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Formulation and Evaluation of Conventional Metronidazole Tablets using Natural Gum Extracted from *Grewia species*

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Authors' contributions

This work was carried out in collaboration between both authors. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The pharmaceutical world has been paying increasing attention to the extraction, development and use of natural gums as binders in the formulation of solid dosage forms. The use of natural gums as binders is more advantageous than the use of synthetic ones due to availability, low cost, biodegradability and biocompatibility. In this study, gum extracted from *Grewia species* was compared with that from*Acacia* in metronidazole tablets.
Study Design: Ten batches of metronidazole tablets were formulated with varied concentration of *Grewiaspp* gum and *Acacia* gum.
Place and Duration of Study: The study was carried out in Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Delta State University, Abraka, Nigeria; between January and December 2019.
Methodology: Five batches of metronidazole tablets containing 0.5, 0.75, 1.0, 1.25 and 1.5% w/w of *Grewia* gum were preparedby wet granulation. Resulting granules were characterised by measuring flow and packing properties. In other experiments, five batches of tablets were formulated using same concentration of gum, with *Acacia* gum substituted for *Grewia* gum. Both sets of granules were compressed into tablets using tableting machine at a load of 27 arbitrary

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units. Tablets so formed were evaluated for hardness, friability, disintegration time, drug content and drug release profiles. Drug – excipient interaction was investigated with FTIR.
Results: The resulting metronidazole tablets showed hardness of 5.46 kgF to 7.87 kgF (*Grewia*gum) and 6.06 kgF-8.20 kgF (*Acacia* gum). Friability percentages of all the batches were above 1% except for A3-A5 and B5 which are less than 1%. All formulations released more than 75 % of the drug content within 60 min. The FTIR analysis revealed no interaction between the metronidazole and *Grewia species* gum.
Conclusion: Metronidazole granules and tablets were successfully prepared using *Grewia*gum and showed comparable pre-compression and post-compression properties with those formulated with *Acacia*.

Keywords: Grewia gum; acacia gum; binder; metronidazole; granules; tablets.

1. INTRODUCTION

It is an open truth that man is gradually going back to nature to provide solutions to his numerous health concerns. The pharmaceutical industries and pharmaceutical scientists are not left out in this trend. The pharmaceutical world has been paying increasing attention to the extraction, development and use of natural gums as binders in the formulation of solid dosage forms. Binders are majorly a class of excipients utilized to hold the active pharmaceutical ingredient (API) and excipients together in a cohesive mass [1]. They are also called granulating agents.They promote size enlargement of fine powders to granules of desired sizes, thereby enhancing the free flowing qualities of powder used in solid dosage form manufacture [2]. The use of natural gums as binders is more advantageous than the use of synthetic ones because binders from nature are commonly available, low in cost, biodegradable and biocompatible [3]. Many natural gums have been used as binders and matrix former in tablets manufacture,for example, *Khaya* gum, *Leucaenaleucocephala* seed gum, *Anacardium occidentale* gum, *Gellan* gum, gum acacia and *okra* gum [1, 4]. Natural gums are derived from animal sources (chitin, chitosan), marine sources (agar, alginic acid), microbial sources (xanthan, dextran) and plant sources (acacia, tragacanth) [4]. Gums and mucilages are monosaccharides produced as a result of hydrolysis of polysaccharides. They contain magnesium, potassium and calcium salts of polyuronic acids [5]. Gums extracted from plants constitute the largest proportion of natural gums and are applied in drug delivery as disintegrants, emulsifying agents, suspending agents and binding agents. They are useful in the formulation of immediate and sustained-release preparations [6]. One of such gums from plant is *Grewia* gum (family, Malvaceae).

The genus, *Grewia* has over 150 species, many of which are edible e.g. G. mollis, G. *tenax*, *G. villosa* etc. G. Mollis Juss is composed of rhamnose, glucose and galacturonic acid [5].The species used in this study is commonly called *ila-oko* or *lakolako* among the Yoruba speaking tribe of Nigeria and is used for its nutritional and medicinal values. Its emulsifying property has earlier been established [7]. In the present study, it is used as a binder in conventional metronidazole tablets formulation.

