Cefixime Niosomes: Fabrication and characterization

Sruthi Marthadu, Jyoshna Medindla
Balaji College of Pharmacy, Sanapa Road, Rudrampeta, Anantapur-515001, AP, India
E-mail address: pharmaanantapur@gmail.com

Abstract - The authors aimed to fabricate and characterize the site precise delivery of Cefixime niosomes to avoid disturbances in gastric dissolution and absorption for desired therapeutic response. Cefixime niosomes were fabricated by an Ether injection procedure with innumerable proportions of Cefixime, cholesterol, and Sorbitans (Span 40, 60 and 80). The fabricated niosomes were characterized for compatibility studies with excipients used, vesicular shape, size, entrapment efficiency, drug content, and in-vitro drug release. The outcomes discovered that the primed niosomes passes and satisfies all the physicochemical characterizations done. The study concludes that Cefixime can be formulated as niosomes by ether injection techniques for enhanced absorption of the drug.

Keywords: niosomes, Spans, Cefixime, Cholesterol, Methanol, Diethyl ether

1. Introduction

Niosomes (NS) are vesicles attained on the hydration of synthetic non-ionic surfactants, stabilized with cholesterol [1].

Cefixime (CFX) is a third-generation antibiotic prescribed majorly to tackle urinary tract infections and lower respiratory tract infections. CFX tablets has absorption between 40- 50% from gut [2]. On the other hand oral suspension has better absorption than solid orals. NS are prepared using non-ionic surfactants stabilized with cholesterol which prevents leakage of contents from vesicle [3].

CFX-NS were made by using spans and cholesterolthen characterized for particle size, shape, uniformity in drug content, entrapment efficiency and *in vitro* drug release.

2. Materials and Methods

2.1. Materials

The resources need for the preparation of NS was listed in **table 1**.

Table 1: Ingredients used in the study with suppliers

Materials	Source
Cefixime	Cipla Limited, Bangalore, India
Span 40, 60 and 80	Loba Chemicals Pvt. Ltd. Hyderabad, India
Sodium hydroxide	Loba Chemicals Pvt. Ltd. Hyderabad, India
Sodium dihydrogen Phosphate	Loba Chemicals Pvt. Ltd. Hyderabad, India
Methanol	Loba Chemicals Pvt. Ltd. Hyderabad, India
Diethyl ether	Loba Chemicals Pvt. Ltd. Hyderabad, India
Double distilled water	Own lab

2.2. Methodology

Identification of the drug

The procured CFX was analysed for its purity and identity

Melting point

A sharp melting point specifies the purity of the CFX and reduced value signposts the presence of foreign substances in it. The melting point of CFX was determined using digital melting point apparatus.

λ_{max} of Cefixime

The $\lambda_{max}$of CFX in 0.1N HCl was determined in the dilution range of 2-10 µg/ml using double beam UV spectrophotometer [4].

Solubility

The solubility of CFX in the aqueous phase is important in dissolution and its availability in blood for its action. The solubility of CFX was assessed in 0.1N HCl, water, methanol, ethanol, and in PBS of pH 7.4 [5].

Partition coefficient of Cefixime

CFX's partition coefficient in n-octanol-water was attained [6].

2.3. Physical drug excipient compatibility

CFX was subjected to DSC studies to find the interaction with excipients used.

2.4. Preparation of NS by modified Ether injection method

Cholesterol and span 40/60/80 were dissolved in 5 ml diethyl ether mixed with2 ml methanol comprising a weighed quantity of CFX.The subsequent solution was slowly injected using a microsyringe at a rate of 1ml/min into 10 ml of hydrating solution phosphate buffer (PBS) of pH 7.4.The solution was enthused unceasingly on a magnetic stirrer at 60±2ºC. This leads to spontaneous vesiculation and formation of NS [7]. Various batches of NS were made to choose an optimized formula. The components of NS were shown in **table 2**.

