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Research Article

Enhancement of Bioavailability of Cefpodoxime Proxetil Using Different Polymeric Microparticles

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Abstract. Poorly water-soluble drugs such as cefpodoxime proxetil (400 μg/ml) offer a challenging problem in drug formulation as poor solubility is generally associated with poor dissolution characteristics and thus poor oral bioavailability. According to these characteristics, preparation of cefpodoxime proxetil microparticle has been achieved using high-speed homogenization. Polymers (methylcellulose, sodium alginate, and chitosan) were precipitated on the surface of cefpodoxime proxetil using sodium citrate and calcium chloride as salting-out agents. The pure drug and the prepared microparticles with different concentrations of polymer (0.05–1.0%) were characterized in terms of solubility, drug content, particle size, thermal behavior (differential scanning calorimeter), surface morphology (scanning electron microscopy), *in vitro* drug release, and stability studies. The *in vivo* performance was assessed by pharmacokinetic study. The dissolution studies demonstrate a marked increase in the dissolution rate in comparison with pure drug. The considerable improvement in the dissolution rate of cefpodoxime proxetil from optimized microparticle was attributed to the wetting effect of polymers, altered surface morphology, and micronization of drug particles. The optimized microparticles exhibited excellent stability on storage at accelerated condition. The *in vivo* studies revealed that the optimized formulations provided improved pharmacokinetic parameter in rats as compared with pure drug. The particle size of drug was drastically reduced during formulation process of microparticles.

KEY WORDS: cefpodoxime proxetil; chitosan; methylcellulose; microparticles; sodium alginate.

INTRODUCTION

One of the major challenges is to synthesize any new molecule that is pharmacologically active for researchers and pharmaceutical companies. Out of this research, around 40% of lipophilic drug candidates fail to reach the market although exhibiting potential pharmacodynamic activities. More than 90% of drugs approved since 1995 have poor solubility, poor permeability, or both (1). Many compounds currently under development are Biopharmaceutical Classification System Class II compounds, *i.e.*, high permeability but poor solubility. These physicochemical characteristics may be inherent in the chemical structure of the drug compounds but may also result from optimization of lead compounds to enable site or receptor specificity (2,3). Poorly water-soluble drugs often show low bioavailability when administered orally because the absorption of the drugs in the gastrointestinal tract can usually be a rate-limiting step (4).

Cefpodoxime proxetil is an orally absorbed, broad spectrum, third-generation cephalosporin ester implicated in treatment of upper respiratory tract and urinary tract infections (5). Although cefpodoxime proxetil, the prodrug ester, is hydrolyzed *in vivo* to its active metabolite, cefpodoxime is designed to improve the permeability and thus bioavailability of the parent molecule cefpodoxime acid (CA); it still has only 50% oral bioavailability when administered orally as a 132-mg tablet, equivalent to 100 mg of cefpodoxime in humans (6). Cefpodoxime proxetil is a non-crystalline, slightly basic compound and is absorbed from the gastrointestinal tract after oral administration and hydrolyzed to its parent moiety CA by nonspecific esterases in the intestinal wall/plasma (7).

The reasons for low oral bioavailability of cefpodoxime proxetil are mainly attributed to low water solubility (400 μg/ml), typical gelation behavior of cefpodoxime proxetil particularly in acidic environments (6–8), and pre-absorption luminal metabolism of its ester side chain by digestive enzymes cholinesterases present in the intestinal lumen into CA (9).

Micronization for dissolution rate enhancement of poorly water-soluble drugs by a precipitation method in the presence of stabilizing agents (*e.g.*, chitosan and different types of cellulose ethers), followed by applying anti-solvent to the formed dispersion, was reported by Rasenack and Müller (10), where the polymer was dissolved in water/dilute glacial acetic acid and the drug was then added into it, homogenized, and then precipitated by rapidly pouring salt solution into the drug solution (10). We tried to utilize the same concept in enhancement of bioavailability of cefpodoxime proxetil. The usage of natural polymers as drug carriers is on an increasing

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Table I. Percent Yield, Percent Drug Content, Percent Drug Released, and Saturated Solubility of Cefpodoxime Proxetil with Different Polymeric Preparations

