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Review Article

FORMULATION AND EVALUATION OF CEFUROXIME AXETIL ORAL SUSPENSION

Balasubramanian V[1]*, Senthil Kumar K L[2], Vijaya K[3]

[*1]Professor, Department of Pharmaceutics, Jainee College of Pharmacy, Dindugal, Tamilnadu. Affiliated The TN Dr MGR Medical University, Chennai, Tamilnadu, India.
[2]Principal, Sri Vijay Vidyalaya College of Pharmacy, Dharmapuri, Tamilnadu. Affiliated The TN Dr MGR Medical University, Chennai, Tamilnadu, India.
[3]Dean, Ultra College of Pharmacy, Madurai, Tamilnadu. Affiliated The TN Dr MGR Medical University, Chennai, Tamilnadu, India.

ABSTRACT
Cefuroxime is the second-generation cephalosporin, which its intravenous and oral dosage forms are available. Oral route is the selective method for administration of most of the drugs. The aim of this study was formulating 'for oral' cefuroxime axetil suspensions. From all formulations, were selected to further investigation. Considering no sedimentation, the sedimentation volume was determined. All selected formulations released which was acceptable. The results of assay test also proved that all formulations contain the drug in acceptable. The viscosity curves showed that the systems were pseudo plastic and thixotrop. Designed cefuroxime axetil formulations had good qualities and could be added as a new product to drug marketing.

Keywords: Cefuroxime, Formulation, Evaluation, oral, Suspension

INTRODUCTION

A Pharmaceutical suspension is a coarse dispersion in which internal phase (therapeutically active ingredient) is dispersed uniformly throughout the external phase.

The internal phase consisting of insoluble solid particles having a range of size (0.5 to 5 microns) which is maintained uniformly throughout the suspending vehicle with aid of single or combination of suspending agent. The external phase (suspending medium) is generally aqueous in some instance, may be an organic or oily liquid for non-oral use [1].

The reasons for the formulation of a pharmaceutical suspension:

- When the drug is insoluble in the delivery vehicle.
- To mask the bitter taste of the drug.
- To increase drug stability.
- To achieve controlled/sustained drug release.

Corresponding Author

Balasubramanian V
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Email :

Applications

- ❖ Suspension is usually applicable for drug which is insoluble (or) poorly soluble.
- ❖ To prevent degradation of drug or to improve stability of drug.
- ❖ To mask the taste of bitter of unpleasant drug.

Advantages

- ➢ Suspension can improve chemical stability of certain drug.
- ➢ Drug in suspension exhibits higher rate of bioavailability than other dosage forms.
- ➢ Duration and onset of action can be controlled.
- ➢ Suspension can mask the unpleasant/ bitter taste of drug [2].

Cefuroxime Axetil

It is an acetoxy ethyl ester prodrug of cefuroxime which is effective orally. The activity depends on *in vivo* hydrolysis and release of cefuroxime tablets [3].

It was patented in 1976 and approved for medical use in 1987.

Second generation cephalosporins are more effective in treating Gram-negative bacilli compared to first generation cephalosporins, which have a greater coverage for Gram-positive cocci. Also, it has been reported that cefuroxime is resistant to hydrolysis by β-lactamases produced by Gram-negative bacteria [4].

Mechanism of Action

Cefuroxime axetil is a second generation cephalosporin that, like penicillins antibiotics, contains a β-lactam ring structure. Cephalosporins works as a bactericidal antibiotic; that by binding to penicillin-binding proteins (PBPs), inhibit the last step of the bacterial cell wall synthesis. Once the β-lactam ring binds to PBPs, cross-linking between peptidoglycan units is inhibited [5].

Materials and Method

Cefuroxime axetil, Micronization silica gel, Pvp k30, Pregelatine starch, Sucrose, Microcrystalline cellulose, Xylitol, Xanthan gum, Aspartame, Acesulfame potassium, Tuttifruti flavor concentrate [6, 7].

METHODOLOGY

Formulation of CA oral suspension

Here the drug crystals mixed with silica gel, the above mixture was micronized. Then it was pass through Sieve No.100-is called mixture 1. PVPK 30 with pregelatinized starch and powders sucrose mix well, then it passes through Sieve No.100-is called mixture 2. Both mixture-1 and 2 blended well with liquid binder. The above blend dried well and screened [8].

