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Preparation, evaluation and in vitro charecterization of biopolymer derived hybrid microcapsules for extended release of cefaclor

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ABSTRACT

The mucoadhesive cefaclor monohydrate microcapsules are prepared by ionotrophic gelation method using different concentration of sodium alginate, xanthan gum, guar gum and pectin in combination with 0.8% chitosan using cross linking agent calcium chloride. The microcapsules were evaluated for percentage yield ,capsule size, entrapment efficiency swelling index, mucoadhesion study by in vitro wash off test and scanning electron microscopy analysis were investigated .Infrared spectroscopy studies confirmed the absence of any drug interaction with polymers .DSC analysis revealed that the drug was uniformly distributed in the microcapsule. The mean particle size increase with increasing the polymer concentration. SEM photomicrograph showed microcapsules with rough surface and oval shape. The entrapment efficiency of all formulations was in the range of between 95% to 99%. The swelling index decreased with increase in sodium alginate concentration. The results of in vitro mucoadhesive showed that the microcapsules were remained adhered to mucus membrane for longer period of time .In vitro drug release studies were performed in simulated gastric fluid [SGF,pH 1.2] for 2 hrs and phosphate buffer [pH 6.5] for 10 hrs at 37± 2° C. In vitro drug release followed. Drug release from the microcapsules was found slow releasing and following zero order kinetics, Korse mayers & Peppas model. The diffusional exponent n, specified anomalous transport and non fickian type and controlled by diffusion through swollen matrix. The above observations suggested that the cefaclor monohydrate can be developed as mucoadhesive drug delivery system with sodium alginate, xanthan gum, chitosan (7.5 :1:0.8).

Keywords: Cefaclor monohydrate, Sodium alginate, Microcapsule, Mucoadhesion, Ionotrophic gelation method.

1. INTRODUCTION

Microcapsule system made up of natural biodegradable polymers have been paid considerable attention for several years in controlling and sustaining of release rate of drugs .Recently dosage forms that can precisely control the release rate and targets drugs to a specific body site have made enormous impact in the formulation and development of novel drug delivery systems. Microcapsules are small, solid and free flowing particulate carriers containing dispersed drug particles either in solution or crystalline form that allow a sustained release [1].

The microcapsules maintain functionality under physiological conditions, can incorporate drug to deliver locally at high concentration ensuring that therapeutic levels are reached at the target site while reducing the side effects by keeping systemic concentration low. It will therefore be advantageous to have means for providing an intimate contact of the drug delivery system with the absorbing membranes. This can be achieved by coupling the bioadhesive characteristics to microcapsules and develop bioadhesive microcapsules bioadhesive microcapsules have advantages such as efficient absorption and enhanced bioavaibality of drugs

owing to high surface to volume ratio, a much more intimate contact to mucus layer and specific targeting of drugs to the absorption site. [2]

Alginate (polysaccharide) is obtained from marine brown algae, alginate can be considered as block polymers which mainly consist of mannuronic acid (M), guluronic acid (G) and mannuronic-guluronic (MG) blocks. The gelation of alginate is caused by forming an egg-box junction to associate divalent metal ions with the GC block of alginate polymer chain. The medicinal use of sodium alginate as a matrix material to achieve controlled release drug delivery is due to its hydrogel forming properties. In this case xanthan gum,guar gum and pectin was used to regulate the drug release pattern. Chitosan was selected as a polymer in preparation of mucoadhesive microcapsules because of their good mucoadhesive and biodegradable properties.[3]

Cefaclor is a broad spectrum antibiotic belonging to the family of second generation cephalosporins. Cefaclor is well absorbed in the body, with a peak serum concentration occurring within 30-60 min, which is significantly reduced in the presence of food, with no change in the total amount of drug absorbed. Cefaclor is rapidly excreted in urine, with an approximate half – life of two hours. Because of its short half – life and large dose, cefaclor is considered a good candidate for sustained release dosage forms.

1.1. Microbiology

Cefaclor has *in vitro* activity against a broad range of gram-positive and gram-negative bacteria. The bactericidal action of cefaclor results from inhibition of cell-wall synthesis. It is used against

1.1.1. Gram-positive aerobes: *Staphylococcus aureus, Streptococcus pneumonia, Streptococcus pyogenes*

1.1.2. Gram-negative aerobes: *Haemophilus influenzae*, *Moraxella catarrhalis*

Cefaclor is indicated for Acute bacterial exacerbations of chronic bronchitis due to *Haemophilus influenzae*, Moraxella *catarrhalis* or *Streptococcus pneumoniae*., Pharyngitis and tonsillitis due to *Streptococcus pyogenes* [4-6]

The purpose of present investigation is to develop mucoadhesive microcapsules with crosslinking agent like calcium chloride and chitosan as mucoadhesive polymer with drug cefaclor monohydrate by ionotrophic gelation method. [7-9]

2. MATERIALS AND METHODS

Cefaclor monohydrate was obtained as a gift sample from Sance laboratories, palai, Cochin. Sodium alginate was purchased from Yarrow Chem Products Mumbai, calcium chloride and xanthan gum,guar gum,and pectin were purchased from Nice chemical private limited, Kochi. Chitosan was purchased from Hi media laboratories Pvt limited, Mumbai.

