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FORMULATION AND EVALUATION OF FAMOTIDINE TABLETS PREPARED BY USING GUAVA STARCH AS BINDING AGENTS

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ABSTRACT

Objective- The release of drug is affected by various excipients presents in formulation. In case of tablets the role of binders is very important for release of drug. Thus in following study an attempt is made to improve the solubility and dissolution rate of a drug by use of natural excipients (Guava Starch).

Methods- The unripe fruit of guava has high content of starch and hence it can be used as a material for extraction of starch. Then the extracted starch was evaluated and used as a binder in different concentrations, in famotidine tablets. The tablets were formulated by wet granulation method by using 2% w/v, 4% w/v, 6% w/v and 8% w/v of guava starch. Then formulated famotidine tablets were further evaluated for various parameters i.e. weight variation, hardness, friability, disintegration time and in-vitro drug release.

Results- The starch obtained is qualitatively and quantitatively comparable to known standard starch. The hardness and disintegration time of the tablets was found to be increased with increase in starch concentration. Tablets with highest binder concentration showed maximum hardness (6.0 kg) and disintegration time (7.4 min) and minimum friability (0.76%). After one hour tablets with 4% w/v starch showed maximum drug release (83.54%).

Conclusion- The results from various evaluations show that guava starch has significant binding characteristics. Hence it can be used as tablet binder in pharmaceutical formulations

Key words: Starch, Binder, Tablets, In-vitro dissolution, Famotidine

INTRODUCTION

Solubility is an important physicochemical factor affecting absorption of drug and its therapeutic effectiveness. Consequences of poor aqueous solubility would lead to failure in formulation development. The poor solubility of drug substances in water and their low dissolution rate in aqueous G.I.T fluid often leads to insufficient bioavailability. The bioavailability of drug is affected by various excipients in formulation.

A binder [1] is a material that is added to a formulation in order to improve the mechanical strength of a tablet. In direct compression, it is generally considered that a binder should have a high compatibility to ensure the mechanical strength of the tablet mixture [2]. The rational choice of a suitable binder in a formulation requires extensive knowledge of which properties of a binder are important for the strength enhancing effect. The role of the binders in direct compression is especially important when a high dose of a poorly compressible drug is included in the formulation [3].

There are different starch [4] used as tablet binder like potato starch, maize starch and corn starch are most commonly used. Binders are agents used to impart cohesive qualities to the powdered material during the production of tablets. They impart cohesiveness to the tablet formulation, which ensures that the tablet remains intact after compression as well as improving the flow property of granules. Binders have been used in both solutions as well as in dry form depending on the other ingredients in the formulations and the method of preparation [5]. The choice of a particular binding agent depends on the binding force required to form granules and its compatibility with the other ingredients particularly the active drug [6]. Starch from different sources have been evaluated and used as excellent binders.

In the present study was done to improve the solubility and dissolution rate of a drug by studying the effect of excipients on it. The starch was isolated from the guava and the isolated starch was evaluated and then used as binder for the preparation of famotidine tablets. Wet granulation method was used for the preparation of tablets. The tablets were then evaluated for the various evaluation parameters.

MATERIALS AND METHODS

Materials

The starch sources was purchased from local market then starch is extracted in laboratory. Famotidine was obtained as gift sample from Sun Pharma, Jammu. Carboxy methyl cellulose, lactose, magnesium stearate, talc (Central Drug House, New Delhi). All other chemicals used were of analytical grade.

Extraction of starch

- Fresh part of all sources were washed with tap water, peeled, washed again, and chopped in to small pieces [7].
- The pieces were mixed with 0.5% w/v NaOH solution in ratio of 1:3 and kept for 2 hr.
- The mass was then strained through muslin cloth and washed with saline solution several times to remove soluble substances, sugar, proteinaceous part and mucilage and other impurities present in it.
- Then the mass was washed many times to get clear supernatant solution.
- For removal of fatty material it is treated with petroleum ether and then filtered the mass and get residue.
- The sedimented starch was collected and again washed with ethanol and then by water until the pH was neutral.
- Then scrapped off it and dried at room temperature.
- Then pulverized it into fine powder and stored in containers prior to use and analysis.

Characterization of Different Starch [8-10]

Identification test

- 1 g of starch was boiled with 50 ml of water separately.
- After cooling to 1 ml of the mucilage, 2 drops of iodine solutions were added and the colour change was noted.

