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Research Article

Selection of excipients for the formulation of Ceftriaxone sodium loaded chitosan Nanoparticle through drug - excipient compatibility testing

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ABSTRACT

Ceftriaxone (CFTX) sodium is a 3rd generation semisynthetic antibiotic that can effectively treat several types of bacterial infections. The best formulation is considered appropriate when no interactions between drug-excipient or excipient-excipient occur. To obtain the best formulation preformulation study is an essential tool and desiring a quick and accurate method to evaluate and choose the best excipients for stable dosage forms. The aim of the present work was to study the compatibility of Ceftriaxone sodium drug substance with the excipients employed in colon target release capsule preformulation by testing the Thermo gravimetric analysis (TGA) study and Fourier transform the Infrared spectrophotometric study (FTIR). Based on the TGA results Ceftriaxone was found to be compatible with Chitosan and Sodium Tri polyphosphate. FTIR was used as supportive techniques for the analysis.

Keywords: Ceftriaxon; Chitosan; FTIR; TGA.

INTRODUCTION

Ceftriaxone (CFTX) sodium is a semisynthetic broad spectrum antibiotic that can effectively treat several types of bacterial infections. CFTX is chemically known as, (Z) -7-[2-(2-aminothiazol-4-yl) -2-methoxyiminoacetyl amido] -3-[(2,5-dihydro-6- hydroxy-2-methyl- 5-Oxo-1,2,4-triazin-3-yl) thiamethyl] -3-cephem-4-carboxylic acid, disodium salt, CFTX is a β-lactamase-resistant cephalosporin with an extremely long serum half-life. The beta lactam moiety of CFTX binds to penicillin binding protein such as caboxypeptidase, endopeptidase, transpeptidase of cell membrane. These enzymes are involved in bacterial cell wall synthesis and cell division. (A.Preetha *et al.,* 2008). CFTX is used for various clinical condition such as Respiratory and urinary tract Infections, Bacterial Otitis Media, Skin infections, Gonorrhea Pelvic Inflammatory Disease, Bacterial Septicemia, Bone Joint Infections and Meningitis (Neu HC *et al*., 1981). The dose will be varying according to the severity of disease conditions. Markedly available formulation- Injection, powder for solution 500 mg (3.6 mEq of sodium/g) - Injection, powder for solution 1 g (3.6 mEq of sodium/g)

Solid nanoparticles were introduced at the beginning of 19 th centuries, as an alternative to solid nanoparticles, emulsions and liposomes in pharmaceutical preparations. (Kurita, K. et al., 2002). Chitosan is easily degradable by colonic bacterial enzyme so it can be used as a polymer for colon drug delivery system and also it has muco adhesive character. TPP is nontoxic, multivalent and able to form gels through ionic interactions.

A good formulation is considered appropriate where there are no interactions between drug excipient or excipient- excipient occur. One attempt was aimed at increasing its functional lipophilicity through the formation of ion pairs by coupling with positively charged chitosan with various P^H (Merisko-Liversidge E *et al.,* 2003).

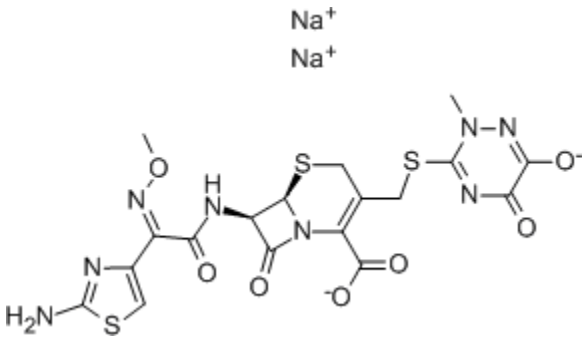

Figure 1: Chemical structure of ceftriaxone sodium

Thermal analysis is one of the most frequently used instrumental techniques on pharmaceutical researches to find out the physical changes of the drug and polymer used for the formulation in the pre formulation stages of solid dosage forms (W. Mehnert *et al.,* 2001) . A quick and accurate method to test and select the best excipients for stable dosage forms constitute a real attempt in the preformulation stage (R.H. Muller *et al.,*2000, Mura P *et al.,*1998).The aim of this work was to evaluate the compatibility between Ceftriaxone sodium and some pharmaceutical excipient, using