2.1. Formulation of mucoadhesive alginate beads

The mucoadhesive alginate beads were prepared by ionotrophic gelation method as per the composition shown in table 1. An aqeous solution of various concentrations of sodium alginate, xanthan gum,guar gum and pectin is prepared with vigorous stirring to form a clear solution. Pectin, guar gum and xanthan gum is used in low concentration whereas high concentration will result in much higher viscosity of solution which was difficult to process for preparing the microcapsules. To this solution the drug Cefaclor monohydrate is added slowly and stirred continuously until a uniform dispersion is obtained. The dispersion is kept undisturbed for 30 minutes. The resultant bubble free, homogeneous dispersion is extruded into polyvalent ion solutions (200 ml) containing 0.8 % chitosan using a hypodermic syringe with 21 gauge needle and stirred at 100rpm in magnetic stirrer. The microcapsules are cured in gelation medium for 15 mins and then collected by decantation technique and the product thus separated is washed with acetone for two times and dried at room temperature for 24 hours[10-14].

2.2. Preformulation studies

2.2.1FTIR studies

FT-IR spectra (Spectrum RX-1 Perkin-Elmer, German) for the drug and various physical mixtures are obtained in a FT-IR spectroscopy in the transmission mode with the wave number region 4000-500cm-1. KBr pellets are prepared by gently mixing 1mg sample powder with 100mg KBr. [7]

2.2.2. DSC studies

To detect any interaction between drug and polymer the DSC thermo grams of pure drug, polymers and physical mixture of drug and polymers were taken using DSC200 TA Instruments, USA. The samples are heated in sealed aluminium pan at a rate of 10°C/min over the temperature range of 5-400℃ under a nitrogen flow of 20 lb/cm.

Table - 1:

Formula	Cefaclor (%m/V)	Sod Alg(%m/V)	Chitosan (%m/V)	$CaCl_2$ (%m/V)	Xanthan gum(%m/V)	Guar gum(%m/V)	Pectin (%m/V)
FX1	5	1.5	0.8	4	0.20	-	-
FX2	5	3.0	0.8	4	0.40	-	-
FX3	5	4.5	0.8	4	0.60	-	-
FX4	5	6.0	0.8	4	0.80	-	-
FX5	5	7.5	0.8	4	1.0	-	-
FX6	5	9.0	0.8	4	1.20	-	-
FG7	5	1.5	0.8	4	-	0.20	-
FG8	5	3.0	0.8	4	-	0.40	-
FG9	5	4.5	0.8	4	-	0.60	-
FG10	5	6.0	0.8	4	-	0.80	-
FG11	5	7.5	0.8	4	-	1.0	-
FG12	5	9.0	0.8	4	-	1.20	-
FP13	5	1.5	0.8	4	-	-	0.20
FP14	5	3.0	0.8	4	-	-	0.40
FP15	5	4.5	0.8	4	-	-	0.60
FP16	5	6.0	0.8	4	-	-	0.80
FP17	5	7.5	0.8	4	-	-	1.0
FP18	5	9.0	0.8	4	-	-	1.20

2.3. Evaluation of mucoadhesive microcapsule

2.3.1. Percentage yield

The percentage yield of microcapsules of various batches are calculated using the weight of final product after drying with respect to the initial total weight of the drug and polymer used for preparation of microcapsules and percent yields is calculated as per the formula mentioned below [15-17].

$$\text{Percentage yield} = \left(\frac{\text{Amount of dried microbeads}}{\text{Amount of drug+ Amount of polymer}} \right) \text{X } 100$$

2.3.2. Drug entrapment efficiency

Drug loaded microcapsules (100 mg) are crushed in glass mortar and pestle and suspended in 100 ml of phosphate buffer (pH 6.5) solution and kept for 24hr. It is stirred for 5 minute and filtered by whatmann filter paper. Drug content in the filtrate is determined by spectrophotometrically. Entrapment efficiency is calculated using the following formula:

$$\text{Entrapment efficiency} = \left(\frac{\text{Actual \% drug content}}{\text{Theoretical \% drug content}} \right) \text{X } 100$$

$$\text{Actual drug content mg (\%)} = \left(\frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \right) \text{X } 100$$

$$\text{Theoretical drug content mg (\%)} = \left(\frac{\text{Weight of drug in microbeads}}{\text{Microbeads sample weight}} \right) \text{X } 100$$

2. 3.3. Swelling studies by weight method:

A known weight (50mg) of microcapsules were placed in basket assembly of dissolution apparatus (USP XXIV) rotated at 500rpm in 500ml of pH 7.2 phosphate buffer solution maintained at 37±0.5^{0}C and allowed to swell for the require period of time. The microcapsules were periodically removed, blotted with filter paper and their changes in weights were measured during the swelling until equilibrium was attained. Finally the weight of the swollen microspheres was recorded after a period of 6 hrs and the swelling ratio (SR) was calculated from the formula.

Swelling index = mass of swollen microcapsules – mass of dried microcapsules X 100

2.3.4. *In vitro* dissolution studies

An accurately weighed amount of drug loaded microcapsules equivalent to 16 mg are taken for *in vitro* dissolution studies. The microcapsules are filled into hard gelatin capsules and it is coated with Eudragit L 100 by dipping and drying method. The study is carried out in the USP Type II apparatus using 900 ml of buffer solution. The rotating speed of paddle is maintained at 50 rpm at 37±1°C. First two hour study is carried out in pH 1.2 and next ten hour study is carried out in phosphate buffer pH6.5. Samples are withdrawn every 15 mins for first one hour and then for every 30 mins. 10 ml of sample is withdrawn from buffer medium, diluted with fresh medium and make upto 100ml. At the same time 10 ml of fresh medium was added to the dissolution medium to maintain the sink condition. 10 ml fresh medium and analyzed for

cefaclor monohydrate content by the absorbance of the sample was determined by UV-Visible spectrophotometer at 264 nm. [12-15]

2.3.5 Release kinetics

In order to understand the mechanism and kinetics of drug release, the drug release data of the in-vitro dissolution study are analyzed with various kinetic equations like zero-order, higuchi and peppas equation. Coefficient of correlation (r) values are calculated for the linear curves obtained by regression analysis of the above plots.

