Original Article

Cefuroxime Axetil Loaded Dispersed Formulation for Enhanced Drug Release and Antibacterial Activity

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ABSTRACT

Aim: Aqueous solubility of drugs is a determining factor for bioavailability in systemic circulation and confronts in the unbeaten formulation of therapeutic agents. Cefuroxime axetil (CA) is a broad-spectrum β-lactamase cephalosporin that pertains to class II drugs under Biopharmaceutical Classification System (BCS) with poor aqueous solubility and high absorption permeability after oral administration. The objective of this current work was to achieve the enhanced solubility in water and subsequent antibacterial activity of CA loaded coarse dispersion (CCD) formulations. **Materials and Methods:** CCDs were prepared by anti-solvent precipitation method by blending CA with a carrier, Microcrystalline cellulose (MCC) at different ratios. *In-vitro* dissolution test using paddle method and antibacterial study against *Staphylococcus aureus* (ATCC 25923) and *Escherichia coli* (ATCC 25922) were carried out for both pure CA and CCDs for performance comparison. **Results:** Among the formulations, CCD-3 exhibited maximized dissolution rate by 1.67-fold higher than that of pure CA with the drug-carrier (CA: MCC) ratio of 1:3. Antibacterial activity of CCD-3 against *S. aureus* and *E. coli* was also found by 1.75-fold and 5.25-fold higher relative zone of inhibition (RZOI), respectively than that of pure drug. **Conclusion:** As an optimized formulation, CCD-3 is a promising to be a fruitful substitute to conventional dosage forms of CA for the modified dissolution rate and antibacterial potency. However, before its recommendation as a novel formulation validation study to point its pharmacokinetics, competence with *in-vivo* antibacterial property and safety is needed.

Keywords: Cefroxime axetil, Coarse dispersion, Solubility, Dissolution, Antibacterial activity.

INTRODUCTION

The oral delivery of drugs has been the most popular and commonly employed route due to its advantages such as ease of administration, high patient compliance, cost-effectiveness, high production output, least need for maintenance of sterile condition and flexibility in the dosage form design.[1] Bioavailability after oral administration of a drug is a very important consideration for therapeutic success and it can be influenced by several factors viz., its solubility in water, permeability through membranes, rate of dissolution, first pass metabolism, biotransformation and sensitivity to efflux mechanisms.[2] Amongst these, dissolution is the rate determining step during absorption of poorly aqueous soluble drugs leading to inadequate bioavailability.[3]

There exists a challenge for the pharmaceutical scientists always to develop formulations that can overcome the hurdle of poor solubility and to maximize the bioavailability in systemic circulation upon oral delivery. To circumvent the obstacles; various techniques improving drug solubility for enhancing bioavailability are in practice for long. The reported approaches are solid dispersion, anti-solvent precipitation, dry suspension and dry emulsion, lipidic dispersion, nanosuspension, drug dispersion

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in carriers, selective adsorption on insoluble carrier, co-solvents, cryogenic techniques etc.[4-5]

In recent years, a number of dispersion techniques have been introduced to stand against the obstacle with poorly water-soluble drugs without requiring expensive equipment or facilities. In dispersion technique, a drug substance is dispersed or embedded in a chemical entity so called carrier or continuous phase. There are a number of ways to classify dispersion, for example, the size and the state of dispersed matter. In general, three types of dispersions, such as- (i) coarse dispersions (e.g., suspensions); (ii) colloidal dispersions (e.g., nanoparticles); and (iii) molecular dispersions (e.g., true solution, liquid or solid state) are categorized. However, dispersion technique may be applied as a simple method to improve dissolution efficiency of poorly aqueous-soluble drugs to solve the difficulties of limited solubility and bioavailability.[6]

Coarse dispersions (CDs) are heterogeneous systems in which the particle size is existing more than 1000 nm. These are ascertained by relatively fast sedimentation of the particles from the continuous phase in filtration mediated by gravity or other forces. The evolution of CDs is effectively employed technique to augment bioavailability of poorly water-soluble drugs as well as to overcome the drawbacks of previously proposed approaches such as formation of salt, using co-solvents and reducing particle size etc. Further, the CD has added advantages like improved oral absorption, dose proportionality, low inter-subject variability apart from its simplicity and cost effectiveness over other techniques. Although various methods can be employed to prepare CDs, anti-solvent precipitation method is much convenient for its fast and ease preparation technique. In addition, this method can be conducted at ambient temperature and pressure avoiding the engagement of expensive equipment.[7]

