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ORIGINAL ARTICLE

Formulation and Evaluation of Atenolol Microspheres

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ABSTRACT

Objective: The aim of present study is to formulate and evaluate atenolol microspheres using excipients like sodium alginate, calcium chloride and starch soluble.

Method: The encapsulation efficiency was higher in formulations with higher polymer concentrations than in the other nine. In order to make microspheres, the ionotropic gelation method was used. High yielding and easy to produce, this technology represents a significant improvement over current procedures.

Conclusion: A granulometric research, bulk and tapped density, mean particle size and angle of repose, drug entrapment efficiency and in-vitro dissolution study were all found to be within acceptable limits in terms of their results

Keywords: Microspheres, Ionotropic gelation technique,sustained release.

INTRODUCTION

A novel, on the other hand, is searching for something out of necessity, as opposed to a medicine delivery mechanism. For chronic patients, the drug must be administered over an extended period of time, and many medications must be taken at the same time. Many types of controlled release dose forms have been developed and tweaked in attempt to improve patient compliance while lowering peak plasma concentrations[1]. In this dose form, the drug is released at a fixed pace over a prolonged period of time, maintaining a generally constant plasma level. Microspheres can be defined as "Monolithic spheres or therapeutic agents distributed throughout the matrix either as a molecular dispersion of particles [2]. Its particle size ranges between and (1-1000nm). Enteric coated/double-layer tablets, which slowly disperse the medication into the body over time over a period of 12-24 hours, are also currently available, although they still result in ineffective systemic distribution and the possibility of gastrointestinal irritation [3].

METHODS OF PREPARATION

Step 1 The precise amount of medication and polymer was measured. Water was used to prepare the polymer solution until it was clear.

Step 2 It was then added to the polymer solution (atenolol) and mixed to create an even clearer mixture of the polymer and the medication.

Step 3 The solution was retained for sonication until the bubbles were eliminated.

Step 4 The resultant solution was injected into a calcium chloride solution-containing petri dish using needle no.26 from a syringe.

Step 5 Whatmann filter paper was used to filter the microspheres after they were created this way.

Step 6 A predetermined temperature was used to dry the filtered spheres in an oven.

Step 7 It was then collected and transported for additional testing of the dried microspheres

Table 1: Formulation table of Sodium alginate microspheres

Formulation code	Atenolol (mg)	Sodium alginate (%)(w/v)	Calcium chloride (%)(w/v)	Starch soluble
F1	500	0.5%	3%	0.5%
F2	500	1%	5%	1%
F3	500	1.5%	7%	1.5%
F4	500	0.25%	5%	0.25%
F5	500	0.5%	5%	0.5%
F6	500	0.75%	5%	0.75%
F7	500	2%	7%	2%
F8	500	2.3%	7%	2.3%
F9	500	2.5%	7%	2.5%

Microspheres made of sodium alginate are prepared [9]: Three batches of microspheres loaded with drugs were synthesised in the first set (F1, F2, F3). In 100ml of deionized water, we made a sodium alginate solution with a w/v concentration of 0.51.5 percent. Wt. ofatenalol was uniformly dispersed in sodium alginate solution, 50 ml. A bubble-free dispersion was injected into a 100ml aqueous calcium chloride solution (3%, 5%, 7%) using a syringe and swirled at 100rpm. Ten minutes after mixing, the spheres were filtered, rinsed, dried, and finely dried in an oven at 600 C for six hours.

Materials Used: Drug was given as a gift sample from zydus. The excipients - sodium alginate, calcium chloride and starch soluble was brought from a local laboratory. Applications are microspheres in vaccine delivery, targeting using micro particulate carriers, monoclonal antibodies mediated microspheres targeting, chemo embolization, imaging, topical porous microspheres.[10-13]

Drug Excipient Compatability Studies: FT-IR and FIR spectroscopy were used to investigate drug-polymer interactions. (ANALYSIS). Potassium bromide mixed atenolol, polymers, and physical mixtures. A little powder was pressed into a thin, semi-transparent pellet. Using air as a reference, 450-4000cm' of pellet IR spectra were analysed for interference.[14-16]

Particle size analysis: Optical microscopy measured microsphere particle size. Samples of formed beads were measured with a calibrated optical micrometre. Before measuring bead size, the microscope was calibrated. Using a calibrated optical microscope, 625 beads were counted. Three-trial average + SD.[17-18]