Particle size determination

- The mean particle size of samples of starch was determined microscopically with the aid of a calibrated eyepiece.

- A small amount of starch was mixed with glycerol and mounted onto a microscope slide with a cover slip and examined by polarized light microscopy and the particle size of each sample was determined [11].

Paste clarity

- The clarity (transmittance % at 650 nm) of starch paste was measured.
- A 1% aqueous suspension of starch was heated in a boiling water bath for 30 min with intermittent shaking.
- After the suspension was cooled for 1 hr at 25°C, the light transmittance at 650 nm was read against water blank.

Moisture content

- A 2 g weight (W_1) each of starch was dried for 24 hr. at 105°C in hot air oven and weight (W_2). Then moisture content calculated as –

$$\text{M.C. (\%)} = \frac{W_1 - W_2}{W_1} \times 100$$

W_1 = Weight of wet sample (grams), and W_2 = Weight of dry sample (grams)

Swelling capacity

- Note the tapped volume of 1 gm of starch (V_d) in a 50 ml measuring cylinder was noted.
- This powder was then dispersed in 8.5 ml of distilled water and volume was made up to 10.0 ml with distilled water.
- After 18 hrs of standing, the volume of the sediment, (V_w) was estimated and the swelling capacity was determined as-

$$\text{Swelling capacity} = \frac{V_w - V_d}{V_d} \%$$

Where, V_w = Volume of the sediment, V_d = Tapped volume

Ash value of starch

- Total 2 g quantity of starch [12] was weighed into a silica crucible and incinerated.
- Determination of ash value was done by measurement of the residue left after complete combustion in a muffle furnace at 350°C.

$$\% \text{ Total ash value} = \frac{\text{Wt. of total ash}}{\text{Wt. of crude drug taken}} \times 100$$

Flow properties of starch [13]

Angle of repose

- It was determined by allowing powder to flow through a funnel and fall freely on to a surface.
- Further addition of powder was stopped as soon as the pile has touched the tip of the funnel. A circle was drawn around the pile without disturbing it.
- The height and diameter of the resulting cone was measured.
- The same procedure was repeated three times and the average value was taken.
- Angle of repose was calculated by using the following equation:

$$\tan \theta = \frac{h}{r}$$

Where, h = height of the powder cone, r = radius of the powder.

Bulk density

- Take about 100 gm of starch [14] in to a dry 250 ml cylinder.
- The cylinder was filled carefully and level of powder was adjusted without compacting and the unsettled apparent volume (Vo) was noted.
- Bulk density was calculated, in g/ml. By using the formula:

$$\text{Bulk density} = M/V_o$$

Where, M = weight of the sample taken, Vo = bulk volume

Tapped density

- Accurately weighed quantity of powder was introduced into a measuring cylinder.
- The cylinder was tapped 500 times and the tapped volume (Va) was measured. Then the tapped density was calculated using the following formula:

$$\text{Tapped density} = M / V_f$$

Where, M = weight of the sample taken, Vf = final tapped volume

Carr's index

- The compressibility index of granules was determined using Carr's compressibility index, as-

$$\text{Carr's index} = \frac{(\text{Tapped density} - \text{Bulk density}) \times 100}{\text{Tapped density}}$$

Tapped density

Hausner's ratio

- The Hausner's ratio was determined using the following formula:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

FORMULATION AND EVALUATION OF FAMOTIDINE TABLETS [17]**Formulation of Famotidine Tablets**

Four batches of the tablet [18] containing 20 mg famotidine were prepared. The batches contained guava starch as binders [19] respectively in concentrations of 2, 4, 6, and 8% w/w. carboxy methyl cellulose used as the disintegrant [20] in 7.5 % with 0.5% magnesium stearate as lubricant.

