The objective of this study was to study the individual effect of Tamarind gum (TG), Locust bean gum (LB) and xyloglucan extracted out from tamarind gum (XG) as a release modifier in the design and development of sustained release matrix tablets of highly water-soluble drug Tramadol hydrochloride. Advantages offered by these natural excipients are that they are non-toxic, less expensive and freely available. Matrix tablets of tramadol hydrochloride were produced by direct compression and wet granulation method. The prepared tablets were evaluated for various physicochemical parameters. To analyze the release mechanism zero-order, first-order, Higuchi, Hixon-Crowell and Korsmeyer-Peppas model were used. Similarity factor f2 was also calculated to compare prepared matrices with the synthetic release retardant HPMC as well as market product Contramal SR (Piramal Healthcare Limited, 100 mg). Xyloglucan of tamarind gum and locust bean gum exhibit higher release retarding ability than tamarind gum.

Keywords: Sustained release matrix, Tramadol hydrochloride, Tamarind gum, Locust bean gum, Xyloglucan.

INTRODUCTION

Generally, controlled drug delivery are formulated with primary objectives of ensuring safety and improving efficacy of drugs as well as patient compliance, which can be achieved by better control of plasma drug levels and less frequent dosing. Physical blending of drug with polymer matrix followed by direct compression, compression molding, injection molding, extrusion, or solvent casting are the most convenient way to achieve controlled release of active agent which results either in monolithic device or in swellable hydrogel matrix. In fact, matrix is defined as a well composite of one or more drugs with a gelling agent i.e. hydrophilic polymer. Extensive use of the natural materials in the field of drug delivery have been owed to their ready availability, cost-effectiveness, eco-friendliness, capability of undergoing multitude of chemical modifications, potential degradability and compatibility due to their natural origin. Past research therefore studied and acknowledged various natural gums like agar, konjac, guar gum, chitosan, xanthan gum, sodium alginate and locust bean gum for potential pharmaceutical and biomedical applications. Hydrophilic matrices containing swellable polymers are referred to as swellable controlled release systems or hydrophilic matrix tablets.

Hydrophilic natural gums are high molecular weight substances, usually insoluble in alcohol, but can be made to dissolve, swell or disperse in water to give viscous or mucilaginous solutions. When solutions of hydrophilic gums are mixed, they interact with each other; this can result in an increase in viscosity, which becomes greater than the viscosity of each solution.

Tamarind gum (Tamarindus indica Linn., Family Leguminosae) consists of a main chain of cellulose with frequent branching at the O-6 positions with short side chains of one or two D-xylopyranosyl capped with D-xylopyranosyl, D-galactopyranosyl or L-arabinofuranosyl units.

Locust bean gum or Carob bean gum (Ceratonia siliqua Family Leguminosae) is a plant seed galactomannan, composed of a 1-4-linked β-D-mannan backbone with 1-6-linked α-D-galactose side groups. The physico-chemical properties of galactomannan are strongly influenced by the galactose content and the distribution of the galactose units along the main chain. Longer galactose side chains produce a stronger synergetic interaction with other polymers and greater functionality. LBG is also used to treat hyperlipidemia (elevated plasma cholesterol levels in healthy subjects).

Xyloglucans are a major class of structural polysaccharides found in the primary cell walls of higher plants. Xyloglucan polysaccharide has the same skeleton, α-1, 4-D-glucan, as cellulose and therefore is not digested by human digestive enzymes (it acts as dietary fiber). Isolation of xyloglucan the polysaccharide from tamarind kernel powder was carried out by aqueous extraction-non aqueous precipitation method. Polysaccharide based matrix tablets were prepared by many researchers.

Developing oral controlled-release tablets for highly water-soluble drugs with constant release rate has always been a challenge to the pharmaceutical technologist. Most of these drugs, if not formulated properly; may readily release the drug at a faster rate and are likely to produce toxic concentrations when administered orally. Tramadol hydrochloride is used in the treatment of osteoarthritis when nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, or COX-2 inhibitors alone produce inadequate pain relief. After oral administration, tramadol hydrochloride is rapidly and almost completely absorbed. Sustained-release tablets reach to peak concentrations after 4-9 hours and have a bioavailability of 87% to 95% compared with capsules. The mean elimination half-life is ~6 hours and requires dosing every 6 hours in order to maintain optimal relief of chronic pain. Consequently, once-daily extended-release tablets have been formulated (tramadol hydrochloride ER). Long-term treatment with sustained-release tramadol hydrochloride once daily is generally safe in patients with osteoarthritis or refractory low back pain and is well tolerated. It has the potential to provide patients increased control over the management of their pain, fewer interruptions in sleep, and improved compliance.

