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MATERIAL AND TABLETING PROPERTIES OF *AZADIRACHTA INDICA* GUM WITH REFERENCE TO OFFICIAL ACACIA GUM

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Abstract: This study determined the material and tableting properties of *Azadirachta indica* gum (NMG) relative to acacia gum (ACA). The morphological properties were assessed with size and shape factors of aspect ratio, roundness, irregularity and equivalent-circle-diameter. The tableting properties of the gums were determined using compressional characteristics, tensile strength (TS), brittle fracture index (BFI) and crushing-strength-friability/disintegration-time ratio (CSFR/DT). The results suggest that NMG possesses larger, irregular and more elongated particles than ACA. The onset and amount of plastic deformation occurring in NMG was faster and higher, respectively, than in ACA. The result shows that, although ACA tablets were stronger, their tendency to cap/laminate was higher than in NMG tablets. The NMG tablets possess lower DT than those of ACA, while the CSFR/DT result suggests that a better balance exists between the strength and weakness of NMG tablets. The study concluded that NMG can be a useful excipient in tablet formulation.

Keywords: neem gum, acacia gum, tensile strength, brittle fracture index, disintegration, crushing strength-friability/disintegration-time ratio

In the production of pharmaceutical tablets, one or more excipients are needed to facilitate the production of good quality tablets, particularly for active pharmaceutical ingredients (API) that have little or no directly compressible properties. One of these excipients is a binder, which is employed in pharmaceutical tablet formulation to provide adequate mechanical properties by promoting the bonding properties existing between the different components of a powder mix in a formulation (1, 2). Various substances such as starches, celluloses and gums have been employed in pharmaceutical tablet formulations as binders (3). Gums have been used in pharmaceutical solid dosage formulations mainly as binders and directly compressible excipients.

Azadirachta indica gum, which belongs to the family of galactan gums (4) is a very complex condensate of heteropolysaccharides and proteins. The proteins are tightly linked to the polysaccharides, which constitute the major component. Drastic degradation of a smaller gum complex component shows that it contains D-glucose, D-glucuronic acid, L-arabinose, L-fucose, mannose and xylose. Investigation of the amino acid composition of the gum shows aspartic acid as the most abundant (5). Acacia gum (gum Arabic) consists of a group of macromolecules characterized by a high proportion of carbohydrates (approximately about 97%), which are predominantly composed of D-galactose and L-arabinose units and a low proportion of proteins (< 3%) (6, 7). However, neem gum has unusual structural features in that it contains appreciable amount of D-glucosamine and proteins (8) unlike other plant gums. Although studies have been done on the characterization and mechanical properties of various gums in pharmaceutical tablet formulations (3, 9–11), not much work has been done on the characterization and suitability of neem gum in tablet formulations.

In the present study, the morphological, compressional, disintegrant and mechanical properties of neem gum (NMG) obtained from the trunk of *Azadirachta indica* (A. Juss) tree were evaluated in comparison with a standard gum binder, acacia BP. The morphological properties were determined using shape factors of aspect ratio, roundness, irregularity and equivalent circle diameter (ECD). The compressional properties were determined by the Heckel and Kawakita equations, whereas its tableting properties were assessed with the aid of tensile strength (T), brittle fracture index (BFI), and the crushing strength – friability/disintegration time ratio (CSFR/DT).

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Although, researchers have carried out studies to elucidate the chemical compositions of neem gum (4, 5, 8), however, no study is available in the literature to specifically evaluate the safety profile of the gum exudate. Thus, this work includes the acute toxicity profile of neem gum using the Lorke's method (12).

EXPERIMENTAL

Materials

The materials used were *Azadirachta indica* gum obtained from the trunk of *Azadirachta indica* (A. Juss) tree and processed as described by Ogunjimi and Alebiowu (2), acetone and 99.8% ethanol (Sigma-Aldrich Laborchemikalien GmbH, Seelze, Germany), and acacia gum BP.

METHODS

Acute toxicity testing

The acute toxicity test on the *Azadirachta indica* gum was carried out using the Lorke's method (12). The toxicity was carried out in two phases using 13 experimental animals (rats). The animals were divided into three groups consisting of three animals per group. In the first phase, neem gum at doses of 10, 100, 1000 mg/kg body weight were administered orally in order to establish the range of doses that could produce toxic effects. The animals were observed for mortality within 24 h of administration. The second phase involved repeating the 1000 mg/kg body weight and new doses of 1600, 2900 and 5000 mg/kg body weight, which were administered orally (n = 1) and were observed for 24 h for mortality. The result obtained was used to determine the LD_{50} of the neem gum.

Particle shape and size characterization

This was determined by optical microscopy (LEICA DM 750 Research Microscope with an integrated icc50 camera, LEICA Microsystems GmbH, Germany). The images were then transferred to a personal computer for analysis. Approximately 300 particles picked randomly in the optical field for each sample were analyzed using the Image Pro Premier software (MediaCybernetics, Bethesda, MD, USA) to determine the particle descriptors of major and minor axis length, perimeter and projected area from which shape factors of aspect ratio, roundness, irregularity and equivalent circle diameter were determined according to the following equations (13):

$$Aspect\ ratio = \frac{b}{l} \qquad \text{Eq. 1}$$

$$Roundness = \frac{4 \times \pi \times A}{p^2} \qquad \text{Eq. 2}$$

$$Irregularity = \frac{p}{l} \qquad \text{Eq. 3}$$

$$Equivalent\ circle\ diameter = 2 \times \sqrt{\frac{A}{\pi}} \qquad \text{Eq. 4}$$

where b = length of the minor axis (minimum Feret diameter), l = length of major diameter (maximum Feret diameter), A = projected area of the particle, p = perimeter.

