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Full Length Research Paper

Isolation, characterzation and compaction properties of *Afzelia africana* gum exudates in hydrochlorothiazide tablet formulations

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***Afzelia* gum was obtained from the bark exudates of *Afzelia africana* plant, characterized and evaluated for its compaction properties in hydrochlorothiazide tablet formulations. Compressional properties of the formulations were analyzed using density measurements and the Heckel equation as assessment parameter. Formulations containing *Afzelia* gum as a binder show a slower onset and lower extent of plastic deformation than those containing the 2 standard binders, tragacanth and gelatin. While retative density Db values for formulations containing tragacanth and gelatin generally increased with increased concentration up to 3% w/w, those containing *Afzelia* gum were at variant with the binder concentrations. Formulations containing *Afzelia* gum were also found to exhibit higher degree of packing than those containing tragacanth and gelatin. Yield values for formulations containing *Afzelia* gum was also found to be at variant with the binder concentration. The values decreased between 1 and 3% w/w and increased at 4% before decreasing again at 5% w/w. *Afzelia* gum improved the fluidity of hydrochlorothiazide granulation better than tragacanth and gelatin. This study suggests that *Afzelia* gum has good physicochemical properties that would make it a useful binder in hydrochlorothiazide tablet formulations.**

Key words: *Afzelia* gum, tragacanth, gelatin, hydrochlorothiazide, Heckel equation, compaction characteristics.

INTRODUCTION

Binders confer the structural strength required by tablets during processing, handling, packaging and transportation. A number of plant gums/hydrocolloids have been used as binding, suspending or emulsifying agents in solid and liquid dosage formulations (Chukwu et al., 1994a, b; Nasipuri et al., 1996, 1997, 1999; Odeku, 1998, 2002, 2005; Emeje et al., 2007, 2008, 2009). These gums have been used in producing tablets with different mechanical strength, consolidation and drug release properties for different pharmaceutical purposes. These gums are generally non-toxic and widely available, hence the continued interest (Odeku, 2005) in their development *Afzelia Africana* belongs to the family *Fabaceae.* It is one of the most widely distributed species in Africa. It is found from Senegal in West Africa to the Sudan, Uganda and Tanzania in the east and also present in south Asia. It is occasionally grown in other tropical countries as an ornamental. The plant is used in local medicine for general pain relief, digestive problems, e.g. constipation and vomiting and for internal bleedings (hemorrhage) (Dalziel, 1937).

A survey of literature reveals that a comprehensive physicochemical characterization of the gum obtained from the seed of *A. africana* have been reported (Yilong et al., 2005). However, it appears that no attempt has been made to study the exudates gum from this plant. In this work therefore, we report for the first time, the

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physicochemical characteristics of *A. africana* gum derived from the bark exudates of *A. africana* plant and its binding properties in a hydrochlorothiazide tablet formulation in comparison with standard binders, Tragacanth (TG) and gelatin (Gel) using the density measurements and the compression equations of Heckel as assessment parameters.

The Heckel plot is the method most frequently used to evaluate the volume reduction of materials when pressure is applied (Luiz et al., 2005). It is assumed that the densification of the powder column follows first order kinetics. Thus, the degree of material densification is correlated to its porosity. The model has often been applied to study powder mixtures and to evaluate granule manufacture (Isimi et al., 2003; Luiz et al., 2005; Emeje and Kunle, 2004). Heckel (1961) equation is expressed as:

$$[1/1 - D] = KP + A \text{ ---------- - - -} \quad i$$

The slope of the linear portion of the curve, K, is the reciprocal of the mean yield pressure, Py, of the material. The intercept of the extrapolated linear region, A, is a function of the original compact volume. It represents 2 stages of consolidation- one due to the initial relative density of the powder and the other due to densification by particle rearrangement. From the value of A, the relative density Da can be calculated using the following equation;

$$Da = 1 - e^{-A} \text{ ----------} \quad ii$$

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

$$Db = Da - Do \text{ ----------} \quad iii$$

MATERIALS AND METHODS

Lactose, gelatin, tragacanth (Sigma-Aldrich, Chemic GmbH, Germany), hydrochlorothiazide (Evans Pharmaceuticals, Nigeria Plc).

METHOD

Extraction and purification of AAG was extracted and purified as previously reported by Emeje et al. (2009) with modification. Endogenous enzymes were inactivated by boiling 100 g of the plant material with 80% ethanol for 1 h. The plant material was heated in water bath at 90°C for 2 h to extract the water soluble gum fraction. The insoluble solids were separated by filtration through a muslin cloth, while the extract was centrifuged at 2000 rpm for 10 min to collect the supernatant. The extract was precipitated by adding 3 volumes of 95% ethanol and washed with absolute ethanol 3 times followed by air drying.

