Preformulation Studies of Pantoprazole Sodium Susquihydrate for Sustained Release Mucoadhesive Microsphere

Rubi Singh, Pramod Kumar Sharma and Prashant Dhakad

Department of Pharmacy, School of Medical and Allied Sciences, Galgotias University, Plot No.2, Sector-17A, Yamuna Expressway, Greater Noida, Gautam Buddh Nagar, Uttar Pradesh, India

Abstract: Pantoprazole 5-(difluoromethoxy)- 2-[(3, 4-dimethoxypyridin-2-yl) methylsulfinyl]- 3H benzoimidazole is a proton pump inhibitor belongs to group of benzimidazole. This drug inhibits gastric acid formation and thereby it is very efficient for the treatment of gastric and duodenal ulcers. In aqueous media more acidic than pH 4 it suffers a practically complete decomposition within a period shorter than 10 minutes. Even in solid state it is sensitive to heat, humidity and light and especially to substances containing an acidic group. Pantoprazole which have an irritant effect on the stomach, can be coated with a substance that will only dissolve in the small intestine. For such types of drugs, enteric coating added to the formulation tends to avoid the stomach's acidic exposure, delivering them instead to a basic pH environment (intestines pH 5.5 and above) where they do not degrade and give their desired action. This stimulate us to formulate and evaluate pantoprazole as an enteric coated formulation.

Key words: Pantoprazole sodium • Antiulcer Drug • pH dependent solubility

INTRODUCTION

Pantoprazole is a Proton Pump Inhibitor (PPI), which inactivates the final step in the gastric acid secretion pathway in gastric parietal cells in a dose-dependent manner. Pantoprazole also exhibits antibacterial activity against Helicobacter pylori in-vitro. Seventeen years of clinical experiences, worldwide have shown pantoprazole to be an effective and well-tolerated treatment option in the management of acid-related disorders, including gastric and duodenal ulcers and Gastro-oesophageal reflux disease (GERD) and the treatment or prevention of gastro-duodenal lesions induced by NSAID’S. Pantoprazole also effective in combination with different regimens for H. pylori eradication and is included in the first-line PPI-based options for this purpose. Pantoprazole is a substituted benzoimidazole, which blocks the H+/K+ - adenosine triphosphate enzyme system of parietal cells and thereby inhibits the basal and stimulated gastric acid secretion. Pantoprazole is highly selective to acid secreting gastric parietal cells and its action is irrespective of the type of stimuli. Despite its several therapeutic benefits including maximal efficacy-safety ratio [1-3] Pantoprazole, like other proton pump inhibitors, undergoes degradation at low pH of the esophagus and stomach, leading to serious bioavailability problems [4]. Consecutively to protect the drug from degradation, a suitably designed formulation may be required which delivers the drug in alkaline environment by circumventing the acidic milieu. Since the gastrointestinal tract has pH variations all along its length, such a goal can be achieved by encapsulating the drugs within solid dosage forms coated with pH sensitive enteric polymers. The different release characteristics of the enteric polymers have profound impact upon the pharmacokinetic parameters of the drug [5-6] An Ideal enteric polymer should possess a hydrophilic and hydrophobic monomeric unit. Meth acrylic acid and methyl methacrylate could make an ideal hydrophilic and hydrophobic unit respectively. Such compositions of polymer are essentially insoluble in gastric fluids and may avail conveyance of drugs across the proximal alimentary tract without degradation [7].

Corresponding Author: Rubi Singh, Department of Pharmacy, School of Medical and Allied Sciences, Galgotias University, Plot No.2, Sector-17A, Yamuna Expressway, Greater Noida, Gautam Buddh Nagar, Uttar Pradesh, India. Tel: 07827642549.
MATERIALS AND METHODS

Pantoprazole sodium sesquihydrate are brought from chemical shop.

