



EXTRACTION AND PURIFICATION OF STEM BARK GUM OF *GREWIA MOLLIS* JUSS. FOR USE AS A DISINTEGRANT IN TABLET FORMULATION

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ABSTRACT

Gums are polysaccharides of natural origin that have been used traditionally as binders in the formulation of tablets by wet granulation. This research aimed at extraction of *Grewia mollis* gum (GG) by dispersing 600 g of the dried and pulverized inner stem bark of the *Grewia mollis* shrub in about 20 litres of demineralized water using an impeller, which was further purified by treatment with 0.1 M hydrochloric acid for about 5 minutes followed by extraction with 25 ml of 95 % Acetone and evaluating the use of bleached acetylated stem bark gum of *Grewia mollis* Juss (BAGG) as a disintegrant in tablet formulations using Ibuprofen as a model drug. The yields of the gums were found to be 58.5, 80.3, and 60.0 % for GG (*Grewia* Gum), AGM (Acetylated *Grewia* Gum), and BAGG (Bleached Acetylated *Grewia* Gum) respectively. The pH values for the gums were 4.83, 4.95, and 4.01 for GG, AGM, and BAGG respectively. The swelling capacities were 1.59 ± 0.00 , 2.90 ± 0.01 , and 2.80 ± 0.00 respectively for GG, AGM, and BAGG. Moisture contents were 0.54 ± 0.01 , 0.13 ± 0.01 , and 0.12 ± 0.01 for GG, AGM and BAGG respectively. The LD₅₀ values of both the native and derivatized gums were both greater than 5000 mg. Tablets weighing 500 mg were prepared by compressing ibuprofen granules containing BAGG as disintegrant at concentrations ranging from 1.25 to 10 % in comparison to maize starch B.P. at the same concentrations. The tablets formulated were kept for about 24 hours and subsequently evaluated for tablet properties. The outcome of the study showed that tablets formulated with BAGG - A as disintegrant with a concentration of 1.25 % had an enhanced disintegration time and dissolution profile comparable to other formulations. Formulation of ibuprofen tablets containing BAGG - A with 1.25 %, as disintegrant was obtained with the following properties; Crushing strength (6.9 ± 1.24 kgf), disintegration time (9.47 ± 3.06 min) and friability (0.78 %). The results of this study had been able to establish that bleached acetylated *Grewia mollis* stem bark gum, concentration 1.25 %, could be used effectively to formulate Ibuprofen tablets that disintegrated within 15 mins.

Keywords: Characterization, Extraction, *Grewia* gum (GG), Purification, Organoleptic properties.

INTRODUCTION

Plants gums/resins due to their properties of non-toxicity, non-polluting, sustainable, recyclable, low costs, eco-friendliness, wide spread availability, biodegradability and biocompatibility have bestowed them unique position in the field of pharmaceuticals, nanoparticles synthesis and food industry

(Irfan et al., 2021). Natural polysaccharides/biopolymers-based nanoparticles have a lot of advantages over similar synthetic entities. These plants polymers do double actions i.e. they act as stabilizing as well as reducing agents for

metal ions while synthesizing nanoparticles (Irfan *et al.*, 2021).

Polysaccharides are abundant in nature and form the major constituent of the cell wall materials of plants (eg cellulose or pectin) (Chen *et al.*, 2018). Plant polysaccharide extracts have been widely used in food and pharmaceutical applications due to their valuable functional properties. In addition, they may also display bioactivity including antidiabetic, antitumor or immunomodulatory properties. These functional characteristics have been related to their chemical composition, molar mass, branching characteristics and functional groups (Kpodo *et al.*, 2019).

A class of polysaccharides that has recently attracted research attention are those extracted from the Malvaceae family of flowering plants (Alba *et al.*, 2021). *Grewia*

mollis is a tropical shrub which belongs to the Malvaceae family and is widely distributed in Africa. Polysaccharide extracts from the inner stem bark of the *Grewia* plant have been useful to the food and pharmaceutical industries as a thickening agent, emulsion stabilizer, or as hydrophilic matrix for tablets (Kpodo *et al.*, 2019).

