



EVALUATION OF *MORINGA OLEIFERA* TREE GUM AS DISINTEGRATING AGENT IN METRONIDAZOLE TABLETS

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ABSTRACT

This research was conducted to extract and purify *Moringa oleifera* gum (MOG) from the bark of the tree and evaluate its disintegrant property in metronidazole tablets. The gum was extracted using a standard method. Thedx gum was used as disintegrant at different concentration (0.25, 0.5, 0.75 and 1.0 %w/v) (F1 – F4) using sodium alginate gum as standard (F5 – F8) and gelatin as binder (1 and 2 %w/v) in metronidazole tablet. The physicochemical properties of the dried gum particles showed excellent flow rate and Carr's compressibility index. The physicochemical properties of the granules show free flowing compact particles. Analysis of the granule percent (%) cumulative size showed that as the concentration of MOG increases, more firm compact granules were formed. Average granule size for all the batches were retained on 500 μ m. The composite granules were used to formulate metronidazole tablets using single punch tablet machine compressed at 2.0 KN. The evaluation of metronidazole tablets yielded acceptable tablets. The batches with 1% w/v gelatin as binder gave disintegration time within the acceptable limit (i.e., less than 30 minutes). The batch F₄ (having 1.0 %w/v moringa gum as disintegrant) with crushing strength 55 N and friability value of 0.90 % is comparable with the batch F₈ (having 1.0 % w/v sodium alginate as disintegrant) with crushing strength of 44 N and friability value of 0.77 %. The result of disintegration shows that the MOG can be effectively used as disintegrant in tablet formulation for conventional tablet at concentration of 1 % and above this concentration; it can be used as release retardant.

Keywords: Moringa tree gum, disintegrant, local disintegrant, wet granulation

INTRODUCTION

Natural gums and mucilages have been widely explored as pharmaceutical excipients. These are widely used in the pharmaceutical industry as thickener, emulsifier, stabilizer, gelling agent, granulating agent, suspending agent, binder, film former, disintegrant and as sustained release matrix. Demand for these natural sources is increasing and new sources are

being developed. Natural gums and mucilages are preferred over semi-synthetic and synthetic excipients in the field of drug delivery because they are cheap and easily available, have soothing action and nonirritant nature. Further, they are eco-friendly, potentially degradable and compatible due to their natural origin, (Chang *et al.*, 2000 ; Kuchekar *et al.*, 2003).

There are several successful research works over three decades that proved the relevance of hydrophilic polymers derived from plant, like guar, carrageenan, karaya, locust bean gum in pharmaceutical preparations (Sujja-Areevath, *et al.*, 1996). For example, Gum karaya has been used as carrier for the dissolution enhancement of a poorly water soluble drug nimodipine (Murali Mohan Babu *et al.*, 2002), *Abelmoschus esculentus* gum has been employed as a mini matrix for the formulation of diclofenac sodium and furosemide tablets (Ofoefule and Chukwu, 2001), Cashew-tree exudates have been utilized as a novel bioligand tool (Nogueira Lima, *et al.*, 2002). Guar gum has been used to design colon specific dosage forms (Tuğcu-Demiröz *et al.*, 2006). Gum from the stem bark of *Moringa oleifera* has been reported to have gel forming potential for topical application (Panda *et al.*, 2006).

The *Moringa oleifera* plant is readily available. The stem of the tree exudes a gum which is initially white in colour but changes progressively from reddish brown to brownish black on exposure. It is sparingly soluble in water but swells in contact with water giving a highly viscous solution. It is polyuronide consisting of arabinose, galactose and glucuronic acid in the proportion of 10:7:2, rhamnose is present in traces (Wealth of India-Raw Materials, 1998).

In a research by Kasolo group (Kasolo *et al.*, 2011), *Moringa oleifera* was found to contain phytochemicals which are non-nutritive chemicals that plants produce as a self-defense mechanism. Phytochemicals present in *Moringa oleifera* include catechol tannins, steroids, triterpenoids, flavonoids, saponins, anthraquinones, alkaloids and reducing sugars (Kasolo *et al.*, 2011).

