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Development, Optimisation, and In Vitro Evaluation of a Deep Eutectic System to Enhance the Solubility and Dissolution of Cefuroxime Axetil

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Abstract: *Cefuroxime Axetil (CA) is a second-generation cephalosporin antibiotic characterised by poor aqueous solubility and low oral bioavailability, leading to variable therapeutic efficacy. Enhancing its solubility and dissolution behaviour remains a significant pharmaceutical challenge. Deep eutectic systems (DES), a novel class of green solvents formed by hydrogen-bond donors (HBDs) and hydrogen-bond acceptors (HBAs), have emerged as promising solubilization platforms. This review focuses on the development, optimisation, and in vitro evaluation of DES for improving the solubility and dissolution of Cefuroxime Axetil. The mechanisms of solubilization, formulation strategies, characterisation techniques, and recent advances are discussed. DES-based systems demonstrate remarkable potential to enhance drug dissolution and bioavailability, offering an efficient alternative to conventional solubility-enhancement techniques.*

Keywords: Cefuroxime axetil, Deep eutectic system (DES), Solubility enhancement, Dissolution improvement, Hydrogen bond donor (HBD), Hydrogen bond acceptor (HBA)

I. INTRODUCTION

Cefuroxime axetil is a β-lactam antibiotic widely used for the treatment of bacterial infections; however, its therapeutic performance is significantly limited by poor aqueous solubility and variable oral bioavailability (1,2). As a prodrug of cefuroxime, it exhibits erratic dissolution behaviour in gastrointestinal fluids, resulting in incomplete absorption and reduced clinical efficacy (3). Being classified under the Biopharmaceutics Classification System (BCS) Class II, its absorption is primarily dissolution-rate limited, with reported oral bioavailability ranging from 30–50% due to poor solubility and enzymatic degradation in the gastrointestinal tract (4,5).

To address these limitations, various formulation strategies such as solid dispersions, nanosuspensions, and self-emulsifying drug delivery systems have been explored to enhance the solubility and dissolution rate of cefuroxime axetil (6–8). Although these approaches have demonstrated some improvement, they are often associated with challenges such as complex processing, physical instability, and difficulties in large-scale production (9,10). Therefore, there is a need for a simple, effective, and scalable approach to improve the solubility and dissolution characteristics of this drug (11).

Deep eutectic systems (DES) have emerged as promising and environmentally friendly alternatives for solubility enhancement (12). DES are formed by combining a hydrogen bond acceptor (HBA) and a hydrogen bond donor (HBD) in specific molar ratios, producing a eutectic mixture with reduced melting point and enhanced solvation capacity (13). These systems enhance drug solubility by disrupting the crystalline structure, improving wettability, and promoting molecular interactions such as hydrogen bonding (14,15).

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In this context, the present study focuses on the development, optimization, and in vitro evaluation of a deep eutectic system aimed at improving the solubility of cefuroxime axetil by enhancing its dissolution behaviour. The study systematically investigates the effect of different DES compositions on drug solubility and dissolution, with the ultimate goal of improving its oral bioavailability and therapeutic effectiveness.

II. MATERIALS AND METHODS

2.1 Materials

• Cefuroxime axetil

It is a second-generation cephalosporin antibiotic used as the active drug component in pharmaceutical formulations.

• Choline chloride

A quaternary ammonium salt commonly used as a hydrogen bond acceptor in deep eutectic solvent preparation.

• Propylene glycol

A colourless, hygroscopic liquid used as a hydrogen bond donor, solvent, and stabilising agent.

• Glycerol, Citricacid andTartaric acid

were employed as hydrogen bond donors (HBDs) for the preparation of deep eutectic systems.

• Methanol

It is used as a solvent during analytical and formulation procedures.

• Orthophosphate of disodium hydrogen

It is used as a Buffering agent

• Potassium orthophosphate dihydrogen

It is used as a Buffering agent

• Sodium Hydroxide

It was utilised for the adjustment of buffer pH where required. (16,17)

2.2 Preparation of Deep Eutectic System

DES were prepared by mixing choline chloride (HBA) with selected hydrogen bond donors (propylene glycol, glycerol, citric acid, and tartaric acid) in specified molar ratios (1:1, 1:2, 1:3). The mixtures were heated at 70–80°C under continuous stirring until a clear, homogeneous liquid was obtained. The prepared DES were cooled to room temperature and stored for further use. (18)

2.3 Drug Loading

Cefuroxime axetil (250 mg) was incorporated into the prepared DES and mixed continuously until completely dissolved. The formulation was allowed to equilibrate for 24 h (19).

III. METHODS

3.1Preformulation Studies

• Melting point- itwas determined using the capillary method.

• Partition coefficient - it was evaluated using the n-octanol/water system.

• UV–visible spectrophotometric UV analysis was performed, and λmax of cefuroxime axetil was found at 276 nm.

• Fourier Transform Infrared Spectroscopy (FTIR) - Used to evaluate drug-excipient compatibility and hydrogen bonding interactions.

• Solubility studies were conducted using the shake flask method followed by centrifugation and UV analysis (20,21,22).

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3.2 Optimisation of DES

Different HBDs and molar ratios were screened to optimise formulation. Further optimisation was carried out using central composite design (CCD) with Design-Expert software. The molar ratios of HBA and HBD were considered as independent variables, and equilibrium solubility was taken as the response (23,24).

A factorial design (3^2 design) was used:

Independent variables:

X1: Molar ratio of HBA:HBD

X2: Water content

Dependent variables:

Y1: Solubility

Y2: Dissolution rate

3.3 Characterisation of DES

Formulations were evaluated for:

- Physical appearance (clarity and homogeneity)
- Equilibrium solubility
- pH (digital pH meter)
- Viscosity (Brookfield viscometer) (25,26,27)

3.4 In Vitro Dissolution Study

Dissolution studies were performed using the USP Type II (paddle) apparatus:

Medium: 900 mL phosphate buffer (pH 6.8)

Temperature: 37 ± 0.5°C

Speed: 100 rpm

Samples were withdrawn at predetermined intervals and analysed at 276 nm using UV spectrophotometer (28,29).