The aspect ratio varies between 0 and 1, with a low value indicative of an elongated particle and a perfect circle having an aspect ratio of 1. Roundness is a measure of how closely the projected area of the powder resembles a circle; a perfect circle has a roundness value of 1. Irregularity measures the surface area compared to the size of the particle; in this case, a perfect circle has an irregularity of p. Equivalent circle diameter (ECD) is a measure of size; it is the diameter of a sphere with the same cross-sectional area as the powder. The higher the equivalent circle diameter, the larger the mean particle size (13).

Determination of swelling capacity of gum

The method described by Bowen and Vadino (14) was used. Five grams of each powdered gum was poured gently into a 100 mL measuring cylinder and the bulk volume (V_0) was measured. Distilled water was added to disperse the gum (at room temperature), and subsequently, made up to the 100 mL mark. The dispersion was allowed to stand for 24 h when the volume (V_1) of the swollen gum was read. The swelling index was calculated as V_1/V_0. The determination was done in triplicate.

Determination of moisture content and sorption (hygroscopicity) of the gum

The moisture content of 10 g each of the gum was determined with an Ohaus moisture balance, model 6010H (Ohaus Scale Corporation, New Jersey, USA) set to emit 2 watts of heat for 2 min, while the moisture sorption of the gum was determined by exposing 1 g of the gum (previously dried at 50°C to a constant weight) to a constant relative humidity of 75% for a period of 72 h. Samples (1 g each) were placed in glass cups of uniform internal dimensions and kept in hygrostats prepared using standard solution of sodium chloride in wells of glass desiccators (15). Percent moisture (M_p) absorbed was determined from the weight gained at the end of 72 h according to equation Eq. 5. The determination was done in triplicate.

$$M_p = (\frac{W_2 - W_1}{W_1}) \times 100 \qquad \text{Eq. 5}$$

where W_1 is the initial weight of sample (1 g) and W_2 is the weight of sample after 72 h.

Determination of density parameters of gum

The apparent particle density of the gum was determined by the pycnometer method using acetone as displacement fluid. The bulk density of each gum powder at zero pressure (loose density) was determined by pouring the powder at an angle of 45° through a funnel into a glass measuring cylinder with a diameter of 22 mm and a volume of 50 mL (16). The relative density, D_o, of each gum powder was obtained from the ratio of its loose density to its particle density. The Hausner`s ratio determined as the ratio of the initial bulk volume to the tapped volume, was obtained by applying 100 taps to 30 g of each gum powder in a graduated cylinder at a standardized rate of 38 taps per minute (17). The Carr's index (CI) was obtained from the relationship:

[(Tapped density – Bulk density)/Tapped density] × 100 Eq. 6

All determinations were performed in quadruplicate.

Determination of angle of repose

The angle of repose was determined by measuring the radius "r" of the base and the height "h" of the conical heap formed by pouring 30 g each of the gum through a glass funnel held at 5 cm from the horizontal onto a flat base. The angle of repose (θ) was calculated as a mean of four determinations as:

$$\theta = \tan^{-1}(\frac{h}{r}) \qquad \text{Eq. 7}$$

Determination of flow rate

The flow rate (F_r) of the powdered gum was determined from the time "t" it took 30 g of the gum to pass through the orifice of an Erweka flow rate meter. The flow rate was calculated as a mean of four determinations as:

$$F_r = \frac{30\ g}{t} \qquad \text{Eq. 8}$$

Determination of compressional properties

The Heckel equation is widely used for relating the relative density, D, of a powder bed during compression to the applied pressure, P. It is written as:

$$\ln[(1/1 - D)] = k_P + A \qquad \text{Eq. 9}$$

The slope of the straight-line portion, K, is the reciprocal of the mean yield pressure, P_y, of the material. From the value of A, the intercept, the relative density, D_a, can be calculated using the following equation (18):

$$D_A = 1 - e^{-A} \qquad \text{Eq. 10}$$

The relative density of the powder at the point when the applied pressure equals zero, D_o, is used to describe the initial rearrangement phase of densification as a result of die filling. The relative density, D_b, describes the phase of rearrangement at low pressures and is the difference between D_A and D_O.

$$D_b = D_A - D_O \qquad \text{Eq. 11}$$

The Kawakita equation is used to study powder compression and the degree of volume reduction, C. It is written as:

$$C = \frac{(v_o - v_P)}{v_o} = abp/(1 + bp) \qquad \text{Eq. 12}$$

The equation in practice can be rearranged to give P/C = P/a + 1/ab, where V_o is the initial bulk volume for granular materials and V_p is the bulk volume after compression. The constant "a" is equal to the minimum porosity of the material before compression, while the constant "b" is related to the plasticity of the material. The expression $(1 - a)$ gives the initial relative density of the material, D_i which has been shown to provide a measure of the packed initial relative density of tablets with the application of small pressure or what may be referred to as tapping. The reciprocal of b gives a pressure term, P_k, which is the pressure required to reduce the powder bed by 50% (16, 19, 20).

Preparation of gum tablets

Tablets (500 mg) were prepared from the gum powder by compressing them using a 12.5 mm die and flat faced punches for 30 s with predetermined loads on a model C, hydraulic hand press (Carver Inc., Menomonee Falls, USA). Tablets with a hole (1.5 mm diameter) at their center were made using an upper punch with a hole and a lower punch with a pin (21). After ejection, the tablets were stored in a desiccator for 24 h to allow for elastic recovery and hardening in order to prevent false low yield values. The tablets weights and dimensions were determined to within ±1 mg and 0.01 mm, respectively, and their relative densities (*D*) were calculated using the equation:

$$D = m/V_t\rho_s \qquad \text{Eq. 13}$$

where m is the weight of the tablets (g), V_t is the volume of tablets and ρ_s is the particle density of the powders.

