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FORMULATION AND EVALUATION OF NANOPARTICLES CONTAINING ATENOLOL BY IONIC GELATION TECHNIQUE

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ABSTRACT

Nanoparticles of atenolol, an antihypertensive agent were prepared to improve absorption and to increase bioavailability. The drug nanoparticles were prepared using chitosan polymer by ionic gelation technique. Nanoparticles of different ratios were formulated and analyzed for drug content, entrapment efficiency, particle size, zeta potential and *in vitro* drug release studies. The particle size ranged between 156±2 to 321±6 nm. The entrapment efficiency of FAN-1 to FAN-5 was ranging from 94.5±0.12 to 99.2±0.23. The drug release studies it was observed that prepared nanoparticles formulation-5 (FAN-5) shows better sustained release (98.75%) for about 24 hrs as compared to other formulations.

KEY WORDS

Nanoparticles, Atenolol, Chitosan, Ionic gelation technique and *In vitro* Evaluation.

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INTRODUCTION

The oral drug administration is desirable but challenging owing to the nature of the gastrointestinal tract. The highly acidic pH in the stomach and the presence of enzymes such as pepsin can cause protein degradation. Secreted pancreatic enzymes in the lumen of the intestine and membrane-bound brush-border enzymes may also cause substantial loss of drug activity. Finally, the

physical barrier of the intestinal cells must be crossed before a drug can reach the circulation. To overcome all this, a new drug delivery system called nanoparticles can be employed without facing above mentioned problems[1-3]. The reason why these nanoparticles are attractive for medical purposes is based on their important and unique features, such as their surface to mass ratio that is much larger than that of other particles, their quantum properties and their ability to absorb and carry other compounds. Nanoparticles have a relatively large (functional) surface which is able to bind, adsorb and carry other compounds such as drugs [4-6].

Nanoparticles may partially protect the entrapped drug or gene from degradation and improve cellular uptake through endocytosis. While a variety of polymers and lipids have been employed to form drug loaded nanoparticles, one biodegradable polymer that has received a good deal of recent attention as a component of oral drug and gene delivery systems is chitosan[7].

Atenolol, a β-blocker, is prescribed widely in diverse cardiovascular diseases, like hypertension, angina pectoris, arrhythmias, and myocardial infarction. The drug is also frequently indicated in the prophylactic treatment of migraine. Administration of conventional tablets of Atenolol has been reported to exhibit fluctuations in the plasma drug levels, resulting in manifestation of side effects or reduction in drug concentration at the receptor site. In this present study an attempt was made to formulate the Atenolol loaded into chitosan nanoparticles[8].

MATERIAL AND METHODS

Atenolol was a gift sample from Novans Pvt. Ltd Mumbai. Chitosan, glacial acetic acid and sodium tripolyphosphate were purchased from Lova Chemicals Ltd, India. All other chemical used were of analytical grade.

Preparation of Atenolol nanoparticles by ionic gelatins method

The preparation of nanoparticle was done by taking different concentration of chitosan in 5% glacial acetic acid and stirred for more than 4 hours continuously and kept overnight to get chitosan after stabilization[9]. The formulation of nanoparticle was done by ionotropic gelation method. The different concentration of chitosan gel (1mg/ml) was taken in 5ml of 0.5% TPP which is acting as cross linking agent[10]. Both the solutions were kept under high speed stirring (3000 rpm) using high speed stirrer. The final solution of chitosan suspensions were centrifuged for 20 minutes. The above mentioned method used for different formulations with various proportion of polymer concentration[11].

CHARACTERIZATION OF ATENOLOL NANOPARTICLES[12-15]

FT-IR Spectroscopy

The FT-IR spectra of pure Atenolol and chitosan nanoparticles loaded with Atenolol were evaluated to check the compatibility of polymer and drug in the nanopartilce formulation.

Particle size measurement and Surface Morphology of nanoparticles

Determination of Particles size and the surface morphology of the nanoparticles were done by scanning electron microscopy (SEM).

Zeta Potential

The Zeta potential of the best formulation of Atenolol nanoparticles was measured by using Malvern Zeta-sizer.

Drug content

The drug content of Atenolol present in nanoparticles was determined by centrifugation method. The nanoparticles suspension was centrifuged at 15,000 rpm for 30 min at 15ºC. The supernatant solution was separated and the free drug concentration of Atenolol in the supernatant solution was determined by UV - Vis spectrophotometer at 226 nm.

