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FORMULATION AND EVALUATION OF NORFLOXACIN BEADS

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ABSTRACT

PURPOSE: The objective of the present study was to Forulation and Evaluation of Norfloxacin Beads for the sustained release of Norfloxacin using various of polymer.

METHOD: Forulation and Evaluation of Norfloxacin Beads were prepared by an emulsion-gelation method. The resultant microspheres were evaluated for average particle size, Measurement of bead size, Swelling study of the beads, Content uniformity, drug efficiency, dissolution studies, . FTIR and SEM were used to investigate the physical state of the drug.

RESULTS: The mean particle size of the beads was influenced by varying drug Polymer and emulsion-gelation method,while drug loading was dependent on drug:polymer. The entrapment efficiency was 76-64 to 93.42%. The Entrapment loading 28.91 to 43.23%, The release of drug from the beads extended upto 8 to 12hrs. The results of FTIR indicated the stable charater of Norfloxacin beads and also abscence of drug polymer interaction. SEM revealed that the beads were porous in nature.

CONCLUSION: The formulated beads have shown higher encapsulation efficiency, drug loading, particle size and very low moisture content. The scanning electron micrographs of beads reveal that the beads are almost spherical. The Formulation F7 released Norfloxacin for prolonged duration (12hr).

INTRODUCTION

The hydro gels have the ability to swell and promote the release of encapsulated drugs by controlling cross linking. This makes them attractive as materials in the sustain release (SR) of drugs. There are many new polymers useful in the SR applications of drugs and pesticides. Sodium alginate (Na-Alg) is a bioerodible polymer that has been widely used in SR applications because it forms strong gels in aqueous media and is bioerodible. From a polymer chemistry point of view, the development of interpenetrating network polymers (IPNs) of Na-Alg is attractive because, by definition, the IPNs contain more than one polymer each in a network form, which can be cross linked in the presence of each other to give a three-dimensional network structure producing free volume for the easy encapsulation of drugs[1].

The sodium alginate has been used as a control release (CR) matrix material in medicine and in agriculture after crosslinking it with calcium chloride. Alginates (polysaccharides) are known to be haemocompatible and do not accumulate in any organs of the human body. Alginate has been investigated as a carrier material in different controlled release system. It was employed in the preparation of controlled release microspheres or minimatrices for a variety of medicinal agents including protein drugs, metoclopramide and cisapride, diclofenac, Indometacin, propranalol, and gentamicin.

In this paper we report the preparation of IPNs of Na-Alg with two other polymers such as carbapol and hydroxyl propyl methyl cellulose[2]. These matrices were used to study the SR of Norfloxacin. Norfloxacin has a biological half-life of 3.0-4.0 hrs for a dose containing between 10 and 30mg of the drug. Its short half life can be enhanced by using the tripolymer based beads developed in this research.

Materials

Sodium alginate, hydroxyl propyl methyl cellulose (K100M), carbapol 934 and calcium chloride were all purchased from s.d. Fine Chemicals, Mumbai, India. Gift sample of Norfloxacin was obtained from Bio-ethical Pharmaceutical ltd., Hubli, India. Water used was double distilled.

Formulation of Norfloxacin beads[3]

Norfloxacin beads were prepared using emulsion-gelation method. Hydroxy propyl methyl cellulose (HPMC) and carbapol are soaked in sufficient amount of distilled water and kept it for overnight. Sodium alginate solution is prepared separately. The mixture of HPMC and carbapol is mixed well and then sodium alginate solution is added slowly. After the formation of a homogenous mixture the drug solution is added slowly and mixed well. With the help of 1ml Insulin syringe the beads were prepared by dropping from a distance of about 10cm. The beads were kept for curing in 1.5%, 2.0% and 2.5% of calcium chloride solution for 15 min ten filtered and dried.

Process variables and process optimization

To investigate the contribution of formulation variables on the release profile of Norfloxacin from alginate beads, the different batches were produced and analyzed for size, shape, ease of preparation, drug loading, entrapment efficiency and drug release. The formulation parameters investigated are concentration of sodium alginate, concentration of calcium chloride, concentration of HPMC, concentration of carbapol, percentage entrapment efficiency and percentage drug loading.

