Evaluation of Various Natural Gums as Release Modifiers in Tablet Formulations

Pranati Srivastava, Rishabha Malviya, Sumedha Gupta, Pramod Kumar Sharma

INTRODUCTION

Oral drug delivery system is the most convenient way for drug delivery. Release of water soluble drug from the matrix system is not easy to control due to different factors such as high solubility and hence dose dumping of drug. This may result in toxicity of drug. Matrix tablets are easy to prepare and they are cost effective and exhibit predictable release behavior. Sustained released products designed to reduce the frequency of dosing by modifying the rate of drug absorption have been available for many years. Natural polymers are generally considered to be stable and safe as release retardant excipients in the development of oral controlled release dosage forms. They are non-toxic, cost effective as well as easily available. The varied structure and chemistry of natural polymers provide ample opportunity for their use in the formulation of sustained release drug delivery systems. Guar gum, a polysaccharide derivative with glycoside linkage has been used as matrix former for controlled release of isoniazide and diltiazem. Gum acacia or gum arabic is often

ABSTRACT

Background and purpose of study: In the present investigation, sustained release tablets of diclofenac sodium were formulated using guar gum and gum arabic (gum acacia) as release modifier.

Methods: Six batches of sustained release matrix tablets of diclofenac sodium were prepared by using different drug:polymer ratios viz., 1:1, 1:1.5, 1:2, 1:2.5, 1:3, and 1:3.5 for both guar gum and gum acacia. The tablets were evaluated for physical characteristics like hardness, weight variation, friability, and drug content. In vitro release of drug was studied in phosphate buffered saline (pH 7.4) for twenty four hours.

Results: All the physical characters of the formulated tablets were found to be within acceptable limits. The tablets with guar gum exhibited greater swelling index than those with gum acacia. A better controlled drug release (98.7%) was obtained with the matrix tablet (F1) made-up of the guar gum.

Conclusion: It is clear through the dissolution profile of matrix tablets prepared using guar gum and gum acacia that these polymers have ability to retard drug release for 24 hrs.

Keywords: Diclofenac sodium, guar gum, gum acacia, sustained release matrix tablets.

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*Author for Correspondence: Email: pranatiparul@gmail.com; Phone: +91-9452962662

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used in the preparation as plasticizer and as a tablet binder.
Gum acacia has been recognized as an acidic polysaccharide containing D-galactose, L-arabinose, L-rhamnose and D-glucuronic acid.\textsuperscript{[5]} Sustained release of ferrous sulphate was achieved for 7 h by preparing gum arabic pellet. All the gums are hydrophilic polymers, which until recently had been limited for use in gelation, thickening, suspending and water based emulsifying properties.\textsuperscript{[6–9]} Drug release from hydrophilic matrices is mainly based on complex interaction involving swelling, diffusion and erosion mechanisms.\textsuperscript{[10–13]} Diclofenac sodium is sodium 2-[(2, 6-dichlorophenyl)-amino] phenyl acetate. Diclofenac is an acetic acid nonsteroidal antiinflammatory drug (NSAID) with analgesic and antipyretic properties. Diclofenac is used to treat pain, dysmenorrhea, ocular inflammation, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and actinic keratosis.\textsuperscript{[14,15]} The present investigation is aimed to formulate the matrix tablet of diclofenac sodium with guar gum and gum arabic using no other varying parameter.

**MATERIAL AND METHODS**

Diclofenac sodium was obtained as gift sample from Alchem Laboratories, Baddi, India. The pharmacopoeial grade of guar gum and gum acacia were obtained from Ranbaxy Fine Chemicals Limited, New Delhi, India. Other materials used were of analytical grade, and procured from commercial sources.

