Design and Development of Terminated Assets of Ibuprofen using Cliquishly Compact Technique for water insoluble drugs

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Abstract
The current survey is aimed to prepare and appraise ibuprofen (IBU) liquid solid compacts (LSC) to improve the termination properties of IBU and its bio accessibility. IBU LSC are organized by means of microcrystalline cellulose (MCC) and lactose as carriers in different ratios like aerosol 200 as coating material, propylene glycol (PG) as vehicle and sodium starch glycolate (SSG) and croscarmellose sodium (CCS) as super disintegrants. The LSC organized by evaluated flow properties are compressed into tablets as direct compression method. The tablets prepared are estimated by weight variation, friability, hardness and in-vitro termination. The FTIR studies reveal that there is less communication among IBU and the recipients used in the formulation. The flow properties of the prepared LSC indicate a good flow property and the post compressed parameters of IBU LSC by all the acceptable restrictions. The in-vitro closure study shows a 1.3-fold increase dissolution that is observed in IBU LSC containing MCC as carrier than the formulations containing lactose also as carrier. The added SSG, CCS, and inulin resulted in 1.47, 1.25, and 1.19-fold increased in IBU released formulations without super disintegrants. The overall formulation of F6 is showed faster by dissolution of IBU along with good physic mechanical and flow properties.

Keywords: Ibuprofen, dissolution properties, LSC, and super disintegrants

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1. Introduction
Among the different routes of drug administration oral way is the nearly all favorite and widely accepted route of drug management due to low cost factor and ease of drug administration. About 40% of the drugs administered through oral route exhibit low aqueous solubility and low bioavailability due to less absorption. Over past few years, many techniques are developed to increase the dissolution distinctiveness of water unsolvable drugs and between them liquid solid compact technique is effective to improve the dissolution characteristics of water insoluble drugs. Liquid solid compacts (LSC) are measured as adequately streaming and compressible powdered types of fluid prescriptions that infer slick fluid medications and arrangements or suspensions of water insoluble strong medications conveyed in appropriate nonvolatile dissolvable frameworks. Present procedure the drug was dissolved in a liquid vehicle and was incorporated in to a carrier material having porous nature and adsorption properties. Then coating materials were added to the wet preparation to give the desired flow properties. LSC of inadequately solvent medications containing a medication atomically scattered in solubilizing vehicle show upgraded drug disintegration because of an expanded surface region of medication, and an improved wet ability of the medication molecule. As needs be, this improved medication disintegration may bring about higher medication retention and consequently, an improved oral bioavailability.
NSAID’s which belongs to BCS class II drug has low aqueous solubility or practically insoluble in water. It is a propionic acid derivative having pharmacological effect as a as anti-inflammatory, analgesic and antipyretic. IBU mechanism by reduce the fabrication of prostaglandins by declining the doings of enzyme cyclooxygenase. The present work focuses on the preparation and evaluation of IBU by LSC to progress the solubility and dissolution properties of the drug.

2. Materials and methods:

Materials
Ibuprofen (IBU) is a gift example obtained by Aurobindo Pharma Pvt ltd, Hyderabad, Aerosil 200 and Propylene glycol purchased from thermo Fischer scientific, India Pvt ltd, Microcrystalline cellulose (MCC), Lactose, croscarmellose, sodium starch glycolate, and inulin are obtained from Loba Chemie Pvt Ltd.

Method
Preparation of LSC
IBU LSC was prepared as per the table 1. Necessary quantity of IBU (100 mg) was weigh and transmits to a gun and detached in propylene glycol (PG). The deliberated quantity of carrier and coating substance is additional to the dispersal and blend in the gun. To this the remaining ingredients are a dditional and blended well. The final mixture was compressed in to tablets physically with multi station rotary tablet punch mechanism.