Preformulation Studies:

Flow Property

 Bulk Density: Density is defined as the weight per unit volume. Bulk density, \( \rho_b \), is defined as the mass of powder divided by the bulk volume and is expressed as gm/cm\(^3\).

\[
\text{Bulk density } (\rho_b) = \frac{\text{Weight of the powder (w)}}{\text{Bulk volume (Vb)}}
\]

 Tapped Density: Tapped density is defined as the weight of powder per unit tapped volume. Tapped density is determined by poured mass of complex into 25 ml of measuring cylinder and 100 tappings is done using tapped density apparatus. This method is repeated three times and the mean value is calculated as result of tapped volume. It is also expressed as gm. /cm\(^3\) [8].

\[
\text{Tapped density } (\rho_t) = \frac{\text{Weight of the powder (w)}}{\text{Tapped volume (Vt)}}
\]

 Angle of Repose: The angle of repose of blend is determined by the funnel method. The accurately weighted powder blend is taken in funnel. The height of the funnel is taken in funnel. The height of the funnel is adjusted in such a way that he tip of the funnel just touched the apex of the powder of the blend. The powder blend is allowed to flow through the funnel freely to the surface. The diameter of the powder cone is measured and angle of repose is calculated using the following formula.

\[
\tan \theta = \frac{h}{r}
\]

\[
\theta = \tan^{-1} \frac{h}{r}
\]

Compressibility Index: The simplest way of measurement of free flow properties of powder is compressibility, a n indication of ease with which a material can be induced to flow given by % compressibility index (% CI ) which is calculated as follows:

\[
\% \text{ CI} = \left( \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \right) \times 100
\]

Hausser’s Ratio: Hausner ratio is an index of ease of powder flow, it’s related to inter-particulate friction as such, could be used to predict powder flow properties. It’s calculated by the following formula:

\[
\text{Hausner’s ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}
\]

Melting Point: The melting point of a drug can be measured using three techniques:-
- Capillary Melting
- Hot Stage Microcopy
- Differential scanning calorimetric or thermal Analysis.

Capillary Melting: Capillary melting gives information about the melting range but it is different to assign an accurate melting point.

Table 1:

<table>
<thead>
<tr>
<th>S.no</th>
<th>Test</th>
<th>Specification</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Character</td>
<td>White to off white crystalline powder</td>
<td>Complies</td>
</tr>
<tr>
<td>2</td>
<td>Solubility</td>
<td>Freely soluble in methanol, water and Soluble in ethanol. Not soluble in Liquid paraffin and Chloroform</td>
<td>Complies</td>
</tr>
</tbody>
</table>

Table 2: Effect of angle of repose \( \theta \) on flow property

<table>
<thead>
<tr>
<th>Angle of repose</th>
<th>Type of flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 25</td>
<td>Excellent</td>
</tr>
<tr>
<td>25-30</td>
<td>Good</td>
</tr>
<tr>
<td>30-40</td>
<td>Passable</td>
</tr>
<tr>
<td>&gt;40</td>
<td>Very poor</td>
</tr>
</tbody>
</table>

Table 3: pre-compression parameter of powder

<table>
<thead>
<tr>
<th>Drug Powder</th>
<th>Bulk-density(gm/cm(^3))</th>
<th>Tapped density(gm/cm(^3))</th>
<th>Carr’s index (%)</th>
<th>Hausner ratio</th>
<th>Angle of repose</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>0.375</td>
<td>0.480</td>
<td>20.33</td>
<td>1.26</td>
<td>35.02</td>
</tr>
</tbody>
</table>
RESULTS

The melting point of Pantoprazole sodium susquihydrate is 140°C.

**Standard Calibration Curve of Pantoprazole:** An accurately weighed 100mg of omeprazole drug is dissolved in 100ml of 0.1 N HCL and used as primary stock solution. From the primary stock, concentration of 5, 10, 15, 20, 25, 30 µg/ml are prepared and the absorbance is measured at 302 nm using UV-Visible spectrophotometer. A plot is drawn taking concentration on x-axis and absorbance on y-axis and regression is determined as in Figure 1.

DISCUSSION

It could be concluded that the developed method for estimation of Pantoprazole in pharmaceutical dosage forms and in bulk is simple, sensitive, relatively precise and economical. The proposed methods are used for the routine analysis of the drugs in the quality control.

REFERENCES