Moringa oleifera gum (MOG), is a water soluble gum. Purified whole gum has been

found to contain L-arabinose, L-galactose, L-glucuronic acid, and L-rhamnose, L-mannose, and L-xylose, (Bhattacharya *et al.*, 1982). In view of the easy availability of the plant, the exudate from the stem of the tree *Moringa oleifera* was investigated for possible application as a disintegrant in conventional tablets.

MATERIALS AND METHODS

Materials

Moringa oleifera tree gum was obtained from inner bark of dried stem of *Moringa oleifera* tree from Langtang, Plateau state. Distilled water and Ethanol (95 %) were of analytical grade.

METHODS

Collection of *Moringa oleifera* Tree Gum

The *Moringa oleifera* tree gum was collected from Langtang local government. An incision was made of the bark of the tree stem, between 5-10 cm deep. A small plastic container was hanged at the edge of the incision. It was left for 5days after which the exudate was collected. Several such incisions and collections were made to obtain enough quantity for this work.

Purification of *Moringa oleifera* Tree Gum

A 500 g quantity of the raw gum was dispersed in 2 L of deionized water and stirred continuously until complete dispersion was obtained after 24 h. The dispersion was then filtered through a clean muslin cloth and the filtrate collected contained the gum. A 5 L volume of ethanol (95%) was added to the mixture until the gum crumbled in the ethanol indicating complete precipitation and total separation from water. The crumble mass was collected in a clean container as the extracted gum

while the filtrate was discarded. The purified gum extracted was cut into pieces and properly spread to dry in open air. Drying was completed in Hot-air Oven (Gallenkamp, England) at 50 °C, for 3 h. The dried purified gum was then pulverized and this was then weighed using a weighing balance and the percentage yield was then determined.

Preparation of granules

To prepare granules, 200 ml of deionised water was measured, warmed and used to

prepare gelatin paste which was added to the powder blend of already weighed excipients. Proper mixing was done to ensure uniform distribution and the mixture was passed through a granulating sieve. The formed granules were air-dried on a clean dry brown paper for 24 h. The dried granules were made to pass through 1600 µm mesh to reduce the particle size. It was then spread over a thin brown paper to ensure that the granules dried well. The dried granules were then passed through 800 µm mesh. Then finally, granules were packed into batches ready for characterization and compression into tablet.

Table 1: Percentage Composition of Granules

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8
Metronidazole (g)	25.0	25.0	25.0	25.0	25.0	25.0	25.0	25.0
Lactose (g)	5.50	5.25	5.00	4.75	5.50	5.25	5.00	4.75
Moringa gum (g)	0.25	0.50	0.75	1.00				
Sodium alginate (g)					0.25	0.50	0.75	1.00
Gelatin (2% w/v)	10ml	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml
Talc (g)	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Magnesium trisilicate (g)	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25

Evaluation of Granules

Measurement of Bulk and Tapped Density

The bulk and tapped densities (B_d and T_d) respectively of the granules are determined by the modification of Kumer and Kofhan

method (1999). Tapped density of a powder is expressed as the ratio of the weight of powder to the volume occupied after tapping for a given period of time.

Voids are reduced by tapping resulting to consolidation.

$$T_d = \frac{\text{weight of powder}}{\text{Tapped volume}}$$

$$B_d = \frac{\text{weight of powder}}{\text{Bulk volume}}$$

Bulk and tapped densities of MOG were determined using 50 g of the gum. It was poured into a 100 ml measuring cylinder and the volume occupied by the bulk noted. The tapped volume was obtained after tapping cylinder 200 times. Bulk and tapped densities were calculated using the equations given below. Carr's index and Hausner's ratio were calculated using the parameters of bulk and tapped densities.

Hausner's Ratio

Hausner's ratio (H) is expressed as;

$$H = \frac{T_d}{B_d}$$

Where, T_d and B_d are tapped and bulk densities respectively.