Entrapment efficiency (EE)

The Atenolol nanoparticles prepared by ionic gelation technique were centrifuged at 15000 rpm for 30 min at 15° C using centrifuge. Then the supernatant solution was analyzed for the free drug content. The entrapment efficiency was calculated by using following formula.

EE = Total drug content - Free drug content / Total drug content ×100

***In vitro* release studies**

The *in vitro* release studies were carried out by using dialysis membrane. The Atenolol nanoparticles equivalent to 5 mg of Atenolol and 10 ml of phosphate buffer pH 7.4 was added to the dialysis tubes and immersing the dialysis tube to the receptor compartment containing 250 ml of phosphate buffer pH 7.4. The medium was agitated continuously using a magnetic stirrer and the temperature was maintained at 37±0.5ºC. The sample of 5 ml was taken at various intervals of time over a period of 24 hrs and fresh buffer was replaced during each sampling. The amount of Atenolol released was determined by UV-spectrophotometer at 226 nm.

RESULTS AND DISCUSSION

CHARACTERIZATION OF ATENOLOL NANOPARTICLES

Compatability studies (Fourier Transform Infrared Spectroscopic studies)

IR Study was carried out to conform the compatibility between the selected polymer Chitosan, drug atenolol and nanoparticles. The spectra obtained from the IR studies it was confirmed that there are no major shifting as well as non less of functional peaks between the spectra of drug, polymer and drug loaded Nanoparticles. The FT-IR spectra of Pure Atenolol, Pure chitosan and chitosan nanoparticles loaded with Atenolol were shown in Figure No.1, 2 and 3.

Particle size measurement and Surface Morphology of nanoparticles

Scanning electron microscopy (SEM) was used to determine the particle size and surface morphology of the nanoparticles. The study reveals that the surface of the nanparticles was smooth and no aggregates were found from the sample used for SEM analysis. The particle size of the nanoparticles was found to be around 156±2 to 321±6 nm. The study results were shown in Table No.2 and Figure No.4.

Zeta Potential

The Zeta potential of the formulations was measured by using Malvern Zeta-sizer and it was found to be ranging from 27.3±0.3, 28.1±0.5, 27.1±0.6, 29.3±0.8 and 31.4±0.1. The results were shown in Table No.2 and Figure No.5.

Drug content & Entrapment efficiency (EE)

The drug content of Atenolol present in nanoparticles was determined by centrifugation method by measuring the concentration of drug in supernatant solution which was obtained after centrifugation. The entrapment efficiency of FAN-1 to FAN-5 was ranging from 94.5 ±0.12 to 99.2±0.23. The results are shown in Table No.2.

***In vitro* Release Studies**

The *In vitro* release studies were carried out by using dialysis membrane. The cumulative percentage drug release after 24 hrs were found to be 83.42%, 89.69%, 93.73%, 95.84% and 98.75% for FA1 to FA5 formulations respectively. The results were shown in Table No. 3 and Figure No. 6.

Table No.1: Formulation of Atenolol Nanoparticles

S.No	Formulation	Amount of drug (mg)	Amount of polymer (mg)
1	FAN-1	50	50
2	FAN-2	50	100
3	FAN-3	50	150
4	FAN-4	50	200
5	FAN-5	50	250

Table No.2: Characterization of Atenolol Nanoparticles

S.No	Formulation	Entrapment efficiency (%)	Particle size (nm)	Zeta potential (mv)
1	FAN-1	94.5 ±0.12	156±2	27.3±0.3
2	FAN-2	95.4±0.23	243±7	28.1 ±0.5
3	FAN-3	96.7 ±0.46	268±5	28.1±0.6
4	FAN-4	97.1±0.50	293±9	29.3±0.8
5	FAN-5	99.2±0.23	321±6	31.4±0.1

Table No.3: Comparative dissolution study of different batches with various ratio's of polymer

S.No	Time in hours	% of drug release FAN-1	% of drug release FAN-2	% of drug release FAN-3	% of drug release FAN-4	% of drug release FAN-5
1	0	0.00	0.00	0.00	0.00	0.00
2	3	6.15	7.44	8.27	9.15	10.37
3	6	12.45	14.74	16.75	18.12	19.92
4	9	23.79	26.13	29.42	32.54	34.38
5	12	38.14	45.52	50.28	53.07	57.76
6	15	49.45	53.17	59.62	62.38	65.72
7	18	60.48	64.29	71.79	75.12	79.83
8	21	72.62	76.78	83.42	87.52	90.35
9	24	83.42	89.69	93.73	95.84	98.75

