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# Formulation development and evaluation of taste masked Cefuroxime axetil dry suspension

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**ABSTRACT**

*Cefuroxime axetil is an oral antibacterial prodrug of cephalosporin antibiotic, cefuroxime. It is used frequently for pediatric conditions like upper respiratory tract infections. The bitter taste of Cefuroxime axetil greatly hinders the further development of suitable formulations of this drug for oral use. Hence, it is important to mask the bitter taste and also to make them suitable for oral use. Lubritab is used as a taste masking agent. The taste masked dry suspension was made by compaction process. The prepared suspension was evaluated for various parameters like sedimentation volume, degree of flocculation, drug content and In-vitro dissolution profile. All the parameters were found to be within limits. When the results were also compared with marketed formulation, the prepared suspension was found to be better with respect to marketed preparation.*

**Keywords:** Cefuroxime axetil, Taste masking, Lubritab, Dry suspension.

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## INTRODUCTION

Undesirable taste is one of the important formulation problems that are encountered with many drugs. Administration of bitter drugs orally with an acceptable level of palatability is a key issue for health care providers. Proven methods for bitterness reduction and inhibition have resulted in improved palatability of oral pharmaceuticals. Most of the bitter tasting drugs have amine functional group. If such functional groups are blocked by complex formation, the bitterness of the drug reduces drastically, many drugs in particular; alkaloids carrying a positive charge at neutral pH elicit a strong bitter taste [1].

In general, bitter substances are hydrophobic, and thus hydrophobic interaction of the substances with the receptor sites contributes greatly to their binding various techniques are reported for masking the unacceptable taste of orally administered pharmaceuticals which include flavors & sweeteners, ion-exchange resins, Carbohydrates, formulation of inclusion complexes with cyclodextrins, proteins, gelatins & prolamines, particle coating, high viscosity liquid matrix. Ion exchange resins are water insoluble, cross linked polymers containing salt forming groups in repeating position in the polymer chain [2].

Cefuroxime axetil, Chemically, 1-Acetoxyethyl (6*R*,7*R*)-3-[(carbamoyloxy)methyl]-7-{[(2*Z*)-2-(2-furyl)-2-(methoxyimino)acetyl]amino}-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (fig.1), is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime [3], which is resistant to degradation by most β -lactamases and is active against a wide range of Gram-positive and Gram-negative organisms. It is used frequently for pediatric conditions like upper respiratory tract infections [4], bitter taste of the drug present problem of poor patient compliance.

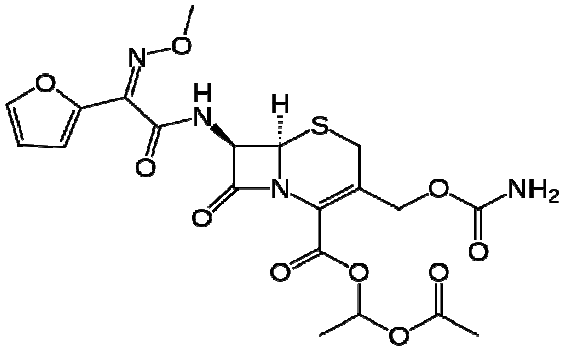

**Figure 1: Structure of Cefuroxime axetil**

Hence in the work undertaken, an attempt was made to mask the taste of the Cefuroxime axetil by dry suspension formulation using lipophilic vehicle [5] such as Hydrogenated cottonseed oil (Lubritab) as taste masking agent.

## MATERIALS AND METHODS

Cefuroxime axetil was procured as gift sample from Aurobindo Pharma Ltd., Hyderabad Lubritab (Hydrogenated Cotton Seed Oil) was procured from S.D. Fine Chemicals, Mumbai. All other ingredients used were of analytical grade.

