The hot water extract of a mixture of stem barks of *Anogeissus leiocarpus* and *Prosopis africana* was formulated into tablets using the wet granulation method of massing and screening. The Heckel equation was used to study the compaction characteristics of the extract formulated with lactose (watersoluble) or magnesium carbonate (waterinsoluble) as diluents. Granules prepared using magnesium carbonate were found to exhibit two stages of deformation – an initial fragmentation followed by plastic flow while those formulated with lactose consolidated mainly by plastic deformation. Compressibility profiles of the formulations were affected by the diluent type. Tensile strength of granules formulated with magnesium carbonate was found to increase as the compression pressure increased from 56.6 to 113.2 MN m\(^{-2}\) while the tensile strength of tablets formulated with lactose had its maximum at a compression force of 84.9 MN m\(^{-2}\).

Keywords: *Anogeissus leiocarpus* (*Combretaceae*), *Prosopis africana* (*Mimosaceae*), stem bark extract, diluent, compaction characteristics, Heckel equation, compressibility, tensile strength, granules, tablets

The hot water extract of a mixture of *Anogeissus leiocarpus* (*Combretaceae*) and *Prosopis africana* (*Mimosaceae*) is widely used in the northern part of Nigeria for the treatment and management of asthma. Preliminary investigations of its pharmacological activities justify its use in folk medicine (1). Urgent need for the development of systems and methods for standardization of traditional medicine has led to the formulation of the extract into tablets using the wet granulation method of massing and screening.

Many compaction techniques have been used to characterize the consolidation behavior of pharmaceutical solids (2, 3). However, due to the complexity of the compression process, many of the expressions used were shown to have limitations. A simple and most widely used approach is the analysis of the Heckel plots. Although the Heckel
The equation has limitations, many authors have successfully used it to differentiate between compression by brittle fracture and plastic deformation (4, 5).

The objectives of the present study were: (i) to characterize the consolidation behavior of the *A. leiocarpus/P. africana* extract in combination with two different diluents, lactose (watersoluble) and magnesium carbonate (water insoluble), and (ii) to investigate the influence of compaction pressure on the compact tensile strength.

EXPERIMENTAL

Excipients

Lactose B.P. 200 mesh (Lactose Co, Ltd., New Zealand), magnesium carbonate (BDH, UK) and maize starch B.P. (Hopkins and Williams, UK) were used.

Methods

Preparation of the extract. – Stem bark of *Anogeissus leiocarpus* and *Prosopis africana* was collected, washed with distilled water, sun-dried and milled to a coarse (1000 μm) powder. The powders were then mixed in a 1:1 ratio and soaked in distilled water in a ratio 1:10 mass to volume, boiled on an electric heater for 10 minutes and left to soak for 24 hours at room temperature. The liquid extract was filtered through a calico cloth and concentrated to a ratio of 5:1 using a rotary evaporator. The concentrated filtrate was then transferred into a tray and dried in an oven at 60 °C until dry. The dry extract was pulverized using a mortar and pestle and then passed through a 150-μm sieve.

Preparation of binder mucilage. – Maize starch suspension was prepared in cold distilled water and then added into hot water until a translucent jelly mass was formed. The mass was made up with hot water to give 2.5/5% (m/m) mucilage and allowed to cool to about 40 °C before it was incorporated as a binder.

Preparation of granules. – The wet granulation method of massing and screening was used. The dry extract (40 g) and the diluent (lactose or magnesium carbonate, 60 g) were mixed in a mortar for 5 minutes. Disintegrant (maize starch, 5 g) was added and mixing continued for another 5 minutes. The liquid binder (2.5 and 5% m/m maize starch mucilage) was added to the powder mix in 2-mL portions and mixed with a pestle. The moistened mass was forced through a 1000-μm sieve, dried at 60 °C for 1 h to give a moisture content of 4–6%, determined on an Ultra X moisture balance (August Gronert Co., Germany). The granules were again passed through a 1000-μm screen to break up agglomerates.

Preparation and analysis of compacts. – Compacts equivalent to 630 mg of granules were produced by compressing the granules for 1 min at various compression pressures using a hydraulic hand press (Model C, Carver Inc., USA). Before each compression, the die (10.5 mm in diameter) and the flat-faced punches were lubricated with a 1% (m/V) dispersion of magnesium stearate in ethanol. After ejection, the tablets were stored over silica gel in a desiccator for 24 h to allow for elastic recovery and hardening (6). The compact diameter (*D*) and thickness (*d*) were determined to the nearest 0.01 mm with a
Mitutoyo model IDC-1012 EB micrometer gauge (Mitutoyo Corporation, Japan). The compact diametral crushing strength ($C_S$) was determined using an Eweka hardness tester (model MT, Germany).

