Taste masking of Lornoxicam by polymer carrier system and formulation of oral disintegrating tablets

Rajesh S. Jadon¹, Swadesh Nayak², Sabita Amlan², Vikas Deep Vaidya³, Prashant Khemariya⁴, Sandip Sumbhate¹, S. Nayak¹

Abstract
Lornoxicam is a non steroidal anti-inflammatory drug with analgesic properties and belongs to the class oxicams. It is extremely bitter in taste. The purpose of this research was to develop a bitterless oral disintegrating tablet of Lornoxicam. Taste masking was done by complexing Lornoxicam with aminoalkyl methacrylate copolymer (Eudragit EPO) in different ratios. In vitro release profile obtained at pH 6.2 indicate that perceivable amount of drug will not be released in saliva while high percentage release (more than 80 % in 30 mins.) would be obtained at acidic pH 1.2 of the stomach. Three super disintegrants were used while preparing the tablets e.g. sodium starch glycolate, crospovidone and crosscarmellose sodium. The tablets were evaluated for different properties like drug content, hardness, friability and disintegration time. The tablets shown good taste and disintegration in oral cavity.

Keywords: Oral disintegrating tablet, Lornoxicam, Eudragit EPO, Super disintegrating agents, Taste masking.

Introduction
In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Considering quality of life, most of these efforts have been focused on ease of medication. Among the various dosage forms developed to improve the ease of administration, the oral disintegrating tablet (ODT) is the most widely preferred commercial products [1, 2].

The ODT has remarkable disintegration properties; it can rapidly disintegrate without water in the mouth within a few seconds. When an ODT is placed in the oral cavity, saliva quickly penetrates into the pores causing rapid disintegration [3]. The ODT presents considerable advantages for the patient (or elder) who can not swallow (Dysphagia), or who is not permitted water intake because of disease. Such tablets can be produced by various methods; Namely, 1) drying after filling the pockets of the press through pack (PTP) with dispersed solution of the drug, 2) drying after low-pressure compression of humid powder granules containing the drug, 3) compression of dry powder granules containing the drug and, shaping by direct compression after mixing excipients and the drug [4].

Lornoxicam is a non steroidal anti-inflammatory drug with analgesic properties and belongs to the class oxicams. The mode of action of Lornoxicam is partly based on inhibition of prostaglandin synthesis.
(inhibition of the cyclo-oxygenase enzyme). Lornoxicam is absorbed rapidly and almost completely from the gastro-intestinal tract [5]. Lornoxicam is very bitter in taste and yet no oral disintegrating taste-masked preparation is available in market, which might be helpful in pediatric and geriatric patients. Therefore, to provide this drug in a more accessible and patient compliant form, in the present study an attempt has been made to mask its bitter taste and formulate it into oral disintegrating tablet [6].

**Materials and Methods**

Lornoxicam was a gift from Hetero drugs Ltd. (Hyderabad, India). Aminoalkyl methacrylate copolymer (Eudragit EPO) was a gift from Degussa India Private Ltd (Mumbai, India). Croscarmellose sodium, sodium starch glycolate, crospovidone, croscarmellose sodium and microcrystalline cellulose IP were obtained as gift samples from Torrent Pharmaceuticals Ltd (Ahmedabad, India). Other chemicals and reagent used were of AR grade.

**Preparation of taste masked granules of Lornoxicam**

Lornoxicam was thoroughly mixed with powdered Eudragit EPO in different ratios. Then 10 % Isopropyl alcohol (IPA) was added to this mixture in a glass beaker and mixed well to make a gelatinous mass. The prepared gel was manually extruded using a syringe. After extrusion of the gel, IPA was removed by evaporation overnight at room temperature. Subsequently the solidified drug polymer complex (DPC) was crushed into granules using a mortar. Three batches were prepared containing drug-Eudragit EPO in the ratio of 1:1, 1:2, and 1:3 in IPA by the above-mentioned method. [7,8]

**Characterization of DPC Drug Content, In Vitro Taste Evaluation**

Drug content was determined by dissolving 100 mg of DPC in 500 mL of simulated gastric fluid (SGF) and analyzing 1mL of appropriately diluted sample at 265 nm (Table 1). In vitro taste was evaluated by determining drug release in simulated salivary fluid (SSF) (pH 6.2) to predict release in the human saliva. DPC, equivalent to 8 mg of Lornoxicam (i.e., its dose), was placed in 10 mL of SSF and shaken for 60 seconds. The amount of drug released was analyzed at 265 nm (Table 1).