Cefuroxime axetil (CA), a broad-spectrum β-lactamase-stable acetoxyethyl ester of cefuroxime has antibacterial sensitivity against both Gram-positive and Gram-negative bacteria.[8] CA has been found very effective in the treatment of genitourinary, skin and soft-tissue infections and erythema migrans associated with early stage of Lyme disease. Moreover, it is safer than other cephalosporin and penicillin antibiotics, because it does not boost any allergic reaction.[9] But being a BCS (Biopharmaceutical Classification System) class II drug, CA is poorly soluble in biological fluids which, upon oral administration may result inadequate bioavailability. Practically, its solubility in water is 107 mg/L at 25°C and it exhibits low and/or inconsistent bioavailability. So, CA requires comparatively higher therapeutic dose to get desired pharmacological effect.[10] Our present investigation provides formulations of CA loaded coarse dispersions (CCDs) using Microcrystalline cellulose (MCC; Avicel PH-102) as a continuous phase to demonstrate the enhanced dissolution and bioavailability in comparison to that of pure CA. Further, enhanced bioavailability was translated to assess the therapeutic implication of optimized CCDs through antibacterial susceptibility study *in-vitro* against both Gram-positive and Gram-negative bacteria. To the best of our knowledge, observation of the present investigation is unique in nature as far as coarse dispersion formulation technique and antibacterial efficacy evaluation are concerned.

MATERIALS AND METHODS

Materials

Cefuroxime axetil (micronized) and Avicel PH-102 (MCC) were generously gifted by Square Pharmaceuticals Ltd., Bangladesh. In this investigation analytical grade chemicals and solvents were used.

Preparation of Coarse Dispersions of Cefuroxime axetil

For preparation of CA loaded coarse dispersions (CCDs) anti-solvent precipitation method was employed. In brief, accurately weighed CA (100 mg) was dissolved in sufficient quantity of acetone and the solution was incorporated drop by drop into 200 mg of MCC dispersed in distilled water (where water served as anti-solvent) with continuous stirring on a hotplate stirrer (Wisd, Korea) at 320 rpm to allow sufficient drug loading into MCC. This preparation (CCD-1) came out as a coarse dispersion with a ratio of 1:2 for CA and MCC. The same procedure was repeated for making CCD-2, CCD-3 and CCD-4 with the ratios of 1:2.5, 1:3 and 1:3.5, respectively by adjusting the quantity of MCC (Table 1).[11]

Dissolution Study

In-vitro dissolution study was performed to demonstrate the drug release pattern of pure CA and CCDs by paddle method (USP Apparatus II) with a dissolution

Table 1: Drug-carrier ratio of coarse dispersion formulations loaded with CA (CCDs).[11]

Formulation	Drug and Carrier	Ratio
CCD-1	CA and MCC	1:2.0
CCD-2	CA and MCC	1:2.5
CCD-3	CA and MCC	1:3.0
CCD-4	CA and MCC	1:3.5

tester (Tianjin Guoming Medicinal Equipment Co. Ltd.).[12-13] Demineralized (DM) water was used as a dissolution medium. In brief, sample equivalent to 13.5 mg of CA from each of CCD was poured in Fisherbrand dialysis tubing (MW: 12,000-14,000; width: 45 mm; wall thickness: 20 μm; dry cylinder diameter: 28.6 mm; volume/cm: 6.42) and immersed in 900 ml of dissolution medium in dissolution vessel. The dissolution conditions such as paddle speed and temperature were maintained at 50±2 rpm and 37.0±0.5°C, respectively. From the vessel the analyte samples (10 ml each) were withdrawn at 1, 5, 15, 30, 60, 120, 150, 180, 210, 240, 270, 300, 360, 420, 480, 540, 600, 660 and 720 min followed by the replacement of an equal volume of fresh dissolution medium. Content of CA at each point was assayed with a UV-spectrophotometer (UV mini-1240, Shimadzu, Japan) at 281 nm using a calibration curve. The mean values were calculated from three replicates of each sample. The average concentration value of CA was plotted against each sampling point to obtain the dissolution profile.