Table 2: Composition of various NS

Ingredients	**Formulations**					
	F-1	**F-2**	**F-3**	**F-4**	**F-5**	**F-6**
Cefixime	20	20	20	20	20	20
Span 40	100	200	-	-	-	-
Span 60	-	-	100	200	-	-
Span 80	-	-	-	-	100	200
Cholesterol	200	200	200	200	200	200
Methanol	2	2	2	2	2	2
Diethyl ether	5	5	5	5	5	5
Phosphate buffer-pH 7.4 (ml)	10	10	10	10	10	10

2.5. Characterization of Niosomes

Vesicle diameter

Optical microscope with calibrated eyepiece micrometer was used to find vesicular diameter of 100 NS of all batches and average was measured [8].

Percentage Cefixime trap

The entrapped CFX formulations were dogged by dialysis. In this niosomal dispersion in dialysis bag was plunged in a beaker with 400 ml of 0.1N HCl, later the beaker was placed on a magnetic stirrer run for 4 h with a speed of 100±20 rpm. Then, the solution inside the receptor compartment was studied for un-entrapped CFX at 268 nm using double beam UV spectrophotometer. The difference of the total amount of drug added and the amount of un-entrapped drug detected, to the total amount of drug added gives the CFX entrapment [9].

Drug content

Suspension of NS equivalent to 20mg of CFX was taken in 100 ml of a volumetric flask, which were dissolved and volume made to 100 ml with 0.1N HCl. Later after that 1ml of this mixture was diluted to10ml by 0.1N HCl and the percentage dug content was observed at 268 nm using double beam UV spectrophotometer [10].

***In-vitro* Drug release**

The releases of CFX from NS formulations were determined using membrane diffusion technique. The NS formulation equivalent to 20mg of CFX was kept in a Dialysis membrane of diameter 2.5cm with an effective length of 8cm (donor compartment). The membrane was placed in a beaker containing 100ml of 0.1N HCl(receptor compartment). The whole assembly was fixed in such a way that the lower end of the membrane containing a suspension was just touching (1-2mm deep) the surface of diffusion medium. The temperature of the receptor medium was maintained at 37±0.5˚C and agitated at 100rpm speed using magnetic stirrer [11]. Aliquots of 5ml sample were withdrawn at regular intervals and sink conditions were maintained. The collected samples were analysed at 268nm in Double beam UV-VIS spectrophotometer using 0.1N HClas a blank.

3. Result and Discussion

3.1. Melting point of Cefixime

The melting of CFX is as described in the monograph, it was observed as222±1.8°C.

3.2. λ_{max} of Cefixime

The λ_{max} of CFX was established as 268 nm, promises its official standards and shown in Fig.1.

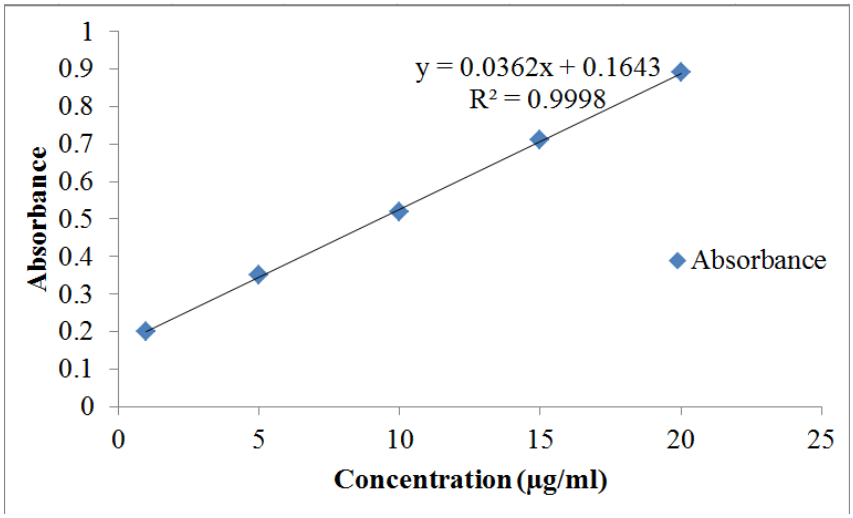

Fig.1. Calibration curve of Cefixime

3.3. Solubility of Cefixime

Pure CFX solubility was compared with its standard, and it indicates that CFX has high solubility in methanol (95%) and practically insoluble in water.