Preparation of powder mixtures

Dried powders of AAG, TG or GEL equivalent to 1.0, 2.0 3.0, 4.0 and 5.0% w/w was mixed with hydrochlorothiazide powder respectively and made up with lactose BP. The mixture was blended thoroughly in a tumbler mixer for 10 min.

Preparation and evaluation of compacts

Compacts equivalent to 50 mg hydrochlorothiazide were produced by compressing the granules for 60 s with predetermined loads (at various compression pressures) using a manesty tableting machine (Shangai, China). 50 tablets were compressed at each pressure. All readings are average of 3 measurements. Before each compression, the die (10.5 mm in diameter) and flat faced punches were lubricated with a 1% w/v dispersion of magnesium stereate in acetone. After ejection, the tablets were stored over silica gel in a dessicator for 24 h to allow for elastic recovery and hardening to prevent falsely low yield values (Krycer et al., 1982) and the dimensions of the compact were determined using the mitutoyo model IDC1012EB (Mitutuyo corporation, Japan) thickness gauge to the nearest 0.01 mm. The Heckel plots were statistically analysed using the microsoft excel computer software.

The relative density of the compacts was calculated using the equation:

$$D = \frac{w}{Vt} \; s \quad \text{---------- (iv)}$$

Where w is the weight of the compact (g), Vt is the volume of the compact (cm^3) and s is the density of granules ($glcm^3$).

Physicochemical characterization of the gum

Solubility test

The gum was evaluated for solubility in water, acetone, chloroform and ethanol in accordance with the British pharmacopoeia specifications (2004).

Swelling index

The method of Ohwoavworhua and Adelakun (2005) was used. 1.0g each of the sample was placed in each of 15 ml plastic centrifuge tubes and the volume occupied was noted. 10 ml of distilled water was added from a 10 ml measuring cylinder and stoppered. The contents were mixed on a vortex mixer (Vortex Gennie Scientific, USA) for 2 min. The mixture was allowed to stand for 10 min and immediately centrifuged at 1000 rpm for 10 min on a bench centrifuge (GallenKamp, England). The supernatant was carefully decanted and the volume of sediment measured. The swelling index was computed using the equation:

$$S = V_2/V_1 \text{ ----------} \quad (v)$$

Where; S = Swelling index.
V1 = Volume occupied by the gum prior to hydration.
V2 = Volume occupied by the gum after hydration.

Loss on drying

The method adopted was a modification of that specified in the B.P (1994) for acacia. A 1.0 g quantity of the sample was transferred each into a petri dish and then dried in an oven at 105°C until a constant weight was obtained. The % moisture content was then determined as the ratio of weight of moisture loss to weight of sample expressed as a %.

pH determination

This was done by shaking a 1% w/v dispersion of the sample in water for 5 min and the pH determined using a pH meter (Corning, model 10 England) (Emeje et al., 2009).

Angle of repose

The static angle of repose, , was measured according to the fixed funnel and free standing cone method (Ohwoavworhua and Adelakun, 2005). A funnel was clamped with its tip 2 cm above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The heights (h), of the powder cones and the mean diameters (D), of the base of the powder cones were determined and the tangent of the angle of repose calculated using the equation:

Tan = 2h/ D
(xvi)

Bulk and tap densities: A 2.0 g quantity each of the powder sample was placed in a 10 ml measuring cylinder and the volume, V_o, occupied by each of the samples without tapping was noted. After 100 taps on the table, the occupied volume V_{100} was read. The bulk and tap densities were calculated as the ratio of weight to volume (Vo and V_{100} respectively).

Hausners index : This was calculated as the ratio of tap density to bulk density of the samples.

Compressibility index: This was calculated using the equation :Compressibility= (Tapped density- bulk density)/Tapped density x 100. (7)Differential scanning calorimetry (DSC). Thermal properties of AAG were characterized using a Netzsch DSC 204 F1 Phoenix (Netzsch, Germany). Nitrogen, at the rate of 20 ml/min, was used as purge gas, 2.7 mg of powdered material was sealed in aluminium pan and heated from 30 °C up to 400 °C at the rate of 10 °C/min, followed by a cooling cycle back to 30 °C at the same rate.