Preparation of cefpodoxime proxetil	Salt solution	Concentration of salt solution (%)	Concentration of polymer solution (%)	Percent yield	Particle size (nm)	Percent drug content	Percent drug released in 30 min	Saturation solubility±SD (μg/ml)	
								Water	Buffer (pH 3)
Cefpodoxime proxetil	–	–	–	–	5,760	–	42.15±2.801	266.67±2.90	305.066±2.82
Methylcellulose	Sodium citrate	22	0.75	97.123±0.633	911	97.913±0.203	94.470±3.296	657.012±2.00	693.723±4.001
Sodium alginate	Calcium chloride	3	0.75	96.243±1.694	5,770	97.471±1.243	94.406±2.156	634.31±5.426	697.33±3.703
Methylcellulose: sodium alginate	Sodium citrate:calcium chloride (1:1)	22.3	0.75	97.618±0.726	516	97.296±0.8578	60.670±3.720	714.88±1.726	817.39±11.962
Chitosan	Sodium citrate	3	0.4	96.816±1.628	571	97.195±1.243	96.051±3.650	744.71±3.384	818.84±4.7891

Fig. 1. Infrared spectra of **a** cefpodoxime proxetil, **b** methylcellulose, **c** methylcellulose formulation, **d** sodium alginate, **e** sodium alginate formulation, **f** methylcellulose–sodium alginate mixture, **g** methylcellulose–sodium alginate formulation, **h** chitosan and **i** chitosan formulation

side because of their low cost, biocompatibility, and biodegradability (11). The main aim of this work was to improve the bioavailability of cefpodoxime after oral administration of cefpodoxime proxetil in different polymeric formulation such as methylcellulose, sodium alginate, and chitosan microparticles.

MATERIALS AND METHODS

Materials

Cefpodoxime proxetil was obtained as a gift sample from Ranbaxy, Gurgaon, India. Chitosan (minimum 85% deacetylated) was procured as a gift sample from crab shells from the National Fisheries Institute, Bhuwneshwar, India. Methylcellulose (300–500 CPS LR grade), sodium alginate (LR grade), and hydrochloric acid (35–38%) were purchased from CDH (P) Ltd., New Delhi, India, and glacial acetic acid (99.5%) was purchased from Qualigens Fine Chemicals, Mumbai, India, respectively. Sodium citrate (99%) was purchased from SRL Pvt. Ltd., Mumbai, India. The solvents used for analysis were of high-performance liquid chromatography (HPLC) grade. All other chemicals were of analytical grade.