### Preparation of Cefuroxime axetil-Lubritab Granules

Cefuroxime axetil and lubritab were sieved through # 30 mesh and mixed in octagonal blender for 30 minutes. The blend was compacted using roller compactor. The compacts were milled using multimill. The milled granules were compacted again using roller compactor. The compacts were milled again using multimill. The same procedure was followed for the Drug: Lubritab ratio 1:3, 1:4, 1:5 and 1:6.

### Formulation of taste masked dry suspension of Cefuroxime axetil

The Drug: Lubritab granules of 1:3, 1:4, 1:5 and 1:6 were used to formulate dry suspension. It was formulated as per following formula (Table. 1). All ingredients were passed through #30 mesh. Xantham gum, Aspartame, Acesulfame potassium and Flavour Tutti Frutti were mixed with part of sucrose. These were added to remaining sucrose and Drug: Lubritab granules and mixed. Finally the dry suspension which was formed (50 gm) is reconstituted up to 100 ml with dimineralised water before use.

**Table 1: Formula for taste masked dry suspension of Cefuroxime axetil**

| S.No. | Ingredients | Ratio (mg/unit) | | | |
|---|---|---|---|---|---|
| | | **1:3** | **1:4** | **1:5** | **1:6** |
| 1. | Cefuroxime axetil :lubritab | 1202.88 | 1503.6 | 1804.32 | 2105.04 |
| 2. | Sucrose | 1257.12 | 956.4 | 655.68 | 354.96 |
| 3. | Xanthan gum | 25 | 25 | 25 | 25 |
| 4. | Flavour Tutti Frutti | 10 | 10 | 10 | 10 |
| 5. | Acesulfame potassium | 2.5 | 2.5 | 2.5 | 2.5 |
| 6. | Aspartame | 2.5 | 2.5 | 2.5 | 2.5 |
| **Average weight** | | **2500** | **2500** | **2500** | **2500** |

Each formulation is equivalent to 300.72 mg of Cefuroxime axetil. Each 5ml of suspension contains 250 mg of Cefuroxime.

### Evaluation of dry suspension

### Sedimentation Volume

The sedimentation volume [6] was determined by keeping 50 ml of each suspension in the stopper measuring cylinder and stored undisturbed at room temperature. The separation of clear liquid was noted at intervals of 1 day and up to 10 days. The sedimentation volume (F) was calculated using the formula F = Vu/Vo, where Vu is the volume of sediment and Vo is the original height of the sample .It is expressed as a percentage.

$$\text{Degree of flocculation } (\beta) = F/F\infty; \quad (\beta) = \frac{Vu/Vo}{V\infty/Vo}$$

$$= Vu/V$$

$$\text{Degree of flocculation } (\beta) = \frac{\text{Ultimate sediment volume of flocculated suspension}}{\text{Ultimate sediment volume of deflocculated suspension}}$$

**Assay for Drug content**
**Sample solution**
An accurately measured portion of Cefuroxime axetil for oral Suspension was transferred to a 100ml volumetric flask, freshly constituted as directed in the labeling, and equivalent to about 250 mg of Cefuroxime mixed and free from air bubbles,. Add about 50 ml of methanol, and shacked by mechanical means for about 10 minutes. Diluted with methanol to volume, and mixed. Filtered a portion of this stock solution, and transferred 5.0 ml of the filtrate to a 50-ml volumetric flask. Add 13.8 ml of methanol and diluted with 0.2 M monobasic ammonium phosphate to volume and mixed well.

Chromatographic condition:
- Mobile phase - 0.2M Monobasic ammonium phosphate and methanol (620:380)
- λ max – 278 nm
- Column- 4.6-mm ×25-cm column containing 5-µm packing L13.
- Flow rate - 1.5 ml/min

***In vitro* release of prepared suspension**
Medium and apparatus used: 0.07 M pH 7.0 phosphate buffer. Apparatus 2: 50 rpm; Time: 30 minutes.

