

**FORMULATION AND EVALUATION OF TERNARY SOLID
DISPERSION OF CEFIXIME TO IMPROVE DISSOLUTION PROFILE****Saral Kumar Singh, Aditi Srivastava, Babita Jaiswal, Lakhshya Veer Singh***Department of Pharmacy, Mahatma Jyotiba Phule Rohilkhand University, Bareilly, 243006
India.Article Received on 05 Sept. 2026,
Article Revised on 25 Sept. 2026,
Article Published on 01 Oct. 2026,<https://doi.org/10.5281/zenodo.23118156>***Corresponding Author****Lakhshya Veer Singh**Department of Pharmacy, Mahatma
Jyotiba Phule Rohilkhand
University, Bareilly, 243006 India.**How to cite this Article:** Saral Kumar Singh, Aditi Srivastava, Babita Jaiswal, Lakhshya Veer Singh*. (2026). Formulation and Evaluation of Ternary Solid Dispersion of Cefixime to Improve Dissolution Profile. World Journal of Pharmaceutical Research, 15(19), 905–914.

This work is licensed under Creative Commons Attribution 4.0 International license.

ABSTRACT

Solubility properties of drugs continue to remain one of the most crucial considerations in the formulation process. Combinatorial chemistry and high throughput screening methods have increased the number of molecules with low water solubility considerably. As a result of the poor water solubility of molecules, 40 to 45 percent of the new chemicals fail to enter the market place. Solubility problems lead to reduced drug bioavailability; therefore, there is a need for improvement in solubility. In the current study, efforts have been made to increase the solubility of BCS class 4 drug cefixime by forming Ternary Solid Dispersion using natural hydrophilic polymers such as xylitol and sodium lauryl sulphate as a surfactant through solvent evaporation method. The complex formed in the ratio of 1:3 between the drug and

polymer exhibited a high dissolution rate. The improved solubility properties of the drug complex were confirmed by determining the dissolution rate in HCl buffer solution with a pH of 1.2. Through identification via UV spectroscopic analysis, organoleptic features, and others, the drug was characterized through various compendial methods. The F3 batch with a dissolution rate of $91.05 \pm 1.11\%$ was selected as the optimized formulation that outperformed others.

KEYWORDS: *Ternary Solid dispersion, Cefixime, Solvent Evaporation, Xylitol, Dissolution.*

INTRODUCTION

Solid dispersion is the most commonly applied technique to enhance the dissolution properties of poorly soluble drugs especially class II and IV drugs of BCS. This process involves mixing the drug substance with a carrier in the solid state as fine, amorphous or molecular form of the drug substance.^[1] There are various reasons for making solid dispersions of active pharmaceutical ingredients. The main reason is the limitation in aqueous solubility that affects the dissolution of these drugs in intestinal fluid leading to reduced bioavailability. Solid dispersions are prepared using a soluble carrier material like polyethylene glycol (PEG), polyvinyl pyrrolidone (PVP), hydroxy propyl methyl cellulose (HPMC), or poloxamers. There are certain mechanisms responsible for enhancement of dissolution properties using solid dispersion technology.^[2]

Firstly, the drug particle size is significantly decreased, to almost molecular size, resulting in increased surface area that is able to be dissolved. Secondly, solid dispersion systems tend to render the drug molecule amorphous. The reason behind this is that amorphous molecules have higher free energy and lower lattice energy compared to crystalline molecules; therefore, they have higher solubility. Finally, the hydrophilic nature of the carrier increases the wetting power of the drug particle, which means that the dissolution media will be able to interact better with the drug molecule.^[3,4]

