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Original Article

Selection of Excipients for Cefixime Floating Tablets through Drug Excipient Compatibility Testing

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ABSTRACT

Cefixime binds to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, causing the inhibition of the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins; it is possible that cefixime interferes with an autolysin inhibitor. Preformulation is the first step in the rational formulation of an active pharmaceutical ingredient (API). For any formulation interactions studies are very important. When there was no interaction between the choosen drug- excipient or excipient-excipient then the formulation will be a appropriate one. The selection of suitable study method to evaluate the interaction between the drug and the excipients is a prime most achievement in the pre-formulation study. The objective of the study was to study the compatibility of drug and polymers like sodium alginate, HPMC and ethylcellulose employed in the preparation of tablets for controlled drug delivery system by adopting Differential Scanning Calorimetric (DSC) study and Fourier transform Infra red spectrophotometric study (FTIR). Based on the DSC and FTIR results Cefixime was found to be compatible with excipients sodium alginate.

Keywords: Cefixime, Sodium alginate, HPMC, Ethylcellulose, FTIR and DSC

1. INTRODUCTION

Cefixime is an antibiotic it as third generation of cephalosporin like ceftriaxone and cefotaxime. Cefixime is highly stable in the presence of beta-lactamase enzymes. As a result, many organisms resistant to penicillins and some cephalosporins due to the presence of beta-lactamases , may be susceptible to cefixime[1]. The antibacterial effect of

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cefixime results from inhibition of mucopeptide synthesis in the bacterial cell wall. cefixime binds to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, causing the inhibition of the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins; it is possible that cefixime interferes with an autolysin inhibitor [2].

Preformulation is an investigation on the physical-chemical properties of the drug substance alone and in combination with excipients. Assessment of the possible incompatibilities between the drug and various excipients is an important part of the preformulation. Study of drug–excipient compatibility is an important process in the early development stage of stable dosage forms. The successful formulation of a stable and effective dosage form depends on a careful selection of the excipients. However, no universally accepted protocol is available for evaluating the drug compatibility with different excipients.[3] In a dosage form, an API comes in direct contact with other components (excipients) of the formulation that facilitate the administration and release of an active component as well as protect it from the environment. Although excipients are pharmacologically inert, they can interact with drugs in the dosage form to affect drug product stability in physical aspects such as organoleptic properties, dissolution slow down or chemically by causing drug degradation. Careful selection of the excipients are required for a robust and effective formulation of dosage forms that make administration easier, improve patient compliance, promote release and bioavailability of the drug and increase its shelf life.

A formulation is considered appropriate when no interaction drug excipient or excipient- excipient occur. In this sense, devising a quick and accurate method to test and select the best excipients for stable dosage forms constitute, a real achievement in the preformulation stage. Thermal analysis is one of the most frequently used instrumental techniques on pharmaceutical researchers to solve technological problems in the preformulation stages of solid dosage forms, In particular, differential scanning calorimetry (DSC) has been proposed as a rapid method for evaluating physico-chemical interactions between the formulation components and therefore selecting excipients with suitable compatibility.[4,5]

The aim of this work was to characterize the compatibility between Cefixime and some pharmaceutical excipients, using Differrential Scanning calorimetry (DSC) and Fourier Transform Infrared Spectroscopy (FTIR).

2. MATERIALS AND METHODS

Cefixime trihydrate, were purchased from Hetero labs, HPMC K5M, EC and sodium alginate were purchased from AR chemicals from Hyderabad. Physical binary mixture cefixime with each excipient alone 1:1 w/w ratio obtained by grinding in the mortar were also studied.

Differential Scanning Calorimetry (DSC)

In this technique, the DSC curves of pure components are compared to the curves obtained from 1:1 physical mixtures. It is assumed that the thermal properties (melting point, change in enthalpy, etc.) of blends are the sum of the individual components if the components are compatible with each other. Samples of Individual components as well as each drug excipient were weighed (balance) ,directly in pierced aluminium crucible pans (5-10 mg) and scanned in the 50^{o} C to 400 ^{o} C temperature range under static air, with heating rate of 10^{o} C/min, using Labindia DSC-60 equipment.[6,7]

Fourier Transform Infrared spectroscopy (FTIR)

The FTIR spectra of sample were recorded on a FTIR equipped with spectrum 11.0.0.0449 software using KBr pellet method. The spectrum for each sample was recorded over than 1000 -3500 cm-1.[8,9]

3. RESULTS AND DISCUSSION

DSC Analysis

The DSC analysis allowed the quantitative evaluation of thermal properties of drug and polymer such as melting point thermogram of Cefixime showed 150 ^{o}c. In majority of the cases, melting endotherm of drug was well preserved with slight changes in terms of broadening or shifting towards the lower temperature. It has been reported that the quantitiy of material used, especially in drug excipient mixture affects the thermogram of the drug. Thus, these minor changes in the melting endotherm of drug could be due to the mixing of drug and excipients which lowers the purity of each component in the mixture and may not necessarily indicates potential incompatibility. However, in the physical mixture of the Cefixime and Sodium alginate no chemical instabilities were found.

FTIR Study

The infrared (FT-IR) spectra were obtained in a KBr pellets using a Perkinelmer FT=IR spectrometer spectrum one at resolution 4cm-1 from 3500 to 1000 cm-1 . A typical FT-IR spectra of novel Cefixime showed absorption at the following wave number in cm-^{1}1688. 1688.23, 1631.65, 1114.66 and 775.42. FTIR spectroscopy has been successfully used for exploring the differences in molecular conformations, crystal packing and hydrogen bonding arrangements for different solid state forms of an organic compound. Spectral variations originates due to alteration in bonds that exhibit characteristic vibrational frequencies, leading to frequency shifts and splitting in absorption peaks. The FTIR spectrum of samples showed characteristic absorption bands 10 which were comparable with absorption bands of individual sample. The results illustrated that, there were no chemical instabilities in drug – excipient combinations.

