DESIGN AND IN-VITRO EVALUATION OF TASTE MASKED FAST DISSOLVING TABLETS OF SUMATRIPTAN SUCCINATE

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ABSTRACT
Sumatriptan succinate is an agonist for 5-HT1 receptors. It is widely prescribed for the treatment of migraine and cluster headaches. Thus formulating Sumatriptan succinate into an orodispersible dosage form would provide fast relief. The Sumatriptan succinate is bitter in taste so Kyron T-114(ion exchange resin) was used to mask the taste and to formulate an orodispersible dosage form using drug resin complex. The tablets were evaluated for the drug content, weight variation, water absorption ratio, wetting time, in-vitro disintegration, dispersion time, hardness, friability, thickness and uniformity. The tablets disintegrated in-vitro within 28 to 39 seconds complete drug were released from tablet within 15 minutes. The results showed that Sumatriptan succinate was successfully formulated into an taste masked orodispersible dosage form.

Keywords: Sumatriptan succinate; Antimigraine; Ion exchange resin; Orodispersible tablets.

INTRODUCTION
Drug delivery system is an efficient tool for enhancing market, extending product life cycles and creating opportunities. Drug delivery system makes a significant contribution to global pharmaceutical sales through market segmentation, and is moving rapidly. Despite of tremendous innovations in drug delivery, the oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, non-invasive method and ease of administration leading to high level of patient compliance. Taste of a pharmaceutical product is an important parameter governing compliance. Hence taste masking of oral pharmaceuticals has become important tool to improve patient compliance and the quality of treatment especially in paediatrics. Hence formulation of taste masked products is a challenge to the pharmacist.

Consumer acceptability certainly affects the commercial success of the product in the market. Various techniques are available to mask the bitter taste or to improve the taste such as by using polymeric coatings, complexation with cyclodextrins, ionexchange...
Ion exchange resins and use of excipients like flavours and sweetners. Ion exchange resins have been increasingly used for this purpose\(^3\).

Ion exchange resins are cross-linked water insoluble polymer-carrying, ionizable functional groups. Ion exchange resins have received considerable attention from pharmaceutical scientists because of their versatile properties as drug delivery vehicles. Research over the last few years has revealed thation exchange resins are equally suitable for drug delivery technologies, that is taste masking. Synthetic ion exchange resins have been used in pharmacy and medicine for taste masking of drug. Drug resin complexation converts drug to amorphous form leading to improved drug dissolution\(^4\).

Drugs can be loaded onto the resins by an exchanging reaction, and hence, a drug-resin complex (drug resinate) is formed. Ion exchange can be defined as a reversible process in which ions of like sign are exchanged between liquid and solid, a highly insoluble body in contact with it. The drug is released from the resinates by exchanging with ions in the gastrointestinal fluid, followed by drug diffusion\(^4\).

The demand for FDT (Fast Disintegrating Tablet) has been increasing from the last decade particularly in geriatric, pediatric and patient with some sort of disabilities in swallowing. FDTs are those tablets which when placed in mouth get dissolved rapidly in saliva without the need of liquid and can be swallowed. European pharmacopoeia adopted the term orodispersible tablet for FDTs. Fast disintegrating tablets are also known as fast melting tablets, orodispersible tablets, fast dissolving/dispersing tablets or melt in mouth tablets\(^5\).

Sumatriptan is structurally similar to serotonin and is a 5-HT agonist. Sumatriptan stimulates 5-HT receptors of the 1D subtype, most likely presynaptic receptors resulting in selective vasoconstriction of inflamed and dilated cranial blood vessels in the carotid circulation. Sumatriptan also blocks the release of vasoactive neuropeptides from perivascular trigeminal axons in the dura mater during migraine and may inhibit the release of inflammatory mediators from the trigeminal nerve\(^6\).

**MATERIAL AND METHODS**

Chemicals used for the study

Sumatriptan Succinate was obtained as gift sample from Dr. Reddy’s Laboratories Limited, Hyderabad. Kyron T-314 and Kyron T-114 were gift samples from Corel
Pharma Chem Limited, Ahmedabad. Crospovidone, Sodium starch glycolate, Avicel pH(102) and Magnesium stearate gift samples from SD Fine Chem Ltd and all chemicals and reagents were used are analytical grade.