Determination of mechanical properties

The tensile strength of the normal tablets (T) and of apparent tensile strength (To) of those containing a hole, were determined at room temperature by

diametral compression (22) using a digital Erweka hardness tester and by applying equation Eq. 14:

$$T = 2F/\pi dt \qquad \text{Eq. 14}$$

where T (or To) is the tensile strength of the tablet (MNm^{-2}), F is the load (MN) needed to cause fracture, d is the tablet diameter (m), and t is tablet thickness (m). Results were taken from tablets, which split cleanly into two halves without any sign of lamination. All measurements were made in quadruplicate. The BFI of the tablets were calculated using Eq. 15:

$$BFI = 0.5\ (T/T_o - 1) \qquad \text{Eq. 15}$$

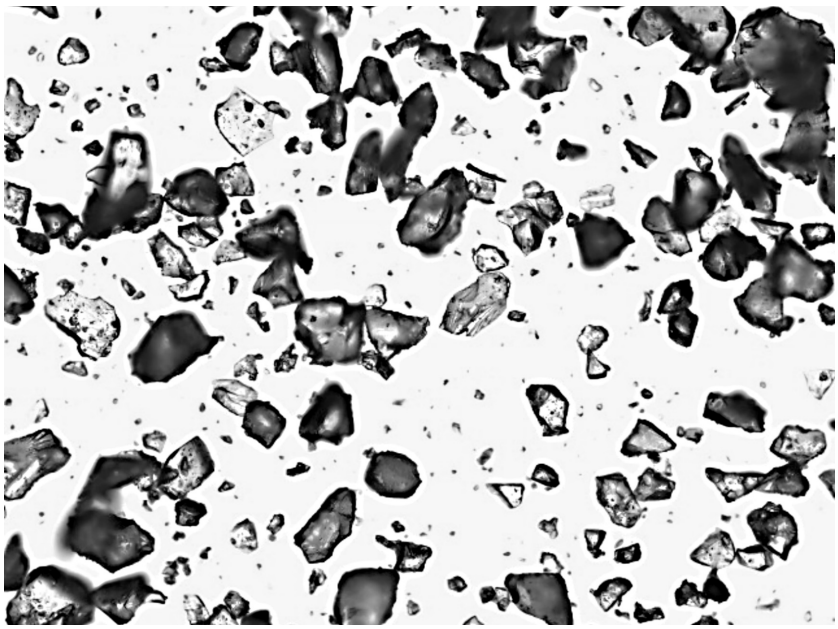

Figure 1. Photomicrograph of neem gum powder (100×)

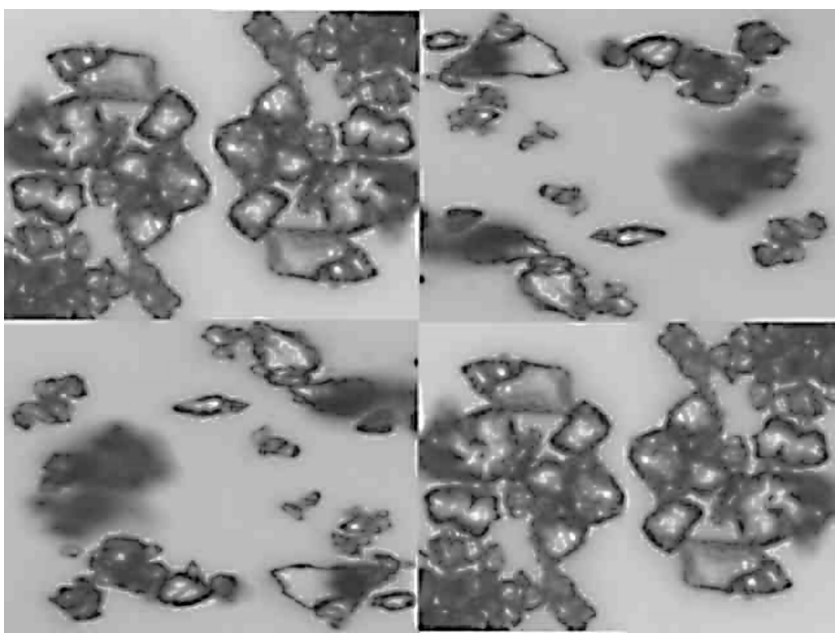

Figure 2. Photomicrograph of acacia gum powder (400×)

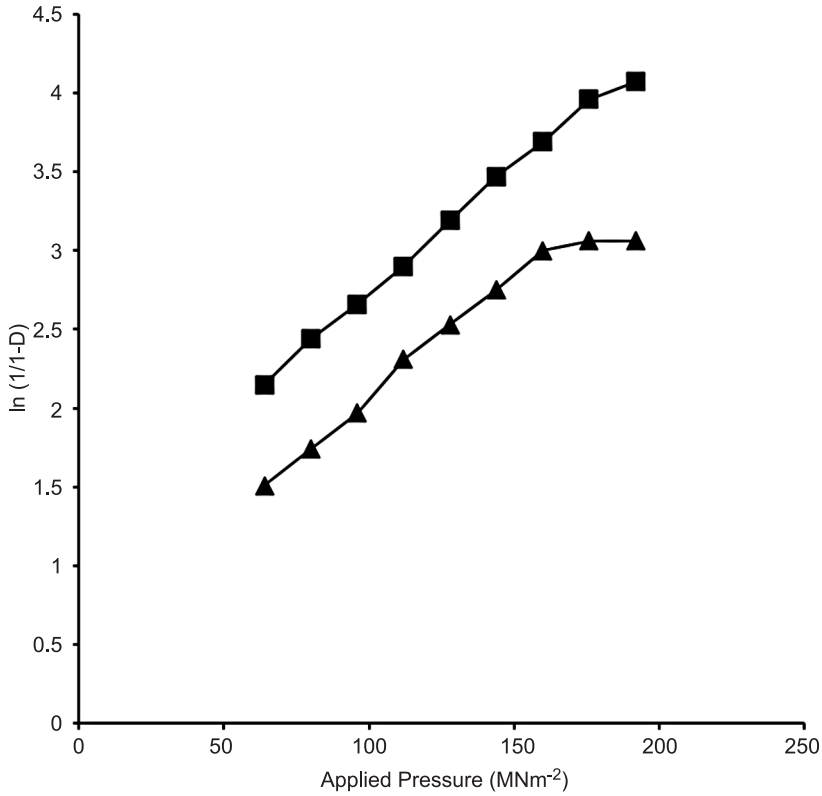

Figure 3. Heckel plots for tablets made from the gums. ■ NMG, ▲ ACA

Determination of tablet crushing strength and friability

A digital Erweka hardness tester was used at room temperature to determine the load required to diametrically break the tablet (crushing strength) into two equal halves. Tablets with signs of lamination and capping were not used. The friability of the tablets was determined using a Roche friabilator (Erweka Apparatebau, Germany) operated at 25 rev/min for 4 min. Ten tablets were used at each relative density. The mean of four determinations was taken for the crushing strength and friability values.