Assay of the drug content:

The content of CA in the suspensions was determined by using a SPD- 10A VP UV-Visible spectrophotometer. The UV detector was operated at 278nm. Solutions of floating tablet of CA Standard were prepared at a concentration of about 0.1 mg/ml of CA was comparatively studied with test tablets [9].

***In vitro* dissolution**

In vitro dissolution behaviors of the two kinds of CA dry suspensions and its commercial dry suspensions were investigated using a type 2 dissolution apparatus (paddle method), and all the test were carried out in triplicate. A volume of 900ml pH 7.0 phosphate buffer was used as the release medium and the temperature was maintained at 37±0.5^{o}c with a paddle speed of 50rpm/min. A certain amount of dry suspensions equivalent to 125mg CA were used in all of the dissolution testes. At pre-determined time intervals (5,10,20,30,40 min), an aliquot of 5ml of the release medium was withdrawn and passed through a 0.22µm filter immediately. An equal volume of fresh medium was replaced. The concentration of CA suspension filtrate was determined using a UV spectrophotometer (Beijing Rayleigh Analytical instrument co.) at 280nm.

The dissolution of commercial dry suspension and dry suspensions prepared by wet granulation method and solid dispersion method were performed in pH 7.0 phosphate buffer and the corresponding profiles Both formulations are higher and faster release than that of the commercial suspension. The solid dispersion suspension displayed a significant improvement in dissolution rate with more than 70% of the drug dissolved within 20 min, owing to the amorphous state of drug in the solid dispersion. In comparison with the self-made formulations, the commercial dry suspension showed a lower and slower release, and only around 50% of the drug dissolved within 20 min.

Modulated Differential Scanning Calorimetry (MDSC)

The thermal analysis was carried out on DSC, TA Q1000. The thermogram was recorded from -20^{0}C to 90^{0}C under the nitrogen flow of 50 mL/min at a heating rate of 10^{0}C per minute with a modulation temperature of 1^{0}C per min.

Weighed about 15 mg sample into aluminum pan and distributed uniformly as a thin layer. The glass transition was recorded as the inflection point up to the step changed base line.

The heat flow was calibrated by enthalpy of indium (28.51J/g) or by the specific heat capacity of Sapphire. The specific heat method used the specific heat of sapphire over a user-defined temperature range. The baseline and sample curves were measured and the calibration was then built automatically. The calibration was checked before running samples by measuring the melting enthalpy of Indium by using the same instrumental parameters [10].

FTIR

The IR spectrum of drugs in KBr/MeOH is presented in IR spectra (KBr pellets) of the different polymorphic forms of the formulations [11].

SEM

In SEM study for different polymorphic forms of the formulations carried out index (Jeol, Japan) after sputter coating with gold in fine coat ION IFC – 1100 sputter (Jeol Japan) [12].

RESULTS

Ft-Ir Spectrum of Cefuroxime Axetil oral Suspensions

FTIR spectrum (fig no: 1) and the interpretations are given in (table no:1, 2, 3) for cefuroxime axetil oral suspensions. FTIR of oral suspension interaction plays a vital role in the release of drug from formulation. FTIR techniques have been used study the physical mixing and chemical interactions between the drug and excipient used. In the present study, chemical interaction between CA and excipients used was found.

DSC OF CEFUROXIME AXETIL ORAL SUSPENSIONS

It shows an endothermic peak at 66^0C(F1), 68^0C(F2) indicating the melting of the cefuroxime axetil oral suspensions.

The figure shows the dsc curve of ca oral suspension kneaded system in 1: 25m.the pure ca showed endothermic peak at 66^0 c,68^0 c. The curve of oral suspension ca displayed wide and strong endothermic effect. which, may be ascribed to dehydration. The characteristic of endothermic peak corresponding to melting peak of ca. represent reduction of temperature due to physical mixture of suspension and kneaded system.

XRD OF CEFUROXIME AXETIL ORAL SUSPENSIONS

XRD pattern of cefuroxime axetil oral suspensions 2theta peak were detected at scattering angles were shown in (table no:3) and the interpretations are given in (figure no:4).