Drug Entrapment Efficiency (DEE): 50mg of microspheres were suspended in 100ml of phosphate buffer pH 7.40.1 to test drug entrapment efficiency. The 24-hour solution was preserved. Next day, it was agitated and filtered. After dilution, Atenolol was measured spectrophotometrically at 243nm using a Shimadzu 1201 UV-visible spectrophotometer.[19]

In-Vitro Dissolution Studies: The medicine is supposed to release from solid dosage forms (granules, tablets, capsules, etc.) and instantly go into molecular solution. This is dissolution.[20]

Procedure: In-vitro dissolving investigations were performed on hard gelatin capsules containing 200mg of Atenolol. The experiment used a USP II spinning basket. Dissolution fluid consists of 900ml of simulated gastrointestinal fluids of changing pH: pH 1.2 (2 hour), pH 6.8 (1 hr), and pH 7.4 (up to 9 hrs), maintained at 37 C0.5 c and 50rpm[21]. After predefined times, aliquots of samples were removed and fresh medium was introduced. Filtered through a 0.45m membrane were withdrawal samples. Standard plots were used to determine sample concentrations and medication release percentages.

SEM analysis: Form and surface properties were determined using gold sputter. Before microscopy, particles were vacuum-dried and gold-palladium-coated to 200 A°. 20nm working distance, 0° tilt, 15kv accelerating voltage were the operating conditions. 50-500x magnifications were used to take the photos. [22].

Release Kineties models: Describe the dissolution profile of a drug by considering its release mechanisms and kinetics, two key features of a drug delivery system. Drug release kinetics and mechanism are studied using mathematical models. The correlation coefficient (R) value of various models is used to select the model that best fits the release data. For the release data, the models with the highest R-value are regarded the best fits.[23-25]

RESULTS AND DISCUSSION

Organoleptic Evaluation: The Physical appearance of the bulk drug was solid, white and amorphous and it has bitter and bland odour.

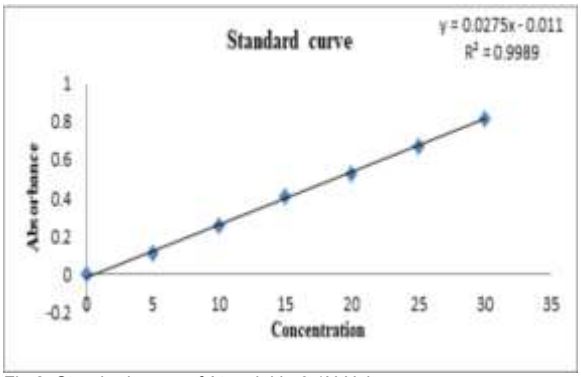

Fig 2: Standard curve of Atenolol in 0.1N Hcl:

Table 2: Standard curve values

Concentration(µg/ml)	Absorbance
0	0
5	0.115
10	0.255
15	0.414
20	0.530
25	0.675
30	0.816

Measurement of flow properties of Atenolol: Adding glidant to the Atenolol preformulation tests improved its compressibility and flow qualities, which were previously shown to be unsatisfactory.

Compatibility studies: FT-IR Analysis of drug-polymer compatibility was carried out by using spectroscopy. Separate scans were done for each individual drug and for each drug with polymers. We analysed the two spectra to see whether there were any shared peaks. Excipients and atenolol were found to be in perfect harmony based on the lack of noticeable differences in peak height, intensity, and location. The medication and polymer do not interact. Hence, it can be said that the medicine is in a state of freedom and that the spectrum it contains can be readily released from the formulation.

Table 3: Flow Properties

Formulation	Angle of repose(θ) (± SD)	Bulk density(g/cc) (± SD)	Tapped density(g/cc) (± SD)	Carr's Index (± SD)	Hausner ratio (± SD)
fm-1	22.1±0.10	0.2±0.06	0.31±0.04	13.9±0.06	1.15±0.054
fm-2	21.6±0.07	0.1±0.08	0.32±0.08	10.8±0.05	1.12±0.06
fm-3	23.5±0.15	0.2±0.08	0.31±0.10	14.4±0.09	1.17±0.07
fm-4	23.6±0.13	0.3±0.11	0.34±0.07	11.1±0.06	1.10±0.08
fm-5	24.1±0.08	0.2±0.11	0.32±0.01	10.3±0.12	1.12±0.04
fm-6	24.2±0.10	0.1±0.07	0.34±0.07	12.3±0.07	1.14±0.06
fm-7	23.1±0.11	0.3±0.08	0.37±0.12	10.9±0.10	1.11±0.08
fm-8	22.6±0.07	0.3±0.13	0.31±0.07	11.3±0.04	1.13±0.02
fm-9	21.1±0.12	0.3±0.14	0.35±0.10	12.8±0.04	1.15±0.01