The plots constructed according to the Heckel equation (7, 8) were used to characterize the consolidation behavior of the formulations:

$$\ln\left[\frac{1}{1-D}\right] = KP + A \quad (1)$$

where $D$ is the ratio of the density of the powder mass at pressure $P$ to the density of the powder mixture (i.e., relative density). $K$, the slope of the straight portion of the graph, reflects the reduction in porosity or the resistance to volume reduction of granules and $A$ is a constant. The yield pressure, $P_Y$, is usually calculated as the reciprocal of the linear portion of the slope of the Heckel plot. The relative density $D_A$ was calculated from the intercept, $A$, using the equation (9):

$$D_A = 1 - e^{-A} \quad (2)$$

$D_B$, the relative density during the rearrangement phase was calculated from the difference between $D_A$ and $D_0$ (relative density of the granules at nil pressure).

The tensile strength ($T_S$) was calculated from:

$$T_S = \frac{2C_S}{\pi Dd} \quad (3)$$
in accordance with Fell and Newton’s expression (10).

Data analysis

The graphs were plotted and analyzed using the Graphpad Prism™ version 2.0 computer software. The data used to plot the graphs were the mean of three readings $\pm$ SD.

RESULTS AND DISCUSSION

Heckel’s equation has been used to classify powders into three types: A, B and C based on their compaction behaviors (11, 12). Fig. 1a depicts the Heckel plots obtained for the granulations formulated with lactose as diluent. Granules formulated with lactose as diluent with no binder or with 2.5% starch as binder gave a linear relationship at all applied pressures, which is typical of A-type materials. This implies that the granules containing lactose, the plant extract and lower concentrations of binder deformed principally by plastic deformation. There was, however, a change in the mode of deformation with an increase in binder concentration, since the granules formulated with 5% binder gave plots with an initial curved region followed by a linear portion, which is typical of B-type materials. Previous studies had indicated that lactose, when subjected to compaction forces, usually first underwent fragmentation, followed by plastic defor-
This intrinsic deformation characteristic of lactose was therefore modified by the plant extract at lower binder concentrations. On the other hand, granules prepared using magnesium carbonate as diluent (Fig. 1b) exhibited two stages of deformation – an initial fragmentation followed by plastic flow. The decrease in slope at higher pressure indicates a decrease in the rate of densitification as the void spaces between particles decrease.

Yield pressure $P_Y$ is an important indication of granule compressibility and it describes the tendency of the material to deform either by plastic flow or fragmentation (14). In general, a low $P_Y$ value (steep slope) reflects low resistance to pressure, good densification and easy compression. A low $P_Y$ value, however, need not necessarily reflect that the compact has an acceptable tensile strength (15). For both diluents used, the highest $P_Y$ values were observed at a 2.5% binder concentration. Formulations made with lactose as diluent gave higher $P_Y$ values than those with magnesium carbonate either without or with 2.5% binder, indicating that the former granules deformed plastically at lower pressures than the latter ones. The lower $P_Y$ values observed for the formu-
lations with magnesium carbonate as diluent may be due to the fragmentation phase of deformation, which comes as a result of low resistance to compression pressure.

Granules formulated with magnesium carbonate as diluent had lower $D_A$ when compared with those of lactose at all concentrations used. This may be attributed to the differences in particle size and shape (16). Granules formulated with lactose as diluent, being larger in size, would not tend to pack as closely as those formulated with magnesium carbonate as diluent.

For granules formulated with either lactose or magnesium carbonate, $D_0$ was found to increase with an increase in granule size. $D_0$ was also found to decrease with an increase in binder concentration. $D_B$ increased with an increase in binder concentration for granules formulated with lactose as diluent, while there was a decrease in $D_B$ values with an increase in binder concentration for granules formulated with magnesium carbonate.

For granules formulated with either lactose or magnesium carbonate, $D_0$ was found to increase with an increase in granule size. $D_0$ was also found to decrease with an increase in binder concentration. $D_B$ increased with an increase in binder concentration for granules formulated with lactose as diluent, while there was a decrease in $D_B$ values with an increase in binder concentration for granules formulated with magnesium carbonate.

Graphs depicting the pressure-tensile strength profile of compacts formulated with lactose/extract and magnesium carbonate/extract are represented in Figs. 2a and 2b, respectively. All the granules exhibited significant sensitivity to changes in the compaction force. For lactose/extract compacts, tensile strength increased up to 84.8 MN m$^{-2}$ for the whole granule size range. Further increase in compaction force results in a decrease in the compact tensile strength. This can be ascribed to the possibility of the work associated with compaction above 84.8 MN m$^{-2}$ being recovered during elastic relaxation, which results in a weakening of the tablet structure (17). The tensile strength of compacts formulated with lactose increased with decrease in granule particle size. This further confirms that the lactose/extract granules deformed mainly by plastic deformation (18).

