

Formulation and Evaluation of Cefixime Nanosuspension for the Enhancement of Oral Bioavailability by Solvent-Antisolvent Method and its Suitable Method Development

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ABSTRACT

Aim: The objective of the present study was to develop and evaluate cefixime nanosuspension to enhance its oral bioavailability. **Materials and Methods:** The method used was solvent/ antisolvent method in which methanol and Millipore water was used as solvent and antisolvent respectively. The surfactants used for the preparation were PVP K30 and HPMC K100 which was found to be compatible in the formulation. Compatibility of the drug and drug with its excipients was found out by FTIR studies. Characterization of the optimized Cefixime Nanosuspension was carried out by particle size analysis, Differential Scanning Calorimetry, Zeta Potential, Drug content, *in-vitro* drug release studies, Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM). The antimicrobial activity of cefixime nanosuspension was done by Disk diffusion method against *E. coli* performed in nutrient agar with different concentrations of the formulation. The Minimum Inhibitory Concentration (MIC) was determined by calculating Zone of inhibition. A method was developed for cefixime nanosuspension and validated by High Performance Thin Layer Chromatography (HPTLC). **Results:** The optimized cefixime nanosuspension was validated for Identification, Linearity, Specificity, Precision and Recovery. The Recovery of cefixime nanosuspension was found to be 95.57%.

Key words: Cefixime nanosuspension, Method development, HPTLC, Solvent/ Antisolvent method, Validation.

Submission Date: 17-05-2019;

Revision Date: 04-09-2019;

Accepted Date: 07-11-2019

DOI: 10.5530/ijper.54.1.7

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INTRODUCTION

Nanotechnology and Nanosuspension

Nanotechnology is probably going to roll out a major improvement in our lives and well-being situation.^{1,2} It is a standout amongst the most vital innovative work territory in the present time. Nanotechnology is a pertinent part of a more extensive territory of nanoscience which is one of the upcoming and very testing just as remunerating key research zone in the cutting edge

logical set up. It is the investigation of little molecule having one of a kind property, which change on modifying the measure of the particle size.

A standout amongst the best systems for the improvement of oral bioavailability of insoluble medications is nanosuspension. These are colloidal scatterings and biphasic framework comprising of medication particles scattered in a watery vehicle in which the measurement of the



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suspended molecule is under 1 μ m in size. They are powerful in conveying the poor dissolvable prescription to concentrate on tissues with their last expanded bio-availability and higher restorative results. They are very ready to focus on the medications to different indispensable organs by excellence of their submicron size or surface adjustments.^{2,3}

Method of preparation of nanosuspension

Preparation of nanosuspension is simple and cost saving used for less soluble drugs for a physically more stable product. For manufacturing nanosuspensions, there are two methods, “Top-down process technology” and “Bottom-up process technology”. The method of preparation of nanosuspension has been showed in Figure 1.

Oral Drug Delivery System

It is one of the easiest routes of delivery of drugs for systemic and local effect as it is safer, the compliance of the patient is better, simpler to ingest with no pain. Liquid forms are better for ingestion than forms. Poorly aqueous soluble drugs have low drug absorption and in turn have insufficient and variable bioavailability. To enhance the same, various techniques are used that is by nano sizing the less dissolving drugs. Nano suspensions are occupied with varied good outcomes for drug delivery. Nano suspension drug delivery system for oral usage has increased dissolution rate and solubility of poorly soluble drugs.^{4,5}

Cefixime

Cefixime fall during a low solubility and low porousness bactericide. Bioavailability of drug is restricted due low solubility and due low solubility i.e. 30%-40%. They provide affordable formulations to improve the bioavailability and drug delivery. The objective of

this study was to develop stable Nano suspension formulation of cefixime, which will eventually improve its solubility, stability and oral bioavailability. Cefixime which falls into category of cephalosporin of third generation antibiotics is used variedly for the diagnosis of infections like pharyngitis, otitis media and gonorrhea, bronchitis and urinary tract infections.^{4,5}

Antibiotics as Nano suspension

Antibiotics or antibacterial are a type of antimicrobials used is the treatment of bacterial infections. They kill or inhibit the expansion of micro-organisms. Cephalosporin's got a huge area of activity against Gram positive and Gram-negative bacteria by inhibiting bacterial cell wall synthesis and it been obtained semi-synthetically from ocean fungi *Cephalosporium acremonium* with antibacterial activity. All the cephalosporins act and are employed as good antibacterials or antibiotics.^{4,6}

Method Development of cefixime by High Performance Thin Layer Chromatography (HPTLC)

High Performance Thin Layer Chromatography is an analytical method for reliability in quantification of analytes at micro and even in nanogram levels. Furthermore, the pictures obtained are so colourful of HPTLC image which fetches excess parameters of visible colour and fluorescence. A CAMAG HPTLC was used for the estimation of cefixime in the nanosuspension (VISIONCATS HP-TLC SOFTWARE).^{5,6}

Method Validation

“A part of validation process which establishes from laboratory studies that the performance characteristics of the method will meet the requirements for the intended analytical application.” Method development and method validation go hand in hand and cannot be separated to detect the developed method and its performance parameters that validation has carried out. The need for validation in analytical laboratories is obtained through International Conference on Harmonization (ICH); Current Good Manufacturing Practices (cGMP); Good Laboratory Practices (GLP); and Good Clinical Practices (GCP). The Validation parameters included are: Identification, Linearity, Precision, Specificity and Recovery.^{7,8}

MATERIALS AND METHODS

Cefixime was a gift sample from Lupin Pharmaceuticals Ltd. Mumbai, India and PVP K30 and HPMC K100 was purchased from Ozone Pharmaceuticals. The test micro-organism used for the antimicrobial study was

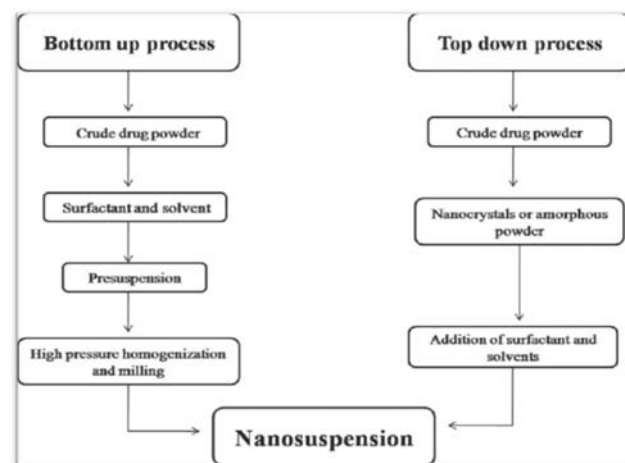


Figure 1: Development of Nano suspension.

