Formulation Development and Evaluation of Microspheres of Cefpodoxime Proxetil - A Broad Spectrum Cephalosporin with Short Half-life

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Abstract- **In present investigation, to develop mucoadhesive microsphere of cefpodoxime proxetil, it was first identified by characteristics infrared spectra and then it was subjected to melting point determination, partition coefficient determination and solubility analysis. After that the drug was analysed in UV spectrophotometer by constructing standard curve in 0.1 N HCl (pH-1.2). It was found that the drug was confirming all the pharmacopoeial standards with respect to melting point, partition coefficient, solubility, wavelength of maximum absorption (λmax) and the characteristics of IR spectra. Polymer used in formulation of microspheres, may interfere in the estimation of drug. The mp of cefpodoxime proxetil was found to be 111^{0}C. The PC of cefpodoxime proxetil was found to be 5.1 (lipophilic). Formulations FC2 and FC4 follows zero order release kinetics with r^2 value of 0.991, 0.998 respectively. From the study it is evident that promising controlled release mucoadhesive microspheres of cefpodoxime proxetil may be developed by solvent evaporation techniques by using polymers for reduced dosing frequency and better patient compliance therapy.**

Keywords**: Bioadhesive, drug release, gastrointestinal tract, melting point determination, microspheres, lipophilic, partition coefficient, polymers, solubility**.

Introduction

Sustained Release Drug Delivery System (SRDDS)

Sampanth *et al*., 2012, SRDDS based formulations are intended to modify / improve the drug actionby increase in their duration of action, decrease the dosing frequency, reduced side effects, decreasing the required dose. In these types of systems, the prior is to maintain or control the release rates and helps in targeting the drug to a specific site (Patel *et al*, 2004).

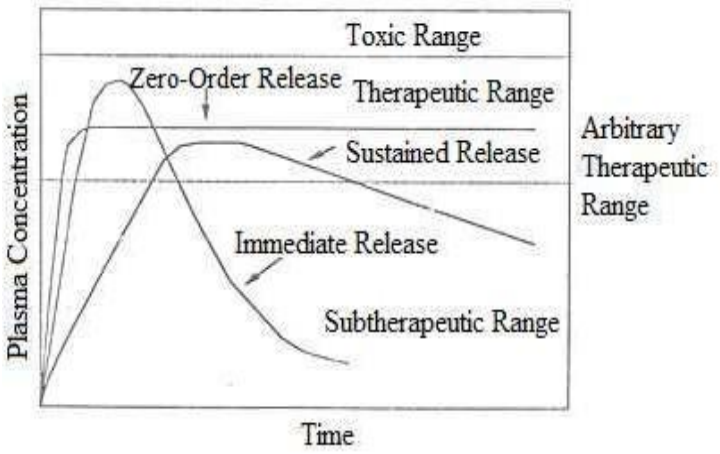


Figure 1: Plasma Drug Concentration Profiles.

Rationale of SRDDS

Heller (1985), several methods are used to enhance the drug releaseswhich are as follows (Robinson and Lee, 1999):

1. Coating drug with polymer to form a Laminate.
2. Dispersing drug in a matrix to form hydrogel.
3. Coating of drug to form Pellets / Micropellets for slow and extended release ofdrug.
4. Addition of drug to a bio adhesive polymer Drug which can adhere to mucus membrane to release drug for prolonged time.
5. Bonding drugs chemically with polymers (Amide or Ester linkages) forcontrol release of drug.

Advantages of sustained release dosage forms

- Reduced quantity of drug-dose required;
- Better Patient compliance;
- More convenient administration of drug;
- Blood concentration is reduced in case of multiple dosing of dosage forms;
- Absorption of drugs can be easily controlled;
- Blood level variations can be reduced;
- Support bioavailability, decreased side effects & drug accumulation.
- Side effects can be reduced by providing high safety margins;.
- Improved therapeutic out-come / bioavailability;
- Economically beneficial.

Disadvantages of sustained release dosage forms

- high cost;
- dose dumping probability;
- increased potential for first pass metabolism;
- dose adjustment potential reduced;
- patient counseling required;
- poor *in vitro* and *in vivo* correlations;
- decreased systemic availability (comparison to immediate release dosage forms)

Controlled Drug Delivery system (CDDS)

Kim *et al*., 2002, stated that CDDS maintain the drug levels within a desired rangeproviding an optimal use of the active moiety and increased patient compliance. Ideally the aim of these controlled-release formulations is to achieve a delivery profile with high blood level.

Advantages of CDDS

- reduced dose ;
- improves the bioavailability ;
- reduced drug accumulation ;
- better patient compliance;
- prevents local / systemic drug toxicity;
- drug level fluctuation in blood is reduced;
- better therapeutic outcome ;
- economical and showcases market and patent expansion ;

Disadvantages of CDDS (Timmins *et al*., 2012)

- Onset of drug action is reduced
- In case of a poor formulation strategy it could lead to dose dumping.
- Undergoes first pass metabolism
- Less accurate dose adjustment in some cases is possible
- When compared with conventional doses cost per unit is higher
- The GI residence time of dosage form is greatly dependent
- Not all drugs are suitable for formulating into ER dosage form.

Burst Release

Huang *et al*., 2001 illustrated that several researches have find the mechanismof burst.

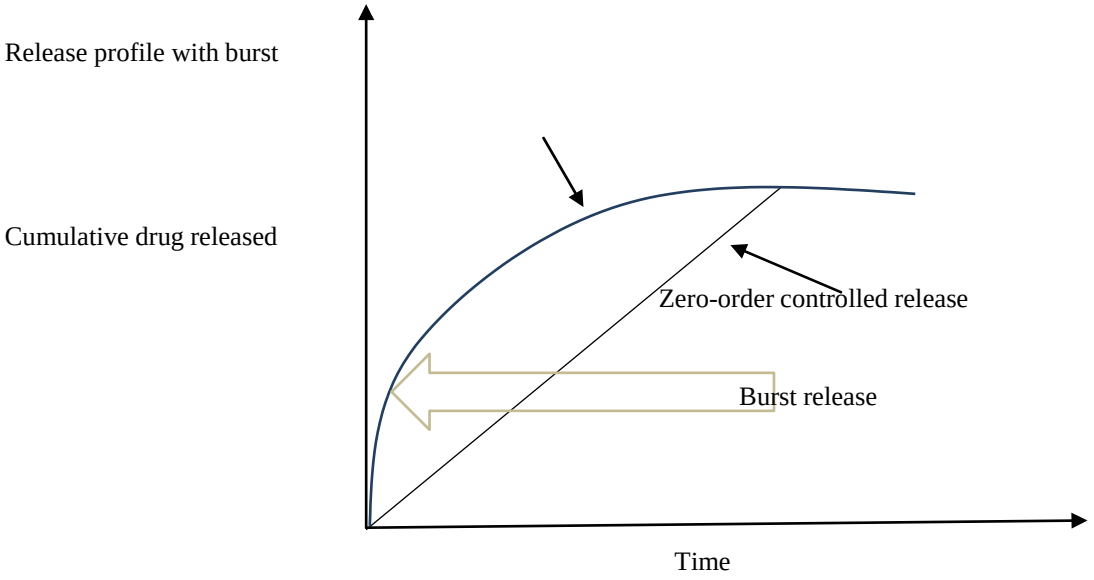


Figure 2 : Burst-effect.

Gastroretentive Drug Delivery System (GDDS)

As oral route are considered as the very successful route as compared to various s routes available for the drug administration. (Dutta *et al*., 2011).

