Studies On The Tabletting Characteristics Of Paracetamol Tablets Using Mucilage Extracted From *Dioscorea Alata*


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ABSTRACT

The aim of this study was to evaluate the binding efficiency of mucilage extracted from *Dioscorea alata* (water yam) by comparing it with two established binders. *Dioscorea alata* mucilage (DA) was extracted from the tuber via maceration followed by precipitation of the viscous fluid with acetone. The extract was dried at 60°C for 25 min and characterized. It was then used to make binding solution of varied concentrations ranging from 2 to 20%. Paracetamol granules were produced by wet granulation, which were compressed into tablets. The same was done using hydroxypropyl methyl cellulose (HPMC) and acacia gum (AC) as binders. Some tests carried out on granules include bulk and tapped densities while tests for tablets include hardness, friability, disintegration time and dissolution rate. The Carr’s index for the different granules ranged from: 19.23 to 35.29 (HPMC), 17.39 to 44.64 (AC), 19.23 to 39.62 (DA). The Hausner’s coefficient were 1.25 to 1.55 (HPMC), 1.21 to 1.81 (AC), 1.11 to 1.66 (DA). The Carr’s index and Hausner’s coefficient decreased with increase in binder concentration. Paracetamol tablets produced using DA had lower friability values (0.71 to 1.02%) and faster disintegration times (0.53 ± 0.11 to 6.16 ± 2.14 min) than those produced with acacia and HPMC. The Physicochemical properties of paracetamol granules and tablets produced using DA was comparable with those of acacia and HPMC. *Dioscorea alata* mucilage has good binding properties and hence can be used as a binder in the formulation of tablets especially those with poor compressibility.

Key words: *Dioscorea alata*, HPMC, acacia gum, binder, mucilage, paracetamol tablets

INTRODUCTION

Binders are pharmaceutical excipients used in the production of pharmaceutical tablets. Their role is to hold the ingredients in a tablet together. Binders ensure that tablets and granules can be formed with required mechanical strength (Aulton, 2007). Examples of binders used in pharmaceutical formulations are starches such as maize starch; modified cellulose such as microcrystalline and hydroxypropyl methyl cellulose; proteins such as gelatin; and partly synthetic polymers such as polyvinylpyrrolidone (PVP), (Cacace, 2011).

Natural polysaccharides are widely used in the pharmaceutical and food industry as excipients and additives due to their low toxicity, biodegradability, availability and low cost (Jani *et al.*, 2009 Deogade *et al.*, 2012). Major disadvantages of natural gums and mucilages are microbial contamination, batch to batch variation, uncontrolled rate of hydration, and reduced viscosity on storage (Kottke and Edward, 2002). Some synthetic polymers have the
disadvantage of being expensive, highly toxic, cause environmental pollution during synthesis and cause adverse side effects on ingestion (Kottke and Edward, 2002; Deogade et al., 2012).

*Dioscorea alata* (Diocoreaceae) commonly known as water yam is widely cultivated in West Africa (Coursey, 1967). It is a readily available source of starch. This has led to research works being done on its starch including its starch components (Okunlola and Odeku, 2008, 2009). However, little is known of the extraction and use of its mucilage as a tablet binder in pharmacy. The objective of this work was therefore to investigate the binding properties of *Dioscorea alata* mucilage (DA) and compare these properties with those of acacia gum (AC) and hydroxyl propylmethyl cellulose (HPMC).

**MATERIALS AND METHODS**

*Dioscorea alata* (water yam) tubers were purchased from a local market in Benin City, Nigeria. Acetone (Sigma-Aldrich, Germany), Sodium metabisulphite (BDH Chemicals Ltd Poole, England), Hydrochloric acid (BDH Chemicals Ltd Poole, England), and dried silica gel. Paracetamol BP, Maize starch BP, Microcrystalline cellulose (undried Avicel PH101) was a gift sample from May and Baker Plc Lagos, acacia gum powder and Hydroxypropyl methylcellulose powder (HPMC) (BDH Chemicals Ltd Poole, England).

**Extraction of the Dioscorea alata mucilage**

The extraction of the mucilage was carried out by a modification of the method of Tavakoli et al., 2004. Briefly, the skin of the yam tuber was peeled off. The tuber was then cut into small pieces and weighed. The pieces of yam were washed with distilled water and 500 g of the yam was blended in 1.5 L of distilled water containing 0.33% of sodium metabisulphite (to prevent oxidation and discolouration) using a blender (Osterizer, USA). The slurry produced was manually strained. The cloudy suspension was allowed to stand and the clear fluid on top was slowly decanted into another container. The mucilage was precipitated from the supernatant solution using acetone in the ratio of 2 parts of decanted fluid to 1 part of acetone (Tavakoli et al., 2004). The precipitated fluid was sent though a spray dryer which condensed it. The fluid was then oven dried at 60°C in glass plates for about 25 min. The dried crust formed was then scraped off the glass plate. The scraped powder obtained was then put in an air tight jar containing sacs of dry silica.

