POTENTIAL OF *BRACHYSTEGIA EURYCOMA* GUM IN AMELIORATING BRITTLE FRACTURE DURING TABLETING.

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**ABSTRACT**

The aim of the present study is to investigate the potential of *Brachystegia eurycoma* gum in ameliorating brittle fracture (i.e., lamination and capping) a problem often encountered during tableting. Granules of metronidazole (test drug) were prepared by wet granulation technique using *Brachystegia eurycoma* or acacia gum at concentrations of 2.5, 5.0, 7.5 or 10%w/w. The resulting granules were evaluated for packing and flow properties. Granules were compressed into tablets with and without a centre hole (as in- built defect) using a compression load of 2.0 arbitrary unit on the load scale. The tablets were evaluated for tensile strength and the data was used to calculate the brittle fracture index (BFI). The compressibility index which is a measure of ease of compaction of the granules upon tapping was < 23.5% while all granules were free flowing with angle of repose < 36.9°. Increase in binder concentration led to an increase in 
P_f and 
T values irrespective of the type of the gum binder used in the formulations. Generally, increasing the binder concentration at a given compression load resulted in a decrease in the brittle fracture tendency of the tablets. For instance, at a binder concentrations of 2.5% w/w the BFI for *Brachystegia eurycoma* and acacia gum were 0.13 and 0.10 respectively while their corresponding values at binder concentration of 7.5% w/w were 0.06 and 0.08. The study has shown that *Brachystegia eurycoma* gum is an effective binder that produces harder tablets with low brittle fracture tendency.

Key words: *Brachystegia eurycoma*, Tableting, brittle fracture index, Compressibility index.

**INTRODUCTION**

Brittle fracture refers to the lamination or capping of tablets which occurs at the point of ejection from the die during their manufacture (Uhumwangho et al., 2009). This phenomenon is associated with the presence of entrapped air pockets arising from high speed of compression such that the air in the die hardly has time to escape before compaction is effected. Air pockets may also arise from the fracture of brittle materials in the tablet formulation during compression or due to elastic recovery of elastic materials upon withdrawal of the upper punch pressure. The brittle fracture tendency was provided by Hiestand et al (1977), who applying the crack theory of Griffiths considered that cracks will propagate from the edge of a void or low density region in a compact when the stress at the edge of the void is three times over the stress in the bulk of the compact.

*Brachystegia eurycoma* Harmos (synonym *B. spiceaformis*) family *leguminosae caesalpinioideae* is a woody plant commonly found in the forest zone in southern Nigeria and Cameroun. The tree is about 35m tall, r. It is commonly called Achi (Igbo), Akalado or Eku (Yoruba), Akpakpa or Apaupan (Ijaw), Okwen (Edo), Okung (Efik) (Ikegwu et al., 2010). The tree bark has found application as fibres, food wrappers and has been used to make containers. The seeds have a hard coat, and is used as a soup condiment, flavour-
Osazuwa & Uhumwngbo

ing agent and for soup thickening in south eastern Nigeria. The seeds are a good source of bioactive compounds comprising flavonoids, alkaloids, phenolic compounds, sapo-
nins and tannins, protein, carbohydrate, lipids and fiber. The seeds are also a good source of water soluble vitamins hence plays a major role in the nutritional status of consumers (Uhegbu et al., 2009). Previously, Brachystegia eurycoma seed gel in combination with snail mucin and honey has been investigated for the treatment of wounds (Adikwu and Enebeke, 2007) but its potential in ameliorating brittle fracture tendency has not been exploited.

Binders are added to tablet formulation to impart plasticity during compression and thus ameliorate brittle fracture tendency within the tablet (Itiola and Pipel, 1986, 1991; Uhumwngho and Okor, 2004). The extent to which this fracture problem can be ameliorated depends in part on the type and concentration of binder used in the tablet formulation. Hence, in the present study, we have investigated the potential of some gum binders on the brittle fracture tendency of metronidazole tablets. Production of these tablets is frequently prone to this brittle fracture problem. Therefore, the outcome of this study will permit the selection of a suitable binder and concentration which is locally available for the production of metronidazole tablets.