XRD was performed to investigate to effect of the physical mixing with suspending agents on the crystallinity of CA with increase of physical mixing of suspensions, in sedimentation volume of the above both the formulations, F2 of suspensions given XRD patterns are shown in the above figure physical mixture of crystalline CA (ammonia crystal F2) was compares with F1 Formulation of suspensions.

The crystalline CA-ammonia(F2) suspensions intense peak at between 10^0 and 20^0 theta, with significance that there is no substantial conversion to crystallinity, often the physical mixing on slight crystalline nature of CA.

SEM OF CEFUROXIME AXETIL ORAL SUSPENSIONS

The above SEM study of CA -oral suspensions (a, b) among all of that prepared from ammonia crystals of CA. The SEM of CA oral suspensions dissolution, adsorption behavior briefly described in formulation “b”. That shows size of CA droplet very clearly dispersed in formulation “b” (size of droplet 103.7 nm).

Table no:1 FTIR Stretching frequencies for pure cefuroxime axetil oral suspension F1

S.NO	NH-Stretching	CH-stretching	C=O stretching	C-O stretching	N-O stretching	6-H,7-H Stretching (β-lactum)
1	3542	2932	1787	1098	1098	3052
2	3545	2976	1776	1009	1087	3094
3	3387	2965	1669	1078	-	-
4	3265	2876	1698	1099	-	-
5	1587	2887	1498	-	-	-
6	1574	2854	-	-	-	-
7	1354	-	-	-	-	-

Table no: 2 FTIR stretching frequencies for pure cefuroxime axetil oral suspension F2

S.NO	NH-Stretching	CH-stretching	C=O stretching	C-O stretching	N-O stretching	6-H,7-H Stretching (β-lactum)
1	3554	2925	1732	1054	1032	3065
2	3543	2921	1721	1054	1043	3043
3	3338	2932	1665	1067	-	-
4	3223	2865	1632	1044	-	-
5	1516	2865	1443	-	-	-
6	1505	2876	-	-	-	-
7	1399	-	-	-	-	-

Table no: 3 FTIR stretching frequencies for pure cefuroxime axetil oral suspension With marketed.

S.NO	NH-Stretching	CH-stretching	C=O stretching	C-O stretching	N-O stretching	6-H,7-H Stretching (β-lactam)
1	3543	2998	1709	1085	1098	3009

2	3554	2976	1798	1061	1009	3087
3	3369	2998	1676	1064	-	-
4	3287	2876	1686	1049	-	-
5	1587	2865	1409	-	-	-
6	1598	2898	-	-	-	-
7	1398	-	-	-	-	-

Table no: 4 XRD Of Cefuroxime Axetil Oral Suspensions

SL.NO		**2 θ**	**PEAK INTENSITY**
F1	1	24.76	08.99
	2	21.73	11.56
	3	19.44	13.54
	4	17.76	15.87
	5	15.29	17.98
F2	1	24.89	10.32
	2	20.12	12.65
	3	18.12	13.76
	4	16.47	15.87
	5	14.54	17.76