3.6. In-vitro Wash - off test for mucoadhesion

The mucoadhesive property of microcapsules was evaluated by an in vitro adhesion testing method known as wash – off method. Freshly excised piece of intestinal mucosa (2x2cm) from sheep intestine were mounted on to glass slides (3x1 inch) with cynoacrylate glue. Two glass slides were connected with a suitable support, about 50 microcapsules were spread on to each wet rinsed tissue specimen and immediately thereafter the support was hung onto the arm of a USP tablet disintegrating test machine. When disintegrating test machine was operated ,the tissue specimen was given slowly , regular up and down moment in the test fluid (500ml pH7.2 buffer) maintained at 37^0C. At the end of 30 minutes, 1 hr and hourly intervals up to 8 hr, the number of microcapsules adhering to tissue were counted.

2.3.7. Scanning electron microscopic studies

The morphology and surface structure of beads are observed using SEM photographs taken with SEM analyser. The beads are made conductive by sputtering thin coat of platinum under vacuum and then the images are recorded with at magnification of 25X.

3.8. X-ray diffraction (X-RD) studies

Different samples were evaluated by X-ray powder diffraction. Diffraction patterns were obtained by using X-ray diffractometer (XRD-Shimadzu 7000) with a radius of 240mm. The Cu, Ka radiation was Ni filtered. A system of diverging and receiving slits of 1° and 0.1mm respectively was used. The pattern was collected with 40 Kv of tube voltage and 30 mA of tube and scanned over the 2Θ range of 5-60°.

4. RESULTS AND DISCUSSION

The objective of the present work is to develop different mucoadhesive formulations of cefaclor. Microcapsules of cefaclor were formulated by ionotrophic gelation method. Eighteen formulations of microcapsules were prepared using different concentrations of sodium alginate, cross linking agent, xanthan gum, guar gum,and pectin and chitosan . The results observed are mentioned in the following sections.

4.1. Physical characterization

In all formulations the alginate microcapsules were more or less spherical in shape and the exterior surfaces were rough. The spherical shape of the microcapsules in wet state was usually lost after drying especially for beads prepared with low concentration of sodium alginate and cross linking agent. With the increase of sodium alginate concentration the shape of the beads retained considerably.

4.2. Scanning electron microscopic studies

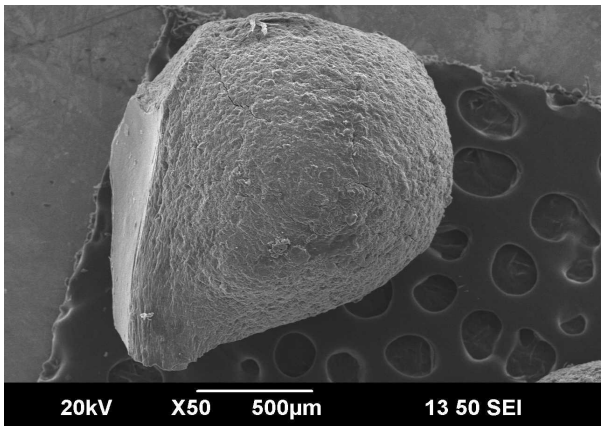


Figure - 1:

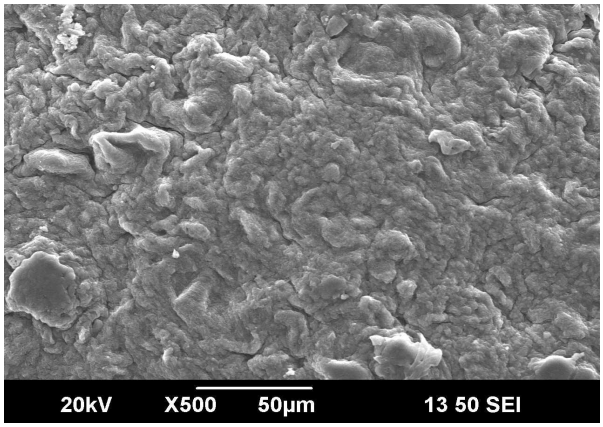


Figure - 2:

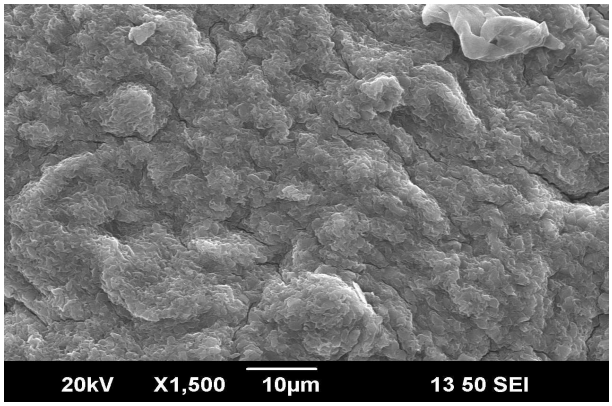


Figure - 3:

