INTRODUCTION

In recent times, the introduction of tablets as sustained release (SR) dosage forms has brought a transformation in pharmaceutical technology. Where the drug was sustained for a prolonged duration of time in the systemic circulation by incorporating in polymeric matrices that have a short-term elimination half-life by releasing the drug in a zero-order pattern and developed as SR dosage forms [1]. These dosage forms offer a number of benefits over an immediate release (SR) dosage forms and developed as SR dosage forms [1]. These dosage forms offer a number of benefits over an immediate release (SR) dosage forms [1]. These dosage forms have a number of benefits over an immediate release (SR) dosage forms and developed as SR dosage forms [1]. These dosage forms have a number of benefits over an immediate release (SR) dosage forms and developed as SR dosage forms [1]. These dosage forms have a number of benefits over an immediate release (SR) dosage forms and developed as SR dosage forms [1]. These dosage forms have a number of benefits over an immediate release (SR) dosage forms and developed as SR dosage forms [1]. These dosage forms have a number of benefits over an immediate release (SR) dosage forms and developed as SR dosage forms [1].

In recent times among other strategies matrix tablets are gaining importance due to its release pattern of the drug, convenient method of formulation, ease of processing, and lesser cost of production. Loading of drug into the polymer matrix can be done by coating or as a bi-layer, either granulation or direct compression can be used to formulate matrix tablet. To choose the appropriate method to formulate matrix tablets rely on the nature of the API and other excipients [3].

Indomethacin (IM) is a nonsteroidal anti-inflammatory drug usually adopted to diminish fever, pain, stiffness in rheumatic disease, and swelling from inflammation. IM inhibits the prostaglandin production; endogenous signaling molecules present these symptoms which were exhibited by inhibiting cyclooxygenase enzyme that catalyzes the production of prostaglandins [4].

MATERIALS AND METHODS

Materials

IM was purchased from Yarrow Cher product, Mumbai, India; Almond gum & (AG) was obtained from a local certified ayurvedic market and exudates; polyvinylpyrrolidone (PVP-30) SRL, Mumbai India; Starch, Talcum, and Mg-Stearate were obtained from Loba, and Isopropyl alcohol was obtained from Merck Mumbai.

Experimental methods

Preformulation studies

Preformulation studies can be termed as the examination of physicochemical characteristics of a drug substance alone. The main reason to perform these studies is to acquire bioavailable and unchanging dosage forms by providing useful information to the formulator.

Development of prolonged release formulation of IM

Wet granulation technique was adopted for formulating the SR matrix tablets. In the current work, SR tablets were formulated by employing varied concentrations of AG along with binder (PVP K30). As shown in Table 1, six preparations of IM were formulated. Ingredients mentioned in Table 1 were weighed, sieved, and finally blended. The obtained blend was then sieved, dried, and compressed [5].

Micromeritics properties

The physical properties of the powder were analyzed for flowability. Carr’s index equation was employed to determine the flow property of the powder blend. In this method, using a Scoopula and the mass occupied by the powder was recorded using a 100ml measuring cylinder. Using well-established formula, that is, weight divided by the volume of the blend,
the bulk density of mixture was measured. Mixture was then allowed to settle by tapping it for a count of 100 times using different cylinders. To measure the tapped density, the process was continued until a constant value was attained. Angle of repose was the most widely used technique for measuring the flowability [by determining the shape of the powder heap]. The formula used to measure the flowability [6].

\[
\tan \theta = h/r
\]

**Table compression**
The talc and mg-stearate were used separately for lubricating the dried granules. Per each tablet, 50 mg of IM equivalent SR granules were weighed, and tablets were compressed using a 10 station lab compressor.

**Physical properties of SR tablets**

**Weight variation**
Initially, 20 units were selected randomly which were then weighed individually, and the average was calculated. In comparison with the percentage given in the pharmacopeia, deviation for any two tablets should not be more than the average weight. Weight variation was carried out using digital balance [7,8].

**Tablet thickness**
In this, 10 tablets were assessed for thickness using electronic Vernier caliper, Mitutoyo, Japan [7,8].