Carr's Compressibility Index

Carr and Neumann developed a simple test to evaluate flowability of a powder by comparing the poured (fluff) density and tapped density of a powder and the rate at which it packed down. A useful, empirical guide is given by:

$$\text{Carr's index (\%)} = \left(\frac{[T_d - B_d]}{T_d} \right) \times 100$$

Determination of Flow Properties of Granules Angle of Repose

A clean plastic funnel of diameter 1.3 cm, and length 10 cm was clamped firmly to a retort stand. A shutter was placed over the orifice. A 50 g of MOG or granules were accurately weighed and transferred into the funnel. The shutter was then removed and the powder was allowed to discharge completely into a plane white paper placed on the bench on a retort stand base. The height of the powder heap and the diameter of the circular base of the powder heap were measured. Average of 3 readings was taken and same procedure was done for the granules.

The angle of repose (θ) was then determined as the tangent of the height of the cone "h" divided by the radius r.

Flow Rate

The measurement of the flow rate was done using the funnel method. A clean dried funnel was clamped on a retort stand 10 cm from the surface of the bench. A 50 g quantity of the MOG powder was poured into the funnel and the time for completely discharge of the granules was recorded. A mean of three determinations was taken.

$$\text{Flow rate (g/sec)} = \frac{\text{Weight of powder}}{\text{Time taken to flow}}$$

Particle size Analysis

A simple method of particle size analysis or distribution was adopted according to U.S.P (2003). The set of sieves used were 850, 500, 355, 250, 180 μm and fine <100 μm collected respectively.

The sieves were arranged on an electric stand and the first batch of the granules was placed on the 850 μm size. The sieves were shaken for 10 minutes using the electric shaker after which the sieves were dismantled and the weight of the powder

retained (i.e. oversize) by individual sieve was determined using electrical balance.

Viscosity Determination

Dispersion of the gum ranging from 0.5 – 2 % w/v were prepared in a 120 ml beaker and the viscosity measured using the Haake viscotester VT-01.

pH Determination

To measure the pH, a 1 % w/v dispersion of the gum was prepared in distilled water. The pH reading was taken with the pH meter (pH-25).

Swelling Index

The swelling index was determined by dispersing 1g of the gum in 100 ml of distilled water prepared in a graduated glass measuring cylinder, 100 ml capacity. The initial volume occupied by the gum was noted and then allowed to stand for 24 h. The final volume was observed after 24 h and the swelling index calculated using the equation below.

$$\% \text{ Swelling index} = \left(\frac{[V_2 - V_1]}{V_1} \right) \times 100$$

Where, V_1 is the initial volume of material before hydration, and V_2 is the final volume of hydrated material.

Loss on Drying (% LOD)

A 10 g portion of the gum powder was weighed in a clean crucible and was heated in an oven at 105⁰c for 24hours. It was then cooled in a dry atmosphere of a desiccator and then reweighed using a weighing balance.

$$\% \text{ LOD} = \left(\frac{[W_1 - W_2]}{W_2} \right) \times 100$$

Compaction of granules

The granules were used to formulate metronidazole tablets. The tablets were compacted in a single punch tableting machine(Erweka, AR 400, Germany) at target weight of 500 mg using 12.5 mm diameter flat faced punch. Both the die and punches were lubricated with magnesium stearate. The tablets were compressed at 2 KN compression force.

Evaluation of Compressed Tablets

Tablet Hardness

Ten tablets obtained from the compression were placed individually between the fixed jaw of the Monsanto hardness tester and the scale adjusted to zero. Pressure was then applied on the tablet by screwing the compression knob until the tablet shattered into pieces. The reading at this point was recorded for other 9 tablets in conformity with the official requirement and guidelines (4 -7kgf, B.P 1988) and the corresponding values recorded in kgf.

Tablet Friability

The abrasion test was performed in a friabilator (Erweka, TA3R, Germany) operated at 25 r.p.m for 4 min. The weight of 10 tablets was taken before and after the test. The friability was calculated as the percentage weight loss.

A maximum weight loss of 1.0% of weight of the tablets being tested is considered acceptable in most products.

$$\text{Friability (\%)} = \left(\frac{[W_I - W_F]}{W_I} \right) \times 100$$

Where, W_I is the initial weight of the 10 tablets and W_F is the final weight of the corresponding tablets.

