Design of aspirin formulation for rapid pain relief

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Summary

Objective: Aspirin has always had excellent pain relief benefits. To reduce the gastric problems in the present study we had made an attempt to make aspirin fast dissolving tablets.

Methods: Aspirin fast dissolving tablets were developed by direct compression method using Indion 254, Indion 214 and croscarmellose as superdisintegrants. Microcrystalline cellulose was used as diluent, and mannitol, as sweetening agent. The tablets were evaluated for weight variation, mechanical strength, in vitro disintegration time, wetting time and drug release characteristics.

Results: Hardness and friability data indicated good mechanical strength of tablets. The results of in vitro disintegration time indicated that formulation FD3 (containing 5 mg Indion 254) as superdisintegrant was found to be suitable tablets as it showed rapid disintegration within 8 to 32 seconds. Dissolution study revealed the release rate of aspirin fast dissolving tablet and these was compared with that of marketed tablet formulation of aspirin.

Conclusion: It was concluded that superdisintegrants addition technique is a useful method for preparing fast dissolving tablets by direct compression method and present study revealed that Indion 254 could produce good superdisintegrating property.

Key words: Aspirin; Indion 254; Superdisintegrants

Introduction

Aspirin has always had excellent pain relief benefits, but it was also recognized that, it could cause digestive problems for some patients when used regularly. Some modified versions of aspirin came onto the market in an effort to achieve the benefits of aspirin while "buffering” the prospect for stomach discomfort. These formulations have no or only minimal impact on the stomach lining.

Fast dissolving tablets (FDT) are solid unit dosage forms which disintegrate or dissolve rapidly in the mouth without chewing and water. FDTs are also called as fast melt, fast disintegrating or orally dispersible tablet. Fast dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery systems which aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. Their growing importance was underlined recently when European Pharmacopoeia adopted the term “oro-dispersible tablet” as a tablet that to be placed in the mouth where it disappears rapidly before swallowing [1-3].

Direct compression using superdisintegrants is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Disintegration and solubilization of directly compressed tablets depends on single or combined action of disintegrants, water soluble excipients and effervescent agent. Ion exchange resins have been increasingly used for the taste masking of bitter taste drug and help to prepare oro-dispersible tablets [4, 5].

Indion 254 is water insoluble, chemically crosslinked acrylic copolymer matrix with carboxylic acid as functional group (potassium form). Swelling property of ion exchange resins makes them ideal candidate as superdisintegrants. In the present study we evaluate the efficacy of ion exchange resins such as Indion 254, Indion 214 as superdisintegrants over the existing one (croscarmellose) in fast dissolving tablets.

Aspirin tablet that melts in the mouth after contact with saliva on the tongue is absorbed by the lining of the mouth, avoiding first-pass metabolism and irritation to the gastro-intestinal tract. Time is critical in the prevention of heart attacks, stroke, or migraine headache, so that a fast-dissolving formulation of aspirin is the best way for rapid absorption. The present investigation is an attempt to design a new formulation of aspirin which can release the medicaments in the mouth within seconds for immediate relief of pain and thereby produce lesser contact time with mucus membrane and may reduce the gastric irritation caused by aspirin.

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Materials and methods

Chemicals
Aspirin (Spectrum Chemicals), magnesium stearate and mannitol (Ozone International) were purchased from the sources indicated. Indion 214, Indion 254 (Colorcon Pvt. Ltd.), croscarmellose (Mapple biotech Pvt. Ltd.), microcrystalline cellulose (Reliance Cellulose Products Pvt. Ltd.) were the gift samples.

Aspirin preparation
Aspirin was mixed in geometric proportions with superdisintegrants, sweeteners, diluent, flavors and lubricants. Various concentrations of superdisintegrants were employed to arrive at an optimum disintegration time and the blend was screened through sieve no:40 and compressed using 16 press rotary punching machine, having flat beveled punches. Composition of fast dissolving tablets of aspirin was shown in Table 1.

Characterization of aspirin FDTs
The prepared formulation were subjected to characterization thikness, weight variation, hardness, percentage friability, wetting time, and disintegration time.

Weight variation
Twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance the average weight of one tablet was determined from the collective weight.

Hardness
The tablet crushing load, which is the force required to break a tablet by compression in the radial direction was measured using a Monsanto hardness tester (Tab-Machines Ltd., India). The test was performed on 10 tablets and the average was calculated.

Friability
Friability of the tablets was determined using Roche friabilator (Electrolab, India) at 25 rpm for 4 minutes. Preweighed sample of 20 tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed.

The friability (F%) is given by the following formula:

\[ F\% = \left[ \frac{1 - W_0/W}{W_0} \right] \times 100 \]

where, W0; weight of the tablets before the test
W; weight of the tablets after the test

Wetting time
A piece of double folded tissue paper was placed in a Petri plate (internal diameter; 6.5 cm) containing 6 ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37°C. Wetting time corresponds to the time for the tablet to disintegrate when kept motionless on the tongue.

Drug content
Five tablets were weighed and powdered to the quantity of power equivalent to 0.5 g of aspirin; add 30 ml of 0.5M sodium hydroxide. Boil gently for 10 min and titrated with 0.5M hydrochloric acid using phenol red solution as indicator. Repeat the operation without the substance being examined. The difference between titration represents the amount of sodium hydroxide required.