Table 1: Formulation of famotidine tablet

| S. No. | Ingredient | Category | Amount mg/tab |
|--------|------------|----------|--------------------|
| 1 | Famotidine | Active | 20 |
| 2 | Lactose | Diluents | Variable (153-140) |

| | | | |
|---|----------------------------------------|--------------|-----------------|
| 3 | Sodium carboxy methyl cellulose (7.5%) | Disinterants | 15 |
| 4 | Guava Starch (2-8%) | Binder | Variable (4-16) |
| 5 | Talc (2.5%) | Glidant | 5.0 |
| 6 | Magnesium stearate (1.5%) | Lubricant | 3.0 |
| 7 | Total Wt. | | 200 |

Wet granulation and compression

Wet granulation method [21] was used for the preparation of tablets. The calculation was made for 30 tablets in each batch. Accurately weighed quantities of famotidine, lactose and sodium carboxymethyl cellulose were mixed in a mortar and passed them through sieve # 44. Then appropriate quantity of starch mucilage of various concentrations (2, 4, 6 and 8% w/w) was added as granulating agents and mixed for 20 min in a mortar until wet mass was formed. The damp mass was sieved with sieve no. # 22 and dried at 50°C in an oven for 6 hrs. The dried granular mass was passed through sieve no. # 44 to obtain uniform sized granules. Then in different batches of the granules calculated amount of the disintegrant were mixed. Now added the magnesium stearate and talc in the granules and compressed the tablets by single punch machine.

EVALUATION OF TABLETS [22,23]

- **Hardness test**

Hardness testing was carried out by using Monsanto hardness tester as per procedure given in I.P. Five tablets were selected at random from each batch to measure the hardness. Then the mean hardness was calculated for each batch. The value of hardness was expressed in kg/cm².

- **Weight uniformity test**

Twenty tablets from each batch were selected randomly and weight individually using a analytical balance. Then their mean weights were calculated.

- **Friability test**

Friability testing was carried out by using Roche friabilator as per procedure given in I.P. 10 tablets were taken and the weight was determined. Then they were placed in the friabilator and allowed to make 100 revolutions at 25 rpm. The tablets were then dusted and reweighed. The percentage weight loss was calculated.

- **Disintegration Test:**

The *in-vitro* disintegration test for all the formulations were done as per official method prescribed in I.P. for uncoated tablets. Disintegration medium used was 900 ml of 0.1 N HCl maintained at temperature between 37°C throughout the experiment. Five tablets selected at random from each batch were placed one in each of the cylindrical tubes of the basket. The time taken for each tablet to break up into small particles was recorded. Mean disintegration time was calculated for each batch.

- **Dissolution studies**

Dissolution studies [24] were performed as per procedure given in I.P. The test is performed by using USP-II dissolution apparatus. 900 ml of 0.1N HCl, pH 1.2 was used as dissolution medium. The temperature of medium was 37±2°C throughout the experiments. The speed of rotation was 100 rpm. The samples were withdrawn at 10, 20, 30, 40, 50 and 60 min. by replacing equal amount of fresh dissolution medium. Then sample were analysed using U V Spectrophotometer and % cumulative drug release was calculated.

RESULTS

The extracted starch shows all the properties comparable to known standard starch. Then the starch was evaluated. Table-1 shows all the characteristics properties of guava starch powder. The tablets of famotidine prepared with guava starch [25] ,used as

binder, were evaluated [26] for different parameters such as hardness, weight variation, friability, disintegration time and *in-vitro* dissolution study. The evaluation parameters [28] of tablets are shown in table-3. The average weight variation of the formulated tablets was found to be within acceptable limits. The hardness of the tablets increased with the increase in binder concentration. The friability was found to be decreased as the binder concentration increases. The friability of first batch was exceeding the acceptable friability limits (more than 1%) but the friability of tablets containing more than 2% of binder was within limits. The disintegration time, were found to be increased with the increasing concentration of cucumber starch. The dissolution study shows the 4 % conc. of binder shows maximum drug release 83.54% after 1 hr as shown in (Table 4).

Table 2: Characterization of Starch [15, 16]

| S. No | Properties | Observation |
|-------|--------------------------------------------------|----------------|
| 1. | Identification test (Color with I ₂) | Black |
| 2. | Starch color | Cream to brown |
| 3. | Particle size (μ) | 8.68 |
| 4. | % Yield | 53 |
| 5. | Paste clarity (%) | 50.4 |
| 6. | Moisture content (%) | 2.56 |
| 7. | Swelling capacity (%) | 4.1 |
| 8. | Ash value (% w/w) | 0.26 |
| 9. | Bulk density (g/ml) | 0.775 |
| 10. | Tapped density (g/ml) | 0.89 |
| 11. | Carr's index (%) | 12.5 |
| 12. | Hausner's ratio | 1.14 |
| 13. | Angle of repose | 11.44 |
| 14. | Flow properties | Excellent |