These factors were evaluated and experimental trials were performed at all possible levels and 10 formulations were prepared as shown in Table 1.

Evaluation of beads.

Measurement of bead size.

The bead size was measured by taking 5 – 10 particles on a glass slide under polarized light. The mean diameter was calculated by measuring the number of divisions of the eye piece micrometer covering the particles[4]. The stage micrometer was previously used to standardize the eye piece micrometer.

TABLE 1: Formulation of Norfloxacin NF

Formulation code	Amount of Norfloxacin (mg)	Amount of sodium alginate	Amount of HPMC	Amount of Carbapol	Amount of water (ml)
NF1	30	0.3%	0.1%	0.25%	Up to 100
NF2	30	0.4%	0.2%	0.25%	Up to 100
NF3	30	0.5%	0.4%	0.25%	Up to 100
NF4	30	0.8%	0.6%	0.25%	Up to 100
NF5	30	1.0%	0.8%	0.25%	Up to 100
NF6	30	1.0%	0.9%	0.5%	Up to 100
NF7	30	1.25%	1.0%	0.5%	Up to 100
NF8	30	1.5%	1.2%	0.5%	Up to 100
NF9	30	1.6%	1.4%	0.5%	Up to 100
NF10	30	1.7%	1.5%	0.5%	Up to 100

Swelling study of the beads.

Swelling property of the beads was studied by measurement of percentage water uptake as a function of time[5]. Three different beads exposed to calcium chloride at different time and at different temperatures were selected and incubated wit distilled water in a watch glass. The mass of all the three beads was taken at different time intervals of time and the average value was calculated. During this process, care should be taken in handling the swollen beads so as to avoid any weight loss due to breaking or erosion of the beads. All the measurements of the swollen beads were taken on a Mettler single pan balance having accuracy up to fifth decimal. Te percentage uptake of water was calculated as

% water uptake = wet weight – dry weight/dry weight x 100.

Determination of content uniformity and encapsulation efficiency.

Beads were evaluated for the Norfloxacin content and this was done by incubating the known mass of beads with 5ml of water for complete swelling. The swollen beads were crushed in an agate mortar and pestle and the solution thus formed was sonicated for 2 min using 60 MHz of frequency[6]. Water was evaporated to form a thick paste to which about 10ml of methanol was added to extract all of the Norfloxacin. The precipitated Na-Alg was removed from methanol by centrifugation for 5 min at 10,000 rpm. Then the absorbance methanol containing the Norfloxacin was taken at 238 nm in a UV spectrophotometer using pure ethanol as a blank.

Percentage encapsulation efficiency was calculated using following formula,

$$\text{Percentage encapsulation efficiency} = AQ / TQ \times 1OO$$

Where AQ is the actual drug content of beads and TQ is the theoretical quantity of drug present in beads.

Dissolution studies

Dissolution experiments were performed at 37^{o}c using a dissolution tester equipped with eight paddles at a paddle speed of 100 rev./min. a 900 ml solution of phosphate buffer solution (pH 7.4) was used as a dissolution medium in order to stimulate the gastrointestinal tract (GIT) conditions, and a 10ml solution was used for analyzing the Norfloxacin content at a fixed interval of time[7]. Whenever necessary, the samples were diluted before assaying Norfloxacin. The dissolution media was always replenished with a fresh stock solution the Norfloxacin released was analyzed by a UV spectrophotometer at 238nm.

Scanning electron microscope (SEM)

The purpose of SEM study is to obtain topographical characteristics of the beads. The sample was deposited on brass hold and sputtered with gold. SEM photographs were taken with JSM 6400 Scanning Microscope at the required magnification at room temperature. The working distance of 10 mm was maintained and the acceleration voltage used was 15 kV, with ETD as a detector[8].