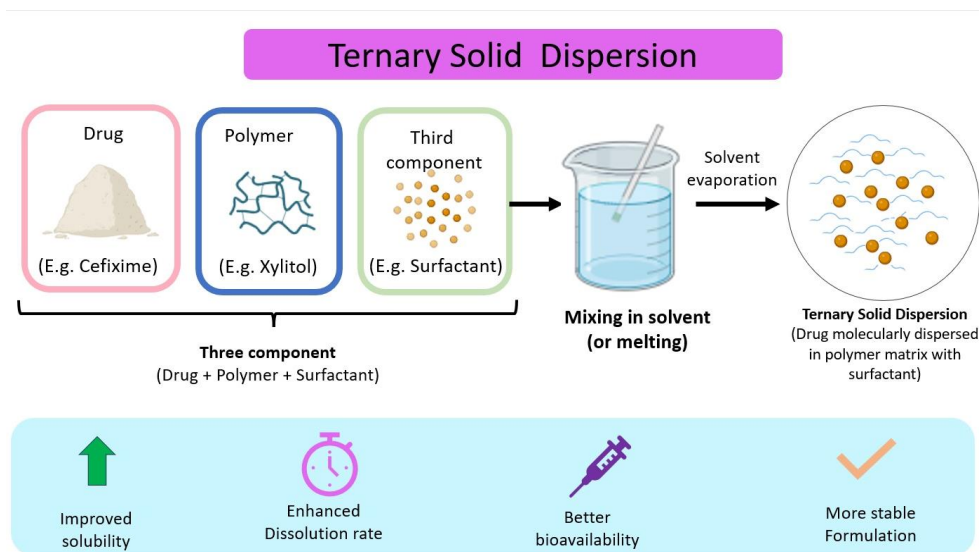
In case of BCS Class II, where high permeability and low solubility exist, dissolution is the rate-limiting step, and thus, to overcome this, solid dispersion technique works very efficiently in improving the dissolution rate and increasing the amount of drug available for absorption.^[5] In BCS Class IV, the drug suffers from low solubility as well as low permeability, and thus, using the technique of solid dispersion, there is improvement in solubility and dissolution rate. Due to this, the concentration of dissolved drug increases, and hence, better drug absorption can be expected. Hence, solid dispersion can be considered an extremely effective approach for improving the efficacy of poorly soluble drugs.^[6]

In ternary solid dispersion (TSD), the drug that possesses poor aqueous solubility is dispersed using two carriers rather than just one in the solid dispersion process. The cooperative effect of the drug and two carriers will enhance drug solubility, dissolution, wettability, and physical stability.^[7] TSD has better effects on solubility and dissolution, drug release, and physical stability than the traditional binary solid dispersions. It not only can decrease the crystallinity of the drug more effectively but can also achieve other effects such as wettability and

recrystallization inhibition.^[8] Consequently, TSD may become a good choice for improving oral absorption of poorly water-soluble drugs.^[9]

Cefixime is an antibacterial agent belonging to the category of third-generation semi-synthetic cephalosporins.^[10] Its main mechanism of action is related to inhibition of bacterial cell wall biosynthesis via interaction with penicillin-binding proteins, which results in bacterial cell death. Cefixime is frequently prescribed for the treatment of infections of respiratory system, urinary system, middle ear infections (otitis media), typhoid fever, and gonococcal urethritis.^[11] In terms of biopharmaceutics, cefixime can be described as having low aqueous solubility. This property can affect the drug's dissolution rate and thus oral absorption.^[12] Cefixime is practically insoluble to slightly soluble in water and its solubility strongly depends on pH. The drug dissolves better in an acid environment compared to a neutral or basic one. As it can be concluded from the above information, due to its low solubility and moderate permeability, cefixime is a difficult-to-formulate medication, therefore different methods of solubility improvement were suggested.^[13]

Graphical Abstract



Experimental data

MATERIALS

Cefixime IP was obtained as gift sample from Arti Pharmaceutical Industrial Area, Baddi, Xylitol of analytical grade was obtained from SDFCL Fine Chemical Limited, Mumbai while Sodium Lauryl Sulphate and Methanol was obtained from Merck Specialities Ltd., Mumbai

having analytical grade and the remaining buffers used to carry out Drug Content and Drug release studies were procured from the institution laboratory.

METHODS

Preformulation studies of Cefixime

Melting point

The melting point of Cefixime was determined by USP method for which a small quantity of drug was placed into sealed capillary tube. The tube was placed in melting point apparatus. The temperature was gradually increased and eventually the temperature at which drug starts to melt was noted as the melting point of drug.^[14]

Spectrophotometric analysis of Cefixime^[15,16]

Preparation of 0.1N HCl solution

For this, 4.13ml of concentrated HCL from laboratory was taken and diluted upto 500ml with distilled water.