**Preparation of sustained release matrix tablets**

Sustained release matrix tablets of diclofenac sodium were prepared by using different drug:polymer ratios viz., 1:1, 1:1.5, 1:2, 1:2.5, 1:3, 1:3.5 for Batch 1, Batch 2, Batch 3, Batch 4, Batch 5 and Batch 6 respectively (Table 1). Guar gum and gum acacia were used as matrix forming material, while microcrystalline cellulose was used as filler to maintain the tablet weight. All ingredients were passed through a # 20 sieve, weighed, and blended. The granulated formulations (which were obtained after wet granulation, using water as granulating agent) were compressed by a direct compression technique, using KBr press (IR press), with the help of 8 mm flat faced punches.\textsuperscript{[16–19]}

**Evaluation of Fabricated Matrix Tablets**

**Weight variation:** All batches of matrix tablets were evaluated for weight variation as per USP XXIV monograph. Twenty tablets of each batch were used to evaluate weight variation among tablets and standard deviation was calculated.\textsuperscript{[18,19]}

**Friability:** Tablets of all batches were used to evaluate friability as per USP XXIV monograph. Friability testing was done by Roche friabilator with triplcitate readings.\textsuperscript{[18,19]}

**Hardness:** Hardness of all batches was determined using Digital Force Gauge (Model: EL = 500 N, ElectroLab). The test was carried out in triplicate for all batches as per USP XXIV monograph for uncoated tablets.\textsuperscript{[18,19]}

<table>
<thead>
<tr>
<th>INGREDIENTS</th>
<th>FORMULATIONS</th>
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<tbody>
<tr>
<td></td>
<td>BATCH F1</td>
</tr>
<tr>
<td>Diclofenac sodium</td>
<td>50 mg</td>
</tr>
<tr>
<td>Polymer *</td>
<td>50 mg</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
<td>200 mg</td>
</tr>
<tr>
<td>Total weight</td>
<td>300 mg</td>
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</tbody>
</table>

\* guar gum and gum acacia for their respective batches.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>FORMULATIONS</th>
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<tbody>
<tr>
<td></td>
<td>BATCH F1</td>
</tr>
<tr>
<td>Weight variation (g)</td>
<td>0.301 ± 0.01</td>
</tr>
<tr>
<td>Friability (%)</td>
<td>0.05 ± 0.01</td>
</tr>
<tr>
<td>Hardness (N)</td>
<td>20.27 ± 0.06</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>4.18 ± 0.03</td>
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</tbody>
</table>

**TABLE 1:** Formulation composition of matrix tablets.

**TABLE 2:** Physical parameters for fabricated guar gum tablets.
**Thickness:** Thickness was measured by vernier caliper as per USP XXIV monograph. The readings were carried out in triplicate and average value was noted.\(^{[18,19]}\)

**Drug content:** The tablets were powdered, and 50 mg equivalent weight of diclofenac sodium in tablet powder was accurately weighed and transferred into a 100 ml volumetric flask. Initially, 10 ml of phosphate buffer (pH 6.6) was added and shaken for 10 min. Then, the volume was made up to 100 ml with buffer. Subsequently, the solution in volumetric flask was filtered, and 1 ml of the filtrate was diluted and analyzed at 276 nm using UV-visible spectrophotometer (Shimadzu UV-2450, Japan). The drug content of each sample was estimated from the standard curve.\(^{[18–21]}\)

**Swelling Behavior of Sustained Release Matrix Tablets**

The extent of swelling was measured in terms of % weight gain by the tablet. The swelling behavior of all formulations was studied. One tablet from each formulation was kept in a petridish containing phosphate buffer (pH 7.4). At the end of 1 h, the tablet was withdrawn, wiped with tissue paper, and weighed. Then for every 2 h, weights of the tablets were noted, and the procedure was continued till the end of 8 h. Percentage weight gain by the tablets (swelling index, S.I.) was calculated by using the formula:

\[
S.I. = \left(\frac{M_t - M_0}{M_0}\right) \times 100,
\]

Where, S.I. = Swelling index, \(M_t\) = weight of tablet at time \(t\) (in sec) and \(M_0\) = weight of tablet at time 0.\(^{[18,19,22,23]}\)

**In vitro drug release study**

**FIGURE 1:** Swelling index profile of guar gum based tablet.

In vitro drug release was studied using LabIndia dissolution apparatus, with 900 ml of dissolution medium maintained at 37 ± 1°C for 24 h, at 50 rpm. 5 ml of sample was withdrawn after every hour, and was replaced by an equal volume of fresh dissolution medium of same pH. Collected samples were analyzed spectrophotometrically, at wavelength of 276 nm, and cumulative percentage drug release was calculated. The study was performed in triplicate and results were recorded.\(^{[18,19,24]}\)

The data obtained in the in vitro dissolution study is grouped according to two modes of data treatment as follows:

1. Percentage drug released Vs time in hrs.
2. Cumulative percentage drug released Vs time in hrs.

In these two methods, drug release profile can be better studied using cumulative percentage drug release Vs time (h) plot.