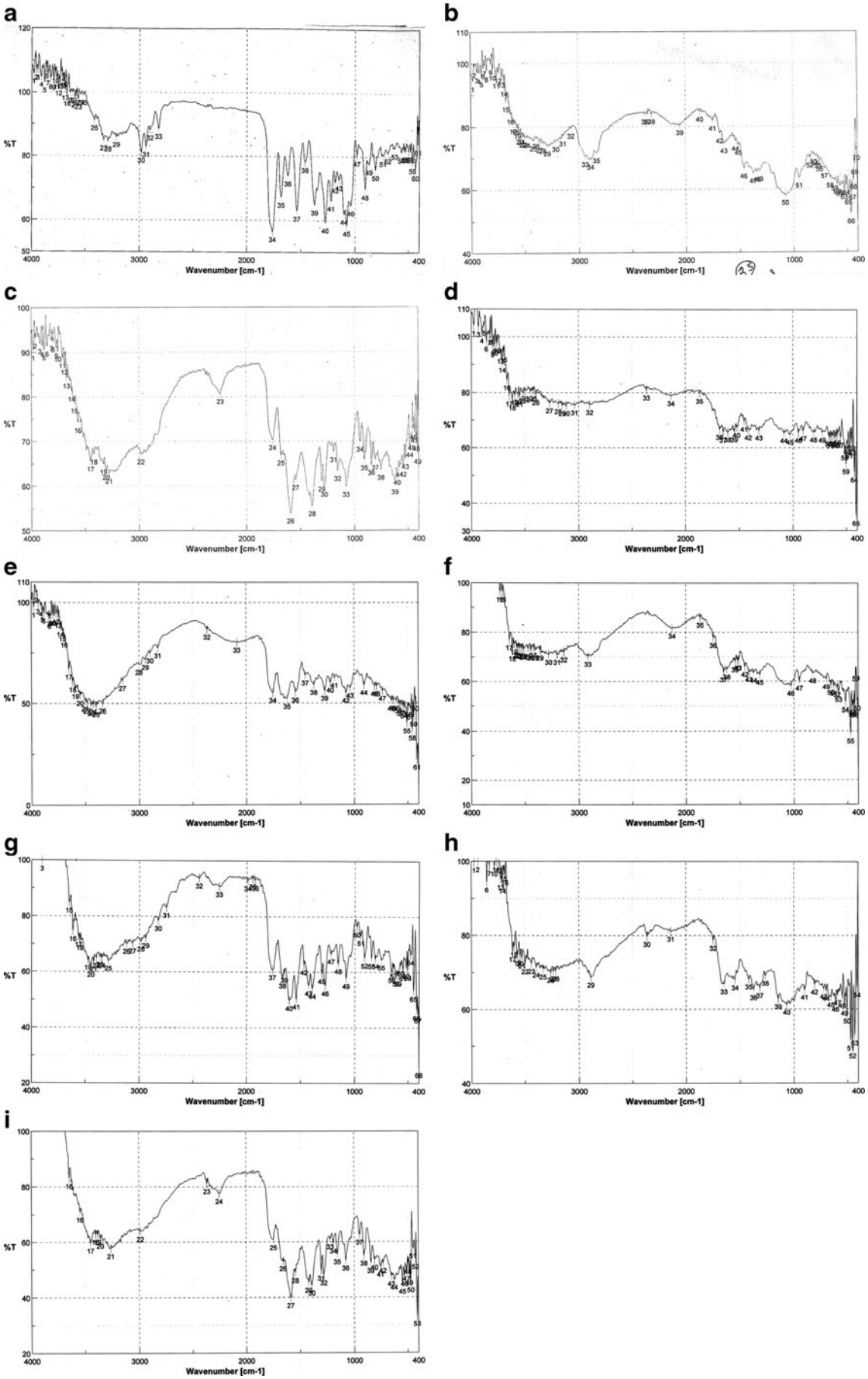
Method

Preparation of Microparticles

A weighed amount of the drug was dispersed in different polymeric solution (30 ml) by using high-speed dispersion homogenizer (Remi Motors, Mumbai) at 18,000 rpm for 20 min. This dispersion was then added to sodium citrate/calcium chloride/mixture of sodium citrate and calcium chloride solution to precipitate polymeric solution on the drug particles (Table I). The precipitate obtained was filtered through Whatman No. 1 filter paper and dried at 60°C for 24 h. The dried product was then passed through sieve No. 85 to obtain a uniform size distribution (12).

Characterization of Microparticles

1. Practical yield
   The percentage practical yield of formulations was calculated by comparing accurately weighed quantity of prepared formulation and sum of initially taken quantity of drug and *polymers* rationally to all formulations (Table I).
2. Solubility
   An excess quantity of cefpodoxime proxetil (5 mg) and prepared microparticles (equivalent to 5 mg drug) was placed in separate bottles containing 10 ml of different solutions (water and buffer pH 3.0±0.1). The bottles were agitated in shaking water bath (100 agitations/min) for 24 h at room temperature. The solution was then passed through a membrane (0.45 μm), and the amount of the drug dissolved


a
b
c
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Wavenumber [cm-1]

was analyzed spectrophotometrically (UV-1700, Shimadzu, Japan) at 260 and 260.5 nm for water and phosphate buffer (pH 3.0±0.1), respectively (Table I).