E. coli maintained on nutrient agar provided by Himedia Lab Ltd. Mumbai.

Preformulation Study

The primary procedure in rational development of dosage forms of a drug substance is preformulation testing. Preformulation testing or study is method of optimization of drug delivery and determining physicochemical properties of the new compound which affects drug performance and development of a proper safe; stable dosage form.

Identification

Determination of melting point

The melting point of cefixime drug was found by Thiele's tube apparatus.

Solubility

The solubility of cefixime was checked in solvents such as methanol; distilled water; ethyl acetate; ethanol; acetone; 6.8 and 7.2 phosphate buffer.^{9,10}

Determination of absorbance maximum of Cefixime

100mg of cefixime was taken in 100mL of volumetric flask and dissolved in 50mL of methanol and made up to the mark with 0.1N HCl. 10ml of the above stock solution was taken in 100ml of volumetric flask and was diluted with 0.1 N HCl to produce a concentration of 100µg/ml which was used as standard stock solution. The standard stock solution was scanned between 200-800nm to determine the maximum absorbance.^{6,11}

Compatibility studies

FTIR Spectroscopy

The compatibility of cefixime used to formulate nanosuspension was established by IR spectroscopy method. FT-IR spectral measurement of cefixime drug and physical mixtures of cefixime+PVP K-30 and cefixime+HPMCK 100M were taken at a proper temperature.^{6,11}

Differential Scanning Calorimetry (DSC)

DSC was done using Shimadzu-DSC – TA 60. The drug samples were put in aluminum solid and liquid pans; crimped and heated under nitrogen gas flow at a scanning rate of 5°C/min from 30°C to 310°C. An empty crimped pan was used as reference. As a function of temperature, the heat flow was measured for both drug and drug-polymer physical mixture.^{6,11}

Table 1: Formulation table for cefixime nanosuspension.

Formulation	Cefixime (mg)	PVP K-30 (mg)	HPMC K 100(mg)	Methanol (mL)	Millipore water (mL)
F1	100	40	40	5	100
F2	200	5	5	5	100
F3	200	20	20	5	100
F4	100	35	35	5	100

Standard calibration curve of cefixime

100mg of cefixime was taken in 100mL of volumetric flask and was dissolved in 50 mL of methanol and made up the volume with 0.1 N HCl. 10ml of above primary stock solution was pipetted in 100 ml volumetric flask and diluted with 0.1 N HCl to produce concentration 100µg/ml. Dilutions were prepared out of secondary stock solution in the concentration range 2 to 12µg/mL. The absorbance was measured by UV spectrophotometer. λ_{max} : 287nm; Beer's range: 2-20mg/mL.^{6,11,12}

Preparation of cefixime nanosuspension

Cefixime nanosuspension was prepared by Solvent/anti-solvent method. Four different types of formulations were formulated. The above given cefixime (drug) from the formulation was weighed and dissolved completely in 5mL of methanol. In a 200mL beaker (kept in a ice bath), 100mL of Millipore water was taken and both the excipients each were added slowly to the beaker and partially dissolved using probe sonicator. The drug solution was then added slowly to the beaker containing 100 ml of Millipore water. The above formulation was sonicated for 15 to 30 mins using probe sonicator ensuring that the formulation did not become hot. Further, the formulation was transferred in an amber coloured bottle and stored in the refrigerator. The sizes of particle analysis of the formulation were carried out.^{11,12} Table 1 summarizes the formulation of cefixime nano suspension

Evaluation parameters for cefixime nanosuspension

Particle size analysis: Particle size analysis of cefixime nanosuspension is characterized by using the instrument Micronanotrak A150. All the prepared cefixime nanosuspension formulations were analysed for particle sizes. The mean particle size (PS) for cefixime nanosuspension was measured.¹⁻³

Polydispersity Index

The mean polydispersity index (PDI) for cefiximenano-suspension was measured using a “Micronanotracer A150” instrument and the samples were measured directly. PDI values of all nanosuspension formulations are less than 0.8.^{11,12}

Scanning Electron Microscopy (SEM)

SEM was used in to examine the particle surface morphology and shape of cefixime nanoparticles. The particle size; sphericity and surface morphology of cefixime nanosuspension were characterized by Scanning Electron Microscope at IIT Delhi.^{12,13}

Transmission Electron Microscopy (TEM)

TEM was used to test the surface morphology and particle size. The images of TEM was found using Transmission electron microscope; at IIT Delhi.¹²⁻¹⁴

Zeta Potential

For the measurement of the electric charges at the surface of the particles; Zeta Potential was used; indicating the physical stability of colloidal systems and it's been shown in Table 4. The assessment was done by determining the electrophoretic mobility of the particles. It was found using a zetaserano ZS (Malvern Instruments; Malvern; UK).^{1,6}

Drug content

100mg of cefixime was taken and dissolved completely on 100ml of 0.1N HCl in a volumetric flask. From above solution; 10ml was withdrawn and diluted to 100ml in a volumetric flask and then analysed in UV Spectrophotometer at a wavelength of 287nm.^{13,14}

In-vitro drug release studies

Drug release of cefixime nanosuspension was studied in phosphate buffer (PBS); at a pH of 7.4 as the medium. An amount of 2ml was taken in a 5ml measuring cylinder and a dialysis membrane was tied to the mouth of the measuring cylinder. The measuring cylinder was then inverted over a 50ml beaker kept on a magnetic stirrer containing PBS. A magnetic bead was then added into the beaker by shaking at 50 rpm at $37 \pm 0.5^\circ\text{C}$. 1 ml of the dispersion was taken and replaced by 1ml of PBS at a determined time interval (1; 5; 10 and 15 min). Each sample was filtered and the amount of cefixime dissolved was determined using a UV Spectrophotometer at a wavelength of 287nm.¹⁴⁻¹⁶

Antimicrobial studies

1.05 g of nutrient agar was dissolved in 50 ml of distilled water. The above mixture was stirred and

heated to dissolve it completely and autoclaved at 121°C for about 15 min. Once the autoclave is completed, it was allowed to cool and poured in each plate and on a sterile surface until it was solidified. The loop was dipped in *E. coli* and removed. All the procedures were performed in aseptic conditions. The agar plate was opened and the loop was touched at the center of the plate. Gently spread it on the surface of the plate. The loop should be sterilized before and after use in the flame. Put the top back onto the agar plate. The 10mm disks were placed. Incubation at 35°C for about 24 hr and the zone of inhibition was measured.¹⁴⁻¹⁷

Method development and Validation by High Performance Thin Layer Chromatography (HPTLC) by VISIONCATS HP-TLC SOFTWARE (CAMAG)