RESULTS AND DISCUSSION

Results in Table 1 show some of the physicochemical parameters of test and reference gums. While AAG was completely soluble in water yielding colorless slimy solution, it was practically insoluble in ethanol, acetone and chloroform. Tragacanth and gelatin which were used but insoluble in ethanol, acetone and chloroform.

The swelling characteristic of AAG in water was studied. The results show that AAG generally has higher swelling index (660 times its original volume) suggesting that the gum may perform well as binder/disintegrant/matrixing agent. The swelling index is in the order AAG > gelatin > TG.

The moisture content of AAG was low (Table 1), suggesting its suitability in formulations containing moisture sensitive drugs. Given suitable temperature moisture will lead to the activation of enzymes and the proliferation of micro organisms, thereby affecting its shelf life. It is important to investigate for the moisture content of a material because the economic importance of an excipient for industrial application lies not only on the cheap and ready availability of the biomaterial but the optimization of production processes such as drying, packaging and storage (Sonnergaard, 1999).

Results in Table 1 also show that, of the 3 materials tested, AAG would be expected to have the best flow based on the compressibility index and angle of repose. The knowledge of compressibility and flow indices is important in scale up processes involving this material as an excipient in a pharmaceutical formulation. Modification regarding the improvement in its flow properties during process development will be minimal compared to tragacanth. Such process development for optimal production process would include glidants or feeders.

Knowledge of the pH of an excipient is an important parameter in determining its suitability in formulations since the stability and physiological activity of most preparations depends on pH (Luiz et al., 2005). The gums (1% w/v) gave pH of 4.3, 5.3 and 7.5 for AAG, tragacanth and gelatin respectively (Table 1). The acidic pH of AAG implies that when used in uncoated tablets, it may be irritating to the gastrointestinal tract. It might also not be useful in the formulation of acidic drugs.

Differential scanning calorimetry (DSC) : Is used to measure the occurrence of exothermal or endothermal changes with increase in temperature. The thermograms of AAG, TG and gelatin are shown in Figure 1, while Table 2 contains the corresponding parameters. The results show that the gum only has an amorphous portion. The glass transition (Tg) temperatures for the gums were 43.7, 74.8 and 213.9 °C for AAG, TG and gelatin respectively. AAG had a lower degree of crystallinity when compared to gelatin as shown by the values of Tg (Ezekiel et al., 2007). AAG was also observed to have the highest enthalpy, this property has been attributed to the shape and size of powder granules (Matthew and Abraham, 2007.

Gelatin showed a sharp endothermic shift and a broad). Melting peak at about 221.9 and 286.6°C respectively. Its onset peak and conclusion temperatures were much higher than the other 2 gums (Table 2) for gelatin. The continuous (broad) endothermic transition that followed the glass transition in gelatin is indicative of crystallite melting occurring over the glass transition range (Donovan, 1979). The knowledge of Tg is essential in production processes and storage as Tg is affected by moisture and other additives, facilitating conversion to the rubbery state and hence facilitating crystallization (Emeje et al., 2009).

The Heckel equation has been used to classify powders into 3 types; A, B and C based on their compaction behaviors (York and Pipel, 1973; Roberts Formulations containing AAG gave a linear relationship at all applied pressures, which is typical of A- type material. plastic flow. There was however a slight change in the deformation character when the concentration of AAG was increased from 1 to 5% w/w.

The monophasic curve obtained for 1% AAG became

Table 1. Some physicochemical characterization of *Afzelia africana, Tragacanth, Gelatin gums.*

Parameters		Results
Afzelia Africana		
Solubility		Slightly soluble in water.
Practically acetone and		Practically insoluble in ethanol, acetone and chloroform
Swelling capacity (%)	In water	660.0
Loss on drying		0.2%
Total ash		2.0%
Acid insoluble ash		1.0%
True density (g/cc)		1.7
Density of powder	Bulk density (g/cc)	0.61 ± 0.05
	Tapped density (g/cc)	0.71 ± 0.00
Compressibility index		14.08%
Hausners quotient		1.16
Angle of repose		10.61 ± 1.17º
pH		4.3
Tragacanth		
Solubility		Slightly soluble in water. Practically insoluble in ethanol, acetone and chloroform.
Swelling capacity (%)	In water	250.0
Loss on drying		0.1%
Total ash		3.0%
Acid insoluble ash		0%
Density of powder	Bulk density (g/cc)	0.56 ± 0.02
	Tapped density (g/cc)	0.79 ± 0.00
Compressibility index		29.11%
Hausners quotient		1.41
Angle of repose		21.77 ± 2.74º
pH		5.3
Gelatin		
Solubility		Slightly soluble in water. Practically insoluble in ethanol, acetone and chloroform
Loss on drying		0.1%
Total ash		2.0%
Acid insoluble ash		0%
Density of powder	Bulk density (g/cc)	0.64 ± 0.00
	Tapped density (g/cc)	0.74 ± 0.01
Compressibility index		13.51%
Hausners quotient		1.16
Angle of repose		10.28 ± 2.23º
pH		7.5