Hydrophilic polymers are becoming very popular in formulating oral controlled-release tablets. As the dissolution medium or biological fluid penetrates the dosage form, the polymer material swells and drug molecules begin to move out of the system by diffusion at a rate determined by the nature and composition of the polymer as well as formulation technology. The objective of this study was to develop matrix sustained-release tablets of tramadol hydrochloride using natural gums (tamarind gum, locust bean gum and xyloglucan of tamarind gum) as suitable hydrophilic matrix systems compared with extensively investigated hydrophilic matrices (i.e., hydroxy propyl methylcellulose [HPMC] / carbomethyl cellulose [CMC] with respect to in vitro drug release rate) and hydration rate of the polymers.

MATERIALS AND METHODS

Materials

Tramadol hydrochloride was obtained from Saga laboratories (Ahmedabad, Gujarat). Microcrystalline cellulose (MCC) PH 101, polyvinyl pyrrolidone (PVP)-K-30, dicalcium phosphate (DCP) and talc were used as the excipients. Hydroxy propyl methylcellulose (HPMC) E 15, maltodextrin and croscarmellose sodium were used as the disintegrants and the binding agents respectively.
were obtained as a gift from Suvik Hitek Private Limited (Gandhinagar, Gujarat). Tamarind gum was obtained as a gift from H.B. Gum Industries Pvt. Ltd. (Kalol, North Gujarat). Locust bean gum was obtained as a gift from Lucid Colloids Ltd. (Mumbai). Magnesium stearate, Sodium hydroxide (NaOH), and Potassium phosphate monobasic (KH2PO4) were obtained from S.D. Fine chemicals Ltd. and Contramal-SR was obtained from retail pharmacy and used as reference product. All other chemicals were pure and of analytical grade.

Methods

Isolation of xyloglucan (XG) from tamarind gum

The isolation of xyloglucan was performed in the following manner. Twenty gram of tamarind kernel powder was added to 200 ml of cold distilled water and slurry prepared. The slurry was slowly poured into 800 ml of boiling distilled water and further boiled for 20 min under stirring condition on a water bath. The resulting mixture was kept overnight and then it was centrifuged at 5000 revolutions per minute (RPM) for 20 min. The supernatant liquid was separated and poured into twice the volume of absolute alcohol by continuous stirring to precipitate the polysaccharide. The revolutions per minute (RPM) for 20 min. The supernatant liquid was measured according to the fixed funnel and free standing cone method 23, 25-26

\[ \theta = \frac{2h}{D} \quad \text{eqn. 2} \]

Where; \( h \) is the height powder cone from base to the apex.

Bulk and tap densities

2g quantity each of the powder sample was placed in a 10ml measuring cylinder and the volume \( V_0 \), occupied by each of the samples without tapping was noted. After 100 taps on the table, the occupied volume \( V_{100} \) was read. The bulk and tap densities were calculated as the ratio of weight to volume \( (V_0 \text{ and } V_{100} \text{ respectively}) \).

Hausner Ratio

This was calculated as the ratio of tapped density to bulk density of the samples.

Compressibility Index (C.I. %)

This was calculated using the equation:

\[ \text{Compressibility} = \left( \frac{\text{Tapped density} - \text{bulk density}}{\text{Tapped density} \times 100} \right) \quad \text{eqn. 3} \]

Viscosity (cps)

Viscosity of 1% w/v solution was determined using Brookfield viscometer (Model LVDV-II), spindle number 61.