An HPTLC method was developed for cefixime nanosuspension. Evaluation of the same was carried out for the performance of separating standard in the sample. The method was finalized based on the criteria of optimum separation using derivatization or without derivatization. Method developed for cefixime nanosuspension and validated used TLC 10×10 plates with the mobile phase Chloroform: Methanol: Water: Acetic acid in the ratio 6: 1.5: 0.5: 2 v/v/v/v. Saturation time given for the mobile phase was 20 min and dried at room temperature. The validation for HPTLC method development for optimized cefixime Nano suspension was performed using parameters like identification, linearity, precision, specificity and recovery.^{18,19}

RESULTS AND DISCUSSION

Preformulation studies

Melting point: The melting point of cefixime was obtained at 220°C . cefixime of melting point of the drug is ranging from $218 - 225^\circ\text{C}$, indicating that the drug which is obtained is pure.^{19,20}

Absorbance maximum (λ_{max}): The λ_{max} of cefixime was 287nm similar to that of literature review indicating drug purity.¹⁹⁻²¹

Solubility studies: The solubility of cefixime was found to be nearly same as that of the standard value. From the solubility study, it was seen that the drug had better solubility in 0.1N HCl and was completely solu-

Table 2: Solubility studies.

Solvents	Solubility
Millipore water	55.1mg/L
0.1 N HCl	78mg/L

Table 3: Absorbance data for standard calibration curve.

Concentration (µg/mL)	Absorbance (nm)
2	0.117±0.01
4	0.213±0.01
6	0.313±0.01
8	0.423±0.02
10	0.518±0.03
12	0.629±0.03

Results expressed as Mean± SD (n=3).

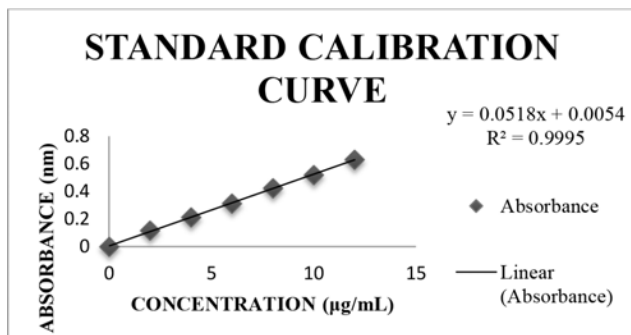


Figure 2: Standard calibration curve for cefixime.

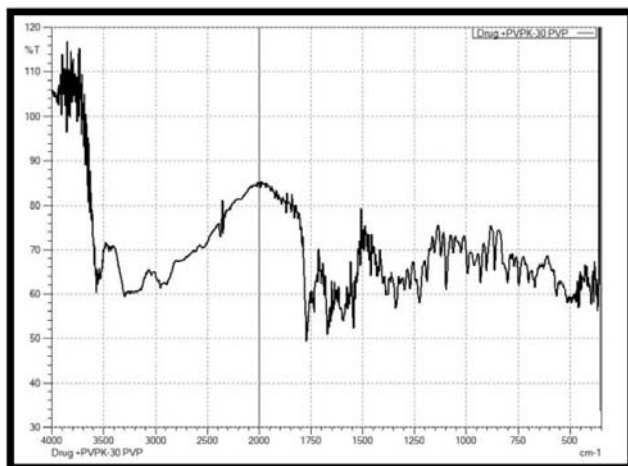


Figure 3: FTIR spectra for cefixime drug.

ble in methanol.^{21,22} Table 2 summarizes the solubility of cefixime in Millipore water and 0.1 N HCl

Compatibility studies

Standard calibration curve: Absorbance maximum of cefixime was observed at 287nm showing better linearity ($r^2=0.9995$) over the concentration range of 2 to 12µg/mL passing from the origin following the Beer-Lambert Law. The equation of linerity was found to be $y=0.0518x+0.0054$.^{23,24}

Absorbance Data for Standard Calibration Curve of Cefixime at 287 nm in 0.1N HCl (Table 3 and Figure 2).

Table 4: Spectral data for FTIR spectroscopy.

Functional Group	IR Range	Pure Drug	Drug+PVP K-30	Drug+HPMC K100M	Cefixime Nanosuspension
C=O(Stretching)	1770-1780	1763.7	1762.5	1763.7	1768.28
C=C(Stretching)	1626-1662	1661.1	1659.5	1659.5	1667.63
N-N(Bending)	1580-1650	1537.7	1540.3	1537.7	1541.08
C-O(Stretching)	1085-1150	1088.0	1084.8	1088.7	1083.81

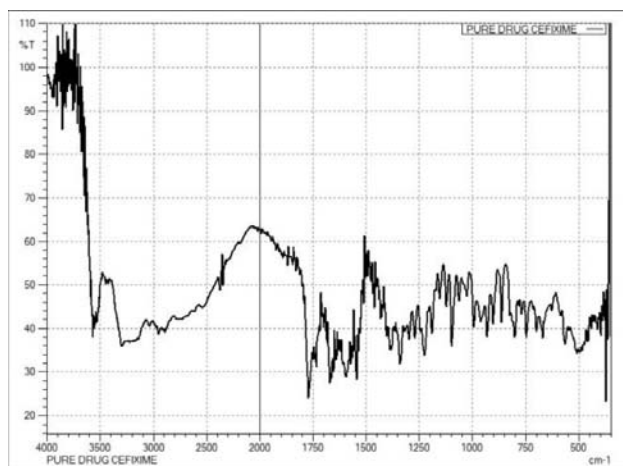


Figure 4: FTIR spectra for cefixime+PVP K30.

FTIR Spectroscopy

FTIR spectrum of cefixime pure drug along with the physical mixtures containing the excipients was observed. The spectra have similar peaks of functional groups of drugs which indicate that the interaction was

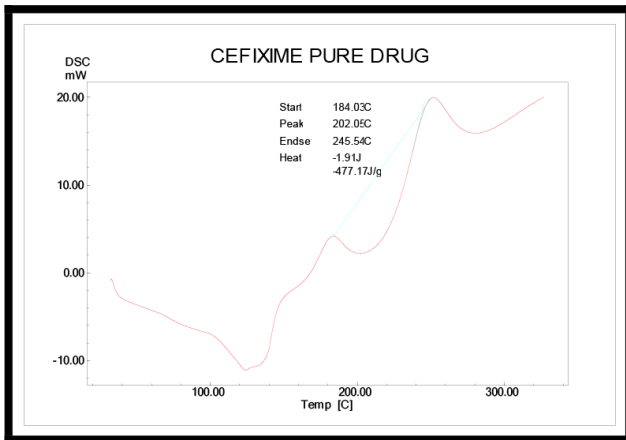


Figure 5: DSC curve for pure drug Cefixime.