**Preparation of Granules**

Wet granulation method was used in the preparation of the granules. Paracetamol powder, Microcrystalline cellulose (Avicel®) (10% w/w), and maize starch (5% w/w) were intimately mixed in a mortar. The various concentrations of DA binder solution were added to produce 6 batches of paracetamol (PCM) granules (see Table 1). The DA solution was added slowly till the desired consistency of the mix was obtained. The mix produced was sieved though a 2.0 mm mesh and then put in the oven to dry at 60°C (Ngwulaka et al., 2010). The dry granules were then passed though an 850 μm sieve. Paracetamol granules were also made with HPMC and acacia binder solutions with the same concentrations as DA. The granules were subsequently characterized before compression into tablets.
Table 1: Formula for Paracetamol granules using the various binder solutions

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Quantity Per Tablet (mg)</th>
<th>Quantity (g) Per Batch (50 Tablets)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paracetamol powder</td>
<td>500.0</td>
<td>25.0</td>
</tr>
<tr>
<td>Microcrystalline cellulose (Avicel® (10% w/w))</td>
<td>50.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Maize starch (10% w/w)</td>
<td>50</td>
<td>2.5</td>
</tr>
<tr>
<td>Binder (DA or HPMC or AC at 2, 5, 7, 10, 15, and 20% w/v)</td>
<td>q.s</td>
<td>q.s</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Talc</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

DA- Dioscorea alata mucilage, HPMC-Hydroxypropyl methyl cellulose, AC- Acacia gum

Evaluation of granules
Compressibility characteristics of the paracetamol granules were evaluated using the following parameters; bulk and tapped densities, Hausner’s quotient, Carr’s compressibility, packing fraction and porosity. Hausner’s quotient and Carr’s compressibility index used to determine the flow and compressibility properties of granules were obtained from equations 1 and 2 (Mohammadi and Harnby, 1997):

\[
\text{Hausner’s quotient} = \frac{\text{Tapped density}}{\text{Bulk density}} \quad \ldots (1)
\]

\[
\text{Carr’s compressibility} = \frac{\text{Tapped density - Bulk density}}{\text{Tapped density}} \times 100/1 \quad \ldots (2)
\]

Preparation of tablets
The tablets were produced using a single punch tabletting machine (type F3, Manesty Machines Ltd, England) at 30 units of arbitrary load. All the tablets were stored in air tight container at ambient temperature in a dessicator prior to evaluation.

Evaluation of the batches of tablets
Properties of tablets investigated include crushing strength, friability, disintegration time and dissolution rate.

Crushing strength
A tablet hardness tester (Thermonic, Model CDHT-200, USA) was employed to determine the mechanical strength of the tablets. The average force required to crush the tablets from each batch was obtained.

Friability testing
To evaluate the degree of friability of the tablets from each batch, ten tablets were randomly selected, dusted and weighed. The tablets were placed in a Roche friabilator (Erweka Gmbh, Germany) and subjected to its tumbling actions at 25 revolutions per minute for four minutes. Afterwards, the tablets were once again dusted and reweighed to determine the percentage loss of weight (USP, 2004). The Percentage friability was determined using equation 3.

\[
\text{Friability} (\%) = \left( \frac{\text{Initial Total weight of tablets} - \text{Final Total weight of tablets}}{\text{Initial Total weight of tablets}} \right) \times 100 \quad \ldots (3)
\]
Disintegration studies on the tablets

Six tablets from each batch were utilized for disintegration studies in distilled water at 37°C using an Educational Sciences Disintegration Apparatus (Es Eagle Scientific Limited, Nottingham, United Kingdom). The disintegration time was taken to be the time no granule of any tablet was left on the mesh of the apparatus (BP, 2003).

In vitro drug release studies

In vitro drug release studies were undertaken using USP type 2 apparatus (paddle method). The dissolution medium was 900 ml of 0.1 N HCl at 37°C for 1 h to simulate the gastric medium where the tablets will disintegrate. In all experiments, 5 ml of sample was withdrawn at 10, 15, 20, 30, 45, 60 min intervals and replaced with fresh medium to maintain sink condition. Samples were filtered and assayed with a UV spectrophotometer at 244 nm (BP, 1980).