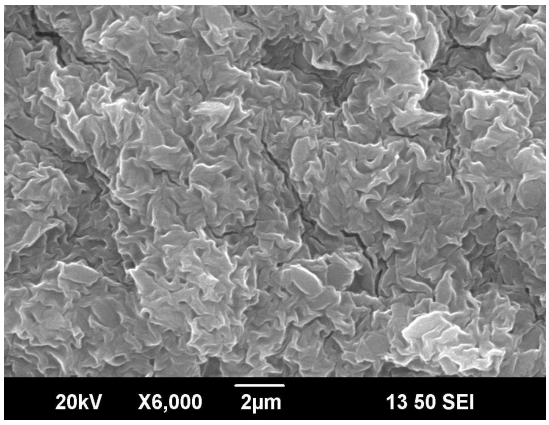


Figure - 4:

4.3. Size analysis of microcapsule

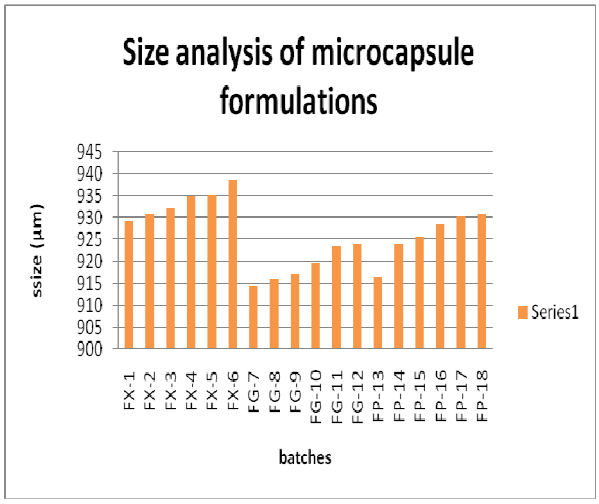


Figure - 5: Size analysis of microcapsules.

4.4. In-vitro Wash - off test for mucoadhesion

The mucoadhesion is a phenomenon in which two materials, atleast one of which is biological are held together by means off interfacial force. The tables shows the muco adhesion data of muco adhesive microcapsule carried out with everted rat intestinal mucosa in presence of phosphate buffer pH 7.2. The percentage of microcapsules retained on everted intestinal mucosa after 6 h in set 1 formulation in the range of 60,55,65,71,68,67 for FX-1,FX-2,FX-3,FX-4,FX-5,FX-6 respectively and set 2 formulation in the range of 65,60,62,60,60,61 for FG-7,FG-8,FG-9,FG-10,FG-11,FG-12 respectively and for set 3 formulation in the range of 60,60,60,67,65 and 66 for FP-13,FP-14,FP-15,FP-16,FP-17,FP-18 respectively .The overall results suggest that concentration and type of mucoadhesive polymer doesn't show much more difference in the mucoadhesive property.Mucoadhesion was more with FX-4 (71%),FP-16 (67%) and FG-8(65%).

4.5 FTIR studies

To check the compatibility of drug with various polymers, IR spectra of drugs, polymers and combination of the drug and polymers were taken. FTIR spectra of cefaclor monohydrate, sodium alginate, xanthan gum, pectin ,guar gum and chitosan were recorded in KBr pellets and are presented in Figure 1.The IR spectral analysis of cefaclor monohydrate pure drug alone showed that principal peaks were observed at wave numbers 3111.67cm^{-1}, 1551.14cm^{-1} . Further in the physical mixture of sodium alginate, xanthan gum,guar gum,pectin, chitosan and cefaclor monohydrate, the major peaks of were observed at 3111.67cm^{-1}, 2940.58cm^{-1}, 1714.69cm^{-1}, 1551.14cm^{-1} and 746.67cm^{-1} suggesting that there is no interaction between the polymers and drug used in the present study.

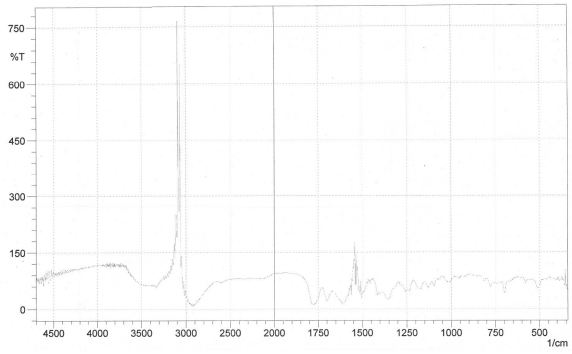


Figure - 6:

Table -2:

Batches	Percentage of microcapsules adhering to tissue at different time interval (%)					
	0hr	0.5hr	2.0 hr	3.0 hr	4.0 hr	6.0 hr
FX-1	50	88	80	64	60	60
FX-2	50	86	74	58	55	55
FX-3	50	96	85	77	65	65
FX-4	50	94	83	74	71	71
FX-5	50	96	88	79	68	68
FX-6	50	93	82	75	67	67

