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# Cefixime Solid Lipid Nanoparticles: Design, Development, and Assessment to Improve Oral Bioavailability

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**ABSTRACT**

Some chemicals don't dissolve well or don't let much through, which makes it hard to make goods that are bioavailable when taken by mouth. Nanotechnology is supposed to make our lives and living conditions a lot better.Acetonitrile was used as the solvent in this method, and Millipore water is used as the antisolvent. PVP and HPMC were the detergents that were used in the mix. It was discovered that these surfactants worked well together in the mixture. FTIR spectroscopy was used to check how well the medicine and its ingredients worked together. The study showed that the cefixime nanosuspension helped the most with healing. A variety of techniques were used to study the improved cefixime nanosuspension, including particle size analysis, differential scanning calorimetry, zeta potential, drug content, in vitro drug release research, scanning electron microscopy, and transmission electron microscopy. The disk diffusion method was used to test Cefixime nanosuspensions antibacterial action against E. coli on nutritional agar at different doses.It could also be said that the nanosuspension form of cefixime is more bioavailable

when taken by mouth than the medicine itself.

**Keywords:** Nanoparticles, solubility, bioavailability, formulation, cefixime.

## INTRODUCTION:

For most restorative purposes, taking medicine by mouth is the best way to get it to work. While some drugs may cause problems, others are perfectly designed to be absorbed by the body through the digestive system. The great solubility and permeability of Class I compounds means that they are easily absorbed when taken by mouth [1-3]. The biggest problem with improving oral dosage forms, though, is that they are not very bioavailable. Bioavailability after oral administration is affected by several things, including how well the drug dissolves in water, how quickly it dissolves, how it is broken down, how quickly it enters the systemic circulation, and how easily it is removed from the body by metabolic processes [2-4].

To get the right concentration of a drug in the bloodstream and the right pharmacological action, solubility is very important. When taken by mouth, medications that don't dissolve well may need big doses to reach the right levels in the bloodstream. One of the hardest things about making new chemical molecules and generic drugs is that they don't dissolve easily in water [3-5]. At the site of absorption, the medicine must be in the form of an aqueous solution in order to be taken. When it comes to liquid pharmaceutical formulas, water is the best solvent. Most drugs don't mix well with water and are either slightly basic or slightly acidic. It is still hard to make medicines more soluble, which means they can be absorbed better when taken by mouth. This is especially true for methods that deliver drugs orally [4-6]. The goals of this work were to create, test, and improve cefixime nanoparticles so that they would be more bioavailable when taken by mouth.

## MATERIAL AND METHODS:

Alkem Pharmaceuticals Ltd., located in Mumbai, India, offered a free sample of cefixime, while Himedia Laboratories sold PVP and HPMC. The antimicrobial study utilized E. coli as the test microorganism, with the nutrient agar being supplied by Himedia Lab Ltd. in Mumbai. Analysis grade solvents were utilized for all remaining solvents.

### Preformulation Study:

Testing before formulation is an important part of creating dosage forms for pharmaceutical drugs in a planned way. Preformulation testing, which is also known as a study, is a way to improve drug delivery and find out the physicochemical qualities of a new molecule that affect how well medicine works and how to make a stable, safe dosage form [5-7].

### Identification:

### Solubility:

Tests were done to see how well cefixime mixed with methanol, pure water, acetone, and ethyl acetate, ethanol, and phosphate buffers with pH levels of 6.8 and 7.2 [6-8].

### Compatibility Study:

### FT-IR Analysis:

Infrared spectroscopy was used to check how compatible cefixime was, which was used to make the nanosuspension. We used FT-IR spectroscopy to find out how cefixime and PVP, as well as cefixime and HPMC, behaved when mixed at the right temperature [7-9].

### DSCAnalysis:

Both solid and liquid pharmaceutical samples were put in metal pans that were then sealed. The temperature was then raised slowly, from 30°C to 310°C at a rate of 5°C per minute

throughout the process. During this whole process, nitrogen gas kept going through the pans. As a guide, an empty crimped pan was used. As the temperature changed, the thermal conductivity of both the drug and the drug-polymer mixture was checked [8-10].