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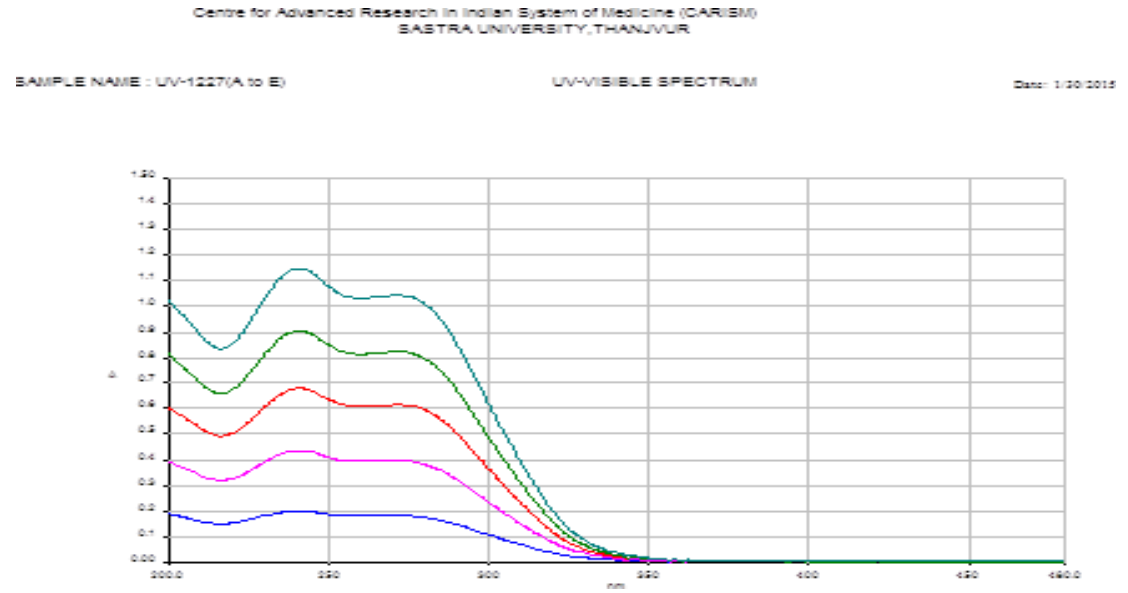

Figure 2: UV-Visible Spectroscopy

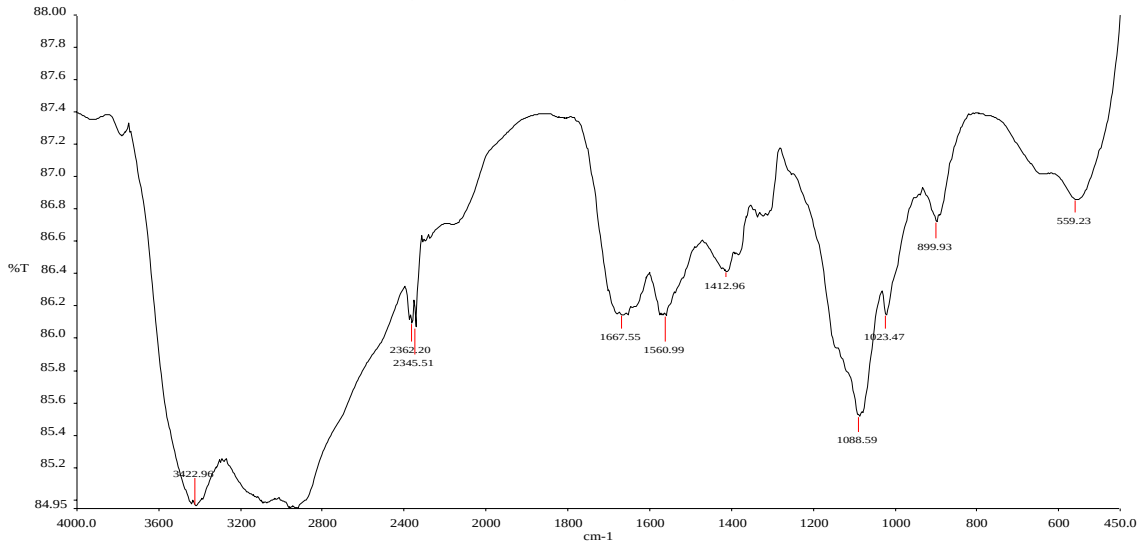

Figure 3: FTIR –Ceftriaxone Sodium

Themo anlytical technique (TGA) and Fourier transform infrared spectroscopy (FTIR).