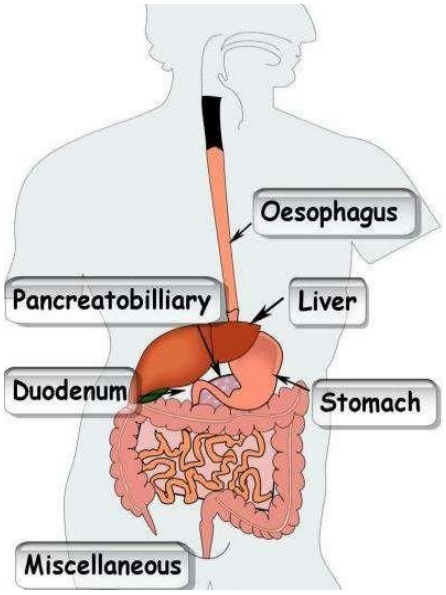


Figure 3: Gastrointestinal Tract.

The controlled drug delivery system possesses more versatility as compare toconventional one. CDDS were developed to achieve better products with greater safety margins who can deliver drugs at a preprogrammed manner for longer duration of time. 'Drug retained in stomach for time longer than usual are known as Gastro Retentive Systems (GRS)**.** GRS are important in case of drugs who get degraded by acidic media of stomach they provide protective action against harsh media of stomach. "If the drugs are poorly soluble in the intestine due to alkaline pH, gastric retention may increase solubility before they are emptied, resulting in improvedbioavailability" (Gudigennavar *et al*, 2012).

Drug Selection Suitable Drugs for GRS

1. Drugs that needed for local action in stomach e.g. misoprostol, antacids etc.
2. Drugs having very small therapeutic window in GIT e.g. Levadopa

Unsuitable Drugs for GRS

1. Low solubility Drugs e.g. Phenytoin
2. Acid Labile Drugs e.g. Erythromycin.
3. Colon Specific Drugs e.g. 5-amino salicylic acid etc.

Types of Gastroretentive System

- Floating drug delivery systems
- Non-effervescent
- Gas-generating (Effervescent) systems
- Expandable systems
- Bio/Muco-adhesive systems
- High-density systems

Advantages of GRS

- Improved Bioavailability because less degradation of drug.
- Reduced dosing frequency with better patient compliance.
- Help to remove limitations of conventional drug delivery.
- Produce Controlled and Sustained action of drug as well as Releases at site of action.
- Site specific Delivery to affected organs.
- Protect drug from degradation in body.
- Improve receptor activity by fluctuating release in case of sustained dosage form.
- Improved Pharmacological responses.
- Avoid unnecessary drug exposure

Microspheres

Varde *et al.,* 2004, summarized that microspheres or microparticles aresame (typically 1 μm to 1000 μm).

Classification of Microspheres

Table 1: Classification of Microspheres

Based on applications	(a) Muco/Bioadhesive microspheres
	(b) Floating microspheres
	(c) Hollow microspheres or microballoons
	(d) Magnetic microspheres
	(e) Radioactive microspheres
	(f) Fluorescent microspheres
Based on type of polymers	(a) Natural Polymeric microspheres: Like Na alginate, starch, chitosan, pectin, guar gum etc.
	(b) Synthetic Polymeric microspheres: Polymers like cellulose derivatives etc.

	(c) Novel polymeric microspheres: Polymers like thiolated polymers, alginate-PEGAc, poloxomer, pluronics and combination.

Mucoadhesive Microsphere

Garg *et al*, 2003, bioadhesive microspheres include microparticles and microcapsules (having a core of the drug) of 1-1000 µm in diameter. These are the carriers used to deliver the drug at the desired site. Shortresidence time at absorption site is the measure problem associated with microspheres. Problem of short residence time can be overcome by preparing a microsphere that can adhere to mucus membrane by replacing normal polymers with mucoadhesive polymers (Parmar *et al*, 2010).

Inability to stay in GIT due to gastric motility and peristaltic movements is the major cause of concern for the scientist working in the field of drug and dosage form design this problem can be overcome. (Lee *et al*, 1999)

Beri *et al*., 2013, illustrated that developing microspheres with mucoadhesive property that can stick to mucus membrane and increases gastric residence time of drug in GI tract and releases drug in a sustained/controlled manner is always beneficial. The contact of dosage form coataning drug with membrane result in improved drug retention time in GI Tract simultaneously increases with overall improvement in therapeutic response.

Carvalho *et al*., 2010, **t**hese novel drug delivery systems have been developed to improve the drug release. This development of systems also helps in increase the bioavailability of the drugs. Microspheres can be potential candidate for the development of targeted and controlled delivery system, if coupled with concept of bio adhesion it has moreadditional advantages e.g. improved absorption and bioavailability and Targeted Delivery to affected site.

Mucoadhesive Polymers

Punitha *et al*, 2010, mucoadhesive polymers are water-soluble and water insoluble polymers, which are swellable networks, jointed by cross-linking agents. These polymers possess optimal polarity to make sure that they permit sufficient wetting by the mucusand optimal fluidity that permits the mutual adsorption and interpenetration of polymer and mucus to take place.

Properties of polymers for mucoadhesive microspheres

- Nontoxic and Non adsorbable from GIT
- Nonirritant to GI Mucosa.
- Must form non covalent bond with the mucin of mucus membrane.
- Adhere to all tissues but must have some site specificity.
- Allow easy molding with drug with no hindrance.
- Must be stable till life cycle of products.
- Should be cost effective in nature so should not affect final cost of dosageform
- Inert in nature and biocompatible.
- It should allow easy incorporation of drug in to the formulation.

Characteristics of an Ideal Mucoadhesive Polymer

Mucoadhesive polymer should have following properties (Patil *et al*, 2006)

- Nontoxic; non-absorbable;
- non-irritant;

Table 2: Properties of Mucoadhesive Polymers.

S. No.	Mucoadhesive Polymers	Properties of polymer	Bioadhesion Property
1.	Alginate Sodium	Anionic polymer, Enhances swelling	High Mucoadhesion
2.	Chitosan	Cationic polymer, High/moderate swelling	High Mucoadhesion
3.	Sodium carboxy methyl Cellulose	Anionic polymer, High swelling properties	High Mucoadhesion

4.	Carbopol	Good water asorption property.	High Mucoadhesion
5.	Hydroxy ethyl cellulose (HEC)	Nonionic polymer,High swelling	Low mucoadhesion
6.	Hydroxy propyl cellulose (HPC)	Non-ionic polymer, Increased swelling	Mild Mucoadhesion
7.	Hydroxypropylmethyl-cellu lose	Non-ionic polymer,High swelling	Mild Mucoadhesion
8.	Polyvinyl alcohol	Less swelling	Mucoadhesive properties
9.	Poly vinyl pyrrolidone	Film Former	Co-adjuvant
10.	Carrageenan	Poor and stable swelling	Less Mucoadhesion
11.	Guar gum	Additive, Mild swelling	Better Mucoadhesion

Table 3: Performance of bioadhesive polymers (Rathore *et al*, 2009).

