ROLE OF ASSAM BORA RICE STARCH AS DIRECT COMPRESSIBLE TABLET EXCIPIENT

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ABSTRACT

Purpose: The aim of this study was to evaluate the possible use of Assam Bora rice starch as directly compressible tablet excipient in comparison to pregelatinized starch. Methods: The starch was extracted from the rice, evaluated for relevant properties and used as direct compression tablet excipient in Ketotifen tablets. The tablets were evaluated for tensile strength, friability, drug content, disintegration and dissolution profiles. Ketotifen tablets containing pregelatinized starch as direct compression tablet excipient were produced and assessed comparatively. Result: The tablets were evaluated for tensile strength, friability, drug content, disintegration and dissolution profiles. Results obtained indicate that Assam Bora rice starch performed as good as pregelatinized starch as a direct compression tablet excipient to Ketotifen tablets. Conclusion: The tablet properties show that Assam Bora rice starch is a useful product for preparation of tablets by direct compression as compared to pregelatinized starch.

KEYWORDS: Assam Bora rice, Direct compression, Pregelatinized starch, Ketotifen tablets.

INTRODUCTION

Recent decades have seen tremendous strides in the designing of novel dosage forms, but tablets still remain an attractive option for pharmaceutical scientists and clinicians because they offer advantages of accurate unit-dosing, better patient compliance, ease of large-scale manufacturing, and low production cost[1]. The total market for excipients is estimated to be US $2.5 billion with an average annual growth of 7% to 8% in volume and 4% to 5% in...
value\textsuperscript{2}. The overall contribution of excipients in dosage form designing can be better appreciated from the fact that more than 70\% of the formulations contain excipients at a concentration higher than the drug\textsuperscript{3}.

It is important to distinguish between true direct compression diluents (i.e., excipients) and active ingredients which are available in a direct compression form. These are usually high dose materials such as aspirin, paracetamol, and ascorbic acid. They can be directly compressed into tablets, the only pretreatment being mixing with a lubricant and perhaps a disintegrating agent. However, such substances are more accurately described as ‘‘pregranulated’’ since the granulation process, either wet or dry, will have been carried out by the excipient manufacturer. It is likely that such materials will contain a binder. For example, ascorbic acid pregranulated with either starch or hydroxypropyl cellulose is commercially available\textsuperscript{4}. The perceived advantages of the direct compression process of tablet manufacture have given rise to a considerable body of literature. Between 1970 and the end of 2000, there were 598 references to ‘‘direct compression’’ in the index of International Pharmaceutical Abstracts. It has been estimated that today, some 40 years after the introduction of diluents specifically designed for direct compression, about 50\% of worldwide tablet production is made by this method\textsuperscript{4}.

The rice granules are the smallest of the grains of starch produced by plants, they average (3 – 8) $\mu$m in size and are polygonal but irregular in shape. Several reports have described the possibility of the use of starch granules as a directly compressible excipient\textsuperscript{5}. Starch is generally regarded as most important constituent of rice in terms of pasting behaviour and functionality. Amylose content is considered as the key determinant of rice texture gelatinization behaviour and pasting behaviour and rheology of rice paste\textsuperscript{6}.

North-east India, including Assam, is recognized as a centre of origin of rice and is endowed with exceptionally rich rice diversity. Among those, Assam Bora rice (a group of glutinous rice) of Assam, characterized by high amylpectin content, was introduced to Assam from Thailand or Burma a considerable time ago\textsuperscript{7}. The rice is known as glutinous or waxy rice when it contains very low amylose, generally less than 3\% by weight, and reported to contain only the traces of amylose (less than 2\%) and these therefore belongs to the glutinous rice. This rice, because of very low amylose content, posses very much adhesiveness and also
called as sticky rice. Researches with this starch in tablets of other active ingredients are necessary because of the high percentage of starch content reported in this plant. The death of primary pharmaceutical industries in some developing economics has led to lack of basic tableting excipients despite the avalanche of unprocessed raw materials. There is the need to bridge this gap. With increasing demand and search for natural starches with desirable properties for use in the pharmaceutical industries, the present work evaluates the possible use of Assam Bora rice starch as directly compressible tablet excipient.