Disintegration test

The disintegration time (DT) of the gum tablet was determined in distilled water at 37 ± 0.5°C in a BP Manesty six station disintegration test unit (Manesty Machines Ltd., Liverpool, UK). Tablets were placed on the wire mesh just above the surface of the distilled water in the tube. The time taken for each tablet to disintegrate and all the granules to go through the wire mesh was recorded. Results were expressed as an average of three determinations.

RESULTS AND DISCUSSION

The acute toxicity results show that the LD_{50} of neem gum is higher than 5000 mg/kg, which suggests that neem gum exudate is safe as there were no deaths recorded at this dose (12).

The photomicrographs (Figs. 1 and 2) show the shape of NMG and ACA, respectively. Both gums are polygonal in shape; however, ACA exists as aggregates. The morphological and physical properties are as presented in Table 1. The result showed that the aspect ratio and roundness of NMG particles were lower than those of ACA, implying that NMG is more elongated than ACA, while the projected area of ACA is closer to a perfect circle. The result also showed that NMG had particle size (ECD) that is larger and more irregular than that of ACA. The flow and packing properties of powder blends have been shown to depend to a large extent on their particle shape and sizes (23, 24). The swelling index result showed that NMG swelled 1.04 times its weight while ACA was soluble in distilled water. The moisture content values of NMG and ACA suggest that their use in formulations containing moisture sensi-

Table 1. Morphological and physical properties of neem and acacia gums.

Properties	Neem gum	Acacia gum
Aspect ratio	0.57	0.62
Roundness	0.44	0.68
Irregularity	3.34	2.75
ECD (mm)	18.90	14.30
Swelling Index	1.040 ± 0.012*	Soluble
Moisture content	7.540 ± 0.214	5.810 ± 0.132
Moisture Sorption	14.500 ± 0.105	7.400 ± 0.201
Particle density	1.476 ± 0.012	1.479 ± 0.015
Bulk density	0.690 ± 0.010	0.708 ± 0.021
Porosity (%)	53.252	52.130
Hausner's Ratio	1.207	1.395
Carr's Index	17.167	28.340
Angle of Repose	22.692	34.994
Flow Rate	3.229 ± 0.020	2.890 ± 0.050

* Mean ± SD, n = 3

Table 2. Parameters obtained from Heckel and Kawakita plots for neem and acacia gum.

	Parameters	Neem gum	Acacia gum
Heckel analysis	P_y (MNm^{-2})	62.112	68.027
	D_o	0.310	0.401
	D_A	0.451	0.678
	D_B	0.141	0.277
Kawakita analysis	D_i	0.348	0.435
	P_k (MNm^{-2})	11.236	14.231

tive active ingredients should be done with caution. However, the result also showed that the moisture content of NMG is higher than that of ACA, which might have resulted from the appreciable amount of polysaccharide and proteins present in neem gum unlike in acacia gum. It could also be due to the tight link between the polysaccharides and the protein (11).

The values of particle and bulk densities obtained for ACA were higher than those of NMG. This could be due to the regularity of ACA, which form fewer arches and bridges than NMG, hence an increase in packing per unit space suggesting that the particle shape has an influence on the density properties of the powders. The result also showed that the porosity of NMG was higher than that of ACA. This could also be due to the regularity of ACA. It has been observed that because of particle geometry, mechanical forces may exist in particles, which tends to influence their packing (25). Hausner's ratio provides an indication of degree of densification of powders/granules that could result from vibration of the feed hopper e.g., during tableting, with values of above 1.2 indicating considerable amount of densification, while Carr's compressibility index (26) is a direct measure of the potential powder/granule arch or bridge strength and stability; a less than 20% standard value suggests free-flowing powder/granules. The HR, CI and angle of repose (a characteristic of internal friction or cohesion of particles) values of NMG were lower than those of ACA suggesting that NMG possesses a higher flow that could be useful in direct compression. These results could be due to the particle size of NMG, which was higher than that of ACA. A decrease in powder particle size has been shown to cause an increase in the surface area per unit mass thus leading to an increase in the cohesive strength of the powder bed thereby reducing flowability [27].