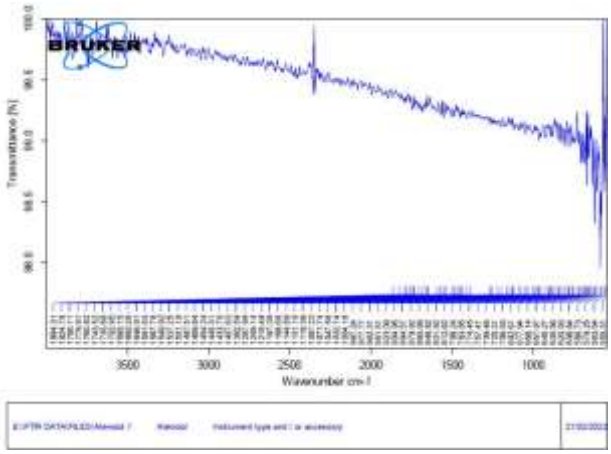

Fig 3: FT-IR Graph

Table 4: Average Particle Size

Code of Formulation	Average Particle Size (µM)
F1	105.4±1.2
F2	110±2.21
F3	103.4±1.42
F4	102.5±1.3
F5	103.2±0.9
F6	103±2.8
F7	108.6±1.7
F8	106±2.35
F9	103.8±1.8

Drug entrapment efficiency and drug content:

Table 5: Percentage Drug Entrapment Efficiency

S.NO.	Preparation code	Percentage yield	% of drug entrapment efficiency	Drug content
1	f-1	93.61±1.11	86.03±1.82	98.46±0.62
2	f-2	87.72±2.10	78.69±2.13	98.48±0.81
3	f-3	92.60±1.17	84.11±1.77	97.59±1.87
4	f-4	85.84±1.79	77.77±1.81	94.64±2.11
5	f-5	94.79±2.15	86.58±2.07	99.46±3.01
6	f-6	86.88±3.04	75.68±1.81	97.78±1.43
7	f-7	93.24±1.27	87.97±2.07	98.11±2.22
8	f-8	85.71±2.11	75.66±2.12	96.46±2.65
9	f-9	93.60±1.30	87.02±1.88	98.95±1.87

In-vitro drug release studies:

These microspheres (F1-F9) were dissolved in USP II dissolving apparatus at 37.5+0.5°C and 224nm UV spectroscopy was used to examine the invitro release tests..

Table 6: Invitro Drug Release Studies

Time in min	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
0	0	0	0	0	0	0	0	0	0

20	21.15	27.2	27.64	11.45	13.18	14.35	5.11	8.47	9.26
40	49.1	58.14	48.95	32.88	33.11	33.64	21.32	25.73	27.74
60	56.34	66.26	59.45	42.56	44.34	45.46	24.61	31.72	34.32
80	62.51	70.22	67.97	49.11	51.45	52.14	29.46	35.77	39.36
100	68.3	74.32	71.56	53.23	55.42	58.54	31.47	38.29	41.33
120	74.25	84.18	83.42	62.67	64.45	67.95	38.74	48.83	49.79

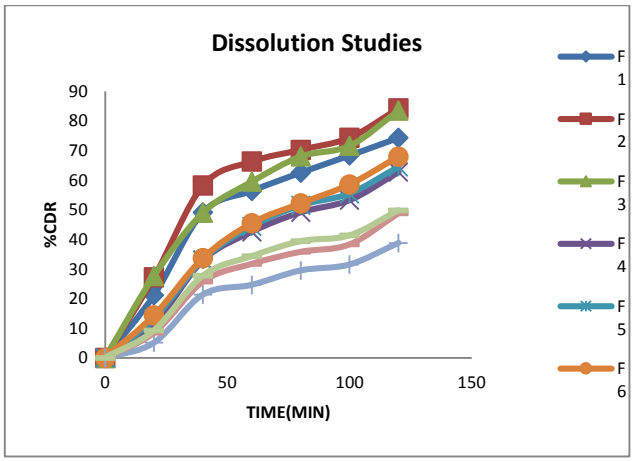

Fig 4: Dissolution plot

Scanning Electron Microscopy: Drug-loaded microspheres were captured by SEM imaging as being spherical. With more polymer, the surface of the microspheres was smoother than that of those with less polymer. The microspheres formed with a smaller amount of polymer had irregular surfaces and larger diameters. This has had a significant impact on the microspheres' morphological characteristics. There was a rise in spherical microspheres with smooth surfaces as the medication to polymer ratio was raised.

