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Research Article

EVALUATION OF THE BINDING PROPERTIES OF *SPONDIAS PURPUREA* GUM IN METRONIDAZOLE TABLET FORMUALTIONS

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ABSTRACT

Objective: this study is aimed at investigating the binding ability/properties of *Spondias purpurea* (also known as plum) bark gum in metronidazole 200mg tablet formulation.

Methods: characterization of the gum was carried out according to the B.P official procedure for percentage yield, organoleptic properties, morphology, loss on drying and particle size determination. The wet granulation method of massing and screening was employed in the formulation of the granules. The gum was used at a 1, 2, 5 and 10%w/w concentrations while pharmaceutical grade gelatin was used as a standard. The granules were evaluated for particle size distribution, moisture content, flow rate, bulk and tapped density, Hausner's ratio and Carr's indices. The granules were compressed at 4.0 metric tonnes (MT) with the target weight of each tablet being 500mg. The tablets were evaluated for uniformity in weight, tablet thickness, crushing strength, friability, disintegration time and dissolution profile.

Results: the gum was observed to be polygonal in shape, crystalline in texture with a neutral pH. There was a linear correlation between concentration and viscosity. The granules possessed good flow properties as indicated by the low angle of repose, Hausner's ratio and Carr's index. Tablet disintegration and dissolution time were observed to increase with increase in gum concentration while friability decreased. *Spondias purpurea* gum produced tablets with better mechanical strength, longer disintegration time and faster onset of drug release at low concentrations.

Conclusion: It can be inferred therefore that *Spondias purpurea* bark gum has binding abilities which can be employed especially when high mechanical strength and fast to moderate release is desired.

Keywords: Metronidazole, *Spondias purpurea* bark gum, Gelatin, Wet granulation, Binder.

INTRODUCTION

Drug substances are rarely administered as they are in their pure state, but rather as part of a dosage form where they are combined with other substances, which could be non-medicinal. These other substances are known as excipients and are defined as pharmacologically inert materials which are combined with active pharmaceutical ingredients to aid their processing into dosage forms suitable for administration to patients[1].

These excipients traditionally were included to provide the necessary weight, consistency and volume for the correct administration of the active ingredient, but in modern pharmaceutical technology, they often fulfill other roles such as improvement of the stability, release and bioavailability of the active ingredient, enhancement of patient acceptability and performance of technological functions that ensure ease of manufacture [2].

Since, excipients have now been included in dosage forms because of their multi-functionality, it is necessary to develop excipients which will meet these needs. Although excipients have been derived from various sources; natural which includes animal (lactose, gelatin, steric acid), plant (e.g. starches, sugars, cellulose, alginates, gums) and synthetic (e.g. PEGs, polysorbates, povidone, etc) [3], those developed from natural origin (plants especially) are said to be of particular interest. This is because they are locally available, biodegradable, bio-compatible, non-toxic, cheaper and with lower production cost and less chances of side and adverse effects than with the synthetic materials [4]. They also minimize reliance upon fossil fuels derived products [5].

Plant gums have been extensively employed as local excipients in pharmaceutical dosage forms. Some examples include the use of *Khaya grandifolia* stem gum has been evaluated as a tablet binder [6], as a directly compressible matrix system for controlled release [7]. *Albizia zygia* gum has also been assessed as a compression coat for colon delivery [8]. Okro mucilage has also been explored as a tablet binder [9]. *Cassia roxburghii* seed gum has been evaluated by Kundlik *et al*, 2009 [10]. Also, the seed powder and mucilage of *plantago ovata* has been evaluated as a superdisintegrant in carbamazepine formulations and it was observed that the formulations containing the plant mucilage exhibited faster drug dissolution and thus, improved bioavailability [11].

Spondias purpurea is a species of flowering plant in the cashew family, Anacardiaceae which is native to tropical regions of America. It is most commonly known as plum, *Jocote*, Red Mombin, Purple Mombin, Hog Plum, Sineguela, and Siriguela. *Spondias purpurea* is a single stemmed tree or shrub which grows up to about 15m high with a medium canopy and a spreading crown.

The plum tree is greatly valued for the taste in their fruits. In most countries, the fruits are sold in local markets and consumed fresh making a significant contribution to the diet of the people in the tropics [12].

The bark of this tree is grey or brown, smooth and thick, becoming rough and warty on large trunks. It develops a poor crooked stem form and shallow lateral root [13] and exudes gum on incision. The plum tree is now widely cultivated in tropical regions throughout the world for its edible fruit, and is also naturalized in some areas, including the Philippines and Nigeria.

The aim of this present study is to explore the suitability of Spondias purpurea (plum) gum as a binder in metronidazole tablet formulations.

MATERIALS AND METHODS

Materials

Metronidazole, Lactose, Gelatin, Maize starch BP all of BDH chemicals Ltd. Poole, England were used, *Spondias purpurea* gum was prepared in the laboratory of the department of Pharmaceutics, Ahmadu Bello University, Zaria, Nigeria. All other chemicals used were of analytical-reagent grade.

Method

Collection and extraction of *spondias purpurea* gum

Spondias pupurea gum was gotten from the bark of plum trees grown around Samaru Zaria town in Kaduna State, Nigeria. The plant

and the gum were identified, authenticated and assigned a voucher number 9852 in the herbarium of the Department of Biological Science Ahmadu Bello University Zaria, Kaduna State, Nigeria.

The collected bark gum was soaked in water overnight (12hours), strained using a cloth (to remove extraneous materials), and then an equal volume of acetone was added to the filtrate to precipitate out the gum. Some more acetone (1:1) was used to wash the precipitate. The precipitated gum was air dried on a tray overnight and was then dried in an oven at 40^0c for 24hrs; the dried sample was size reduced, packaged and stored in an air tight container.

Physicochemical properties

The powdered plum gum was evaluated for its solubility in water, acetone, chloroform, ethanol and its particle size distribution was determined by using the sieve method. The morphology was determined by the simple method of photomicrography. The ash value and acid insoluble ash were determined, the pH was also determined using the pH Oaklon pH meter. The viscosity of 1, 2, 5, 10%w/v concentrations of gum at 50 r.p.m. were determined using the Brookfield Viscometer (model DV-1 PRIME). The true particle density of the gum was determined by the method of Odeku [14].

The flow parameters evaluated were angle of repose, bulk, tapped densities, from which the Hausner's ratio and the Carr's indices were determined.

Preparation of granules

Granules containing metronidazole 200mg were prepared using the massing and screening method of wet granulation. Plum gum was employed as tablet binder in concentrations of 1, 2, 5 and 20%w/w and gelatin was used as the standard binder (Table 1).

Metronidazole powder was geometrically diluted with lactose (the diluent) and then with maize starch (BP) (the disintegrant) in a porcelain mortar. The binder mucilage prepared from the concentrations of the gum was incorporated into the content of the mortar until a damp coherent mass was obtained. The damp mass was then passed through a 1.7mm sieve (to break down the mass) and then dried at 40^0c in the oven for 30 minutes. The granular mass was again passed through a 0.8mm sieve to obtain uniform sized granules and this was further dried in the oven at 40^0c for 20 minutes. The granules were packaged and kept for further analysis.

Table 1: Composition of different formulations of metronidazole 200mg tablets.

Parameters	PG 1	PG 2	PG 3	PG 4	GL 1	GL 2	GL 3	GL 4
Metronidazole	20	20	20	20	20	20	20	20
Lactose	23.75	23.25	21.75	19.25	23.75	23.25	21.75	19.25
PM Gum	0.5	1	2.5	5	-	-	-	-
Gelatin	-	-	-	-	0.5	1	2.5	5
MS BP	5	5	5	5	5	5	5	5
Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Mag.Stearate	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Total weight	50	50	50	50	50	50	50	50

Key: PG- plum gum, GL-gelatin, 1, 2, 3, 4- 1%w/w, 2%w/w, 5%w/w, 10%w/w.

Analysis of granules

The granule analysis carried out were angle of repose, flow rate, bulk and tapped densities, Hausner's ratio and Carr's index.

Compression of granules

The granules were mixed with the extra-granular excipients (talc and magnesium stearate) for five (5) minutes and then compressed using the Erweka single punch laboratory tableting machine, (Erweka Ar400 Germany) at compression pressure of 4 metric tons. Batches of 100 tablets were prepared according to the formular in Table 1. The tablets were left for 24 hours before evaluation to allow for elastic recovery.

Evaluation of tablets

The tablets were evaluated for uniformity of weight, thickness, crushing strength (hardness), friability and disintegration time.

***In-vitro* studies**

The dissolution rates of the drug were determined using the DGN multipurpose drug test machine (China) Shanghai. The basket method of dissolution was employed. The dissolution media was 0.1N HCL at 37 ± 0.5ºC. Samples (10ml) were withdrawn at intervals and these were replaced with equivalent volume of the dissolution media. The withdrawn samples were diluted 1 in 10 and analysed at a wavelength of 277nm using the B.Bran Scientific Spectrum Lab 752s spectrophotometer and the percentage drug release was determined using the Beer's calibration curve for metronidazole.

RESULTS AND DISCUSSION

The results of the organoleptic properties of *Spondias purpurea* (plum) gum as shown in Table 2 describes the gum as crystalline, cream in colour, odourless, tasteless with neutral pH and polygonal in shape (Fig. 1).

Table 2: Organoleptic and physicochemical properties of *spondias purpurea* gum.

Parameters	PG
Yield (%)	63
Colour	Cream
Odour	Odourless
Taste	Tasteless
Texture	Crystalline
Solubility:	
Acetone	Insoluble
Chloroform	Insoluble
Ethanol	Insoluble
Water	Soluble
Shape of particle	Polygonal
pH 1%w/v	7.2
Viscosity (mPas) 1%w/v	26.4
2%w/v	31.2
5%w/v	121.3
10%w/v	299.9
Loss on drying (%)	17
Ash value (%)	5.5
Acid insoluble ash (%)	1
Mean particle size (µm)	145.7
Angle of repose (^{0})	23.7
Flow rate (g/sec)	9.15
Bulk density (g/ml)	0.77
Tapped density (g/ml)	0.95
Hausner's ratio	1.23
Carr's index (%)	18.95

The viscosity was found to increase with increase in gum concentration and this could be attributed to reduced quantity of liquid required to completely fill the spaces between the particles of the gum and hence increasing its polymer content. The gum was

found to be insoluble in acetone, chloroform and ethanol and this is because organic solvents have been said to precipitate gums [15] but was found to be sparingly soluble in water. Gums are polysaccharides with numerous sugar molecules and, therefore partially dissolve in water. The observed sparing solubility of plum gum in water may also be due to the linear nature of the polymer, which has been reported to be less soluble compared to the branched components [16]. The acid insoluble ash value was found to be 1% and this indicates low levels of contamination during gathering, processing, and handling of the crude *Spondias purpurea* gum.

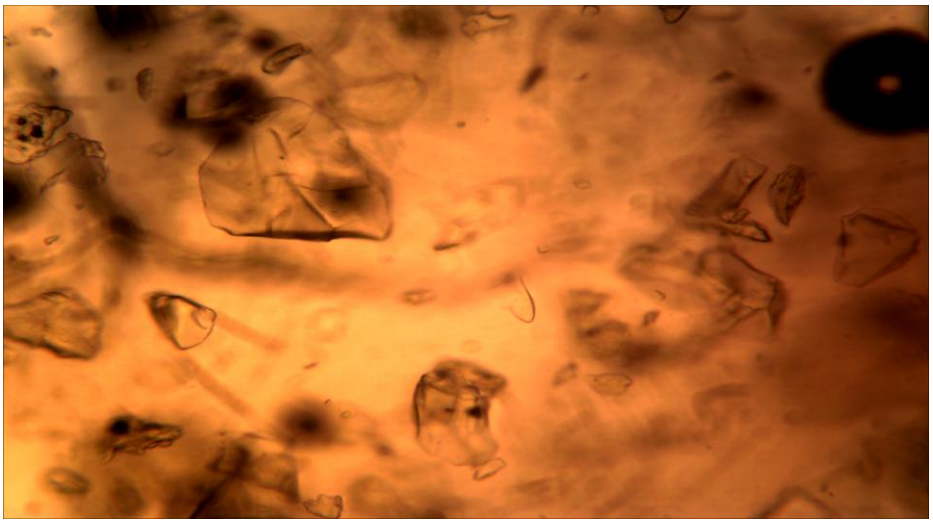

Fig. 1: Photomicrograph of *Spondias purpurea* gum (X 100mag.)