**Procedure**
Test 5.0 ml of constituted Cefuroxime axetil for oral Suspension equivalent to 250 mg of cefuroxime. Determine the amount of Cefuroxime equivalent dissolved by employing UV absorption at the wavelength of maximum absorbance at about 280 nm on filtered portions of the solution under test, suitably diluted with dissolution medium, if necessary, in comparison with a Standard solution having a known concentration of USP Cefuroxime Axetil RS in the same medium.

**Stability studies** [7]
**Drug content determination**
The chemical stability of Cefuroxime axetil is important because the physicochemical characteristics of Cefuroxime axetil depends on excipients employed in preparation. Hence the preparations were subjected for stability studies. The stability of Cefuroxime axetil was assessed by evaluating the percentage of the initial concentration remaining after a specific period of time under different conditions. A difference in concentration by ± 10% was considered a notable change in drug stability.

**pH measurements**
Change in pH of the suspension followed by reconstitution was measured for the optimised formulation (1:3 ratio) using a digital pH meter on day 1 and day 10 at 25˚C.

**Comparison with marketed preparation**
*In vitro* release of prepared suspension and marketed preparation was compared.

## RESULTS AND DISCUSSION

**Sedimentation volume**
It is observed that the sedimentation volume is between 1-10 at the end of 10 days, it shows good stability of suspension .The shape of the curve shows good stability of suspension. This was shown in the fig.2.

**Degree of flocculation**

Degree of flocculation **β**=27/25
=1. 08; It shows the greater the stability**.**
If the **β** value is nearer to 1, then the suspension does not represent a flocculated suspension. It indicates that the system under study is deflocculated system. But **β** can assume any value greater than 1.In general, the higher the value of B, the greater is the physical stability.

**Drug Content**
Assay value of the suspension was found to be 99.56%.

**Stability studies**
There is no significant change in pH and drug content of the suspension. The prepared formulation shows good stability for 10 days.

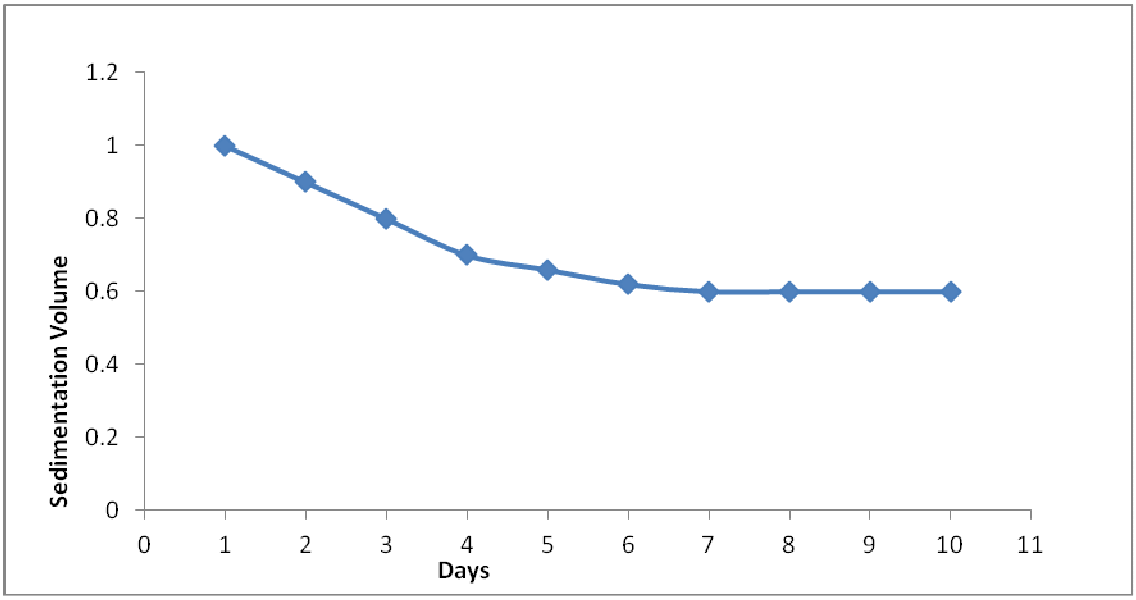


**Figure 2: Sedimentation Volume**

**Table 2: Physical properties of reconstituted suspension of optimised batch**

| Optimised batch formulation (1:3 Ratio) | pH of the formulation at 25°C | Drug content% |
|---|---|---|
| Day 1 | 5.6 | 99.56 |
| Day 10 | 5.9 | 99.12 |

