Original Article……!!!

PREPARATION AND EVALUATION OF SUSPENSION OF CEFUROXIME AXETIL

Dumbare A.S.*, Shelke P.V, Gadhave M.V, Banerjee S.K.

Department of Pharmaceutics, Vishal Institute of Pharmaceutical Education & Research, Ale, Pune, India, 412411

Keywords:
Cefuroxime axetil, Taste Masking, ion exchange resin

For Correspondence:
Dumbare A.S.
Department of Pharmaceutics, Vishal Institute of Pharmaceutical Education & Research, Ale, Pune, India, 412411

E-mail: dumbareavinash@gmail.com

ABSTRACT

Cefuroxime axetil (CA) is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime. Cefuroxime axetil (CA) is an antibacterial belonging to second generation of antibiotics. CA is used frequently for pediatric conditions like Upper respiratory tract infections. The bitter taste of the drug presents problem of poor patient compliance. So in the work undertaken, an attempt was made to mask the taste of the CA.
INTRODUCTION
Taste is an important parameter in administering drugs orally. Undesirable taste is one of the important formulation problems that are encountered with many drugs. Administration of bitter drugs orally with 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 drug reduces drastically, many drugs in particular; alkaloids carrying a positive charge at neutral pH elicit a strong bitter taste. Taste is a function of concentration of drug dissolved in saliva reduction of solubility of drug in saliva also forms the major approach towards taste masking. 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 on the polymer chain. Drug resin complexes (DRC) are insoluble hence DRC of bitter drugs have virtually no taste. Because of less counterion concentration and pH of saliva the drug bound to Cefuroxime axetil (CA) is an oral prodrug of the bactericidal cephalosporin antibiotic cefuroxime, which is resistant to degradation by most β-lactamases and is active against a wide range of Gram-positive and Gram-negative organisms. CA is an antibacterial belonging to second generation of antibiotics and is used frequently for pediatric conditions like upper respiratory tract infections, bitter taste of the drug presents problem of poor patient compliance.

MATERIALS AND METHODS
Cefuroxime Axetil, (Maxim Pharmaceuticals, Pune), Indion 214, Indion 204, Indion 234 (having crosslinked polyacrylate matrix type, exchange capacity of 10.0 meq/g and size ≤0.15mm), Eudragit EPO (Rohm Pharma, Germany) were obtained as gift. CA was analyzed by UV spectroscopy using Jasco 550 uv/vis spectrophotometer at λ-max 280 nm. Resinates were prepared using batch method. The weighed quantity of resin (Indion 214, Indion 264 and Indion 234) was stirred with equal quantity of CA keeping drug: resin ratio as 1:1 using a mechanical
stirrer for 4 hours which was found to be sufficient time for attainment of loading equilibrium. The slurry was decanted and filtered using Whatman filter paper no. 40. Resinate was washed with 10ml of methanol and dried. This was added to the filtrate and unbound drug in the combined filtrate was estimated at 280nm using distilled water as solvent for preparing dilutions and drug loading efficiency was calculated.

**EVALUATION**

Determination of drug content:-

Prepared resinate was evaluated for the drug content. 100 mg of the resinate was stirred with 100ml of 1M HCl for 4 hours using a mechanical stirrer and then the solution was filtered. Further dilutions were made using 1N HCl as solvent and the drug content was determined spectrophotometrically at 280nm using 1N HCl as blank.

Taste Evaluation :-

Determination of threshold bitterness concentration :-

Various concentrations (10-50 mcg /ml) of drug were prepared in phosphate buffer pH 6.7. Mouth was rinsed with buffer solution and then, 10 ml of most dilute solution was tasted by swirling it in the mouth mainly near the base of the tongue for 30 seconds. If the bitter sensation was no longer felt in the mouth after 30 seconds, the solution was spat out and waited for 1 minute to ascertain whether this is due to delayed sensitivity.

Then mouth was rinsed with safe drinking water. The threshold bitter concentration is the lowest concentration at which a material continues to provoke a bitter sensation after 30 seconds. After the first series of tests, mouth was rinsed thoroughly with safe drinking water until no bitter sensation remained. Interval of at least 10 minutes was observed between two tests.

**RESULT AND DISCUSSION**

For the preparation of resinites, batch method and kneading method were used. Indion 214 shows maximum (87.71%) adsorption of CA which may be attributed to the difference of cross-linking, exchange capacity and form of resin.
Calibration curve for Cefuroxime Axetil in phosphate buffer (pH 6.8)

**RELATIONSHIP BETWEEN ANGLE OF REPOSE (θ), % COMPRESSIBILITY & FLOWABILITY**

<table>
<thead>
<tr>
<th>Angle of repose (θ)</th>
<th>% Compressibility</th>
<th>Flowability</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>15</td>
<td>Excellent</td>
</tr>
<tr>
<td>30</td>
<td>16</td>
<td>Good</td>
</tr>
<tr>
<td>34</td>
<td>21</td>
<td>Passable</td>
</tr>
<tr>
<td>40</td>
<td>35</td>
<td>Poor</td>
</tr>
<tr>
<td>----</td>
<td>38</td>
<td>Very poor</td>
</tr>
</tbody>
</table>

**DETERMINATION OF THRESHOLD BITTERNESS CONCENTRATION**

<table>
<thead>
<tr>
<th>Concentration of drug(µg/ml)</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of candidate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
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 drug in pediatric and geriatric formulation is challenge to the pharmacist in the present world.

Various techniques like ion exchange resin, coating and inclusion complex with β-cyclodextrin were used to mask the bitter taste of CA. CA forms complex with Indion-214 by two methods like batch method and kneading. All taste masked products were characterized by drug content, in-vitro dissolution and micromeritic properties. Taste was evaluated using in-vitro method suggested as per WHO guidelines for evaluation of bitter medicinal plants. The product which showed best taste masking and drug release was formulated into suspension. Suspension was again evaluated and in vivo studies were carried out to check the bioavailability of suspension.

REFERENCES