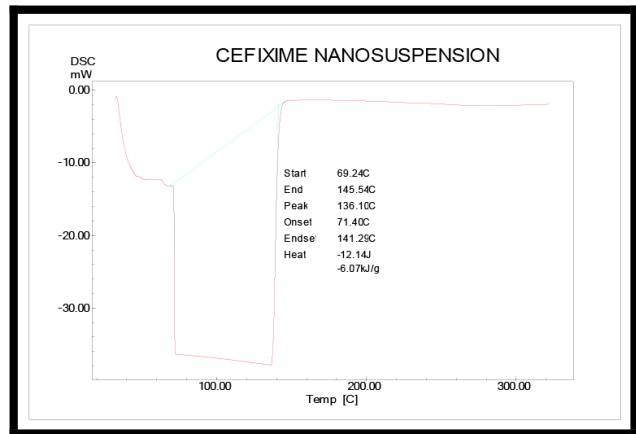


Figure 8: DSC curve for formulated cefixime nanosuspension.

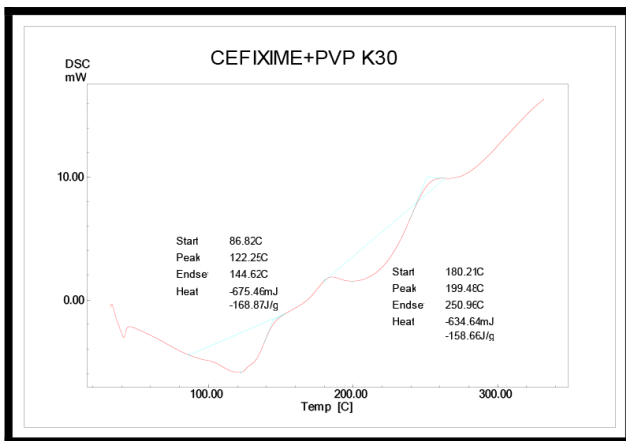


Figure 6: DSC curve for Cefixime + PVP K-30.

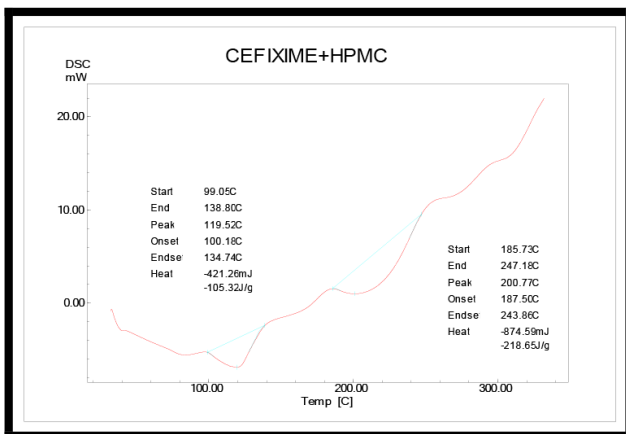


Figure 7: DSC curve for cefixime + HPMC Figure K100M.

not found between the drug and the polymers. The FTIR spectral data has been shown in Table 4, Figure 3 and 4.^{25,26}

Differential Scanning Calorimetry (DSC)

The melting point of the pure API cefixime was found between 218-225°C. Pure cefixime showed a smooth,

Table 5: Particle sizes and Polydispersity index of four formulations.		
Formulation	Particle Size (nm)	Polydispersity Index
F1	284.9nm	0.831
F2	338.0nm	0.2670
F3	360.0nm	0.2238
F4(Optimised)	288.3nm	0.1422

blunt peak at 202.0°C. Similarly, Cefixime along with its excipients, PVP K-30 showed peak at 122°C and HPMC K 100M showed peak at 138.8°C which has shown in Figure 5-7. Whereas DSC curve for liquid formulation of cefixime nanosuspension has been shown in Figure 5,6,7 and 8.²⁷

Particle size analysis and Polydispersity Index

Particle sizes analysis and polydispersity index was generated from Micronanotracs A150. The particle sizes were consistent in the range 200 to 300nm with polydispersity index or particle size distribution less than 0.8 indicating good results (Table 5 and Figure 9).²⁷

Scanning Electron Microscopy: SEM image of cefixime nanoparticles shown in Figure 10 concludes that nanoparticles are found in nano size.

Transmission Electron Microscopy: TEM cefixime nanoparticles in Figure 11; TEM image of optimized cefixime nanosuspension shows spherical size of the nanoparticles.

Zeta Potential: Zeta Potential of optimized cefixime nanosuspension was found to be - 15.5 mV shown in Figure 12; which indicates good stability and stabilizes more on longer storage.

Drug Content: The drug content of cefixime nanosuspension resulted more than 80% which determines

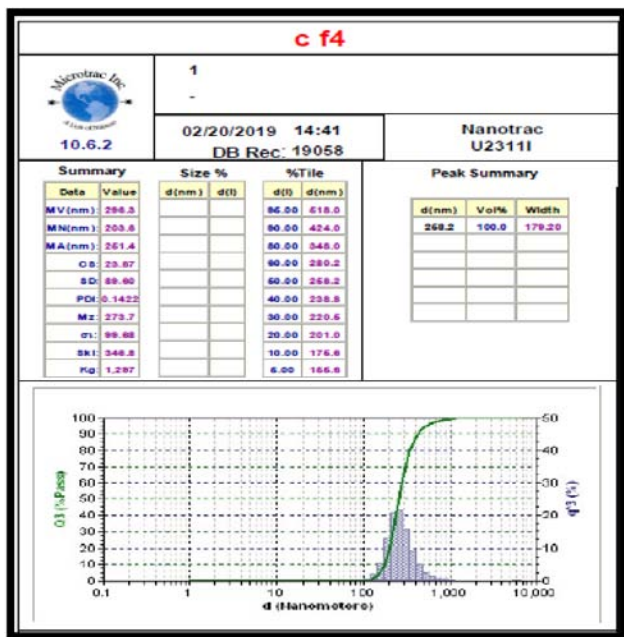


Figure 9: Particle size and polydispersity index of Cefixime nanosuspension (Formulation-4).

