

Afzelia africana seed gum: potential binder for tablet formulations

Ibezim, E. C¹., Khanna, M²., Singh, S² and Uzuegbunam, C.E.¹

1. Department Of Pharmaceutics, University Of Nigeria, Nsukka.

2. Department Of Pharmaceutics, Central Drug Research Institute, Lucknow, India

Abstract

The physico-technical properties as well as the application of a novel polysaccharide from the seeds of *Afzelia africana* as a tablet binder have been studied. The following physico-chemical properties of the gum, extracted by cold maceration in distilled water were evaluated by standard methods: presence of starch, saponin, tannin, reducing sugar, glycosides, alkaloids, oils, flavonoids and steroidal aglycones; solubility profiles, rheology and densities. Differential Scanning Calorimeter (DSC). Nuclear Magnetic Resonance (NMR) spectroscopy and Mass Spectroscopy (MS) of the polysaccharide were also carried out. The granulating as well as tableting characteristics of the gum in 100 mg 5-aminosalicylic acid tablets were studied and compared to a similar formulation with acacia. The yellowish-brown, translucent gum, with angular and irregularly shaped particles, contained saponin, glycoside, reducing sugars, protein and steroidal aglycone. The gum swells in water, and was soluble in 1% sodium hydroxide. A 2% solution had a viscosity of 143 cp and an acidic pH of 4.58. Other physico-technical properties were similar to those of acacia, a standard tablet binder. The DSC scan showed the gum to absorb heat at 140 - 150 °C while the NMR spectra show it to be a polysaccharide possibly with CH₂O-R units at the region 3.369. The Electro-spray MS shows the presence of negative (M-HT groups of disaccharides, trisaccharides, tetrasaccharides and pentasaccharides. The percentage; of C, N and H in the gum were 0.00, 48.09 and 1.11 respectively. Granules formed with *Afzelia* gum were free flowing, having a percentage compressibility of 22.8, angle of repose of 35 ± 0.64°, bulk density of 0.29 g/cm³ and tapped density of 0.37 g/cm³. The tablets prepared with *Afzelia* gum showed better tablet properties with lactose as diluent than with microcrystalline cellulose. The overall tablet characteristics were within the acceptable official ranges and compared favourably with the tablets formed using acacia.

Keywords: *Afzelia africana* gum, binder, granules, tablets.

Introduction

Gums of natural origin have found varying uses in pharmaceutical formulations (1, 2). One of the key areas where they have employed is in tablet formulations where they serve as binder, or as matrices for sustained release dosage forms. Binders give strength to tablets and as such, evaluation of granule and tablet properties gives an index of binder efficiency (3). Agents that have been employed as binders include acacia, starch, gelatin, ethyl cellulose, tragacanth and *albizia* gum. *Afzelia africana* gum is obtained from the seeds of the tropical food plant grown widely in West Africa. The seeds are used locally as thickener in soups and other food preparations. The drug, 5-amino salicylic acid (Mesalazine®) employed in the study is used in the treatment and maintenance of patients suffering from ulcerative colitis (4).

In this study, the gum obtained from the seed of *Afzelia africana* is evaluated for its binding properties in 5-amino salicylic acid tablets.

Materials and methods

Materials

The following materials of analytical grade were used as procured from their respective manufacturers: acacia (Merck, England) and 5-amino salicylic acid (FMC USA). *Azzeria africana* seeds were collected from Utonkon in Benue State Nigeria.

Methods extraction of gum

The gum was extracted from the dehauled and pulverized seeds of *A. africana*, by maceration using the method of Keshri and Srivastava (5). The precipitated gum was dried at 60°C in an oven for 12 hours, pulverized and passed through a sieve of 125 urn mesh size.

Physico-chemical properties microscopy

The microscopic appearance of the gum was observed in a Leitz Microscope (Leitz, Germany), by mounting a little quantity of the powdered gum in an immersion oil and viewing under a x40 objective lens and x 100 eye piece.

Solubility

The solubility profile of the gum was evaluated in varying solvents by adding 5 mg quantity in 5 ml of the respective solvent.

Rheology

The rheological properties of a 2 % w/v dispersion of the gum in water were measured with a Rotovisco viscometer at 25 °C. A 20 ml quantity of the gum dispersion was placed in the cup of the viscometer and the reading on the instrument scale noted, which is later converted to centipoises.