**Preparation of nano formulation:**
The solvent/anti-solvent method was used to make the cefixime nanosuspension. Four separate recipes were made. An amount of 5 milliliters of methanol was used to correctly measure and completely dissolve the cefixime in the above mixture. By adding each of the ingredients one at a time to a 200 mL beaker along with 100 mL of Millipore water, the mix was made. After that, a probe sonicator was used to break up some of the excipients. After that, the drug solution was slowly added to the beaker that had 100 milliliters of Millipore water in it. A probe sonicator was used to sonicate the mentioned formulation for 15 to 30 minutes so that too much heat wouldn't be produced. Additionally, the mixture was put into an amber-colored jar and kept in the fridge. The particle sizes of the mixture were looked at in a study. In table 1, you can see how the cefixime nano suspension was made [9-11].

**Table 1: Formulation table**

| Sr. No. | Batches | Drug (mg) | PVP | HPMC | Solvent | Water |
|---|---|---|---|---|---|---|
| 1. | F1 | 100 | 30 | 30 | 5 | 100 |
| 2. | F2 | 200 | 5.0 | 5.0 | 5 | 100 |
| 3. | F3 | 200 | 15 | 15 | 5 | 100 |
| 4. | F4 | 100 | 30 | 30 | 5 | 100 |
| 5. | F5 | 300 | 10 | 15 | 5 | 100 |
| 6. | F6 | 200 | 15 | 10 | 5 | 100 |

**Evaluation of optimised formulation:**
**Particle size, PDI and Zeta Potential:**
We used the Zeta Potential to measure the electric charges on the particles' surfaces. This number tells us about how stable colloidal systems are physically. The test was done by measuring how easily the particles moved along an electrophoretic field. A Zetasizerano ZS was used to find it. A tool named "Micronanotrac A150" was used to measure the polydispersity index (PDI) of the cefixime nanosuspension. The readings were taken in a direct way. The PDI number for all nanosuspension formulations is less than 0.8. For measuring the particle sizes of cefixime nanosuspension, the Malvern zetasizer device is used. The sizes of the particles in each cefixime nanosuspension mixture were studied. It was found out what the mean particle size (PS) of the cefixime nanosuspension was [12-15].

**Drug Content:**
The 100 mg of cefixime was mixed thoroughly with 100 ml of 0.1N HCl in a volumetric flask. A 10 mL sample of the above solution was taken out, diluted in a volumetric flask until it had a volume of 100 mL, and then it was looked at with a UV Spectrophotometer at a wavelength of 287 nm [16-19].

***In-vitro* drug release study:**
We looked at how the cefixime nanosuspension drug released in phosphate buffer (PBS) with a pH of 7.4. Two milliliters of liquid were put into a five-milliliter measuring cylinder, and then a dialysis membrane was put over the mouth of the cylinder. After that, the measuring cylinder was placed upside down on top of a 50-ml beaker that contained PBS

and was being stirred with a magnetic mixer. After that, the beaker was stirred at a speed of 50 turns per minute and a temperature of 37±0.5°C so that a magnetic bead could be added. One milliliter of the dispersion was taken out and replaced with one milliliter of PBS at set times (1, 5, 10, and 15 minutes). After filtering, a UV Spectrophotometer was used to measure the amount of dissolved cefixime in each sample at a range of 287 nm [20-25].

**Antimicrobial studies:**

One gram of healthy agar was mixed with fifty milliliters of clean water. It was heated and stirred until the mixture was fully dissolved, and then it was put in an autoclave at 121°C for about 15 minutes. After the autoclave cycle was over, the material was allowed to cool down before being put on separate plates and left to harden on a clean surface. The loop was taken off after putting it in E. coli. All of the procedures took place in a clean area. The top of the agar plate was taken off, and the loop was gently pressed against the middle of the plate to check its temperature. Spread it out carefully so that it covers the whole surface of the plate. There must be sterilization of the flame both before and after it is used. Put the top back on top of the agar plate. The 10 mm disks were put in order. We looked at the zone of blocking after the samples were left to sit at 35°C for about 24 hours [26-32].

## RESULTS AND DISCUSSION:

**Preformulation study:**

**Melting point:**

The temperature at which cefixime melts was found to be 220°C. The cefixime medicine has a freezing point of between 218 and 225°C, which shows that it is pure.