Statistical analysis

The data obtained were entered into Microsoft Excel® database. Inferential statistics was done using Microsoft Instat version (3) statistical package. Differences in means of variables were determined using Student t-test. A p-value < 0.05 was considered significant.

RESULTS AND DISCUSSION

Properties of granules

Wet granulation is a pharmaceutical process of tabletting which provides better uniformity of content, controls product bulk density as well as compaction (Faure et al., 2001). Furthermore, it improves flow and handling, appearance, mixture’s resistance to segregation and reduces variation in tablet dissolution (Westerhuis and Coenegracht, 1997; McConville et al., 2004). The type of binder used in granulating influences the properties of the granules as well as the quality of the tablets produced (Becker et al., 1997).

Tapped density is an important experimentally determined value to those industries where powder packing is a critical process parameter, particularly pharmaceuticals (Foster and Leatherman, 1995). The values of the tapped density of all the paracetamol granules tested were higher than the bulk density values. This showed that the granules had good compaction characteristics (Foster and Leatherman, 1995). There was no statistical significant difference between the values (p > 0.05) (Table 2).

Granules prepared using 2% and 5% DA and AC exhibited poor flow with Carr’s Index > 25%. While those prepared using 10, 15 and 20% DA and AC exhibited good flow properties with Carr’s index between 15 and 25%. All the granules made with HPMC, except 2% HPMC, had a Carr’s index between 15% and 25%. Hausner’s ratio was < 1.25 for DA at 10, 15, and 20% concentrations; Hausner’s ratio for HPMC was > 1.25 for all concentrations except 7 and 10%. Hausner’s ratio for the granules made with Acacia decreased steadily with 7, 10, 15, and 20% having a value < 1.25. There was no statistical significant difference between the values (Table 3).

Tablet properties

Friability is a mechanical property of a tablet with compendial (USP, 2004) specification of not more than 1%. While crushing strength test is a test of bulk deformation of the tablet. The crushing strength test shows the ability of tablets to withstand pressure or stress during handling, packaging and transportation (Aulton, 2007). It is the property of a tablet that is measured to assess its resistance to permanent deformation. Paracetamol tablets containing 10% DA gave the highest value of 1.02%.
Table 2: Bulk and Flow properties of Paracetamol granules prepared using DA, HPMC, and AC. Results are mean ± Sd.

<table>
<thead>
<tr>
<th>Binder Conc. (%w/v)</th>
<th>Bulk Density (g/cm³)</th>
<th>Tapped Density (g/cm³)</th>
<th>Carr’s index (%)</th>
<th>Hausner’s Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>DA</td>
<td>HPMC</td>
<td>AC</td>
<td>DA</td>
<td>HPMC</td>
</tr>
<tr>
<td>2</td>
<td>0.40 ± 0.04</td>
<td>0.43 ± 0.01</td>
<td>0.39 ± 0.04</td>
<td>0.67 ± 0.02</td>
</tr>
<tr>
<td>5</td>
<td>0.39 ± 0.04</td>
<td>0.45 ± 0.02</td>
<td>0.45 ± 0.03</td>
<td>0.57 ± 0.04</td>
</tr>
<tr>
<td>7</td>
<td>0.50 ± 0.03</td>
<td>0.47 ± 0.02</td>
<td>0.44 ± 0.02</td>
<td>0.55 ± 0.01</td>
</tr>
<tr>
<td>10</td>
<td>0.43 ± 0.02</td>
<td>0.45 ± 0.01</td>
<td>0.44 ± 0.01</td>
<td>0.53 ± 0.02</td>
</tr>
<tr>
<td>15</td>
<td>0.47 ± 0.02</td>
<td>0.46 ± 0.02</td>
<td>0.53 ± 0.01</td>
<td>0.51 ± 0.01</td>
</tr>
<tr>
<td>20</td>
<td>0.49 ± 0.01</td>
<td>0.44 ± 0.01</td>
<td>0.52 ± 0.01</td>
<td>0.62 ± 0.01</td>
</tr>
</tbody>
</table>

Table 3: Friability and Hardness Values of Paracetamol Tablets Compressed Using DA, HPMC and the AC gum