3.5 Drug Release Kinetics

Use to determine the mechanism of drug release

- zero-order
- first-order
- Higuchi models (30,31).

IV. RESULTS AND DISCUSSION

4.1 Preformulation Studies

4.1.1 Melting Point

The melting point of cefuroxime axetil was determined using the capillary method and was found to be in the range of 178.67 ± 0.58 °C to 182.33 ± 1.53 °C. This observed range is consistent with the reported literature value (~181 °C), confirming the purity and identity of the drug sample.

Sr.no	Parameter	Observation
1	Method Used	Capillary Method
2	Observed Melting Point Range	178.67 ± 0.58 °C to 182.33 ± 1.53 °C
3	Reported Literature Value	~181 °C
4	Interpretation	Observed range is consistent with the literature value, confirming the purity and identity of the drug

Table :1 Melting Point Study

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4.1.2 UV Spectroscopic Analysis

The absorption maxima (λmax) of cefuroxime axetil in methanol was identified using UV–visible spectrophotometry. The drug exhibited a characteristic peak at 276 nm, which was selected for further quantitative analysis. This wavelength is suitable due to its specificity and sensitivity for cefuroxime axetil estimation.

SR.NO.	Parameter	Observation
1	Method Used	UV–Visible Spectrophotometry
2	Solvent	Methanol
3	Absorption Maxima (λmax)	276 nm
4	Application	Selected for quantitative analysis
5	Interpretation	Wavelength shows good specificity and sensitivity for estimation of cefuroxime axetil

Table:2 UV Spectroscopic Analysis

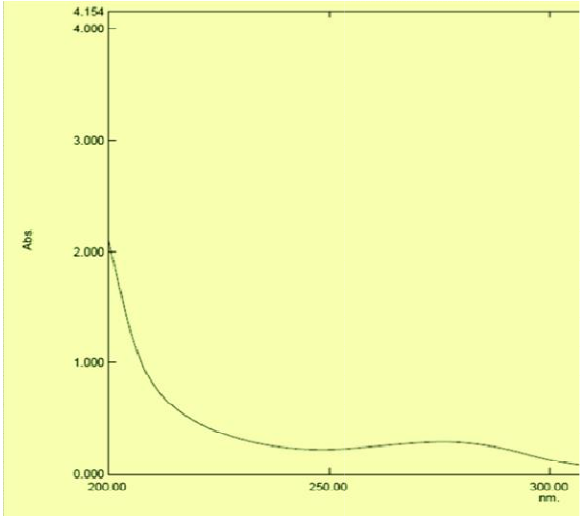

Figure 4.1.2: Cefuroxime axetil absorption maximum in methanol (4µg/mL)

4.1.3 Preparation of Linear Standard Calibration Curve

The Lambert-Beer law was used to prepare the linear standard calibration curve at 276 nm for the quantitative measurement of cefuroxime axetil in test samples. For the preparation of the standard calibration curve, the concentration range of 2–18µg/ml was used. As shown in Figure 4.1, the standards calibration curve showed a linear connection between concentration and absorbance with a linear equation of Y=0.045x-0.0017 and a linear coefficient of 0.999. 0.999.

SR.NO	Concentration (µg/mL)	Trial 1	Trial 2	Trial 3	average	Std. Deviation
1	0	00.017	00.018	0.016	00.017	00.001
2	1	00.062	00.063	0.061	00.062	00.001
3	3	00.152	00.153	0.151	00.152	00.001
4	5	00.242	00.244	0.241	00.242	00.002
5	7	00.332	00.334	0.331	00.332	00.002
6	9	0.422	0.424	0.421	0.422	0.002
7	12	0.557	0.559	0.556	0.557	0.002
8	15	0.692	0.694	0.691	0.692	0.002

Table 4.1.3 : The value of absorbance of different concentrations of cefuroxime axetil at 276nm in methanol

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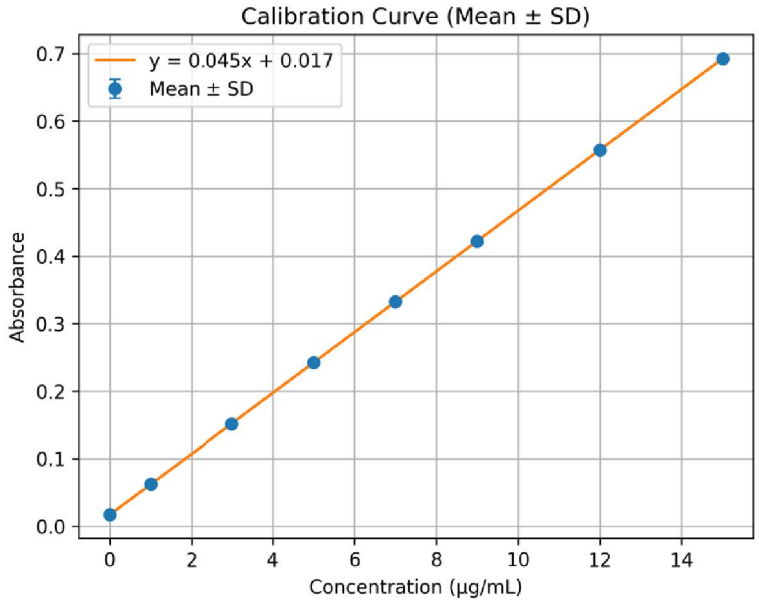

Figure 4.2: A Linear relationship graph between concentration and absorbance at 276nm in methanol

4.1.4 Partition Coefficient

The partition coefficient of cefuroxime axetil was determined using the n-octanol/water system by the shake flask method. The obtained value was 0.867 ± 0.016, indicating the drug possesses moderate lipophilic characteristics. This suggests limited aqueous solubility, supporting its classification as a poorly water-soluble drug.