Preparation of Tramadol hydrochloride Matrix Tablets

Preparation of Tramadol hydrochloride Matrix Tablets by direct compression method (DC)

Matrix tablets of tramadol hydrochloride (dose 100 mg) were prepared by direct compression method and wet granulation method. For direct compression (DC), concentrations of gums used were 30 to 70%. All ingredients were sieved through an ASTM #60 sieve (250μm size), and then weighed quantity of drug was physically mixed with all auxiliary excipients by geometric addition using a glass mortar and pestle for about 10 min. Then magnesium stearate and talc were added as the lubricant/ glidant and thoroughly mixed (zip bag) for 5min. This was the Granules Ready for Compression (GRC). From the GRC, the homogeneous powder mixture for a single matrix was weighed, fed manually into the die of an eight station automatic rotary tablet machine (Karnavati Engineering Ltd., Kadi) equipped with biconcave die-punch set of 8mm diameter and compressed to a target weight of 400mg and an average hardness of 5–6 kg/cm² for all tablets. The obtained matrices were subjected to various pharmacopoeial and physical properties evaluation like weight variation, thickness (Vernier calipers), hardness (Monsanto hardness tester, Campbell electronics), Friability (Roche Friabilator, Labtronik), drug content, in vitro drug release and swelling behavior of the matrix tablets.

Formulation codes (Batch F1 and F2) and composition of the batches are shown in Table 1.

Preparation of Tramadol hydrochloride Matrix Tablets by wet granulation method (WG)

For wet granulation method, mucilage of gums were prepared and added to the mixture of previously shifted and weighed quantity of drug and other auxiliary excipients to make a wet mass using a glass mortar and pestle; then passed through sieve to prepare granules; dried in hot air oven at 60°C for 30 min; then magnesium stearate and talc were added as the lubricant/ glidant and thoroughly blended for 5min and were sieved through ASTM sieve #20 sieve (841μm) and retained on #40 sieve (420μm). This was the Granules Ready for Compression (GRC). The rest of the procedure was same as used for direct compression.

Formulation codes (F3 to F8) and composition of the batches are shown in Table 1.
Determination of Drug Content

The tramadol hydrochloride matrix tablets were tested for their drug content. Twenty tablets were finely powdered; 400 mg of the powder was accurately weighed and transferred to a 50-ml volumetric flask. Then the volume was made up with 0.1N HCl and shaken for 10 minutes to ensure complete solubility of the drug. The mixture was centrifuged and 10 ml of the supernatant liquid was diluted 20 times with 0.1N HCl, and after centrifugation the absorbance was determined spectrophotometrically (UV-visible 1800, Shimadzu) at 271 nm.

In Vitro Drug Release Studies

As per USP monographs for extended-release dosage forms, the percent of drug released after more than one time point is required. Therefore, the percent of drug release after every hour up to 12 h (Qt) was selected as the response variables (Figure 1).

To analyze the in vitro release data various kinetic models were used to describe the release kinetics. The zero order rate equation (Eq. (5)) describes the systems where the drug release rate is independent of its concentration. The first order Eq. (6) describes the release from system where release rate is concentration dependent. Higuchi Eq. (7) describes the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion. The Hixon-Crowell cube root law Eq. (8) describes the release from systems where there is a change in surface area and diameter of particles or tablets.

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In Vitro Drug Release Studies

As per USP monographs for extended-release dosage forms, the percent of drug released after more than one time point is required. Therefore, the percent of drug release after every hour up to 12 h (Qt) was selected as the response variables (Figure 1).

Table 1: Composition of batches prepared to produce matrix tablets of tramadol hydrochloride*

<table>
<thead>
<tr>
<th>Formulation</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol hydrochloride</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>TG</td>
<td>160</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>XG</td>
<td>-----</td>
<td>160</td>
<td>160</td>
<td>160</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>LB</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>160</td>
<td>160</td>
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<td>160</td>
<td>160</td>
</tr>
<tr>
<td>HPMC K100M</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
</tr>
<tr>
<td>PVP K-30</td>
<td>128</td>
<td>128</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>-----</td>
<td>128</td>
<td>-----</td>
</tr>
<tr>
<td>DCP</td>
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<td>128</td>
<td>128</td>
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<td>64</td>
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<td>-----</td>
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<td>64</td>
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<td>8</td>
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<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>MgStearate</td>
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<td>4</td>
<td>4</td>
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<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td>400</td>
<td>400</td>
</tr>
</tbody>
</table>

*All quantity are in mg.

Study of Release Kinetics

To compare the release profile of the prepared matrices with the market product, similarity factor f2 was calculated using the following equation:

\[ f_2 = 50 \log \left( \frac{100}{\sqrt{\frac{\sum (Ti - Ri)^2}{n}}} \right) \]

Where, Ti and Ri show the average percents dissolved from test and reference products at the time point(t), and n is the number of time points.