On the basis of these observations Drug polymer ratio 1:3 was finalized for further study [3].

**Table-1 Drug Content and In Vitro Taste Evaluation of DPCS in SSF**

<table>
<thead>
<tr>
<th>Serial No.</th>
<th>Drug-Polymer Ratio in DPC</th>
<th>% drug content in DPC*</th>
<th>% Drug Dissolved in SSF*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1:1</td>
<td>94.21 ± 0.48</td>
<td>45 ± 0.32</td>
</tr>
<tr>
<td>2.</td>
<td>1:2</td>
<td>49.52 ± 0.05</td>
<td>19 ± 0.21</td>
</tr>
<tr>
<td>3.</td>
<td>1:3</td>
<td>31.85 ± 0.32</td>
<td>4.60 ± 0.42</td>
</tr>
</tbody>
</table>

*Results are the mean of 3 observations ± SD.

**Formulation of oral disintegrating tablets (ODTs)**

Direct compression method was used to prepare the ODTs of Lornoxicam: Eudragit EPO complex. Different excipients incorporated are Mannitol, Avicel PH 102 (as diluent), Aerosil (as lubricant) and Aspartame (as sweetener). Superdisintegrants such as, croscarmellose sodium, crospovidone and sodium starch glycolate were also used in different concentrations [9, 10] (Table-2).

**Evaluation of ODTs**

**Hardness**

It is the tensile strength of tablets expressed in kg/cm². It is the pressure required to break the tablet in to two halves by compression [11].

**Weight Variation**

Weight variation test is done with 20 tablets. It is the individual variation of tablet weight from the average weight of 20 tablets [12].
Friability
This test is performed to know the effect of friction and shocks on tablets. Preweighed sample of tablets was placed in the friabilator (Roche friabilator), and operated for 100 revolutions. Tablets were dusted and reweighed. The test complies if tablets not lose more than 1% of their weigh [13].

Content Uniformity
Five tablets were crushed and from this, quantity equivalent to 8 mg of lornoxicam was dissolved in suitable quantity of pH 1.2 solution. Solution was filtered and diluted and analyzed for drug content [14].

Disintegration Time
Disintegration time for ODTs was determined using USP disintegration apparatus with SSF (pH 6.2, 900 ml at 37°C) as the disintegrating medium. To comply the test all tablets should disintegrate within 3 minutes [15].

Dissolution Study of Tablets
On the basis of disintegration data, formulation F6 was chosen for dissolution study, as it was showing least disintegration time i.e. 38 seconds. In vitro dissolution study on prepared tablets was performed in SSF (pH 6.2) and SGF (pH 1.2) without enzymes using USP type II (paddle) apparatus operated at 50 rpm (900 ml) for 60 minutes (37 ± 0.5°C).[16]

![Fig-1 Dissolution profile of batch F6](image)

### Table-2 Formulation table of batch F1-F6

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Formulations and their excipients (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
</tr>
<tr>
<td>DPC equivalent to 8 mg of drug</td>
<td>25.2</td>
</tr>
<tr>
<td>Mannitol</td>
<td>66</td>
</tr>
<tr>
<td>Avicel PH 102</td>
<td>45</td>
</tr>
<tr>
<td>Sodium Starch Glycolate</td>
<td>2</td>
</tr>
<tr>
<td>Crospovidone</td>
<td>-</td>
</tr>
<tr>
<td>Crosscarmellose Sodium</td>
<td>-</td>
</tr>
<tr>
<td>Aerosil</td>
<td>1.8</td>
</tr>
<tr>
<td>Aspartame</td>
<td>5</td>
</tr>
<tr>
<td>Tablet Weight</td>
<td>145</td>
</tr>
</tbody>
</table>

