



**DISINTEGRANT PROPERTIES OF BLEACHED ACETYLATED GUM FROM STEM BARK OF
GREWIA MOLLIS JUSS. 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 evaluating the disintegrant properties of BAGG (Bleached Acetylated Grewia Gum) obtained from the Stem Bark of *Grewia mollis* Juss in tablet formulation, using Ibuprofen as a model drug. Median Lethal Dose (LD₅₀) values of both the native and derivatized gums were each greater than 5000 mg. The mean weight for the BAGG formulations ranged from (501, 502 ± 9.19 mg). For the MS tablets, mean weight ranged from (499,504 ± 11.74 mg). Tablet friability was highest for BAGG – B (1.56) and lowest for BAGG – C (0.77), while the crushing strength was highest for MS – D (11.2 ± 1.35) and lowest for BAGG – B (6.5 ± 1.17). Tablet thickness was highest with MS - B and C (3.97 ± 0.06) mm and lowest with MS – D (3.72 ± 0.11) mm. Disintegration time was highest for GG (89.00 ± 0.05) min. and lowest for MS – C (2.58 ± 1.10) min. respectively. 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; crushing strength (6.9 ± 1.24 kgf), disintegration time (9.47 ± 3.06 min) and friability (0.78%) at 1.25%. The results of this study have established that BAGG, at 1.25 % concentration, could be used effectively to formulate ibuprofen tablets that disintegrate within 15 mins.

Keywords: BAGG, Disintegrant, Evaluation, Formulation, GG, Tablet

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INTRODUCTION

Oral drug delivery remains the preferred route of administration for various drugs [1]. Solid dosage forms, such as tablets and capsules, are popular because of their ease of administration, dosing accuracy, inappropriate self-medication, pain evasion and most importantly, patient compliance [2]. Disintegrating tablets constitute by far the bulk of pharmaceutical products [3]. By choosing suitable ingredients, tablets can be formulated to either release their active pharmaceutical ingredient (API) immediately following oral administration (immediate-release tablets) or to modify the drug release profile with the aim to achieve improved therapeutic efficacy, reduced toxicity, and improved patient compliance and convenience (modified release tablets) [3].

The performance of tablets as a solid dosage form has been credited to their ability to release the

embedded drug when swallowed or ingested. Tablet formulations usually contain other ingredients, called excipient, that facilitate the processing and manufacturability of tablets. In addition, these excipients are added to aid the functionality of tablets. One of such excipients is known as the disintegrant. To facilitate rapid release of drug, disintegrating agents are added to the formulation [2].

Despite increasing interest in controlled-release drug delivery systems, the most common tablets are those intended to be swallowed whole and to disintegrate and release their APIs rapidly in the gastrointestinal tract (GIT). The choice of disintegrant and its consistency of performance are of critical importance to the formulation or development of such tablets. Drug release from a solid dosage form can be enhanced by addition of suitable disintegrants [4]. 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 [4]. In immediate-release tablets, disintegration is a necessary requirement for dissolution; therefore, the disintegration performance has a direct impact on the therapeutic effect of the medication and must be assessed, and ideally quantified using specifically designed disintegration tests [3].

The disintegration process is an integral step in ensuring, and maximizing the bioavailability of the API from the majority of solid dosage forms. With the exception of diffusion-controlled matrix systems, the wetting and subsequent disintegration of the powder compact in tablets is the first step towards the liberation of the API from the dosage form. Without disintegration, only the API near the surface of the tablet would be able to dissolve and hence the reproducible and full disintegration of the tablet upon exposure to the dissolution medium is of critical importance to achieve a reliable clinical performance of the dosage form [3].

The most widely used disintegrants are synthetic polymers such as crospovidone (XPVP), croscarmellose sodium (CCS) and sodium starch glycolate (SSG).

MATERIALS AND METHODS

Materials

Grewia mollis Juss (Nigerian College of Aviation Technology, Zaria, Kaduna State). Magnesium stearate, Talc, Lactose and Maize starch (BDH Chemicals Ltd, England). Acetic Anhydride 98.5% and Acetone 95% (M & B Laboratory Reagent, England). Ibuprofen powder (Needham Market Suffolk, England).

Equipment

Magnetic stirrer, centrifuge and weighing balance (Mettler Toledo-ME 303E), pH meter (Mettler Toledo), Moisture content analyser (OHAUS MB 45), Water bath (Karl Kolb Sci. Co. Germany), UV Spectrophotometer (Cary-60, UV-Vis, Agilent technologies, UK), Single Punch Tablet Machine (Erweka, Germany), Monsanto Tablet Hardness Tester (Monsanto Chemical Co., USA), Brookfield Viscometer (Model RVF, Stoughton, MA), Tablet Friabilator (Type TA3R, Erweka - Apparatebau - G.m.b.H Heusenstamm, Made in West Germany), Disintegration Test Unit (Type ZT3, Erweka – Apparatebau - G.m.b.H Heusenstamm, Made in West Germany), Dissolution Test Apparatus (Type DT, Erweka - Apparatebau - G.m.b.H Heusenstamm, Made in West Germany), Screw Gauge Micrometer (965M, Moore & Wright Sheffield, England).

Methods

Toxicity studies:

Five mice each weighing 20 g were randomly selected from animal house in the Department of Pharmacology and Therapeutics and marked to permit individual identification and kept in their cages for at least five days prior to dosing for acclimatization to the laboratory conditions. The mice were fasted prior to dosing and weighed. A dose of 2000 mg were 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 survival of the previously dosed mice [5]. Attention was directed to observation of signs of toxicity such as tremors, convulsions, salivation diarrhoea, lethargy and coma, over a period of 24 h for two weeks (14 days) and mortality observed thereafter.

Tablet formulation

Grewia gum was successfully extracted from the stem bark of *Grewia mollis* by maceration in water at room temperature for 72 hours, acetylated using acetic anhydride, and bleached using Sodium hypochlorite solution (10 % w/v) for 1 hour to get a buff – coloured BAGG, which was used in our tablet formulations.

Tablets containing ibuprofen with bleached acetylated *Grewia mollis* gum (BAGG) as disintegrant were formulated by wet granulation method, using maize starch (BDH Chemicals Ltd, England) as a binder. Ibuprofen tablets with batch size of 100 and tablet weight of 500 mg, were formulated according to the formula in Table 1, using Erweka (Germany) Single Punch Tablet Press with a 12 mm punch and compression force of 6 KN.

Table 1: Composition of ibuprofen tablets containing *grewia* gum (GG), bleached acetylated *grewia* gum (BAGG) and maize starch (MS)

Materials	GG		BAGG			MS			
	A	A	B	C	D	A	B	C	D
Ibuprofen	20	20	20	20	20	20	20	20	20
Lactose	22.75	22.75	21.50	20.25	19.00	22.75	21.50	20.25	19.00
GG (disintegrant)	1.25	-	-	-	-	-	-	-	-
BAGG (disintegrant)	-	1.25	2.50	3.75	5.00	-	-	-	-
MS (disintegrant)	-	-	-	-	-	1.25	2.50	3.75	5.00
MS (binder)	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Magnesium Stearate	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Talc	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50	0.50
Total	50.0	50.00	50.00	50.00	50.00	50.00	50.00	50.00	50.00

A, B, C and D = Formulations at 1.25, 2.50, 3.75 and 5.00% Concentrations of different gum types as disintegrants, respectively.

Evaluation of tablet properties

Weight variation

This was carried out according to [6], to confirm the uniformity in the formulated tablets, in order to ascertain the variation between the tablets. Five (5) tablets each from formulations containing GG, BAGG and MS granules as disintegrants, were picked at random and weighed individually. The mean and standard deviations of each of the tablets were computed to determine the weight variation.

Crushing strength

The crushing strength was conducted according to [7]. Six tablets were crushed using the Mosanto hardness tester, and the mean of the six tablets was calculated.

Friability

Friability test was conducted according to [8]. Five (5) tablets each from formulations containing GG, BAGG and MS granules as disintegrants, were accurately weighed and placed in the Erweka Friability tester and then rotated at 25 rpm for 4 min. The tablets were removed after 4 mins, de-dusted and re-weighed. The tablets pass the test if the percentage friability value is ≤ 1 %.

Friability (%)

$$= \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100 \dots \dots \dots 1.1$$

Disintegration test

The disintegration time for each batch of tablets was determined in distilled water at $37 \pm 0.5^\circ\text{C}$ using the Erweka disintegration test apparatus (Type ZT3, Erweka – Apparatebau - G.m.b.H Heusenstamm, West Germany). Six tablets were tested and the time taken for each tablet to break into small particles and pass through the mesh was recorded as the disintegration time [9].

Pharmaceutical interaction study

Pharmaceutical interaction study (Drug release study) was done in phosphate buffer (pH 7.2) solution. Tablets containing BAGG were used for this study. A tablet was placed in a basket and immersed into a vessel containing 900 mL of the dissolution medium and maintained at 37°C under mild agitation (50 rpm). The samples were analysed for the dissolution, amount of drug release in percentage (%), at regular time intervals of 5, 10, 15, 20, 30, 45 and 60 mins, using the UV spectrophotometer (Cary-60, UV-Vis) at 221 nm [9]. The entire process was repeated for tablet formulations containing GG and MS as dis-integrants.

Data analysis

Data were analysed and/or presented as mean of readings \pm standard deviation. And values ≥ 0.05 were considered statistically significant.

RESULTS

Properties of ibuprofen tablets containing BAGG and MS as disintegrants

The results for the tablet properties are shown in Table 2. The mean weight for the BAGG formulations ranged from (501, 502 ± 9.19 mg). For the MS tablets, mean weight ranged from ($499, 504 \pm 11.74$ mg). Tablet friability was highest for BAGG – B (1.56) and lowest for BAGG – C (0.77), while the crushing strength was highest for MS – D (11.2 ± 1.35) and lowest for BAGG – B (6.5 ± 1.17). Tablet thickness was highest with MS – B and C (3.97 ± 0.06) mm and lowest with MS – D (3.72 ± 0.11) mm. Disintegration time was highest for GG (89.00 ± 0.05) min. and lowest for MS – C (2.58 ± 1.10) min. respectively

Table 2: Properties of ibuprofen tablets containing GG, BAGG and MS as disintegrants

Formulation	Weight Variation (mg)	Friability (%) w/w	Hardness (Kgf)	Thickness (mm)	Disintegration time (min)
BAGG-A	502 ± 9.19	0.78	6.9 ± 1.24	3.95 ± 0.11	9.47 ± 3.06
BAGG-B	501 ± 5.68	1.56	6.5 ± 1.17	3.95 ± 0.05	21.00 ± 5.98
BAGG-C	501 ± 7.38	0.77	9.3 ± 1.30	3.84 ± 0.09	42.59 ± 4.60
BAGG-D	501 ± 5.68	0.78	10.8 ± 0.57	3.74 ± 0.13	79.00 ± 0.05
MS-A	502 ± 6.29	1.18	6.6 ± 1.29	3.91 ± 0.06	3.77 ± 1.93
MS-B	503 ± 8.23	1.12	7.2 ± 1.04	3.97 ± 0.06	7.82 ± 2.54
MS-C	499 ± 14.49	1.19	8.2 ± 1.15	3.97 ± 0.06	2.58 ± 1.10
MS-D	504 ± 11.74	1.24	11.2 ± 1.35	3.72 ± 0.11	3.92 ± 1.33

Values are presented as mean of readings \pm standard deviation.

Key: GG = Formulation at 1.25% Concentration of *Grewia* gum (GG) as disintegrant. BAGG – A, B, C, D = Formulations at 1.25, 2.50, 3.75 and 5.00% Concentrations of Bleached Acetylated *Grewia* Gum (BAGG) as disintegrants, respectively.

MS – A, B, C, D = Formulations at 1.25, 2.50, 3.75 and 5.00% Concentrations of Maize Starch (MS) as disintegrants, respectively.

Pharmaceutical interaction study

The Pharmaceutical Interaction Study (Drug release profile) of Ibuprofen tablets containing BAGG - A, B, C and - D as disintegrants is as shown in Figure 1. The percentage(s) of drug released after 60 minutes ranged from 76.37, 93.81, 100 and 100% for BAGG - C, D, B and - A respectively.

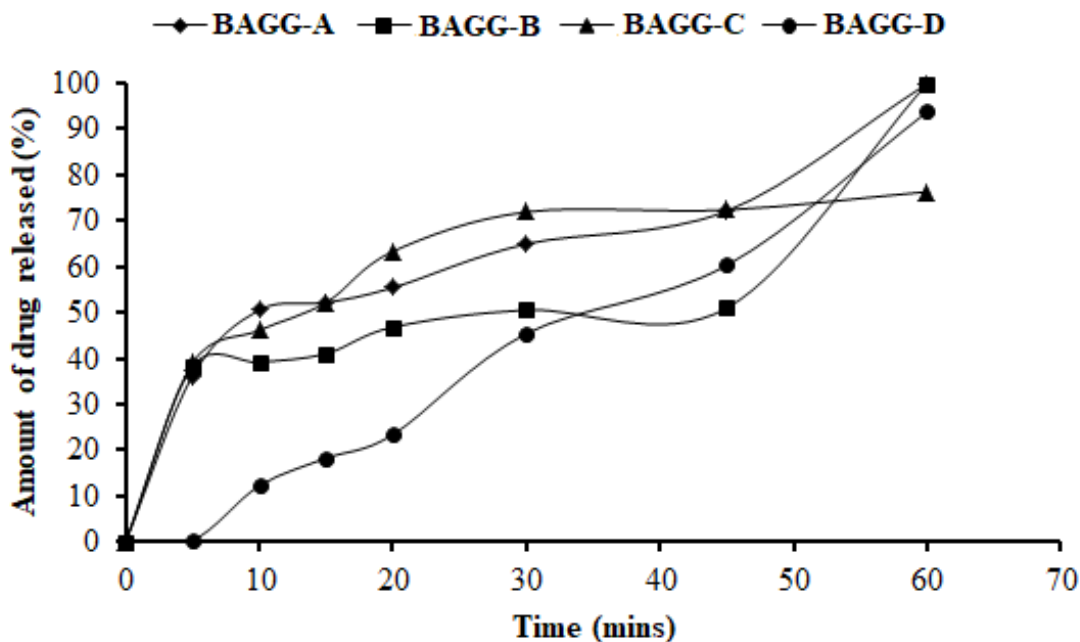


Figure 1: Pharmaceutical Interaction Study (Drug Release Profile) of Ibuprofen Tablets Containing BAGG A, B, C and D, as Disintegrants, at 1.25, 2.50, 3.75 and 5.00% concentrations, respectively

DISCUSSION

Grewia polysaccharide gum is a natural resource that could be used as an excipient in the pharmaceutical industry to increase the production of pharmaceutical products.

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 [5]. Medium lethal dose (LD₅₀) of both the GG and BAGG were 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 gums were said to be non-toxic and relatively safe for use in humans.

The properties of the tablets containing Bleached Acetylated *Grewia* Gum (BAGG) showed that BAGG - A formulation tablets with 1.25%

concentration of the derivatized gum, having an average disintegration time of 9.47 ± 3.06 minutes, successfully passed the test, amongst the different formulations, and complied with the official tests, with Disintegration time ≤ 15 mins [9, 10]. Hence, BAGG - A formulation ibuprofen tablet(s) were developed, using BAGG as the disintegrant. However, when compared with the control formulations containing GG and maize starch as the disintegrant, GG formulation batch tablets with same concentration (1.25%), performed poorly as disintegrant, as the tablets took a longer time to disintegrate (average disintegration time of 89.00 ± 0.05 minutes) whereas MS - A formulation batch tablets with same concentration (1.25%), performed better as disintegrant, as the tablets disintegrated faster (average disintegration time of 3.77 ± 1.93 minutes) than the BAGG - A formulated tablets (9.47 ± 3.06 minutes), but still the tablets were able to disintegrate within 15 mins, which invariably justified the aim of the study.

The pharmaceutical interaction study (Drug release profile) of the developed Ibuprofen Tablets

containing BAGG as the disintegrant showed that the formulations containing BAGG – A, B and D seemed to release the drug at a much faster rate (100, 100 and 93.81% drug release) than the other formulation. As such, BAGG – A, B and D formulations of the developed tablets, passed the USP dissolution test for Ibuprofen tablets, which specifies that not less than 80 % of the drug dissolves in solution after 60 mins. [9]. Hence, the BAGG – A, B and D tablet formulations had a better dissolution profile compared to the other (BAGG - C), suggesting an enhanced and/or faster disintegration time, having a drug release of ≥ 80 %.

CONCLUSION

From the result obtained, it can be concluded that bleached acetylated *Grewia mollis* gum BAGG, has potential to be used as disintegrant in conventional tablet formulations. Other chemical functionalization of the gum such as carboxylation, etherification, and cross-linking reactions of hydroxyl groups can be considered by researchers to improve the physicochemical properties of the gum and open prospects for extending the application of the native gum.

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