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used for each individual time point. The increase in weight due to absorbed liquid (Q) was estimated at each time point from the following equation:

\[ Q = (W_f - W_i) \times 100 \]  \[ (\text{10}) \]

where \( W_f \) is the mass of the hydrated sample before drying and \( W_i \) is the final weight of the dried and partially eroded sample. The percentage erosion (E) was estimated from the following equation:

\[ E = \left( \frac{W_f - W_i}{W_f} \right) \times 100 \]  \[ (\text{11}) \]

where \( W_i \) is the initial weight of the dry sample.

**RESULTS AND DISCUSSION**

**Physicochemical characterization of the gums**

Various physicochemical parameters for the gums were tested and are shown in Table 2. It was observed that XG has higher swelling index and less viscosity than TG and LB. Total bacterial count of the gums and tests for pathogens were carried out from time to time as prescribed in BP under the heading “Microbiological testing of nonsterile pharmaceuticals”23. The result of the TBC was found within the limit and all gums were free from pathogens.

<table>
<thead>
<tr>
<th>Source</th>
<th>Swelling Index (%)</th>
<th>Loss on Drying (%)</th>
<th>pH (1%w/v soln.)</th>
<th>Angle of Repose (°)</th>
<th>Bulk density (gm/ml)</th>
<th>Tapped density (gm/ml)</th>
<th>H.R.</th>
<th>C.I. (%)</th>
<th>Viscosity (cps) (1%w/v soln.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG</td>
<td>1.5-1.8</td>
<td>4.4</td>
<td>6-7</td>
<td>28</td>
<td>0.45</td>
<td>0.77</td>
<td>1.71</td>
<td>42</td>
<td>800</td>
</tr>
<tr>
<td>LB</td>
<td>6.2-6.4</td>
<td>5</td>
<td>5.5-7</td>
<td>25</td>
<td>0.42</td>
<td>0.68</td>
<td>1.62</td>
<td>38</td>
<td>2235</td>
</tr>
<tr>
<td>XG</td>
<td>80</td>
<td>5.5</td>
<td>5-7</td>
<td>13</td>
<td>0.28</td>
<td>0.36</td>
<td>1.29</td>
<td>22.2</td>
<td>50</td>
</tr>
</tbody>
</table>

**Preparation of Tramadol hydrochloride Matrix tablet**

**Optimization of sustained release formulation**

Many Batches were prepared by direct compression method using 30, 40, 50, 60 and 70% of gums. Release retarding ability was very poor in case of 30% while more than 50% gum was unable to compress by DC. Wet granulation method was not effective in producing sustained release tablet in case of TG. Table 1 shows only the optimized batches containing 40% of the gum. In DC method PVP-K-30 was used as filler and dry binder while in wet granulation method MCC and/or DCP were used as filler and mucilage of gum was incorporated as binder. The optimization of the batch was done based on the hardness and friability of the prepared tablet and obtained in vitro release behavior.

**Physicochemical Investigation of prepared matrix tablets**

The prepared matrices were evaluated for thickness, weight variation, hardness, friability, drug content (Table 3) and release rate (Figure 1). All the tablets were of 8mm diameter and biconcave in shape. The data are shown in Table 3.

The hardness of the tablets was ranged from 5-7 Kg/Cm². All formulations satisfied the content uniformity of tramadol hydrochloride and friability between 0.4% and 0.8%.

**Determination of Drug Content**

All formulations passed the drug content uniformity as per official specification (Table 3).

**In Vitro Drug Release Studies**

In vitro release profile of the prepared matrices and market product of tramadol hydrochloride are shown in Figure 1. Comparison of the prepared matrices were carried out with the reference product, for %cumulative release after 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 h. Compared to the market product, an initial burst release (>30%) of %cumulative release after 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 h. Composed to the market product, an initial burst release (>30%) of the drug was observed with almost all matrices except batch F2, F5 and F8. Such a burst effect was also observed by other investigators who suggested the addition of other hydrocolloids such as HPMC in relatively large amounts31. It was also reported that increasing the concentration of either HPMC K-4M or HPMC K-100M is expected to decrease the drug release. Such delay in drug release may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature.

PH 101 was included, not showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature. While batch F5 in which MCC was included, it showed desired controlled release, may be due to its hydrophilic nature.