### Table-3 Evaluation of various batches of ODTs

<table>
<thead>
<tr>
<th>Formulation No.</th>
<th>Hardness (kg/cm²)</th>
<th>Friability (%)</th>
<th>Weight variation</th>
<th>Thickness (mm) ±S.D</th>
<th>Drug Content (%)</th>
<th>Disintegration time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>3.96± 0.01</td>
<td>0.28</td>
<td>Passes</td>
<td>2.51± 0.1</td>
<td>101.21</td>
<td>1 min. 25 sec.</td>
</tr>
<tr>
<td>F2</td>
<td>4.00± 0.01</td>
<td>0.21</td>
<td>Passes</td>
<td>2.49± 0.1</td>
<td>100.07</td>
<td>56 sec.</td>
</tr>
<tr>
<td>F3</td>
<td>3.94± 0.01</td>
<td>0.31</td>
<td>Passes</td>
<td>2.55± 0.1</td>
<td>99.90</td>
<td>1 min. 15 sec.</td>
</tr>
<tr>
<td>F4</td>
<td>4.06± 0.005</td>
<td>0.18</td>
<td>Passes</td>
<td>2.48± 0.1</td>
<td>100.12</td>
<td>52 sec.</td>
</tr>
<tr>
<td>F5</td>
<td>3.96± 0.01</td>
<td>0.24</td>
<td>Passes</td>
<td>2.54± 0.1</td>
<td>98.95</td>
<td>1 min 05 sec.</td>
</tr>
<tr>
<td>F6</td>
<td>4.04± 0.01</td>
<td>0.21</td>
<td>Passes</td>
<td>2.48± 0.1</td>
<td>100.25</td>
<td>38 sec.</td>
</tr>
</tbody>
</table>
Results and Discussion

Eudragit EPO was chosen for the taste masking of Lornoxicam. The Drug-polymer complex (taste-masked granules) was prepared by simple mass extrusion technique using syringe [7]. The drug polymer ratio that gave the best taste masking was 1:3. Drug content was found to be 31.85% in the complex (Table-1).

Six formulations F1-F6 were prepared using various excipients and three different superdisintegrants (crosscarmellose sodium, crospovidone and sodium starch glycolate) in different concentrations.

ODTs were prepared by direct compression [9, 10] and evaluated for Hardness [11], weight variation[12], friability[13], content uniformity[14], disintegration time [15] and dissolution [16]. The % drug content was found in the range of 98.95 - 101.21% (within the acceptable range) and the hardness was found between 3.94 - 4.06 kg/cm². Thickness of ODTs was found in between 2.48-2.4 mm. Friability of was found below 1% indicating good resistance against mechanical shear (Table-3).

Among the different formulations, F-6 was chosen as optimized batch containing crosscarmellose sodium as superdisintegrant, as it has produced the ODT having least disintegration time of 33 sec. The dissolution study was carried out in SSF and SGF, yielding about 10% and 90% dissolution respectively in 60 minutes. These results shown that taste masking effective

On the basis of above results it can be concluded that an oral disintegrating tablet of Lornoxicam can be prepared. Eudragit EPO also found to be efficient in taste-masking.

Acknowledgements

The authors are thankful to Hetero drugs Ltd. (Hyderabad, India) for the gift sample of lornoxicam Degussa India Private Ltd (Mumbai, India) for Aminoalkyl methacrylate copolymer (Eudragit EPO) and Torrent Pharmaceuticals Ltd (Ahmedabad, India) for Croscarmellose sodium, sodium starch glycolate, crospovidone, crosscarmellose sodium and microcrystalline cellulose IP.

References