Antibacterial Activity of Pure CA and CCD-3 Formulation

Source of Bacteria

The antibacterial activity study of pure CA and CCD-3 (with the highest drug release among CCDs) was performed against *S. aureus* and *E. coli*. Bacterial strains were collected from the Microbiology Department of Rajshahi Medical College, Bangladesh.

Preparation of Antimicrobial Disks of CCD-3

10 ml of sample from CCD-3 were withdrawn from dissolution vessel at 60, 120, 180, 240, 300, 360, 420, 480, 540, 600, 660 and 720 min, respectively. The sample from each point was extracted separately with 5 ml of chloroform and this process was repeated 3 times. The aliquots were kept in small vials and allowed for drying. After complete drying, 300 μl of acetone were incorporated into each vial and shaken vigorously until the extracts are completely soluble in acetone. Each extracted sample was applied to a sterilized blank disk (Bio Maxima SA Poland); kept onto a sterilized Petri dish to get the theoretical concentration of CA by 30 μg/disk. Three replicates of each sample were prepared in this way. Finally, acetone was allowed to evaporate completely from the disk to make readily available for antibacterial testing.

Antibacterial activity Testing

The antibacterial efficacy of CCD-3 and pure CA was determined following disk diffusion method described by Kirby–Bauer. Colonies of both *S. aureus* and *E. coli* from fresh bacterial culture grown on Nutrient agar and MacConkey's agar respectively were inoculated into 5 ml of 0.9% saline solution. Inoculum's turbidity was matched with 0.5 McFarland standards to optimize inoculation at a concentration of 10^7 colony-forming units (CFU)/ml. 100 μl of inoculums were spread gently onto the surface of freshly prepared Mueller-Hinton agar medium using sterilized cotton buds. Care was taken to keep the culture plate free from accumulated moisture on its lid or surface of the agar before using the plates for inoculation. The test was performed by applying 5 μl aliquots of each culture on the agar plates. The bacterial inoculums without CA were added on each plate to determine the bacterial growth and medium for sterility control. Then antimicrobial disk of test samples withdrawn at different time were placed onto the inoculated medium and was allowed for diffusion into refrigerator for 3 hrs before final incubation. For comparison of zone of inhibition (ZOI) between CCD-3 and pure CA, disk prepared from pure drug (CA) was applied a reference at the centre of the medium and allowed to incubate at 37°C overnight. The ZOI around the disks was measured in mm.[14]

Determination of Relative Zone of Inhibition (RZOI)

To determine the RZOI, the diameter of ZOI of samples were divided by that of control disk on the same Petri dish by using the following equation:

$$RZOI = \frac{ZOIs}{ZOIc} \quad (i)$$

Where, RZOI = Relative zone of inhibition; ZOIs= Diameter of ZOI of sample; ZOIc= Diameter of ZOI of control

Statistical Analysis

Results were expressed as mean ± standard deviation (S.D.). Unpaired *t*-test using GraphPad Prism 8.0.1 was applied for assessing differences among groups. $p<0.05$ was considered statistically significant.

RESULTS

Dissolution Study

The dissolution results of CCDs and pure CA were plotted in MS Excel and the profiles are presented in Table 2 and Figure 1. The formulations (CCD-1, CCD-2, CCD-3 and CCD-4) showed enhanced drug dissolution than that of pure CA by 1.67, 2.00, 6.87 and 2.17-fold, respectively. The drug concentration 6.05 μg/ml produced by CA at 480 min was marked as the peak which is comparable with that of CCD-1, CCD-2 at

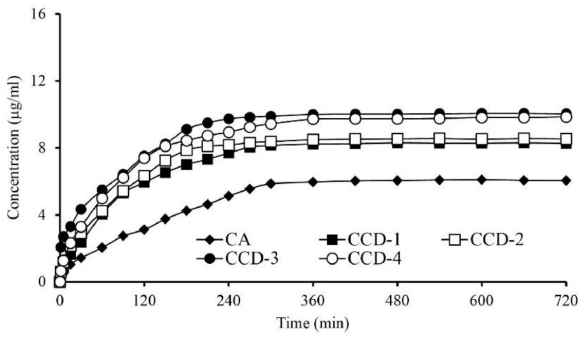

Figure 1: Dissolution profile of CA, CCD-1, CCD-2 and CCD-3. Each value represents mean ± S.D. (*n*=3).

120 min and of CCD-3, CCD-4 at 90 min, revealing the capability of CCD-3 and CCD-4 for faster drug release in water. Furthermore, the peak drug concentration obtained from CCD-1, CCD-2, CCD-3 and CCD-4 was 8.30, 8.56, 10.06 and 9.85 µg/ml at 480, 540, 600 and 720 min, respectively. Among the coarse dispersion formulations, significantly higher ($p<0.001$) drug concentration was found with CCD-3 as compared to CCD-1, CCD-2 and CCD-4 (Table 2). In a consequence, the formulation of CCD-3 with drug carrier ratio of 1:3 (CA: MCC) was taken into account as the best one for the superior drug release profile. Hence, CCD-3 was subjected for the test of antibacterial activity.

In-vitro Antibacterial activity of Pure CA and CCD-3

The optimized CCD-3 and pure CA were subjected for *in-vitro* antibacterial activity testing against both *Staphylococcus aureus* and *Escherichia coli*.

Relative zone of inhibition of CCD-3 against Staphylococcus aureus

The antibacterial activity testing of CCD-3 showed increase in RZOI gradually over pure CA against *Staphylococcus aureus* (Table 3 and Figure 2) up to 300 min and it was statistically significant ($p<0.01$).

Relative zone of inhibition of CCD-3 against Escherichia coli

Like *Staphylococcus aureus,* in case of *Escherichia coli*, RZOI exhibited gradual increment with time than pure CA (Table 4 and Figure 3) up to 480, which was also statistically significant ($p<0.001$).

DISCUSSION

The essential objective of a delivery system is to release therapeutic agents in adequate at the desired anatomical site and to keep up the systemic drug concentration between the margin of minimum effective concentration and minimum toxic concentration. Over the past decades, pharmaceutical engineering has taken great interest in enabling formulation for many drugs especially for the candidates having poor dissolution features. The efficient techniques viz minimizing a drug's size to improve its dissolution and bioavailability, can be accomplished only by specialized dispersion methods. The drugs that are poorly soluble in water and especially biopharmaceutical classification system (BCS) II ones, are preferably designed for oral dosage forms provided the dissolution limit can be improved.[15]

To ameliorate the oral bioavailability, coarse dispersion formulations of Cefuroxime axetil were carried out using MCC (Avicel PH-102) as carrier and anti-solvent precipitation as dispersion technique in the present study. Engineering of particles by anti-solvent precipitation is a trouble-free and efficient approach under bottom up methods for development of poorly water-soluble drug properties, in which mixing a drug solution with an anti-solvent creates super saturation resulting nucleation and simultaneous growth by condensation and coagulation. In our study, acetone was used as a solvent for CA and water was used as anti-solvent. Among various polar solvents that are capable to dissolve CA, acetone was employed because the drug of experiment is highly soluble in this solvent that rapidly evaporates at low temperature. Beside this, distilled water played as an anti-solvent due to its safety, availability and low cost.[16]

Through dissolution study, we observed the elevated drug release from CCD-3 (10.06 µg/ml) by 1.67-fold than that of pure CA at 600 min (Table 2 and Figure 1). This dissolution improvement of CA from drug-carrier systems can be attributed to several factors such as, minimizing drug's crystallinity, i.e. amorphization, increased wettability and dispersibility and particle size reduction. Increased hydrophilicity and amorphization through preparation of CCDs are thought to be the possible reasons of the improvement of dissolution. As indicative from dissolution data of physical mixtures, improvement could be attributed to higher wettability and dispersibility. Physical mixing of a hydrophobic drug and a hydrophilic carrier accelerates greater wetting affinity and increases available surfaces for dissolution by reducing interfacial tension between drug and dissolution media. In addition, as the drug micro-crystals were embedded in the water-soluble matrix and the hydrophilic carrier possesses the ability to be dissolved rapidly in dissolution medium, fast wetting of CA occurred resulting improvement in its dissolution rate.[17]

In literature review we found no work reporting such a formulation technique where MCC is used as a

Table 2: Dissolution profiles of coarse dispersions loaded with CA.