Fourier Transform Infra-Red measurements (FTIR)

FTIR measurements were taken at ambient temperature using a Nicolet, Model Impact 410. About 2mg of the samples were ground thoroughly with KBr and pellets were formed under a hydraulic pressure of 600 kg/cm^2.

RESULTS AND DISCUSSION

To optimize the parameters affecting the formation of beads, experiments were carried out under different conditions[9]. The tripolymer based beads of Norfloxacin were prepared by emulsion-gelation method and influence of exposure time to calcium chloride on particle size, as well as the concentration of HPMC on the release rate of Norfloxacin from beads were studied. Drug encapsulation efficiency ranged from 78.64% to 93.42% and drug loading capacity of beads ranged from 28.91 to 43.23%. There was no considerable effect of exposure time of the beads to calcium chloride on encapsulation efficiency and drug loading capacity of the beads. The percentage encapsulation efficiency was high because bead formation was carried out in calcium chloride in which Norfloxacin is insoluble and with a lesser possibility of leaching of Norfloxacin during encapsulation. Drug encapsulation efficiency and drug loading capacity of the prepared beads of Norfloxacin are shown in the table 2.

Microscopical characteristics of the beads

Microscopical characteristics of beads are shown in the Table 2. It was observed that the particle size of the formed beads ranged from 0.7mm to 1.5mm. The obtained results indicated that particle size of the beads increased on increasing the exposure time to calcium chloride[10].

Determination of moisture content

Low moisture content in all the Norfloxacin beads indicated the effectiveness of the adopted drying conditions. Low moisture level ensures better stability of the Norfloxacin in the beads Table 2

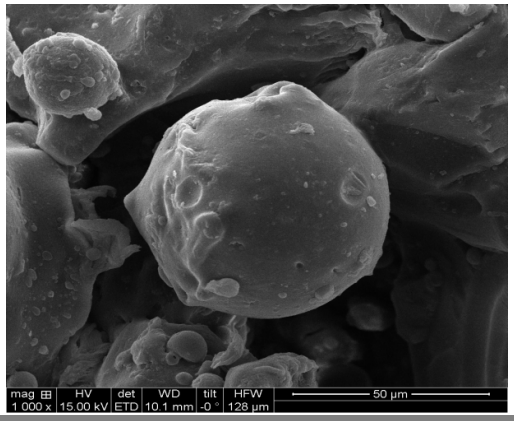
Table 2: Particle size and moisture content of the Norfloxacin beads

Formulations Codes	Particle size (mm)	%Moisture content	% Drug entrapment efficiency	%Drug Loading
NF1	0.749±0.001	0.99±0.44	78.64	36.43
NF2	0.721±0.03	1.74±0.79	79.21	34.68
NF3	0.735±0.02	2.20±0.59	79.91	33.69
NF4	0.755±0.02	1.28±0.47	82.08	31.00
NF5	0.955±0.02	1.67±0.57	84.68	40.21
NF6	0.736±0.04	1.65±0.56	89.59	31.91
NF7	**0.851±0.01**	**1.82±0.58**	**93.42**	**43.23**
NF8	0.844±0.05	1.76±0.72	87.11	28.91
NF9	0.917±0.01	1.87±0.73	82.63	34.12
NF10	1.573±0.02	2.30±0.60	81.98	30.46

SEM of the Norfloxacin beads[11]

SEM photographs of the Norfloxacin beads given in the Fig. 1 indicate smooth surfaces without any pores as shown in Fig 1.

Fig. 1 SEM photographs of Norfloxacin beads



FTIR data

FTIR measurements were taken at ambient temperature using a Nicolet, About 2mg of the samples were ground thoroughly with KBr and pellets.FTIR Spectrum of Norfloxacin + HPMC + Sodium alginates + Carbopol as shown in Fig. 2 & 3, The IR interpretation of Pure drug & Drug in Polymer as shown in Table 4.