SR.NO	Parameter	Observation
1	Method Used	Shake Flask Method
2	System n	Octanol / Water
3	Partition Coefficient	(Log P) 0.867 ± 0.016
4	Nature of Drug	Moderately lipophilic
5	Interpretation	Indicates limited aqueous solubility and supports classification as a poorly water-soluble drug

Table:4 Partition Coefficient study

4.1.5 FTIR Analysis

In The FT-IR spectra of pure CA showed two distinct absorption bands for N–H stretching (primary amide) at 3313.71 cm-1 and 3190.68 cm-1, and C=O stretching of β-lactam, carbamyl, and amide groups at 1761.47 and 1678.97 cm-1 and 1532.37 cm-1, respectively.In the deep eutectic mixed solvent formulation CCDES14, the drug peak was not observed at a lower intensity

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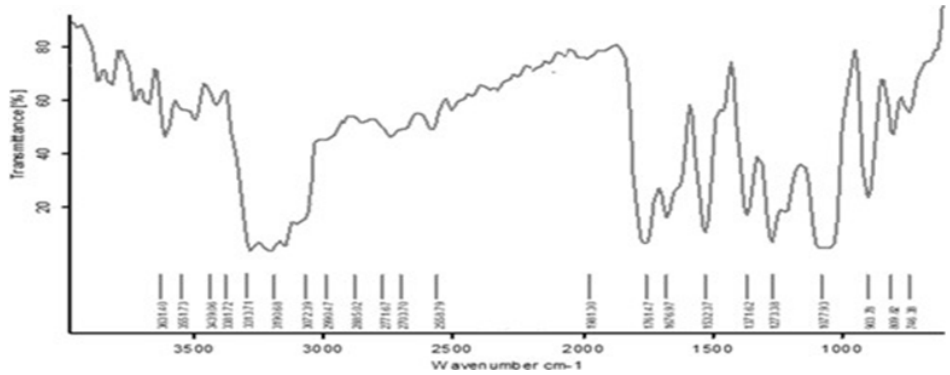

Figure 4.3: Overlay the FTIR spectrum of cefuroxime axetil

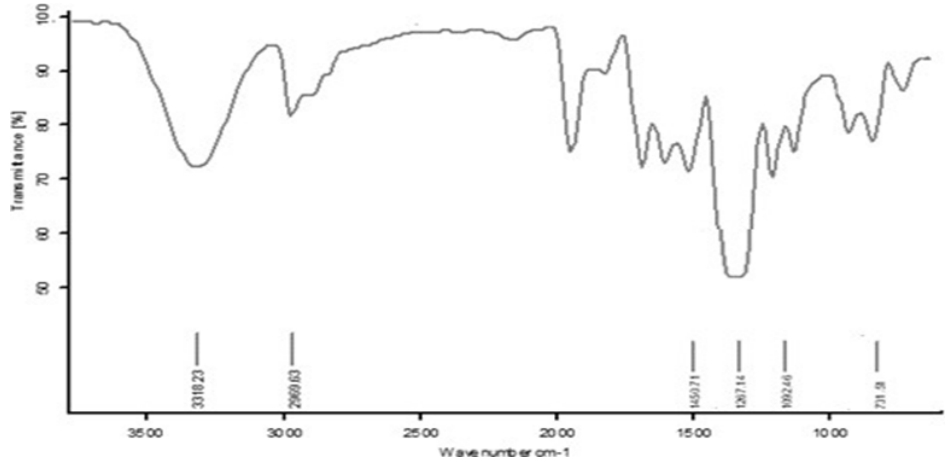

Figure 4.4: Overlay the FTIR spectrum of Optimized deep eutectic mixture CCDES14

4.1.6 Solubility Studies in Different Solvents

SR.NO	Solvent	Solubility (mg/mL)	Interpretation
1	0.1 N HCl	6.601 ± 0.045	Maximum solubility observed
2	Methanol	1.979 ± 0.002	High solubility
3	Water	0.458 ± 0.005	Moderate solubility
4	Ethanol	0.129 ± 0.001	Low solubility
5	Phosphate Buffer (pH 6.8)	0.053 ± 0.001	Very low solubility

Table: 6 Solubility Studies in Different Solvents

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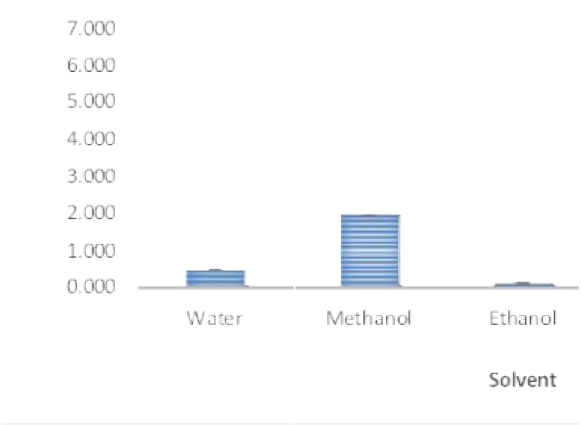

Figure 4.5: A bar graph of solubility of cefuroxime axetil in different solvents.

The data in table on 4 displayed that the cefuroxime axetil displayed maximum solubility 0.1NHcl followed by alcohols. In water it displayed solubility 0.458±0.005mg/ml.

4.2 Preparation of Cefuroxime Axetil-Loaded Deep Eutectic Systems (DES)

Various techniques, such as vacuum, heating, and freeze-drying, have been suggested over the years for producing DESs. Given its ease and widespread use, heating was the approach that was most frequently used in this investigation.