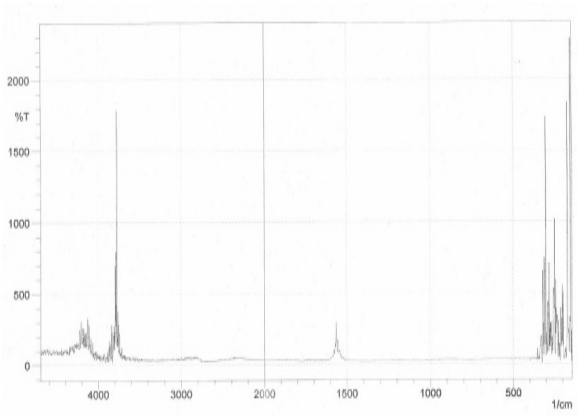
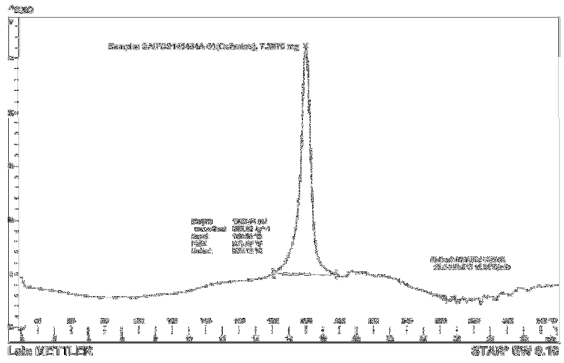


Figure - 7:

4.6. DSC studies

The DSC thermogram of pure drug and the different polymers were shown in the Figure 2. A sharp exothermic peak at about 201.59˚c was observed for pure cefaclor. It was observed that the large exothermic peak of pure drug was a bit smaller and shifted to 201.94˚C in physical mixture revealing its unchanged nature. This indicates that the drug has not undergone any chemical interaction with the polymer backbone.



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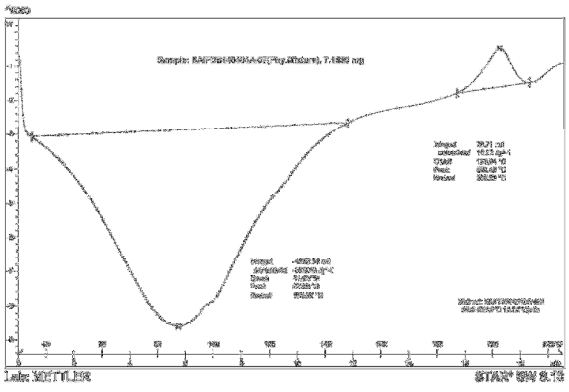

Figure - 9:

4.7. X-ray diffraction (X-RD) studies

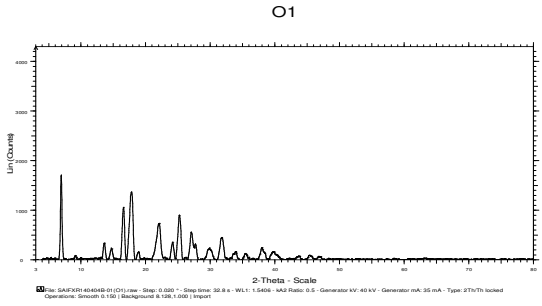

Figure - 10:

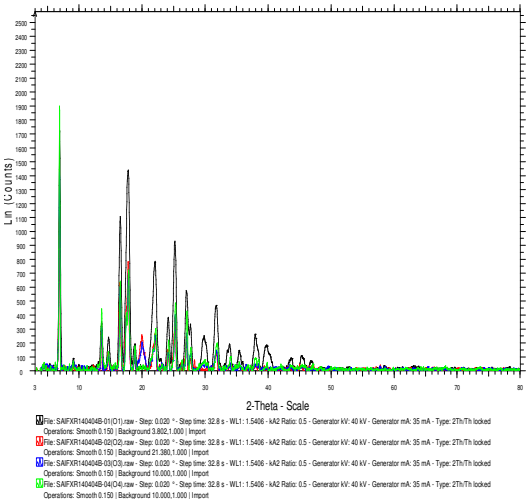

Figure - 11:

4.8. Evaluation of mucoadhesive microcapsules

4.8.1. Percentage yield

The percentage yield of microcapsules prepared by ionotrophic gelation method were found to be between 83.45 % and 95.56 %. It was found that percentage yield of prepared microcapsules in calcium chloride was greater than xanthan gum, guar gum and pectin. A significant decrease in the production yield was observed with increase of alginate concentration. The probable reason behind this may be due to high viscosity of the solution which decreases its syringe ability resulting in blocking of needle and wastage of the drug polymer solution which ultimately decreased the production yield[17].

The percentage yield of FX- formulations were in the range of 89.46±0.78 to 95.56 ±0.31

FG - Formulations in the range of 83.55±0.21 to 89.25 ± 0.5

FP - Formulations in the range of 83.45±0.64 to 89.34 ± 0.45 the production yield was manageable with little loss of drug during the formulation stage

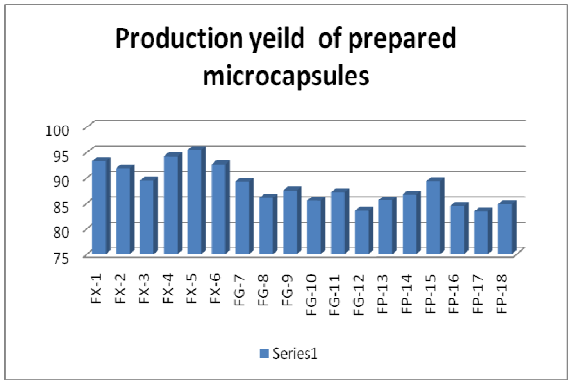

Figure - 12:

4.8.2. Drug entrapment efficiency

The drug entrapment efficiency of all formulations was in the range between 95% and 99%. This is probably due to more firmness in the alginate-chitosan complex during gelation caused by increased ionic interactions between the carboxylate groups in the alginate and the protonated amine groups in the chitosan. The results of drug entrapment efficiencies were shown in graph. Pectin showed maximum drug entrapment efficiency then guar gum and xanthan gum.