Table 1. Composition of Ibuprofen tablets by LSC technique:

<table>
<thead>
<tr>
<th>S.No</th>
<th>Formulation</th>
<th>Liquid Vehicle</th>
<th>Carrier</th>
<th>Disintegrant (3%)</th>
<th>Liquid load factor (L&lt;sub&gt;f&lt;/sub&gt;)</th>
<th>Aerosil (mg)</th>
<th>Unit dose Weight (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F 1</td>
<td>PG</td>
<td>MCC</td>
<td>-</td>
<td>0.11</td>
<td>19</td>
<td>400</td>
</tr>
<tr>
<td>2</td>
<td>F 2</td>
<td>PG</td>
<td>MCC</td>
<td>-</td>
<td>0.14</td>
<td>20</td>
<td>400</td>
</tr>
<tr>
<td>3</td>
<td>F 3</td>
<td>PG</td>
<td>MCC</td>
<td>-</td>
<td>0.24</td>
<td>21.5</td>
<td>400</td>
</tr>
<tr>
<td>4</td>
<td>F 4</td>
<td>PG</td>
<td>Lactose</td>
<td>-</td>
<td>0.11</td>
<td>19</td>
<td>400</td>
</tr>
<tr>
<td>5</td>
<td>F 5</td>
<td>PG</td>
<td>Lactose</td>
<td>-</td>
<td>0.14</td>
<td>20</td>
<td>400</td>
</tr>
<tr>
<td>6</td>
<td>F 6</td>
<td>PG</td>
<td>Lactose</td>
<td>-</td>
<td>0.24</td>
<td>21.5</td>
<td>400</td>
</tr>
<tr>
<td>7</td>
<td>F 7</td>
<td>PG</td>
<td>MCC</td>
<td>Sodium starch glycolate</td>
<td>0.14</td>
<td>20</td>
<td>400</td>
</tr>
<tr>
<td>8</td>
<td>F 8</td>
<td>PG</td>
<td>MCC</td>
<td>Croscarmellose sodium</td>
<td>0.14</td>
<td>20</td>
<td>400</td>
</tr>
<tr>
<td>9</td>
<td>F 9</td>
<td>PG</td>
<td>MCC</td>
<td>Inulin</td>
<td>0.14</td>
<td>20</td>
<td>400</td>
</tr>
</tbody>
</table>

Liquid load factor L<sub>f</sub>= W/Q ultimate tablet load contain 1% of lubricant

EVALUATION of LSC
Flow behavior
Before compressing in to the tablet the powder mixture is subjected to different flow properties such as angle of repose, Carr’s index ad Hausner’s ratio to reduce the dose variation in the production of dosage forms."

Angle of relaxation
Fixed funnel technique is worn to establish the angle of relaxation for powder mixture, precisely weighed powder mixture is in use of funnel and is permitted to flow freely by the funnel on to the surface of the powder cone was estimated point of rest was determined utilizing the accompanying equation. Tan θ= h/r wherever, θ is the angle of relaxation, h is the height in cm r is the radius in cm.
**Mass thickness**
The mass thickness is indomitable with bulk density apparatus. The powder mix was poured in to a graduated chamber and the weight and mass volume of the powder was determined\(^6\). The mass thickness is resoluted utilizing the formula:

\[
BD = \frac{M}{Vb}
\]

wherever, M is the mass of powder, Vb is bulk volume of powder.

**Tap thickness**
A deliberated mass of powder was filled in a cylinder and tapped continuously up to a set time. The volume that was engaged by the powder blend and weight of the powder was noted and tapped density is intended by the following formula\(^6\):

\[
Dt = \frac{M}{Vt}
\]

where, M is the mass of powder, Vt is tapped volume of powder

**Carr’s Index (%)**
Carr’s index is the simple way of calculated flow properties of the powder and it was an indirect method to decide the bulk density, size and shape of the particles\(^6\). Values were given in table 2. Cars index is considered by the next formula:

\[
CI (\%) = \frac{[(Tapped\ density - Bulk\ density) / Tapped\ density]}{x\ 100}
\]

**Hausner’s Ratio**
The ease of powder flow can be indirectly determined through Hausner’s ratio and the formula to verified Hausner’s ratio was as follows\(^6\):

\[
Hausner's\ Ratio = \frac{Tapped\ density\ (pt)}{Bulk\ density\ (pb)}
\]

Hausner’s ratio standards are mentioned in table 2.