Polymers	Bioadhesive nature
Tragacanth	+++
Carbopol 934	+++
Carboxy methyl cellulose	+++*
Hydroxy Ethyl cellulose	+++
Polycarbophil	+++
Poly(acrylic acid /divinyl benzene)	+++
Sodium alginate	+++
Guar gum	++
Gelatin	++
Karaya Gum	++
Polyvinyl pyrrolidone	+
Polyethylene glycol	+
Thermally modified starch	+
Acacia	+
Pectin	+
Hydroxy propyl cellulose	+
Hydroxy ethyl methacrylate	+
Chitosan	+

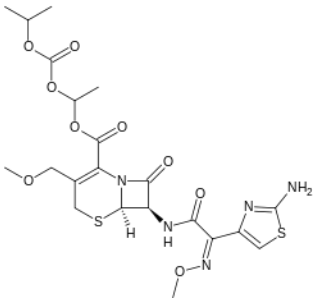
+++*Very High; ++High; +Moderate.

The drug shows relatively higher bioavailability in fed conditions than fasted conditions. It is stable and well absorbed within pH range 1-4. Above pH 4 it undergoes hydrolysis to form active cefpodoxime. But the active metabolite cefpodoxime is not absorbed from gastrointestinal tract. So the bioavailability of cefpodoxime proxetil may be increased by reducing its hydrolysis. The short half life of cefpodoxime proxetil (2-3 hrs) suggests that it is rational drug for sustained delivery. In this investigation carbopol-934P, sodium CMC and sodium alginate were used as as a mucoadhesive polymer and prepare mucoadhesive microsphere which adhere to gastric mucosa and release the drug in controlled release manner.

Materials and Methods

Drug Profile

Name: Cefpodoxime Proxetil (CP) (Goswami *et al*., 2012;Sivaneswari ., 2013)



Description: Cefpodoxime proxetil is used orally for the treatment of mild to moderate respiratory tract infections, uncomplicated gonorrhea and urinary tract infections.
Mol. Formula: $C_{21}H_{27}N_5O_9S_2$
Mol. Weight: 557.6
Melting point: 111-113°C
Bioavailability: 50% of the administered cefpodoxime dose.
pKa value: 3.22 and 4.16
Color: White to yellowish powder.
State: solid.
Odor: odorless.
Solubility: It is readily soluble in DMSO and methanol. Cefpodoxime proxetil exhibited a pH dependent solubility phenomenon in various aqueous buffers. Very high solubility of cefpodoxime proxetil was observed in acidic pH values, while the solubility dropped rapidly as the pH increased.

Cefpodoxime proxetil Gift sample from Apco Pharma Ltd, Haridwar (UK)Polymers. Cemicals (AR Grade Chemicals): Sodium carboxy methyl cellulose, Propylene glycol, Methanol, Acetone, Potassium hydroxide, Potassium dihydrogen phosphate, Sodium dihydrogen phosphate, Liquid paraffin, Carbopol-934, Sodium alginate etc.

Pre-formulation Studies

Identification of Drug

Infrared Spectrum

The KBr pellets were prepared and examined by FTIR (8400S,Shimadzu Corporation, Japan). The scanning was done using KBr dispersion pellets. Scanned between 4000-400 cm^{-1};

Ultraviolet Spectrum

The λmax of cefpodoxime proxetil was determined determine using Double Beam UV Spectrophotometer (Systronic 2201, India). Dilutions (2-20 µg/ml) were prepared from standard stock (100 mg / 100 ml;100 µg/ml).

Determination of Melting Point (mp) : As per SOP / SAP.

Partition Coefficient (PC)

The PC was analysed by as per SOP / SAP. PC of cefpodoxime proxetil was determined in solvent system. Kept to equilibrate by shaking in orbital shaker incubator for 24 hrs and after shaking, materials were transferred into a separating funnel, kept overnight at room temperature. Equation :

$Po/w = (C_{organic} / C_{aqueous})$ $Pw/o = (C_{aqueous} / C_{organic})$

Determination of Solubility

Solubility studies of cefpodoxime proxetil were performed by SOP / SAP in different solvent (buffers of pH values 1.2,

6.8, acetonitrile, methanol, dehydrated alcohol, dimethyl sulphoxide etc). Saturated solutions of drug were prepared in different solvent by adding the excess drug tothe vehicles and shaking in screw capped tubes on the shaker for 48 hrs at 25^0C under constant vibration.

Compatibility Studies

The drug and polymer compatibility was characterized by SOP / SAP using FTIR spectroscopy.

Method of Analysis of Drug

Calibration curve

Cefpodoxime proxetil was estimated by UV spectrophotometer (Systronic UV-2202, double beam spectrophotometer) method. Pure cefpodoxime proxetil was taken and the solutions were prepared by using acidic buffer solution (pH 1.2) as solvent and absorbance was measured at 263 nm (Systronic 2201).

Determination of interference

Polymers used in the formulation of cefpodoxime proxetil mucoadhesive microspheres, may interfere in the estimation of drug. Hence the interference due to these polymers was checked using the maximum concentration used in the formulation. Polymers were dissolved in the standard solution of cefpodoxime proxetil prepared. Solution was subjected to UV scanning between 220-400nm.

Method of Preparation of Formulation:

Method of Preparation of Microspheres without Drug

Microspheres without drug were prepared by SOP / SAP.

Table 4 : Microspheres without drug

Formulation	Sod. Alginate (mg)	Carbopol-934P	Sod. CMC (mg)
MS1	1000	--	--
MS2	--	1000	--
MS3	--	--	1000
MS4	500	500	--
MS5	500	--	500
MS6	--	500	500
MS7	334	333	333

All batches were prepared at 2% polymer concentration and every batch wasprepared at two different stirring speeds (500 rpm and1000 rpm).

Table 5: Microspheres without drug for accessing the effect of polymerconc. on the particle size (PS) of microspheres.

Formulation code	Sod. alginate (mg)	Carbopol-934P (mg)	SCMC (mg)
MC1	1000	--	--
MC2	--	1000	--
MC3	--	--	1000
MC4	500	500	--
MC5	500	--	500
MC6	--	500	500
MC7	334	333	333

All batches were prepared at 1000 rpm stirring speed and every batch were prepared at two different polymer concentrations (1%, 2%).

Method of Preparation of Microspheres with Drug

Drug loaded microsphere were prepared by water in oil (w/o)emulsification solvent evaporation method (SOP/SAP).

Table 6: Composition of drug loaded microspheres formulation.

Formulation	Drug (mg)	Sod. alginate	Carbopol-934P	SCMC
FC-1	200	800	--	--
FC-2	200	--	800	--
FC-3	200	--	--	800
FC-4	200	400	400	--
FC-5	200	400	--	400
FC-6	200	--	400	400
FC-7	200	267	266	267

2% polymer concentration (1000 rpm); Span 80 (1.5% v/v).

Evaluation of Microspheres

Surface Morphology

SOP was used for SEM analysis using SEM, EVO 40, Zeiss Germany; AIRF at JNU, New Delhi.

Particle size Analysis

SOP / SAP were used for particle size analysis of mucoadhesiveusing optical microscope.

Swelling Index

SOP / SAP were used for swelling in SGF (pH -1.2) for 4 hrs.

Drug entrapment Efficacy

SOP / SAP were used to determine entrapment efficacy of microsphereand drug content was analysed at 263 nm.

***In-vitro* Mucoadhesion Analysis :** As per SOP/SAP (*in-vitro* wash off method).

Drug Release

Determined using USP-DT apparatus (1 basket type and absorbance was measured at 263 nm.

Modeling of Release Profile : As per SOP.

Stability Studies : Sample was analysed for residual drug content at the time interval of 15 days.