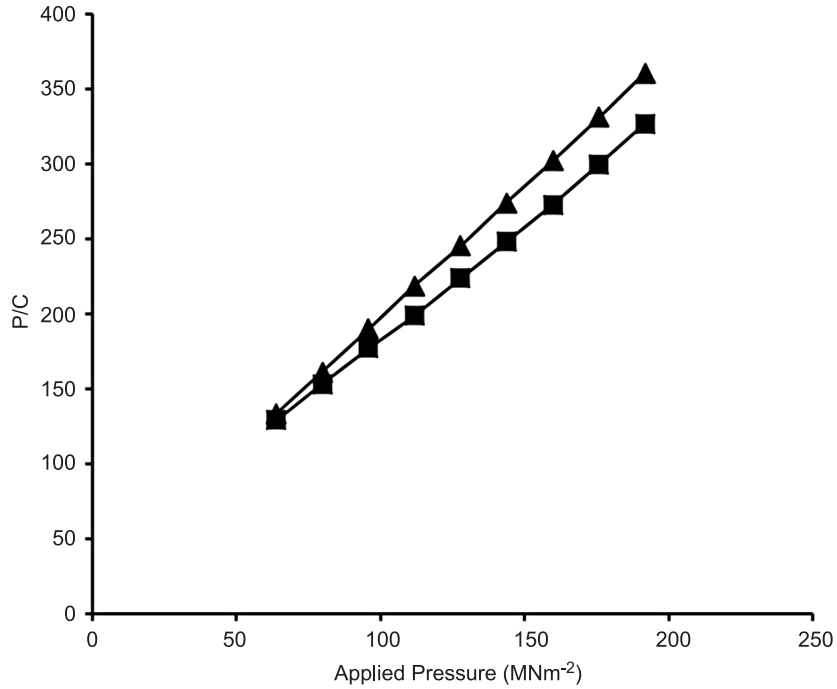

Figure 4. Kawakita plots for tablets made from the gums. ■ NMG, ▲ ACA

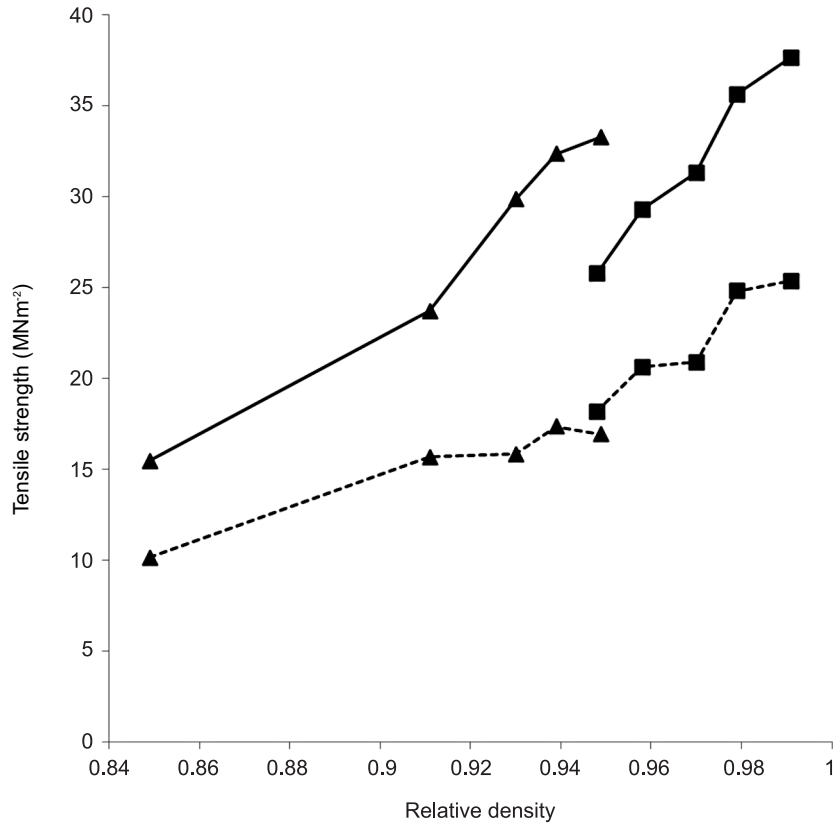

Figure 5. Plot of tensile strength *versus* relative density for gum tablets. ■ NMG, ▲ ACA. (———) Tablets without holes and (– – – –) tablets with holes

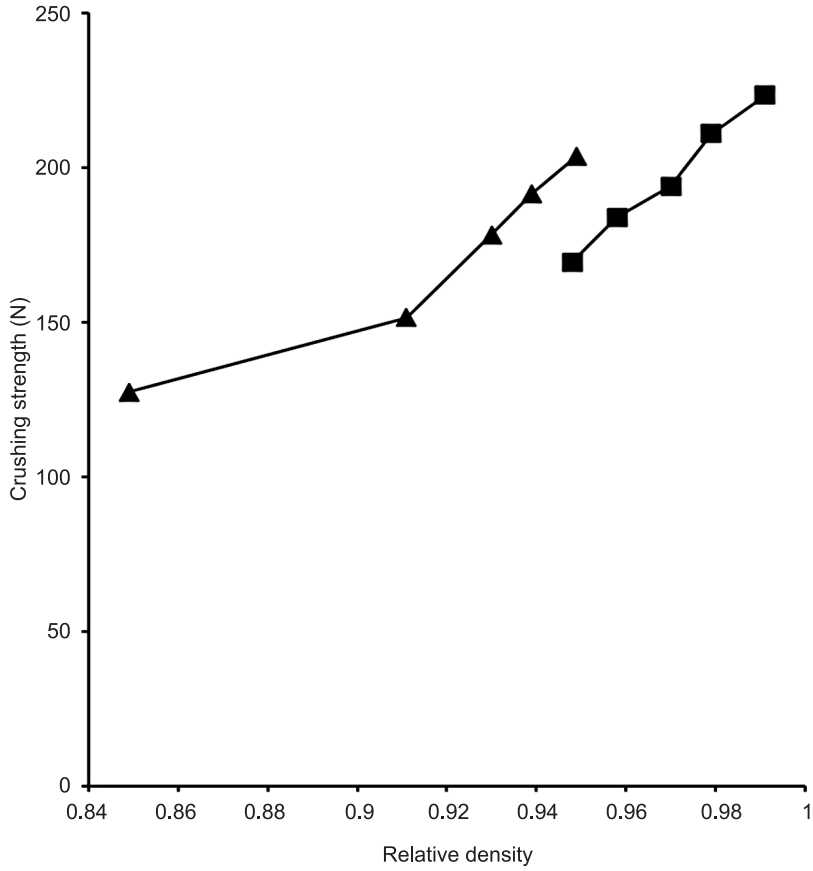

Figure 6. Plot of crushing strength *versus* relative density for gum tablets. ■ NMG, ▲ ACA

Table 3. Values of tensile strength (T or T_o), brittle fracture index (BFI), crushing strength (CS), disintegration time (DT), friability (FR) and crushing strength-fraiblity/disintegration time ratio (CSFR/DT) of gum tablets at relative density of 0.90.