Densities

The relative density of a 2 % w/v dispersion of gum in water was determined with a Pycnometer by determining the weight of 10 ml volume of the gum dispersion contained in the Pycnometer, relative to the weight of a similar volume of distilled water. The densities (bulked and tapped) were determined by the 3 - tap method (6).

PH

The pH of the 2 % gum dispersion was determined immediately after preparation and after storage for 8 weeks using a pH meter (Systronics, India).

DSC Scan

This was carried out on the powdered gum using a Mettler TA 4000 System at the rate of 10 k/min.

NMR Spectroscopy

An NMR study was carried out on the gum dispersed in dimethyl sulphoxide (DMSO) using a dP x 200 Instrument.

Electrospray mass spectroscopy(ems)

The Electrospray Mass Spectra of the powdered gum sample was recorded on a Micromass Quattro II Triple quadrupole Mass Spectrometer. The nitrogen, carbon and hydrogen contents of the powdered gum were equally determined by elemental analysis by the EMS.

Granulation and Granule properties

Granules of 5-amino salicylic acid were prepared with *A. africana* seed gum according to the following formula: 5-amino salicylic acid 2.0211 g; Magnesium stearate 0.1076 g; Microcrystalline cellulose 2.6580 g; *A. africana* seed gum 2.2000 g.

The powders were mixed together in a mortar, and the gum in form of mucilage added. The wet mass was then passed through a No 60 sieve and the resulting granules dried at 60 °C in an oven. A similar formulation was made with acacia in place of *A. africana* gum for the purpose of comparison.

The flow rates, angles of repose, % compressibility, densities (bulk and tapped) and % fines were determined according to standard procedures (7, 8). The flow rate was determined by noting the time for 10 g of the granules to completely flow out of a funnel fixed at a distance of 20 cm from a horizontal surface. The angle of repose was measured by determining the angle formed by heap (cone) formed by 10 g of the granules falling from a funnel fixed at a distance of 20 cm from a flat surface. The bulk density was determined by measuring the volume occupied by 2 g of the granules placed in a measuring cylinder while the tapped density was obtained by measuring the volume occupied by 2 g of the granules after tapping the cylinder on a hard surface for 20 times.

Tableting properties

Tablets (300 mg) were prepared from the granules using a Korsch Single Punch Tableting machine at a force of 4 kgf according to the following formula:

5 - amino salicylic acid 100mg

Magnesium stearate 3 mg

A. Africana gum 5% or 10 %

Microcrystalline cellulose 132.5 mg

Lactose was used in place of microcrystalline cellulose in another batch of formulations to reduce bulk and improve hardness.

Similar formulations were also made with acacia for the purpose of comparison. Tablet properties like friability, hardness, uniformity of weight, surface area, dissolution profile and disintegration time were evaluated. The friability test was carried out in Friability tester (IEC, India) by determining the percentage loss in weight after 20 tablets had been rotated in the friabilator for 4 mins at a speed of 25 rpm.

The hardness was measured by placing the tablet between the spindle and anvil of the Monsanto tablet tester and noting the pressure required to just break the tablet. The mean of five determinations was taken. The surface area was measured with the aid of a Micrometer Screw Gauge. The mean of five measurements was taken. The dissolution profile was determined in a Dissolution rate USP XXI Apparatus (IEC, India) by measuring the amount of drug released to the dissolution medium (0.1 N HCl) at a temperature of 37°C and a rotation speed of 100 rpm at 10 minutes intervals. The disintegration study was carried in a USP Disintegration Tester (Electrolab, India) using five tablets and noting the time taken for the tablets to disintegrate. The uniformity of weight was determined following the BP specifications. The average weight of 20 tablets was taken and the deviations of the

individual weights of the tablets compared the average weight.

Results and discussion

The extraction process yielded a yellowish brown gum with a bland taste and smooth texture. When mounted and examined under the microscope, the gum particles were translucent, angular and irregular in shape with size ranges of 12-20 μm . Saponin, glycoside, reducing sugars, protein and steroidal aglycones were present in the gum. Starch, alkaloids, tannins, oils and flavonoids were however absent. The gum swole somewhat in water to yield a slightly viscous mass. It was insoluble in methanol, propylene glycol and diethyl glycol but swole in dimethyl sulphoxide. It was however soluble in 1% sodium hydroxide solution. From Table 1, a 2% gum dispersion in water had a pH of 4.58, and exhibited a viscosity (μrel) of ~ 143.4 cP, which was found to decrease with increase in temperature (Fig. 1). These were comparable to the viscosity and pH of a similar dispersion of acacia, which were ~ 139.6 cP and 4.33 respectively. The results of relative densities, bulk densities, tapped densities, and % compressibility, presented in Table 1 show that *A. africana* gum possesses good physico-chemical properties comparable to those of acacia, a standard binder in tablet formulations.