MATERIALS AND METHODS

Materials

The test drug was metronidazole (Baif Laboratories Limited, Pune, India) and it was received as a gift sample from Sam Pharmaceutical Nigeria Ltd. Acacia gum (Kapadia gum Industries Pvt. Ltd Mumbai, India) was used as binder in varying concentration (2.5%, 5.0%, 7.5% and 10% w/w) for comparative study. Magnesium stearate (S.D. Fine Chemicals Ltd., Mumbai, India) was used as lubricant at concentration of 1.0 % w/w. All other reagents used were of analytical grade.

Extraction of Brachystegia eurycoma gum:

Undehulled Brachystegia eurycoma seeds were purchased from a local Market in Edo state, Nigeria. The dried seeds were roasted and soaked in 1500 mls of distilled water for 48 hours and macerated to remove the shells. The dehulled seeds were dried completely, milled and weighed accordingly. Five hundred (500) gram of the milled seed was defatted with chloroform-methanol mixture in the ratio of 2:1. At intervals of 1h, the mixture was shaken to enhance proper defatting. The mixture was sieved with a porcelain cloth to remove the fat. The residue (Brachystegia eurycoma powder) was sundried for 1h to allow complete evaporation of the chloroform-methanol. Sufficient quantity of hot water was then poured in the Brachystegia eurycoma powder in a clean bowel and triturated severally and left for 24 h. The paste obtained was manually strained through a white muslin cloth to extract the gum. The filtrate was treated with acetone in the ratio 1:1 to precipitate the gum. The precipitate formed was dried under the oven at 50°C for 3 h. The dry flakes were pulverized using a electric blender and stored in an air tight dessicator containing silica gel.

Measurement of viscosity of the gum:

The viscosities of 2.5%, 5.0%, 7.5% and 10% w/w of Brachystegia eurycoma gum or acacia were determined using Brookfield synchro-electric viscometer (model number NDJ-5S). The dispersion (50 ml) was poured into a clean beaker and the viscosity measured using spindle number 3. The viscosity for each concentration was measured and the readings recorded. This determination was done in triplicate.

Granulation technique:

Granules were formed by wet massing a sample of metronidazole powder (100 g) with a determined volume of the Brachystegia eurycoma or acacia gum. The wet mass was screened through sieve (aperture size, 1000 µm) and then dried in a hot air oven (Kotterman, Germany) at 50°C for 0.5 h, to a moisture content of 1.9±1.0 % w/w. This was further screened through a 750 µm sieve. Based on the volume of gum used in the wet massing the final binder concentration in the granules were 2.5, 5.0, 7.5 and 10% w/w.

Determination of packing and flow properties of granules:

These were determined by
measuring the bulk density (BD) and tapped density (TB) using standard procedures (Richards, 1972). From the data compressibility index (CI) values of the granules were calculated as $CI = \{TB-BD\}/TB\times100\%$ (Carr, 1965). The flowability of the granules was determined by measuring the angle of repose formed when a sample of the granules (20g) was allowed to fall freely from the stem of a funnel to a horizontal surface (Travers, 1972). The angle of repose ($q$) was calculated using the expression: $q = \arctan H/r$ (1)

**Tableting technique:** Flat faced tablets of mean weight 400±6 mg and diameter, 12.5 mm were produced using a single punch machine (Karl Kolb) at a compression load of 2, arbitrary units on the load scale. In each case the maximum load was held on the tablet for 30 s before releasing it to allow for consolidation of the tablet. Also, the punch and die surfaces were lubricated with a 1% dispersion of magnesium stearate (BDH) in chloroform to prevent sticking and hence allow easy ejection of the tablets from the die. In order to form tablets with a center hole (needed for estimation of BFI) lower punches with a center pin and upper punches with a center through hole (diameter, 0.6 mm) were used in the compression process. Details of the procedure have been described previously (Uhumwangho and Okor, 2004; Uhumwangho et al., 2009).