For magnesium/extract compacts, earlier found to consolidate by fragmentation as well as by plastic deformation, the tensile strength increased with an increase in compaction pressure from 5.6 to 113.2 MN m$^{-2}$. This can be a result of fragmentation of deformed particles (19), leading to the formation of new potential bonding areas (20). The tensile strength of the magnesium carbonate/extract compacts was found to increase with an increase in the granule particle size. The observed increase in tensile strength

<table>
<thead>
<tr>
<th>Diluent</th>
<th>Starch (binder) (%)</th>
<th>Moisture content, mean ± SD$^a$ (%)</th>
<th>Mean granule size (μm)</th>
<th>$P_Y$ (MN m$^{-2}$)</th>
<th>$D_A$</th>
<th>$D_0$</th>
<th>$D_B$</th>
<th>$K \times 10^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose</td>
<td>0</td>
<td>6.1 ± 0.1</td>
<td>687.5</td>
<td>572.3</td>
<td>0.88</td>
<td>0.33</td>
<td>0.54</td>
<td>1.75</td>
</tr>
<tr>
<td>MgCO$_3$</td>
<td>3.2</td>
<td>3.2 ± 0.1</td>
<td>583.3</td>
<td>294.7</td>
<td>0.87</td>
<td>0.24</td>
<td>0.63</td>
<td>3.39</td>
</tr>
<tr>
<td>Lactose</td>
<td>2.5</td>
<td>5.9 ± 0.1</td>
<td>562.5</td>
<td>1302</td>
<td>0.92</td>
<td>0.28</td>
<td>0.64</td>
<td>0.77</td>
</tr>
<tr>
<td>MgCO$_3$</td>
<td>3.8</td>
<td>3.8 ± 0.1</td>
<td>375.0</td>
<td>610.4</td>
<td>0.83</td>
<td>0.23</td>
<td>0.60</td>
<td>1.64</td>
</tr>
<tr>
<td>Lactose</td>
<td>5.0</td>
<td>5.7 ± 0.1</td>
<td>791.6</td>
<td>257.9</td>
<td>0.90</td>
<td>0.27</td>
<td>0.65</td>
<td>3.87</td>
</tr>
<tr>
<td>MgCO$_3$</td>
<td>4.2</td>
<td>4.2 ± 0.1</td>
<td>875.0</td>
<td>444.7</td>
<td>0.75</td>
<td>0.22</td>
<td>0.54</td>
<td>2.24</td>
</tr>
</tbody>
</table>

*a n = 3*
could be a result of an increased surface irregularity, leading to an increased number of binding surface areas (21).

CONCLUSIONS

A study of the compaction properties of the hot water extract of *Anogeissus leiocarpus* and *Prosopis africana* stem has been performed. From the evidence provided in this study, it can be concluded that the Heckel plot was successfully used to explain the compaction characteristics of the *A. leiocarpus*/*P. africana* formulations. Examination of the compressibility profile suggests the optimum compression pressure of 84.8 MN m⁻² for formulation when lactose is used as a diluent, whereas both compaction and compressibility profiles of the extract were greatly affected by the diluent type. Further work on the formulation studies of *A. leiocarpus*/*P. africana* extract is currently going on in our laboratory.

Acknowledgement. – The authors are grateful to the management of NIPRD for financial support and to Mr. A. Garuba of NIPRD for technical assistance.
REFERENCES

Učinak vrste punila na kompresijska svojstva tableta priređenih iz ekstrakta kore Anogeissus leiocarpus i Prosopis africana

C. Y. ISIMI, R. N. NASIPURI, J. B. OJILE, Y. K. E. IBRAHIM i M. EMEJE

Vodeni ekstrakt smjese kore biljaka Anogeissus leiocarpus i Prosopis africana tabletiran je metodom vlažne granulacije. Pomoću Heckelove jednadžbe proučavana je kompaktnost pripravaka oblikovanih s laktozom (vodotopljivim punilom) i magnezijevim karbonatom (punilom netopljivim u vodi). Granule priređene s magnezijevim karbonatom pokazivale su dva stupnja deformacije – početno fragmentiranje iza kojeg slijedi plastično tečenje, dok se pripravci priređeni s laktozom konsolidiraju uglavnom plastičnom deformacijom. Vrsta punila utjecala je na profil kompresibilnosti pripravaka. Čvrstoća granula priređenih s magnezijevim karbonatom povećava se s povećanjem tlaka za komprimiranje od 56,6 do 113,2 MN m–2, dok je čvrstoća tableta priređenih s laktozom maksimalna ako je tlak za kompresiju 84,9 MN m–2.

Ključne riječi: Anogeissus leiocarpus (Combretaceae), Prosopis africana (Mimosaceae), ekstrakt kore, punilo, kompaktnost, Heckelova jednadžba, kompresibilnost, čvrstoća, granule, tablete

Department of Pharmaceutical Technology and Raw Material Development, National Institute for Pharmaceutical Research and Development, P.M.B. 21, Garki, Abuja, Nigeria

Department of Pharmaceutics and Pharmaceutical Microbiology, Ahmadu Bello University Zaria, Nigeria