Preparation of Standard Solution (100ug/ml)

To prepare this, 10mg of drug was weighed, transferred in 100ml of volumetric flask and dissolved in 100ml of 0.1N HCl solution to get standard solution.

Preparation of Standard Curve

10ml of standard solution was taken and diluted up to 100ml using 0.1N HCl solution to get stock solution of 10ug/ml. Further from this solution, successive dilutions were prepared and was then analysed using UV-Vis Spectrophotometer.

Formulation of Ternary Solid Dispersion

Cefixime ternary solid dispersions were formulated using Xylitol as hydrophilic matrix and Sodium Lauryl Sulphate as surfactant through solvent evaporation technique. It was done by dissolving the drug in methanol. This was followed by the addition of Xylitol and Sodium Lauryl Sulphate to get homogenous solution. Evaporation of solvent yielded solid mass which was then dried, powdered, sieved and stored in desiccators for further evaluation. These formulated ternary solid dispersions were further tested for physiochemical characteristics, improved solubility and dissolution studies.^[17,18]

Table 1: Formulation Composition for Various Batches of Cefixime.

S. No.	Indigent	F1	F2	F3	F4
1.	Drug	100mg	100mg	100mg	100mg
2.	Xylitol	100mg	200mg	300mg	400mg
3.	Methanol	20 ml	20 ml	20 ml	20 ml
4.	Sodium lauryl sulphate	20 mg	20 mg	20 mg	20 mg

Evaluation of Ternary Solid Dispersion

1. Angle of repose It refers to the maximum angle formed by the powder pile surface with the horizontal plane. Angle of repose can be used in evaluation of the flow properties of powders and granules. A smaller angle of repose means better flow properties while a larger one suggests poor flow properties.^[19]

2. Hausner ratio It is an indirect method of evaluating the flow properties of a powder. It is the ratio of the tapped density to bulk density of the powder. Hausner ratio is used to evaluate the flow properties of powders and granules. Hausner ratio is less than 1.25 when there are good flow properties, but it is greater than 1.25 when there are poor flow properties.^[20]

3. Tapped density It is the mass of the powder divided by the volume of the powder that has been mechanically tapped for a certain period. Tapped density is used in evaluation of the packing and flow properties of powders and granules.^[21]

4. Bulk density It is defined as the mass of powder divided by the bulk volume of the powder before mechanical tapping. Bulk density shows the packing characteristics of the powder.^[22]

5. Carr's index It refers to the indirect determination of the compressibility and flow properties of a powder. It is determined using the bulk and tapped densities of the powder.^[23]

6. Drug content The Drug Content of the ternary solid dispersion that contained 100mg of Cefixime was done by dissolving it in 100ml of Methanol. The sample was filtered using Whatmann filter paper and analysed using a UV spectrophotometer at 288nm.^[24]

7. In vitro release The in vitro drug release study was conducted using a ternary solid dispersion that contained 100mg of Cefixime, which was placed in a beaker containing 900ml of 0.1N HCL. An aliquot of 1ml was drawn from the beaker at different time points. The

sample taken was replaced by the same volume of medium used to maintain the volume constant. The absorbance was determined using a UV spectrophotometer at 288nm.^[25]

RESULT AND DISCUSSION

Melting point

The melting point of Cefixime when determined using USP method was found to be 218-225°C which is in agreement with the melting point of Cefixime as given in literature.

Spectrophotometric analysis

Standard Curve of Cefixime

Table 2: Standard Curve of Cefixime.