**Study of Release Kinetics**

To compare the release profile and release behavior of the prepared matrices of tramadol hydrochloride with the market product, similarity factor \( f_1 \) was calculated (Table 4). The two dissolution profiles are considered significantly similar when the \( f_1 \) value is in the range of 50 to 100. Here, all batches except batch- F4 showed similarity factor value above 50. Analysis of release profiles were also carried out using zero order, first order, Higuchi, Korsemeyer-Peppas and Hixon-Crowell models. Drug release exponent (DRE) i.e. ‘n’ was taken into consideration to decide the mechanism of drug release. Data analysis of release profiles according to different kinetic models is shown in Table 4.

**Table 2: Physicochemical parameters for the gums used in preparation of matrices**

<table>
<thead>
<tr>
<th>Source</th>
<th>Swelling Index (%)</th>
<th>Loss on Drying (%)</th>
<th>pH (1%w/v soln.)</th>
<th>Angle of Repose (°)</th>
<th>Bulk density (gm/ml)</th>
<th>Tapped density (gm/ml)</th>
<th>H.R.</th>
<th>C.I. (%)</th>
<th>Viscosity (cps) (1%w/v soln.)</th>
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</thead>
<tbody>
<tr>
<td>TG</td>
<td>1.5-1.8</td>
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<td>0.45</td>
<td>0.77</td>
<td>1.71</td>
<td>42</td>
<td>800</td>
</tr>
<tr>
<td>LB</td>
<td>6.2-6.4</td>
<td>5</td>
<td>5.5-7</td>
<td>25</td>
<td>0.42</td>
<td>0.68</td>
<td>1.62</td>
<td>38</td>
<td>2235</td>
</tr>
<tr>
<td>XG</td>
<td>80</td>
<td>5.5</td>
<td>5-7</td>
<td>13</td>
<td>0.28</td>
<td>0.36</td>
<td>1.29</td>
<td>22.2</td>
<td>50</td>
</tr>
</tbody>
</table>

**Table 3: Physicochemical parameters of tramadol hydrochloride matrices prepared by direct compression and wet granulation method**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Average drug content (mg) ± SD</th>
<th>Hardness (Kg/Cm²) ± SD</th>
<th>Friability (%)</th>
<th>weight(mg) (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contramal SR</td>
<td>98.5 ± 2.6</td>
<td>5.8±0.5</td>
<td>0.57</td>
<td>399.40 ± 1.14</td>
</tr>
<tr>
<td>F1</td>
<td>99.8 ± 1.2</td>
<td>5.8±0.6</td>
<td>0.4</td>
<td>399.61 ± 1.18</td>
</tr>
<tr>
<td>F2</td>
<td>100.5 ± 2.8</td>
<td>5.8±0.8</td>
<td>0.57</td>
<td>400.48 ± 0.29</td>
</tr>
<tr>
<td>F3</td>
<td>99.3 ± 2.0</td>
<td>5.0±0.8</td>
<td>0.66</td>
<td>399.28 ± 0.34</td>
</tr>
<tr>
<td>F4</td>
<td>99.5 ± 4.0</td>
<td>5.0±0.3</td>
<td>0.35</td>
<td>399.99 ± 0.75</td>
</tr>
<tr>
<td>F5</td>
<td>96.8 ± 2.8</td>
<td>5.8±0.2</td>
<td>0.6</td>
<td>401.2 ± 0.88</td>
</tr>
<tr>
<td>F6</td>
<td>100.0 ± 3.4</td>
<td>5.3±0.6</td>
<td>0.62</td>
<td>399.76 ± 0.84</td>
</tr>
<tr>
<td>F7</td>
<td>100.1 ± 4.5</td>
<td>5.6±0.7</td>
<td>0.52</td>
<td>399.53 ± 0.75</td>
</tr>
<tr>
<td>F8</td>
<td>100.05 ± 1.2</td>
<td>6.0 ± 0.1</td>
<td>0.45</td>
<td>399.95 ± 0.67</td>
</tr>
</tbody>
</table>

*n=3
Fig. 1: In-vitro release profiles of the sustained release matrices of tramadol hydrochloride

Table 4: Similarity factor ($f_2$) and Drug Release Exponent ($n$), Regression Coefficient ($r^2$) and best fit model for Tramadol hydrochloride matrix tablets After model fitting ($n = 3$)