***In Vitro* Drug Release Profile**

***In Vitro*** drug release profiles of different batches were studied in 0.07 M pH 7.0 phosphate buffer. The results obtained for different batches are tabulated in the following Table 3. From the, Fig. 3 it was found that trial batch with Drug: Lubritab of 1:3 ratio show better release with excellent taste masking. Hence 1:3 batch was selected for further studies.

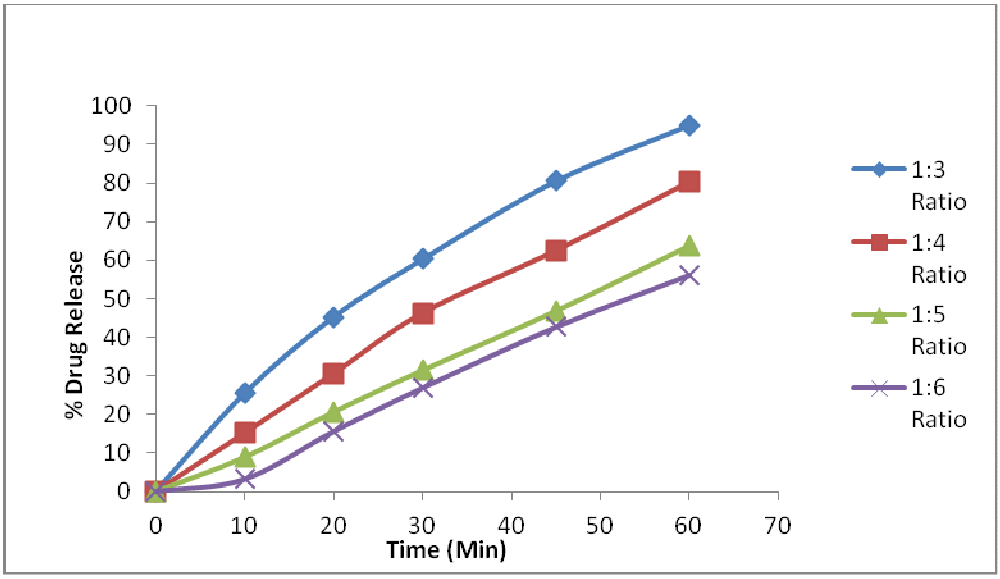


**Figure 3: *In vitro* drug release profile of trial batches**

**Table 3: *In vitro* release profile of trial batches**

| Time in min | % Drug Release of trial batches | | | |
|---|---|---|---|---|
| | 1:3 ratio | 1:4 ratio | 1:5 ratio | 1:6 ratio |
| 0 | 0 | 0 | 0 | 0 |
| 10 | 25.5 | 15.2 | 8.9 | 3.2 |
| 20 | 45.3 | 30.6 | 20.6 | 15.6 |
| 30 | 60.3 | 46.3 | 31.4 | 26.9 |
| 45 | 80.6 | 62.5 | 46.8 | 42.7 |
| 60 | 95.1 | 80.3 | 63.7 | 56.2 |

**Comparison of *In Vitro* drug release profile of optimised formulation with marketed formulation (Ceftin)**

The release profile of optimised formulation (1:3 ratio) of Cefuroxime axetil suspension was better as compared to marketed formulation (Ceftin) as shown in the table 4 and fig 3.