In Nigeria, *Grewia mollis* from which the gum is extracted grows abundantly (wild or cultivated) in the middle belt region of the country where it has been used as a thickener in local delicacies and can be propagated by seed or seedlings (Ologunagba *et al.*, 2020). The low solubility of the gum was attributed to insoluble cell wall materials making up a larger proportion of the gum (Pahwa, 2017). The gum was reported to possess excellent binding property in sodium salicylate tablets (Alobo and Arueya, 2017).



Plate I: *Grewia mollis* Juss plant (collected from NCAT, Zaria) Voucher specimen no. 161.

Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. The emphasis on the availability of drug highlights the importance of the relatively rapid disintegration of a tablet as a criterion for

ensuring uninhibited drug dissolution behaviour (Bhowmik *et al.*, 2018).

In more recent years, increasing attention has been paid to formulating fast dissolving and/or disintegrating tablets that are swallowed, but also orally disintegrating

tablets that are intended to dissolve and/or disintegrate rapidly in the mouth (Bhowmik *et al.*, 2018). Thus, disintegrant is a substance added to a formulation to enhance its dissolution and/or breakdown.

The study aimed at collecting, identifying and extracting the gum from the stem bark of *Grewia mollis* Juss and chemically derivatize the gum by acetylation using acetic anhydride as the derivatisation agent.

MATERIALS AND METHODS

Materials

Grewia mollis Juss (Nigerian College of Aviation Technology, Zaria, Kaduna State). 0.1 M hydrochloric acid and Acetone 95 % (M & B Laboratory Reagent, England), Demineralized water, impeller, Muslin cloth.

Methods

Extraction and Purification of *Grewia mollis* Juss Gum

Grewia mollis Juss was collected from Nigerian College of Aviation, Zaria, and was identified and authenticated at the herbarium of the department of botany, Ahmadu Bello University, Zaria, with the Voucher Number of 161. The extraction of the gum was carried out by dispersing 600 g of the dried and pulverized inner stem bark of the *Grewia mollis* shrub, in about 20 litres of demineralized water using an impeller. The fibrous material from the dispersed mucilage was removed by straining through a muslin cloth. Thereafter, the mucilage was centrifuged at 20 rpm before extraction of the gum with 100 ml of 95 % acetone. The extracted gum was then redispersed in 5 litres of water and re-extracted to get a beige-coloured gum which was subsequently dried in an oven at 50 °C for 8 h (Nep *et al.*, 2013). The gum was further purified by

treatment with 0.1 M hydrochloric acid for about 5 minutes followed by extraction with 25 ml of 95 % Acetone (Nep *et al.*, 2013).

Organoleptic Properties

The colour, taste, odour, and texture of the GG were examined and the results were documented.

Toxicity Studies

Five mice each weighing 20 g were randomly selected from animal houses in the Department of Pharmacology and Therapeutics, marked for individual identification and kept in their cages for at least five days before dosing for acclimatization to the laboratory conditions. The mice were fasted before dosing and weighed. A dose of 2000 mg was administered using an oral cannula and observed for signs of toxicity for three days. Then a higher dose of 5000 mg/kg body weight was also administered using 500 mg of the GG and BAGG in 10ml of solution respectively. Treatment of the mice at the next higher dose was delayed until we were confident of the survival of the previously dosed mice. Attention was directed to the observation of signs of toxicity such as tremors, convulsions, salivation, diarrhoea, lethargy, and coma, throughout 24 hours for two weeks (14 days), and mortality observed thereafter.

Bulk and Tapped Densities

Ten (10) g quantity of the extracted GG was placed into a clean 50 ml measuring cylinder and the volume, *V*₀ (bulk volume), occupied by the gum without tapping was noted. The cylinder was tapped several times on a hard table top and the tapped volume was recorded. The bulk and tapped densities were calculated as the ratio of mass to volume. The experiment was repeated in triplicates and the average obtained.

Carr's Compressibility Index and Hausner's ratio

This was the percentage difference between the tapped density and the bulk density also referred to as the compressibility index. Hausner's ratio was the ratio of the tapped density to bulk density.