EXPERIMENTAL

Materials
Assam Bora rice starch (prepared in our laboratory), Ketotifen fumarate (Torrent Pharmaceuticals Ltd. Ahmedabad, India), pregelatinized starch (S.A. Pharmachem Pvt. Ltd., Mumbai, India), Magnesium stearate (Vivimed Labs Ltd. Hyderabad, India), Colloidal silica (Vivimed Labs Ltd. Hyderabad, India). The other used materials were of analytical quality.

Extraction of Assam Bora rice starch
Assam Bora rice was collected, washed and sun dried for 7 days. About 8 parts of broken Assam Bora rice were steeped in about 16 parts of a 0.4 % solution of caustic soda. The mass was stirred every six hours and the liquor changed every eighteen to twenty four hours; the process was completed when the grain can be crushed between two fingers. The steeped rice was blended with 2 parts of the dilute soda to each part of the steeped rice and a milky fluid result. The starch suspension was diluted and allowed to settle in vats. The thick suspension was allowed pass through a muslin cloth and the damp starch was transferred to oven at (50-60) °C. After drying it was passed through 125 µm sieve.

Solubility determination
A 2% w/w dispersion of starch was prepared in a 50 ml volumetric flask. The dispersion was shaken frequently for some time and allowed to stand for about 8 hrs. It was then filtered with a filter paper and 30 ml of the clear filtrate evaporated to dryness in a pre-weighed dry crucible. The weight of starch residue obtained was determined by difference. Solubility was calculated in g/dm³ and mg %. This was repeated five times for the pregelatinized starch and average solubility recorded.

Particle size distribution
The particle size distribution was estimated by the microscopic method.
True density
Liquid displacement method using glass pycnometer was used to determine the true density. In this determination benzene was used as intrusion fluid. This was repeated five times for the pregelatinized starch and average true density was recorded.

Bulk and Tapped densities
Exactly 50 g of starch was weighed on chemical balance and transferred into a 100 ml measuring cylinder. The volume occupied by the starch recorded as the bulk volume. The cylinder was dropped on a wooden platform from a height of 2.5 cm three times at 2 seconds intervals until the volume occupied by the starch remained constant. This was repeated five times for the pregelatinized starch and average bulk and tapped volumes recorded. The data generated were used in computing the compressibility index and Hausner’s quotient for the two starches.

Angle of repose
Angle of repose was determined by fixed funnel method. The accurately weighed starch was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the starch. The starch was allowed to flow through the funnel freely onto the surface. The height and diameter of the starch cone was measured and angle of repose was calculated. This was repeated five times for the pregelatinized starch and average angle of repose was recorded.

Tablet preparation
Two batches of the tablet containing 1 mg Ketotifen fumarate were prepared. The batches contained Assam Bora rice starch and pregelatinized starch as filler-binder respectively in concentrations of 98.3% w/w with 1% magnesium stearate as lubricant and 0.2% colloidal silica as glidant were compacted in Tablet Punching Machine using 9.0 mm circular standard flat punch.

EVALUATION OF COMPRESSED TABLETS
Tensile Strength
This was carried out using hardness tester, Pfizer type (Elite Scientific Corp., Mumbai). The lower plunger is placed in contact with the tablet, and a zero reading is taken. The upper plunger is then forced against a spring until the tablet fractures. It was expressed in Kg/cm².
Friability
The friability of the tablets was determined by using friabilator (Roche, USA). Ten tablets were weighed from each batch and placed in the friabilator and operated for 4 min. at 25 rpm. The tablets were then made free from dust and reweighed. The percentage friability was calculated for each batch of the tablets.