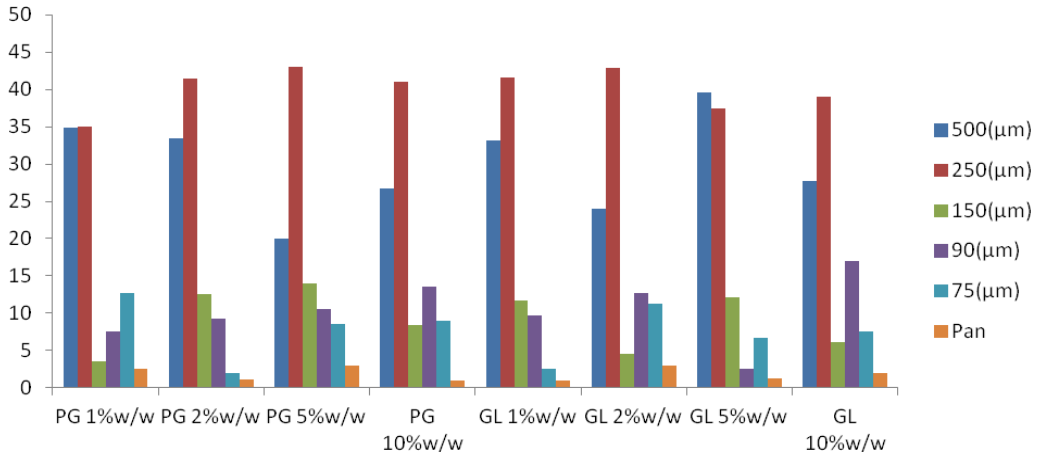

Fig. 2: Particle size distribution of metronidazole 200mg granules

The plum gum was found to possess good flow property as seen from its low angle of repose (23.7º) and moderate compressibility (18.95%). These properties are usually evaluated to give an insight into the processibility of a material during the scaling-up in formulations.

The loss on drying of *Spondias purpurea* gum was found to be 17% and this high value indicates that the gum is susceptible to microbial and physicochemical deterioration if not properly stored [17].

Table 3: Physico-chemical properties of metronidazole 200mg granules.

	Batches							
Parameters	**PG 1**	**PG 2**	**PG 3**	**PG 4**	**GL 1**	**GL 2**	**GL 3**	**GL 4**
Angle of repose (º)	28.50	23.80	27.50	26.70	28.70	26.30	26.80	25.10
Flow rate (g/sec)	5.57	6.13	6.50	5.97	5.00	5.68	4.83	5.10
Bulk density (g/ml)	0.59	0.57	0.67	0.60	0.53	0.51	0.50	0.50
Tapped density (g/ml)	0.71	0.67	0.83	0.70	0.67	0.61	0.61	0.60
Hausner's ratio	1.20	1.17	1.23	1.23	1.24	1.20	1.22	1.20
Carr's index	16.90	14.25	19.30	22.00	20.8	16.40	18.00	16.7

From the results in table 3, the graunles were observed to have good flow property as indicated by the low angles of repose. The granules were observed to have a moderate compressibility profile as observed from the Carr's indices and Hausner's ratio. These compressibility indices have been said to show the ability of the granules to form compact and decrease in volume under applied pressure (which will eventually produce strong tablets). There was no direct correlation observed between the concentrations of the gum used and flow properties, this has also been reported by OforiKwaye *et al* [18]. The results however

generally revealed that the formulated granules possessed good flow properties and also had prospects of producing tablets with minimal weight variation.