3. Drug content
   For the determination of drug content, prepared microparticles (10 mg) were dissolved in 10 ml of phosphate buffer (pH 1.2), and finally, the volume was made up to 100 ml with the same. The solution was filtered through a membrane (0.45 μm) and analyzed spectrophotometrically for drug content after sufficient dilution with phosphate buffer (pH 1.2), and results are given in Table I.
4. Particle size determination
   The mean particle size of pure drug and prepared microparticles was determined by laser light scattering technique using Malvern (CIS-50) particle size analyzer (Malvern, USA). Results are given in Table I.
5. Infrared (IR) spectroscopy
   Infrared (IR) spectroscopy was conducted using a Fourier transform infrared spectrophotometer (FTIR 470 *plus* JASCO-SPEC, Japan), and the spectrum was recorded in the wavelength region of 4,000–400 cm^{-1}. The procedure consisted of dispersing a sample (drug alone, mixture of drug and polymers, or prepared co-microparticles) in KBr. The sample was placed in the light path in sample holder, and the spectrum was recorded. All spectra were collected at a resolution of 2 cm^{-1} (Fig. 1) (13).
6. Differential scanning calorimetry (DSC)
   Differential scanning calorimetry (DSC) was performed using Jade DSC (Perkin Elmer, Japan) calorimeter to study the thermal behavior of plain drug and prepared microparticles. The instrument comprised of calorimeter (DSC 60), flow controller (FCL60), thermal analyzer (TA 60), and operating software (Pyris 6 DSC). The samples were heated in hermetically sealed aluminum pans under nitrogen flow (20 ml/min) at a scanning rate of 10°C/min (Fig. 2).
7. Surface morphology
   (a) Light microscopy
   The surface morphology of pure drug and prepared formulation was studied by light microscope (LABOMED CXR2, Japan) at ×400. The sample was mounted on a glass slide, covered with cover slip, and viewed under light microscope.
   (b) Scanning electron microscopy (SEM)
   The surface characteristics of the pure drug and prepared microparticles with different polymer were studied by scanning electron microscopy (SEM) (JEOL, JSM 50A, Tokyo, Japan) at various resolution. The samples were mounted on double-sided adhesive tape that has previously been secured on glass stubs, air-dried, and stub were then placed into fine coat ion sputter for gold coating and analyzed for surface morphology of microparticles (Fig. 3).
8. Dissolution studies
   Dissolution of cefpodoxime proxetil is pH dependent (14); *in vitro* dissolution studies were carried out using USP type 1 dissolution apparatus (Scientific Ltd., Mumbai, India). The study was carried out in 900 ml of buffer (pH 3.0). Dissolution medium was kept in a thermostatically controlled water bath, maintained at 37±0.5°C. The basket was rotated at 50 rpm. At predetermined time intervals, 5 ml of samples was withdrawn and assessed for drug release spectrophotometrically at λmax 260 nm.

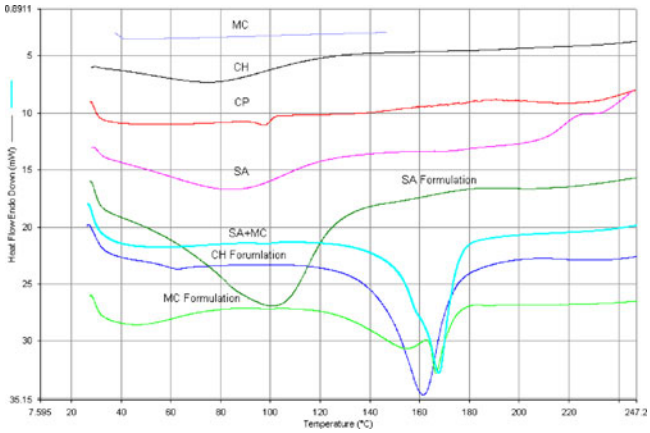

Fig. 2. Differential scanning thermograms of drug and polymers. *CP* cefpodoxime proxetil, *MC* methylcellulose, *SA* sodium alginate, *CH* chitosan, *MC:SA* methylcellulose:sodium alginate formulation, *MC formulation* methylcellulose formulation, *SA formulation* sodium alginate formulation, *CH formulation* chitosan formulation

   At each withdrawal, 5 ml of fresh dissolution medium was added to dissolution jar. Results are shown in Fig. 4.
9. Stability studies
   After determining the drug content, the optimized crystals were charged for the accelerated stability studies according to ICH guidelines (40±2°C and 75±5% RH) for a period of 6 months in stability chamber (Thermolab, Mumbai, India). The samples were placed in USP type 1 flint vials and hermetically sealed with bromobutyl rubber plugs and aluminum caps. Five milligrams of the stored crystals (n=3) were taken out at 15, 30, 60, 90, and 180 days and evaluated for the drug content and physical changes (Table II).
10. *In vivo* studies
    (a) Animal and dosing procedure
    Male Wistar rats weighing 200–250 g were divided into five groups corresponding to the four formulations and one group as control; each group comprises of six rats. The single oral dose of formulations MCR, SAR, MCSAR, DCHR, and pure drug was administered to rats of groups 1, 2, 3, 4, and 5, respectively, as in galenic form. The amount of cefpodoxime proxetil in each one of these formulation was adjusted to contain equivalent to 10 mg/kg of CA as active metabolites of prodrug. Animals were anesthetized by diethyl ether, and anesthesia was maintained by addition dose of diethyl ether. Blood sample (about 0.3 ml) was collected from the retro-orbital route just before (0 h) and after dosing: up to 12 h in a heparinized microcentrifuge tube, stored on ice until further analysis. All studies were approved by the Institutional Animal Care and Use Committee and were conducted in accordance with the NIH guidelines for the care and use of laboratory animals (15,16,17).
    (b) Sample preparation
    Plasma samples were precipitated with 12% perchloric acid in a 1:2 ratio of plasma and perchloric acid; the supernatant was mixed with organic solvent mixture (chloroform:1-butanol=3:1) in a 1:1 ratio and centrifuged at 6,000×g for 3 min at room temperature. The supernatant (20 μL) was injected into the HPLC system (15).