Purification of ion exchange resins:-

All the resins were given a pre-treatment to remove the impurities associated with industrial scale manufacture. The resins were purified by rinsing 10 gm of wet resin with 3 portions of 5ml of deionized water, 1 portion of 50 ml 95% ethanol and 1 portion of 50 ml deionized water. Each stage of treatment lasted 1 hour under magnetic stirring. The resin was then conditioned with 60 ml of 2M NaOH and 60 ml 2M HCl and with deionized water after each treatment. Finally the resins were recovered by vacuum filtration, washed thoroughly with deionized water and dried. Then ground and passed through sieve number 100 to get a uniform size particles.

Preparation of drug - resinate complex:

Taste masking of Sumatriptan succinate is done by complexation with ion exchange resins like kyron T-114 as per the following procedure:

Drug and resin were accurately weighed in required ratio. Then slurry of resin was made with demineralised water and stirred for half an hour at 500 rpm, in order to allow the polymer structure to swell uniformly. The drug was dissolved in solution using 10 ml of methanol. Then drug solution was added slowly under stirred condition. The drug resin mixtures were then continuously stirred for 8 to 10 hrs at 500 to 600 rpm and the volume was made up to 100 ml. filtered the drug-resinates so formed through Whatman filter paper. Washed the drug-resinates with distilled water and dried at about 60°C under vacuum. The drug content in the filtrate was analyzed by UV-visible spectroscopy at 282nm. The amount of drug loaded on the complexes was obtained by subtracting the remaining amount of drug in the filtrate from the initial amount.

Evaluation of granules:

Determination of angle of repose

Angle of repose is an indication of the frictional forces excited between granule particles. It is the maximum angle possible between the surface of the pile of granules and the horizontal plane. 

\[ \tan \theta = \frac{h}{r} \]
Where, \( \theta \) = the angle of repose

\[ h = \text{height of the heap of the powder} \]

\[ r = \text{radius of the heap of the powder} \]

**Hausner’s Ratio:**

It indicates the flow properties of the granules and is measured by the ratio of tapped density to the bulk density\(^9\).

\[
\text{Hausner’s Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}
\]

**Compressibility index (Carr’s Index):**

Compressibility index is an important measure that can be obtained from the bulk and tapped densities. In theory, the less compressible a material the more flow able it is. A material having values of less than 20% has good flow property\(^10,11\).

\[
\text{CI} = \frac{(\text{Tapped Density} – \text{Bulk Density}) \times 100}{\text{Tapped Density}}
\]

**Preparation of tablets:**

Granules of drug-resinate earlier obtained were mixed with flavouring agents (mint flavour) and talc (2%). Before compression hardness was adjusted. Drug-resinates equivalent to 25mg of Sumatriptan succinate were compressed on Cadmach single punch tablet press machine equipped with 10mm flat faced beveled edge punches and same hardness was used for the required number tablets\(^12\).
TABLE NO 1: DESIGN AND IN-VITRO EVALUATION OF TASTE MASKED FAST DISSOLVING TABLETS OF SUMATRIPTAN SUCCINATE

<table>
<thead>
<tr>
<th>FORMULA CODE</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>
<th>F9</th>
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</thead>
<tbody>
<tr>
<td>SUMATRIPTAN SUCCINATE (DRC 1:5)</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
<td>150</td>
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<td>150</td>
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<tr>
<td>KYRON T-314</td>
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<td>20</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CROSPovidone</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10</td>
<td>15</td>
<td>20</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>10</td>
<td>15</td>
<td>20</td>
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<tr>
<td>MCC</td>
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<td>39</td>
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<td>39</td>
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<td>5</td>
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<td>5</td>
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<td>5</td>
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<tr>
<td>SODIUM SACCHARIN</td>
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<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
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<td>FLAVOUR</td>
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<td>1</td>
<td>1</td>
<td>1</td>
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<td>1</td>
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<td>1</td>
</tr>
<tr>
<td>MAGNESIUM STEARATE</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
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<tr>
<td>TALC</td>
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<td>2</td>
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<td>2</td>
<td>2</td>
<td>2</td>
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<td>TOTAL WEIGHT</td>
<td>250</td>
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<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
<td>250</td>
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</tbody>
</table>

*All quantities are in milligrams (mg) only

Evaluation of tablet:

Diameter and Thickness It was measured by using vernier calliper scale.