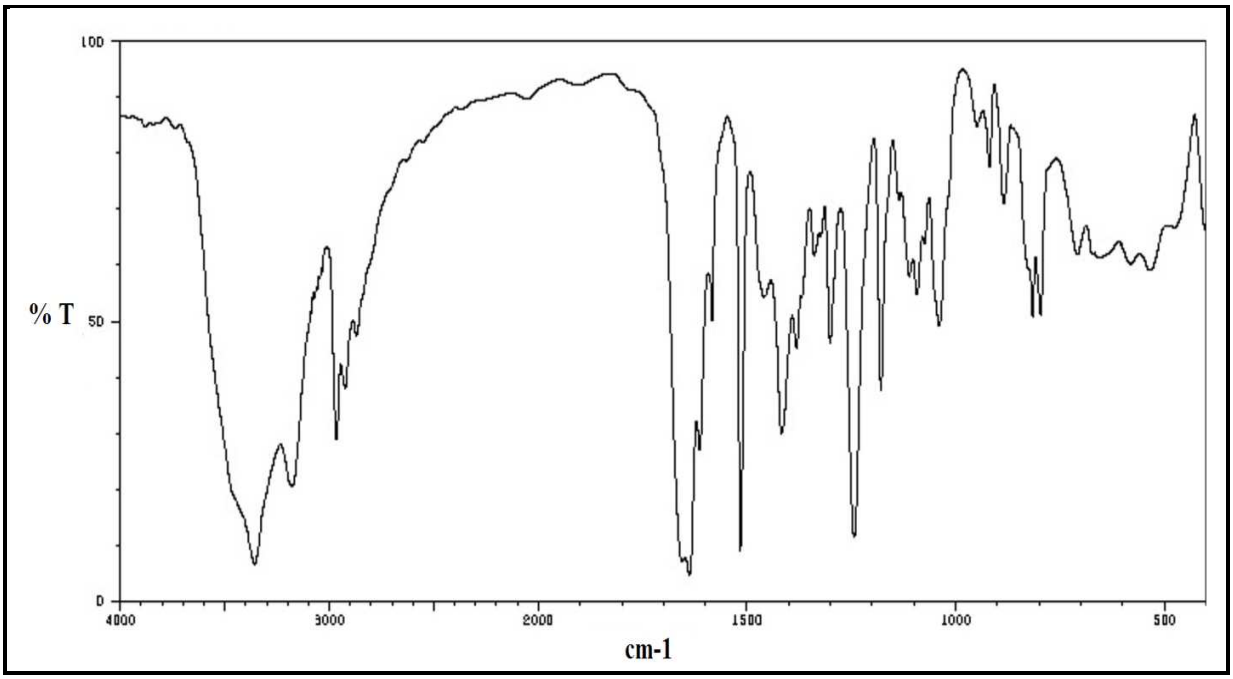

Figure No.1: FT-IR spectra of pure atenolol

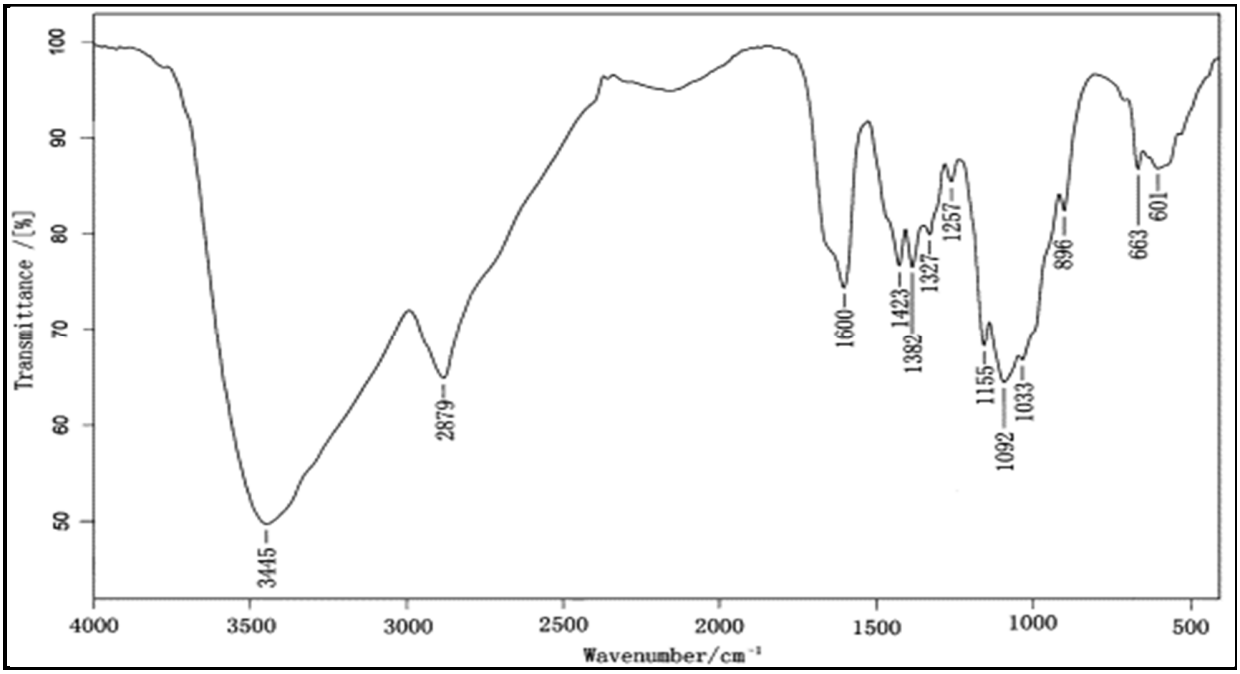

