IMPROVEMENT OF DISSOLUTION PROFILE OF LORNOXICAM BY SOLID DISPERSION USING SPRAY DRYING TECHNIQUE

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ABSTRACT

The objective of the present study was to enhance the dissolution of poorly water soluble drug Lornoxicam by formulating its solid dispersion. Solid dispersion of Lornoxicam was formulated using hydrophilic polymers like gelucire 44/14 and crosspovidone by spray drying technique. Physical mixture and solid dispersion were prepared at three molar ratio as drug: polymer, 1:2, 1:4, 1:6 for both the polymers. Solid dispersion batches prepared using gelucire 44/14 had given rapid and more extent of drug release as compared to crosspovidone containing batches and hence were selected for further characterizations. The formulated solid dispersion batches were characterized by DSC and FTIR. The optimized solid dispersion batch was further used to prepare fast dissolving tablets using super disintegrant microcrystalline cellulose and cross carmellose cellulose. Prepared fast dissolving tablets of optimized batch had shown superior dissolution profile [94.37 % drug release in 10 min] than that of marketed tablet [59.73s% drug release in 10 min.]. Thus, from present work it can be concluded that dissolution and ultimately the bioavailability of Lornoxicam can be greatly increased by its solid dispersion formulation with gelucire 44/14 using spray drying technique.
INTRODUCTION:
Enhancement of bioavailability of hydrophobic drugs is one of the major challenges in drug development. Oral bioavailability of a drug depends on its solubility and/or dissolution rate, and dissolution may be rate determining step for appearance of medicinal effect, therefore efforts to increase dissolution of drug with limited water solubility is often needed. Many methods are available to improve these characteristics, including salt formation, micronization and addition of solvent or surface active agents\textsuperscript{1-3}. Among the various approaches, the solid dispersion technique has often proved to be the most successful in improving the dissolution and bioavailability of poorly soluble, active pharmaceutical ingredients because it is simple, economical, and advantageous. Solid dispersion (SD) involves a dispersion of one or more active ingredients in an inner carrier or matrix in solid state prepared by melting, dissolution in solvent or melting solvent method\textsuperscript{1}. Solid dispersions in water-soluble carriers have attracted considerable interest as a means of improving the dissolution rate, and hence possibly bioavailability of a range of hydrophobic drugs. Recently spray drying process is widely used to improve dissolution rate and bioavailability of poorly soluble drugs. Spray drying is a one step process in which drug-polymer solution is spray dried in a stream of hot air, results in rapid evaporation of solvent from the droplets. The dried particles then separated and collected by cyclone separator. It is observed that spray drying process produce amorphous material because of rapid solvent evaporation and super-saturation of drug in polymer\textsuperscript{4}. The present work was planned with the aim to enhance the dissolution of poorly water soluble drug Lornoxicam by formulating its solid dispersion.

MATERIALS AND METHODS:

Materials
Lornoxicam was gift sample from Aristo Pharma, Mumbai. All reagents and solvents used were of analytical grade. All the chemicals and solvents used in the study were of analytical grade.

Experimental study:

Preparation of solid dispersions of Lornoxicam
Aiming to improve the dissolution behavior of Lornoxicam in gastric conditions, solid dispersions of Lornoxicam with Gelucire 44/14 and crosspovdone were prepared at three molar ratios, namely, 1:1, 1:2 and 1:3 (drug: polymer), using spray drying technique. Physical mixtures of the same polymers were also prepared in the same molar ratios for comparison.
Table 1. Formulation of solid dispersion batches

<table>
<thead>
<tr>
<th>Batch No.</th>
<th>Lornoxicam (mg)</th>
<th>Gelucire 44/14 (mg)</th>
<th>Crosspovidone (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>800</td>
<td>1600</td>
<td>-</td>
</tr>
<tr>
<td>B</td>
<td>800</td>
<td>3200</td>
<td>-</td>
</tr>
<tr>
<td>C</td>
<td>800</td>
<td>4800</td>
<td>-</td>
</tr>
<tr>
<td>D</td>
<td>800</td>
<td>-</td>
<td>1600</td>
</tr>
<tr>
<td>E</td>
<td>800</td>
<td>-</td>
<td>3200</td>
</tr>
<tr>
<td>F</td>
<td>800</td>
<td>-</td>
<td>4800</td>
</tr>
</tbody>
</table>

Spray drying method:
Lornoxicam with Gelucire 44/14 and crosspovidone was dissolved separately in sufficient amount of solvent chloroform to get clear solutions. Spray drying of these solutions was carried out using laboratory scale spray dryer under following set of conditions: inlet temperature, 45-50°C; outlet temperature, 90-100°C; feed rate, 2 mL/min; atomization air pressure, 2 kg/cm² and aspiration, 40%.