MATERIALS AND METHODS

Ceftriaxone sodium were gifted from Hospira health care india Pvt Ltd. chitosan (MW= 60–90 kDa; degree of deacetylation 85%) were purchased from Himedia lab and sodium tripolyphosphate (TPP) were purchased from Sigma Aldrich, USA. All other chemicals were used laoratery grade.

Melting point

A capillary tube was taken, one end was sealed with the help of Bunsen burner and other end was filled with the drug. Then this capillary tube which was filled with the drug was placed in a melting point viewer(Mel temp) along with thermometer .Then the temperature was slowely increased at one point the drug gets melts and become liquid that temperature was noted down and it was considered as the melting point of the drug.

Solubility profile of Ceftriaxone sodium in different solvents (at 25°C)

Solubility of the drug is predicted I.P method. Ceftriaxone was weighed at 1 gm and dissolved in water in the proportions of 1 ml, 10 ml, 30 ml and 100 ml.The solubility was predicted by measuring the absorbance by using UV-Visible Spectroscopy method.

UV–visible spectroscopy

The UV–visible spectra were obtained from UV–visible spectrophotometer, Shimadzu UV-1800 model, Japan. Ceftriaxone sodium stock solution (10mg/ ml) was prepared. Aliquots were withdrawn and making concentration of 5 ; 10 ; 15; 20; 25 mg/ml. Absorbance was taken at 257nm. (Table 1)

Table 1: Fourier Transformed Infrared Spectroscopy Analysis

Slope	0.001593
Regression coefficient	0.99682

Table 2: Fourier Transformed Infrared Spectroscopy Analysis

Concentration (µg/ml)	Absorbance
0	0
5	0.0102
10	0.0166
15	0.0242
20	0.0321
25	0.0411