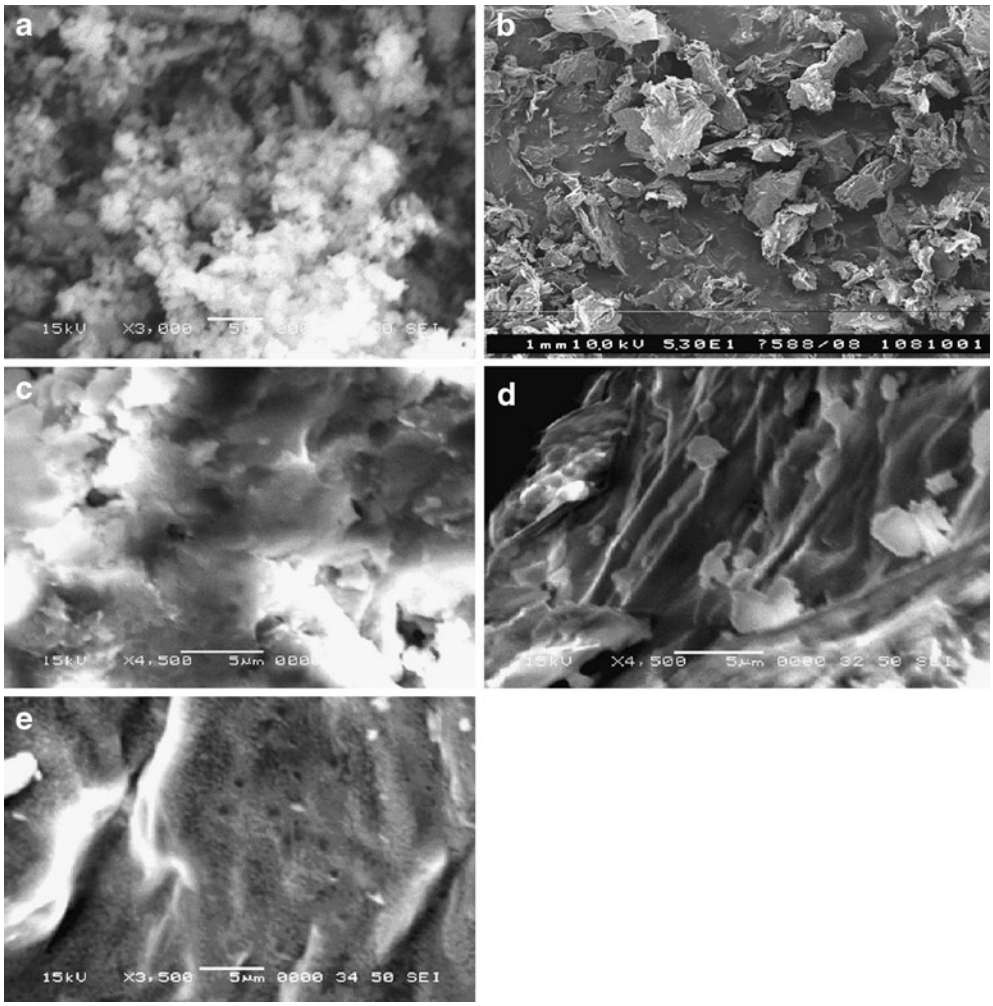

Fig. 3. SEM photograph of **a** cefpodoxime proxetil (×3,000), **b** methylcellulose microparticles (×1,600), **c** sodium alginate microparticles (×4,500), **d** methylcellulose:sodium alginate microparticles (2:3; ×4,500), and **e** chitosan microparticles (×3,500)