Weight variation The USP weight variation test is run by weighing 20 tablets individually, and comparing individual weight to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

Hardness The Pfizer tester was used.

Disintegration time This test was carried out using USP disintegration apparatus.

Content uniformity

The tablets were tested for their drug content uniformity. At random 20 tablets were weighed and powdered. The powder equivalent to 100 mg was weighed accurately and dissolved in 100ml of water. The solution was shaken thoroughly. The undissolved matter was removed by filtration through Whatmann No.41 filter paper. Then the serial dilutions were carried out. The absorbance of the diluted solutions was measured at 282 nm. The concentration of the drug was computed from the standard curve of the Sumatriptan succinate in water.

In-vitro dissolution studies
Dissolution testing of Sumatriptan succinate fast dissolving tablets was carried out with paddle type in USP dissolution apparatus at rpm 50 and temperature 37±0.5°C in water. At each specified intervals of time 5 ml sample was withdrawn and replaced by fresh media. The samples were analytically tested to determine the concentration by UV spectroscopy method at wavelength of 282 nm.

**FT-IR study**

This study was carried out to check incompatibility between drug and excipients by using IR spectrophotometer.

**RESULTS AND DISCUSSION**

In the present study, a total of 9 formulations of fast dissolving tablets of Sumatriptan succinate were prepared using ion exchange resins by direct compression method. In order to select the best formulation, various parameters were checked and subjected to in-vitro dissolution studies, release profile was observed and compared. Evaluation for general appearance, physical parameters, drug content and release studies were performed according to official method and also with modified official methods. All the above tests are described in methodology section 4. Stability studies were performed for a two month and parameters like physical appearance hardness, drug content and in-vitro dissolution studies of the best formulations were evaluated.

**Table 2: Angle of Repose, Loose Bulk Density, Tapped Bulk Density**

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Angle of Repose (θ)</th>
<th>Loose Bulk Density (gm/cm³)</th>
<th>Tapped Bulk Density (gm/cm³)</th>
<th>% Compressibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>18.13</td>
<td>0.45</td>
<td>0.53</td>
<td>13.20</td>
</tr>
<tr>
<td>F2</td>
<td>18.33</td>
<td>0.45</td>
<td>0.54</td>
<td>12.96</td>
</tr>
<tr>
<td>F3</td>
<td>18.00</td>
<td>0.43</td>
<td>0.51</td>
<td>11.52</td>
</tr>
<tr>
<td>F4</td>
<td>22.30</td>
<td>0.58</td>
<td>0.68</td>
<td>14.00</td>
</tr>
<tr>
<td>F5</td>
<td>21.28</td>
<td>0.57</td>
<td>0.66</td>
<td>13.63</td>
</tr>
<tr>
<td>F6</td>
<td>18.56</td>
<td>0.55</td>
<td>0.62</td>
<td>12.90</td>
</tr>
<tr>
<td>F7</td>
<td>23.93</td>
<td>0.53</td>
<td>0.65</td>
<td>15.48</td>
</tr>
<tr>
<td>F8</td>
<td>21.30</td>
<td>0.52</td>
<td>0.62</td>
<td>14.51</td>
</tr>
<tr>
<td>F9</td>
<td>20.10</td>
<td>0.57</td>
<td>0.60</td>
<td>13.33</td>
</tr>
</tbody>
</table>
### TABLE 3: EVALUATION OF TABLET PARAMETERS