Angle of Repose

A clean glass funnel was clamped on a retort stand such that the perpendicular height of the tip of the funnel was 10 cm from the flat table surface with a clean sheet of paper. 10 g of the GG sample was poured into the funnel, with the opening of the funnel blocked with a cotton wool, after which it was removed and a gum heap formed. The height of the gum sample was measured as H (cm). The diameter of the circumference of the heap was divided to give the radius R and the angle of repose was calculated using the eqtn 1;

$$\tan \theta = h / r \dots\dots\dots \text{Eqtn 1}$$

Where θ = angle of repose, h = height of the gum heap, and r = radius of heap base.

Characterization of *Grewia* Gum (GG)

Percentage Yield

The percentage yield of the GG was calculated as the weight of the GG obtained with respect to the original weight of the gum from which it was extracted (i.e. total weight of the plant collected). It was calculated using the equation 2 below:

$$\text{Yield (\%)} = \frac{\text{Total weight of the gum extracted (g)}}{\text{Original weight of the gum from which it was extracted (g)}} \times 100 \dots\dots\dots \text{Eqtn 2}$$

pH measurement

The pH of the GG solution was measured using a pH meter (Mettler Toledo) with a microprocessor. A 1 % dispersion of the GG was prepared, and the pH was taken at room temperature (25 ° C). This was performed in triplicates and the average was obtained.

Viscosity

The apparent viscosity of the extracted gum was determined using a Brookfield Viscometer (Model RVF, Stoughton, MA). The gum slurry (5%) was placed in a boiling bath for 15 minutes and then cooled to 22 ° c. Cold paste viscosity was determined using a spindle at 25 ° C.

Moisture Content

Determination of the moisture content of GG was carried out with the aid of a moisture content analyzer (OHAUS MB 45). A 1 g sample of the GG was weighed with the aid of a weighing balance (Mettler Toledo ME 303E) and placed in the moisture content analyzer that was set at 100 ° C for 10 min. The moisture content was performed in triplicates and the average was obtained.

Swelling Capacity

The swelling capacity was determined according to the method adopted by Babu and Parimalavalli (2012) by making a dispersion of 1 g of GG in 10 mL of distilled water in a pre-weighed centrifuge tube. This was placed in a water bath (Karl Kolb Sci. Co, Germany) equilibrated at 90 ° C and the sample was allowed to stand with agitations for 30 min. The swollen gum was cooled to 25 ° C, centrifuged at 1,500 rpm for 10 min, and the supernatant was discarded. The weight of the tube with the swollen gum gel was further weighed and the swelling capacity calculated using equation 3.

$$\text{Swelling Capacity} = \frac{\text{weight of swollen granules}}{\text{weight of dry sample}} \dots\dots\dots \text{Eqtn 3}$$

FT-IR Analysis

IR scan of GG was collected over a range of 4000 – 650 cm⁻¹ using a Cary 630 FT-IR Spectrometer (Agilent Technologies, USA). The sample was subjected to an average of 32 scans at a nominal resolution of 8 cm⁻¹, employing a background spectrum of gold. The Cary 630 Micro Lab PC software was used for data collection and analysis.

Scanning Electron Microscopy (SEM)

The scanning electron microscope (JOEL-JSM 7600F, Germany) was used to determine the morphology, shape, and surface characteristics of native gum, GG. The sample was prepared by sprinkling the dispersed gum onto double-sided adhesive carbon conductive tape which was mounted on a microscopic stub of copper. Then the

sample was sputter-coated with gold using an ion sputtering device of the equipment.

The elemental contents were analysed by inductively coupled plasma-optical emission spectroscopy (ICP-OES) and ICP-mass spectrometry (ICP-MS), in the microwave assisted digested samples after validating the applied methods via quality assurance parameters

RESULTS

Percentage Yield and Organoleptic Properties of GG

The organoleptic properties of GG and its yield are presented in Table I. GG was found to be odourless, brown in colour having a bland taste with a rough texture. The percentage yield of GG was found to be 58.5 % and the LD₅₀ greater than 5000 mg/kg.