Properties	Neem gum	Acacia gum
T (MN/m^{-2})	13.85 (0.12)*	25.95 (0.18)
T_o (MN/m^{-2})	8.943 (0.08)	14.631 (0.20)
BFI	0.270 (0.01)	0.390 (0.02)
CS (N)	105.001 (2.64)	165.540 (4.26)
FR (%)	1.020 (0.03)	1.303 (0.02)
DT (min)	15.603 (0.35)	32.195 (0.42)
CSFR/DT	6.598	3.946

* Mean ± SD, n = 3

The flow rate result also suggests that NMG has a higher flow than ACA. This result could be due to the same reason given above.

Figure 3 shows the Heckel plot for neem and acacia gums. Values of mean yield pressure, P_y, were calculated from region of the plots showing the highest correlation coefficient of linearity. The intercept, A, was determined from the extrapolation of the region for calculating P_y, while the values of D_A and D_B were calculated from Eq. 2 and 3, respectively. The values of P_y, D_o, D_A and D_B are shown in Table 2.

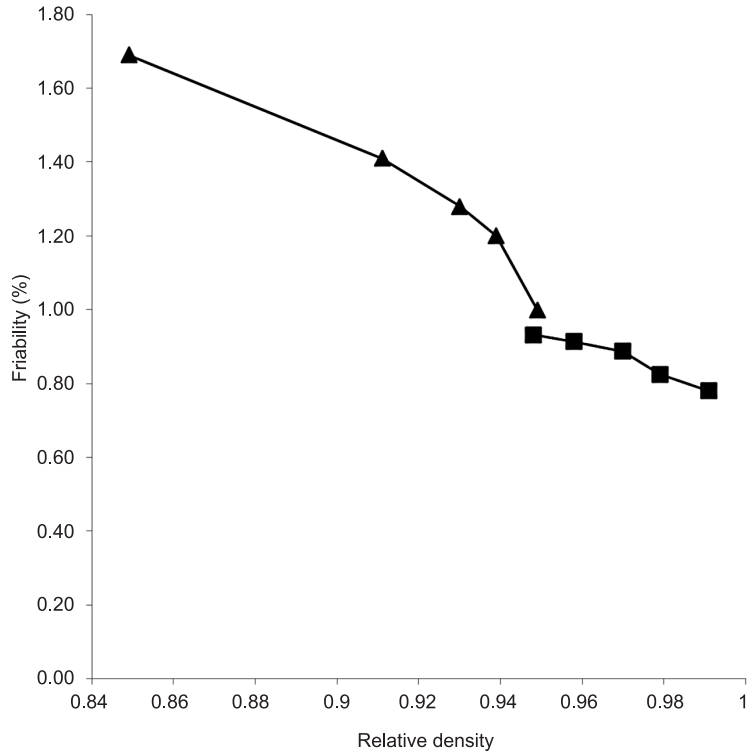

Figure 7. Plot of friability *versus* relative density for gum tablets. ■ NMG, ▲ ACA

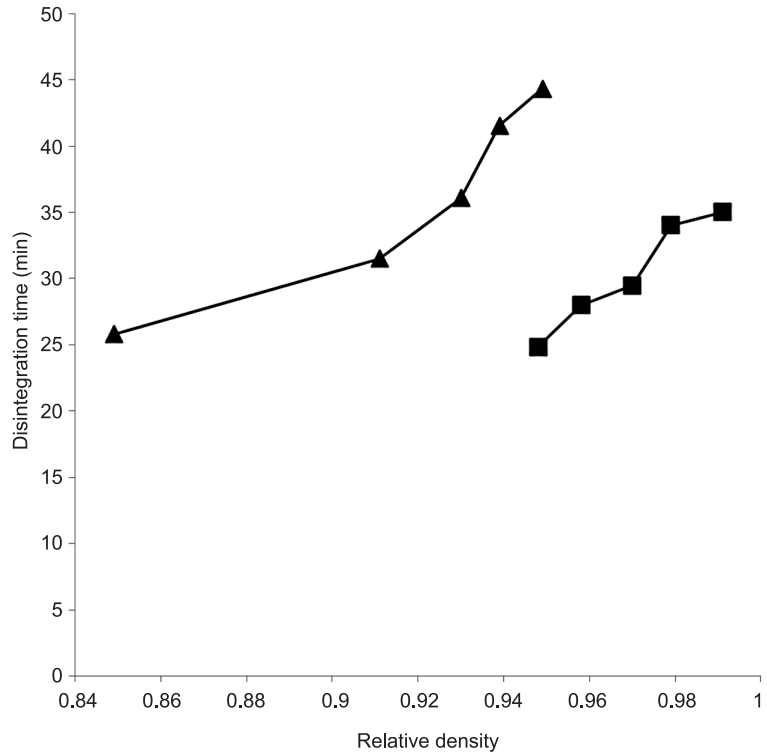

Figure 8. Plot of disintegration time *versus* relative density for gum tablets. ■ NMG, ▲ ACA

The result shows that the D_o value of ACA was higher than that of NMG. This suggests more initial packing of ACA in the die as a result of die filling than NMG. This result could be due to the regularity and smaller particle size of ACA when compared to NMG. D_B represents the phase of rearrangement of particles at low pressure. The result shows that the D_B value of NMG was lower than that of ACA. This suggests more fragmentation of ACA particles at low pressures than NMG. The D_A value of ACA, which represent the total degree of packing at zero and low pressures, was higher than that of NMG.

The mean yield pressure, P_y, is inversely related to the ability of the material to deform plastically under pressure. The value of P_y for ACA was higher than that of NMG. This implies that the onset of plastic deformation in ACA occurred at a higher pressure.