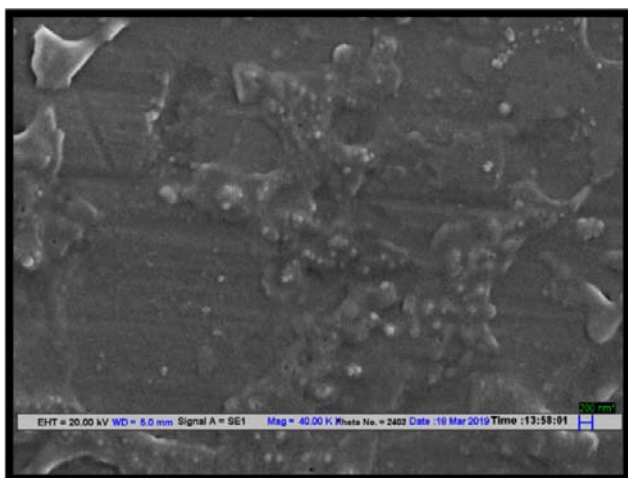


Figure 10: TEM image of cefixime nanosuspension of optimized formulation.

minimum drug loss. The drug content for all the four formulations are shown in the Table 6.

In-vitro drug release studies: The *in vitro* release studies were carried by diffusion method with phosphate buffer 7.4. And the results of all the optimized formulation are shown in Table 7 and graph Figure 13.

Antimicrobial Studies

The antimicrobial activity of cefixime nanosuspension was determined by *E. coli*. Using disk diffusion method. The average values of zone of inhibition of F1; F2; F3 and F4 are given in Table 8. And the images of the zone of inhibition of the optimized formulation are shown in Figure 14.

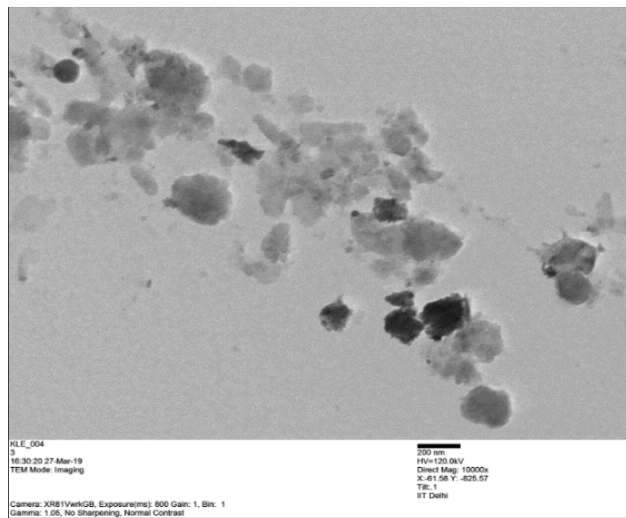


Figure 11: SEM image of cefixime nanosuspension.



Figure 12: Zeta Potential data for cefixime nanosuspension.

Table 6: Drug content of cefixime nanosuspension.

Formulation	Absorbance (nm)	%Drug Content
F1	0.458	87.37
F2	0.429	81.77
F3	0.468	89.3
F4(Optimised)	0.473	90.2

Table 7: Drug release study of optimised Cefixime nanosuspension Formulation 4 (F4).

Time	Absorbance	µg/ml	mg/ml×10	mg/50ml	CDR	%CDR
1 min	0.012	0.127	0.00127	0.635	0.635	63
5 min	0.016	0.204	0.00204	0.102	0.73	73
10 min	0.018	0.243	0.00243	0.121	0.85	85
15 min	0.018	0.243	0.00243	0.121	0.971	97.1

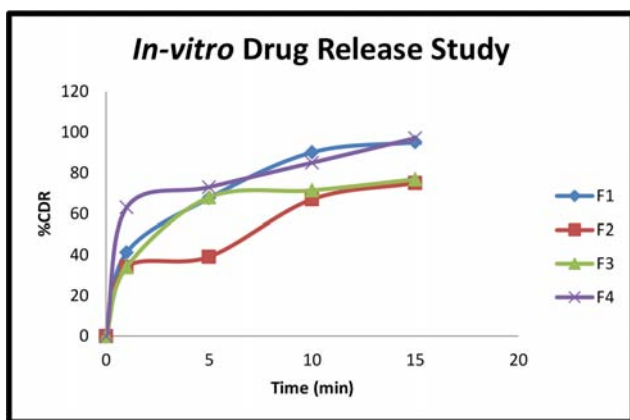


Figure 13: In-vitro Drug Release Study.

Table 8: Antimicrobial zone of inhibition data.

Formulation	MIC (Zone of Inhibition) (mm)
F1	7.2
F2	7.1
F3	6.9
F4(Optimised)	7.6

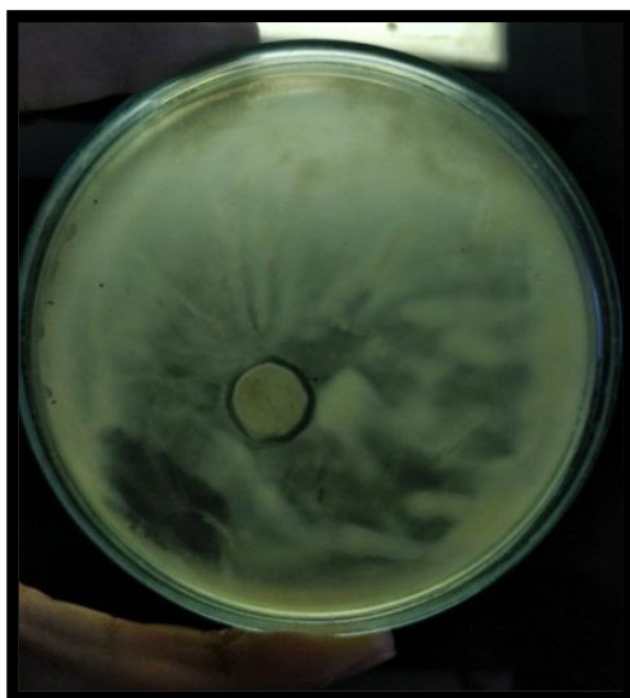


Figure 14: Antimicrobial activity of the optimized cefixime nano-suspension of formulation 4 (F4).

Method development of cefixime nano-suspension by High Performance Thin Layer Chromatography (HPTLC) Method.

The method was developed for cefixime Nano suspension using TLC 10×10 plates was Chloroform: Methanol: Water: Acetic acid in the ratio 6:1.5:0.5: 2 v/v/v/v. The

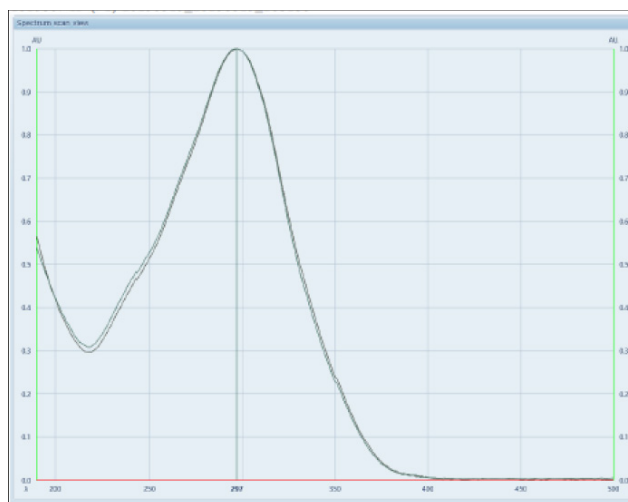


Figure 15: Spectral overlay of cefixime standard and Cefixime in Nano suspension.