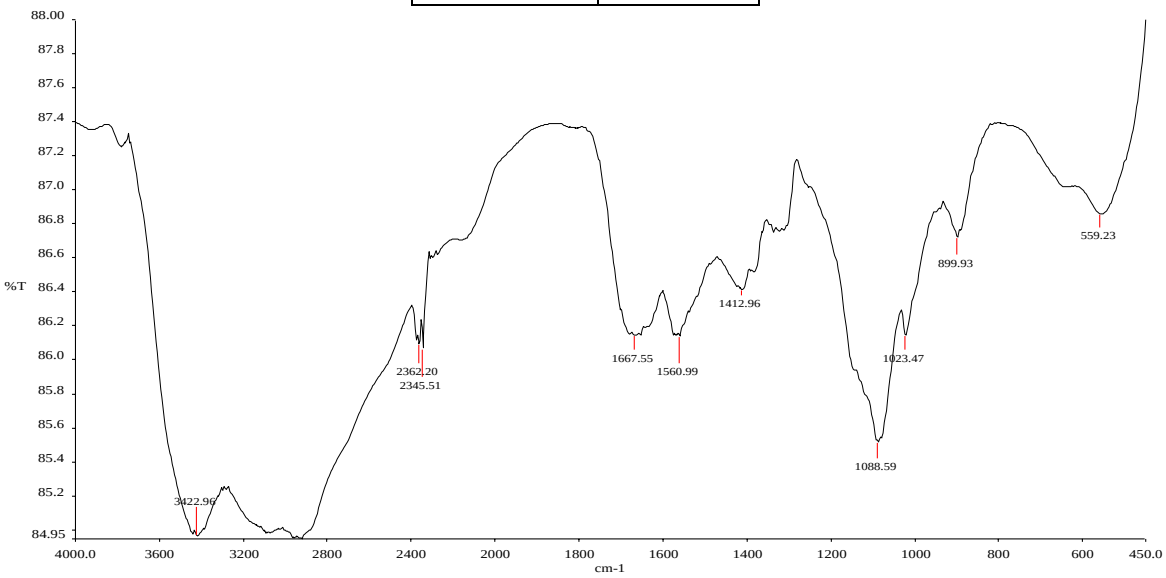

Figure 4: FTIR –Ceftriaxone Sodium

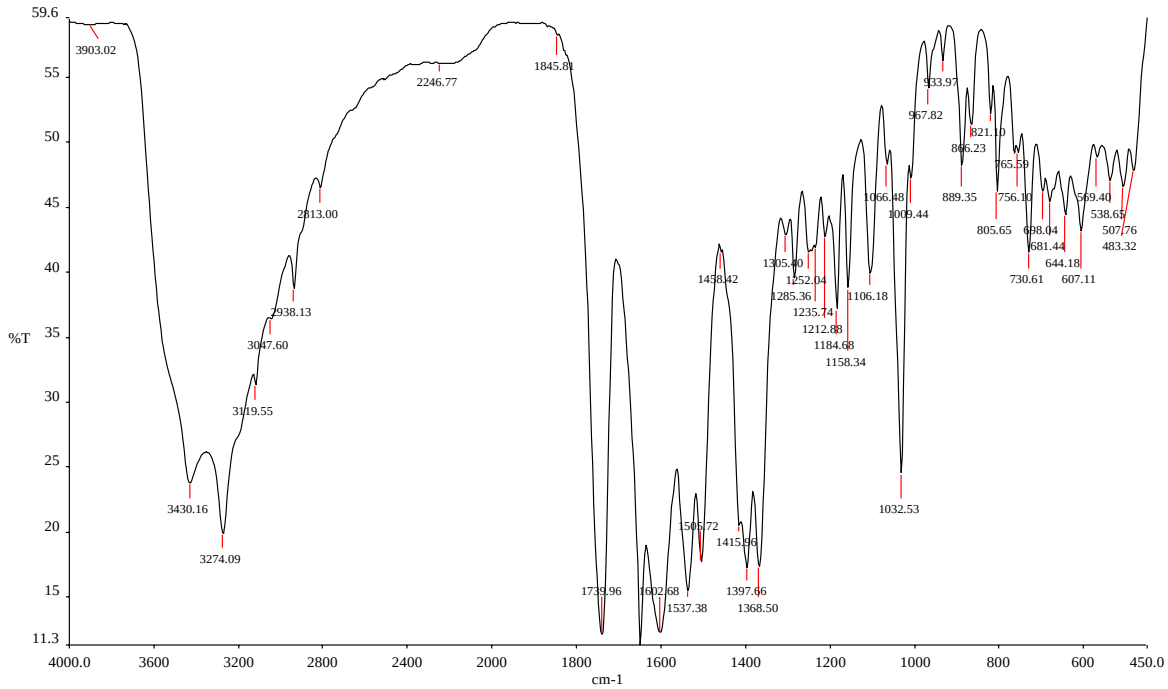

Figure 5: FTIR-Ceftriaxone sodium Chitosan Complex

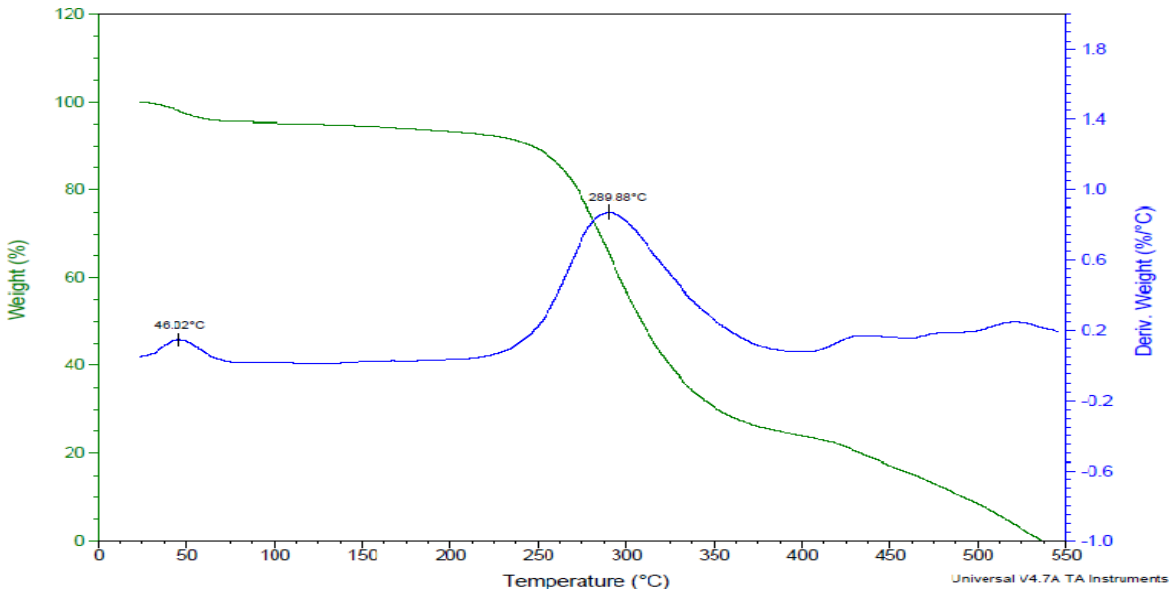

Figure 6: Thermo gravimetric Analysis

FT-IR analysis

The FT-IR analysis was performed with Perkin-Elmer, FT-IR spectrophotometer, USA.FTIR spectrum was taken within the range of 4000–400 cm−1. An equal proportion of drug, Chitosan and Tri sodium polyphosphate was mixed with 100 mg of KBr and compressed into pellet using a hydraulic press. All spectra were corrected against the reference spectrum of KBr pellet.