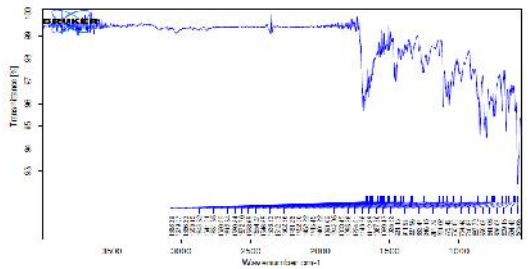

Fig 1: FTIR Studies of Pure Drug (Cefixime)

Table 1: Characteristic Peaks and frequency of Cefixime

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	3500-3000	1688
2	OH Bending	3000-2500	1631.65
3	C-H stretching	2000-1500	1140.66
4	C=O stretching	1500-1000	775.42

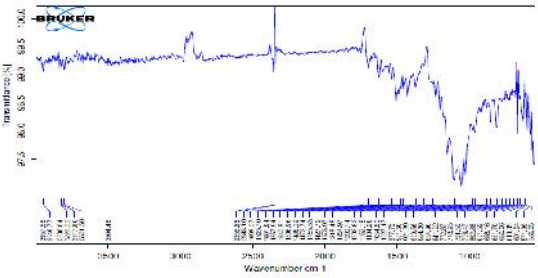

Fig 2: FTIR Studies of Cefixime and sodium alginate

Table 2: Characteristic Peaks Cefixime and Sodium alginate

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	3500-3000	3504.46
2	OH Bending	1000-1500	706.47
3	C-H stretching	2500-2000	1557.94
4	C=O stretching	2000-1500	1104.28

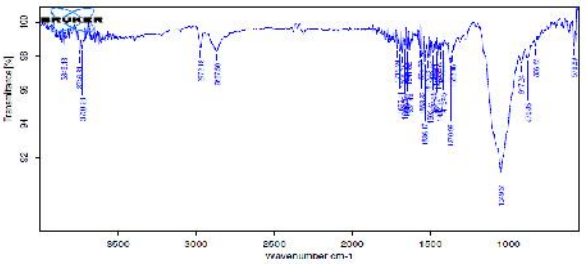

Fig 3: FTIR Studies of Cefixime and HPMC

Table 3: Characteristic Peaks Cefixime and HPMC

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	3500-3000	2972.18
2	OH Bending	1000-1500	1049.31
3	C-H stretching	3000-2500	2867.50
4	C=O stretching	2000-1500	1692.11

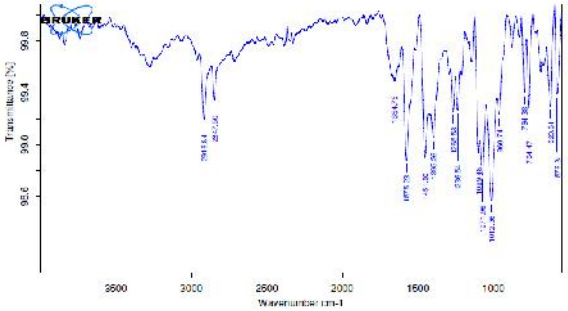

Fig 4: FTIR Studies of Cefixime and Ethyl cellulose

Table 4: Characteristic Peaks Cefixime and Ethylcellulose

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	3000-2500	2916.84
2	OH Bending	1100-1070	1071.96
3	C=O stretching	2000-1500	1575.23

DSC Analysis

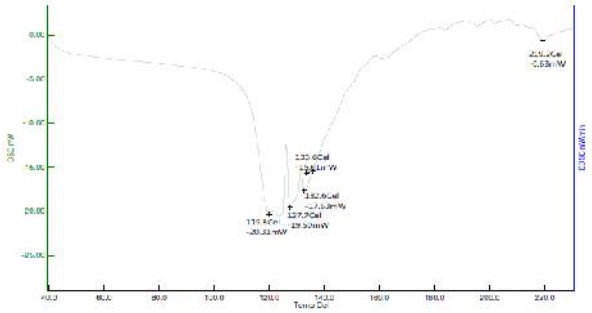

Fig 5: DSC Studies of Cefixime

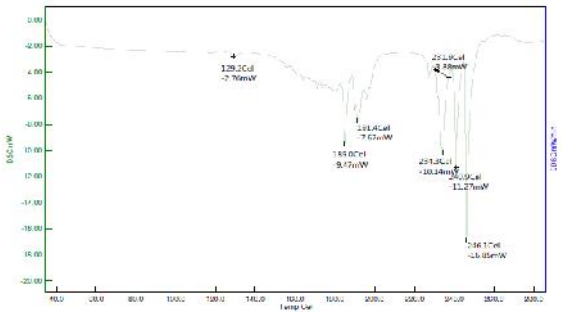

Fig 6: DSC Studies of Cefixime and sodium alginate

4. CONCLUSION

From the results of FTIR and DSC methods, it is proven that FTIR and DSC as fast screening tools to check compatibility in early stages of a preformulation process. Based on our results, all mentioned excipients were found to be fully compatible with. It is conclude that the selected excipients can be further used for preparing cefixime floating tablets.

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