Time (min)	Concentration (µg/ml)				
	CA	CCD-1	CCD-2	CCD-3	CCD-4
1	0.30±0.050	0.50±0.055**^{c}	0.60±0.089**^{c}	2.06±0.056***	0.65±0.065**^{c}
5	0.51±0.058	0.85±0.085**^{c}	1.17±0.117***^{c}	2.70±0.116***	1.27±0.037***^{c}
15	1.03±0.076	1.64±0.115**^{c}	2.14±0.121***^{c}	3.30±0.128***	2.31±0.099***^{c}
30	1.43±0.029	2.36±0.169***^{c}	2.91±0.058***^{c}	4.33±0.096***	3.28±0.063***^{c}
60	2.04±0.086	4.04±0.111***^{c}	4.23±0.147***^{c}	5.50±0.167***	4.99±0.112***^{a}
90	2.74±0.050	5.30±0.032***^{c}	5.42±0.154***^{c}	6.43±0.085***	6.22±0.171***
120	3.12±0.160	5.94±0.139***^{c}	6.33±0.135***^{c}	7.52±0.032***	7.39±0.130***
150	3.75±0.125	6.53±0.146***^{c}	7.24±0.089***^{c}	8.24±0.160***	8.10±0.194***
180	4.24±0.132	7.01±0.178***^{c}	7.86±0.117***^{c}	9.11±0.147***	8.44±0.135***^{b}
210	4.63±0.086	7.32±0.128***^{c}	8.10±0.058***^{c}	9.50±0.111***	8.73±0.198***^{b}
240	5.13±0.100	7.69±0.055***^{c}	8.17±0.121***^{c}	9.74±0.195***	8.94±0.065***^{b}
270	5.55±0.104	8.04±0.194***^{c}	8.31±0.067***^{c}	9.83±0.096***	9.24±0.075***^{b}
300	5.86±0.152	8.15±0.085***^{c}	8.37±0.034***^{c}	9.89±0.192***	9.44±0.099***^{a}
360	5.96±0.125	8.23±0.178***^{c}	8.49±0.187***^{c}	10.00±0.056***	9.72±0.112***^{a}
420	6.03±0.050	8.25±0.146***^{c}	8.52±0.034***^{c}	10.02±0.064***	9.74±0.187***
480	6.05±0.076	8.30±0.200***^{c}	8.54±0.147***^{c}	10.02±0.170***	9.74±0.198***
540	6.03±0.100	8.28±0.085***^{c}	8.56±0.058***^{c}	10.04±0.179***	9.76±0.163***
600	6.03±0.115	8.28±0.169***^{c}	8.52±0.168***^{c}	10.06±0.167***	9.81±0.135***
660	6.05±0.144	8.30±0.055***^{c}	8.56±0.135***^{c}	10.06±0.192***	9.81±0.099***
720	6.05±0.058	8.27±0.128***^{c}	8.54±0.147***^{c}	10.04±0.116***	9.85±0.194***

Results are presented as mean ± S.D. (n=3) *p<0.05, **p<0.01, ***p<0.001 vs. CA and ^{a}p<0.05, ^{b}p<0.01, ^{c}p<0.001 vs. CCD-3.

Table 3: Relative zone of inhibition (RZOI) of CCD-3 against *S. aureus*.

Time (min)	Zone of inhibition (mm) of sample		Zone of inhibition(mm) of control		Relative zone of inhibition	
	CA	CCD-3	CA	CCD-3	CA	CCD-3
60	17	29	43	42	0.40±0.010	0.69±0.015***
120	23	30			0.53±0.015	0.71±0.021***
180	28	31			0.65±0.020	0.74±0.025**
240	29	32			0.67±0.021	0.76±0.023**
300	30	33			0.70±0.026	0.79±0.010**
360	33	35			0.77±0.012	0.83±0.026*
420	34	35			0.79±0.030	0.84±0.006*
480	35	36			0.81±0.006	0.86±0.012**
540	35	36			0.81±0.030	0.86±0.005*
600	36	37			0.84±0.011	0.88±0.020*
660	36	37			0.84±0.018	0.88±0.007*
720	37	38			0.86±0.016	0.90±0.005*

Results are presented as the mean ± S.D. (n=3). *p< 0.05, **p< 0.01, ***p< 0.001 vs. CA.

carrier for the purpose of enhancing the solubility and bioavailability of CA. So, our findings are not exactly concordant with that of others. But alike ours, Sadeghi *et al.* (2016) reported that the dissolution of Curcumin was increased by anti-solvent precipitation technique using PVP K30 as carrier, acetone as solvent and water as anti-solvent.[7] In another report, Mahapatra and Murthy (2014) described that inclusion complexation and liquid anti-solvent precipitation methods using various carriers can improve the solubility and dissolution rate of Efavirenz significantly.[17] Although different drugs and carriers used in those works are different than of us but as far as the technique and its outcomes are concerned, these reports corroborate with the findings of this study that CCDs using carrier are able to enhance the aqueous solubility of CA and in consequence its dissolution rate as well as bioavailability can be improved.