Figure no:1 FT-IR Spectrum of cefuroxime axetil oral suspensions

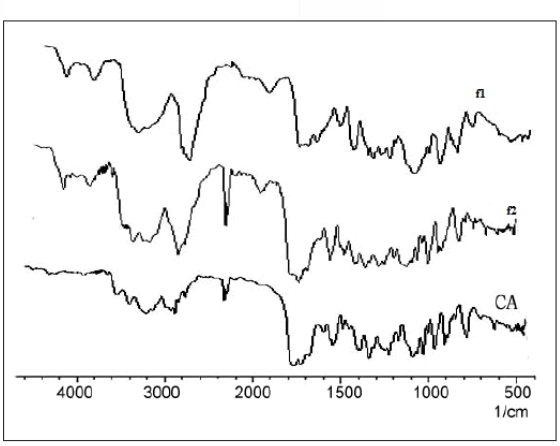


Figure no:3 DSC Of Cefuroxime Axetil Oral Suspensions

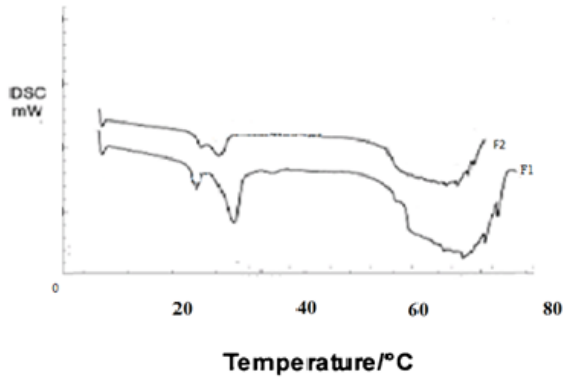


Figure no:4 XRD Of Cefuroxime Axetil Oral Suspensions

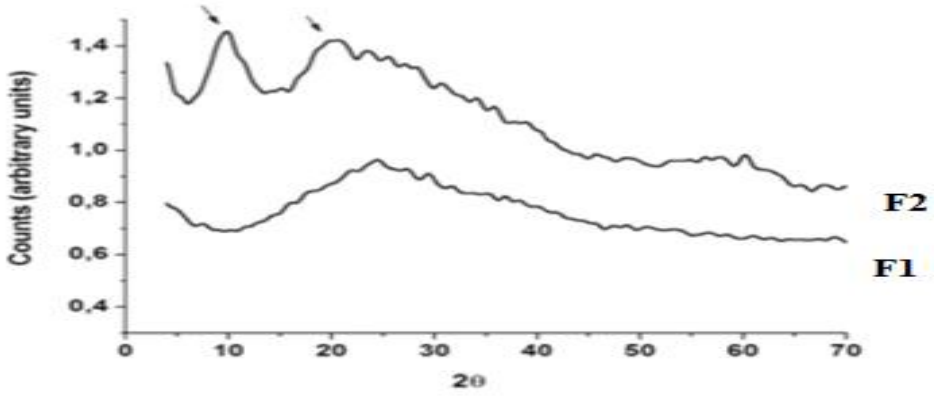


Figure no: 5 SEM of cefuroxime axetil oral suspensions

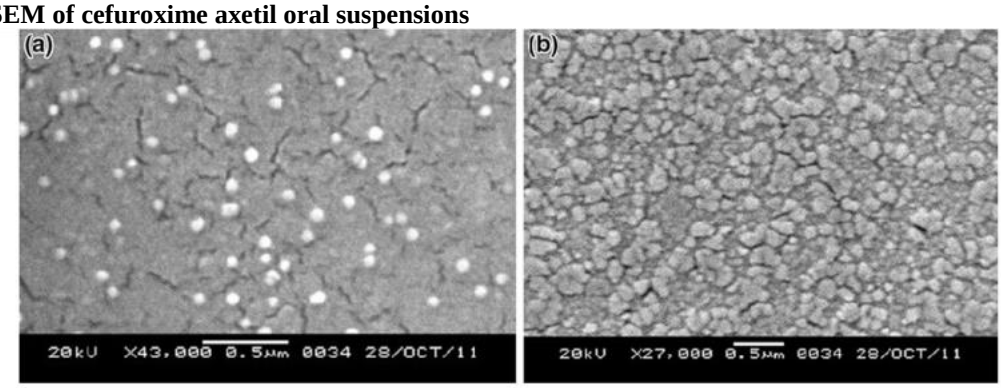


Figure no: 6 FT-IR stability study of cefuroxime axetil oral suspension (3 months)	**Figure no:7 FT-IR stability study of cefuroxime axetil oral suspension (6 months)**

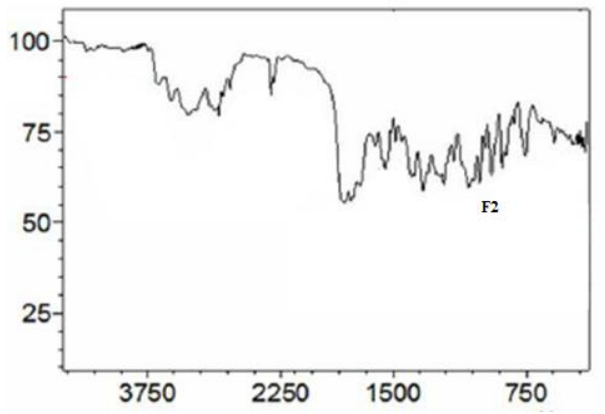
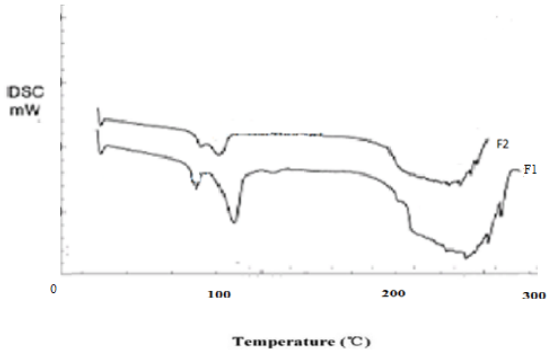