SR.NO	Parameter	Description
1	Method Used	Heating Method
2	Reason for Selection	Simple and efficient
3	Hydrogen Bond Acceptor (HBA)	Choline Chloride (ChCl)
4	Hydrogen Bond Donors (HBDs)	Propylene glycol, Glycerol, Organic acids
5	Principle of Formation	Hydrogen bonding between HBA and HBD leading to melting point depression
6	Physical Appearance	Clear, homogeneous liquids at low temperature
7	Confirmation of DES Formation	Formation of stable liquid system indicates successful DES formation
8	Advantages	Low toxicity, biodegradable, non-volatile, easy to prepare
9	Pharmaceutical Relevance	Suitable alternative to conventional organic solvents and ionic liquids

Table: 6 Preparation of Cefuroxime Axetil-Loaded Deep Eutectic Systems (DES)

4.3 Optimization of the cefuroxime axetil containing deep eutectic mixture (CDES)

4.3.1 Screening of the several kinds of hydrogen bonds donner

For the solubility studies, various classes of DESs, or deep eutectic solvents, were prepared. Choline chloride was selected as the hydrogen bond acceptor, and urea, polyalcohols (propylene glycol and glycerol), and organic acids (citric, malonic, and tartaric acids) were used as hydrogen bond donors. The generated DES formulations were evaluated according to their equilibrium solubility with cefuroxime axetil and their capacity to form clear and transparent liquids, as indicated in Table 4.3.

Table 4.3: Physical appearance of the tested cefuroxime axetil containing deep eutectic mixture

Formulation code	Liquification
CDES1	Clear transparent liquid, stable at room temperature
CDES2	Cleartransparentliquid,stableatroomtemperature
CDES3	Noliquid was created

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CDES4	Noliquidwascreated
CDES5	Noliquidwas created
CDES6	Cleartransparentliquid,stableatroomtemperature

CDES1, CDES2, and CDES6 were clear, transparent liquids that remained stable at room temperature among the six deep eutectic mixture formulations examined; by contrast, CDES3, CDES4, and CDES5 did not take on a liquid form and were not regarded as deep eutectic mixtures formulations and not further selected for the determination of the equilibrium solubility of the cefuroxime axetil.

Formulation code Liquification

4.3.1.1 Solubility in equilibrium

Solubility in equilibrium of the clear, transparent liquid formulations were determined and its equilibrium solubility were shown in table 4.4.

Table 4.4: Physical appearance of the tested cefuroxime axetil containing deep eutectic mixture

Formulation code	Equilibriumsolubility(mg/ml)
CDES1	102.730±1.215
CDES2	144.010±0.709
CDES6	36.652±1.111

Among all three formulations, the CDES1 and CDES2 formulations were selected; both formulations have a higher equilibrium solubility of the cefuroxime axetil.

4.3.2 Examining the various hydrogen bond donor molar ratios

For the solubility experiments, a number of different classes of DES were prepared. Propylene glycol and glycerol were chosen for further evaluation of the process parameters according to the findings of a study that employed various hydrogen bond donors. This paper investigated the effects of different molar ratios of hydrogen bond donors on the equilibrium solubility of cefuroxime axetil in the deep eutectic mixture. The produced deep eutectic combination was assessed for its equilibrium solubility with the cefuroxime axetil and its capacity to produce a clear, transparent liquid formulation, as shown in table 4.5.

Table 4.5: Physical appearance of the tested cefuroxime axetil containing deep eutectic mixture

Formulation code	Liquification
CDES7	Noliquidwas created
CDES8	Noliquidwas created
CDES1	Cleartransparentliquid,stableatroomtemperature
CDES9	Cleartransparentliquid,stableatroomtemperature
CDES10	Noliquidwas created
CDES11	Noliquidwascreated
CDES2	Cleartransparentliquid,stableatroomtemperature
CDES12	Cleartransparentliquid,stableatroomtemperature

CDES7, CDES8, CDES10, and CDES11 did not convert into liquid form and, therefore, were not regarded as deep eutectic solvent (DES) formulations. As a result, they were excluded from further evaluation of the equilibrium solubility of cefuroxime axetil. In contrast, CDES1, CDES2, CDES9, and CDES12 formed clear, transparent liquids that, at room temperature, did not change. These results suggest that the formation of a deep eutectic system requires a suitable ratio of hydrogen bond donor to hydrogen bond acceptor.

deep eutectic mixture occurred when the hydrogen bond donner's molar ratio was increased further.

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4.3.2.1 Solubility in equilibrium

Solubility in equilibrium of the clear, transparent liquid formulations was selected and its equilibrium solubility was shown in table 7.6.

Table 4.6: Physical appearance of the tested cefuroxime axetil containing deep eutectic mixture

Formulation code	Equilibriumsolubility(mg/ml)
CDES1	102.730±1.215
CDES9	130.618±1.229
CDES2	144.010±0.709
CDES12	161.376±0.995

Among the all deep eutectic mixture consisted propylene glycol as hydrogen dong donner shown higher equilibrium solubility of the cefuroxime axetil as compare to the hydrogen bond donner glycerol. Both formulations have higher equilibrium solubility of the cefuroxime axetil. Formulation CDES12 have higher equilibrium solubility 161.376±0.995mg/ml.

4.3.1 Screening of Hydrogen Bond Donors

Several kinds of DES were developed for the solubility tests. Based on the findings of the investigation using several hydrogen bond donors, propylene glycol was selected for further process parameter assessment. This study looked at how different hydrogen bond acceptor molar ratios affected the equilibrium solubility of cefuroxime axetil in the deep eutectic mixture. The produced deep eutectic combination was assessed for its capacity to produce a translucent, clear liquid formulation and its equilibrium solubility with the cefuroxime axetil, as shown in table 4.7.

Table 4.7: Physical appearance of the tested cefuroxime axetil containing deep eutectic mixture

Formulation code	Liquification
CDES12	Cleartransparentliquid,stableatroomtemperature
CDES13	Cleartransparentliquid,stableatroomtemperature
CDES14	Noliquidwas formed

4.3.1.1 Equilibrium Solubility Studies

The clear, transparent liquid formulations' equilibrium solubility was chosen, and table 4.8 displays this equilibrium solubility.