The Kawakita plots of neem and acacia plots are shown in Figure 4. A linear relationship was obtained at all compression pressures used with a correlation coefficient of 0.999 for the gums, thus, the Kawakita equation was used to predict the densification mechanism of the two gums. Values of *a* and *ab* were obtained from the slope and intercept of the plots, respectively.

The D_i value of ACA was higher than that of NMG. The D_i values are also seen to be higher than the values of D_o. Bearing in mind that the methods of determination of D_o and D_i have their limitations, (28), the differences in the values of D_o and D_i are probably due to the fact that while D_o describes the loose initial relative density of the batches due to die filling, D_i provides a measure of the packed initial relative density of the batches with the application of small pressure or what may be referred to as tapping of the granules (20).

The P_k is an inverse measure of the amount of plastic deformation occurring during compression, with low values depicting materials that are soft and readily deform under pressure. Table 2 shows that NMG exhibited the highest amount of plastic deformation when compared to ACA. Odeku and Itiola (29) have shown that P_y is different from P_k in that while the P_y value relates essentially to the onset of plastic deformation during compression, the P_k value appears to relate to the total amount of plastic deformation occurring during the compression process. Thus, the present result showed that NMG had a faster onset of plastic flow and a higher of amount of plastic deformation when compared to ACA.

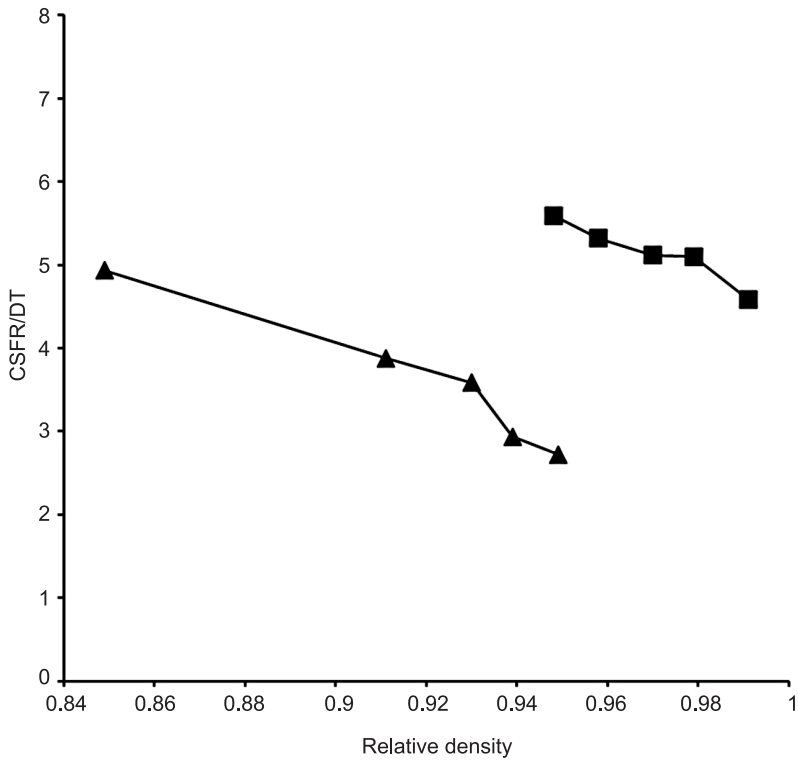

Figure 9. Plot of CSFR/DT *versus* relative density for gum tablets. ■ NMG, ▲ ACA

The result of tensile strength test on the gum tablets generally fits the equation:

$$T \text{ or } T_o = AD + B \text{ .....} \quad \text{(Eq. 15)}$$

with correlation coefficient of > 0.927. A and B are constants, which depend on the nature of the gum and on whether the tablet had a hole in it or not. Plots of tensile strength *versus* relative density of NMG and ACA are presented in Figure 5. It can be seen that at all relative densities the tensile strength (T) of a tablet with a hole was lower than that of the same without a hole, the hole acting as a stress concentrator (21, 30).

The value of T and BFI of the gum tablet at a relative density of 0.90 are presented in Table 3. The result shows that ACA has a higher T and BFI when compared to NMG. This suggests that ACA produced stronger gum tablets; however, the tendency of ACA tablets to cap or laminate is also higher when compared to NMG.

Although low P_k values of powders have been shown to be responsible for high T values, as higher total plastic deformation would lead to more contact points for interparticulate bonding (31), the result showed that ACA which had a slightly higher P_k value (Table 2) than NMG had a higher T. This result could be due to the brittleness (BFI) (Table 3) of ACA, which caused more breakages in the material on application of pressure, and this would lead to creation of more contact points for bonding, thus making the ACA tablets to have a higher T.

Crushing strength provides a measure of strength while friability measures the weakness of a tablet (3). Plots of crushing strength *versus* relative density of NMG and ACA gum tablets are shown in Figure 6. It is observed from the figure that as the relative density increased, the crushing strength of the tablets also increased. This could be due to the decrease in porosity and subsequent increase in the number of contact points, hence, an increase in the degree of bonding between the particles (21). It can also be seen from the result (Table 3) that the crushing strength of ACA tablets was higher than that of NMG tablets. This could be due to the brittleness of ACA gum, which caused more breakages and consequent creation of more particle-particle contact points, hence leading to higher crushing strength values.

Figure 7 shows the plot of friability *versus* relative density for gum tablets of NMG and ACA. It is observed that friability decreased with an increase in relative density for both gum tablets. At a relative density of 0.90 (Table 3), the friability of ACA tablet was higher than that of NMG. This result could be due to the brittleness of ACA gum, which caused more breakage and chipping off in the friabilator drum.