triphasic which did not fit into the any of the 3 classes above. A similar result was obtained for gelatin and TG, with the effect of concentration being more pronounced with formulations containing TG than with those containing gelatin. This is consistent with an earlier report (Emeje and Kunle, 2004) where the Heckel equation w/w AAG with TG and gelatin as comparing standards.

This implies that this formulation deformed principally by and Rowe, 1986). Figures 2 and 3 show representtative Heckel plots for HCTZ formulations containing 1 and 5% could not be used to classify some formulations.

The yield pressure Py is an important indication of granule compressibility and describes the tendency of the material to deform either by plastic flow or fragmentation (Paronen and Juslin, 1983). In general, a low Py value (steep slope) reflects low resistance to pressure, good densification and easy compression (Isimi et al., 2003). The highest Py value was observed at 1 and 4% AAG concentrations while the lowest value was recorded for formulation containing 1 and 2% tragacanth (Table 3). Based on this, the order of plastic deformation would be AAG > TG > gelatin. The lower Py values observed for the

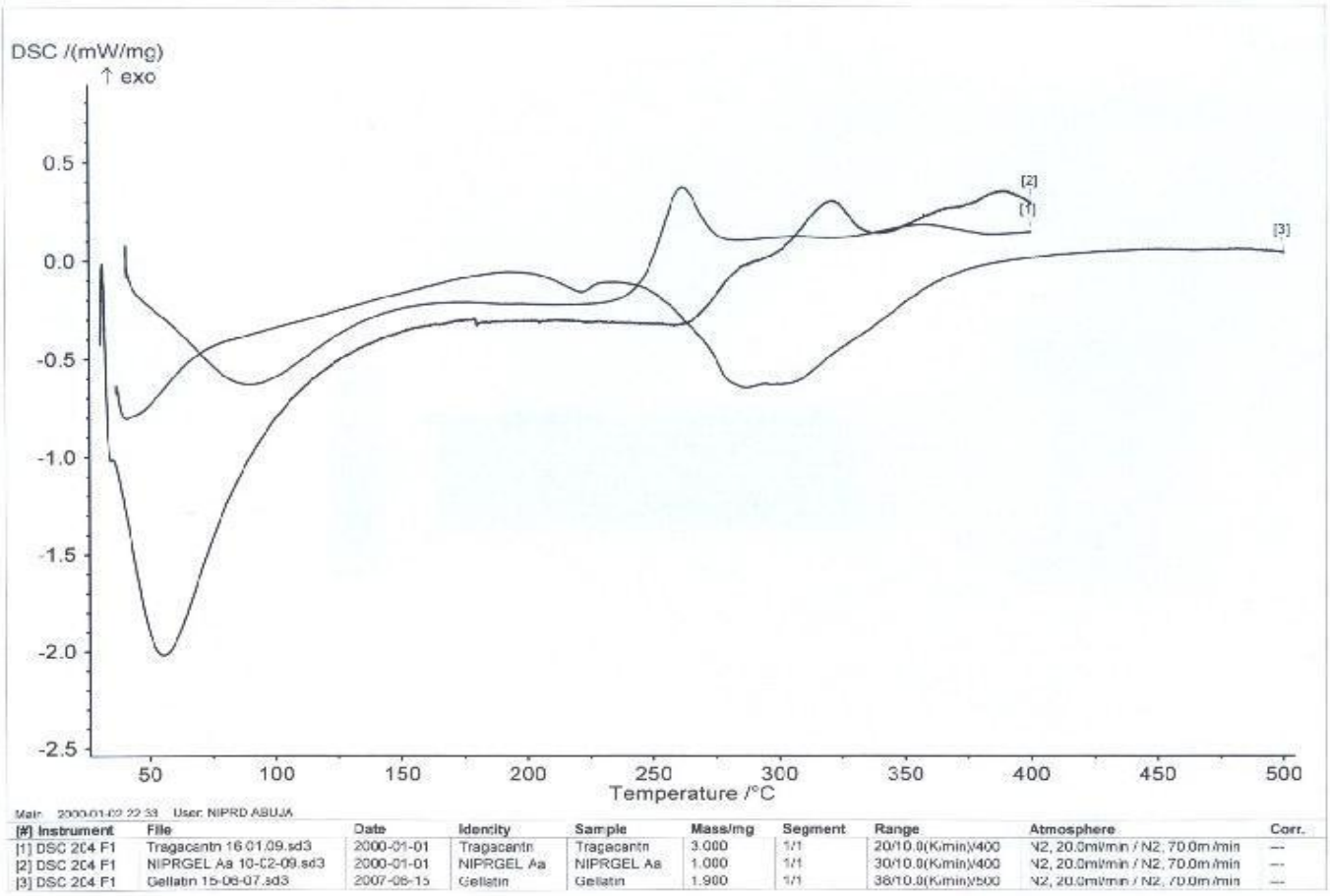

Figure 1. DSC thermograms of *Afzelia* gum (1), Tragacanth (2) and Gelatin (3).

Table 2. Thermal properties of the gums.

Parameter	*Afzelia Africana* gum	Gelatin gum	Tragacanth gum
Onset temperature (°C)	37.0	271.6	62.0
Peak temperature (°C)	43.7	279.8	88.8
Endset temperature (°C)	47.8	288.0	87.6
Delta Cp [J/(g*K)]	4.4	2.0	1.9