**Tensile strength (T):** The load (P) needed to fracture the tablet was determined by diametrical compression with a Monsanto hardness tester (Brook and Marshall, 1968). Ten tablets were used in each determination. T is the stress needed to fracture a tablet by diametral compression. It is given by the expression (Fell and Newton, 1970):

$$T = 2P/\pi rt$$
(2)

where $P$ is the crushing load that causes tensile failure of a tablet of diameter, D and thickness t. The mean values of the fracture load were used to calculate the T values for tablets of the various formulations.

**Brittle fracture index (BFI):** This is a measure of the tablet tendency to laminate or cap during manufacture. It is given by the equation (3) below developed by Hiestand et al. (1977), thus:

$$BFI= 0.5 \left( \frac{T}{T_0} - 1 \right)$$
(3)

where $T_0$ and $T$ are the tensile strength of tablets with and without a centre hole, respectively. The fracture tendency is considered high when the BFI value is $\geq 0.5$.

### Determination of tablet packing fraction ($P_t$): This is a measure of the degree of consolidation of the tablet upon compaction. $P_t$ values are obtained from the expression (4):

$$P_t = \frac{w}{\pi r^2 \rho}$$
(4)

where: $w$ is the mean weight of tablets of radius ($r$), and thickness ($t$), $\rho$ is the particle density of the powder from which the tablets were made, in this case metronidazole powder. The $\rho$ value of metronidazole granules was determined to be 1.41 g.cm$^{-3}$ using a fluid (liquid paraffin) displacement method as described previously (Sugita et al., 1995). The mean weight of ten tablets were determined accurately to 0.001 g using an electronic balance (Mettler Toledo B154, Switzerland) while their mean thickness and diameter were measured accurately to 0.01mm using a digital micrometer (Model GMBH 500 –U- Poland).

### RESULTS AND DISCUSSION

**Packing and flow properties of the granules**

The bulk density, tapped density and compressibility index values of the granules are presented in Table 1. It was observed that there was no statistically significant difference in the densities with increase in concentrations of the gum binders ($p >0.05$). The compressibility index which is a measure of ease of compaction of the granules upon tapping was $< 23.5\%$ this was irrespective of the type of gum binder and concentration used in the tablet formulation (See Table 1). All granules were free flowing with angle of repose $< 36.9^0$.

**Table 1: The flowability of the granules**

<table>
<thead>
<tr>
<th>Concentration of gum (%w/w)</th>
<th>Bulk density (g/cm$^3$)</th>
<th>Tap density (g/cm$^3$)</th>
<th>Carr's index</th>
<th>Hausner's ratio</th>
<th>Angle of repose ($^\circ$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Brachystegia eurycoma</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>0.56±0.02</td>
<td>0.71±0.03</td>
<td>21.1</td>
<td>1.27</td>
<td>36.9</td>
</tr>
<tr>
<td>5.0</td>
<td>0.56±0.02</td>
<td>0.56±0.02</td>
<td>10.8</td>
<td>1.12</td>
<td>35.3</td>
</tr>
<tr>
<td>7.5</td>
<td>0.48±0.02</td>
<td>0.56±0.03</td>
<td>14.3</td>
<td>1.17</td>
<td>33.3</td>
</tr>
<tr>
<td>10.0</td>
<td>0.47±0.04</td>
<td>0.60±0.02</td>
<td>21.7</td>
<td>1.28</td>
<td>31.4</td>
</tr>
<tr>
<td><em>Acacia</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>0.53±0.02</td>
<td>0.68±0.01</td>
<td>23.5</td>
<td>1.31</td>
<td>34.9</td>
</tr>
<tr>
<td>5.0</td>
<td>0.58±0.03</td>
<td>0.63±0.02</td>
<td>7.9</td>
<td>1.09</td>
<td>31.8</td>
</tr>
<tr>
<td>7.5</td>
<td>0.50±0.04</td>
<td>0.54±0.02</td>
<td>7.4</td>
<td>1.08</td>
<td>29.7</td>
</tr>
<tr>
<td>10.0</td>
<td>0.48±0.02</td>
<td>0.58±0.03</td>
<td>17.2</td>
<td>1.23</td>
<td>28.9</td>
</tr>
</tbody>
</table>
**Table 1: Physical parameters of the granules**