(c) Analytical methods

HPLC analytical method was utilized for detecting the quantities of cefpodoxime proxetil and CA from the biological samples. The detection of cefpodoxime proxetil and CA was performed by two separate HPLC methods based on reversed phase columns. An HPLC system (Shimadzu Corporation, Japan), equipped with a UV–Vis spectrophotometric detector and data acquisition software (CLASS-VP, version 6.14 SPD), was utilized for the purpose. Both HPLC methods employed acetonitrile:ammonium acetate buffer (pH 5.0) as mobile phase (at 40:60 and 25:75 for cefpodoxime proxetil and CA, respectively), pumped at a flow rate of 1 ml/min, and analysis was carried out at a temperature of 30°C and at 235 nm. The method employed for quantifying the cefpodoxime proxetil had a calibration range of 5–150 µg/ml with an LOQ of 900 ng/ml, an accuracy of 98.45–101.63%, and intra- and inter-day precision values of %RSD of 0.95–4.29. Similarly, the analytical method employed for quantification of CA had an LOQ of 50 ng/ml and operated in concentration range of 2.5–80 µgml at a detection of 269 nm with an accuracy of 93.68–107.09% and intra- and inter-day precision values with a %RSD in the range of 0.76–4.7 (06). The results of pharmacokinetic data are given in Table III.

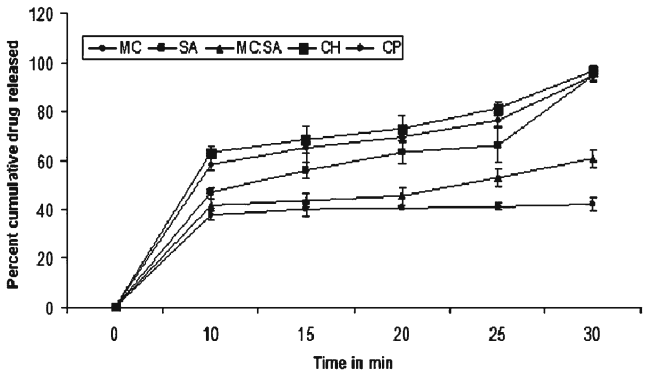

Fig. 4. Percent cumulative drug released from microparticles

RESULTS AND DISCUSSION

The solubility, dissolution pattern, and gelation behavior of cefpodoxime proxetil, particularly in acidic environments, are the main concern of its oral bioavailability. The solubility data of cefpodoxime proxetil reveals that it is poorly soluble in water. Therefore, the improvement of cefpodoxime prox-

Table II. Stability Study of Different Formulations

Formulation code	Time in days					
	0 day	15 days	30 days	60 days	90 days	180 days
MC	100±0.00	99.65±0.56	99.15±0.61	98.93±0.67	97.88±0.78	96.76±0.72
SA	100±0.00	99.48±0.39	99.23±0.49	98.82±0.72	97.78±0.66	96.39±0.73
MC:SA	100±0.00	99.57±0.63	99.34±0.52	98.45±0.92	97.74±0.84	96.56±0.62
CH	100±0.00	99.87±0.52	99.13±0.65	98.19±0.73	97.34±0.76	96.34±0.62

MC methylcellulose, *SA* sodium alginate, *MC:SA* methylcellulose:sodium alginate, *CH* chitosan

etil dissolution and avoidance of gelation behavior from its oral solid dosage forms is of great importance.

It has been reported that polymers with positively or negatively charged groups interact with molecules of opposite charges to form three-dimensional networks. The reaction of methylcellulose, sodium alginate, and chitosan with multivalent anions like sodium citrate and calcium chloride (anion cross-linker) allows the formation of bridges between the polymeric chains and results in inter-cross-linking (by electrostatic interaction) between the polymer molecules, which might have eventually resulted in efficient adsorption of polymer on drug particles. Hence, in the present work, we prepared different polymeric-based microparticulate systems in order to improve the solubility and dissolution of cefpodoxime proxetil in aqueous and acidic media, which could improve its oral bioavailability problems. For this purpose, we selected different polymers (sodium alginate, methylcellulose, and chitosan), which could get precipitated on the surface of micronized drug particles and prevent its gel formation and aggregation at the site of absorption and improve its bioavailability. The developed microparticles were characterized for solubility, drug content, particle size, thermal behavior (DSC), surface morphology, *in vitro* drug release, stability studies, and *in vivo* pharmacokinetic studied of formulations.

Practical Yield, Solubility, Drug Content, and Particle Size Study

The practical yields of formulations ranged from 96% to 97%. The results showed that no significant difference in yield of microparticles was observed with different polymers. Results are given in Table I.