Melting point (°C)	-----	286.6	----

formulations containing TG and gelatin may be due to fragmentation as a result of low resistance to compression pressure. The values of Da were lower for formulations containing AAG compared to those 3). In contrast, formulations containing TG had lower Da when containing gelatin at all concentrations except 2% (Table compared to those containing AAG at all concentrations except 3 and 4% w/w gelatin. These observation maybe attributed to the differences in particle size and shape of the mixtures (Itiola, 1991).

The Do values for all the formulations increased with increase in binder concentration up to 3% w/w and decreased as the concentration increased to 5%. Do which shows the density of the powder without any external pressure indicates the extent of packing of the particles in the powder bed. It is influenced largely by the particle size and shape, with ovoid shaped particles facilitating these interlocking and hence closer packing than round ones. The high value of Do obtained for the formulation containing 3% AAG is also an indication of weak electrostatic forces that could prevent the close packing of particles in the precompression stage. All the formulations have low Db values, since Do describes the phase of particle rearrangement in the powder consolidation process; the low values indicate that fragmentation was not extensive. This observation corroborates our earlier deduction

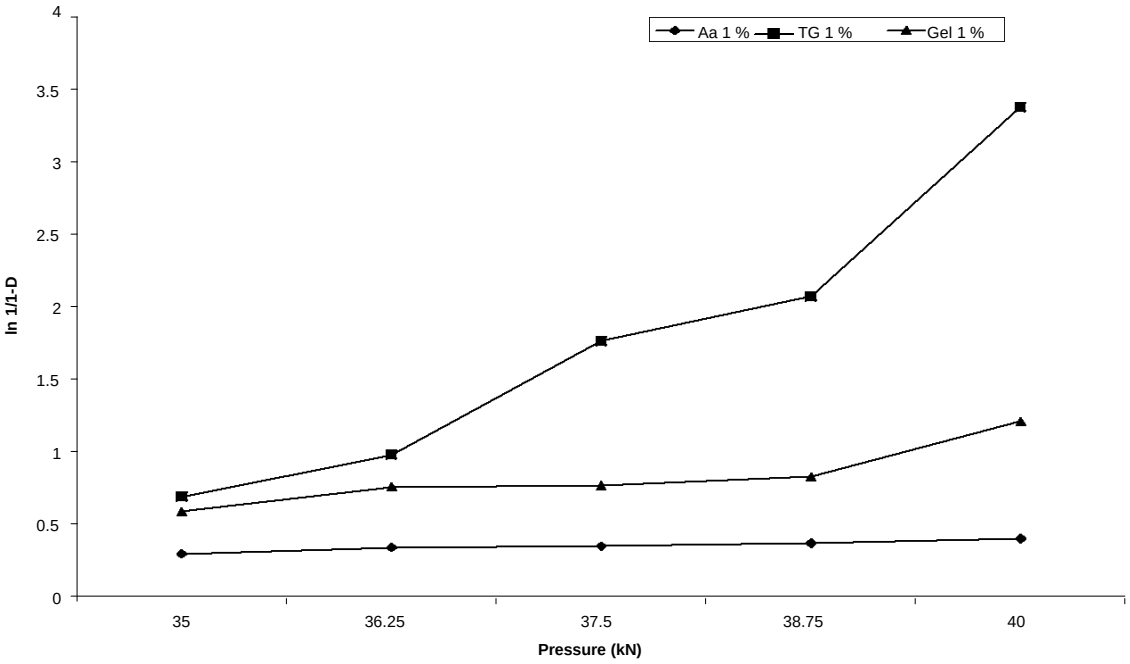

Figure 2. Effect of binder type on the Heckel plots.Aa, Afzelia africana; TG, Tragacanth; Gel, Gelatin.