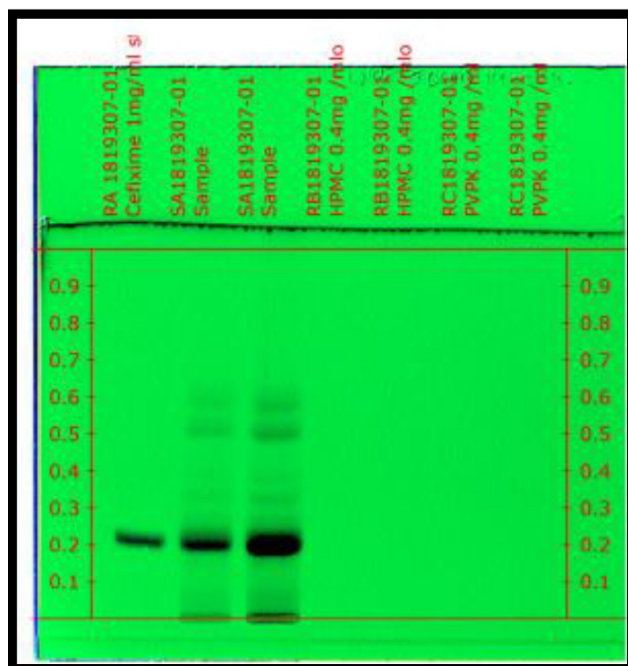


Figure 16: R 256.

results obtained from the validation of the same is given below.²²⁻²⁶

Identification of cefixime

The spectral of cefixime standard and formulation are shown in Figure 15 and the scanning data of cefixime at 254nm and 366 nm is shown in Figure 16 and 17 respectively.²²

Data Acquisition

Linearity: The calibration graph for linearity of cefixime scanned at 366nm is shown in Figure 18 and the 3D image of evaluation has been shown in Figure 19.

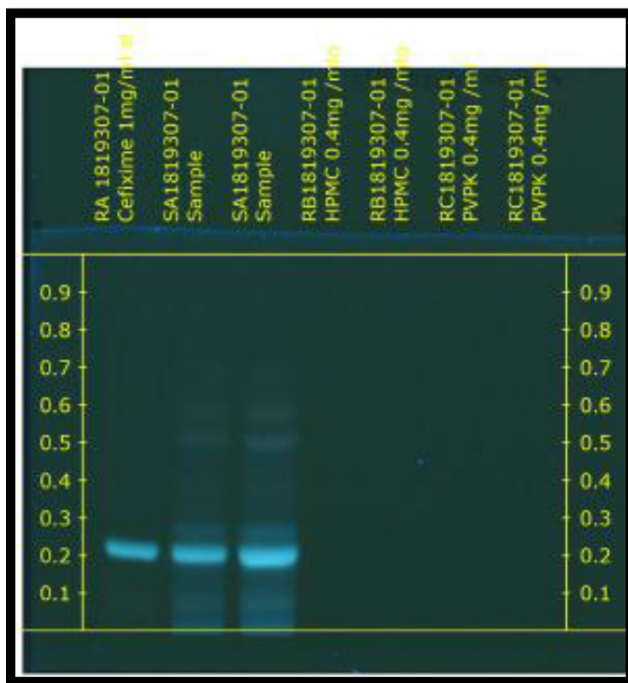


Figure 17: R 366.

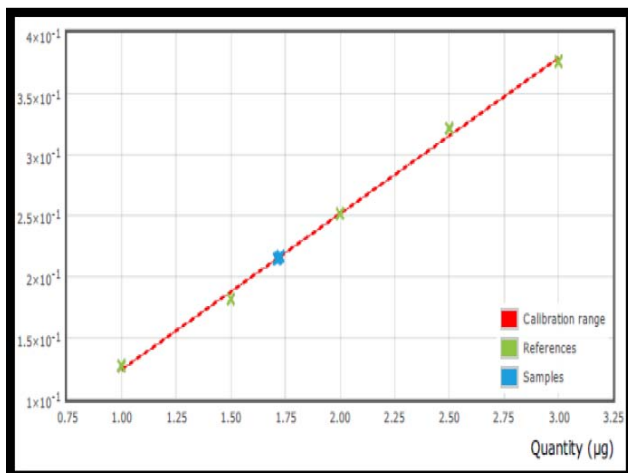


Figure 18: Calibration graph of linearity for cefixime at 366nm.

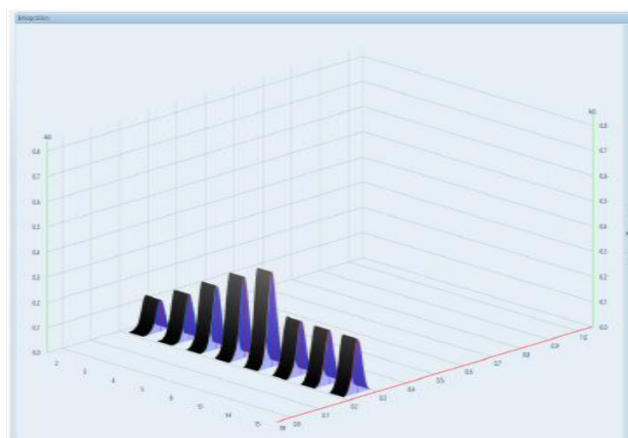


Figure 19: 3D image of quantification.

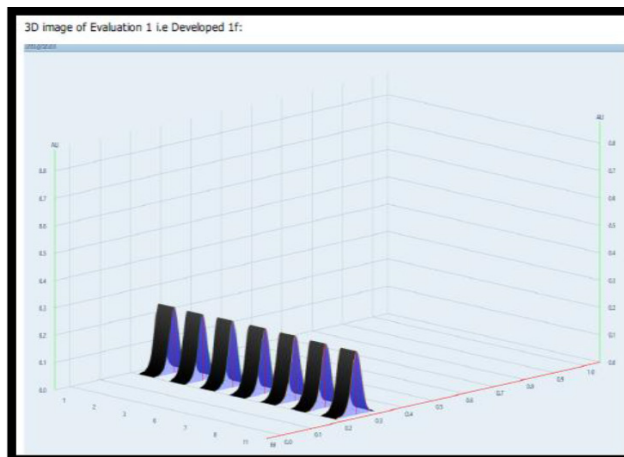


Figure 20: 3D image of evaluation.