Drug Content
The tablets were crushed in a mortar. A mass of powder equivalent with the average weight of one tablet was transferred into a 100 ml volumetric flask and 50 ml of methanol was added. The flask was then shaken automatically for 20 min., the resulting solution made up to the mark with methanol, and mixed thoroughly. A 20 ml aliquot was centrifuged at 4000 rpm. The absorbance of the clear supernatant was measured at 296 nm against methanol. A reference solution of Ketotifen hydrogen fumarate 2,5-hydrate was prepared, and absorbance measured at 296 nm against methanol. From the absorbance obtained the Ketotifen content in one tablet was calculated out. Mean drug content was calculated for each batch and thus their standard deviations.

Disintegration time
The method specified in the USP/NF (2003) was used. The machine was Tablet Disintegration Test Machine IP/BP/USP Std. (Tab-Machines, Mumbai). Disintegration medium used was 0.1 N HCl. Five tablets selected at random from each batch and the time taken for each tablet to break up into small particles and pass out through the mesh was recorded. Mean disintegration time was calculated for each batch.

Dissolution study
The in vitro dissolution study was carried out using USP Type II dissolution apparatus. The dissolution study was carried out in 900 ml of 0.1 N HCl. The dissolution medium was kept in thermostatically controlled water bath, maintained at 37 ± 0.5°C. The concentration of Ketotifen was measured spectrophotometrically at 300 nm (Hitachi, U-2001, Japan).

RESULT
Table 1 shows the various properties of the Assam Bora rice starch in comparison to the pregelatinized starch. The pregelatinized starch exhibited a comparatively higher solubility than the Assam Bora rice starch in cold water with values of 4.99 ± 0.14 and 1.01 ± 0.08 g/dm³ respectively. The low bulk and tapped densities of both Assam Bora rice starch and pregelatinized starch indicate that both materials are not highly porous and are poor flowing...
powders. The low bulk density results when the void spaces created by larger powder particles are not filled by smaller particles in distribution leading to consolidation of powder particles. The confirmation of the non-free flowing nature of Assam Bora rice starch and pregelatinized starch were gotten from the fact that their Hausner’s quotient of 1.47 ± 0.06 and 1.54 ± 0.03 respectively are greater than 1.2 which indicate low inter particulate friction in powder⁸. However, Assam Bora rice starch possessed better flow properties than pregelatinized starch with Carr’s compressibility index of 31.93 ± 2.88% and 35.06 ± 0.24% respectively. This index as a one point measurement does not always show the ease of consolidation of powders. Angle of repose showed Assam Bora rice starch and pregelatinized starch having fair and passable flow properties with values 40.31 ± 1.52° and 41.87± 0.64° respectively. The in vitro tablet properties are shown in Table 2. The tablet tensile strength was generally higher with the Assam Bora rice starch than pregelatinized starch. The same trend was found with the friability for Assam Bora rice starch and pregelatinized starch with values 0.65 ± 0.08% and 0.85 ± 0.04% respectively, both are below 1.0% friability. The drug content in both the batches of Assam Bora rice starch and pregelatinized starch were found within the limits of 97.8 to 101.8% with values 99.70 ± 0.06% and 98.90 ± 0.05% respectively. In case of disintegration time, it was found that the batch containing Assam Bora rice starch took higher time than the batch containing pregelatinized starch with values of 330 ± 7.91 seconds and 205 ± 10.37 seconds respectively. In dissolution study the percentage dissolved in 30 min. for the batch containing Assam Bora rice starch and pregelatinized starch are found to be 95.05± 4.60% and 90.0 ± 5.23% respectively.

Table 1. Properties of Assam Bora rice starch and pregelatinized starch.