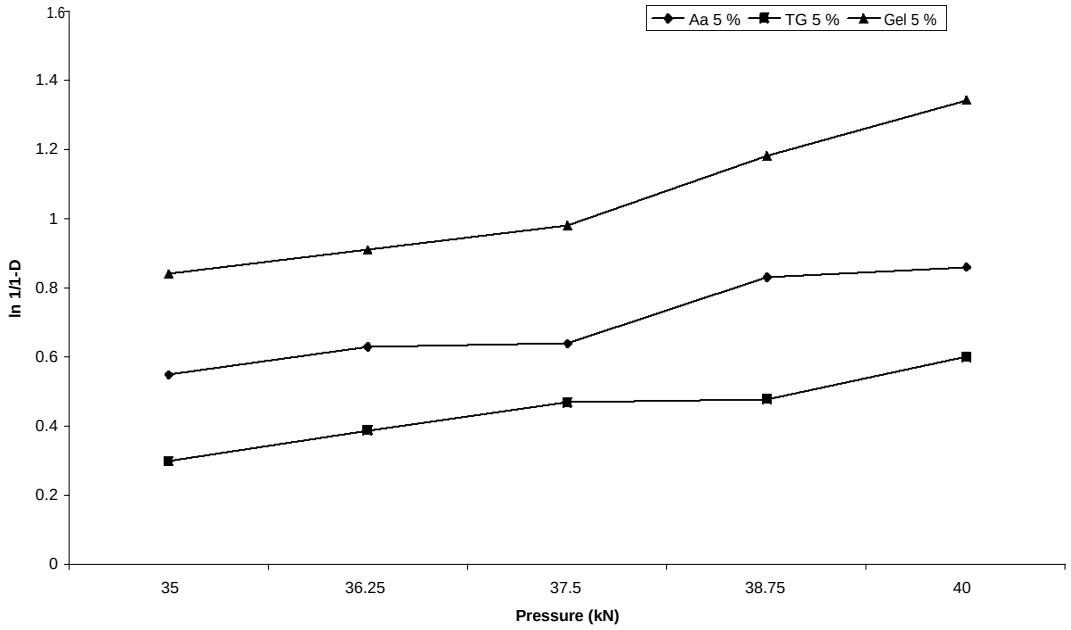

Figure 3. Effect of binding type on the Heckel plots.Aa, Afzelia africana; TG, Tragacanth; Gel, Gelatin.

from the Heckel plots that compact formation was mainly by plastic deformation. The lower values of Db as compared to Do confirmed the absence of fragmentation of the particles at the applied pressures.

Conclusions

The results presented here shows that the gum obtained from *A. africana* has good physicochemical properties that would make it suitable as a binder in hydrochlorothiazide tablet formulation. Compaction studies showed that formulations containing *A. africana* gum as a binder exhibited slower onset and lower plastic deformation than those containing TG or gelatin. It compared favorably with these standard binders. Gum obtained from the exudates of *A. africana* may therefore be a useful binder in

Table 3. Parameters obtained from Heckel plots for hydrochlorothiazide tablet formulations.

Binder type	Binder conc. (%w/w)	Do	Py (kN)	Da	Db
AAG	1.0	0.158	43	0.261	0.103
	2.0	0.305	32	0.393	0.089
	3.0	0.429	26	0.274	0.155
	4.0	0.328	43	0.428	0.100
	5.0	0.318	12	0.366	0.048
TG	1.0	0.132	2	0.174	0.042
	2.0	0.132	2	0.184	0.052
	3.0	0.349	14	0.386	0.037
	4.0	0.336	27	0.486	0.150
	5.0	0.026	14	0.214	0.146
Gel	1.0	0.345	8	0.368	0.023
	2.0	0.345	8	0.368	0.023
	3.0	0.372	13	0.372	0.014
	4.0	0.313	14	0.503	0.190
	5.0	0.320	8	0.488	0.168

hydrochlorothiazide tablet formulations.

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