Figure No.2: FT-IR spectra of pure Chitosan

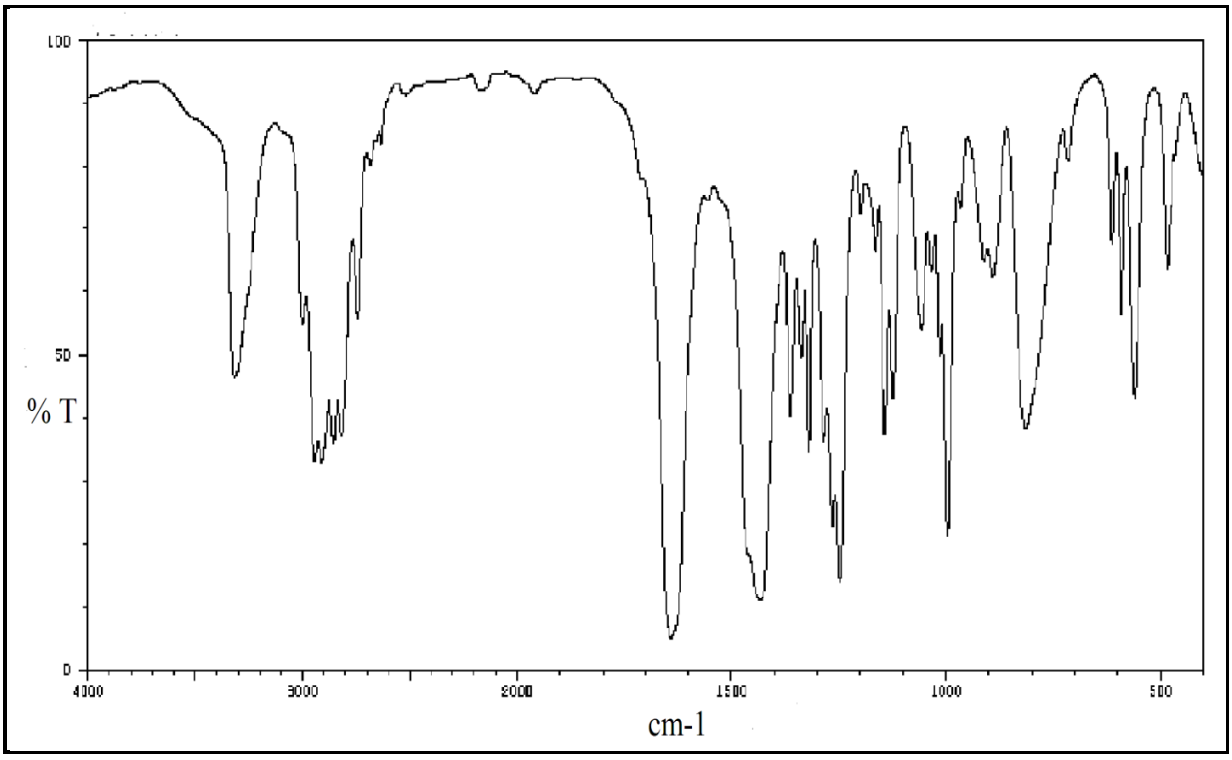

Figure No.3: FT-IR spectra of Formulation-5(FAN-5)