The solubility of cefpodoxime proxetil in distilled water was very less (266.67±2.90 μg/ml) as compared to buffer (pH 3) solution (305.066±2.82 μg/ml). The solubility of drug in formulations was found to be increased due to optimum homogenization and complete adsorption/co-precipitation of polymers on the surface drug particles. The other reason for increased solubility might be due to the particle size reduction, as the particles of the drug underwent impact and attrition during homogenization and resulted into size reduction that influenced the surface area of particles which improved the solubility of cefpodoxime proxetil. The results are summarized in Table I.

The drug content was found to be superior and uniform (97%) for all formulations, as all formulations formed clear homogenized dispersion which could entrapped maximum amount of drug (Table I).

The particle size of all the prepared formulation was considerably reduced during the preparation process. This might be due to high attrition during the homogenization process. The pure drug cefpodoxime proxetil showed an average particle size at 5,760 nm. The size reduction was achieved with all formulations, however, as the average particles size was found to be much reduced with microparticles of combination of methylcellulose and sodium alginate (MC:SA) and chitosan microparticles as compared with other formulation and pure drug particles. These formulations exhibited the highest solubility and dissolution rate of cefpodoxime proxetile as compared to pure drug particles.

Infrared (IR) Spectroscopy

The possible interaction between the drug and excipients was studied by IR spectroscopy. IR spectra of pure cefpodoxime proxetil, sodium alginate, chitosan, mixture of sodium alginate and methylcellulose, and prepared formulations were determined with FTIR spectrophotometer (Shimadzu, Japan). Pure cefpodoxime proxetil showed major peaks at

Table III. Pharmacokinetic Parameters for Drug and Formulation

Pharmacokinetic parameters	Drug	Methylcellulose formulation	Sodium alginate formulation	Methylcellulose and sodium alginate (2:3) formulation	Chitosan formulation
K (/h)	0.207±0.003	0.224±0.038	0.398±0.021	0.130±0.049	0.189±0.034
Ka (/h)	0.573±0.024	0.570±0.098	0.506±0.129	0.535±0.174	0.538±0.116
C_{max} (μg/ml)	5.886±0.403	16.590±0.772	15.831±0.791	12.371±0.674	19.771±1.283
t_{max} (h)	2.780±0.171	2.691±0.123	2.302±0.131	3.480±0.134	2.991±0.073
$t_{1/2}$ (h)	3.346±0.091	3.091±0.175	1.741±0.044	5.318±0.097	3.656±0.162
Cl (ml/min)	0.207±0.0481	0.224±0.043	0.398±0.078	0.130±0.005	0.189±0.002
AUC (μgmin/ml)	25.822±1.298	73.172±2.660	61.015±1.780	56.851±2.513	75.491±3.104
Comparative bioavailability	100%	280%	234%	215%	290%

2,823.28, 1,760.69, 1,780.66, 1,618.95, 1,274.72, 808.992, and 693.28 cm^{-1}, while prepared formulations were also shown their respective peaks at different wave numbers. The IR spectra of formulations showed all characteristic peaks (3,418, 1,754, 1,678, 1,078, 805, and 620 cm^{-1}) of pure drug and polymers, and no extra characteristic peaks were observed in the IR spectra of formulations which indicated the absence of any interaction between drug and polymers (Fig. 1a–i).

Differential Scanning Calorimetry (DSC)

The DSC of pure drug and formulations was carried out at temperatures ranging between 30°C and 400°C with heat flow rate of 100°C/min. The results of DSC studies of pure cefpodoxime proxetil did not show any sharp melting endotherm between 30°C and 250°C, whereas in case of physical mixture of drug and different polymers (cefpodoxime proxetil+methylcellulose/sodium alginate/chitosan), there was no considerable change in the melting endotherms as compared to when pure drug was observed. This observation indicated the absence of any chemical interaction between the drug and polymers used in preparation (Fig. 2).

Surface Morphology

In order to clarify the causes of significant difference in the dissolution rate and solubility, the surface morphology of the preparation was examined by optical microscope and SEM. The remarkable change in surface morphology of formulation as compared to drug particles was visualized through both optical microscopy and SEM.

In case of pure drug larger particles, sticky and hazy structures were seen in all photographs; however, fine and fluffy state along with porous and rough surface structure was observed in case of formulations. The change in surface morphology and fluffy physical state of formulations may also contribute to the enhanced solubility and dissolution rate of cefpodoxime proxetil from the formulations; the SEM photographs are given in Fig. 3a–e.