Table 4.8: Physical appearance of the tested cefuroxime axetil containing deep eutectic

Formulation code	Equilibrium solubility(mg/ml)
CDES12	161.376±0.995
CDES13	151.442±0.892

Table 8: Equilibrium Solubility Studies

4.3.3 Optimisation Using Central Composite Design (CCD)

Formulation code Factor 14.3.4 Central composited design for optimisation

We selected a central composite design for improving the cefuroxime axetil formulation. For cefuroxime axetil 250mg, one response variable and two independent variables were used in a central composite design. A reaction is the equilibrium solubility.

variable. The independent variables are the hydrogen-bond acceptor (X1) and donor molar ratios (X2), and Table 4.9 displays all equilibrium solubility parameters of cefuroxime axetil for 13 formulations.

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Formulation code	Factor1 X1:HBAmolar ratio	Factor2 X2:HBD molarratio	Response 1 Equilibriumsolubility (mg/ml)
CCDES1	1.103	2.25	161.523
CCDES2	0.5	2.0	140.919
CCDES3	0.75	1.896	143.127
CCDES4	0.75	2.25	159.610
CCDES5	0.75	2.603	150.044
CCDES6	0.396	2.25	140.551
CCDES7	0.75	2.25	160.125
CCDES8	0.75	2.25	160.714
CCDES9	0.5	2.5	142.170
CCDES10	0.75	2.25	159.683
CCDES11	1.0	2.5	160.051
CCDES12	1.0	2.0	152.840
CCDES13	0.75	2.25	159.169

Table 4.9: Composition of the formulation as per the central composite design

Mathematical Model and ANOVA Results

software was utilized to develop mathematical relationships for the measured response, namely polynomial equations representing the cefuroxime axetil equilibrium solubility. The relationship between the response and the independent variables is seen in the following equation:

Equilibrium solubility =159.860+7.432X1+2.280X2+1.490X1X2-4.365X12-6.6591X22.

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob>F	
Model	881.615	5	176.323	744.125	<0.0001	Significant
X1-HBAmolarratio	441.925	1	441.925	1865.029	<0.0001	
X2-HBDmolarratio	41.605	1	41.605	175.585	<0.0001	
X1X2	8.881	1	8.881	37.481	0.0005	
$X1^2$	132.569	1	132.569	559.475	<0.0001	
$X2^2$	302.229	1	302.229	1275.480	<0.0001	
Residual	1.659	7	0.237			
LackofFit	0.288	3	0.096	0.280	0.8380	Not significant
PureError	1.371	4	0.343			
CorTotal	883.273	12				
Std. Dev.	0.487		R-Squared		0.998	
Mean	153.118		Adj R-Squared		0.997	

Table: 11 Mathematical Model and ANOVA Results

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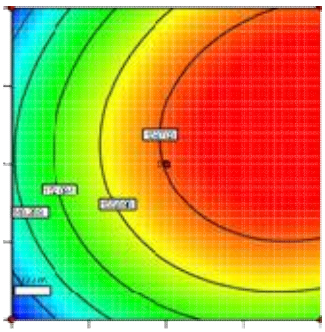

Figure 4.6: Contour plot showing the effect ofThe hydrogen bond donor to hydrogen bond acceptor molar ratio on the deep eutectic mixture's equilibrium solubility.

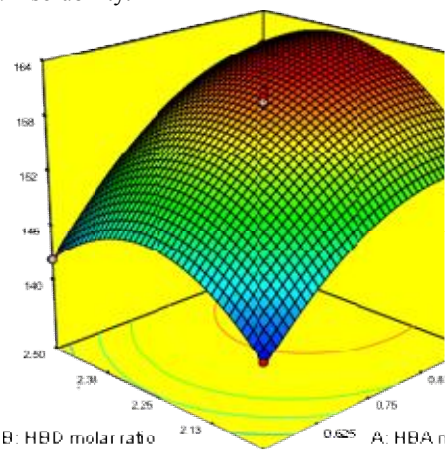

Figure 4.7: Three-dimension response graph showing the impact on equilibrium solubility in a deep eutectic mixture of the hydrogen bond donor to hydrogen bond acceptor molar ratio. Cefuroxime axetil independent variable optimization Response surface analysis provided one solution where the cefuroxime axetil equilibrium The deep eutectic mixture's solubility was found to be within bounds. Response variable composition, projected values, and experimental
Table 7.12 has a list of values.

Number	HBA molar ratio	HBD molar ratio	Predicted Equilibrium solubility
CCDES14	0.9571	2.21	162.4508708

Table 4.11: Composition of the optimized formulation

4.3.4.2 Confirmation of cefuroxime axetil RSM results

Cefuroxime Axetil's equilibrium solubility in a deep eutectic mixture was found to be within bounds in a single solution supplied by the response surface methodology. Table 4.12 (23) provides a list of the response variables' composition, experimental values, and predicted values.

Number	HBA molar ratio	HBD molar ratio	Predicted valueof equilibrium solubility	Experimental value of equilibrium solubility
CCDES14	0.9571	2.21	162.451	161.302

Table 4.12: The response variables anticipated and experimental values, as well as the optimized formulation's composition

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4.4 Evaluation of cefuroxime axetil containing deep eutectic mixture

4.4.1 Physical appearance

Physical appearance of all prepared deep eutectic mixture formulations was shown in table 4.13.

Table 4.13: Physical characteristics of every created formulation

Formulation code	Physical appearance
CCDES1	Clear and transparent liquid
CCDES2	Clear and transparent liquid
CCDES3	Clear and transparent liquid
CCDES4	Clear and transparent liquid
CCDES5	Clear and transparent liquid
CCDES6	Clear and transparent liquid
CCDES7	Clear and transparent liquid
CCDES8	Clear and transparent liquid
CCDES9	Clear and transparent liquid
CCDES10	Clear and transparent liquid
CCDES11	Clear and transparent liquid
CCDES12	Clear and transparent liquid
CCDES13	Clear and transparent liquid
CCDES14	Clear and transparent liquid

Table 4.13 demonstrated that all the prepared cefuroxime axetil containing deep eutectic mixtures were Clear transparent liquids

Equilibrium Solubility

DES systems significantly enhance the solubility of cefuroxime axetil compared to pure drug in water. This improvement is one of the primary advantages of DES-based formulations.