3.4. Partition coefficient of Cefixime

The partition coefficient of CFX was calculated as 3.5, which indicates that CFX is practically insoluble in water and has high affinity towards lipid. So this can be incorporated into NS for efficient delivery.

3.5. DSC studies

The DSC points were procured for CFX and physical blend. The thermo grams of CFX with excipient blend were shifted towards left indicating proper impregnation of CFX with excipients without negative signs. The DSC spectrums were shown in **fig 2**.

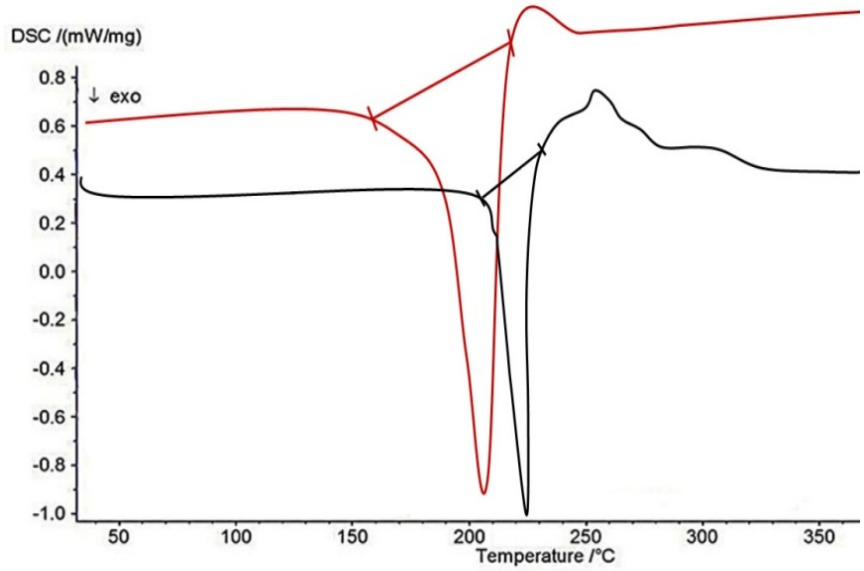

Fig.2. DSC thermo gram of A) Pure Cefixime (CFX) B) CFX formulation blend

3.6. Characterization of niosomes

Drug content was determined for all NS formulations in triplicates. *In vitro* release of CFX from NS was studied using dialysis tube method. Particle size was estimated. After all the characterizations it was found that F-4 was better NS formulation than others.

3.7. Size and size distribution

The vesicular size was ranged between 215 and 400 nm (**fig.3**).