<table>
<thead>
<tr>
<th>Formulation</th>
<th>$f_2$</th>
<th>$n$</th>
<th>$r^2$</th>
<th>Best fit model</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>51.19</td>
<td>0.2847</td>
<td>0.9951</td>
<td>Korsemeyer-Peppas</td>
</tr>
<tr>
<td>F2</td>
<td>73.19</td>
<td>0.4618</td>
<td>0.9947</td>
<td>Korsemeyer-Peppas</td>
</tr>
<tr>
<td>F3</td>
<td>53.94</td>
<td>0.3099</td>
<td>0.8902</td>
<td>Korsemeyer-Peppas</td>
</tr>
<tr>
<td>F4</td>
<td>37.99</td>
<td>0.2555</td>
<td>0.9578</td>
<td>Korsemeyer-Peppas</td>
</tr>
<tr>
<td>F5</td>
<td>75.22</td>
<td>0.3802</td>
<td>0.977</td>
<td>Korsemeyer-Peppas</td>
</tr>
<tr>
<td>F6</td>
<td>59.92</td>
<td>0.2722</td>
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<tr>
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</tr>
<tr>
<td>F8</td>
<td>68.08</td>
<td>0.4423</td>
<td>0.9872</td>
<td>Korsemeyer-Peppas</td>
</tr>
<tr>
<td>Market Product</td>
<td>Reference</td>
<td>0.5414</td>
<td>0.9975</td>
<td>Korsemeyer-Peppas</td>
</tr>
</tbody>
</table>

For all batches prepared, drug release profile better fits with Korsemeyer and Peppas equation. Further, mechanism of release was decided on the basis of value of DRE which was indicative of the anomalous diffusion in case of batch F2 which was comparable to that of market product (Table 4). XG plays an important role in drug release especially at the beginning of the release study as evident from drug release profile of batch F2. This was owing to its high swelling index as apparent from Table 2. Therefore, the quick hydration and subsequent gel formation is a foremost and important property of an excipient for it to be used in sustained-release formulations as reported\(^\text{35}\). The overall rate of release of tramadol hydrochloride from batch F2, F5 and F8 was significantly similar to the release obtained from the market product (Figure 1). These results are clear indication that XG and LB has higher drug retarding ability than TG. Also it can be concluded that HPMC has in the similar line to that of natural gums in release retarding ability. Reference product followed a Peppas model indicating anomalous diffusion of the drug (Table 4). Initial burst release (>30% in the first hour) from the matrices could probably be attributed to the dissolution of drug from the surface of the tablet. Furthermore, The hydrophilic matrix system could control the release only up to 14 hours as reported for Hydrophilic matrix of HPMC which could not control the tramadol hydrochloride release effectively beyond 12 hour\(^\text{35}\).

Water uptake and erosion studies

The swelling process of batch F5 containing LB was not uniform and the zones of high LB concentration appeared more swollen. In the case of LB matrix, a rapid erosion of the hydrated layer was observed, releasing most of the drug content after 4 h. This is because LB does not exhibit a controlled release effect but has a synergistic action with the DCP and/or MCC as in batch F5, F6 and F7 to produce a controlled release effect. Among which batch F5 showed more controlled release as evident from $f_2$ value of batch F5 (Table 4).

The swelling behavior indicates the rate at which this formulation absorbs water from dissolution media and swells. The change in weight is characteristic of the water uptake and swelling which started immediately and continued for 8 h (Figure 2). Batch F2 matrix exhibited a high degree of swelling. Visual observation showed that the matrices appeared swollen almost from the beginning and a viscous gel mass was created when they came into contact with the dissolution medium. The matrix erosion measured the weight loss from matrix tablets immersed in dissolution media as a function of time. The weight loss of the tablets was steady up to 8 h (Figure 3) and was about 50%.
CONCLUSION

It can be concluded from our study that gums alone cannot efficiently control drug release, particularly in the beginning of dissolution study. Xyloglucan and locust bean gum have higher drug retarding ability than tamarind gum. However, according to similarity factor $f_2$, batch F2, F5 and F8 are the most similar formulations to Reference product. Natural gum was able to give comparable sustained release as synthetic polymer like HPMC. It was also reported that combination of the hydrophilic polymers were effective than when used alone. Therefore we can include natural gums in combination in the formulation of sustained release matrix tablets as that of synthetic release retardants.

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REFERENCES