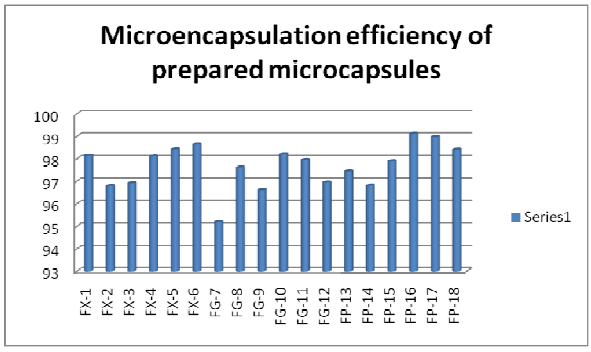

Figure - 13:

Drug entrapment efficiency of alginate beads increases with increase in concentration of polymers. The higher viscosity of the polymer solution at the highest polymer proportion would be expected to decrease the diffusion of the drug into the external phase which would result higher entrapment efficiency. This may be attributed to the greater availability of active binding sites in polymeric chains and consequently the greater degree of cross linking as the quantity of alginate increased. [20]

4.8.3. Swelling studies

The swelling depends upon the polymer concentration, ionic strength as well as presence of water. The relative swelling of mucoadhesive microcapsules of set 1 formulations found in the range of 1.38,1.42,1.48,1.16,1,32 and 1.2 for FX-1,FX-2,FX-3,FX-4,FX-5,FX-6 respectively. For set 2 formulations found in the range of 1.0.9,0.98,1.06,0.94,0.98, and 1.02 for FG-7,FG-8,FG-9,FG-10,FG-11,FG-12 respectively ,where as for set 3 formulations found in the range of 0.94,1.06,1.08,1.02,0.98 and 1.12 for FP-13,FP-14,FP-15,FP-16,FP-17,FP-18 respectively at the end of 6 hr .In all the formulations as the concentration of sodium alginate increases the relative swelling increases which further depend on the type of mucoadhesive polymers. The results clearly suggested swelling ratio depends upon concentration of polymer and type of mucoadhesive polymer used in the formulation . Swelling ratio shows direct relationship with sodium alginate concentration and increased with increasing concentration of sodium alginate .In all three set, formulations having xanthan gum exhibited good swelling property compared to other mucoadhesive polymers

4.9. Stability test

The stability of formulation FX-5,FG-8 were tested at various conditions .The microcapsule FX-5 stored at $4^0 \pm 1^0$C, $25^0 \pm 2^0$C (60 ± 5% RH) and $37^0 \pm 2^0$C (65 ± 5% RH) for 90 days showed drug release of 97.03%,97.63 % and 97.43% respectively. Initially, the same formulation showed 97.84 0.46% release of drug.

The microcapsule FG- 8 stored at $4^0 \pm 1^0$C, $25^0 \pm 2^0$C (60 ± 5% RH) and $37^0 \pm 2^0$C (65 ± 5% RH) for 90 days showed drug release of 96.12%,96.30 % and 96.22% respectively. Initially, the same formulation showed 96.73 0.47 % release of drug.The result indicated that the selected formulation FX-5,FG-8 ensured stability during its shelf life.

4.10. *In-vitro* dissolution studies

The results of *in-vitro* drug release studies from the mucoadhesive alginate microcapsules are shown in Figures FX, FG, FP and respectively.

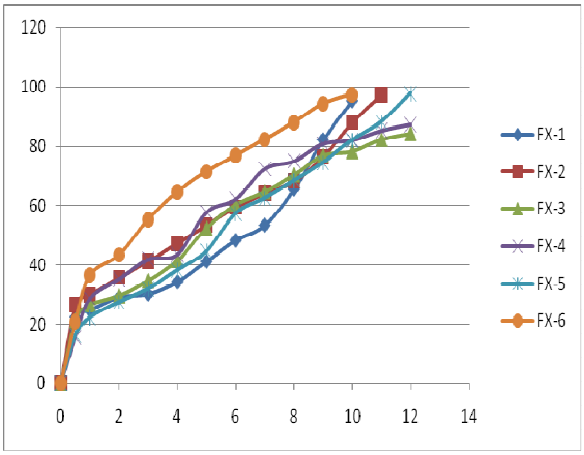

Figure - 14:

The microcapsules did not show any drug release at pH 1.2 and it released the drug at pH 6.5. Above pH 6.0 Eudragit L 100 coating started to dissolve and exposed the microcapsules for drug release. So it protected the release of drug from the acidic medium to minimize the side effects. [18]

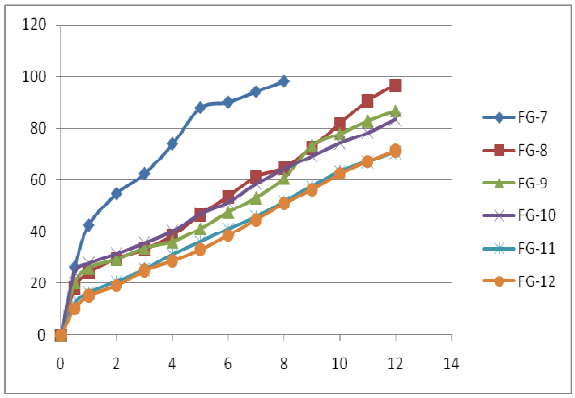

Figure - 15:

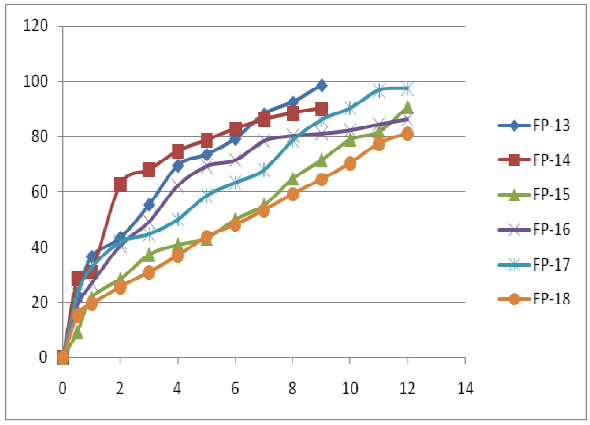

Figure - 16:

4.11. Release kinetics

Further the drug releases were subjected for mathematical treatment to check whether the release is following first order kinetics or zero order kinetics. The correlation co efficient values are shown in table 3

Table - 3:

	Zero order		First order		Higuchi		Korsem Peppas		Hixon crowel	
	R^2	Ko	R^2	$K1$	R^2	KH	R^2	N	R^2	KHC
FX-1	0.926	7.582	0.702	-0.091	0.856	25.23	0.458	0.805	0.808	-0.218
FX-2	0.948	7.044	0.756	-0.098	0.957	25.78	0.444	0.777	0.883	-0.221
FX-3	0.949	6.393	0.987	-0.064	0.980	24.82	0.513	0.804	0.987	-0.170
FX-4	0.931	6.698	0.989	-0.073	0.987	26.35	0.551	0.857	0.985	-0.187
FX-5	0.985	7.294	0.788	-0.098	0.957	27.46	0.587	0.881	0.920	-0.223
FX-6	0.914	8.556	0.931	-0.136	0.996	30.90	0.468	0.876	0.984	-0.292
FG-7	0.891	0.139	0.221	-5.232	0.867	0.4208	0.391	0.908	0.979	-0.387
FG-8	0.980	7.057	0.816	-0.093	0.952	26.57	0.550	0.841	0.918	-0.214
FG-9	0.963	6.315	0.924	-0.064	0.939	23.82	0.491	0.765	0.952	-0.169
FG-10	0.951	5.806	0.965	-0.056	0.972	22.41	0.462	0.744	0.966	-0.149
FG-11	0.985	5.415	0.982	-0.041	0.968	20.51	0.612	0.846	0.990	-0.121
FG-12	0.989	5.513	0.970	-0.041	0.956	20.70	0.648	0.878	0.987	-0.123
FP-13	0.923	9.660	0.883	-0.161	0.995	32.77	0.444	0.900	0.975	-0.337
FP-14	0.791	8.521	0.966	-0.108	0.947	30.47	0.398	0.854	0.920	-0.259
FP-15	0.975	6.775	0.917	-0.071	0.968	25.79	0.643	0.933	0.963	-0.182
FP-16	0.843	6.374	0.965	-0.071	0.971	26.13	0.515	0.835	0.934	-0.180
FP-17	0.947	7.103	0.882	-0.117	0.983	27.63	0.486	0.802	0.958	-0.248
FP-18	0.980	6.060	0.968	-0.053	0.976	23.10	0.580	0.844	0.985	-0.149

The r values of zero order plots were between 0.981 to 0.986 and first order plot between 0.925 and 0.982. The r^2values indicate all these formulations followed zero order kinetics. The values of co efficient of correlation were found to be best fitted to Korse meyer peppas and Higuchi model. The R^2 values are closer to one in zero order kinetics, so it follows zero order kinetics. The diffusional exponent, n, specifies the mechanism of release. For alginate beads, values of 'n' between 0.43 and 0.85 are an indication of both diffusion controlled drug release and

swelling controlled drug release (anomalous transport or non-fickian diffusion). Values above 0.85 indicate case II transport which relate to polymer [19-25].

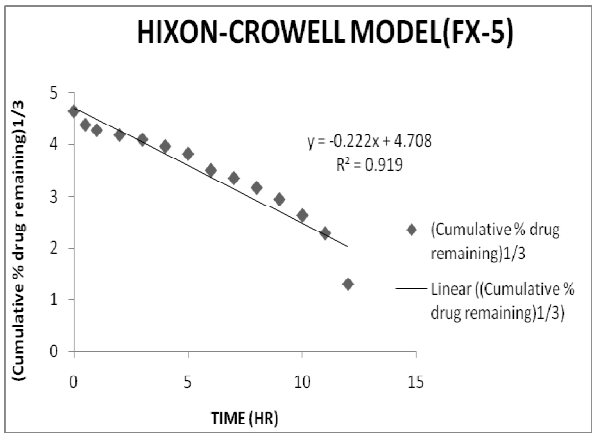

Figure - 17:

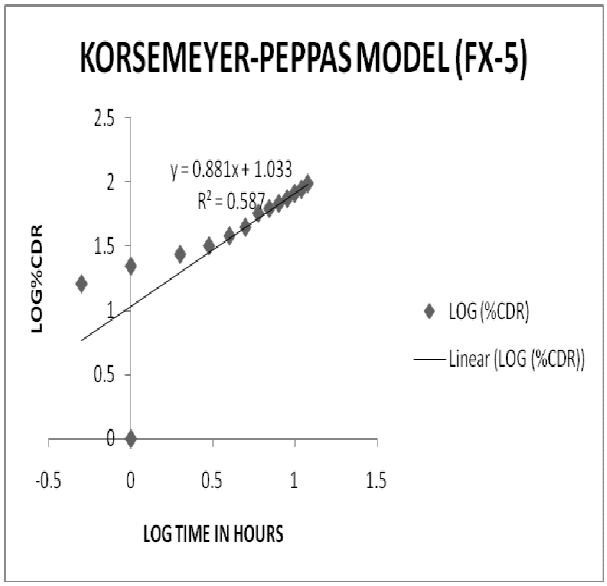

Figure - 18:

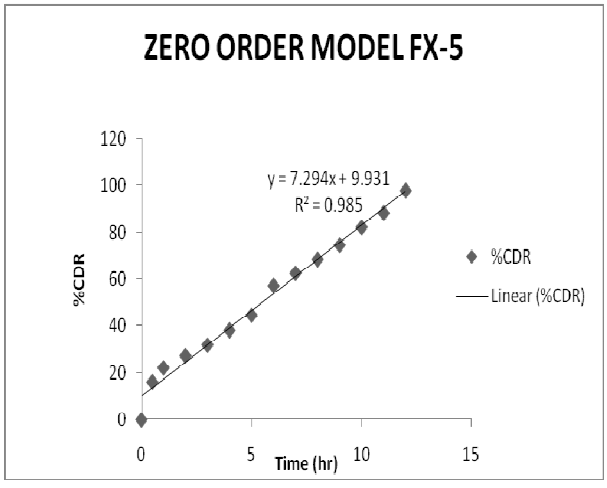

Figure - 19:

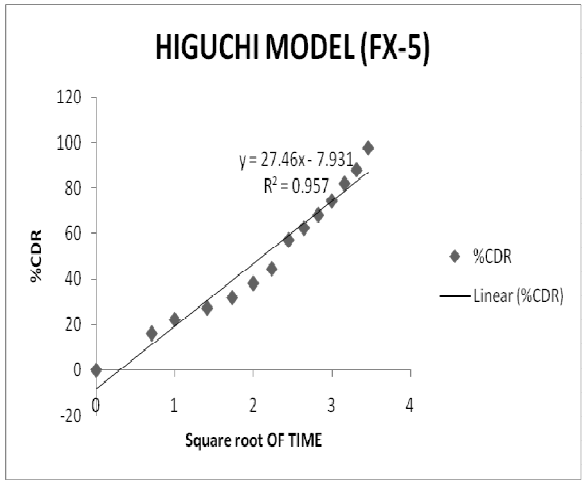

Figure - 20:

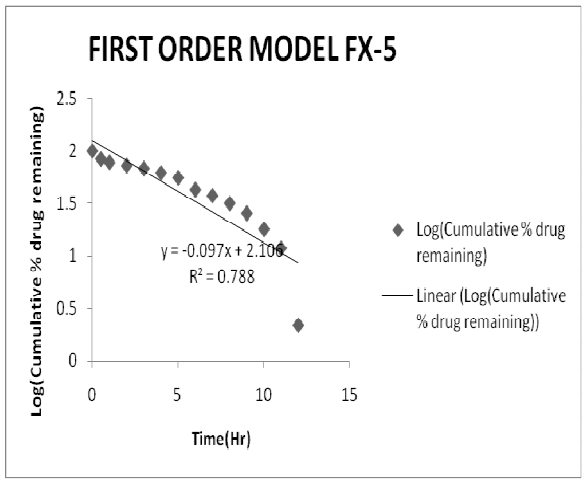

Figure - 21:

The melting point of pure cefaclor monohydrate was found at 327°C following exothermic reaction with on-set and end-set at 160.58°C & 167.23°C respectively with a glass transition lag around 6.67°C & the same found in all compositions with no change in both melting point and glass transition lag. Special peaks were found indicating melting point of sodium alginate at 204.42°C, Guar gum at 105.07°C, Pectin at 102.04°C, Xanthan gum at 106.93°C, chitosan at 270°C Influence of excipients was found only in changing on's and end's of melting point peak of cefaclor monohydrate by absorbing heat but not by interactions indicating unchanged crystalline nature of the drug without undergoing polymorphism in all formulations. X-ray diffractogram of confirmed its crystalline nature as evidenced from the number of sharp & intense peaks. The diffractogram of cefaclor monohydrate with polymers showed diffused peaks indicating polymers amorphous nature. Diffraction pattern of samples spectra represent availability of crystalline peaks of drug situated at 16.23, 19.56, 21.12, and 23.56 (2θ) similar to the pure drug. The obtained 2θ values as characteristic peaks were

found at the same position in all compositions but the intensities got reduced because of diffused peaks & more orientation in case of polymers. The DSC and XRD data states that the crystallinity of pure drug found unchanged & stable, and indirectly determines the compositions are compatible

5. CONCLUSION

It was found that sodium alginate along with chitosan and xanthan gum substantially controlling the release of cefaclor monohydrate from the microcapsules. Results of the *in vitro* drug release indicated that the controlled drug release upto 12 hours. These studies demonstrated that cefaclor monohydrate can be encapsulated into microcapsules having sodium alginate, chitosan and xanthan gum backbone by ionic gelation technique having good yield, particle size, entrapment efficiency and *in vitro* drug release profile of microcapsules. The microcapsules also showed considerable swelling behavior. The prepared microcapsules showed controlled drug delivery behavior as can be inferred from the release kinetics data, as it follows zero order as well as Higuchi model which confirm its diffusion controlled release behavior although the Korsemeyer-Peppas plot shows anomalous transport suggests that the release is controlled by diffusion as well as by other factors like swelling of the microcapsules.

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