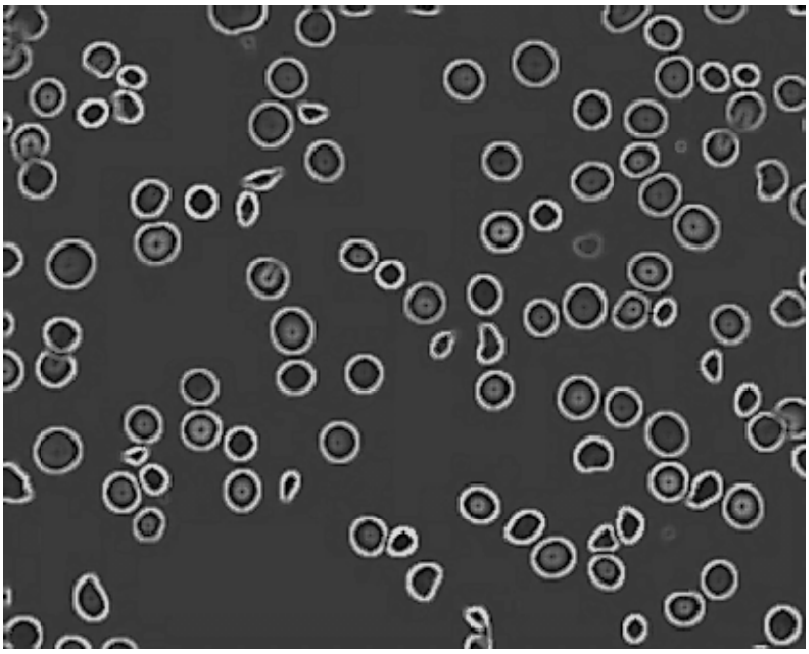

Fig.3. Morphology of niosomes

3.8. Entrapment efficiency

FormulationF-4 has the highest entrapment efficiency(**fig4**) compared to other formulations.

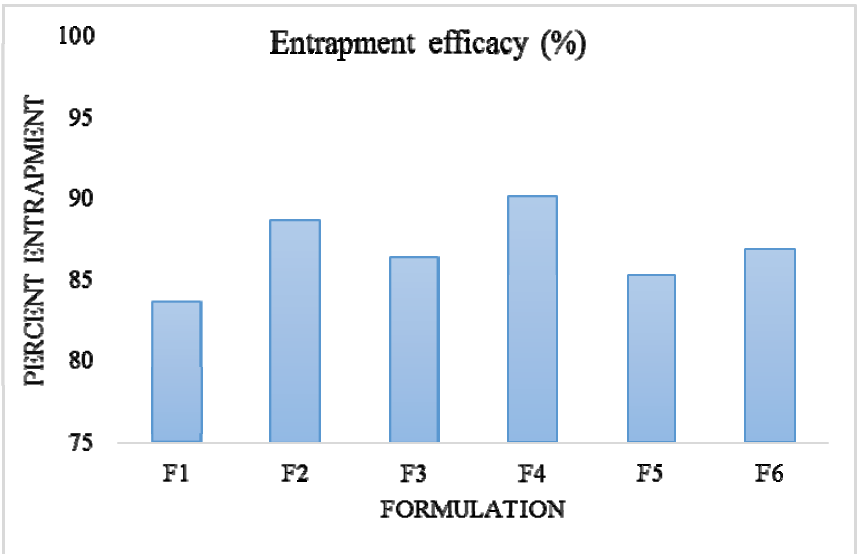

Fig.4. Entrapment efficacy of prepared niosomes

3.8. Drug content

The amount of CFX present in the formulations was in the range of 89.62 to 96.84 %(**table 3**)

3.9. *In vitro* release

Among the NS, F4 formulation has a highest percentage drug release and illustrated in **fig 5**.