**Solubility studies:**

The amount of cefixime that could be dissolved was about the same as the average number. After studying how well the drug dissolves, it was shown that it dissolves completely in methanol and more completely in 0.1N HCl. Millipore water and 0.1 N HCl were used to test how well cefixime dissolved.

**Compatibility studies:**

**FT-IR Analysis:**

The FTIR spectra of the pure cefixime drug were studied along with the physical mixes that contained the fillers. The fact that the drug's functional groups show similar peaks across the spectrum shows that the drug and the polymers are not interacting with each other. Figures 1 and 2 and Table 2 show the FTIR spectrum data.

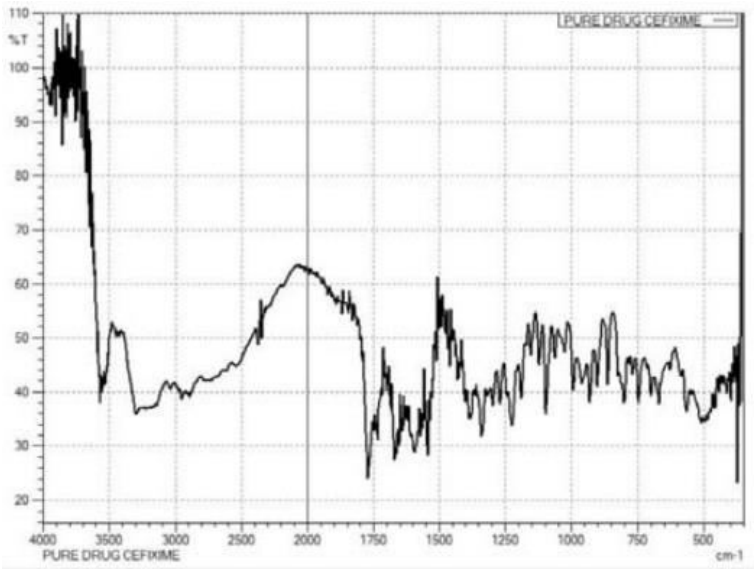


**Figure 1: FTIR spectra for drug**

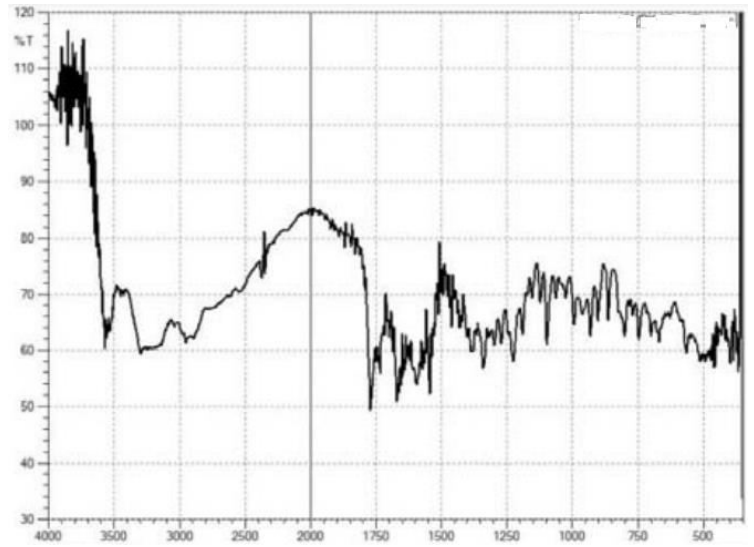


**Figure 2: FTIR spectra for mixture**

**DSC Analysis:**

It was found that pure API cefixime has a freezing point of 218–225°C. At a temperature of 202.0°C, the peak of pure cefixime was round and smooth. In Figures 3 and 4, you can see that cefixime and its components PVP and HPMC reached their highest points at 122.5°C and 138.5°C, respectively.