Table I: Percentage Yield and Organoleptic Properties of GG

Properties	GG
% yield	58.5
pH	4.83
Viscosity, (50, 100 rmp)	12.82, 11.67
Colour	Brown
Taste	Bland
Odour	Odourless
Texture	Rough
Toxicity studies Non-toxic, LD ₅₀ > 5000 mg	

LD₅₀ = Lethal dose; GG = Native *Grewia* Gum

Table II: Physicochemical Properties of GG

Material	BD (g/mL)	TD (g/mL)	HR (%)	CI (%)	AoR (°)	SC	MC (%)
GG	0.14 ± 0.00	0.20 ± 0.00	1.43 ± 0.04	30.03 ± 2.02	49.70±1.94	1.59 ± 0.00	0.54 ± 0.01

Values are presented as the mean of triplicate readings ± standard deviation

GG – *Grewia mollis* gum

FTIR Image of GG

The IR spectrum presented in Figure 3 shows the absorption spectrum of GG.

Scanning Electron Microscopy (SEM)

The SEM image of GG is as shown in Plate II (a, b and c).

Elemental Composition of GG Using SEM Analysis

The SEM image of particles/elements of GG analysed by inductively coupled plasma-optical emission spectroscopy (ICP-OES) and ICP-mass spectrometry (ICP-MS), shows sixteen elements with atomic concentration ranging from 0.00 to 48.09, as shown in Table III. The highest of which is calcium and the lowest Titanium respectively.

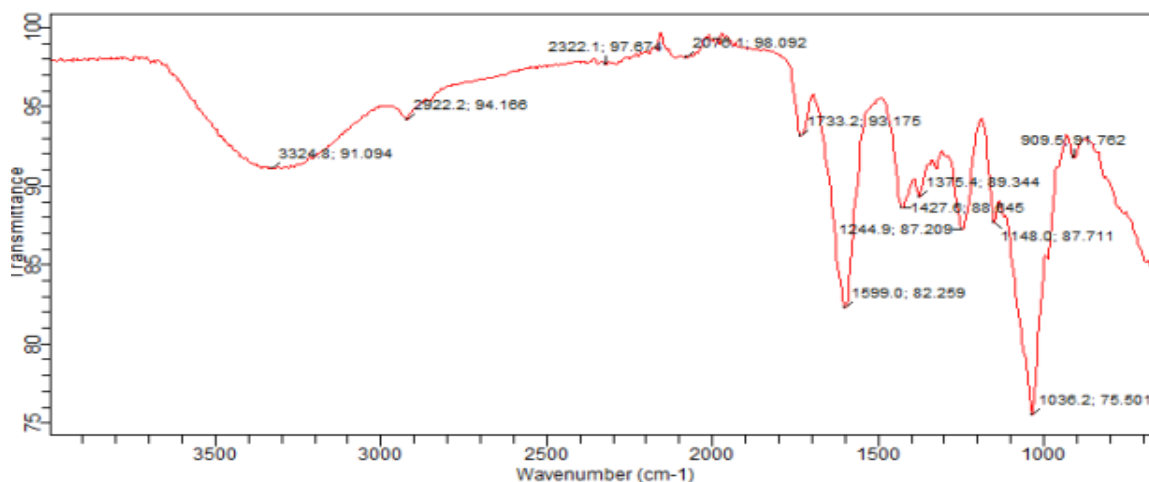


Figure 3: FT-IR Scan of GG

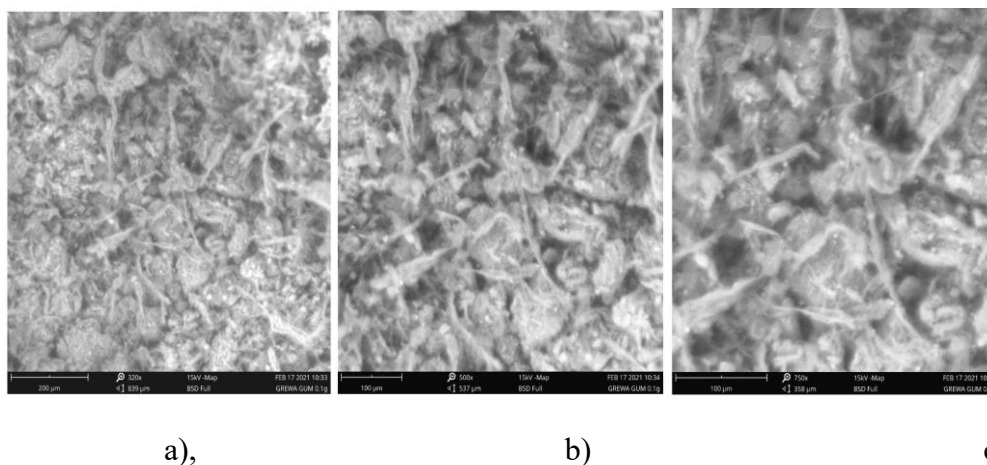


Plate II: Scanning Electron Micrograph of GG at a) 320 ×, b) 500 × and c) 750 × Magnifications