The RZOI of CCD-3 was found to be increased by 1.75 and 5.25-fold ($p<0.001$) than that of pure CA at 60 min against *S. aureus* and *E. coli,* respectively in *in-vitro* antibacterial activity test (Table 3, 4 and Figure 2, 3). This significant difference in antibacterial activity can be attributed to the fact that the improved solubility of CA achieved through CCD formulation ensured better diffusion and consequent antibacterial efficacy. Our findings on antibacterial activity are compared with study of Khan *et al.* (2016) where nanoparticles loaded with cefixime exhibited better antibacterial activity than to pure cefixime against *S. aureus* and *E. coli* by agar well diffusion method.[18] In another study, Omolo *et al.* (2018) demonstrated that nanosuspension of fusidic acid using poloxamer 188 as carrier had antibacterial activity superior to that of pure drug.[19] Furthermore, it was revealed that both *in-vitro* and *in-vivo* test of CA

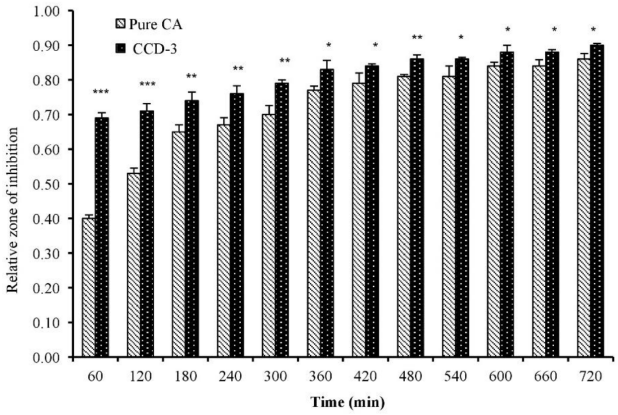

Figure 2: Relative zone of inhibition of pure CA and CCD-3 against *S. aureus*. Each value represents mean ± S.D. (*n*=3).

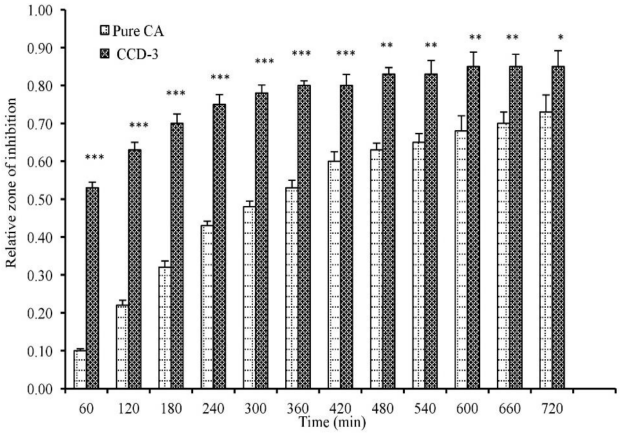

Figure 3: Relative zone of inhibition of pure CA and CCD-3 against *E. coli*. Each value represents mean ± S.D. (*n*=3).

Table 4: Relative zone of inhibition (RZOI) of CCD-3 against *E. coli*.

