In vitro studies on guar gum based colon targeted delivery of aceclofenac

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INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body promptly thereby to maintain the desired drug concentration i.e. the drug delivery system should deliver the drug at a rate desired by the needs of the body over a specified period of treatment[1].

The colon targeting is also exploited for systemic delivery of active drug for certain diseases such as arthritis, nocturnal asthma and angina for delivering the drug consistently with the circadian rhythm of the disease[2].

Arthritic diseases such as rheumatoid arthritis, osteoarthritis, ankylosing spondylitis and gout exhibit profound circadian rhythms in the manifestation and intensity of symptoms. Patients with osteoarthritis tend to have less pain in the morning and more at night whereas, rheumatoid arthritis pain usually peaks in the morning and decreases as the day wears off.

In case of ankylosing spondylitis, back stiffness and pain are prominent between 6 a.m and 9 a.m. Chronotherapy for all forms of arthritis uses standard treatment of NSAID. The drugs are to be delivered to synchronize the circadian rhythms of the above diseases.

The present work exploits the use of polysaccha-
ride–guar gum in the preparation of Colon Specific Drug Delivery (CSDD) system of aceclofenac. The gum hydrates and swells forming viscous colloidal dispersions which retard the drug release from the tablet into the intestine. The in vitro release profile confirms that the vast micro flora and the enzymes present in the colon leads to the degradation of the polymer in the colon\[3\].

**MATERIALS AND METHODS**

**Materials**

Aceclofenac was obtained from M/s. Padmaja Pharmaceutical’s, Vijayawada., Guar Gum from M/s. Romet labs Pvt.Ltd, Chennai. All other chemicals were of analytical grade.

**Methods**

**Preparation of aceclofenac matrix tablets using guar gum**\[4\]

Granules were prepared by wet granulation method (TABLE 1).

**TABLE 1: Preparation of matrix tablets of aceclofenac and guar gum**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Quantity (mg) present in each tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GG(_1)</td>
</tr>
<tr>
<td>Aceclofenac</td>
<td>100</td>
</tr>
<tr>
<td>Guar gum</td>
<td>180</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>50</td>
</tr>
<tr>
<td>Lactose</td>
<td>122</td>
</tr>
<tr>
<td>Starch paste</td>
<td>20</td>
</tr>
</tbody>
</table>

**Evaluation of granules and tablets**

Granules were evaluated for angle of repose and compressibility index. Prepared tablets were evaluated for weight variation, thickness, hardness, friability, and drug content followed by in vitro release studies. In vitro release studies of tablets in media of different pH

**RESULTS AND DISCUSSION**

**In vitro release study**

1. **Simulated gastric fluid (SGF) pH 0.1 N HCl**

Dissolution test was carried out as per USP XXI rotating basket method. 0.1M HCl was used as the dissolution medium (900ml), at 100 rpm, temperature maintained at 37\(^\circ\)±1\(^\circ\)C. Samples of 5 ml were withdrawn at regular time intervals, filtered, diluted suitably and assayed spectrophotometrically at 275 nm (UV-1601 shimadzu).
increased from the GG1 to GG4, the amount of the drug released was found to be less. This was due to the protective effect of guar gum, which swells to form a barrier to release the drug. The data are represented in figure 1.

2. In simulated intestinal fluid (SIF) and simulated colonic fluid (SCF)

In SIF batch GG1 showed 47.56% of drug release at the end of 7th h and the tablet remained intact but showed very loose gel like appearance. The cumulative percentage drug release for the batch GG1 in pH 7.4 buffer with rat cecal contents was 111.1%. The amount of drug released from GG2 matrix tablet at the end of 8th h was found to be 50% (SIF) and 108.78% at the end of 8th h in pH 7.4 buffer with rat cecal contents. The data are represented in figure 2 and 3.

The amount of drug released from the GG1 tablets in the simulated intestinal fluid study was found to be 45.20% at the end of 24 h (SIF) and it was found that 92.25% of drug was released at the end of 24h in the SCF dissolution medium containing rat cecal contents. The GG1 batch of tablets have released 42.13% at the end of 24th h in the stimulated intestinal fluid and it was found that 83.3% of drug was released from the GG4 batch in the pH 7.4 buffer solution with rat cecal contents. The data are represented in figures 4 and 5.

It was observed that a drug release of maximum 40.15% was found in 0.1 N HCL from GG1 and minimum 10.95% and 8.46% from the GG3 and GG4 batches respectively. It is evident from the data that GG3 and GG4 batches release small quantity of drug in the stomach media, so they can be considered as moderate formulae. The release of drug from GG1, GG2, GG3 and GG4 tablets in SIF, it was found that GG1 and...
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GG, tablets which were containing 38% and 47% of guar gum could not protect the drug release in the stomach media and 50% of drug was released from both the batches at the end of the studies without rat cecal contents (SIF). The GG, and GG, batches released 45.20% and 42.13% of drug at the end of 24th hr respectively. The matrix tablets containing 55% and 64% of guar gum in the batches GG, and GG, were considered suitable for colon targeting but in comparison to the percentage of drug released in the presence of rat cecal matter, the GG, batch was releasing a maximum of 92.25% of the drug whereas the GG, batch released 83.3% of drug at the end of 24th h of the study.

CONCLUSION

This suggests that the amount of guar gum present in GG, batch was enough to retard the drug release in the upper G.I tract Amongst all the approaches used for colon targeting, a microbiually controlled delivery system is the most appealing as it relies on a unique enzymatic ability of the colonic microflora and enables a more specific targeting independent of pH variation along the GI tract in the present work 55% of guar gum have been concluded as an optimised percentage in designing colon specific delivery of aceclofenac for the treatment of chronobiological symptoms of arthritis.

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REFERENCES