<table>
<thead>
<tr>
<th>Binder Conc. (% w/v)</th>
<th>Friability</th>
<th>Hardness (Kg)</th>
<th>Disintegration Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DA</td>
<td>HPMC</td>
<td>AC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0.98</td>
<td>1.63</td>
<td>1.60</td>
</tr>
<tr>
<td>5</td>
<td>0.84</td>
<td>1.3</td>
<td>0.84</td>
</tr>
<tr>
<td>7</td>
<td>0.79</td>
<td>1.28</td>
<td>1.28</td>
</tr>
<tr>
<td>10</td>
<td>1.02</td>
<td>0.96</td>
<td>0.95</td>
</tr>
<tr>
<td>15</td>
<td>0.77</td>
<td>0.96</td>
<td>0.95</td>
</tr>
<tr>
<td>20</td>
<td>0.71</td>
<td>0.97</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Table 2: Bulk and Flow properties of Paracetamol granules prepared using DA, HPMC, and AC. Results are mean ± Sd.
DA- Dioscorea alata mucilage, HPMC-Hydroxypropyl methyl cellulose, AC- Acacia gum
Tablets containing other amounts of DA met the compendial specification for friability with values < 1% (USP, 2004). Tablets made with HPMC at 2, 5 and 7% mucilage concentration had friability values of 1.6%, 1.3%, and 1.3%, respectively, while tablets made with 10%, 15%, and 20% HPMC met compendial specification with friability values of 0.96%, 0.96%, and 0.97%, respectively. The percentage friability of paracetamol tablets containing HPMC and AC were similar. There was no statistical significant difference between the values (p > 0.05).

All the tablets passed the crushing strength test with values higher than 4 Kg (Allen et al., 2004). The HPMC paracetamol tablets gave the highest values, with the 20 % w/v paracetamol tablets giving hardness values of > 12.5 Kg. The tablet strength as indicated by the crushing strength (hardness) of the tablets was seen to increase with increase in concentration of the binder (Table 4). It has been suggested that the mechanical strength is governed by the interparticulate bonding mechanisms and the area over which these bonds interact (Nystrom et al., 1993). The increase in tablet hardness with increase in binder concentration could be attributed to more particle-particle contact points of the binding agents as well as the drug particles which help to create more solid bonds and also due to the formation of thicker adhesive coats around the particles (Allen et al., 2004). There was no statistical significant difference among the values for the different binders (p > 0.05).

Effect of binder type and concentration on disintegration time

The rate of disintegration is influenced by the rate of influx of water into the tablets which is also dependent on the porosity of the tablets. When the porosity is high, disintegration is hardly influenced by tablet formulation; otherwise, disintegration will be affected by the excipients (Bi et al., 1999). Only tablets made with DA at all its different concentrations met the BP specification for disintegration which states that uncoated tablets should disintegrate within 15 min. Tablets produced with HPMC and acacia at all concentrations except 20% w/v disintegrated within 15 min. Tablets containing 20% HPMC disintegrated after 30 min (Table 3). It was observed that the disintegration times of all the formulated tablets increased with an increase in binder concentration (Table 3). This could be attributed to an increment in the number and strength of interparticulate bonding. Formation of a thick film of gum mucilage as the tablet comes into contact with the disintegrating fluid with the film being converted into a mucilaginous viscous barrier could also contribute to the result seen (Adetogun and Alebiowu, 2009).

In vitro drug release studies

The drug release profiles of paracetamol tablets made with DA was comparable with those prepared with HPMC and AC. All the DA tablets attained over 70% release, with 2% having up to 99% drug released, and 5, 7, and 10% had 98% drug released after 30 min. All the tablets made with HPMC met BP specification for dissolution rate. All the tablets made with HPMC except for those containing 20% HPMC release their content within 15 min. Tablets prepared with 20% HPMC had 92% release after 30 min and 100% release at 45 min (Figure 3). All the tablets prepared with AC had over 95% dissolution within 30 min. (Figure 4). It was observed that there was an increase in dissolution rate with decrease in binder concentration. Dissolution plays an important role in the bioavailability and therapeutic efficacy of a drug in the body. The factors that affect the dissolution rate include type and concentration of binder, hardness.
CONCLUSION

Paracetamol granules prepared with *D. alata* mucilage had satisfactory compressibility characteristics when compared with paracetamol granules made with HPMC and AC. The physical characteristics of tablets made with *D. alata* mucilage were also comparable to those made with HPMC and AC. Paracetamol tablets produced with DA had fast disintegration time and a satisfactory dissolution rate. This suggests that *D. alata* mucilage with further research will be a suitable binder. Therefore, the dried mucilage of *Dioscorea alata* tuber can be used as a pharmaceutical tablet binder as a suitable substitute for the presently existing binders.

REFERENCES


British Pharmacopeia (1980) Published by The Stationery Office Crown Copyright UK Vol I, p 326


Figure 1a, b and c: Effect of Binder concentration on the dissolution profile of paracetamol tablets (key: (a) AC-Acacia gum; (b) HPMC- Hydroxypropyl methyl cellulose, and (c) DA- *Dioscorea alata* mucilage.