Thermogravimetric analysis (TGA)

Themogravimetric analysis was carried out with the help of Perkin-Elmer Model of TGA-7 thermo

gravimetric system. It's having temperature control with a microprocessor driven unit. The psycho chemical property of a drug against the temperature changes at a variable time was determined using TGA. The weight of the sample was taken for thermogravimetric analysis in the range of 2–3 mg. The sample was taken in the sample pan which is placed on the balance system equipment and the temperature was raised from 25 to 800 ◦C at a heating rate of 10 ◦C per minute with the nitrogen flow rate of 50cm3/min. The weight changes of the sample against the temperature were continuously recorded.

RESULT AND DISCUSSION

Melting point: Melting point was found to be 179° C. The physical property of a compound helps to identify the impurity of drugs. (Bodmeier, R *et al.,* 1989).

Solubility: Freely soluble in water at P^H 1.2, 5.5, 6.8, 7.4, sparingly soluble in methanol, very slightly soluble in Ethanol Acetone and Octanol.at 25°C. (Lipinski, C.A *et al.,* 2000).

Selection of analytical wave length and calibration of standard curve

The diluted stock solution was scanned for maximum wavelength and it was found to be 247 nm, which was selected as the maximum wavelength for UV-Visible Spectroscopy. (Lakshmi K.S. *et al* 2009)

FTIR studies for Ceftriaxone showed (Fig.2) characteristic peaks at 3432.7 cm-1 (N-H stretching mode of H-bonded amide group), 1741 cm-1 (β-lactam C=O stretching vibrations) and 1592 cm-1 oxime C=N stretching vibrations). 3505.69cm-1 N- H stretching (amides) 3376.67 cm-1 N-H asymmetric (sulfonamide) 3237.06 cm-1 symmetric vibration 3103.86 cm-1 C-H stretching (Alkene) 1331.03 cm-1 Asymmetric (-SO_2 Stretching vibration) 1171.3 cm-1 symmetric (-SO_2 Stretching vibration) 902.074 cm-1 N- H Stretching . There are three characterization peaks of chitosan at 3440 cm−1 of O-H stretching , 1078 cm−1 of (C- O-C) and 1642 cm −1 of NH2. The spectrum of pure chitosan exhibited an amine deformation peak at 1600cm-1 and amide I carbonyl stretch at 1643cm-1 (Samuels, 1981).The IR spectral interpretation shows that the spectra obtained from the formulation matches with original spectra of drug. Similarly characteristic peaks, for the polymers were also noticed in the formulation spectrum. There was no change of any characteristic peaks which confirms that the absence of chemical interaction between the drug and polymers.

Fig- Thermogravimetric analysis (TGA) is a simple analytical technique which is used to study the thermal stability of the sample and their weight loss at different temperatures. It also confirms the successful loading of ceftiraxone within CS-NP. We observed a four step decomposition pattern on ceftriaxone sodium loaded CS-NP (Fig. 4). Initially, 39% weight loss was observed at 40.02°C, due to the release of water molecules. The second step in the curve is about 75% weight loss at 289.88°C indicating the decomposition of CS and the third step was observed at 450◦C with the weight loss of 19% could be due to the decomposition of both CS and ceftriaxone sodium. Finally the fourth step of decomposition was examined at5 35◦C of about 09.79%,

which might be due to the decomposition of pure Ceftriaxone sodium. Similar decomposition pattern of ceftriaxone was also observed in solid lipid nanoparticle [29] and our result correlates well with this report. By comparing the thermogram of ceftriaxone and chitosan nano particle, we confirmed the loading of ceftriaxone sodium within chitosan nano particle.

CONCLUSION

The present study confirms that there is no chemical interaction between drug and excipient. From the results of FTIR and TGA methods, it is proven that FTIR and TGA are fast screening tools to check compatibility in early stages of a pre formulation process. Based on our results, all excipients were found to be compatible ceftriaxone sodium. It is conclude that the selected excipients can be further used for formulating ceftriaxone sodium chitosan coated nanoparticle

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