S. No	Concentration($\mu\text{g/ml}$)	Absorbance
1.	0	0
2.	20	0.107
3.	40	0.19
4.	60	0.285
5.	80	0.382
6.	100	0.489

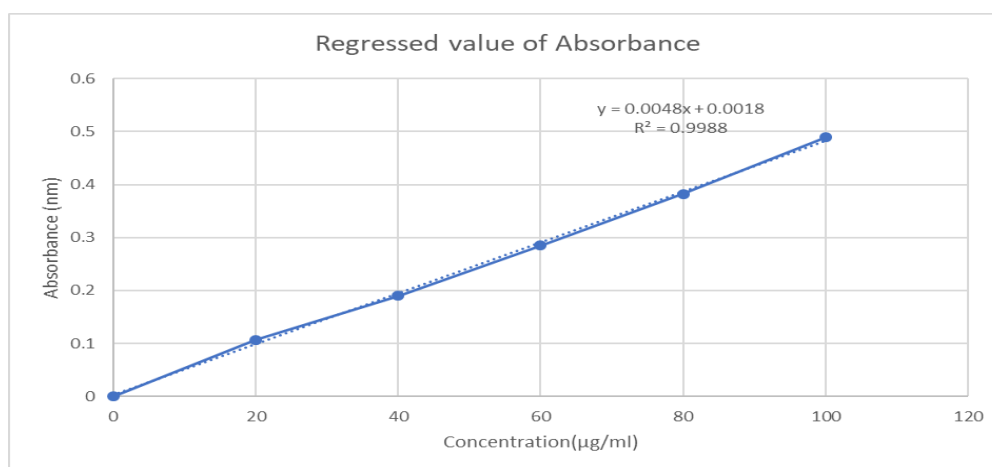


Fig: 2 Standard curve for Cefixime.

Evaluation of Ternary Solid Dispersion

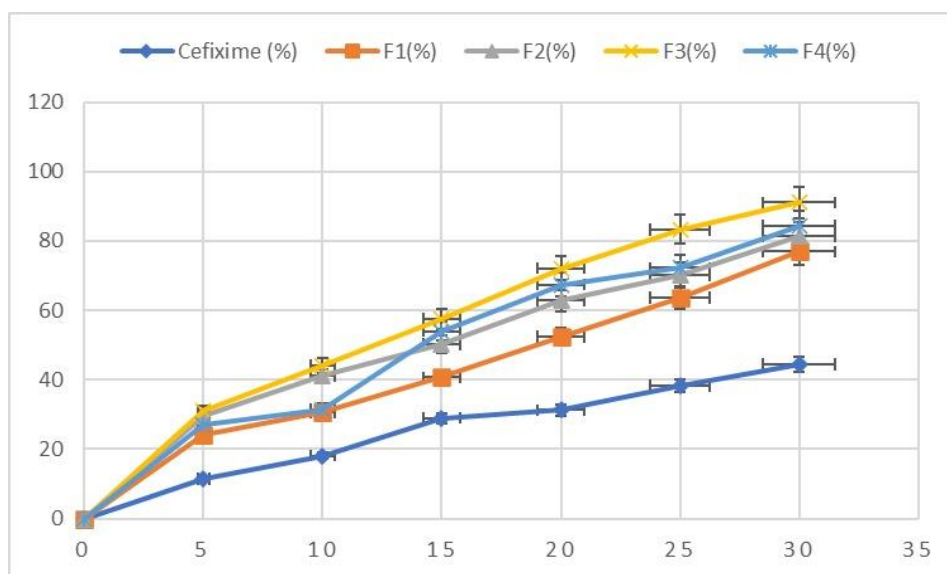
Table 3: Evaluation result of Ternary Solid Dispersion.

S. No	Property	Cefixime	F1	F2	F3	F4
1.	Angle of repose	37.88 ± 1.03	35.4 ± 1.15	31.52 ± 1.45	29.03 ± 1.6	31.92 ± 1.57
2.	Hausner's Ratio	1.53	1.61	1.04	1.94	1.10
3.	Tapped Density	0.67	0.53 ± 0.12	0.32 ± 0.35	0.56 ± 0.42	0.36 ± 0.05
4.	Bulk Density	0.44	0.33	0.31	0.29	0.33

5.	Carr's Index	34.33	37.74	31.25	48.22	35.72
6.	Drug content	-	76.88± 5.54	74.68± 2.37	91.12± 1.39	84.23± 2.30

Table 4: Result of In-Vitro Release Studies.