Tablet Thickness and Diameter

The vernier caliper was used to measure the thickness and diameter of twenty tablets sampled from the batch. The mean and standard deviation were calculated.

Tablet Disintegration Time

Disintegration apparatus (Erweka, ZT3, Germany) was employed. Three tablets were used, one tablet was placed in each compartment of the disintegrating basket which was lowered into a glass beaker (1L capacity) filled with deionised water to 800 ml mark and in turn was placed in a water bath maintained at 37 °C. The time taken for the dissociated tablet particles to pass through the mesh was recorded as the disintegration time.

Weight Uniformity

The weight uniformity test was performed according to the B.P 1980. Twenty tablets

were randomly selected from each batch and weighed. The average weight and the standard deviation was reported.

RESULTS AND DISCUSSION

The gum was used as disintegrant at different concentration (0.25, 0.5, 0.75 and 1.0 %w/v) (F1 – F4) using sodium alginate gum as standard (F5 – F8) and gelatin as binder (1 and 2 %w/v) in metronidazole tablet (Table 1).

The physicochemical properties of the dried gum particles showed excellent flow based on the parameters of flow rate and angle of repose (Table 2). MOG possessed high swelling index, 440 % (Table 2). The swelling index, availability and high percentage yield of 74 % are some advantages of MOG that positioned it as a potential material for local industries as a replacement for imported natural disintegrant like sodium alginate.

Table 2: Physicochemical Properties of *Moringa oleifera* Tree Gum

Material	Flow Rate(g/s) (n=3)	Angle of Repose (o) (n=3)	Bulk Density (g/cm ³) (n=3)	Tapped Density (g/cm ³) (n=3)	Compress-ibility Index (%)	Hausner Ratio	Swelling Index (%) (n=3)	pH	Loss on drying (%)	% Yield MOG
<i>Moringa Oleifera</i> gum	21.26±0.30	20.6±0.1	0.721±0.012	0.883±0.022	21.2±0.2	1.2±0.0	440±2.0	6.62	0.65±0.02	74

The viscosity of dispersion of MOG increases with increase in concentration as shown in Figure 1. At a constant shear rate (50 rpm) the viscosity doubled with the concentration, a property of an ideal polymer for pharmaceutical application (Moris, 1984). At a zero-shear and constant shear rate, viscosity of dispersion of biopolymers increases with increase in concentrations (Moris, 1984). As the

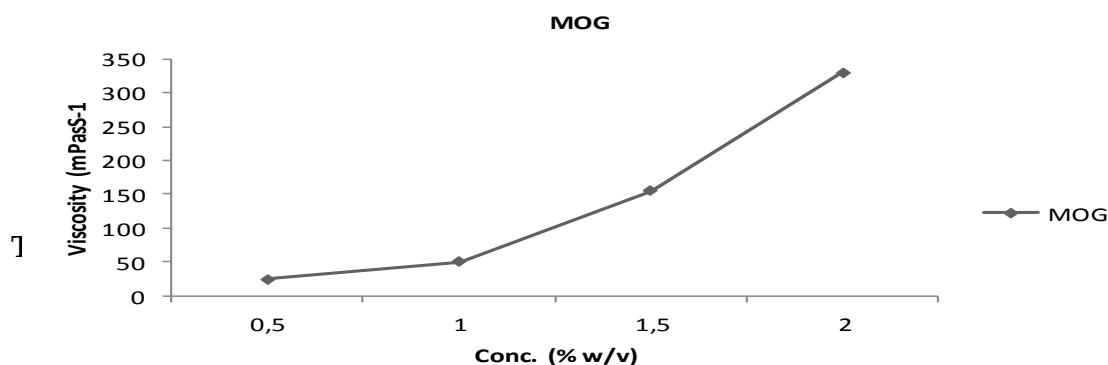
concentration increases a critical point is reached and the slope increases abruptly (Moris, 1984). This abrupt increase in viscosity is believed to be caused by a change from a solution of freely moving biopolymer coils to a region of entangled chains as the concentration exceeds the critical value (Moris, 1984).

The physicochemical properties of the granules showed free flowing compact particles as reflected by both flow rate and the angle of repose for F1 – F8, (Table 3). All batches possessed good flow property (angle of repose ranged from 25 – 30).