Results and Discussions
Compatibility Studies

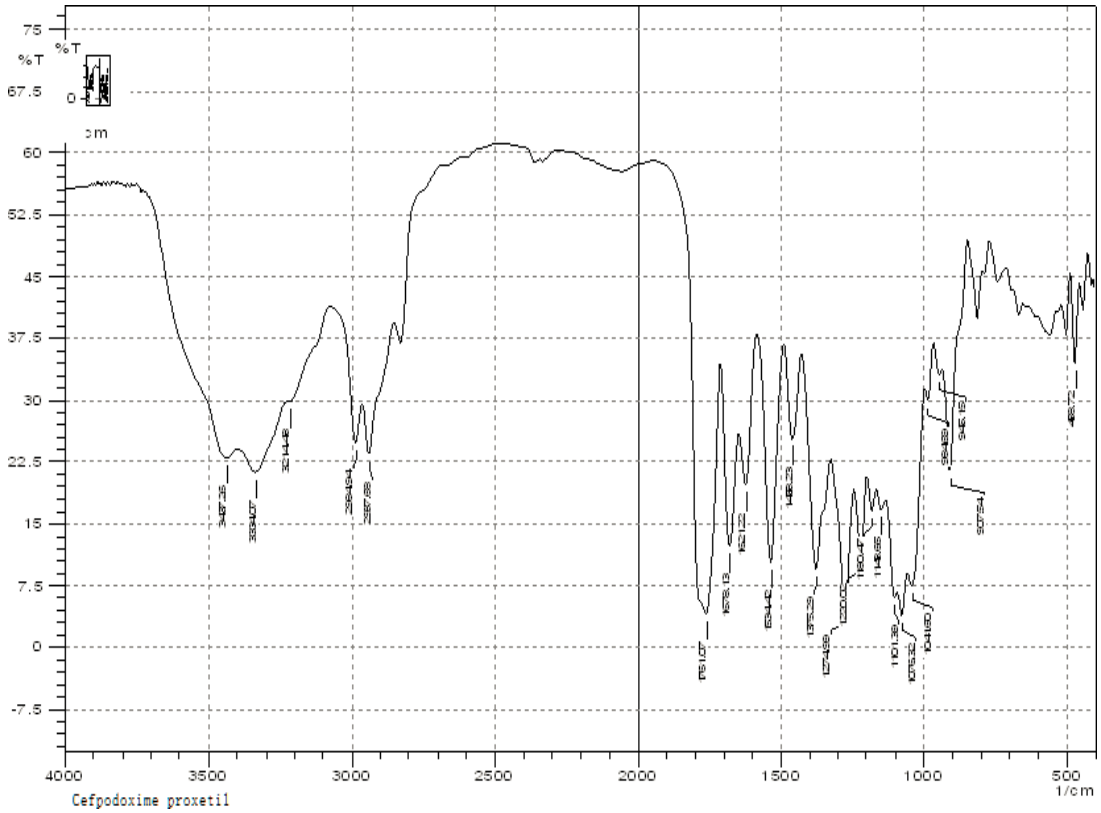


Figure 4 : FTIR spectra of cefpodoxime proxetil.

Table 7: Cefpodoxime proxetil FTIR.

Peak	Interpretation
2937	C-H
2984	C-H
3330	N-H
1074;1099	C-O
1761	C=O
1274	C-N
1375	C-H

Table 8: FTIR spectra of SCMC.

Peak (cm^{-1})	Groups
1751.12	C=O stretching
1419.12	Carboxylate ion stretching
1319.23	C-O stretching in sec. alcohol
1085.26	C-O-C stretching

Table 9 : FTIR of sod. alginate.

Peak (cm^{-1})	Groups
2921.31	O-H
2850.12	C=H
1419.12	Carboxylate ion
1033.13	C-O

Table 10 : FTIR analysis of carbopol-934P.

Peak (cm^{-1})	Groups
3602.31	O-H
1712.12	C=O
1452.23	C-H
1409.26	C-OH

Table 11 : FTIR spectra of Drug with SCMC.

Peak	Interpretation
1618	N-H
1638	C=N
1074, 1099	C-O
1274	C-N
1375	C-H

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Table 12: FTIR spectrum of cefpodoxime proxetil and Carbopol-934P.

Peak observed (cm^{-1})	Interpretation
1074, 1099	C-O
1761	C=O
674	C-S-C
1274	C-N
1375	C-H

Melting Point

Table 13 : Melting point of cefpodoxime proxetil.

S. No.	Reported	Observed
1.	111-113^{0}C	111^{0}C

Partition Coefficient

Table 14 : Partition coefficient of cefpodoxime proxetil in Octanol/0.1 N HCl.

S. No.	o/w system	Reported	Partition coefficient(observed)
1.	Octanol/0.1 N HCl	5	5.1

Solubility Studies

Table 15: Solubility of Cefpodoxime proxetil in various solvent.

Solvent	Solubility
Methanol	soluble
Dimethyl sulphoxide	Soluble (freely)
0.1 N HCl	Soluble
Acetonitrile	Soluble
Dehydrated alcohol	Freely soluble
Phosphate buffer (pH 6.8)	Slightly Soluble
Water	Sparingly soluble

SEM Analysis Photographs

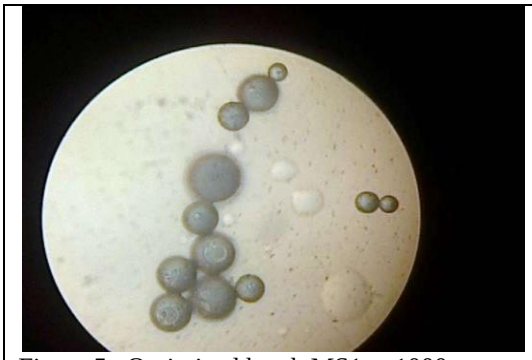


Figure 5 : Optimized batch MS1 at 1000 rpm.

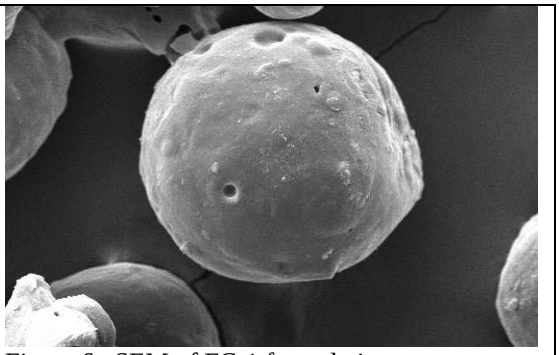


Figure 6 : SEM of FC-1 formulation.

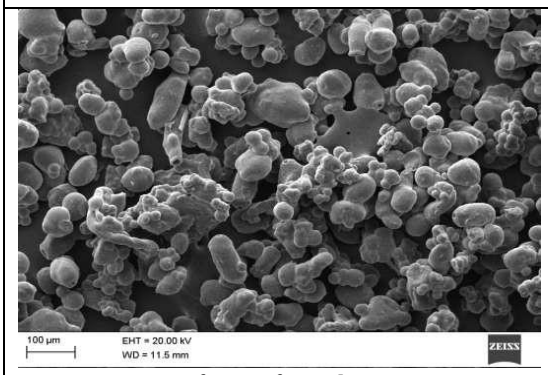


Figure 7: SEM of FC-2 formulation.