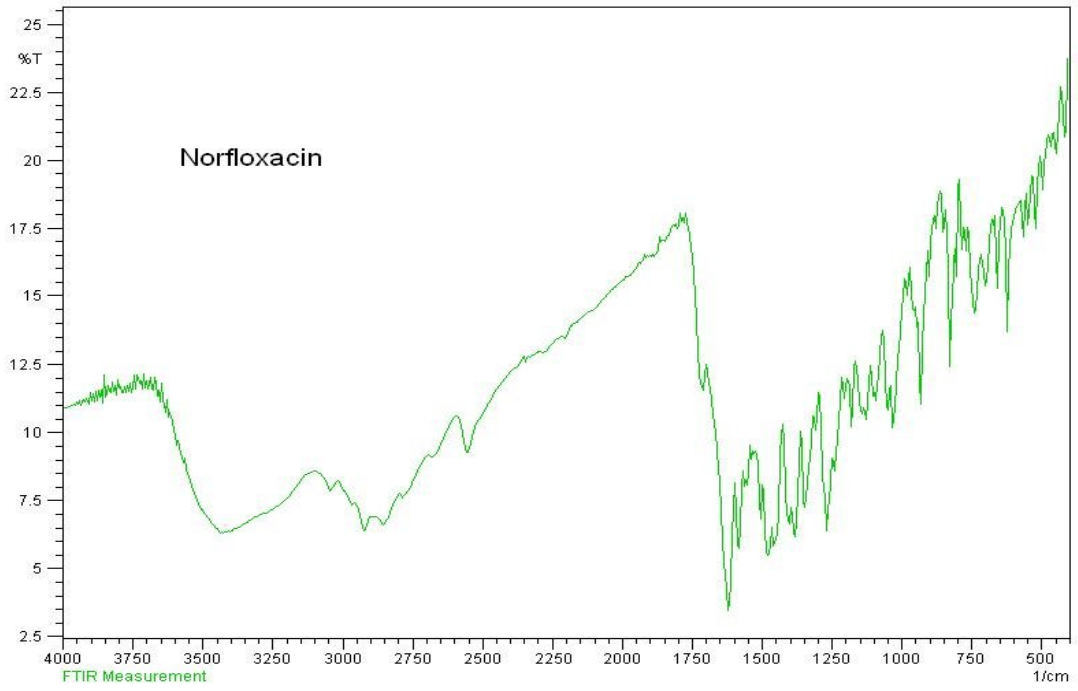


Fig. 2 FTIR Spectrum of Norfloxacin

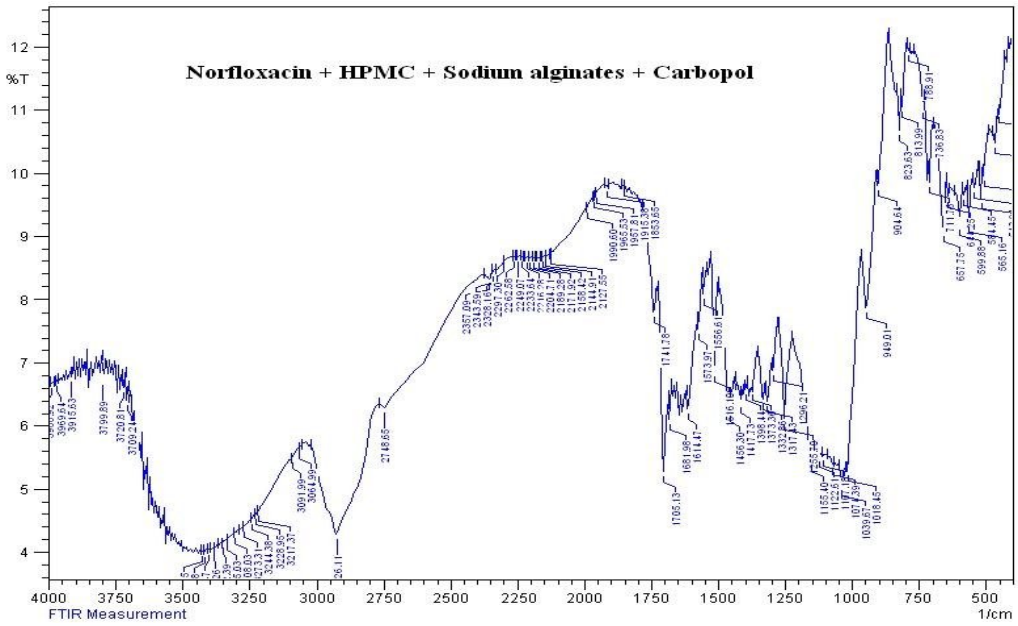


Fig. 3 FTIR Spectrum of Norfloxacin + HPMC + Sodium alginates + Carbopol

Table 4 FTIR Interpretation of Pure drug (Norfloxacin) & Drug in Polymers (Norfloxacin + HPMC + Sodium alginate + Carbopol)

SI. No	FUNCTIONAL GROUPS	PURE DRUG	DRUG IN POLYMERS
1.	NH-	3416.05	3414.09
2.	C=O	1763.71, 1749.61	1772.62, 1741.78
3.	C – S	711.76	711.78
4.	C – O – C	1147.68	1155.40
5.	C=N	1618.33	1616.09
6.	C=C	1608.69	1614.47
7.	CH – (aliphatic)	2966.62	2976.25
8.	CH – (aromatic)	3084.28	3091.99
9.	C – N	1444.73	1456.30

On observing the IR values of the functional groups in pure drug as well as the drug in the polymers it was found that there is no significant difference between the peaks. The IR spectral values were found almost similar which indicates that the drug is well compatible with the polymers used.

In Vitro drug release studies[12]

The in vitro dissolution studies of the prepared Norfloxacin formulations were performed to investigate the percentage drug release at 1hr (T1), 6hr (T6) and 12hr (T12). From the results of in vitro dissolution studies, amongst the