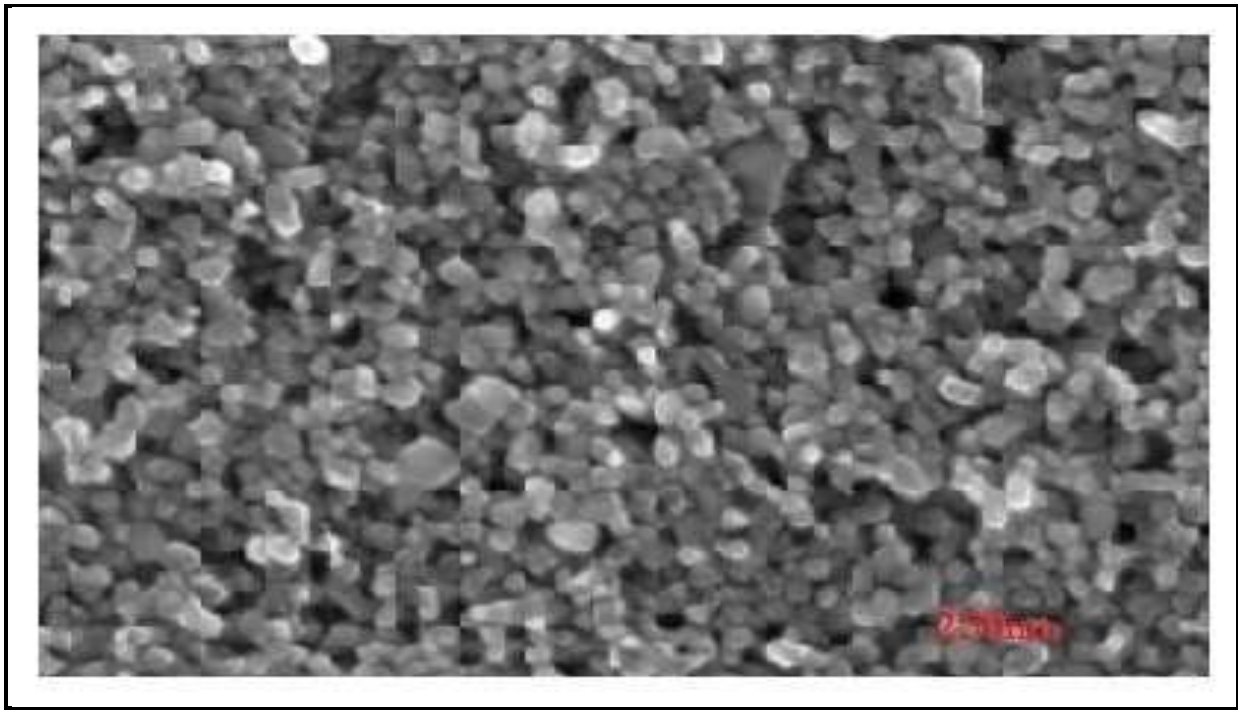

Figure No.4: Surface Morphology of nanoparticles (FAN-5)