Table III: Elements Found in the SEM Image of GG

Element Number	Element Symbol	Element Name	Atomic Conc.	Weight Conc.
20	Ca	Calcium	48.09	52.25
19	K	Potassium	22.49	23.83
47	Ag	Silver	1.67	4.87
17	Cl	Chlorine	3.32	3.19
12	Mg	Magnesium	3.25	2.14
16	S	Sulfur	2.42	2.10
26	Fe	Iron	1.38	2.09
15	P	Phosphorus	2.37	1.99
8	O	Oxygen	3.91	1.70
14	Si	Silicon	2.21	1.68
6	C	Carbon	5.07	1.65
13	Al	Aluminium	2.16	1.58
11	Na	Sodium	1.23	0.76
7	N	Nitrogen	0.43	0.17
23	V	Vanadium	0.00	0.00
22	Ti	Titanium	0.00	0.00

Differential Scanning Calorimetry DSC

The DSC thermogram of GG is as shown in Figure 4. The GG thermogram showed an

endotherm at about 73 °C which broadened and maintained over a certain temperature up to about 240C

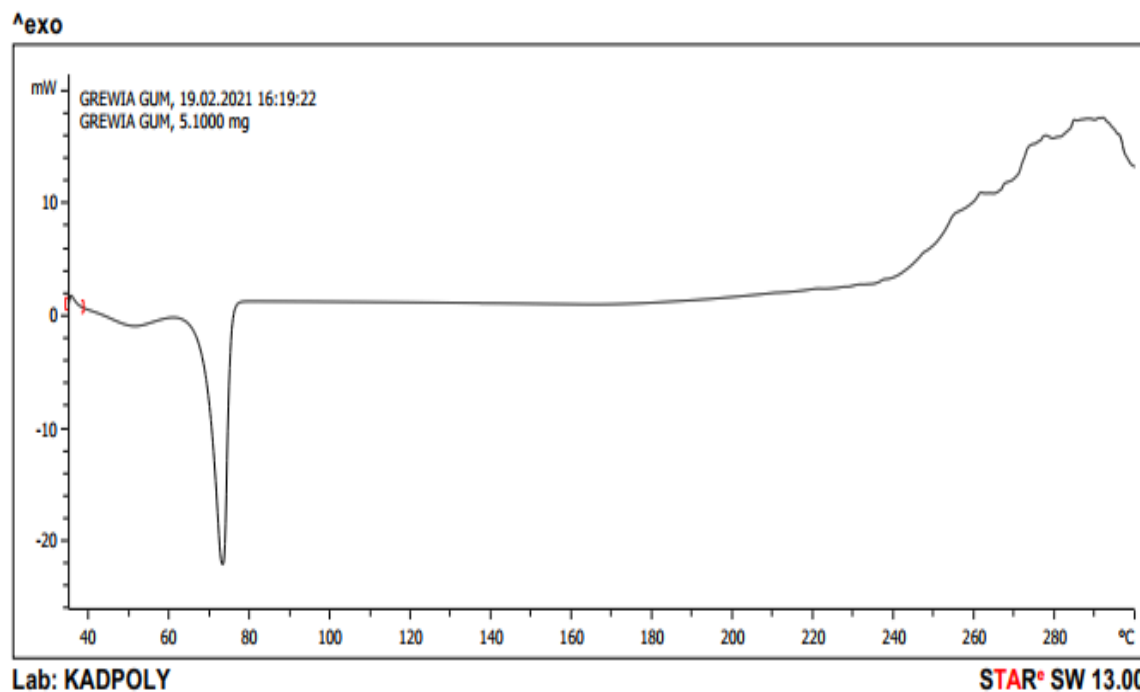


Figure 4: DSC Thermogram of GG

DISCUSSION

Grewia polysaccharide gum is a natural resource that could be used as an excipient in the pharmaceutical industry to increase in the production of pharmaceutical products. *Grewia mollis* Juss has considerable potentials for use as pharmaceutical excipient. The yield of *Grewia mollis* Juss in this study was found to be 58.5 % w/w, which was higher than the 32 % w/w reported by Olayemi *et al.* (2015). The difference in these values might be due to disparities in the content of the gum in terms of the species, the stage at which it was harvested, environmental and climatic conditions. In addition, the method employed during the processing of these gums (Olayemi *et al.*, 2015).