**FTIR studies**
The similarity among IBU and excipients utilized for the readiness of LSC were controlled by FTIR\(^3\). Tests were dissected by utilizing an ATR-FTIR spectrometer (Bruker, Germany) over the wave number scope of 4000-600 cm\(^{-1}\) at a goal of 1.0 cm\(^{-1}\). The FTIR spectra of both IBU and IBU LSC were recorded to assess the similarity of IBU with excipients utilized in the definition

**IBU Content**
The prepared LSC mixtures were assayed for IBU content. 10 mg of LSC mixture was weighed and dissolve in sufficient amount of methanol\(^8\). The above arrangement was reasonably weakened with pH 7.2 cradle and the IBU content was resolved utilizing UV spectrophotometer at 222nm.

**Hardness**
The rigidity of the IBU LSC compact tablets is calculated with Pfizer hardness tester and the values were expressed in kg/cm\(^2\) and given in Table 3. Hardness of the tablets was checked by taking a set of three tablets haphazardly by every formulation and the mean values are noted\(^3\).

**Friability:**
Roche fryolator is the equipment which is used for the determination of friability. A set of pre weighed tablets were located in a friability chamber that rotate at 25rpm and they are subjected to fall from a height of 6 inches for concerning 100 revolutions\(^9\). The weight of the tablets before and after subjecting to friability test was noted and the percentage of friability is considered by using the subsequent method and the values were given in Table3.

\[
F = \frac{(W\ initial) - (W\ final)}{(W\ initial)} \times 100
\]
In-vitro Dissolution studies
The in vitro drug disintegration study is executed by utilizing USP disintegration type II device (LABINDIA DS-8000) at 50 rpm using phosphate buffer pH 7.2 phosphate buffer (900 ml) as dissolution medium preserved at $37 \pm 0.5 \degree C$. 5ml of aliquots are inhibited at respective time intervals and filtered through 0.45µm filter paper and replaced with 5ml of fresh dissolution medium. The samples were then analyzed at 222nm by UV-visible spectrophotometer. The cumulative amount of drug released was calculated as a function of time to construct release profile graphs. The release data is built-into dissimilar kinetic representations.

3. RESULTS AND DISCUSSION
In the present investigation LSC were prepared using various carriers like MCC and lactose, and super disintegrants like SSG, CCS and inulin. The tablets are equipped by direct compression method and are estimated for a variety of physic mechanical properties and in vitro drug release profile.

Evaluation of LSC
3.2.1 Flow Properties
The prepared mixtures of LSC flow properties were determined by angle of repose, Carr’s index and Hausner’s ratio. The results were given in table 2. From the results it is observed that there is 1.17- and 1.30-fold increase in angle of relaxation and Carr’s index for the formulation containing MCC as carrier compared to formulations containing lactose as carrier. The addition of super disintegrants didn’t show any significant effect on the flow properties of LSC. Overall the formulations showed good flow ability.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Angle of repose</th>
<th>Carr’s index</th>
<th>Hausner’s ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>27.85±0.50</td>
<td>16.35±0.26</td>
<td>1.12±0.12</td>
</tr>
<tr>
<td>F2</td>
<td>31.26±0.18</td>
<td>14.65±0.3</td>
<td>1.14±0.06</td>
</tr>
<tr>
<td>F3</td>
<td>29.84±0.25</td>
<td>18.33±0.52</td>
<td>1.10±0.62</td>
</tr>
<tr>
<td>F4</td>
<td>32.23±0.63</td>
<td>21.22±0.68</td>
<td>1.12±0.88</td>
</tr>
<tr>
<td>F5</td>
<td>30.22±0.38</td>
<td>24.56±0.12</td>
<td>1.11±0.28</td>
</tr>
<tr>
<td>F6</td>
<td>32.61±0.41</td>
<td>22.03±0.44</td>
<td>1.15±0.03</td>
</tr>
<tr>
<td>F7</td>
<td>32.16±0.22</td>
<td>20.98±0.12</td>
<td>1.3±0.08</td>
</tr>
<tr>
<td>F8</td>
<td>31.63±0.20</td>
<td>22.68±0.08</td>
<td>1.03±0.64</td>
</tr>
<tr>
<td>F9</td>
<td>33.53±0.19</td>
<td>21.63±0.13</td>
<td>1.14±0.24</td>
</tr>
</tbody>
</table>
FTIR studies
The FTIR range of unadulterated IBU and IBU LSC were appeared in Fig 1. The FTIR spectra of IBU showed trademark tops at 2918.50cm⁻¹ because of alkane extending, (C-H extending), 1698.84cm⁻¹ (C=O extending of the carboxyl particle). All the peaks were retained in IBU LSC demonstrating non interaction of IBU and excipients within the formulat