	

Figure no:9 DSC Stability study of cefuroxime axetil oral suspension (6 months)	**Figure no:10 XRD Stability study of cefuroxime axetil Oral Suspension (3 months)**

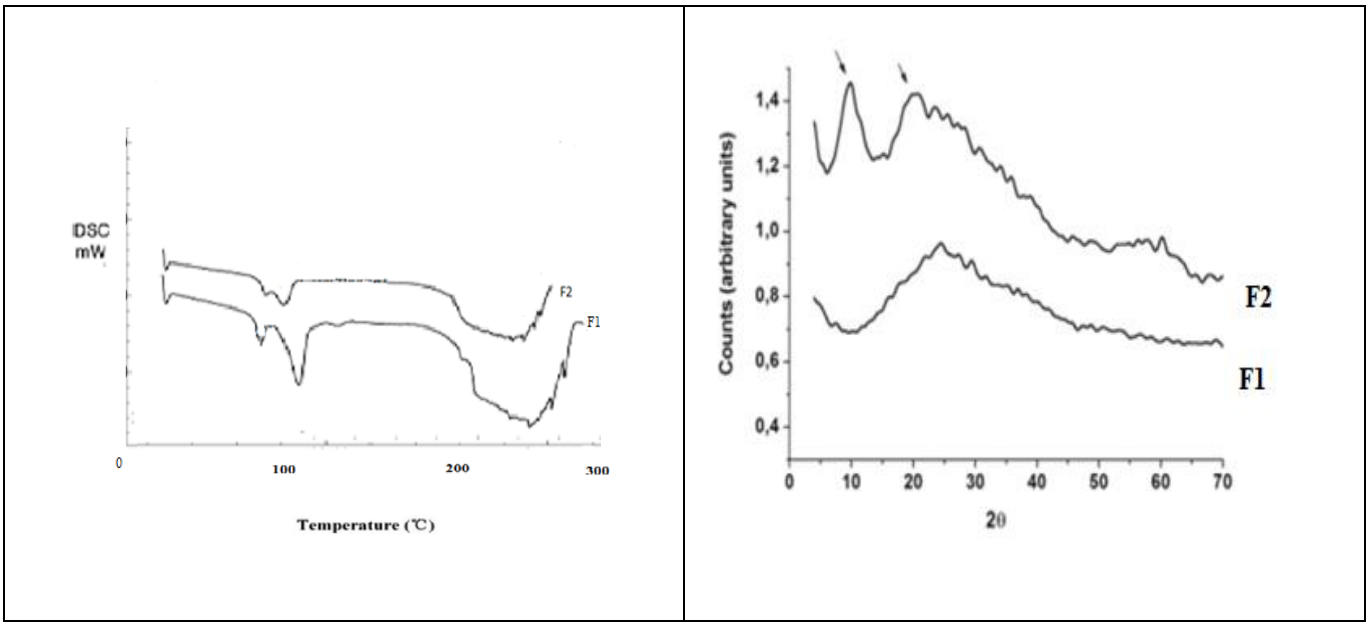


Figure no:11 XRD Stability study of cefuroxime axetil Oral Suspension (6 months)