The acute toxicity studies also known as single dose studies, were conducted to determine the short-term adverse effects of a drug or any substance when administered in a single dose, or in multiple doses over a period of 24 h in an animal species. It provides information on potential for acute toxicity in humans, an estimate of safe acute doses for humans and on doses that should be used in subsequent studies (Colerangle, 2016). In this study, the LD₅₀ of GG was found to be greater than 5000 mg/kg, since all the mice were able to survive after two weeks, and there was no mortality, hence the gum was said to be non-toxic and relatively safe for use in humans.

The angle of repose indicated the flowability of powdered material or a granular substance. Materials with angle of repose less than 20° have excellent flow, 20-30° have good flow, 30-34° passable flow and greater than 40° indicate very poor flow (Aulton, 2015). *Grewia* gum GG, with angle of repose of 49.70°, had very poor

flowability when compared to that reported by Olayemi *et al.*, 2015, with angle of repose of 27°.

The presence of moisture affects the physicochemical properties of active ingredients and excipients, the crystal structure, flow properties, compaction, dissolution rate and the permeability of gums/polymers in solid dosage forms (Olayemi *et al.*, 2015). In addition, it can lead to the growth of micro-organisms in the formulation. The moisture content obtained in this study for GG was 0.54 % which was lower than that reported by the Olayemi *et al.* (2015), 7.33 %. This reduced moisture content of the extracted gum as compared to that reported by the Olayemi *et al.* (2015), was as a result of the difference in environmental conditions (Saraugi *et al.*, 2022). The bulk densities of the GG (0.14 g/mL) was lower than the tapped densities (0.20 g/mL), which could be due to the presence of inter-particulate spaces or voids in the bulk volume. Tapping brings about a reduction in the volume of the powder bed due to re-arrangement of the particle packing geometry. This reduction gives rise to a tightly packed powder bed which would be easy to compress on application of pressure (Olayemi *et al.*, 2015).

Compressibility index is used to access the flow property of a material while Hausner ratio indicates the cohesive nature of the material. Compressibility value ≤ 15 % are said to have excellent flow and those with Hausner ratio ≤ 1.25 are less cohesive and flow more freely (Olayemi *et al.*, 2015). The compressibility index (30.03 %) and Hausner ratio (1.43 %) of GG showed that it had moderate to poor flow profile. This implied that on application of pressure, GG might not produce good compacts, but the addition of other tableting excipients and

processing of the GG into granules could improve their compressibility (Bamiro, 2017). The IR spectrum of GG showed the absorption spectrum of GG. Here, there were presence of a narrow vibration band at 3400 cm^{-1} and sharp absorption bands at 909.5 and 1733.2 cm^{-1} respectively, which retained same characteristics of the native gum, as reported by the Olayemi *et al.* (2015), which invariably showed the hydrophilic character of the native gum.

The calorimetric thermogram of the Native gum, showed an endotherm at about $73\text{ }^{\circ}\text{C}$ which broadened and maintained over a certain temperature up to about $240\text{ }^{\circ}\text{C}$, over which the gum was degraded. This implied that the native gum could undergo melting, but on acetylation, crystallization of the gum could be achieved, hence improving its functionality in tablet formulations (Burton, 2015). The structural characteristics (SEM image) of native gum revealed that the structures assumed spheroidal, cuboidal and/or squamous shape(s), with a relatively smoother edge(s) at all magnifications, which invariably showed relative swelling and water penetration capacity.

Conclusion

From the result obtained, *Grewia* gum GG as a natural resource had potential pharmaceutical values that have been established, which invariably could be used as an excipient to be explored for the unmet needs in drug formulation, design and/or delivery.

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