![Fig.1. FTIR Spectra of (a) Pure IBU, (b) IBU LSC F9.](image)

Drug Content
The medication content was inside the worthy reach for all details demonstrating uniform dissemination of IBU in all the plans. IBU content was found to be 97% to 101% in all the prepared formulations.

Hardness
The hardness of the prepared LSC tablets is calculated with Pfizer hardness tester and was found to be in the range of 4.5 kg/cm². The carrier doesn’t show any major consequence on the hardness of the tablets. However, the concentration of MCC showed a slight consequence on the hardness of the tablets i.e as the concentration of MCC increases the hardness of the tablet increased. The consequences are revealed in table.3.

Friability
The friability of the tablets was within the limits as per I.P i.e. <1% and values were given in table 3. Test results indicate that tablet can overcome shock and wear without being destroyed during the production process, packing and transporting of the dosageform.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Hardness</th>
<th>Friability</th>
<th>Drug content</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>4.2±0.3</td>
<td>0.86±0.02</td>
<td>96.42±1.86</td>
</tr>
<tr>
<td>F2</td>
<td>4.3±0.2</td>
<td>0.79±0.05</td>
<td>95.33±0.88</td>
</tr>
<tr>
<td>F3</td>
<td>4.1±0.6</td>
<td>0.84±0.02</td>
<td>98.63±2.23</td>
</tr>
<tr>
<td>F4</td>
<td>4.4±0.1</td>
<td>0.81±0.06</td>
<td>97.21±1.27</td>
</tr>
<tr>
<td>F5</td>
<td>4.2±0.4</td>
<td>0.86±0.01</td>
<td>95.41±0.59</td>
</tr>
<tr>
<td>F6</td>
<td>4.4±0.1</td>
<td>0.85±0.09</td>
<td>96.81±2.21</td>
</tr>
<tr>
<td>F7</td>
<td>4.2±0.8</td>
<td>0.82±0.03</td>
<td>97.71±1.63</td>
</tr>
<tr>
<td>F8</td>
<td>4.1±0.3</td>
<td>0.80±0.02</td>
<td>98.26±1.45</td>
</tr>
<tr>
<td>F9</td>
<td>4.3±0.8</td>
<td>0.84±0.10</td>
<td>96.83±0.76</td>
</tr>
</tbody>
</table>

Table 3. Evaluation of IBU LSC Tablets
Fig. 3 Comparative in-Vitro dissolution profiles of (a) IBU LSC (containing super disintegrants) and (b) IBU LSC (containing carriers)

Dissolution

The dissolution profiles of IBU LSC tablets are revealed in Fig. 2. From the results it is experimented by concentration of carrier increase the dissolution of IBU increased. A 1.23 fold increase in IBU release was observed in formulation F3 containing MCC as carrier compared to formulation F6 containing lactose as carrier. Further trails were carried out to study the effect of super disintegrants like Sodium starch glycolate, croscarmellose sodium and inulin on the discharge of IBU from the formulations; it is experimented that a faster drug discharge was observed in the formulations containing super disintegrants than the formulations without super disintegrants. A 1.78, 1.51, and 1.44 folds increase in IBU release was observed in formulation F7, F8, and F9 respectively containing SSG, CCS, and inulin than formulation F3 without super disintegrants. Among the three super disintegrants used formulation F (7) containing S.S.G showed faster dissolution than CCS and inulin.

4. CONCLUSION

From this investigation, it can be concluded that IBU can be successfully formulated as LSC. From the results it is observed that the nature of carrier had shown significant effect on dissolution properties of IBU. In addition, super disintegrants was found to play a crucial role on the IBU release rates. Faster drug release rates from LSCs may provide quick onset of action with enhanced oral bioavailability and therapeutic efficacy.

5. REFERENCES