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Uniformity of Thickness (n=3) (mm)</th>
<th>Hardness (n=3) (kg/cm²)</th>
<th>Friability % (n=10)</th>
<th>Uniformity of Weight (n=20) (mg)</th>
<th>Drug Content (%)</th>
<th>Wetting Time (n=3)</th>
<th>Water Absorption Ratio (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>4.5 ± 0.01</td>
<td>3.44 ± 0.25</td>
<td>0.3296</td>
<td>249.95±1.011</td>
<td>93.51±0.57</td>
<td>51 ± 1.06</td>
<td>83.61 ± 0.23</td>
</tr>
<tr>
<td>F2</td>
<td>4.5 ± 0.02</td>
<td>3.33 ± 0.27</td>
<td>0.2988</td>
<td>249.95±1.120</td>
<td>95.92±0.42</td>
<td>50 ± 1.17</td>
<td>85.73 ± 0.12</td>
</tr>
<tr>
<td>F3</td>
<td>4.5 ± 0.04</td>
<td>3.16 ± 0.25</td>
<td>0.2985</td>
<td>250.3 ± 1.123</td>
<td>95.75±0.32</td>
<td>48 ± 0.15</td>
<td>87.76 ± 1.12</td>
</tr>
<tr>
<td>F4</td>
<td>4.5 ± 0.01</td>
<td>3.52 ± 0.23</td>
<td>0.3788</td>
<td>251.0 ± 1.775</td>
<td>97.5±0.27</td>
<td>52 ± 1.09</td>
<td>88.00 ± 0.89</td>
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<tr>
<td>F5</td>
<td>4.5 ± 0.02</td>
<td>3.51 ± 0.24</td>
<td>0.3485</td>
<td>250.05±1.00</td>
<td>96.20±0.89</td>
<td>51 ± 1.07</td>
<td>89.00 ± 0.24</td>
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<tr>
<td>F6</td>
<td>4.5 ± 0.03</td>
<td>3.52 ± 0.26</td>
<td>0.2993</td>
<td>250.55±1.11</td>
<td>96.85±0.42</td>
<td>49 ± 1.23</td>
<td>90.00 ± 0.91</td>
</tr>
<tr>
<td>F7</td>
<td>4.5 ± 0.04</td>
<td>3.70 ± 0.24</td>
<td>0.3791</td>
<td>250.55±1.15</td>
<td>96.57±0.84</td>
<td>53 ± 1.04</td>
<td>89.10 ± 0.85</td>
</tr>
<tr>
<td>F8</td>
<td>4.5 ± 0.03</td>
<td>3.63±0.24</td>
<td>0.3492</td>
<td>255.25±1.5</td>
<td>97.87±0.42</td>
<td>52 ± 0.30</td>
<td>90.50 ± 0.32</td>
</tr>
<tr>
<td>F9</td>
<td>4.5 ± 0.04</td>
<td>3.61±0.24</td>
<td>0.3296</td>
<td>254.00±1.80</td>
<td>98.79±0.42</td>
<td>51 ± 1.05</td>
<td>92.00 ± 0.45</td>
</tr>
</tbody>
</table>

Figure 1: In-vitro drug release studies of Sumatriptan succinate FDTs.
IN-VITRO DRUG RELEASE STUDIES OF SUMATRIPTAN SUCCINATE

Figure 2: In-vitro drug release studies of Sumatriptan succinate FDTs.

Best formulation comparison with marketed product

Figure 3: Best formulation F3 comparison with marketed product
CONCLUSION

Orodispersible tablets of Sumatriptan succinate can be prepared by direct compression technique using the different super disintegrants, namely Kyron T-314, Sodium starch glycolate and crospovidone. Preformulation studies of Sumatriptan succinate were performed. The FTIR analysis revealed that the super disintegrants and excipients used were compatible with Sumatriptan succinate. Among all the formulations, formulation containing Kyron T-314 as super disintegrants is fulfilling all the parameters satisfactorily. It has shown excellent in-vitro disintegration, in-vitro dispersion time, compared to other super disintegrants. Overall, formulations F3 containing Kyron T-314 & F6 containing Crospovidone and F9 containing, Sodium starch glycolate tablets disintegrated rapidly to release the drug. The formulations F3, F6, F9 were selected for stability studies on the basis of their better and satisfactory evaluation studies parameter. In formulations showed there was not much variation in any parameter even after the period of 60 days. From these results it was concluded that, formulations F3, F6, F9 are found to be stable and retained their original properties.

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