**Viscosity of the gums**
The viscosity values of the *Brachystegia eurycoma* or acacia gum equilibrated at room temperature 28°C are presented in Figure 1. The results showed that acacia gum were slightly more viscous than *Brachystegia eurycoma* gum although there was no statistically significant differences in their viscosities (p > 0.05). Generally, as the concentration of the different gums increased their viscosities also increased. These differences will determine the binder effectiveness of the gums.

**Fig 1: Effect of binder type and concentration (2.5%, 5.0%, 7.5% AND 10.0% w/w) on the brittle fracture tendency of metronidazole tablet, where AC = Acacia gum and BE = Brachystegia eurycoma gum**

**Effect of binder type and concentration on the degree of consolidation and tensile strengths of the tablets**
The results of the degree of consolidation and tensile strengths of the tablets are presented in Table 2. Generally, increasing the binder concentration at a given compression load resulted in a decrease in the brittle fracture tendency of the tablets (See Table 2). Similar finding has been reported previously (Okor et al., 1998; Uhumwangho et al., 2004). Hence, increase in binder concentration ameliorate brittle fracture tendency of tablets by promoting plastic deformation of particles within the tablet during diametral compression (e.g. by die wall stress). For instance, at a binder concentrations of 2.5% w/w the BFI for *Brachystegia eurycoma* and acacia gum were 0.13 and 0.10 respectively while their corresponding values at binder concentration of 7.5%w/w were 0.06 and 0.08. However, there were no statistically significant differences (p >0.05) between their BFI values.

**Table 2: Effect of binder type and concentration on the brittle fracture tendency of the tablets**

<table>
<thead>
<tr>
<th>Concentration of gum (%w/w)</th>
<th>T (MN/m²)</th>
<th>T₀ (MN/m²)</th>
<th>Pᵣ</th>
<th>BFI</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Brachystegia eurycoma</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5</td>
<td>0.102±0.02</td>
<td>0.08±0.03</td>
<td>0.77</td>
<td>0.13</td>
</tr>
<tr>
<td>5.0</td>
<td>0.121±0.03</td>
<td>0.101±0.02</td>
<td>0.78</td>
<td>0.10</td>
</tr>
<tr>
<td>7.5</td>
<td>0.152±0.01</td>
<td>0.131±0.02</td>
<td>0.79</td>
<td>0.08</td>
</tr>
<tr>
<td>10.0</td>
<td>0.172±0.02</td>
<td>0.156±0.03</td>
<td>0.79</td>
<td>0.05</td>
</tr>
<tr>
<td><em>Acacia</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5</td>
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<td>0.102±0.03</td>
<td>0.78</td>
<td>0.10</td>
</tr>
<tr>
<td>5.0</td>
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<td>0.131±0.01</td>
<td>0.79</td>
<td>0.08</td>
</tr>
<tr>
<td>7.5</td>
<td>0.172±0.03</td>
<td>0.153±0.02</td>
<td>0.80</td>
<td>0.06</td>
</tr>
<tr>
<td>10.0</td>
<td>0.193±0.02</td>
<td>0.182±0.03</td>
<td>0.81</td>
<td>0.03</td>
</tr>
</tbody>
</table>

**CONCLUSION**
The study has shown that *Brachystegia eurycoma* gum is an effective binder that produces harder tablets with low brittle fracture tendency.

**REFERENCES**


Uhumwangho, M.U., Okor, R.S. and Eichie, F.E. (2004). Effect of cation contentof certain ammoniomethacrylate copolymers type A (RL) and B (RS) on their