Analysis of the granule percent (%) cumulative size showed that as the concentration of MOG increases, more firm compact granules were formed (Fig.2).

Average granule size for all the batches were retained on 500 μm . This characteristic favours adequate tablet weight.

Evaluation of metronidazole tablets yielded acceptable tablets (Table 4a & b). Batches F1 – F8 have acceptable tablet weight variations attributed to good granule size distribution with mean granule size of 500 μm that favours good flow, and constant die filling.



Batch	Flow Rate(g/s) (n =3)	Angle of Repose(o) (n =3)	Bulk Density (g/cm ³) (n =3)	Tapped Density (g/cm ³) (n =3)	Compress- ibility Index (%)	Hausner Ratio	Loss on drying (%) (n =3)
F1	2.09±0.03	30.20±0.01	0.501±0.01	0.697±0.03	16.6±0.3	1.2±0.0	6.5±0.4
F2	2.17±0.03	31.74±0.02	0.527±0.03	0.672±0.03	21.6±0.3	1.2±0.0	6.3±0.1
F3	2.96±0.02	29.53±0.06	0.545±0.05	0.668±0.01	18.4±0.2	1.2±0.0	6.4±0.2
F4	4.24±0.04	28.48±0.12	0.558±0.08	0.663±0.03	15.7±0.2	1.1±0.3	6.0±0.0
F5	3.40±0.00	26.62±0.00	0.523±0.02	0.618±0.02	15.3±0.0	1.1±0.0	6.5±0.1
F6	3.58±0.02	27.62±0.22	0.524±0.01	0.651±0.02	19.5±0.4	1.2±0.0	6.2±0.0
F7	3.80±0.01	29.63±0.16	0.543±0.03	0.670±0.00	19.0±0.3	1.2±0.0	5.9±0.3
F8	4.04±0.02	29.27±0.13	0.563±0.06	0.693±0.03	18.6±0.3	1.2±0.0	5.7±0.8