S. No.	Time(min)	Cefixime (%)	F1(%)	F2(%)	F3(%)	F4(%)
1.	5	11.48 ± 4.48	24.07 ± 2.20	29.62 ± 4.00	31.12 ± 1.12	27.13 ± 2.35
2.	10	18.08 ± 3.56	30.58 ± 4.47	41.06 ± 2.94	44.24 ± 2.08	31.54 ± 1.27
3.	15	28.97 ± 4.28	40.69 ± 3.18	50.31 ± 5.77	57.65 ± 1.09	54.06 ± 2.34
4.	20	31.33 ± 2.22	52.47 ± 2.57	62.88 ± 3.71	72.17 ± 1.22	67.42 ± 2.08
5.	25	38.28 ± 3.07	63.67 ± 1.42	70.16 ± 2.91	83.28 ± 2.06	72.26 ± 1.08
6.	30	44.41 ± 2.57	76.92 ± 1.44	81.26 ± 3.74	91.05 ± 1.11	84.32 ± 2.26

**Figure: 3 %Cumulative release vs Time graph.**

The ternary solid dispersions of Cefixime prepared using Xylitol and Sodium Lauryl Sulphate by the solvent evaporation method were successfully evaluated for their physicochemical properties and dissolution behaviour. The flow properties of the prepared formulations were found to be improved in comparison with pure Cefixime. The angle of repose values indicated acceptable flow characteristics, with formulation F3 showing the lowest angle of repose ($29.03 \pm 1.6^\circ$), suggesting better flowability. Similarly, the Hausner ratio and Carr's index values demonstrated improved flow properties for formulations F2 and F3.

Drug content analysis revealed that all formulations contained satisfactory amounts of Cefixime, indicating uniform distribution of the drug within the carrier matrix. Among all formulations, F3 exhibited the highest drug content ($91.12 \pm 1.39\%$), indicating efficient incorporation of the drug during the preparation process.

The *in vitro* dissolution studies demonstrated a significant enhancement in the drug release profile of the ternary solid dispersions compared to pure Cefixime. The percentage drug release increased with increasing concentration of Xylitol up to formulation F3. Formulation F3 showed the highest cumulative drug release of $91.05 \pm 1.11\%$ at 30 minutes, whereas pure Cefixime exhibited the lowest release of $44.41 \pm 2.57\%$. The enhanced dissolution may be attributed to the hydrophilic nature of Xylitol and the surfactant effect of Sodium Lauryl Sulphate, which improved the wettability, dispersibility, and solubility of Cefixime.

Based on the overall evaluation, formulation F3 was considered the optimized formulation as it exhibited superior flow properties, highest drug content, and maximum drug release among all the formulations.

CONCLUSION

The solid dispersions of Cefixime with the Xylitol as carrier were prepared and evaluated. The solubility and dissolution studies have shown that there is a possibility of improved solubility of Cefixime through solid dispersion with natural polymer viz. Xylitol. A maximum increase in dissolution rate was obtained with Cefixime-Xylitol solid dispersion with a weight ratio of 1:3 prepared by solvent evaporation method.

REFERENCES

1. Rose HS, Golan DE. Pharmacodynamics. In: Golan DE, Tashjian AR, Armstrong EJ, Armstrong AW (eds) Principles of Pharmacology: The Pathophysiologic Basis of Drug Therapy. Baltimore: Lippincott Williams & Wilkins, 2008; 19-30.
2. Rose S. Gastrointestinal and Hepatobiliary Pathophysiology, 2nd ed. North Carolina: Hayes Barton Press, 2004; 507-535.
3. Ryan JA. Compressed pellet X-ray diffraction monitoring for optimization of crystallinity in lyophilized solids: Imipenem-cilastan sodium case. J. Pharm. Sci., 1986; 75(8): 805-807.