**RESULTS AND DISCUSSION**

The formulated matrix tablets met the pharmacopoeial requirement of uniformity of weight. All the tablets confirmed to the requirement of assay, as per I.P. Hardness, percentage friability and thickness were within the acceptable limits (Table 2, Table 3).\(^{[18,19]}\) It has less absorption through gastric fluid due to less solubility at the pH studied. Sustained, but complete drug release was displayed by all the formulations in phosphate buffer (pH 7.4). Thus it can be concluded, that drug dissolution was a function of drug solubility, at various pH ranges. When pH rises above pK_a, rapid increase in solubility occurs.

**TABLE 3:** Various evaluation parameters for fabricated gum acacia tablets.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>BATCH F1</th>
<th>BATCH F2</th>
<th>BATCH F3</th>
<th>BATCH F4</th>
<th>BATCH F5</th>
<th>BATCH F6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight variation (g)</td>
<td>0.301 ± 0.01</td>
<td>0.293 ± 0.02</td>
<td>0.299 ± 0.01</td>
<td>0.298 ± 0.01</td>
<td>0.301 ± 0.01</td>
<td>0.302 ± 0.01</td>
</tr>
<tr>
<td>Friability (%)</td>
<td>0.03 ± 0.01</td>
<td>0.02 ± 0.01</td>
<td>0.02 ± 0.01</td>
<td>0.02 ± 0.01</td>
<td>0.01 ± 0.01</td>
<td>0.01 ± 0.01</td>
</tr>
<tr>
<td>Hardness (N)</td>
<td>20.07 ± 0.06</td>
<td>20.20 ± 0.00</td>
<td>20.37 ± 0.06</td>
<td>20.53 ± 0.06</td>
<td>20.63 ± 0.06</td>
<td>20.83 ± 0.06</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>3.503 ± 0.02</td>
<td>3.560 ± 0.08</td>
<td>3.740 ± 0.04</td>
<td>3.683 ± 0.03</td>
<td>3.777 ± 0.04</td>
<td>4.04 ± 0.07</td>
</tr>
</tbody>
</table>
The swelling index was calculated with respect to time. As time increases, the swelling index was increased, because weight gain by tablet increased proportionally with rate of hydration up to a certain limit. Later on, it decreases gradually due to dissolution of outermost gelled layer of tablet into dissolution medium (Figure 1, Figure 2, Figure 3). A direct relationship was observed between swelling index and gum concentration, and as gum concentration increases, swelling index was increased.\textsuperscript{[22,23]} It has been observed that the cumulative percentage drug release decreases with increasing concentration of gum and swelling index. The reason attributed to this fact is the slow erosion of the gelled layer from the tablets containing higher amount of guar gum. This slow release is because of the formation of a thick gel structure that delays drug release from tablet matrix.

It has been observed that the cumulative percentage drug release decreases with increasing concentration of polymer and swelling index. The reason attributed to this fact is slow erosion of the gelled layer from the tablets containing higher amount of natural polymer. This slow release is due to the formation of a thick gel structure that delays drug release from tablet matrix.\textsuperscript{[24–26]} From the findings, obtained so far it can be concluded that guar gum in the concentration ratio of 1:4 (G4) was promising concentration for oral controlled release tablet of diclofenac (Figure 4, Figure 5).

The drug release profile including the cumulative drug release for six batches of each polymer can be elucidated by plotting the graph of cumulative release vs. time. This can help in determining the release characteristics and matrix forming ability of natural polymers under study.

**CONCLUSION**

Natural polymers when used as release retardent exhibits uniform release over longer period of time. Hence it can be concluded that, guar gum which is a
natural polymer can be used as a promising drug release retardant in comparison to the stabilized gum acacia in a particular concentration range.

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REFERENCES