The results of the sieve analysis of the granules (Figure 2) shows that the granules were generally distributed along the 250 sieve size which means that the granules were of moderate sizes.

Table 4: Mean weight, crushing strength, friability and disintegration times of metronidazole 200mg tablets.

Parameters	Batches							
	PG 1	PG 2	PG 3	PG 4	GL 1	GL 2	GL 3	GL 4
Mean tablet weight (mg)	508.5 ±1.95	498.9 ±0.25	498.9 ±0.37	499.2 ±0.18	501.8 ±0.41	500.5 ±0.11	500.2 ±0.04	506 ±1.38
Tablet thickness (mm)	4.09 ±0.45	4.07 ±0.35	4.02 ±0.01	4.11 ±0.05	4.06 ±0.03	4.05 ±0.02	4.04 ±0.02	4.09 ±0.04
Tablet hardness (KgF)	8.5	9	11	12.5	3.5	5	7.5	11
Tablet friability (%)	1	0.9	0.89	0.8	0.99	0.81	0.61	0.4
Tablet disintegration (mins)	1.19	2.17	30.67	47.83	0.55	1.2	5.67	16.88

The evaluation of the tablets (Table 4) revealed tablets with uniform weights and low deviations from the official specifications shoes that the granules had good flow and thus, filled the compression is uniformly thereby, producing tablets of minimal weight variations. Tablet thickness has been said to vary with the density of the granules, applied pressure and the speed of compression which in-turn affects tablet disintegration and dissolution and from the results, the tablets were observed to have uniform thickness across the concentrations used and this can be attributed to their similar bulk and tapped densities and to the same compression force used during compression.

Crushing strength has been said to be the ability of tablets to withstand pressure or stress during handling, packaging and transportation. It is the property of a tablet that is measured to assess its resistance to permanent deformation [19] and also a measure of cohesiveness or structural strength of a tablet [21].

It was also observed that the crushing strengths of tablets increased with increase in concentrations used and this could be attributed to the formation of more particle- particle contact between the binder as well as with the particles of the drugs which also helped in creating more solid bonds.

The formulations with plum gum were observed to have greater mechanical strength as indicated by their generally higher crushing strengths across the different concentration used. This could probably be attributed to a gel-like foaming property of plum gum in the tablet matrix and it could also be due to the said versatile role of natural gums which include "matrix-formation" among others [4].

Friability is another mechanical property of tablets specified by the official compendium [21] and is expected not to exceed a value of 1%. Friability is a surface deformation of the tablet which could be as a result of the morphology of the tablet [22] and the rougher the surface of the tablet, the more friable it would be [19]. It was observed that all the formulations met the official specification. Furthermore, there was a general decrease in friability of the tablets with increase in binder concentrations. The decrease in friability can be explained based on the fact that there was increase in crushing strength with increase in binder concentration and therefore increase in tablet mechanical strength thereby conferring resistance to tablet abrasion.

A general increase in disintegration time with increase in binder concentration was observed and this could be due to the fact that more plum gum and gelatin were forced into the inter-particulate spaces thereby increasing the area of contact and thus formation of additional solid bonds. This in-turn produced a reduction in the size of the capillary spaces between the particles and thus, a reduction in the penetration of liquid into the tablet to cause bond separation and therefore, prolongation of the disintegration (break-up) time. It was also observed that tablets formulated with plum gum had longer disintegration times than those of gelatin. This is attributable to the already stated higher crushing strengths which caused a reduction in the available spaces between the particles and their by increase in disintegration time needed to effect bond separation. It is worthy of note to state that only formulations with plum gum 1%w/w, 2%w/w and gelatin 1%w/w, 2%w/w and 5%w/w passed the official disintegration test specification for uncoated tablets [23].