The DSC scan of the powdered *A. africana* gum showed that it absorbed heat between the temperature range of 140 and 150°C at which it probably underwent glass transition (Fig 2). The NMR spectra indicate that the gum is a polysaccharide possibly with $\text{CH}_2\text{O-R}$ units mainly present at the region of 3.369 (Fig. 3). Other peaks at regions 2.536 and 1.266 may represent some $-\text{CH}_2$ units of rhamnose. The Electrospray MS showed the presence of negative (M-II) groups of disaccharide, trisaccharides (base peak), tetrasaccharides and pentasaccharides (Fig 4). The percentages of C, N, and H in the gum sample were found to be 0.00, 48.09 and 1.11 respectively.

Properties of granules formulated with both *Afzelia* and acacia gums are presented in Table 2.

Table 1: Some physical properties of granules formulated with *A africana* and acacia

Granule type	Physical property						
	PH	Viscosity (cP)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Relative density	% compressibility	Angle of
<i>Afzelia africana</i>	4.58	143.4	0.37	0.51	1.018	27.16	.
Acacia	4.33	139.6	0.63	0.83	1.017	25.00	-

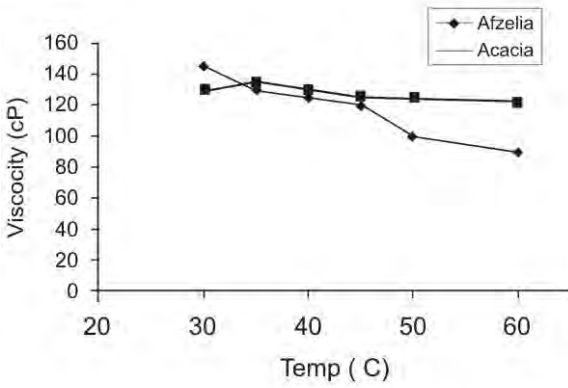


Fig 1: Graph of viscosity versus temperature for 2% dispersions of Afzelia and acacia gums

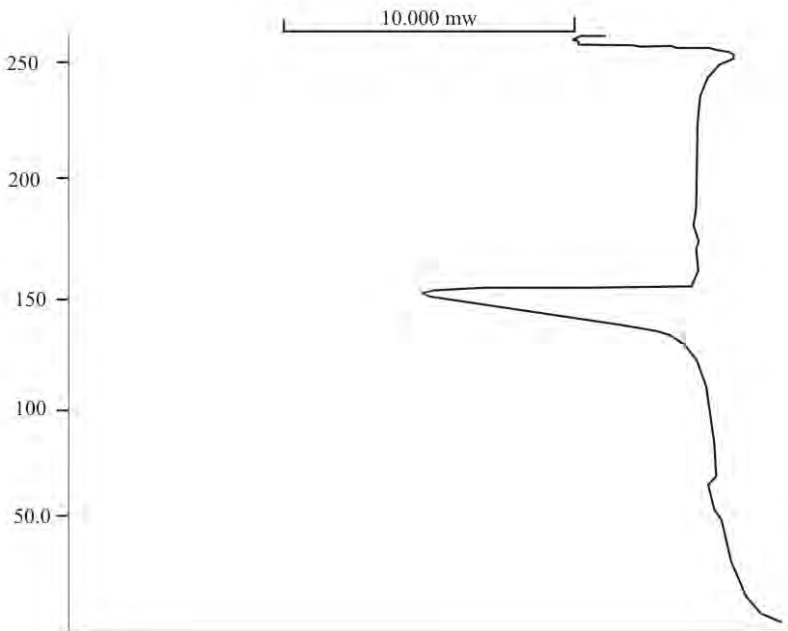


Fig. 2: DCS scan of Afzelia africana seed gum

SEED START

***** METTI 1001 YSTEM *****

GREEN
7-OCT-9814:03
SCAN PARAMETERS
START TEMPS °C 30
RATE K/MIN 10
END TIME °C 300
TIME ISO. MIN 0
PLOT CM 15
RANGE FS MW 25
OFFSET O/O 70
PAN TYPE ½ 1
LIMIT MW 0
SCREEN
DYN / ISO ½ 0
IDENT. NO. 3. (AFLEZIA)
WEIGHT MG 5.286
TEMPERATURE °C HEAT FLOW
EXOTHERMAC ---->