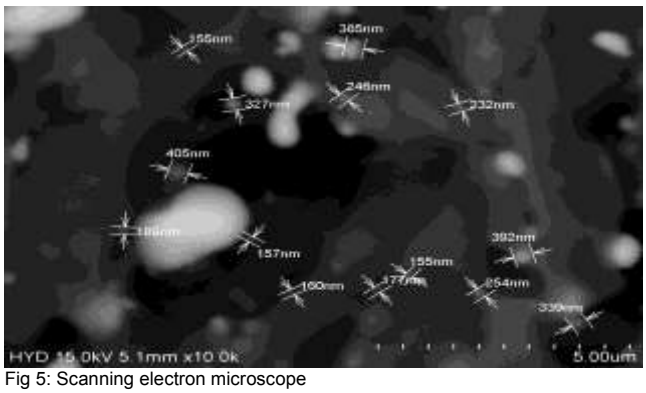

Fig 5: Scanning electron microscope

In-Vitro Drug Release Kinetics: Higuchi and korsmeyer-peppas equations were used to fit F3 in vitro dissolution data. F3's optimised R value is 0.9482. The enhanced formulation's drug release followed zero order kinetics, as shown by the greater R 2 values in the zero order figure. In the korsmeyer and peppas plot, n = 0.45 is Case I or Fickian diffusion, 0.45 n 0.89 is non-Fickian transport, n = 0.89 is case II transport, and n 0.89 is Super case II transport.

The release exponent value of n=0.536 shows that swelling and erosion, which are always connected with diffusion, was the predominant mechanism of drug release from the optimised formulation matrix.

Non-Fickian kinetics or anomalous transport could be responsible.

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Fig 6: Plot of Zero order

Fig 7: Plot of First order

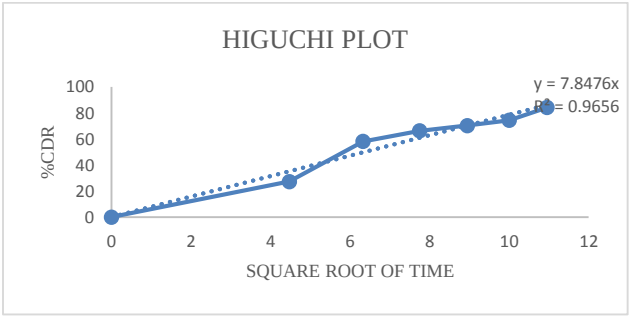

Fig 8: Higuchi Plot

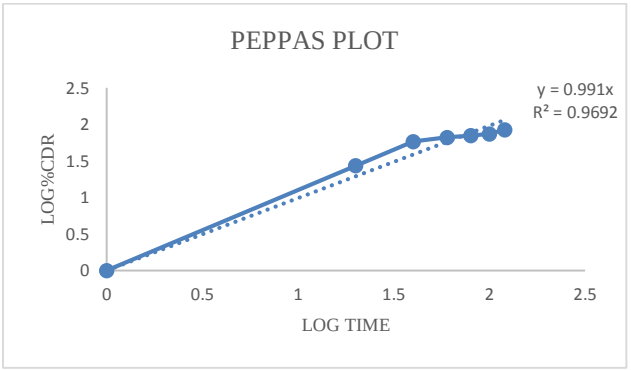

Fig 9: Peppas Plot

CONCLUSION

There were nine formulations tested, each with a different ratio of release drug modifiers including sodium alginate and calcium chloride, and their physicochemical qualities and in-vitro drug release capability were assessed. A granulometric research, bulk and tapped density, mean particle size and angle of repose, drug entrapment efficiency and in-vitro dissolution study were all found to be within acceptable limits in terms of their results.

Formulations F1 and F3 released sodium alginate more slowly in an in-vitro release trial than did formulation F2. However, the most optimal degree of sustained release effect was found in the batch of sodium alginate polymers in formulations 4 through 6 (F7–F9) that demonstrated less release than formulations.

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