**Hardness**
Hardness is defined as the resistance of a material to permanent deformation such as indentation, wear, abrasion, and scratch. Monsanto Hardness is defined as the resistance of a material to permanent deformation which can be measured by a specific type of hardness instrument known as a hardness testing device. Hardness is usually measured in a unit called Vickers hardness numbers (VHN). The VHN is the ratio of the force applied to the area of the indent. The VHN is determined by the following formula:

\[
\text{VHN} = \frac{4FL}{d^2}
\]

where:
- \(F\) is the applied load in kgf.
- \(L\) is the diagonal length of the Vickers indentation in mm.
- \(d\) is the diagonal length of the Vickers indentation in mm.

**Table 1: Composition of IM formulations with different AG concentrations along with starch as filler**

<table>
<thead>
<tr>
<th>Composition</th>
<th>IM (mg)</th>
<th>AG (mg)</th>
<th>PVP K30 (mg)</th>
<th>Starch (mg)</th>
<th>Talcum (mg)</th>
<th>Magnesium stearate (mg)</th>
<th>IPA (mL)</th>
<th>Total (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>50</td>
<td>15</td>
<td>0</td>
<td>125</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>F2</td>
<td>50</td>
<td>20</td>
<td>0</td>
<td>90</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>F3</td>
<td>50</td>
<td>25</td>
<td>0</td>
<td>115</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>F4</td>
<td>50</td>
<td>30</td>
<td>0</td>
<td>80</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>F5</td>
<td>50</td>
<td>35</td>
<td>0</td>
<td>80</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>F6</td>
<td>50</td>
<td>40</td>
<td>0</td>
<td>80</td>
<td>5</td>
<td>5</td>
<td>1</td>
<td>200</td>
</tr>
</tbody>
</table>

**Tanθ = h/r**

**Table 2: Micromeritic properties of granules**

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Angle of repose (°)</th>
<th>Loose bulk density (g/mL)</th>
<th>Tapped bulk density (g/mL)</th>
<th>Compressibility index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>24.02±0.05</td>
<td>0.41±0.01</td>
<td>0.55±0.05</td>
<td>15.01±0.21</td>
</tr>
<tr>
<td>F2</td>
<td>25.01±0.03</td>
<td>0.46±0.03</td>
<td>0.53±0.03</td>
<td>15.06±0.13</td>
</tr>
<tr>
<td>F3</td>
<td>24.21±0.14</td>
<td>0.41±0.02</td>
<td>0.50±0.09</td>
<td>12.07±0.17</td>
</tr>
<tr>
<td>F4</td>
<td>24.13±0.09</td>
<td>0.45±0.09</td>
<td>0.51±0.02</td>
<td>11.09±0.23</td>
</tr>
<tr>
<td>F5</td>
<td>24.01±0.04</td>
<td>0.43±0.08</td>
<td>0.50±0.04</td>
<td>14.02±0.26</td>
</tr>
<tr>
<td>F6</td>
<td>24.23±0.05</td>
<td>0.41±0.05</td>
<td>0.51±0.01</td>
<td>12.09±0.17</td>
</tr>
</tbody>
</table>

**Table 3: Physical properties of the tablet**

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Weight variation (%)</th>
<th>Hardness (kg/cm²)</th>
<th>Thickness (mm)</th>
<th>Friability (% w/w)</th>
<th>Drug content (mg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>20±1.26</td>
<td>5.2±0.12</td>
<td>4.5±0.15</td>
<td>0.48±0.12</td>
<td>98.03±0.12</td>
</tr>
<tr>
<td>F2</td>
<td>199±2.37</td>
<td>4.3±0.04</td>
<td>4.4±0.12</td>
<td>0.53±0.12</td>
<td>97.09±0.12</td>
</tr>
<tr>
<td>F3</td>
<td>199±3.42</td>
<td>5.2±0.03</td>
<td>4.6±0.08</td>
<td>0.41±0.02</td>
<td>98.03±0.12</td>
</tr>
<tr>
<td>F4</td>
<td>200±1.06</td>
<td>5.3±0.08</td>
<td>4.4±0.16</td>
<td>0.43±0.05</td>
<td>97.07±0.03</td>
</tr>
<tr>
<td>F5</td>
<td>201±1.06</td>
<td>4.3±0.06</td>
<td>4.4±0.09</td>
<td>0.61±0.11</td>
<td>97.09±0.12</td>
</tr>
<tr>
<td>F6</td>
<td>199±0.77</td>
<td>4.3±0.12</td>
<td>4.6±0.28</td>
<td>0.55±0.04</td>
<td>94.03±0.12</td>
</tr>
</tbody>
</table>

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Bulk density
The bulk density values ranged from 0.41±0.1 to 0.45±0.09 (Table 2) suggesting that the obtained results were within the prescribed limits.