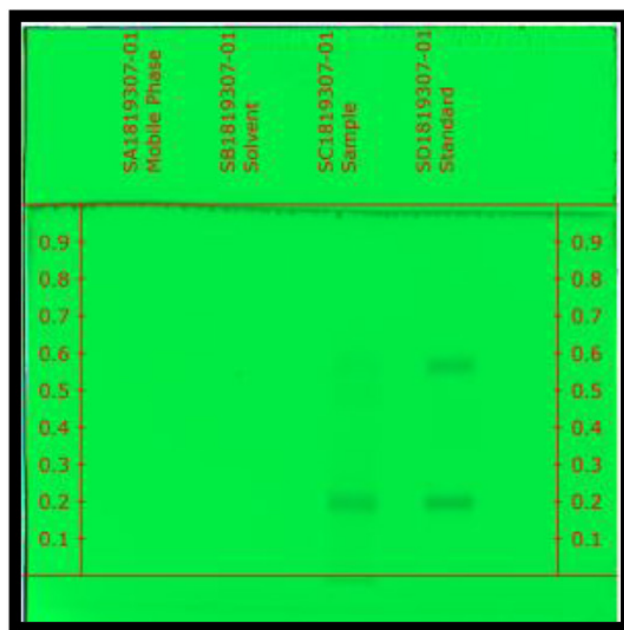


Figure 21: Scanning At R 254.

Calibration results

Precision: The 3D image for the evaluation for precision is shown in Figure 20 and it shows that the method developed was precise.

Specificity: Specificity was done by examining the sample solution in relation to interference from formulation ingredients. The scanning results are given below in Figure 21 and 22 and the 3D image for evaluation in Figure 23.

Data acquisition

Recovery of cefixime: The results for recovery determine 95.57% of recovery of cefixime are shown in Table 9.

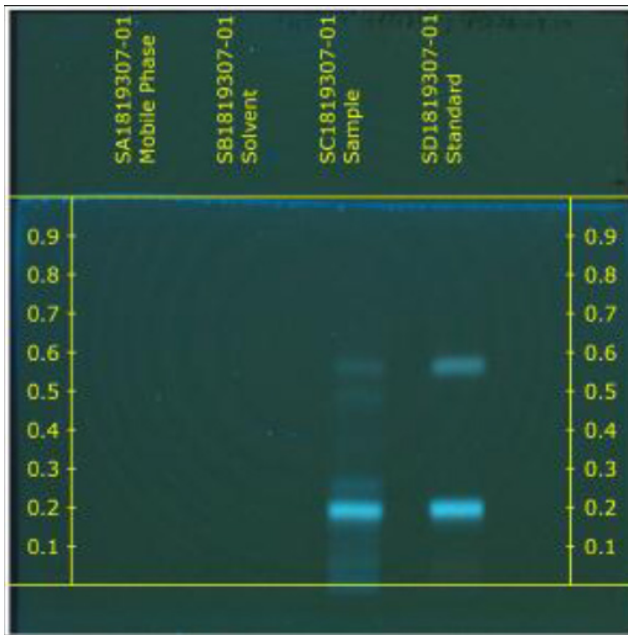


Figure 22: Scanning At R 366.

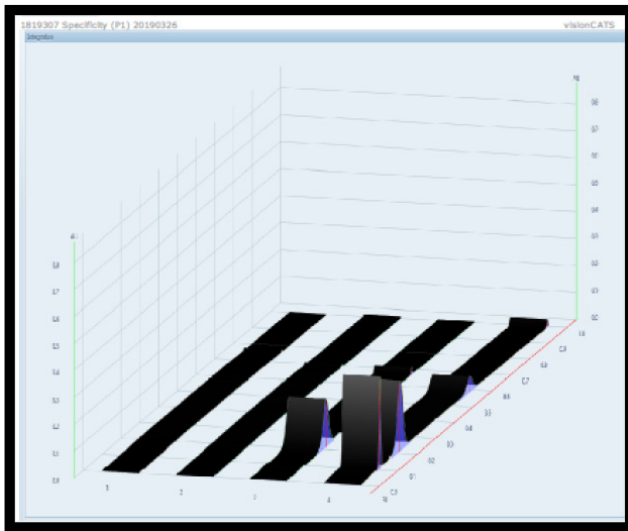


Figure 23: 3D image of scanned data.

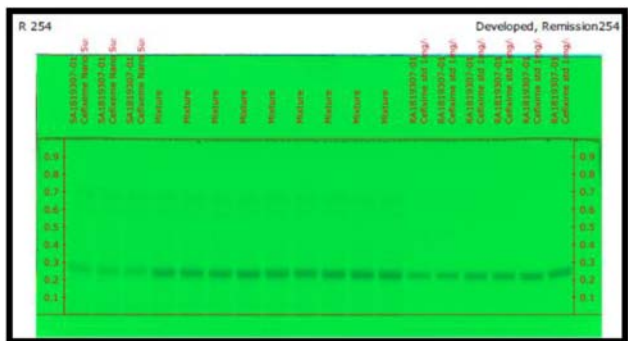


Figure 24: Scanning data at R 254nm.

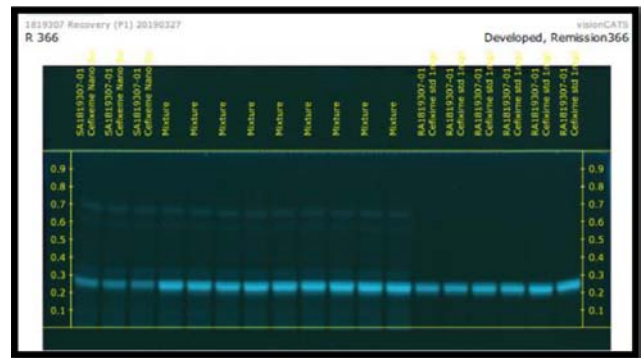


Figure 25: Scanning data at R 366nm.

Scanning data

The Scanning data in at 254 nm and at 366 nm has been shown in Figure 24 and 25 respectively.