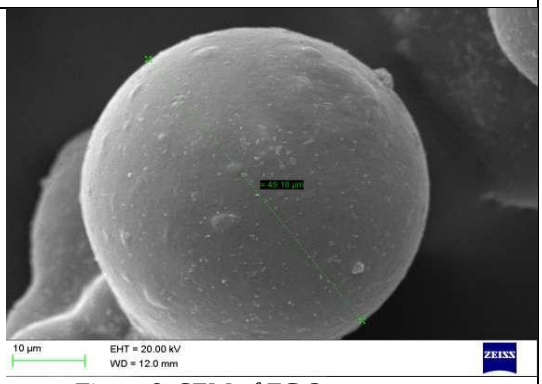


Figure 8: SEM of FC-3

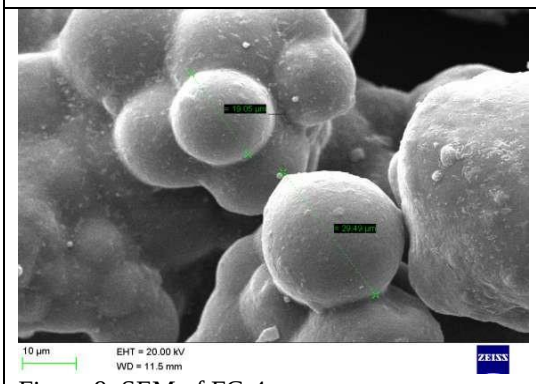


Figure 9: SEM of FC-4.

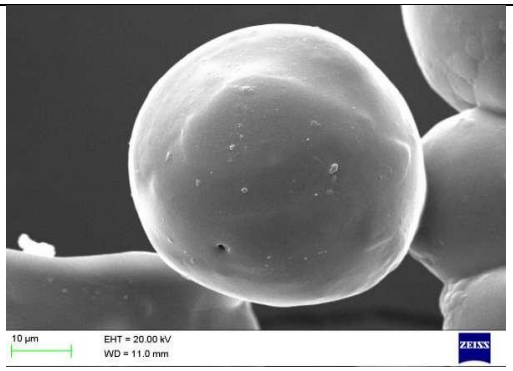


Figure 10: SEM of FC-5.

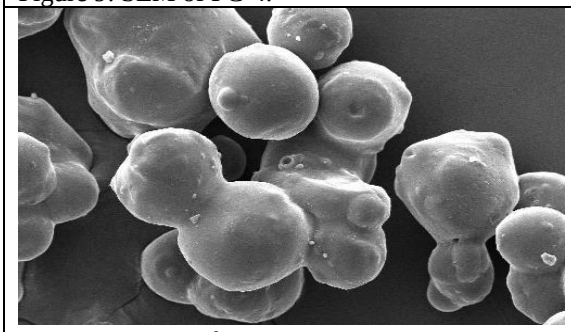


Figure 11: SEM of FC-6.

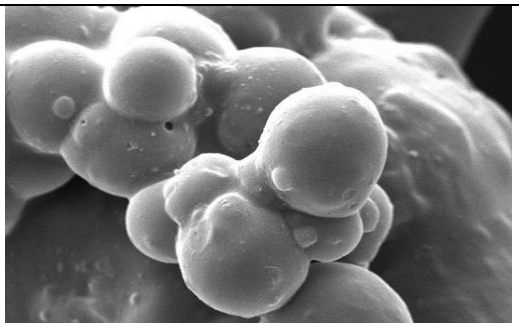


Figure 12: SEM of FC-7.

RPM Optimization

Table 16: Effect of stirring speed.

Code (MS)	PS (µm) at 500 rpm	PS (µm) at 1000 rpm
1	59.39±2.54	41.46±3.32
2	54.67±1.78	33.30±1.93
3	49.18±3.22	37.63±2.71
4	47.23±2.46	36.57±3.28
5	48.43±2.32	34.42±2.64
6	47.67±3.23	38.66±2.38
7	49.62±2.56	39.56±2.42

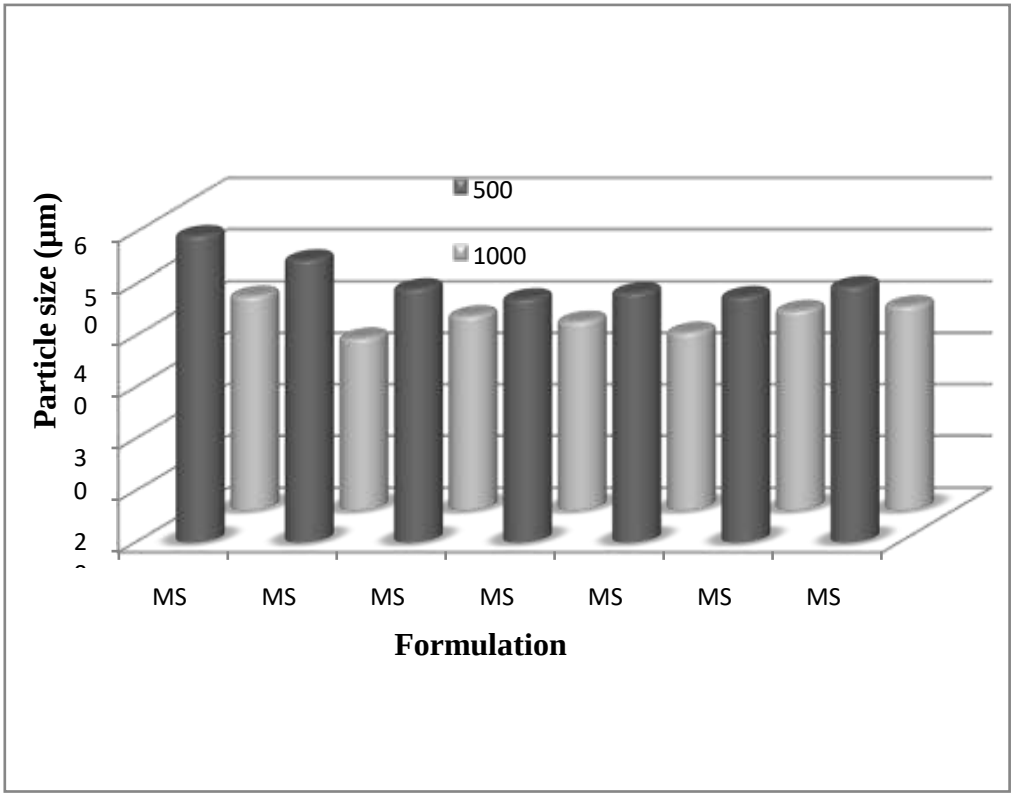


Figure 13: Effect of stirring speed on particle size.

Concentration Optimization

Table 17 : Effect of polymer conc. on Particle size (PS).

Formulation code	PS (µm) (1% polymer Conc.)	PS (µm) (2% polymer Conc.)
MC-1	34.45±2.42	41.46±3.32
MC-2	29.64±1.85	33.30±1.93
MC-3	33.56±1.68	37.63±2.71
MC-4	31.68±1.82	36.57±3.28
MC-5	30.45±2.53	34.42±2.64
MC-6	34.89±2.74	38.66±2.38
MC-7	35.73±1.68	39.56±2.42