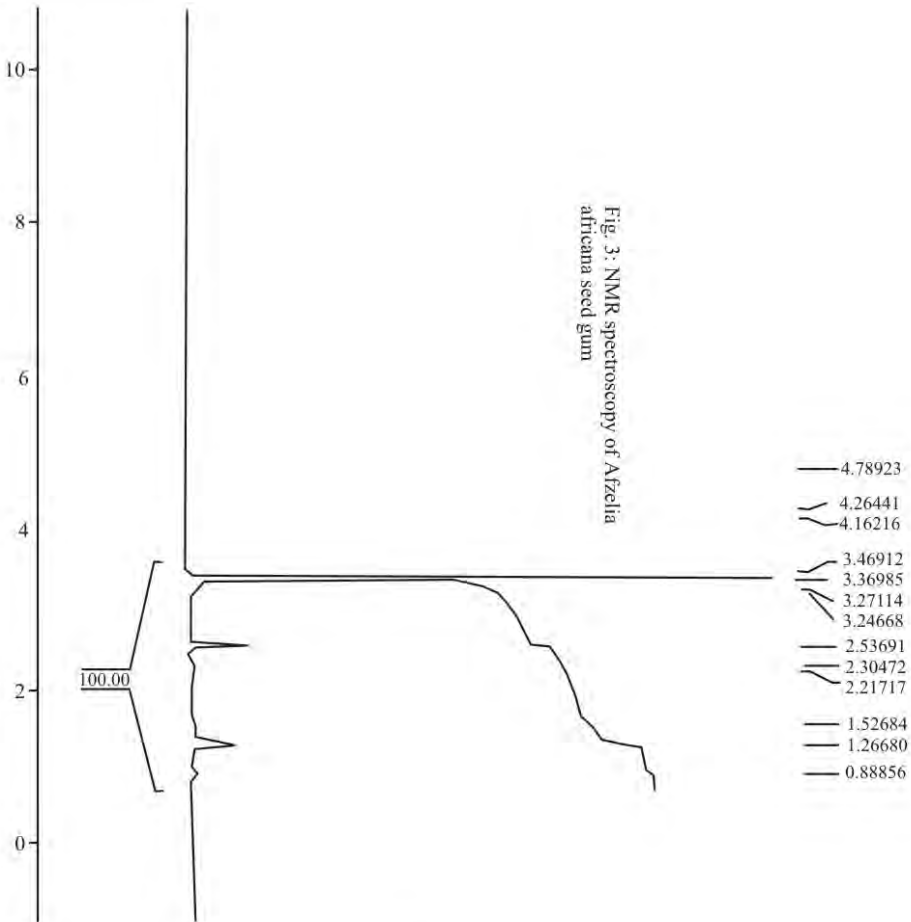


Fig. 3: NMR spectroscopy of Afzelia africana seed gum

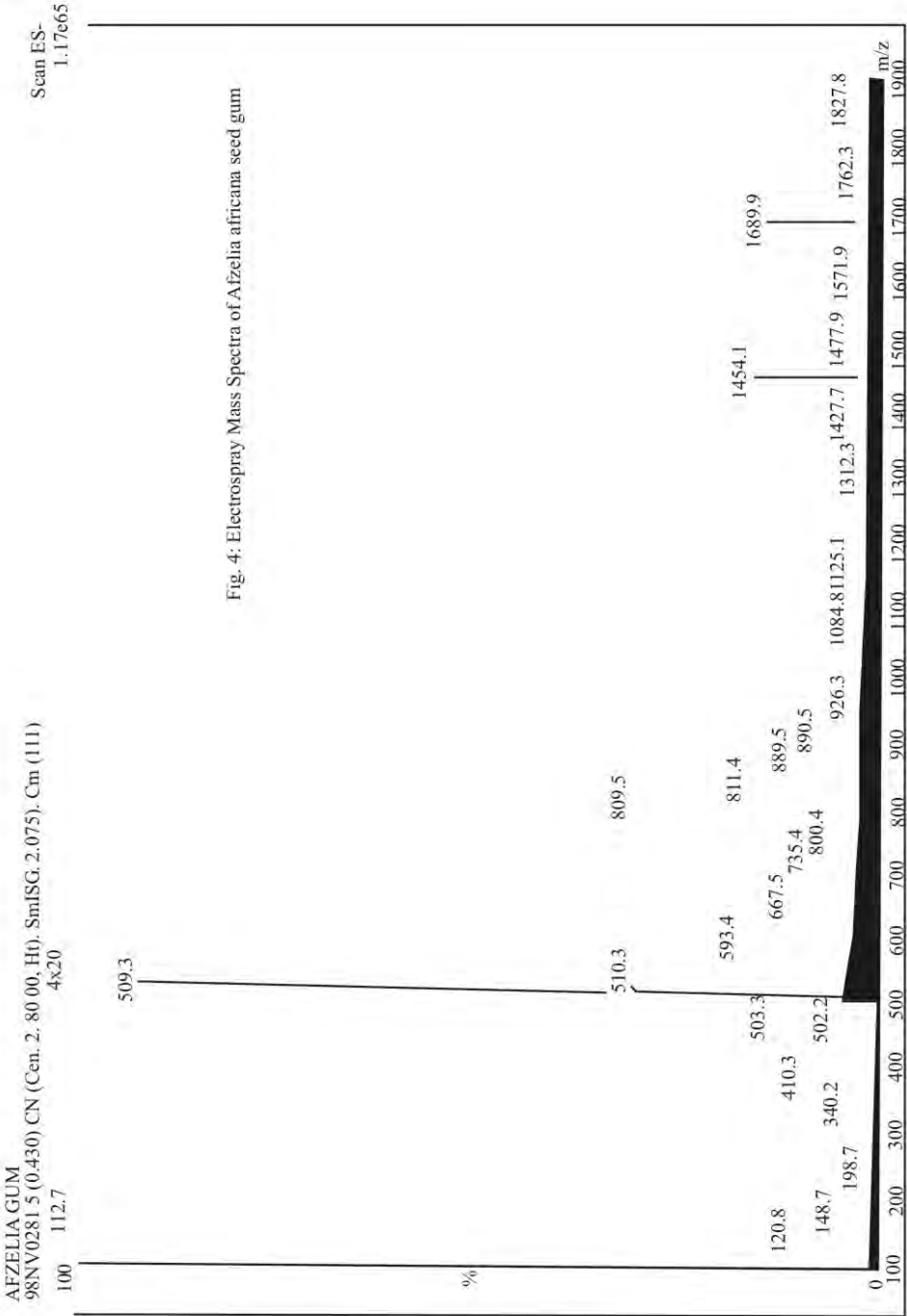


Table 2: Properties of granules prepared with Afzelia and acacia

type	Granule properties				
	Flow rate g/sec	% compressibility	Angle of repose (o)	Bulk density (g/cm ³)	Tapped density (g/cm ³)
A.africana	1.85 ± 0.09	22.8	35.15 ± 0.64	0.29	0.37
Acacia	1.26 ± 0.02	24.0	33.62 ± 2.04	0.30	0.39