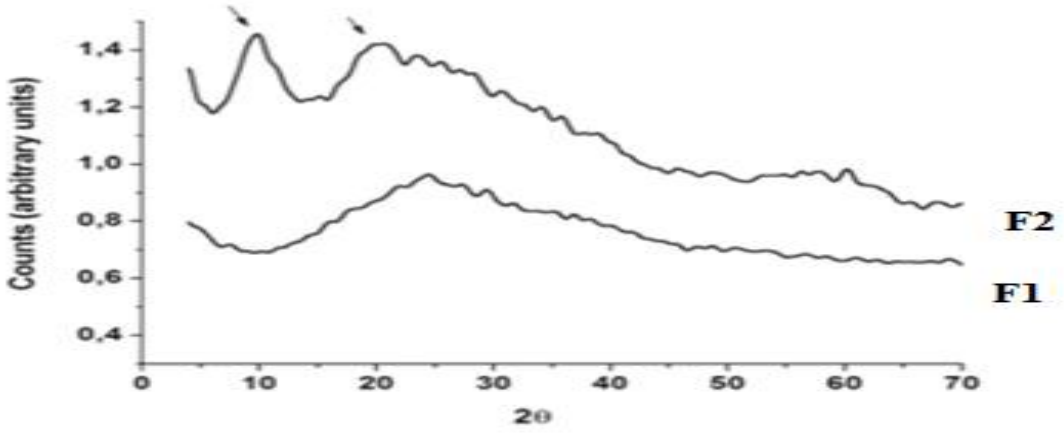


Figure no:12 SEM stability study of cefuroxime axetil oral suspensions (3 months)

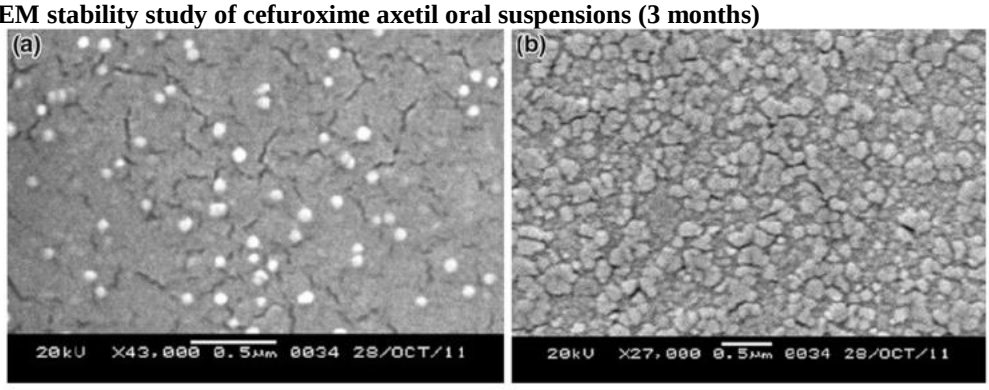
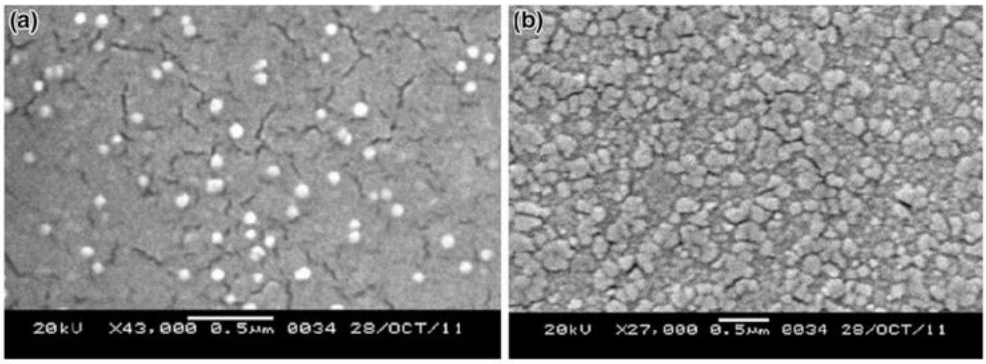


Figure no:13 SEM stability study of cefuroxime axetil oral suspensions (6 months)



DISCUSSSION

General criteria for selecting a suitable suspension can be considered as proper appearance of Formulation development, Sedimentaion rate, Invitro Drug Release studies According to these properties a general discussion is presented. Formulations were were pourable and had ideal characteristics to continue more other tests. There was no sediment in selected formulations. This involved in the formulation of stable formulations in other words, polymer bridging was the main mechanism for controlled flocculation in the present work.

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