<table>
<thead>
<tr>
<th>Properties</th>
<th>Assam Bora rice starch</th>
<th>Pregelatinized starch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold Water Solubility (g/dm³)</td>
<td>1.01 ± 0.08</td>
<td>4.99 ± 0.14</td>
</tr>
<tr>
<td>Average Particle Size d₅₀ (µm)</td>
<td>21.75 ± 12.65</td>
<td>40.56 ± 19.97</td>
</tr>
<tr>
<td>True density (g/cm³)</td>
<td>1.74 ± 0.03</td>
<td>1.54 ± 0.84</td>
</tr>
<tr>
<td>Bulk density (g/cm³)</td>
<td>0.31 ± 0.06</td>
<td>0.30 ± 0.02</td>
</tr>
<tr>
<td>Tapped density (g/cm³)</td>
<td>0.46 ± 0.01</td>
<td>0.46 ± 0.04</td>
</tr>
<tr>
<td>Carr’s Compressibility Index (%)</td>
<td>31.93 ± 2.88</td>
<td>35.06 ± 0.24</td>
</tr>
<tr>
<td>Hausner Ratio</td>
<td>1.47 ± 0.06</td>
<td>1.54 ± 0.03</td>
</tr>
<tr>
<td>Angle of Repose (°)</td>
<td>40.31 ± 1.52</td>
<td>41.87± 0.64</td>
</tr>
</tbody>
</table>

Each value represents the mean ± S.D of 10 determinations.
Table 2. *In vitro* tablet properties with *Assam Bora* rice starch and pregelatinized starch as filler-binder.

<table>
<thead>
<tr>
<th>Properties</th>
<th><em>Assam Bora</em> rice starch</th>
<th>Pregelatinized starch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tensile Strength (Kg/cm²)</td>
<td>11.63 ± 0.44</td>
<td>8.64 ± 0.36</td>
</tr>
<tr>
<td>Friability (%)</td>
<td>0.65 ± 0.08</td>
<td>0.85 ± 0.04</td>
</tr>
<tr>
<td>Drug Content (%)</td>
<td>99.70 ± 0.06</td>
<td>98.90 ± 0.05</td>
</tr>
<tr>
<td>Disintegration Time (sec.)</td>
<td>330 ± 7.91</td>
<td>205 ± 10.37</td>
</tr>
<tr>
<td>$t_{50%}$ (min.)</td>
<td>12 ± 3.45</td>
<td>17 ± 6.4</td>
</tr>
<tr>
<td>$t_{90%}$ (min.)</td>
<td>28 ± 4.25</td>
<td>30 ± 4.32</td>
</tr>
<tr>
<td>% dissolved in 30 min.</td>
<td>95.05 ± 4.60</td>
<td>90.0 ± 5.23</td>
</tr>
</tbody>
</table>

Each value represents the mean ± S.D of 10 determinations.
DISCUSSION
The cold water solubility of starches is related to their amylose/amylopectin constituents. The higher the water soluble amylopectin constituent the higher the cold water solubility of the candidate starch. The pregelatinized starch exhibited a comparatively higher solubility than the Assam Bora rice starch in cold water. The low bulk and tapped densities of both Assam Bora rice starch and pregelatinized starch indicate that both are poor flowing powders which is been further confirmed by Hausner’s quotient, Carr’s compressibility index & Angle of repose. The tensile strength & friability of tablets containing Assam Bora rice starch was found to be better as compared to tablets containing pregelatinized starch. In dissolution study it was found that the t_{50\%} and t_{90\%} of that the batch containing Assam Bora rice starch and pregelatinized starch are comparable with values 13, 28 and 17, 30 min. respectively. It could be said that the pregelatinized starch and Assam Bora rice starch showed comparative effectiveness as directly compressible tablet excipient to Ketotifen tablets. Studies found that Assam Bora rice starch can be used as a drug carrier for an effective colon targeted delivery system for drugs effective against the large intestine resident disease condition[9]. Studies been also reported for the possible use of Assam Bora Rice Starch as a plasma volume expander[10].

CONCLUSION
In conclusion, Assam Bora rice starch could compete favorably with pregelatinized starch as direct compressible table excipient.

REFERENCES