Time (min)	Zone of inhibition (mm) of sample		Zone of inhibition(mm) of control		Relative zone of inhibition	
	CA	CCD-3	CA	CCD-3	CA	CCD-3
60	4	21	40	40	0.10±0.005	0.53±0.015***
120	9	25			0.22±0.013	0.63±0.020***
180	13	28			0.32±0.017	0.70±0.025***
240	17	30			0.43±0.012	0.75±0.026***
300	19	31			0.48±0.015	0.78±0.021***
360	21	32			0.53±0.020	0.80±0.012***
420	24	32			0.60±0.025	0.80±0.029***
480	25	33			0.63±0.018	0.83±0.017***
540	26	33			0.65±0.023	0.83±0.036**
600	27	34			0.68±0.040	0.85±0.038**
660	28	34			0.70±0.030	0.85±0.032**
720	29	34			0.73±0.045	0.85±0.042*

Results are presented as the mean ± S.D. (*n*=3). *$p<0.05$, **$p<0.01$, ***$p<0.001$ vs. CA.

amorphous ultrafine particles by high gravity anti-solvent precipitation (HGAP) technique possessed better dissolution rate and stronger antibacterial activity by agar dilution method against *S. aureus* and *E. coli*.[20] Regardless of dispersion techniques and drugs, it has been proved that formulations always have reportedly better antibacterial efficacy in significant over the pure drug.

CONCLUSION

This study proposed a drug delivery approach using solvent/anti-solvent precipitation technique, where CA dissolved in acetone was allowed to precipitate onto MCC dispersion resulting the increased dissolution rate and antibacterial efficacy. The technique is very simple and practical and uses safe materials. Among the dispersion formulations, CCD-3 possessed the superiority considering its drug release property and antibacterial efficiency. Thus, this newer formulation of CA can be an effective substitute to its conventional dosage forms. Before recommending as a novel formulation additional studies like pharmacokinetic parameters, *in-vivo* antibacterial properties and safety issues should be considered.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

ABBREVIATIONS

ATCC: American type culture collection; **BCS:** Biopharmaceutical classification system; **CA:** Cefuroxime axetil; **CCDs:** CA loaded coarse dispersions; **CD:** Coarse dispersion; **CFU:** Colony forming units; **MCC:** Microcrystalline cellulose; **RZOI:** Relative zone of inhibition; **S.D.:** Standard deviation.

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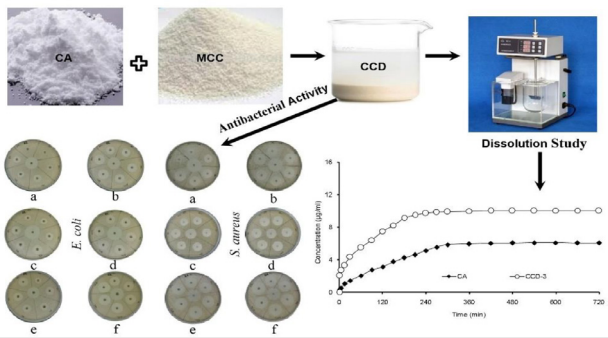
PICTORIAL ABSTRACT



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SUMMARY

Bioavailability of a drug after oral administration is a very important consideration for therapeutic success and it can be influenced by several factors. Dissolution is the rate limiting step in absorption of aqueous soluble drugs leading to inadequate bioavailability. Cefuroxime axetil (CA) is a prodrug of cefuroxime belonging to BCS class-II drugs that exhibit poor aqueous solubility and oral bioavailability. The present investigation reveals that CA loaded coarse dispersions (CCDs) using microcrystalline cellulose (MCC) as a carrier has enhanced solubility and bioavailability with consequent increased *in-vitro* antibacterial activity. CCDs were formulated by anti-solvent precipitation method, using Avicel PH-102 as a carrier at different ratios. Dissolution study reveals that extent of *in-vitro* CA release from all CCDs were significantly ($p<0.01$) higher than that of pure CA. Among all formulations, CCD-3 showed the highest drug release by 1.67-fold than pure CA. Also CCD-3 showed drug release by 6.87-fold than pure CA at initial sampling point (1 min). In addition, CCD-3 exhibited drug release (6.43 μg/ml) at 90 min comparable to corresponding maximum release by pure CA (6.05 μg/ml) at 480 min demonstrating apparently significant faster release by CCD-3. The comparative *in-vitro* antibacterial activity testing for CCD-3 against both *S. aureus* and *E. coli* showed higher RZOI by 1.75-fold and 5.25-fold, respectively ($p<0.05$) than pure CA. It may be concluded that, CCD-3 is an improved drug delivery technique considering both dissolution rate and antibacterial efficiency parameters. So, CCD-3 has the potential to be an alternative as more effective to conventional CA delivery systems. However, additional *in-vivo* studies are required to reinforce the pharmacokinetics and antibacterial efficacy including safety margin of CCD-3 to consider it as a novel technique.

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