SR.NO	Parameter	Observation
1	Pure Drug Solubility (Water)	0.458 ± 0.883 mg/mL
2	DES Solubility Range	140.552 ± 0.662 – 161.523 ± 0.883 mg/mL
3	Optimized Formulation	CCDES14
4	Maximum Solubility	161.302 ± 0.220 mg/mL
5	Interpretation	Significant enhancement in solubility

Table 4.14: Equilibrium solubility

Formulation code	Equilibrium Solubility(mg/ml)
Puredrug	0.458±0.883
CCDES1	161.523±0.883
CCDES2	140.920±0.637
CCDES3	143.127±0.337
CCDES4	159.610±0.919
CCDES5	150.044±1.168
CCDES6	140.552±0.662
CCDES7	160.125±1.132
CCDES8	160.714±0.709
CCDES9	142.171±0.919
CCDES10	159.684±1.436
CCDES11	160.052±1.348

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CCDES12	152.840±1.627
CCDES13	159.169±1.330
CCDES14	161.302±0.220

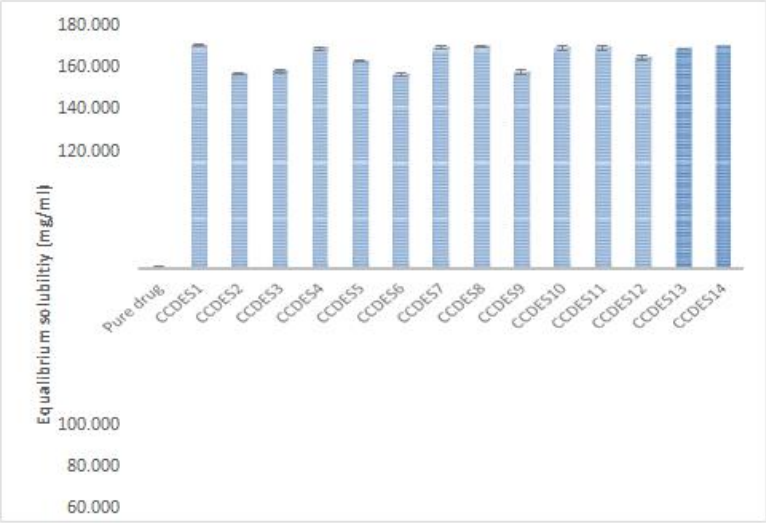

Figure 4.8: Equilibrium solubility of drug containing deep eutectic mixture in the distilled water.

pH and Viscosity Analysis

DES formulations generally exhibit slightly acidic pH and moderate viscosity, which are suitable for pharmaceutical applications and influence drug release behaviour.

4.4.3 pHall formulation ph shown in table 7.15.

Table 4.15: all prepared formulation ph

Formulation code no.	pH values
CCDES1	5.520±0.010
CCDES2	5.607±0.015
CCDES3	5.477±0.014
CCDES4	5.540±0.020
CCDES5	5.597±0.031
CCDES6	5.490±0.020
CCDES7	5.580±0.026
CCDES8	5.497±0.038
CCDES9	5.500±0.036
CCDES10	5.767±0.025
CCDES11	5.640±0.026
CCDES12	5.580±0.030
CCDES13	5.620±0.021
CCDES14	5.480±0.026

Figure 4.9: all prepared formulation ph

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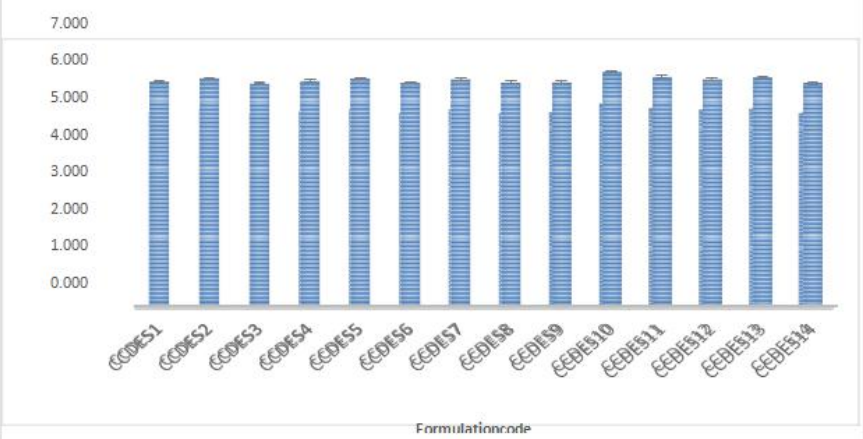

Figure 4.9: all prepared formulation ph

7 Viscosity Viscosity of all the prepared formulations 4.16

Formulation code no.	Viscosity range(mPa.s)
CCDES1	1004.840±0.691
zCCDES2	894.233±1.083
CCDES3	913.543±0.122
CCDES4	922.233±0.472
CCDES5	943.920±1.565
CCDES6	965.293±1.487
CCDES7	966.980±1.506
CCDES8	956.837±0.467
CCDES9	940.940±1.457
CCDES10	959.697±1.492
CCDES11	988.687±0.632
CCDES12	974.483±0.537
CCDES13	968.057±1.603
CCDES14	979.857±1.295