The disintegration time of the gum tablets obtained generally increased with an increase in relative density of the tablets as shown in the plots of disintegration time against relative density for gum tablets of NMG and ACA (Fig. 8). With an increase in relative density, there is usually an accompanying decrease in porosity (32), which consequently slows down water penetration into tablets. Also, when porosity decreases, more solid bridges are formed, making destruction of interparticulate forces difficult (33, 34). The result also showed that at a relative density of 0.90 (Table 3), the disintegration time of ACA tablets was significantly higher than that of NMG tablets. This could be due partly to the brittleness of ACA gum, which caused more breakages and consequent creation of more particle-particle contact points thereby reducing the rate of liquid penetration into the micropores of ACA gum tablets.

The crushing strength friability/disintegration time ratio (CSFR/DT) has been suggested as a better index for measuring tablet strength (crushing) and weakness (friability), it simultaneously evaluates all negative effects of these parameters on disintegration time (35). A higher value of CSFR/DT ratio indicates a better balance between binding and disintegration properties. The values of CSFR/DT for NMG and ACA gum tablet at a relative density of 0.90 are as shown in Table 3. Higher values of CSFR/DT obtained for NMG gum tablet suggests that NMG gum tablets will produce a better balance between the mechanical and disintegration properties of tablets when used in directly compressible formulations. This could be due to the high CS of ACA tablets which ultimately led to longer DT of the tablets.

CONCLUSION

The results obtained from the present work showed that:

- the morphology of a gum powder material influences its tableting properties;
- the NMG powder would lead to the production of tablets with lower TS and lower tendency to cap or laminate when used in a directly compressible formulation relative to ACA gum powder;
- the NMG powder is more likely to produce tablets with a better balance between mechanical and disintegration properties than that of ACA powder as reflected in the CSFR/DT values when used in direct compression.

REFERENCES

1. Joneja S.K., Harcum W.W., Skinner G., Barnum P.E., Guo J.H.: Drug Dev. Ind. Pharm. 25, 1129 (1999).
2. Ogunjimi A.T., Alebiowu G.: Braz. J. Pharm. Sci. 46, 205 (2010).
3. Adetogun E.A., Alebiowu G.: Acta Pol. Pharm. Drug Res. 66, 433 (2009).
4. Aspinal G.O.: Advances in carbohydrate chemistry and biochemistry. Wolfrom M.L., and Tipson R.S. Eds., Vol. 24, p. 333, Academic Press, New York 1969.
5. van der Nata J.M., van der Siuisa W.G., de Silvab K.T.D., Labadie R.P.: J. Ethnopharmacol. 35, 1 (1991).
6. Islam A.M., Phillips G.O., Sljivo A., Snowden M.J., Williams P.A.: Food Hydrocolloid., 11, 493 (1997).
7. Montenegro M.A., Boiero M.L., Valle L., Borsarelli C.D.: Gum Arabic: more than an edible emulsifier. In Products and Applications of Biopolymers, pp. 3-24, Johan Verbeek Ed., Intech, Rijeka 2012.
8. Ushalakshmi S., Pattabiraman, T.N.: Indian J. Biochem., 4, 181 (1967).
9. Kulkarni G.T., Gowthamarajan K., Suresh B.: Indian Drugs 39, 422 (2002)
10. Odeku O.A., Itiola O.A.: Drug Dev. Ind. Pharm. 28, 329 (2002).
11. Panda D.S., Choudhury N.S.L., Yedukondalu M., Si S., Gupta R.: Indian J. Pharm. Sci. 70, 614 (2008).
12. Lorke D.: Arch. Toxicol. 54, 275(1983).
13. Bodhmage A.: M.Sc. Thesis, Saskatchewan University, Canada (2006) (unpublished).
14. Bowen F.E., Vadino W.A.: Drug Dev. Ind. Pharm. 10, 505 (1984).
15. Nyqvist H.: Int. J. Pharm. Technol. Prod. Manuf. 4, 47 (1983).
16. Alebiowu G., Osinoiki K.A.: Farmacia 58, 341 (2010).
17. British Standard 1460. British Standard Institution, London 1970.
18. Humbert-Droz P., Gurny R., Mordier D., Doelker E.: Int. J. Pharm. Tech, Prod. Manuf. 4, 29 (1983).
19. Lin C., Cham T.: Int. J. Pharm. 118, 169 (1995).
20. Podczeck F., Sharma M.: Int. J. Pharm. 137, 41 (1996).
21. Alebiowu G., Itiola O.A.: Drug Dev. Ind. Pharm. 28, 663 (2002).
22. Fell J.T., Newton J.M.: J. Pharm. Sci. 59, 688 (1970).
23. Johansson B., Nicklasson F., Alderborn G.: Int. J. Pharm. 163, 35 (1998).
24. Itiola O.A., Odeku O.A.: Trop. J. Pharm. Res. 4, 363 (2005).
25. Harwood C.F., Pilpel N.: J. Pharm. Sci. 57, 478 (1968).
26. Carr R.L.: Chem. Eng. 72, 163 (1965).
27. Sameh A., Firas A., Gabrielle B.: Int. J. Pharm. 413, 29 (2011).
28. Celik M.: Drug Dev. Ind. Pharm. 18, 767 (1992).
29. Odeku O.A, Itiola O.A.: Pharm. Pharmacol. Commun. 4, 183 (1998).
30. Hiestand E.N., Wells J.F., Poet C.B., Ochs J.F.: J. Pharm. Sci. 66, 510 (1977).
31. Itiola O.A., Pilpel N.: J. Pharm. Pharmacol. 43, 145 (1991).
32. Zhang Y., Law Y., Chakrabarti S.: AAPS PharmSciTech. 4, article 62 (2003).
33. Bi Y., Yonezawa Y., Sunada H.: J. Pharm Sci. 88, 1004 (1999).
34. Gohil U.C., Podzeck F., Turnbull N.: Int. J. Pharm. 285, 51 (2004).
35. Upadrashta S.M., Katikaneni P.R., Nuessla N.O.: Drug Dev. Ind. Pharm. 18, 1701 (1992).

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