Tapped density
The values for the tapped density were within the range of 0.50±0.09–0.55±0.05 (Table 2) assuring the free flow of granules.

Angle of repose
The results were ranged between 24.01±0.04 and 25.01±0.03 (Table 2) that is <30° which assures excellent flow properties of the powder.

Compressibility index
The values obtained were found to fall in the range of 11.09±0.23–15.08±0.13 (Table 2). These observations suggested that the granules of all batches have showed good flow characters, and hence, were suitable for compression into matrix tablets.

Physical properties of matrix tablet
Formulated SR tablets of IM were analyzed for post-compression parameters such as weight variation, thickness, hardness, friability, and drug content. The results were depicted in Table 3. From the results, it was evident that values from all the tests were within the limits prescribed by pharmacopeia.

Weight variation
The results from the weight variation varied from 199±0.77 to 201±2.26 and were found to be within the pharmacopeial specifications that is ±7.5% (Table 3).

Tablet thickness
The formulated sustained matrix tablets loaded with IM had showed thickness varying from 4.4±0.09 to 4.6±0.28 (Table 3), and the average value of thickness was found to be within the range ±5% as prescribed by pharmacopeia.

Hardness
The variation in hardness of the formulated sustained matrix tablets loaded with IM was in the range of 4.3±0.04–5.3±0.08 kg (Table 2), suggesting acceptable mechanical strength with a capability to endure mechanical and physical stress circumstances while handling and shipping.

Friability
Decrease in the weight of the sustained matrix formulations due to friability was observed to be in the range of 0.4±0.02%–0.55±0.04% (Table 3), results suggested that formulated tablets were mechanically stable.

Drug content
Drug content values obtained from various formulations were highly uniform and within the range of 94.03±0.12–98.03±0.12 (Table 3). The maximum percentage drug content among various formulations was found to be 98.03±0.12%. The minimum percentage of drug content was found to be 94.03±0.12% for all the batches. All the values of the drug content were within limits specified by pharmacopeia.

Surface topography of matrix tablet by SEM
By employing SEM, the surface morphology of SR layer of matrix tablet was determined. From, Fig. 1. SEM photographs exhibit the intact SR layer of IM after 1 h, 4 h, and 8 h of dissolution study. SEM photomicrograph taken at different time intervals of sustained matrix tablet after the dissolution study presented that the matrix was unimpaired and the matrix had pores throughout its surface. Table surface also exhibited erosion of matrix has proportionately enhanced with reference to time as indicated by the photocopies at 2, 4, and 8 h and explaining that there is an increase in the diameter of the pores. The formation of gelling structure was explained by these photomicrographs revealing the probability of swelling of the formulated dosage form (Fig. 1). The release of IM from developed formulation was due to the formation of the pores and gelling structures (due to diffusion and erosion mechanism) on the table surface.

Dissolution study
Dissolution of the formulated IM SR matrix tablets takes place by swelling between the polymer networks by which the drug is getting diffused into the dissolution medium. Thus, the release of the active agent from the matrix tablet takes place by the diffusion mechanism. As shown in Fig. 2, formulation F4 had shown the accurate and complete release of the drug by 10 h. From the results, it can be inferred that formulation F4 can be considered as optimized formulation as it had SR of IM up to 10 h [14].

CONCLUSION
Matrix tablets loaded with IM was formulated using wet granulation method to sustain the release of drug for a period of time. The pre-compressional (micromeritics properties) and the post-compressional parameters (physical properties) were found to be within the pharmacopeial limits. From the various formulations F4 with 30 mg
of almond gum, 30 mg of PVP and 80 mg of starch were considered as optimized formulation based on its drug release pattern, i.e., 10 h, which was better when compared with other formulations. SEM photographs of F4 suggested that tablet surface exhibited erosion of matrix with reference to the time at 2, 4, and 8 h, which explains the increase in diameter of the pores and facilitates the drug release from the uniform surface of the matrix tablet. Therefore, it can be concluded that IM matrix tablets can be used for enhancing both the therapeutic efficacy and patient acceptance by reducing the dosing intervals.

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AUTHORS’ CONTRIBUTIONS

The author is a faculty in division of pharmaceutics, and the work contributed on faculty development program in the institution.

CONFLICTS OF INTEREST

The author confirms that this article content has no conflicts of interest.

REFERENCES