Table 4.16: Viscosity of all the prepared formulations

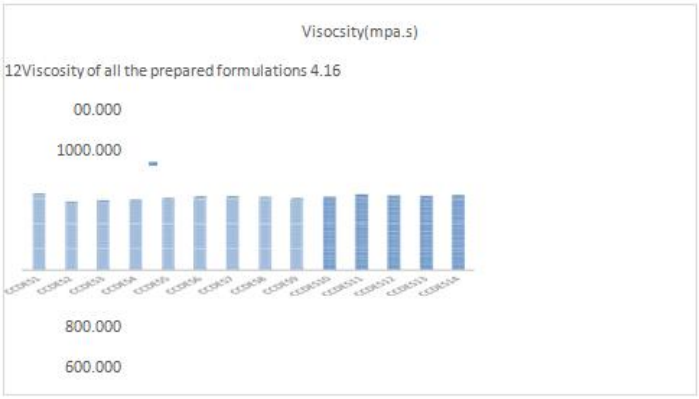

Figure 4.10: Viscosity of the fully prepared formulation

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The Viscosity of every prepared mixture was discovered to be in a range of the 894.233±1.083mPa.s to 1004.840±0.691mPas. The viscosity of the optimized formulation CCDES14 was found to be in a range of the 979.857±1.295mPas

In Vitro Dissolution Study

In pharmaceutical technology, an API's solubility is a crucial factor. Here, we assessed how well the liquid DES dissolved in phosphate buffer pH 6.8 and 0.1 M NHCl as measured by the percentage drug release versus dissolution time

Table 18:Table 4.17: Comparison of percentage dissolution of cefuroxime axetil containing deep eutectic mixture and cefuroxime axetil bulk in 0.1NHcl with pH 6.8 phosphate buffer

Time (minute)	%Drugrelease of pure drug in 0.1NHCl solution	%Drug release of pure medication in a pH 6.8 phosphate buffer solution	% Drug release of formulation CCDES14in 0.1NHCl	%Drugreleaseof formulation CCDES14 in a pH 6.8 phosphate buffer solution
0	0	0	0	0
5	4.744±0.899	4.784±0.393	12.374±0.450	11.062±0.281
10	8.599±0.169	8.241±0.337	25.089±0.221	23.499±0.105
15	10.744±0.160	10.188±0.169	34.268±0.284	25.287±0.116
20	12.572±0.281	12.016±0.050	52.546±0.101	35.579±0.048
25	15.274±0.843	14.360±0.001	61.963±0.112	48.294±0.225
30	17.221±0.674	16.268±0.112	79.248±0.098	63.115±0.445
35	19.685±0.225	19.168±0.086	92.344±0.562	65.325±0.990
40	19.923±0.112	19.327±0.285	95.126±0.987	76.848±0.482
60	20.042±0.056	19.446±0.119	98.305±0.001	84.397±1.686

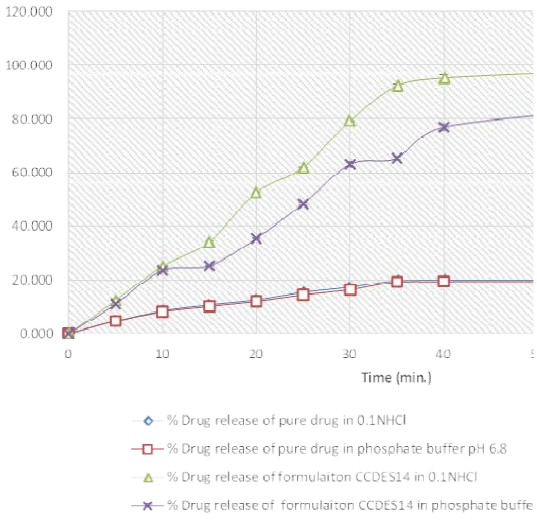

Figure 4.11: A compression graph of in vitro drug release between the of percentage dissolution of cefuroxime axetil containing deep eutectic mixture (CCDES14) and cefuroxime axetil bulk in 0.1NHcl and phosphate buffer pH 6.8

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Drug Release Kinetics

Drug release from DES systems commonly follows first-order kinetics, indicating concentration-dependent release governed by dissolution processes.

SR.NO.	Medium	Model	R^2 Value	Interpretation
1	0.1 N HCl	First-order	0.9411	Concentration-dependent release
2	pH 6.8 Buffer	First-order	0.9679	Follows dissolution-controlled release

Table: 19 Drug Release Kinetics

4.4.6 In-vitro Drug release kinetic of cefuroxime axetil containing deep eutectic mixture CCDES14 in 0.1NHcland pH 6.8 phosphate buffer

Cefuroxime axetil's in vitro drug release kinetics in 0.1NHcl and pH 6.8 phosphate buffer with the deep eutectic combination CCDES14 as shown below:

Zero order

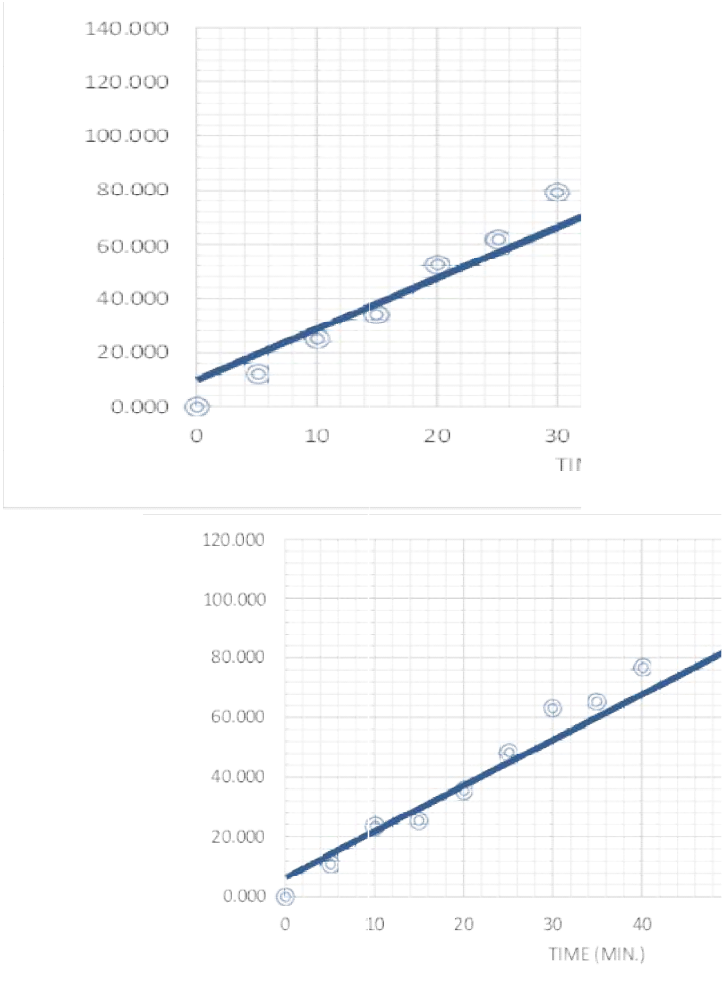

Figure 4.13: Zero order kinetic graph for CCDES14 in phosphate buffer pH 6.8

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First order

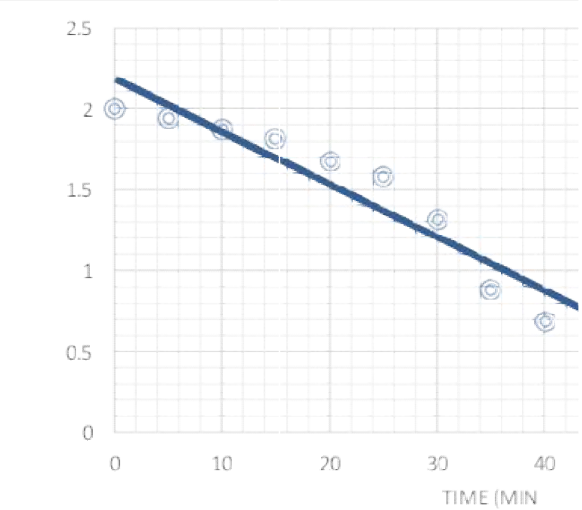

Figure 4.14: First order kinetic graph for CCDES14 in 0.1NHcl

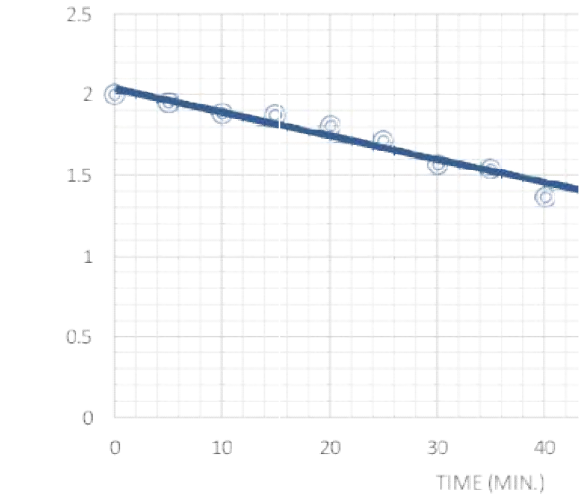

Figure 4.15: First order kinetic graph for CCDES14 in phosphate buffer pH 6.8

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Higuchi Model

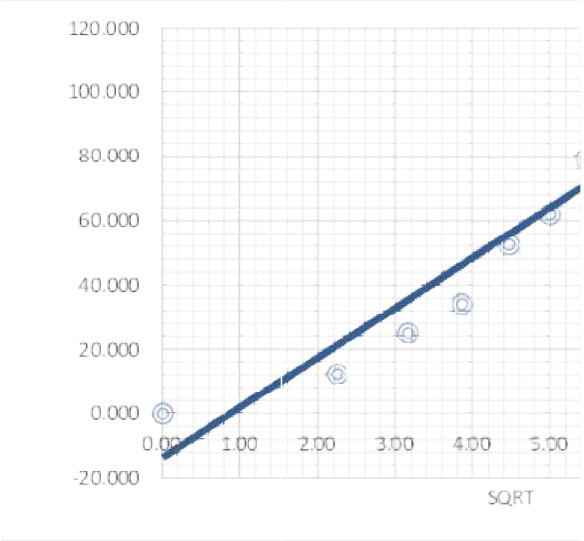

Figure 4.16: Higuchi order kinetic graph for CCDES14 in 0.1NHcl

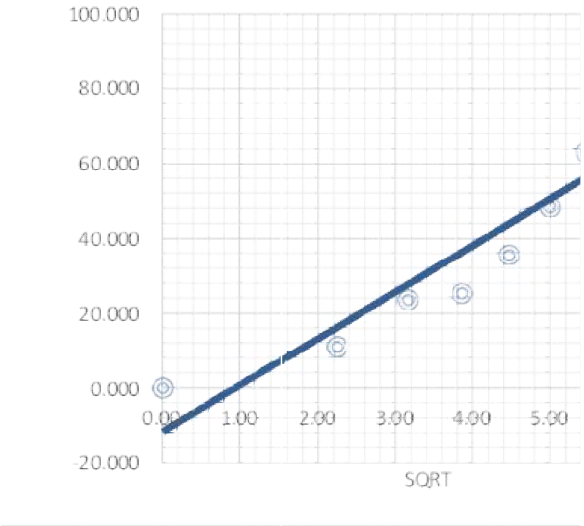

Figure 4.17: Higuchi order kinetic graph for CCDES14 in phosphate buffer pH 6.8

Conclusion

The present study successfully demonstrated that deep eutectic systems (DES) are an effective approach for enhancing the solubility and dissolution of cefuroxime axetil. Preformulation studies confirmed the drug's poor aqueous solubility and the need for solubility enhancement strategies. DES formulations prepared using choline chloride and suitable hydrogen bond donors showed significant improvement in equilibrium solubility. Optimisation using central composite design identified CCDES14 as the optimised formulation with maximum solubility. FTIR analysis confirmed the absence of drug–excipient incompatibility, indicating formulation stability. The optimised DES exhibited favourable physicochemical properties, including suitable pH and viscosity. In vitro dissolution studies revealed a marked increase

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in drug release compared to the pure drug. Overall, DES-based formulations offer a simple, efficient, and promising strategy to improve the bioavailability of poorly soluble drugs like cefuroxime axetil.

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