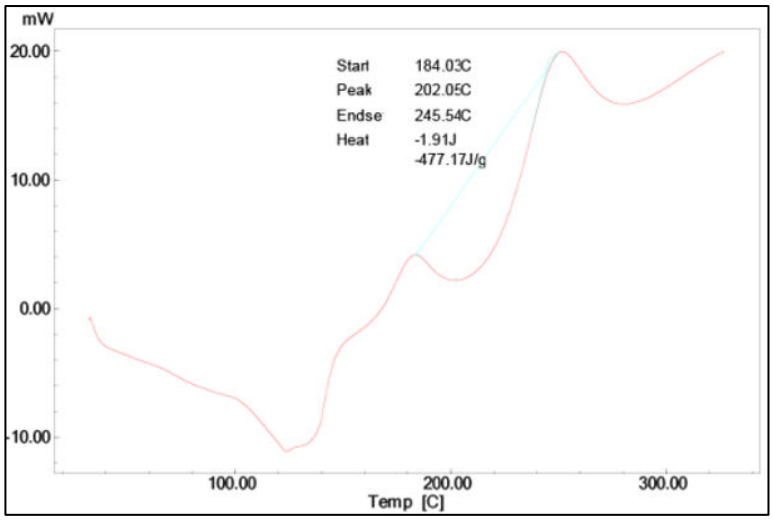


**Figure 3: DSC curve for pure drug Cefixime**

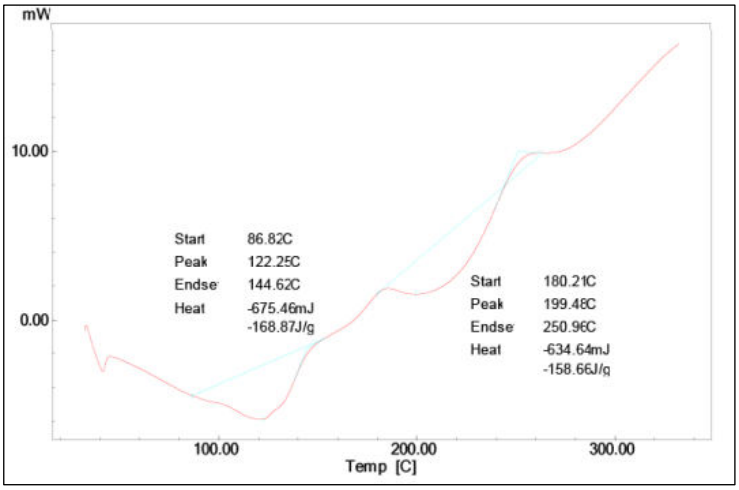


**Figure 4: DSC curve for Mixture**

**Particle size, PDI and Zeta Potential:**

The Malvern Zetasizer was used to measure the polydispersity index and look at the particle sizes. Particle sizes that stayed the same, between 210 and 310 nm, and a polydispersity index (a measure of particle size distribution) below 0.8 were signs of good results. The adjusted cefixime nanosuspension in Figure 5 was found to have a Zeta Potential of -12.2 mV, which means it is very stable and will stay stable over time when stored.

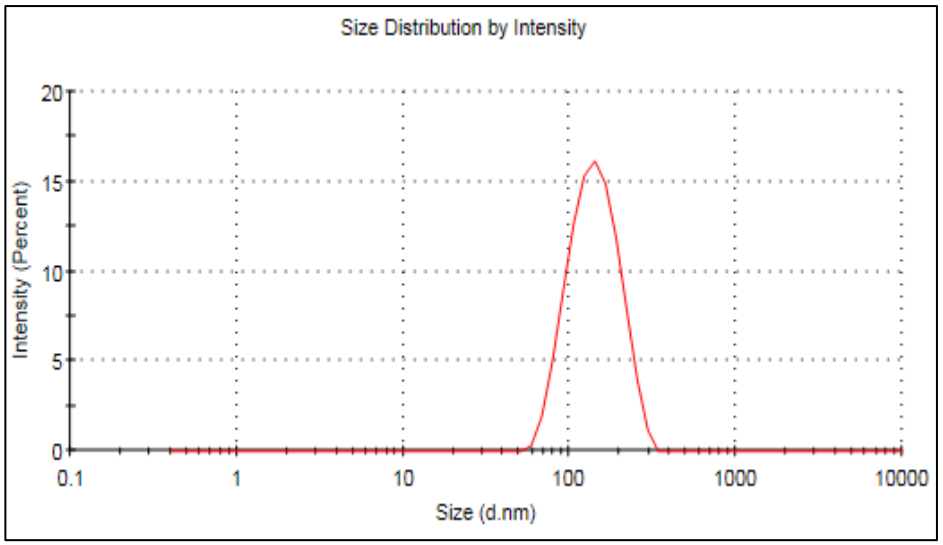


**Figure 5: Particle size and PDI analysis**

**Drug Content:**

The lowest amount of drug lost depends on how much drug is in the cefixime nanosuspension. It has been found to be over 80% (Table 3).