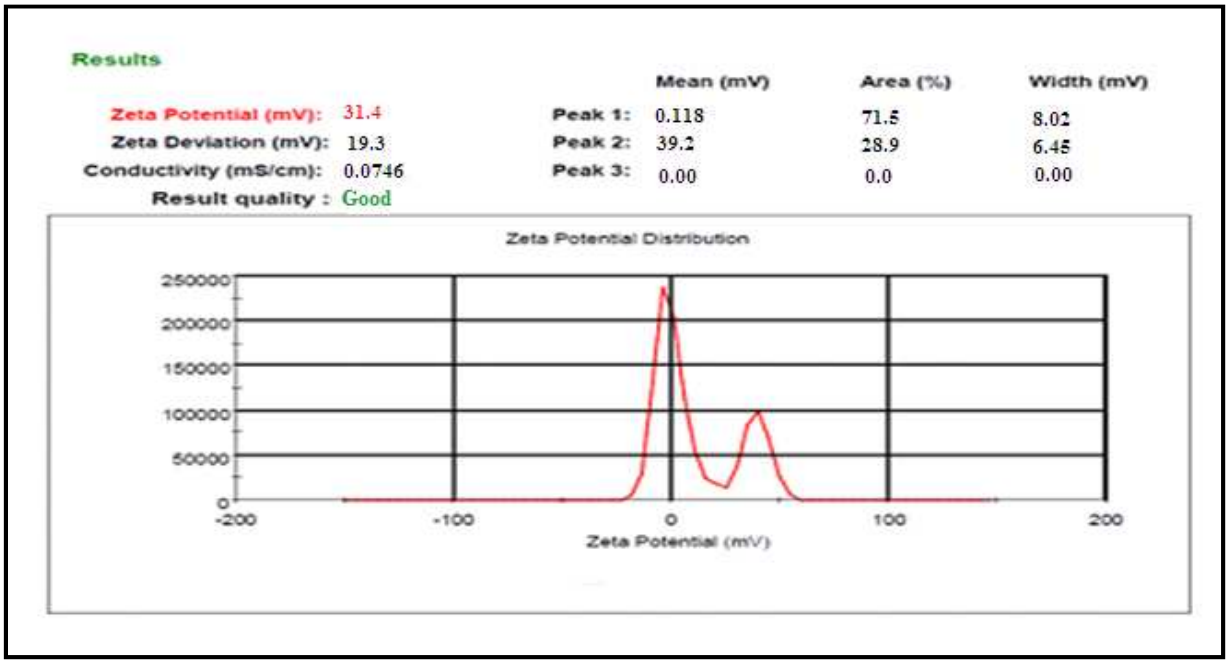

Figure No.5: Zeta Potential of Formulation-5 (FAN-5)

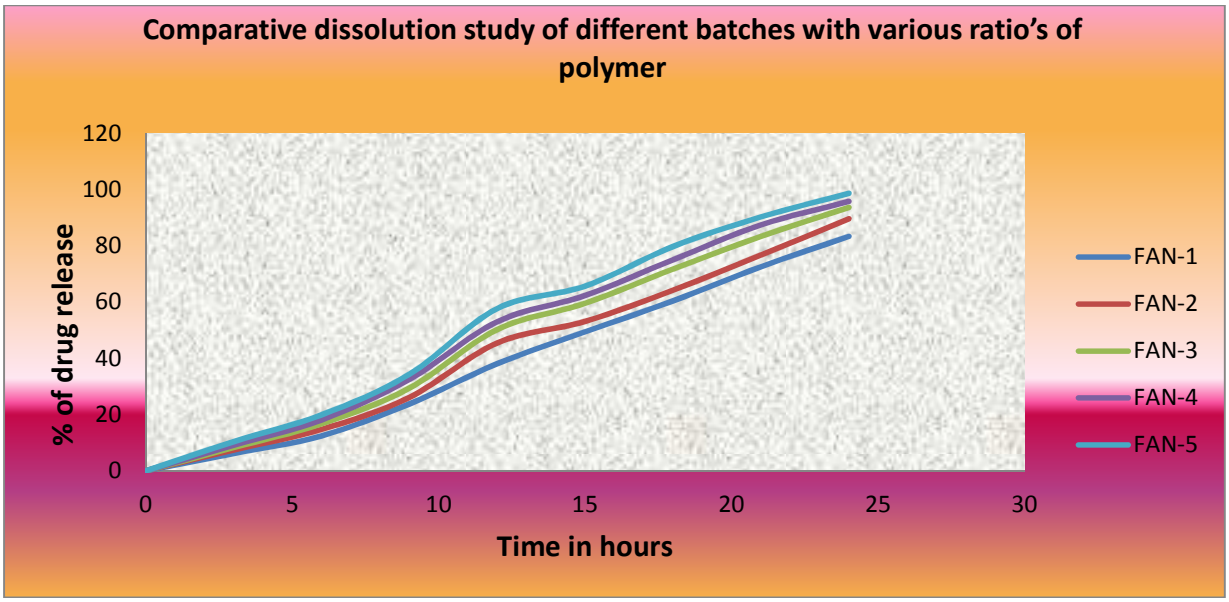

Figure No.6: Comparative dissolution study of different batches with various ratio's of polymer

CONCLUSION

The Atenolol nanoparticles was prepared by ionic gelation technique and evaluated for various evaluation parameters like particle size, drug polymer compatibility, entrapment efficiency, *in vitro* drug release. The results were conclude that FAN-5 can be considered as an optimized formula for sustaining the release of drug for over 24 hours and the formulation can be considered as best alternate to sustained release tablets for the treatment of HYPERTENTION and can be best used with minimal or without any major side effects associated with sustained release tablets.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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