formulations, formulation F7 shows maximum percent cumulative release with in 12hrs. This shows that F7 was having the good sustained release of the Norfloxacin up to the 12th hr. hence it can be concluded that a new sustained release system of tri polymer based Norfloxacin beads were designed and prepared by an emulsion-gelation method and it's morphological and release characteristics were studied. The prepared beads were easy to prepare and evaluate as shown in Fig. 4.

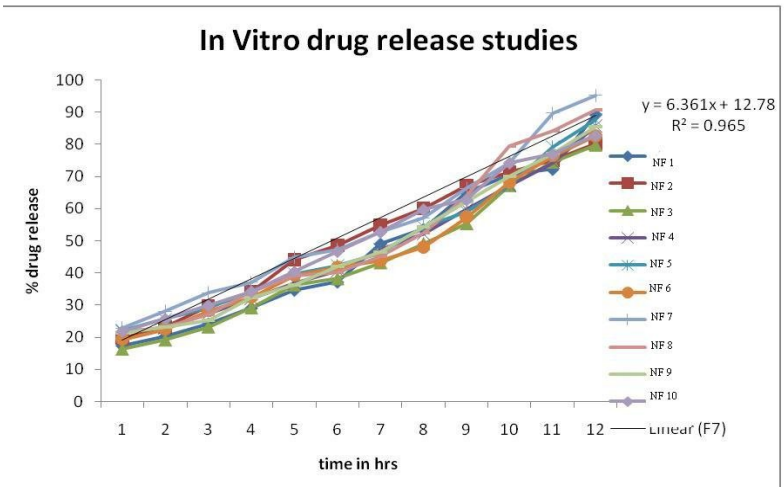


Fig. 4 In Vitro drug release studies

CONCLUSION

The tripolymer based Norfloxacin beads were successfully prepared by emulsion gelation method. Good linearity was shown by the method adopted for the estimation of Norfloxacin. The formulated beads have shown higher encapsulation efficiency, drug loading, particle size and very low moisture content. The scanning electron micrographs of beads reveal that the beads are almost spherical. In vitro dissolution study showed that, amongst the formulations,

formulation F7 released Norfloxacin for prolonged duration (12hr). This optimized formulation F7 showed best fit in zero order models.

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