4. Sammour OA, Hammad MA, Megrab NA, Zidan AS. Formulation and optimization of mouth dissolve tablets containing rofecoxib solid dispersion. *AAPS Pharm. Sci. Tech.*, 2006; 7(2): 1-9.
5. Samyuktha RB, Vedha HBN. Niosomal formulation of orlistat: Formulation and in-vitro evaluation. *Int. J. Drug Dev. Res.*, 2011; 3(3): 300-311.
6. Sarkar R, AL-Hossain M, Islam S, Faroque ABM. Effect of hydrophilic swellable polymers on dissolution rate of atorvastatin using simple physical mixing technique. *Ind. J. Novel Drug. Del.*, 2012; 4(2): 130-138.
7. Schwartz JB, Simonelli AP, Higuchi WI. Drug release from wax matrices. I. Analysis of data with first-order kinetics and with the diffusion-controlled model. *J. Pharm. Sci.*, 1968; 57(2): 274-277.
8. Shah S, Joshi S, Lin S, Madan PL. Preparation and characterization of spironolactone solid dispersions using hydrophilic carriers. *Asian J Phram. Sci.*, 2012; 7(1): 40-49.
9. Shinde SS, Patil SS, Mevekari FI, Satpute AS. An approach for solubility enhancement: Solid dispersion. *Int. J. Adv. Pharm. Sci.*, 2010; 1: 299-308.
10. Sreenivasa RK, Iqbal MM, Shirse P. Preparation and evaluation of cyclodextrin inclusion complexes of water insoluble drug-glimipiride. *Int. J. Res. Pharm. Biomed. Sci.*, 2012; 2(1): 428-434.
11. Swami G, Koshy MK, Pandey M, Saraf SA. Preparation and characterization of Domperidone- β -cyclodextrin complexes prepared by kneading method. *Int. J. Adv. Pharm. Sci.*, 2010; 1: 68-74.
12. Tantishaiyakul V, Kaewnopparat N, Ingkatawornwong. Properties of solid dispersions of piroxicam in polyvinylpyrrolidone. *Int. J. Pharm.*, 1996; 1: 59-68.
13. Waite M, Keenan J. *CPD for Non-Medical Prescribers: A Practical Guide*. Oxford: Blackwell Publishing Ltd., 2010; 97-100.
14. Yogesh R, Rajshree M, Mayur S, Jolly S. Effect of hydrophilic swellable polymers on dissolution enhancement of carbamazepine solid dispersions studied using response surface methodology. *AAPS Pharm. Sci. Tech.*, 2007; 8(2): 1-11.
15. Zhao G, Duane J, Xie Y, Lin G, Luo H, Li G, Yuan X. Effects of solid dispersion and self-emulsifying formulations on the solubility, dissolution, permeability and pharmacokinetics of isorhamnetin, quercetin and kaempferol in total flavones of *Hippophae rhamnoides* L. *Drug Dev. Ind. Pharm.*, 2012; 1-9 (Ahead of Print) (doi: 10.3109/03639045.2012.699066)

16. Hitoshi S, Masahiro N, Takaichi A. Inhibitory effects of polyvinylpyrrolidone on the crystallization of drugs. *Chem. Pharm. Bull.* 1978; 26: 118-126.
17. Imai T, Nishiyama T, Ueno M, Otagiri M. Enhancement of the dissolution rates of poorly water-soluble drugs by water-soluble gelatin. *Chem. Pharm Bull.* 1989 Aug; 37(8): 2251-2.
18. Kagan L, Hoffman A. Selection of drug candidates for gastroretentive dosage forms; pharmacokinetics following continuous intragastric mode of administration in a rat model. *Eur. J. Pharm. Biopharma.*, 2008; 69(1): 238-246.
19. Eleonora Mircia, Emese Sipos, Silvia Imre, Veronica Avrigeanu, Gabriel Hancu, Barna Iantovics, Teodora Balaci. New modified release tablets with pentoxifylline based on lipophilic matrix. *Farmacia*, 2012; 60, 2: 218-226.
20. Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersion. *Eur. J. Pharm. Biopharm.*, 2000; 50: 47-60.
21. Mircioiu C, Mircioiu I, Voicu V, et al. Dissolution – Bioequivalence non-correlations. *Basic Clin. Pharmacol. Toxicol.*, 2005; 96(3): 262-264.
22. Mircioiu C, Prasacu I, Sandulovici R, et al. Release of metoprolol from solid dosage forms. Choice and validation of theoretical model. *Farmacia* 2009; 57(1): 89-98.
23. Moore J, Flanner H. Mathematical comparison of dissolution profiles. *Pharm. Tech.*, 1996; 20: 64-74.
24. Pairet M, Van Ryn J, Schierok H, Hauz A, Trummlitz G, Engelhardt G. Differential inhibition of cyclooxygenase-1 and -2 by meloxicam and its 4- isomer. *Inflamm. Res.*, 1998; 47(6): 270-276.
25. Patel RP, Patel MM. Physiochemical characterization and dissolution study of solid dispersion of lovastatin with polyethylene glycol 4000 and polyvinylpyrrolidone K30. *Pharm. Dev. Technol.*, 2007; 12(1): 21-33.