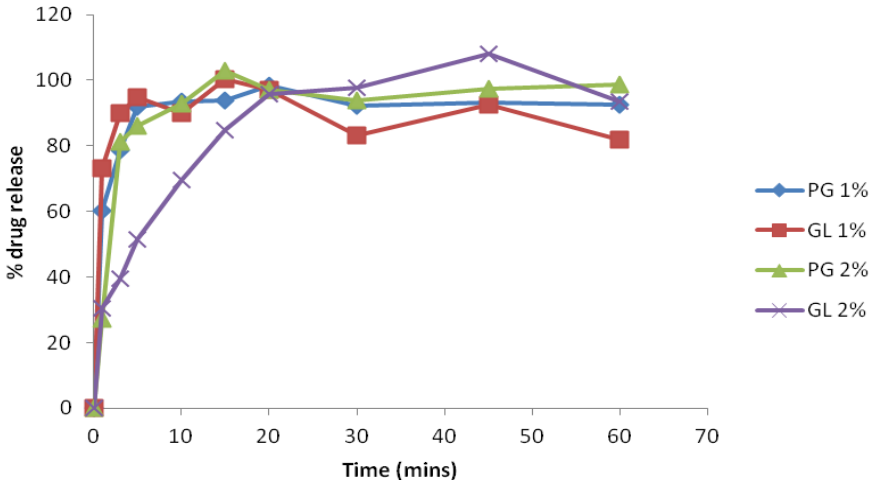

Fig. 3: Dissolution profile of metronidazole 200mg tablets formulated with 1%ww and 2%w/w binders.

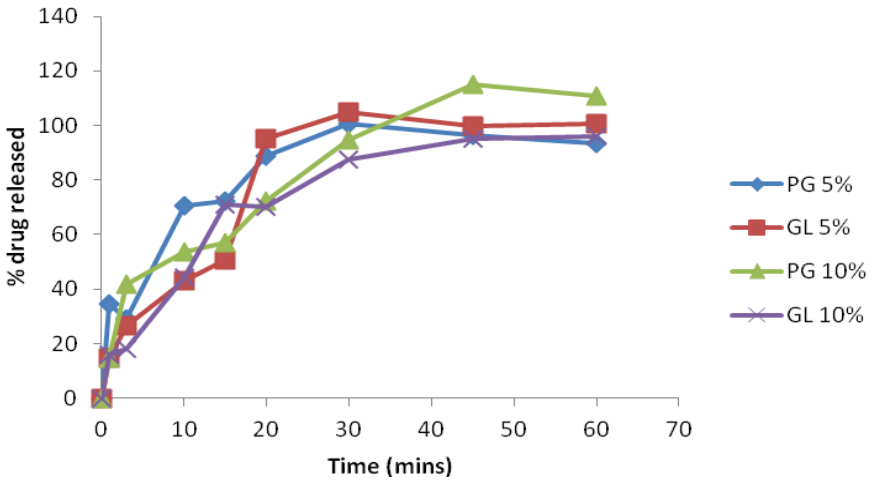

Fig. 4: Dissolution profile of metronidazole 200mg tablets formulated with 5%ww and 10%w/w binders.

Disintegration is an important step in the release of drugs from pharmaceutical dosage forms and the rate of disintegration is said to be directly proportional to the rate of dissolution [20].

The dissolution studies give an insight into the rate of release of drug from a dosage form. There are certain factors that affect drug dissolution which include the type and concentration of binder, hardness of the tablet, surface area, distance of diffusion, solubility of the drug, manufacturing process (wet granulation, dry granulation or direct compression) and diluents included in the formulation. As the concentrations of the binders increased, the rate of drug release decreased. It is observed that the plum formulations had a faster onset and higher release rate at lower concentrations (1 and 2%w/w) but had when employed at 5 and 10%w/w, the release was observed to be slower at the onset but increased steadiliy. Overall, plum gum formulations showed a comparable release profile to gelatin formulations across the concentrations used.

All the formulations passed the official dissolution specification [24] for tablets which specifies that at least 70% of the drug should be in solution after 30 minutes.

CONCLUSION

This work has been able to establish some physicochemical properties of *Spondias purpurea* (plum) bark gum. It has also been able to establish that formulations produced from plum gum had greater mechanical strength than those of gelatin even though the formulations had a faster onset of drug release at lower concentrations and the higher concentrations had a slower onset but steadily increasing release. These properties of plum gum could be of advantage when an excipient that can provide high bond strength and a fast dissolution profile is desired.

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