In vitro dissolution testing
Dissolution study was conducted for all the formulation using USP type-II apparatus (Electolab, Mumbai, India). The dissolution test was performed using 500 ml of phosphate buffer (pH 4.5) as the dissolution medium at 50 rpm and 37°C±0.5°C. Five millilitres of aliquots were periodically withdrawn and the sample volume was replaced with an equal volume of fresh dissolution medium. The samples were analyzed spectrophotometrically at 265 nm.

<table>
<thead>
<tr>
<th>Table 1. Composition of fast dissolving tablets of aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingredient</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Aspirin</td>
</tr>
<tr>
<td>Indion 214</td>
</tr>
<tr>
<td>Indion 254</td>
</tr>
<tr>
<td>Croscarmellose</td>
</tr>
<tr>
<td>Microcrystalline cellulose</td>
</tr>
<tr>
<td>Talc</td>
</tr>
<tr>
<td>Mannitol</td>
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</tbody>
</table>

Total tablet mass is 350 mg.
Table 2. Characterization of fast dissolving aspirin tablets

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Thickness (mm)</th>
<th>Weight variation</th>
<th>Hardness (kg/cm²)</th>
<th>Friability (%)</th>
<th>Wetting time (sec)</th>
<th>Drug content (mg)</th>
<th>Disintegration time (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FD1</td>
<td>16</td>
<td>+0.0594 / -0.0453</td>
<td>4.6±0.2</td>
<td>0.42</td>
<td>21±0.91</td>
<td>98</td>
<td>32</td>
</tr>
<tr>
<td>FD2</td>
<td>16</td>
<td>+0.0397 / -0.0369</td>
<td>4.0±0.3</td>
<td>0.39</td>
<td>22±0.23</td>
<td>99.8</td>
<td>14</td>
</tr>
<tr>
<td>FD3</td>
<td>16</td>
<td>+0.0312 / -0.0312</td>
<td>4.2±0.14</td>
<td>0.43</td>
<td>10±0.54</td>
<td>96.5</td>
<td>8.5</td>
</tr>
<tr>
<td>FD4</td>
<td>16</td>
<td>+0.0370 / -0.0398</td>
<td>4.2±0.6</td>
<td>0.7</td>
<td>7±0.58</td>
<td>100</td>
<td>12.75</td>
</tr>
<tr>
<td>FD5</td>
<td>16</td>
<td>+0.0418 / -0.0698</td>
<td>4.9±0.82</td>
<td>0.4</td>
<td>17±0.45</td>
<td>97.2</td>
<td>18.75</td>
</tr>
<tr>
<td>FD6</td>
<td>16</td>
<td>+0.0638 / -0.0444</td>
<td>4.9±0.04</td>
<td>0.86</td>
<td>21±0.35</td>
<td>94.3</td>
<td>10.5</td>
</tr>
<tr>
<td>FD7</td>
<td>16</td>
<td>+0.0604 / -0.0576</td>
<td>4.65±0.12</td>
<td>0.88</td>
<td>47±0.14</td>
<td>99.7</td>
<td>58.5</td>
</tr>
</tbody>
</table>

Results and discussion

The results for evaluation of different formulations of aspirin fast dissolving tablets prepared by direct compression method are shown in Table 2. Percent weight variation was observed in between 3.0 to 6.1 which were well within the acceptable limit for uncoated tablet as per Indian Pharmacopoeia (IP).

Hardness of tablet was determined and was found to be in the range of 4.0-4.9 kg/cm². These good hardness and friability data indicates good mechanical resistance of tablets. In vitro disintegration time for different formulations FD3, FD4, FD5 was found to be 8, 14 and 12 seconds, respectively.

The in vitro disintegration time of different formulations with different concentrations of superdisintegrants were given in Fig. 1. The tablet formulations containing disintegration time of 8 to 12 seconds was produced by formulations containing 5 and 10 mg of Indion 254, disintegration time of 14 to 32 seconds and 10 to 18 seconds were produced by formulations containing 5 and 10 mg of Indion 214 and croscarmellose, respectively. This result of in vitro disintegration time indicates that the formulation FD3 containing 5 mg tablet of Indion 254 showed minimum time of 8 seconds to disintegrate.

Wetting time was determined to get idea of wetting lag time before disintegration. The wetting time for FD3 was 10 seconds, which shows that very small amount of water is required for wetting of tablet. It has been reported that wetting is closely related to the inner structure of the tablet and the hydrophilicity of the excipients. Thus these results indicate that these tablets would disintegrate almost instantaneously when they will come in contact with even slight quantity of saliva in the mouth.

Invitro dissolution studies (Fig.2) shows that the cumulative percentage drug release increased with increased in concentration of superdisintegrant in the formulations containing Indion 214 and croscarmellose. At 10% concentration of Indion
214 and croscarmellose the cumulative percentage drug release were found to be 94.33 and 93.4%, respectively, at the end of 180 seconds. Whereas at 5% concentration of Indion 254 the cumulative percentage drug release was found to be 94.55% release at the end of 150 sec; this did not correlate with above statement. Indion 254 was found to have a very good superdisintegrant property at low concentrations.

In conclusion, new aspirin tablets which have optimum physicochemical properties were formulated for more compliance and palatable melt in mouth. The ion exchange resin Indion 254 could be successfully used as superdisintegrant, thus making the formulation cost effective.

The tablets exhibited an invitro disintegration time of 8 seconds. This can be easily employed for large-scale manufacturing.

References