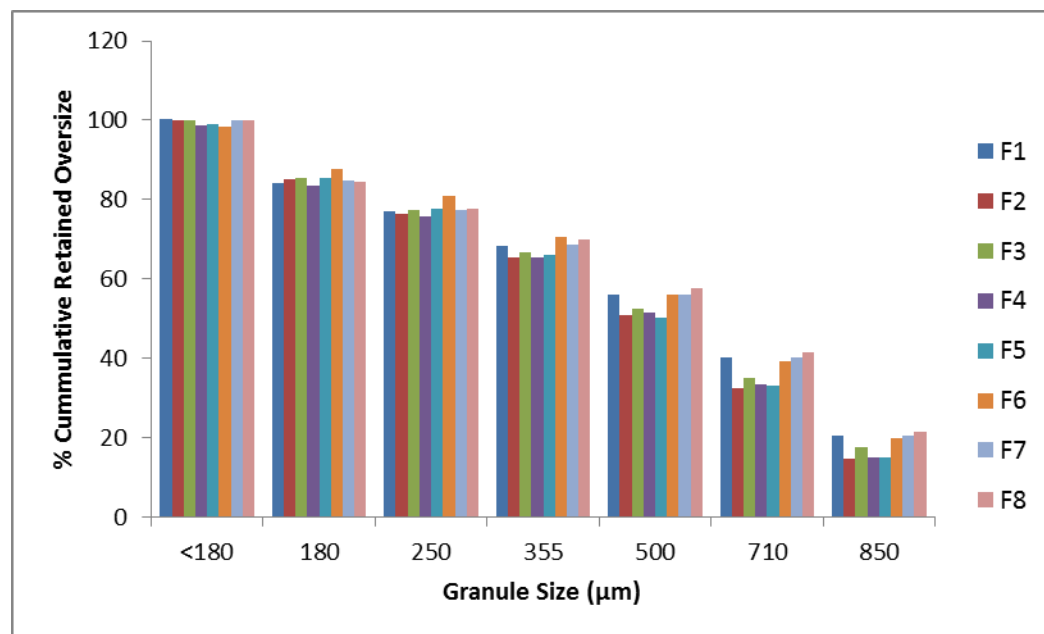


Fig 2: Granule size (µm) vs % cumulative retained oversize

Table 4a: Compact Properties of Compressed Tablets with 1 % Gelatin as Binder

Batch	Tablet Wt (g)	Tablet Thickness (cm)	Tablet Diameter (cm)	Tablet Crushing Strength (N)	Friability (%)	Disinte-gration Time (min)	% Drug Release
F1	0.505±0.05	0.35±0.00	1.25±0.00	30±3	1.30±0.00	26±1	97.50
F2	0.500±0.00	0.35±0.01	1.25±0.00	33±5	1.20±0.02	23±2	96.70
F3	0.500±0.00	0.35±0.01	1.25±0.00	45±5	1.12±0.02	21±2	97.90
F4	0.505±0.05	0.35±0.00	1.25±0.00	55±4	0.90±0.01	20±1	96.80
F5	0.500±0.05	0.34±0.00	1.25±0.00	20±2	2.70±0.10	15±3	98.70
F6	0.501±0.03	0.34±0.01	1.25±0.00	30±2	2.00±0.05	14±2	97.50
F7	0.520±0.10	0.35±0.00	1.25±0.00	40±2	1.08±0.04	12±1	96.80
F8	0.505±0.00	0.35±0.00	1.25±0.00	43±3	1.00±0.01	11±2	98.50

Compression pressure 2.0 KN

Table 4b: Compact Properties of Compressed Tablets with 2 % Gelatin as Binder

Batch	Tablet Wt (g)	Tablet Thickness (cm)	Tablet Diameter (cm)	Tablet Crushing Strength (N)	Friability (%)	Disintegration Time (min)	% Drug Release
F1	0.521±0.13	0.34±0.00	1.26±0.00	32±1	1.29±0.03	60±0	98.70
F2	0.500±0.00	0.34±0.02	1.26±0.00	40±1	1.15±0.05	52±2	98.50
F3	0.500±0.00	0.34±0.00	1.26±0.00	50±3	2.26±0.20	55±2	98.90
F4	0.501±0.01	0.35±0.01	1.26±0.00	44±2	0.77±0.03	58±4	98.70
F5	0.500±0.00	0.35±0.00	1.26±0.00	30±0	2.52±0.50	28±0	99.00
F6	0.500±0.00	0.34±0.00	1.26±0.00	35±1	1.98±0.42	30±0	98.60
F7	0.531±0.20	0.34±0.00	1.26±0.00	42±2	0.08±0.02	28±1	98.90
F8	0.507±0.05	0.34±0.01	1.26±0.00	47±1	0.22±0.01	30±0	97.90

The batches with 1% w/v gelatin as binder (Table 4a), gave disintegration time within the acceptable limit (i.e., 15 - 30 min., B.P. 1988). The batch F₄ (having 1.0 %w/v moringa gum as disintegrant) with crushing strength 55 N and friability value of 0.90 % is comparable with the batch F₈ (having 1.0 % w/v sodium alginate as disintegrant) with crushing strength of 44 N and friability value of 0.77 %. It could be seen that F₄ formed better compact than F₈. But the results of disintegration shows that the MOG at 1 %w/v as disintegrant for F₁ – F₄ were higher than that of sodium alginate 1 % disintegrant (F₅ – F₈), Table 4a. Sodium alginate is a soluble form of alginate. Alginates are hydrophilic colloidal substances which has high sorption capacity.

They are classified as a super-disintegrant at concentration range of 2.5 – 10% (Debjit, *et al.*, 2010). MOG can be used effectively as disintegrant in tablet formulation for conventional tablet at concentration of 1 % and above.

CONCLUSION

In this present study, the disintegrant property of the gum powder of *Moringa oleifera* has been studied in comparison with a natural gum disintegrant (sodium alginate). MOG exhibits acceptable disintegration time at 1 %w/v. MOG is eco-friendly and biodegradable (Chang *et al.*, 2000; Kuchekar *et al.*, 2003). Future research will investigate a higher concentration of MOG as a superdisintegrant.

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