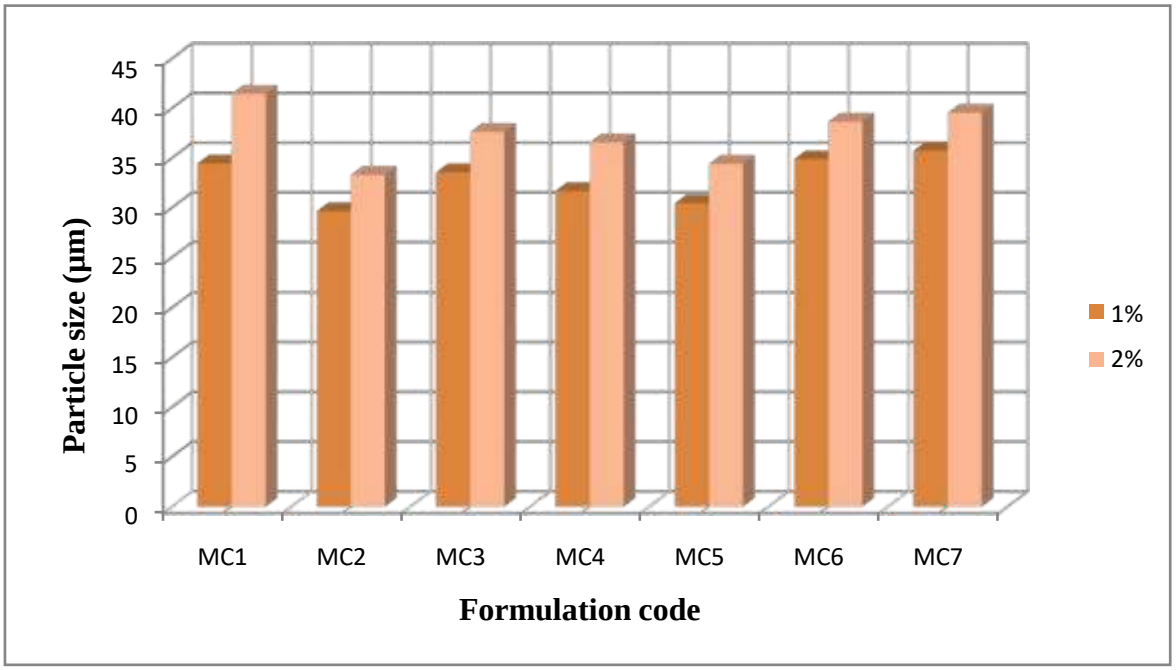


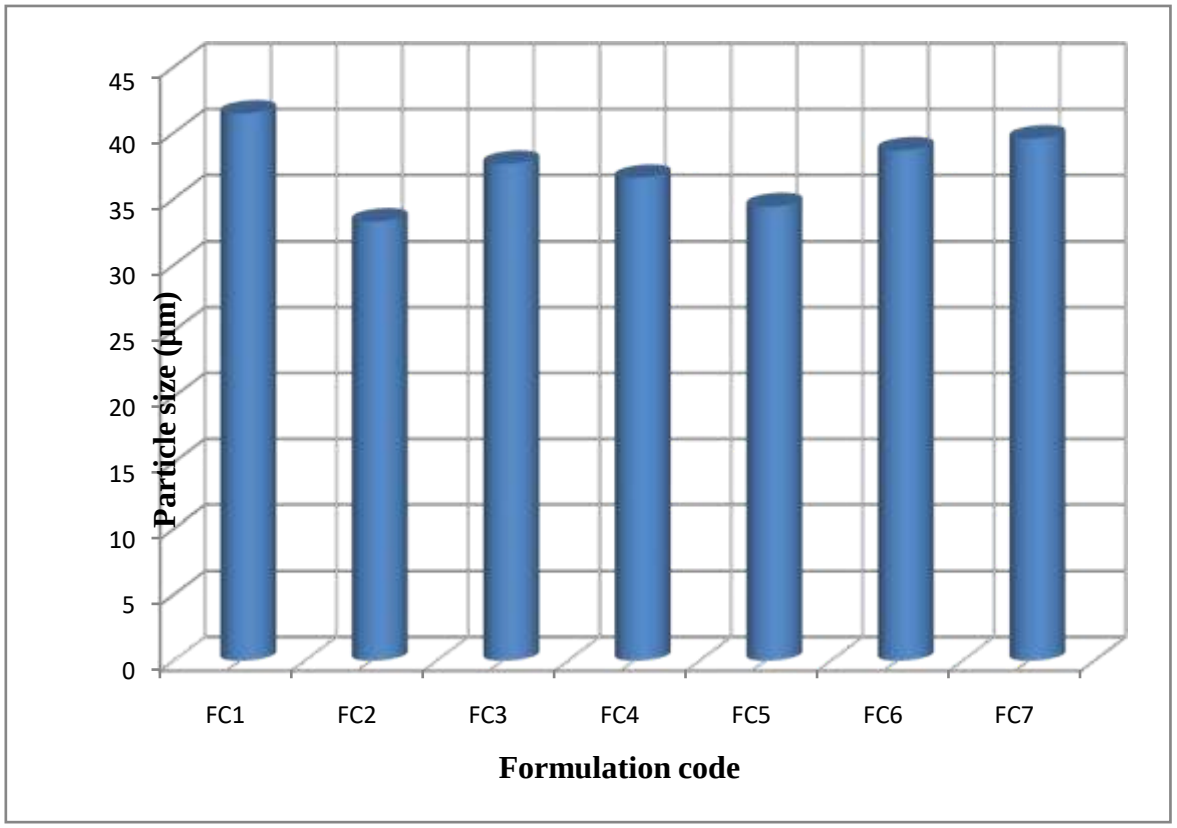
Figure 14: Effect of polymer concentration on Particle size.

Particle Size (PS) Analysis

Table 18 : Particle size of microsphere of formulations.

Formulation code	Particle size (μm)
FC1	41.46±3.32
FC2	33.30±1.93
FC3	37.63±2.71
FC4	36.57±3.28
FC5	34.42±2.64
FC6	38.66±2.38
FC7	39.56±2.42

Figure 15 : Particle size of microsphere.



Swelling Index (SI)

Table 1 9 : Swelling Index of mucoadhesive microspheres of formulations.

Formulation code	Swelling index
FC-1	0.66±0.09
FC-2	1.62±0.08
FC-3	0.94±0.12
FC-4	1.28±0.16
FC-5	1.12±0.11
FC-6	1.24±0.18
FC-7	1.26±0.15

Drug Entrapment Efficiency (DEE)

Table 20: Drug Entrapment Efficiency of microspheres of formulations.

S. No.	Formulation code	Theoretical Loading (mg)	Practical loading (mg)	% Drug entrapment
1.	FC1	200	106	53±2.65
2.	FC2	200	128	68±3.44
3.	FC3	200	120	60±2.32
4.	FC4	200	102	51±3.45
5.	FC5	200	114	57±2.76
6.	FC6	200	124	62±2.68
7.	FC7	200	98	49±3.24

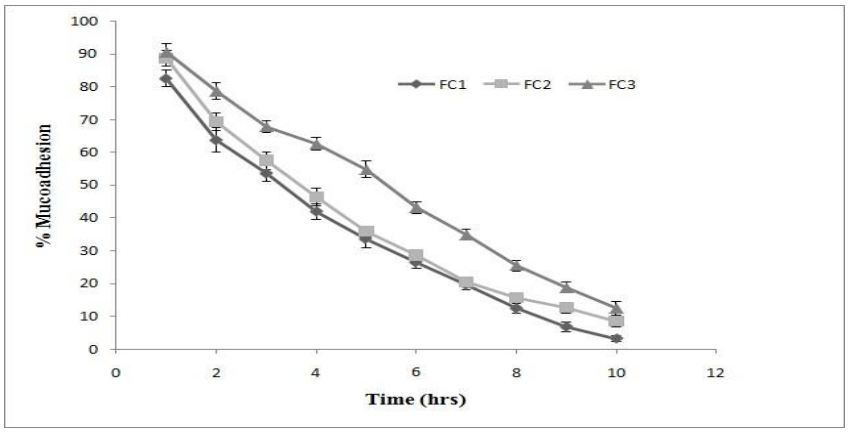


Figure 16: Comparative % mucoadhesion of microspheres of formulations.