CONCLUSION

The present research work has been satisfactory and efficient success and attempt to formulate cefixime Nano suspension by solvent/antisolvent method using probe sonication. The use of surfactants like PVP K30 as well as HPMC K100 has been compatible with the drug and its formulation as determined by compatibility studies like FTIR and DSC. Enhancement in the concentration in the surfactant enhances the particle size and enhancement in the polymer concentration enhances the drug content and particle size. Cefixime Nano suspension along with PVP K30 and HPMC K100 was found to be stable and showed particle sizes in range and a good percentage yield than formulating alone with PVP K30 and HPMC K100. Solubility and *in-vitro* studies determined that the diffusion rates were phenomenally increased by formulating as a Nano suspension dosage form. *In-vitro* drug release pattern resulted that the drug released in a sustained manner and upto 15 min which showed fast release. Therefore, it can be concluded that solvent/antisolvent method using probe sonication technique offer an easy, time saving and efficient method than other conventional methods. It can be also concluded that cefixime formulated as a Nano suspension dosage form is orally active with increased bioavailability than the drug alone. Furthermore, it has been determined that the method development and its validation which was done by High Performance Thin Layer Chromatography with cefixime Nano suspension were found to be suitable.

ACKNOWLEDGEMENT

The authors would like to sincerely thank the Principal, KLE College of Pharmacy, Belagavi. Lupin Phar-

Table 9: The result for recovery of cefixime.

Track No.	Area x 10 ⁶	Average	Expected Value	Percentage	Mean Percentage
1	0.00448582				
2	0.00450164	0.004517			
3	0.00456419				
4	0.01461337				
5	0.01414917	0.014243			
6	0.01396682		0.014862086	95.83528725	
7	0.01682123				
8	0.01667609	0.016776	0.017817241	94.15356159	95.57665234
9	0.01682938				
10	0.01942537		0.020047652	96.74110818	
11	0.01956179	0.019394			
12	0.01919581				
13	0.01032149				
14	0.01036825	0.010345			
15	0.0131819				
16	0.01341815	0.0133			
17	0.01573217				
18	0.0153287	0.01553			

maceuticals Ltd., Mumbai for providing with cefixime API as a gift sample. I would like to thank Anchrome Enterprises, Mumbai for carrying out HPTLC analysis of the formulation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

ICH: International Council for Harmonization; **HPTLC:** High Performance Thin Layer Chromatography; **CFX:** Cefixime; **CFX NP:** Cefixime Nanoparticles; **CFX NS:** Cefixime Nanosuspension; **DDS:** Drug delivery system; **OF:** Optimized Formulation; **r²:** Correlation Coefficient; **PS:** Particle Size; **PDI:** Polydispersity Index; **SEM:** Scanning Electron Microscopy; **TEM:** Transmission Electron Microscopy; **UV:** Ultra violet; **UV/VIS:** Ultra-violet/Visible; **IR:** Infrared; **FTIR:** Fourier Transform Infrared; **DSC:** Differential Scanning Calorimetry; **ZP:** Zeta Potential; **Abs:** Absorbance; **v/v/v:** Volume/ Volume/ Volume; **w/v:** Weight/ Volume; **w/w:** Weight/ Weight; **E.coli :** *Escherichia coli*; **RPM:** Rotations per minute; **PVP:** Polyvinyl pyrrolidone/ Povidone; **HPMC:** Hydroxy propyl methyl cellulose; **FFT:** Fast Fourier Transform; **CDR:** Cumulative Drug Release; **F:** Formulation; **IP:** Indian Pharmacopoeia; **USP:** United States Pharmacopoeia;

λ_{max}: Absorbance maximum; **β-L:** Beta-Lactum; **μg:** Micro gram; **nm:** Nano meter; **mg:** Milligram; **ml:** Milliliter; **min:** Minutes; **g:** Gram; **ng:** Nano gram; **°C:** Degree Centigrade.

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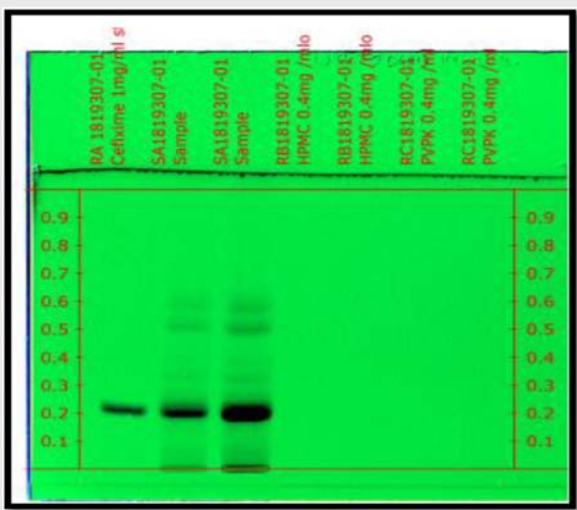
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SUMMARY

Cefixime is the only antibiotic drug belonging to third generation cephalosporin's of BCS classification IV. It is an orally active drug used in the treatment of UTI; Upper and Lower Respiratory Tract Infections; Acute Otitis media; and Gonococcal urethritis. It is of both low solubility and permeability antibacterial having bioavailability of 30-50% oral drug absorbed. Therefore, in the present study; an effort has been done to formulate such a dosage form so as to enhance its oral bioavailability. This is why; an oral cefixime nanosuspension was formulated to increase its bioavailability. Cefixime nanosuspension was successfully developed by probe sonication with the solvent/anti-solvent method, using PVP K30 and HPMC K100 as surfactants and using methanol as a solvent and Millipore water as an antisolvent. The formulation was examined for varied preformulation and evaluation tests such as sizes of the particles; polydispersity index, drug content, *in vitro* drug release, surface morphology and antimicrobial studies which determined that the prepared formulation showed acceptable results. Surface morphology studies determined that the nanoparticles have a spherical shape and sizes of about 200nm whereas the nanoparticle sizes varied from 200 to 300nm with PDI less than 0.8. Differential scanning calorimetry suggested that cefixime was molecularly dispersed and was compatible with its physical mixtures. The *in-vitro* drug release results generated that a total of 97.1% and drug content of 90.2% for the optimized Cefixime formulation (F4). The surface charge of the nanoparticles (zeta potential) -15.5mV indicating good stability. The zone diameter of the optimized formulation of cefixime nanosuspension (F4) detected 8mm by using *E. coli* bacterial strain. The method developed for cefixime Chloroform: Methanol: Water: Acetic acid in the ratio 6: 1.5: 0.5: 2 v/v/v/v and validated according to the ICH Guidelines. The validation parameters used were Linearity, Specificity, Precision and Recovery of Cefixime. The recovery of Cefixime was detected to be 95.57%.

PICTORIAL ABSTRACT



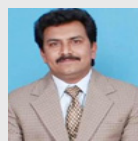
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Cite this article: Mastiholmath VS, Rajendra BA, Mannur VS, Dandagi PM, Gadad AP, Khanal P. Formulation and Evaluation of Cefixime Nanosuspension for the Enhancement of Oral Bioavailability by Solvent-Antisolvent Method and its Suitable Method Development. Indian J of Pharmaceutical Education and Research. 2020;54(1):56-67.