Evaluation of Surface Solid Dispersion

Drug content determination of prepared solid dispersions⁵:
Solid dispersions equivalent to 10 mg of Lornoxicam were weighed accurately and dissolved in suitable quantity of solvent mixture chloroform. The drug content was determined at 354 nm by UV spectrophotometer with suitable.

Determination of saturation solubility of prepared solid dispersions⁶:
Excess amount of different solid dispersion formulations of Lornoxicam were added to 10mL of 0.1N HCl and phosphate buffer pH 6.8, separately in 10 mL volumetric flasks. Samples were shaken using mechanical shaker for 48 hours. Samples were then filtered, diluted suitably and analyzed spectrophotometrically at 354nm.

Fourier transform infrared spectroscopy (FTIR):
Infrared spectra of solid dispersion powder were obtained using FTIR spectrometer FT/IR Jasco 4100. About 3-4 mg sample was directly placed on the stage of spectrometer and scanned from 4000-400 cm⁻¹.

Differential scanning calorimetry (DSC):
DSC studies were carried out using thermal analyzer (TA SDT-2790). The samples were hermetically sealed in an aluminum pans and heated at constant rate of 10⁰C/min over a temperature range of 0-300⁰C. Inert atmosphere was maintained by purging nitrogen gas at a flow of 50 mL/min.
**In-vitro dissolution studies of Lornoxicam solid dispersion systems:**

Preliminary dissolution tests under gastric conditions, intended for selecting the solid dispersion system with superior dissolution properties to be incorporated into the formulation of fast dissolving tablet, were performed using the United States Pharmacopoeia (USP) dissolution apparatus II at 50 rpm. A sample equivalent to 8mg of Lornoxicam was placed in the dissolution vessel containing 900mL of 0.1N HCL maintained at 37 ±0.5°C. At appropriate intervals, samples from the dissolution medium were withdrawn and filtered, and concentrations of Lornoxicam were determined spectrophotometrically at 354 nm. The dissolution studies were conducted in triplicate and the mean values were plotted versus time.

**RESULTS AND DISCUSSION:**

**Percent drug content of lornoxicam in prepared solid dispersions:**

Percent drug content of Lornoxicam in spray dried solid dispersions was found decrease with increasing molar ratio of polymer. The percent drug content values of Lornoxicam in different solid dispersion batches are shown in Table 2.

<table>
<thead>
<tr>
<th>Batch</th>
<th>Equivalent weight of powder (mg)</th>
<th>% drug content</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10</td>
<td>45</td>
</tr>
<tr>
<td>B</td>
<td>10</td>
<td>50</td>
</tr>
<tr>
<td>C</td>
<td>10</td>
<td>27</td>
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<td>D</td>
<td>10</td>
<td>36.36</td>
</tr>
<tr>
<td>E</td>
<td>10</td>
<td>55</td>
</tr>
<tr>
<td>F</td>
<td>10</td>
<td>20.27</td>
</tr>
</tbody>
</table>

**In vitro dissolution studies of lornoxicam solid dispersion systems:**

Figure 1 and 2 indicate the dissolution profiles of pure Lornoxicam, physical mixtures and solid dispersion batches. From saturation solubility data it was found that Lornoxicam is a typical poorly water soluble drug having pH dependent solubility. Dissolution profile of pure Lornoxicam manifesting zero percent drug release upto 60 min. Dissolution enhancement of Lornoxicam was elicited by both polymers (gelucire 44/14 and crosspovidone) from their physical mixtures and spray dried solid dispersions.
Fourier transform infrared spectroscopy (FTIR) studies:

FTIR spectra of pure lornoxicam, Gelucire 44/14, physical mixtures and solid dispersion batches are shown in Figure 3 and 4. From this observation it can be assume that there is strong hydrogen bonding interaction between lornoxicam and gelucire 44/14 which may resulted in solubility enhancement. It is reported that hydrogen bonding is generally occur between hydrogen bond acceptor and hydrogen bond donor group.
Figure 4. IR Spectra of Lornoxicam + crosspovidone

Differential scanning calorimetry (DSC):

DSC thermograms over the temperature range 0-300°C. The DSC thermogram of lornoxicam exhibited a sharp exothermic peak at 224.88°C corresponding to its crystallinity and melting point. This indicates lornoxicam is completely crystalline in nature. 106°C and softening point near 180°C. Sharp exothermic peak of pure lornoxicam at 224°C was disappeared in the DSC scans.

Figure 5. DSC thermograms of Lornoxicam
CONCLUSION

In present work efforts were taken to enhance the dissolution of poorly water soluble lornoxicam by formulation spray dried solid dispersion. The study demonstrates the high potential of spray drying technique for successful preparation of lornoxicam solid dispersion using Gelucire 44/14 and crosspovidone.

REFERENCES: