Gastric Ulcer Prevention by Lansoprazole

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Abstract

The objective of the current investigation is to formulate ethyl cellulose and hydroxypropyle methyle cellulose based sustained release microspheres, containing lansoprazole as model drugs. Lansoprazole is type II anti-ulcer agent when administered shows synergistic effect in their action. Microspheres were prepared by W/O/O double emulsion solvent evaporation method with different stabilizer concentration and at different speeds of emulsification while maintaining constant amount of lansoprazole. Drug excipient compatibility study was performed prior to formulation development and only compatible excipients were used in the fabrication of microspheres. Prepared microsphere formulations were characterized by percentage yield, particle size analysis, entrapment efficiency, invitro release behavior, differential scanning colorimetry (DSC) and scanning electron microscopy (SEM). SEM studies showed that the microspheres were spherical with rough surface morphology. The drug loaded microspheres showed 10.4-57.9% entrapment capacity for lansoprazole and The invitro release profile showed a slow and steady release pattern for lansoprazole. A 95-98% was releases within a period of 12 hrs . The drug release was found to be diffusion controlled mechanism. The n value of Korsmeyer Pepas equation indicated non Fickian type of diffusion.

Keywords: microspheres; lansoprazole; hydroxypropyle methyle cellulose; ethyl cellulose; double emulsion solvent evaporation method; FTIR;SEM; DSC

Introduction

Sustained Release Formulation

For decades an acute or chronic illness is being clinically treated through delivery of drugs to the patients in form of some pharmaceutical dosage forms like tablets, capsules, liquids, creams, pills, aerosols, injectable, and suppositories with their main discrepancy to maintain drug levels within the therapeutic range. However, these conventional dosage forms have some drawbacks. Multiple daily dosing is inconvenient to the patient and can result in missed doses, made up doses and patient incompliance with the therapeutic regimen. When conventional immediate release dosage forms are taken on schedule and more than once daily, there are sequential therapeutically blood peaks and valley associated with their actions. Microspheres were prepared by W/O/O double emulsion solvent evaporation method with different stabilizer concentration and at different speeds of emulsification while maintaining constant amount of lansoprazole. Drug excipient compatibility study was performed prior to formulation development and only compatible excipients were used in the fabrication of microspheres. Prepared microsphere formulations were characterized by percentage yield, particle size analysis, entrapment efficiency, invitro release behavior, differential scanning colorimetry (DSC) and scanning electron microscopy (SEM). SEM studies showed that the microspheres were spherical with rough surface morphology. The drug loaded microspheres showed 10.4-57.9% entrapment capacity for lansoprazole and The invitro release profile showed a slow and steady release pattern for lansoprazole. A 95-98% was releases within a period of 12 hrs . The drug release was found to be diffusion controlled mechanism. The n value of Korsmeyer Pepas equation indicated non Fickian type of diffusion.

Table 1: List of materials used and supplier

<table>
<thead>
<tr>
<th>S.No</th>
<th>CHEMICAL NAME</th>
<th>SOURCE</th>
<th>PURPOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lansoprazole</td>
<td>MSN Laboratories, Hyderabad, India</td>
<td>Drug</td>
</tr>
<tr>
<td>2</td>
<td>Ethyl Cellulose</td>
<td>SD Fine chemical Ltd, Mumbai, India</td>
<td>Olymer</td>
</tr>
<tr>
<td>3</td>
<td>Dichloro Methane (DCM)</td>
<td>SD Fine chemical Ltd, Mumbai, India</td>
<td>Polymer</td>
</tr>
<tr>
<td>4</td>
<td>Paraffin Liquid (light)</td>
<td>SD Fine chemical Ltd, Mumbai, India</td>
<td>Solvent</td>
</tr>
<tr>
<td>5</td>
<td>Span 80</td>
<td>SD Fine chemical Ltd, Mumbai, India</td>
<td>Stabilizer</td>
</tr>
<tr>
<td>6</td>
<td>N- Hexane</td>
<td>SD Fine chemical Ltd, Mumbai, India</td>
<td>Solvent</td>
</tr>
<tr>
<td>8</td>
<td>Potassium dihydrogen Phosphate</td>
<td>SD Fine chemical Ltd, Mumbai, India</td>
<td>Buffer ingradient</td>
</tr>
<tr>
<td>9</td>
<td>NAOH pellets</td>
<td>SD Fine chemical Ltd, Mumbai, India</td>
<td>Buffer ingradient</td>
</tr>
</tbody>
</table>

Lansoprazole

Lansoprazole belongs to class of antisecretry compounds, the substituted benzimidazoles that donot exhibit antocholinergic or histamine H2 receptor antagonist properties but rather supress gastric acid secretion by inhibition of the H+, K+ ions.

Lansoprazole has been characterised as a gastric acid pump inhibitor in that it blocks the final step of acid production. This effect is dose related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus.
Analytical method development

Preparation of buffer pH 6.8

50 ml of the potassium dihydrogen phosphate (0.2M) was placed in 200 ml volumetric flask and to it 22.4 ml of sodium hydroxide solution (0.2M) was added and the volume was made up to 200 ml with distilled water.

Preparation of standard solution of lansoprazole:

Procedure: Accurately weighed 100 mg of lansoprazole drug was dissolved in 100 mL of (Conc. 1000 µg/mL). From this solution, 10 mL was pipetted out into 100 mL volumetric flask and volume was made up to with methanol (Conc. 100 µg/mL). Further 10 ml aliquot was taken from this solution (100 µg/ml) and diluted to 100 ml with methanol to give 10 µg/ml standard solution of drug. Similarly, standard stock solution was prepared in phosphate buffer pH 6.8 and methanol.

Preparation of microspheres

For the preparation of microspheres the double emulsion method was used as suggested by Rama Rao et al. (2005) with slight modifications. The polymer was dissolved in a mixed solvent system (MSS) of acetone and dichloromethane. To this polymer solution glipizide was added and mixed. Then metformin was dissolved separately in 3 ml of distilled water and added to the polymer solution while stirring to form a primary emulsion. This primary emulsion was stirred at 450 rpm for 15 min using a mechanical stirrer. Then, this w/o emulsion was poured into liquid paraffin containing Span180 as the non solvent. This was stirred using a mechanical stirrer for 3 h, for the complete evaporation of the solvent. 10 ml of n-hexane was added as the non solvent after 2 h of the stirring process. 47

Treatment and randomization

All patients who met the inclusion and exclusion criteria received a 1 week course of antibacterial therapy containing lansoprazole 30 mg, amoxicillin 1 g and clarithromycin 500 mg, given twice daily. This was followed by treatment with lansoprazole 30 mg, given daily for 4 weeks. Repeat endoscopy was performed at the end of treatment to check for healing of ulcers and eradication of H. pylori using the methods described above. Patients with unhealed ulcers would be given 30 mg of lansoprazole daily for another 4 weeks. Patients who failed H. pylori eradication, defined as a positive rapid urease test or histology, would receive another 1 week course of triple therapy containing ranitidine bismuth citrate 400 mg, amoxicillin 1 g and metronidazole 400 mg, given twice daily. Patients with unhealed ulcers and two unsuccessful eradication treatments of H. pylori were taken out of the study.

Results and Discussion

In the present investigation an attempt has been made to formulate microspheres of lansoprazole by using biocompatible polymer like ethyl cellulose and hydroxypropyl methyl cellulose as carrier for sustained release. Microspheres were prepared by double emulsion solvent evaporation method. Prepared microspheres are subjected for characterization and evaluation studies.

Characteristics of patients

Among 102 patients screened during the study period, 45 were suitable for entry into the trial and were given a 1 week course of triple therapy, followed by treatment with lansoprazole. Reasons for exclusion are given in Figure 1. Two patients had persistent H. pylori infection after the first course of eradication therapy; they received the second antibacterial therapy and H. pylori was eradicated in both patients. Two patients had persistent ulcers after repeated antibacterial treatment and were excluded from the study. The remaining 43 patients were given naproxen 750 mg daily and randomly assigned to receive lansoprazole treatment (n = 22) or no treatment (n = 21).

Preformulation Studies

Preformulation study for lansoprazole has been performed to know the drug physical properties so as to design it to a suitable formulation.
### Physical property | lansoprazole
---|---
Empirical Formula | C_{11}H_{15}N_{4}HCl
Molecular Weight | 369.36 daltons
Color and odour | White brownish colour powder
Taste | Slightly bitter in taste
Appearance | Crystalline powder

**Table:** Description data of lansoprazole

**Surface Morphology By Sem**

![Particles in spherical shape](image_url)

**Conclusion**

From the study it is evident that promising sustained release microspheres of lansoprazole may be developed by W/O/O double emulsion solvent diffusion technique by using ethyl cellulose and hydroxyl prople methyle cellulose polymer.

**References**

9. Patel J. Bioadhesion is a topic of current interest in the design of controlled or targeted drug delivery system.