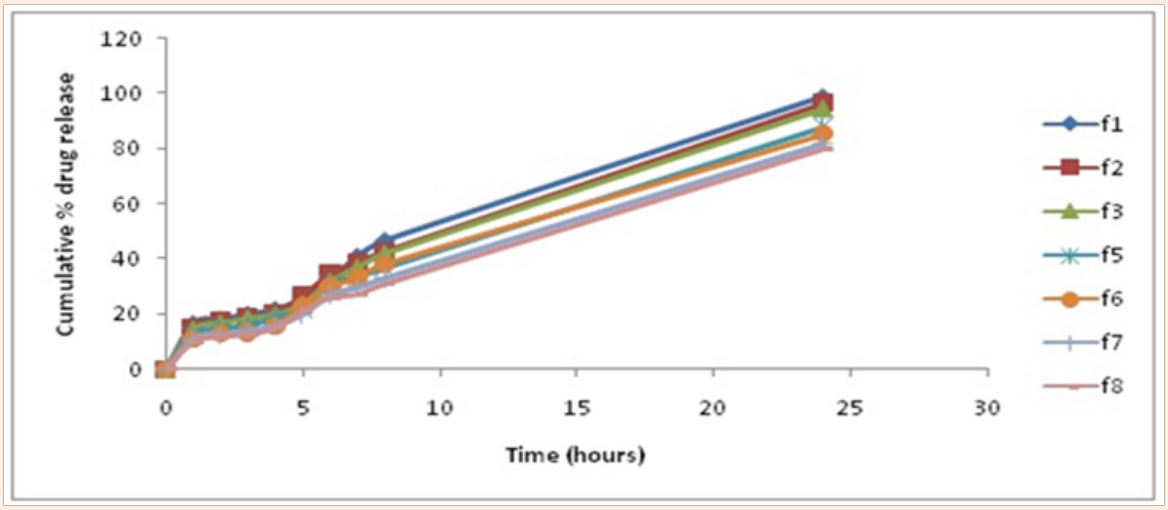

Figure 4: Zero order curves of Atenolol nanoparticles.

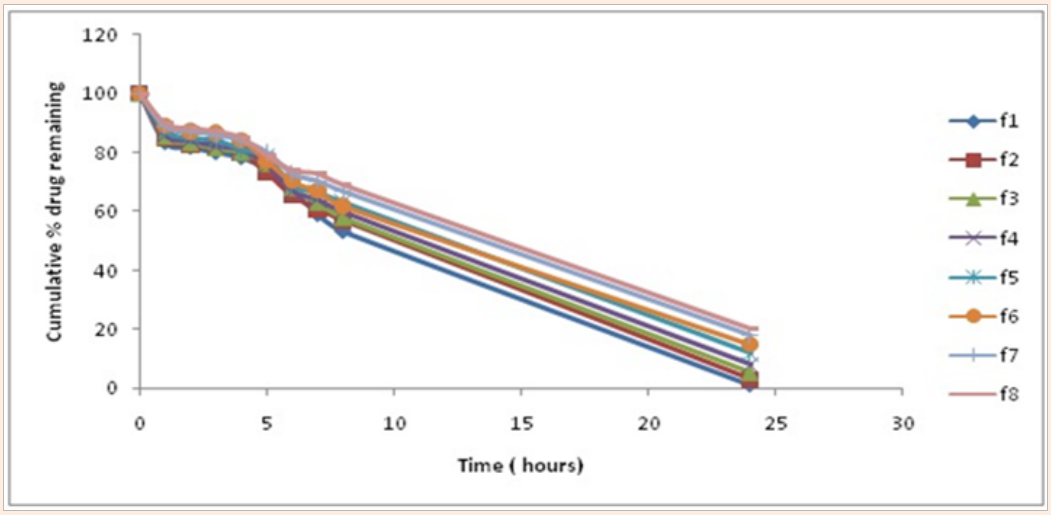

Figure 5: First order curve of Atenolol nanoparticles.

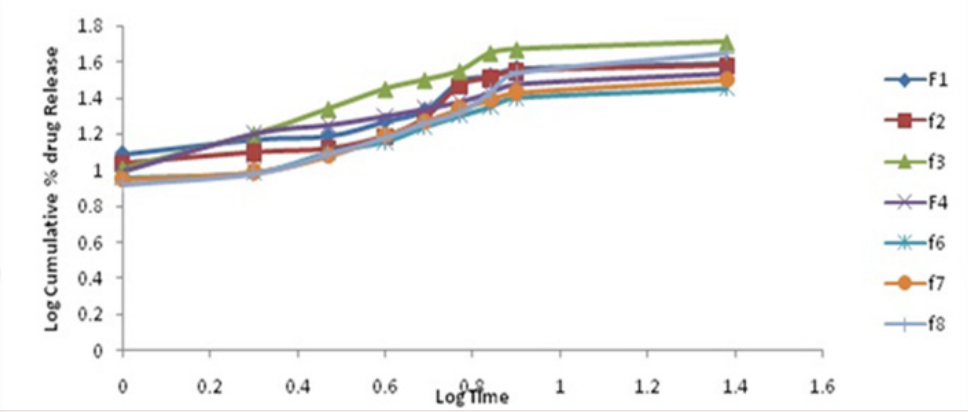

Figure 6: Korsmeyer-Peppas plot of Atenolol nanoparticle.

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Conclusion

In the present study, an attempt was made to develop nanoparticles of Atenolol for treatment of glaucoma with a view to provide targeted action to the required site and helps to provides the controlled action and thus reduces the dose frequency and increases the patient compliance. Nanoparticles were successfully prepared by nano-precipitation method. The method was able to produce discrete, free-flowing nanoparticles.

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