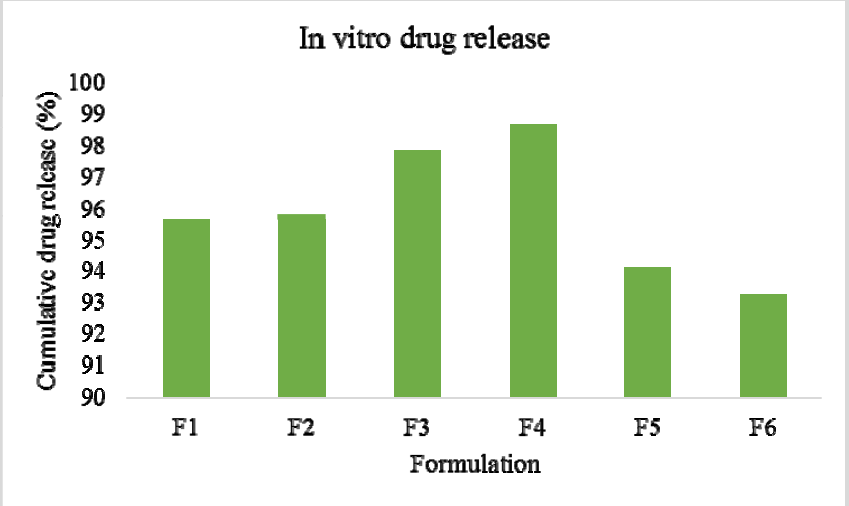

Fig.5. *In vitro* release comparison curve of all formulations

Table 3: Characterization of Formulations by variousEvaluation Methods

Formulation	Entrapment efficacy	Particle size	Drug content	In vitro drug release
F1	83.7	5.29	96.84	95.68
F2	88.7	5.16	89.62	95.81
F3	86.4	5.22	94.15	97.84
F4	90.1	4.99	92.35	98.67
F5	85.3	5.06	90.98	94.12
F6	86.9	5.11	93.87	93.28

4. Conclusion

From the extensive research work the authors concludes that, Cefixime can be fabricated as niosomes for efficient drug release rate.

Acknowledgement

The authors would like to thank Cipla Limited Pvt.Ltd, Bangalore, India for providing the gift sample of Cefixime.

References

[1] Srishti A, Sheikh M, Sreejith R, Ankit KR, Toru M and Sakthi KD.Formulation, characterization and evaluation of morusin loaded niosomes for potentiation of anticancer therapy, RSC Adv., 2018, 8, 32621-32636.
[2] Tripathi KD. 5thed. New Delhi: Jaypee Brothers Medical Publishers; 2003. Essentials of Medical Pharmacology.
[3] Ahad HA, Padmaja BS, Sravanthi M, Ramyasree P, Kavitha K. Phytochemical screening and anti-inflammatory actions of Alangiumsalviifolium root extract. Natural product research. 2012 Sep 1;26(17):1649-53.
[4] Ahad HA, Rani EM, Kranthi G, Gupta PR, Reddy MN, Prakash G. Spectrophotometric Determination of Cefadroxil in Cefadroxil Tablets by Bromination Method. Analytical Chemistry Letters. 2011 Jan 1;1(2):185-8.
[5] Annepogu H, Ahad HA, Nayakanti D. Valuing Best Poloxamer Carrier for Thiocolchicoside Solid Dispersions. Asian J Pharm Clin Res, Vol 12, Issue 3, 2019, 250-255.
[6] Bartelds R, Nematollahi MH, Pols T, Stuart MCA, Pardakhty A, Asadikaram G et al. Niosomes, an alternative for liposomal delivery, PLoS One. 2018 Apr 12; 13(4):e0194179.
[7] Mahmoud G, Jafar A, Hamidreza K, Hossein D, Ali S.Niosome: A Promising Nanocarrier for Natural Drug Delivery through Blood-Brain Barrier, Advances in Pharmacological Sciences, 2018; Article ID 6847971.
[8] Abdul Ahad H, Sreeramulu J, Padmaja BS, Reddy MN, Prakash PG. Preparation of Fluconazole β-Cyclodextrin Complex Ocuserts: In Vitro and In Vivo Evaluation. ISRN pharmaceutics. 2011, 237501.
[9] Hindustan AA, Sreenivasulu R, Mallapu Rani E, Reddy BV. Preparation and evaluation of famotidine high density gastro retentive microspheres with synthetic and natural polymers. Journal of Pharmaceutical Education & Research. 2011 Jun 1;2(1).
[10] Patel MP, Patel MM, Patel KN. Formulation and optimization of controlled released floating matrix tablets of cefixime. J Pharm Res. 2009; 2:1110–2.
[11] Indian Pharmacopoeia, New Delhi, India: Ministry of Health and Family Welfare; 2010. Indian Pharmacopoeia, Controller of Publication, Govt. of India; p. 185.