Dissolution Studies

Among the various methods investigated to select suitable dissolution medium, the selected media (phosphate buffer pH 3) containing surfactants were proposed as a suitable method for dissolution studies of drug. As various surfactants are present in the gastrointestinal fluid, *e.g.*, bile salts, lecithin, cholesterol, and its esters, in the present study, the glycine was added into the dissolution media to simulate the gastric fed condition because food has been shown to alter the cefpodoxime bioavailability from tablets by increasing the extent of absorption of cefpodoxime proxetil (18).

The pure drug showed the maximum cumulative drug release of 42.15±2.801% that was very less compared to all dissolution values of formulations. The maximum dissolution of drug was found to be with chitosan particles (96.051±3.6%). The decrease dissolution rate was observed with MC:SA microparticles, which can be attributed to viscous gel formation by polymers on the surface of drug particles.

Stability Studies

The results of accelerated stability studies carried out according to ICH guidelines indicated that microparticles did not show any physical changes during the study period, and the drug content was found to be more than 96% at the end of 6 months in accelerated conditions. The values for drug content (n=3; mean±SD) in microparticles were given in Table II. The results indicated that the formulations were quite stable at accelerated storage conditions.

In Vivo Studies

Generally, the degradation of the prodrug esters progressed faster in intestinal juice than in phosphate buffer (19). Comparative data of CA plasma concentration of test and reference at each sampling time in all the rats are shown in Table III. The time to reach maximum plasma concentration (t_{max}) in all the rats was 2.3 to 3.5 h. Plasma concentration–time profiles for all the formulations are shown in Fig. 5. The results clearly indicated the higher values of plasma concentration of all formulation as compared with pure drug at each sampling time for all the rats.

The bioavailability parameters *viz* C_{max}, t_{max}, and area under the curve (AUC; 0–12 h) for all the formulations are also shown in Table III. From the data, it can be concluded that there was a significant difference in the rate of absorption of cefpodoxime proxetil from these formulations. Absorption rate constant (Ka), half life ($t_{1/2}$), and elimination rate constant (CL) of sodium alginate or combination with sodium alginate were found to be lowest because sodium alginate gets converted into alginic acid that forms gel-like structure in acidic media, which reduces the absorption, $t_{1/2}$, and elimination of drug through gastrointestinal tract.

The C_{max} and AUC of chitosan and methylcellulose were found to be much more than other polymeric formulations. It revealed that the maximum amount and extent of drug absorption were achieved by chitosan and methylcellulose formulation, which is attributed to more particle size reduction of these formulations, which improves their absorption and bioavailability of drug (Table III). The t_{max} of mixture of methylcellulose and sodium alginate formulation was observed to be greater than other polymeric formulation, due to the thick coating of drug particles with polymers which

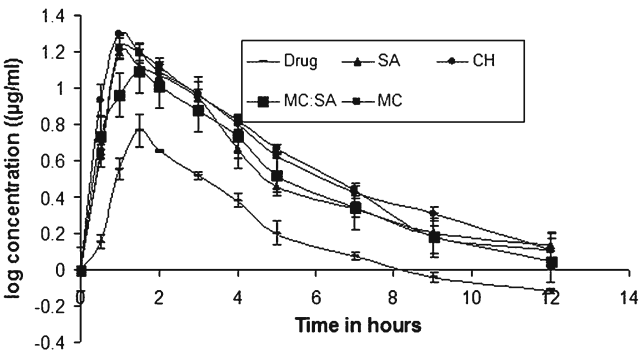

Fig. 5. Comparative *in vivo* release (concentration *versus* time) of cefpodoxime proxetil from different polymeric microparticles

act as a barrier for release of drug from the system and resulted into delay absorption of drug.

CONCLUSIONS

It has been shown that formulations of cefpodoxime proxetil as microparticles have met great success in regards to dissolution rate and saturation solubility enhancement. In an acidic environment, the drug particles get aggregated and form fluffy gel-like structure which interrupt the exposure of drug to dissolving media, and finally, the solubility of drug suffered. The adsorption of polymer on the drug surface provided the barrier between drug particles to come in direct contact with dissolution medium, by which gelling of the drug could be avoided. The *in vivo* studies in albino rat showed improved pharmacokinetic parameter as Ka, $t_{1/2}$, AUC, and bioavailability of drug due to maximum absorption of drug from gastrointestinal route as a resultant of size reduction and prevention of gel formation of drug molecules. It facilitates maximum drug in solution which improves the dissolution rate followed by solubility of drug and hence absorption.

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