Table 3: Evaluation of famotidine tablets with guava starch

| S. No. | Parameter | Binder concentration | | | |
|--------|-------------------------------------------|----------------------|------------|------------|------------|
| | | 2% | 4% | 6% | 8% |
| 1 | Hardness (kg) | 4.3±0.11 | 4.5±0.08 | 5.8±0.06 | 6.0±0.09 |
| 2 | Weight variation (gm) | 198 ±0.55 | 205 ±0.66 | 207±0.24 | 202±0.34 |
| 3 | Friability (%) | 1.4±0.25 | 0.99±0.28 | 0.84±0.54 | 0.76±0.41 |
| 4 | Thickness (mm) | 4.58±0.28 | 4.57±0.45 | 4.48±0.34 | 4.59±0.26 |
| 5 | Disintegration time (min.) | 3.5±0.22 | 4.0±0.80 | 6.5±0.90 | 7.4±0.60 |
| 6 | <i>In vitro</i> drug release (after 1 hr) | 70.43±0.12 | 81.84±0.15 | 65.47±0.15 | 58.65±0.31 |

Note: Results have been expressed as mean ± S.D. (n = 3).

Table 4: *In vitro* dissolution studies of famotidine tablets with guava starch

| S.No. | Time (min.) | Percentage cumulative drug release | | | |
|-------|-------------|------------------------------------|------------|------------|------------|
| | | 2% | 4% | 6% | 8% |
| 1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 2 | 10 | 11.23±0.09 | 15.12±0.11 | 10.11±0.15 | 8.54±0.41 |
| 3 | 20 | 21.21±0.04 | 28.02±0.45 | 18.18±0.13 | 15.90±0.11 |
| 4 | 30 | 32.13±0.45 | 39.27±0.39 | 27.09±0.56 | 26.56±0.47 |
| 6 | 40 | 42.04±0.19 | 55.15±0.44 | 39.38±0.41 | 33.21±0.15 |
| 7 | 50 | 61.05±0.14 | 75.04±0.23 | 57.72±0.26 | 48.89±0.12 |
| 8 | 60 | 73.03±0.12 | 83.54±0.15 | 69.47±0.15 | 62.65±0.01 |

Note: Results have been expressed as mean ± S.D. (n = 3).

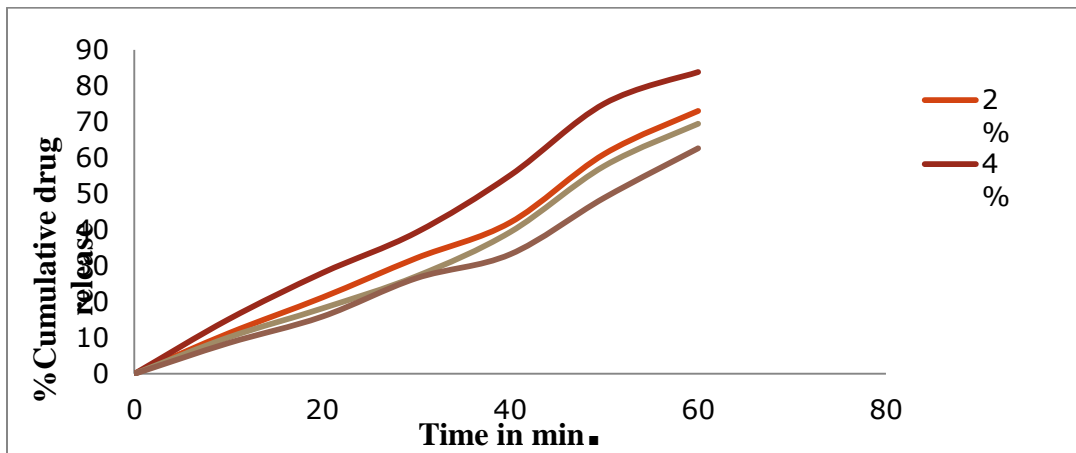


Figure 1: *In vitro* release profile of famotidine tablets

CONCLUSION

From the results of following study it was concluded the guava starch showed significant binding properties. Hence it can be used as tablet binder in pharmaceutical formulations and serve as alternatives for the production of industrial products.

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