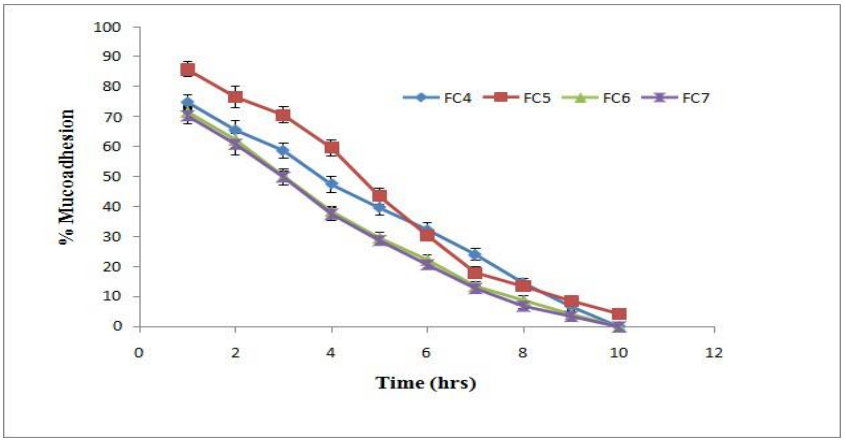


Figure 17 : Comparative % mucoadhesion.

Table 21: Comparative % mucoadhesion.

S.NO.	Formulation code	% Mucoadhesion after 1 hrs	% Drug entrapment	Particle size (µm)	% yield
1.	FC1	82.45±2.56	53±2.65	41.46±3.32	74.86±3.24
2.	FC2	88.68±2.45	68±3.44	33.30±1.93	70.76±2.43
3.	FC3	90.56±2.67	60±2.32	37.63±2.71	72.68±2.82
4.	FC4	74.88±2.44	51±3.45	36.57±3.28	73.36±2.48
5.	FC5	85.75±2.48	57±2.76	34.42±2.64	72.77±2.23
6.	FC6	71.66±1.86	62±2.68	38.66±2.38	70.58±2.64
7.	FC7	70.33±2.54	49±3.24	39.56±2.42	68.83±2.44

Values are represented as mean ± standard deviation (n=3).
All formulation were prepared at 2% polymer concentration and 1000 rpm stirring speed.

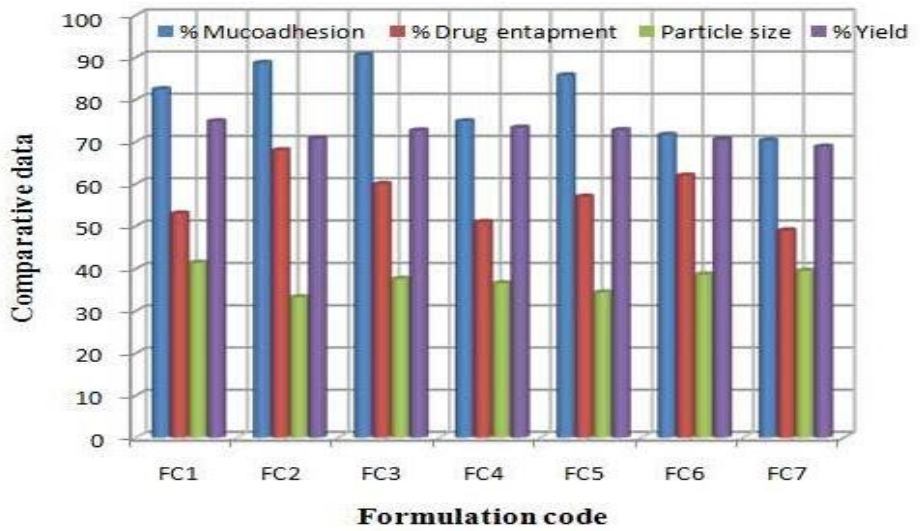


Figure 18 : Comparative % mucoadhesion, DEE, PS and % yield of formulations.

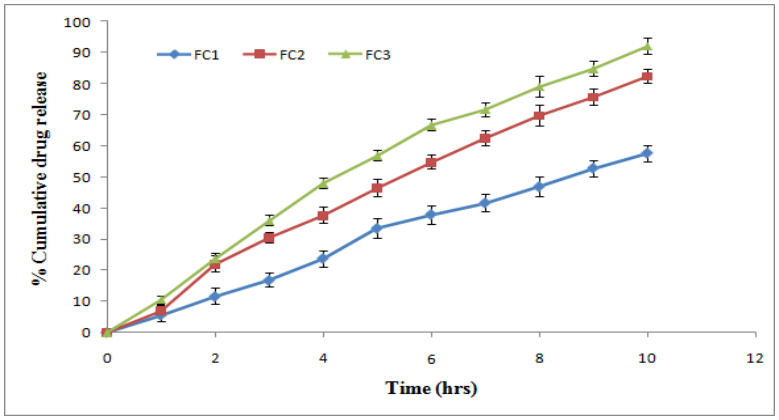


Figure 19 : Comparative cumulative (CC) drug release.

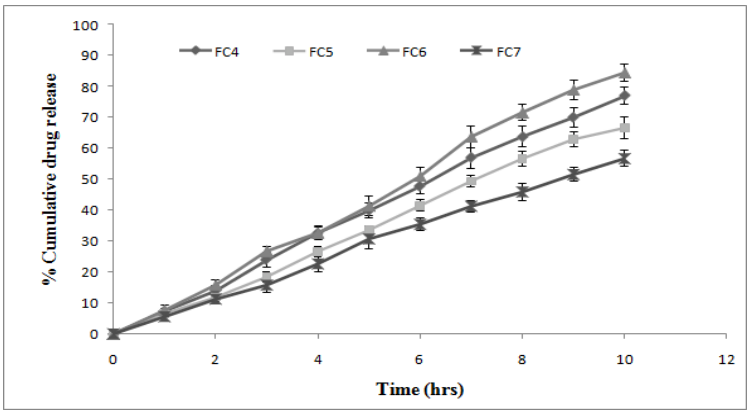


Figure 20 : Comparative cumulative % drug release.

Stability Studies

Table 22 : Stability study of FC-1 and FC-2.

S. No.	Time (days)	% Drug retained					
		At 25^{0}C		At 40^{0}C		At 50^{0}C	
		F1	F2	F1	F2	F1	F2
1.	0	100	100	100	100	100	100
2.	15	99.48	99.61	99.26	99.27	99.22	99.14
3.	30	98.43	98.72	98.74	98.66	97.79	98.83

4.	45	97.88	97.78	97.52	97.64	97.40	97.55
5.	60	95.34	95.86	95.22	94.71	95.17	94.66
6.	75	92.77	91.61	92.33	90.44	91.05	91.68
7.	90	90.16	89.19	89.37	88.74	88.63	87.44

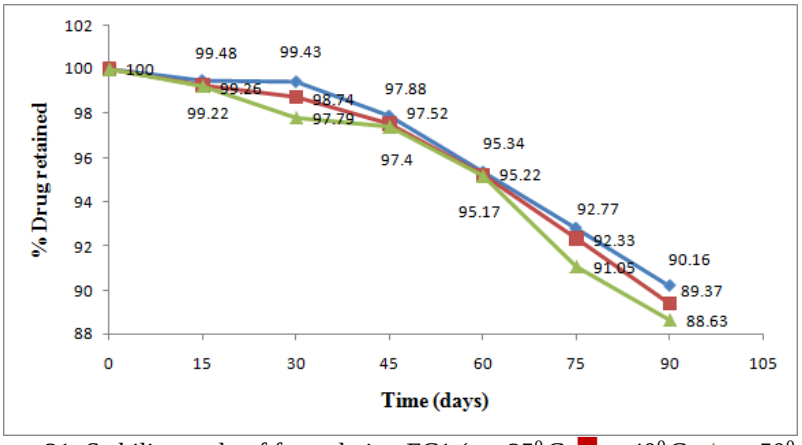


Figure 21: Stability study of formulation FC1 (♦at 25^{0}C, ■ at 40^{0}C, ▲ at 50^{0}C).