**Table 3: Drug content**

| Batches | Abs.(nm) | %DrugContent |
|---|---|---|
| F1 | 0.458 | 85.12 |
| F2 | 0.429 | 80.33 |
| F3 | 0.468 | 87.40 |
| F4 | 0.473 | 88.21 |
| F5 | 0.451 | 90.10 |
| F6 | 0.436 | 82.30 |

***In-vitro* drug release:**

For the in vitro release studies, a phosphate buffer with a pH of 7.4 was used in the diffusion method. The outcomes of each improved formulation are also shown in Table 4 and Graph Figure 6.

**Table 4: Drug release study**

| Sr. No. | Time | Abs. | Mg/50ml | CDR | %CDR |
|---|---|---|---|---|---|
| 1. | 1min | 0.013 | ).641 | 0.642 | 62 |
| 2. | 5min | 0.017 | ).112 | 0.729 | 72 |
| 3. | 10min | 0.019 | ).123 | 0.849 | 84 |
| 4. | 15min | 0.020 | ).125 | 0.969 | 97 |

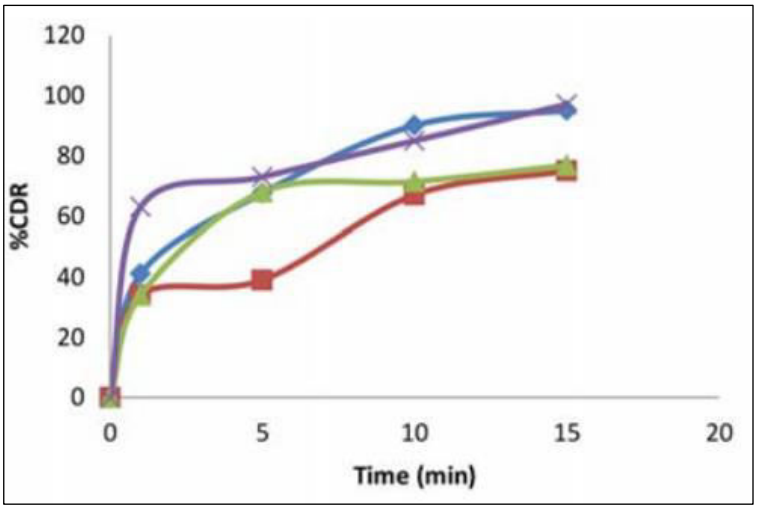


**Figure 6: *In-vitro* Drug Release**

**Antimicrobial Assay:**

E. coli was used as a test organism to see how well cefixime nanosuspension killed germs. Using the method of disk diffusion. In Table 5, you can see the average values of the zone of inhibition for F1, F2, F3, F4, F5, and F6. There are also pictures of the zone of inhibition for the best version.

**Table 5: MIC Data**

| Sr. No. | Batches | MIC (mm) |
|---|---|---|
| 1. | F1 | 7.3 |
| 2. | F2 | 7.0 |
| 3. | F3 | 6.1 |
| 4. | F4 | 6.0 |
| 5. | F5 | 7.6 |
| 6. | F6 | 6.2 |

**CONCLUSION:**

This research made a successful cefixime nano suspension using solvent/antisolvent and probe sonication. The medicine and its formulation function well with surfactants like PVPand HPMC, according to FTIR and DSC measurements. Surfactant concentration increases particle size, although polymer concentration increases medication amount and particle size. Solubility and in vitro studies demonstrated that nano suspension dosage forms considerably accelerated diffusion. The in vitro drug release pattern shows rapid and constant release for 15 minutes. Finally, probe sonication technology's solvent/antisolvent technique is simple, fast, and effective. Additionally, cefixime is more bioavailable when administered orally as a nano suspension dose rather than the medication itself.

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None
**Conflict of Interest:**
None

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