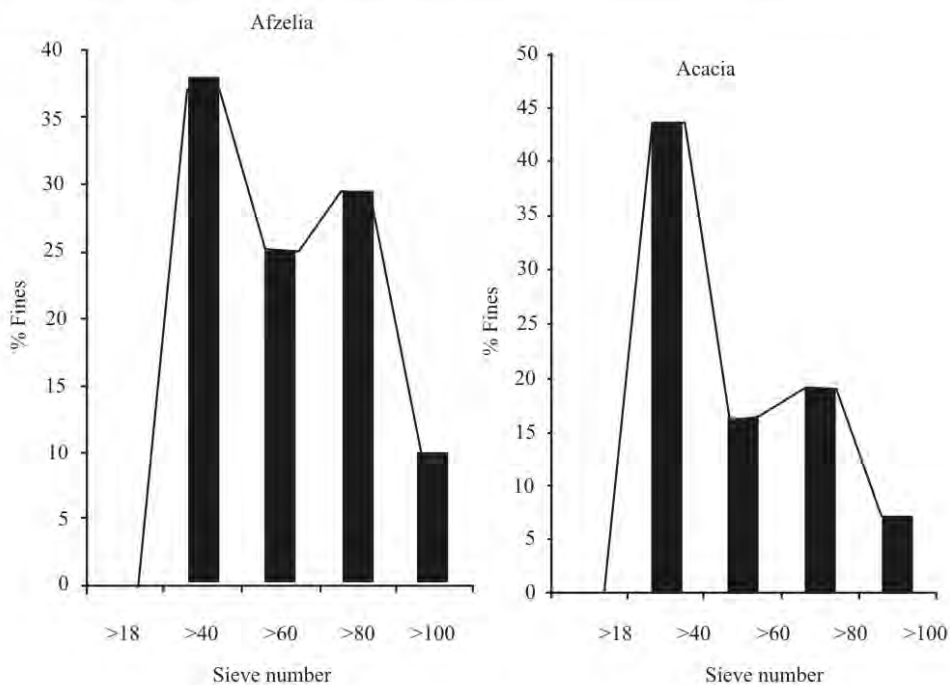


Fig. 5% Distribution of fines in granules prepared with Afzelia and acacia gums

The results above indicate that both granules possessed similar properties. The percentage fines of the granules are presented in Fig. 5.

Table 3 shows the characteristics of the tablets formulated with *Afzelia africana* and acacia gums using different methods, diluents and gum concentrations. The results obtained for the tablets formed by wet granulation were similar to those obtained using the dry granulation method. The tablets prepared by dry granulation method with lactose as diluent exhibited increased hardness, disintegration time and dissolution times (Figs 6 and 7). The tablet friabilities were similar but generally reduced with increase in gum concentration (Table 4), while the hardness expectedly increased (11-14).

All the tablets conformed to the BP specifications for uniformity of weight. The hardness values for the tablets containing microcrystalline cellulose were low making the tablets brittle, which suggests that microcrystalline cellulose may be unsuitable as a diluent in this formulation. The tablets prepared with *Afzelia* gum generally exhibited acceptable disintegration times though some disintegrated rather fast. The BP requirement is that the tablet should disintegrate within 15 mins. The tablets containing acacia were however slow in disintegration, a reflection of the high hardness results earlier obtained. This is not very favourable in therapy where it is expected that the tablet should disintegrate promptly to release its drug contents. The results of the dissolution test however showed that all the tablets released their drug contents within 1 hour, suggesting that *Afzelia africana* gum can be used as matrix for normal but not sustained release of the drug 5 - amino salicylic acid.

Table 3: Characteristics of 5-amino salicylic acid tablets prepared with *Afzelia* and acacia gums

Tablet composition	Tablet weight (g)		Hardness (kg/cm ²)		% friability	Surface area (mm ²)		Disintegration time (min)
	Mean	% CV	SD	% CV		Mean	% CV	
	SD	CV	SD	CV	Mean	CV		
5 % <i>Afzelia</i> in lactose (Dry granulation)	0.2965 0.0019	0.64	4.41 0.413	9.35	1.06	220.39 0.4502	1.11	6.5
5 % Acacia in lactose (Dry granulation)	0.2965 0.0019	0.64	8.75 0.634	8.75	0.63	211.19 0.8887	0.40	48
10 % <i>Afzelia</i> in lactose (Dry)	0.2950 0.0075	2.54	5.08 0.716	14.1	0.57	215.65 1.8198	0.84	11.0
10 % Acacia in lactose (Dry)	0.2980 0.0000	0.00	8.73 0.573	6.57	0.67	213.98 1.1399	0.53	52.0

Table 3 Contd

Tablet composition	Tablet weight (g)		Hardness (kg/cm ²)		% friability	Surface area (mm ²)		Disintegration time (min)
	Mean	% CV	SD	% CV		Mean	%CV	
5 % <i>Amelia</i> in lactose (Wet granulation)	0.3003 0.0020	0.67	3.28 0.035	1.07	0.38	215.0 0.6171	0.29	1.00
5 % Acacia in lactose (Wet granulation)	0.2982 0.0056	1.88	4.20 0.000	0.00	0.28	0.18 0.3817		1.25
5 % <i>Afielia</i> in MCC (Dry)	0.2475 0.0040	0.02	3.19 0.122	3.82	0.95	226.7 0.8239	0.36	8.50
5% Acacia in MCC (Dry)	0.2510 0.0024	0.96	3.99 0.171	4.29	0.43	225.8 2.2652	1.00	7.00

Conclusion

It has been demonstrated in this study that the novel gum from the seed of *Afzelia africana* possesses good physico-chemical, granulation and binding properties, comparable to those exhibited by acacia, an official binder in tablet formulations. It can thus be exploited for future use as a binder in tablet formulations in view of the rising cost and increasing unavailability of the official gums (15, 16).

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