**Table 4: *In vitro* drug release of formulation compared with marketed formulation**

| Time in min | % Drug Release | |
|---|---|---|
| | Cefuroxime axetil Suspension | Marketed Suspension (Ceftin) |
| 0 | 0 | 0 |
| 10 | 25.5 | 19.1 |
| 20 | 45.3 | 39.2 |
| 30 | 60.3 | 54.1 |
| 45 | 80.6 | 73.9 |
| 60 | 95.1 | 89.6 |

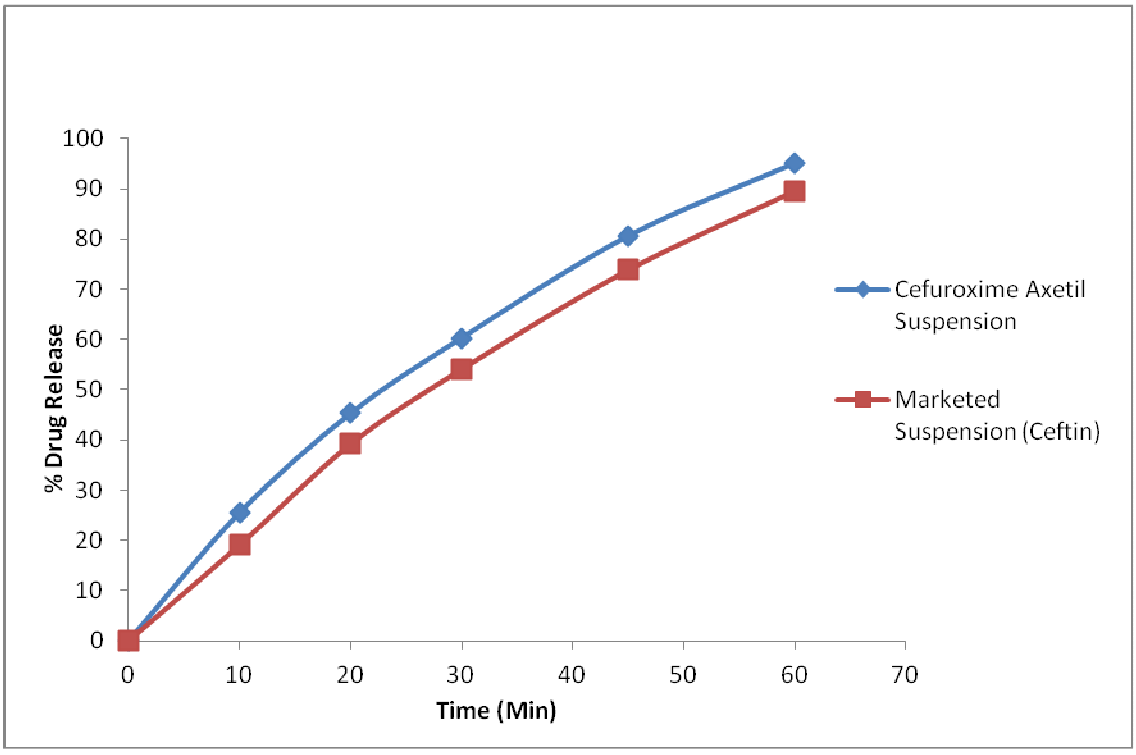


**Fig. 4: *In vitro* drug release comparison with marketed formulation**

## CONCLUSION

Taste masking enhances patient compliance & product appeal resulting in completion of therapy, better therapeutic results & promotion of sales. The problem of bitter and obnoxious taste of the drug in pediatric and geriatric formulation is a challenge to the pharmacist in the present world. In the present study, granules of Cefuroxime axetil were prepared by using different ratios of Cefuroxime axetil to lubritab. The granules show good taste masking property for Cefuroxime axetil and lubritab from 1:3 to 1:6 ratios. Trial batch with 1:3 ratio shows better drug release profile for Cefuroxime axetil. The Prepared suspension of Cefuroxime axetil shows good taste as compared to marketed preparation.

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