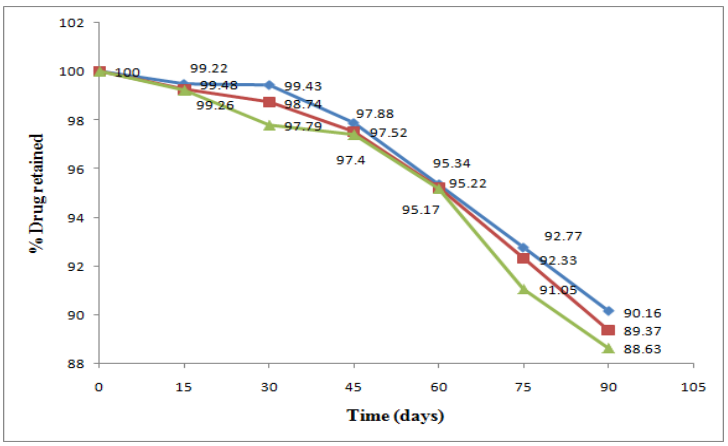


Figure 22: Stability study of formulation FC2 (♦at 25^{0}C, ■ at 40^{0}C, ▲ at 50^{0}C).

Table 23 : Stability study of formulations FC3 and FC4.

S. No.	Time (days)	% Drug retained					
		At 25^{0}C		At 40^{0}C		At 50^{0}C	
		F3	F4	F3	F4	F3	F4
1.	0	100	100	100	100	100	100
2.	15	99.58	99.61	99.26	99.27	99.22	99.14
3.	30	98.43	98.32	98.27	98.26	98.04	97.83
4.	45	97.61	97.10	97.53	97.89	97.44	96.64
5.	60	95.74	95.86	95.18	95.72	95.08	95.61
6.	75	92.52	92.42	92.28	91.58	91.88	92.14
7.	90	90.43	89.41	89.67	88.34	88.56	88.26

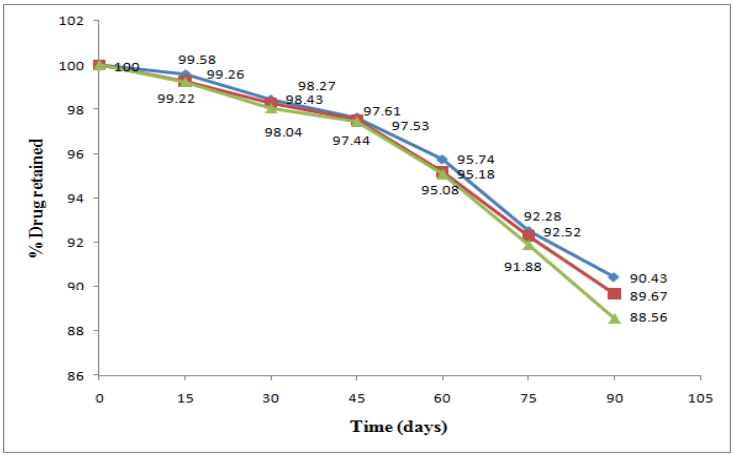


Figure 23: Stability study of formulation FC3 (♦ at 25^0 C, ■ at 40^0 C, ▲ at 50^0 C).

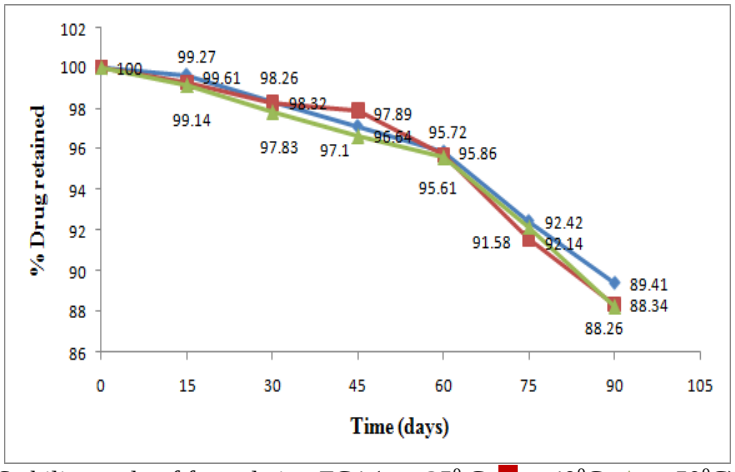


Figure 24 : Stability study of formulation FC4 (♦at 25^0 C, ■ at 40^0C, ▲ at 50^0C).

In order to develope mucoadhesive microsphere of cefpodoxime proxetil, it was first identified by characteristics infrared spectra and then it was subjected to melting point determination, partition coefficient determination and solubility analysis. After that the drug was analysed in UV spectrophotometer by constructing standard curve in 0.1 N HCl (pH-1.2). It was found that the drug was confirming all the pharmacopoeial standards with respect to melting point, partition coefficient, solubility, wavelength of maximum absorption (λmax) and the characteristics of I R spectra. The plain sodium CMC absorption peaks found at 1751.43, 1419, 1319.35, 1085.13 and 1033. The plain sodium alginate absorption peaks found at 2921.43, 2850, 1419.35, 1085.13 and 1033cm^{-1}. The plain carbopol-934 absorption peaks found at 3602.31, 2954.16, 1712.31, 1452.34, 1409 and 1244 and λmax was 263 nm.

Polymer used in formulation of microspheres, may interfere in the estimation of drug. Hence the interference due to these polymers was checked by using the maximum concentration of polymers with drug solution. This polymer and drug solution was filtered and then suitably diluted. This diluted solution was subjected to UV scanning between 220-400 nm. The data tells that there is no significant interference of polymers observed inestimation of drug. The mp of cefpodoxime proxetil was found to be 111^0C. The PC of cefpodoxime proxetil was found to be 5.1 (lipophilic). The SEM of microspheres of formulation. The data of the various models revealed that formulation FC1, FC3, FC5, FC6, FC7 follows Peppas model with r^2 value of 0.995, 0.985, 0.996, 0.996, 0.997 and n value of 1.094, 1.032, 1.042, 1.054, 1.042 respectively. Values of n are above 0.89 and thus release can be concluded as by super case 2 transport. Formulations FC2 and FC4 follows zero order release kinetics with r^2 value of 0.991,0.998 respectively.

Conclusions

In order to develop mucoadhesive microsphere of cefpodoxime proxetil, it was first identified by characteristics infrared spectra and then it was subjected to melting point determination, partition coefficient determination and solubility analysis. The PC of cefpodoxime proxetil was found to be 5.1 (lipophilic). From the study it is evident that promising controlled release mucoadhesive microspheres of cefpodoxime proxetil can be developed by solvent evaporation techniques by using polymers for reduced dosing frequency and better patient compliance therapy.

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