Metronidazole, an antimicrobial chemotherapeutic agent commonly referred to as: “an old warhorse” has become a major player in the treatment of anaerobic infections all over the world and ranks amongst the ‘essential medicines’ as defined by the World Health Organization, WHO [8]. Metronidazole was developed in 1959 by Cosar and Julou specifically for the treatment of trichomoniasis, an infection of the genital tract caused by the microaerophilic parasite - *Trichomonasvaginalis* - that was ravaging the world and very difficult to treat at that time [9].

Despite history of long period of frequent use, metronidazole still remained reliable for the treatment of most anaerobic/microaerophilic infections, thus setting it apart from many other antimicrobial agents to which resistance emerge much more quickly [10]. This is attributable, unequivocally, to its pleiotropic mechanism of action. Here metronidazole targets numerous molecules in the cell, unlike many other chemotherapeutic agents that attack a few or just a single molecule. The mechanism of action of metronidazole is extremely simple: it gains entrance into the cell without the assistance of any known transporting mechanisms and then unfold its destructive power, after reduction to its nitro group (a reaction which takes place only in the presence of very low concentration of oxygen) [8].

In this study, conventional metronidazole tablets were formulated with gum extracted locally from *Grewia spp*, by wet granulation technique. Properties of tablets so formed were compared with tablets formulated with an already established gum – acacia. Metronidazole – excipients interaction was investigated with Fourier transform infrared (FTIR) spectrophotometer.

2. MATERIALS AND METHODS

2.1 Materials

The test drug, metronidazole BP (Tonxiang Zhejiang, China), corn starch BP, magnesium stearate, talc, lactose (Pharmaceuticals AliyaliPalghar, India), acetone (Guangdong Guangzhou chemicals, China), acacia gum (BDH Chemicals Ltd, Poole England) and freshly collected pods of *Grewia species* (obtained from the tropical forest of Okitipupa, Ondo state, Nigeria and authenticated by the Plant Curator, Pharmacognosy and Traditional Medicine Department, Delta State University, Abraka, Nigeria).

2.2 Methods

2.2.1 Extraction of gum

The methods described by Okafo and Chukwu [11],Avbunudiogba*et al* [7] were adopted for the extraction process with slight modification. In these method, fresh *Grewia* pods, collected from the wide were washed properly, chopped into bits, air-dried and pulverized using a manual grinding machine. The powder blendwas sieved using a 1.18 mm sieve to remove the shaft. The powder was weighed using a top loading balance (Uni Bloc balance, TX4202L) and transferred into a stainless steel container. A sample of distilled water (4000 mL) was added. The mixture was heated until mucilage was formed. The mucilage was filtered using a muslin bag to obtain a viscous filtrate. A 1000 mL sample of the viscous filtrate was measured, transferred into a bowl and an equivalent amount of acetone solution (1000 mL) was added to precipitate the gum. The remaining viscous filtrate was also mixed with acetone in the ratio 1:1 in order to precipitate the gum. The gum was collected by sieving using a muslin bag and dried in hot air oven at 60 ± 1^{o}C for 24 h. The dried mass of gum was pulverized, passed through a sieve (710 µm sieve) and the percentage yield computed using Equation (1):

$$Percentage\ yield = \frac{W_f}{W_0} * \frac{100}{1} \ldots . (1)$$

Where W_0 is initial weight of powdered plant materials before extraction, while $W_f$is the final weight of extracted gum after drying.

2.2.2 Characterization of *Grewiaspp* gum

The extracted gum has earlier been characterized (e.g. Flow/packing properties, pH, viscosity, and swelling index) and published [7]

2.2.3 Preparation of metronidazole tablets

To prepare conventional metronidazole tablets, granules were first prepared according to the formula in Table 1. A sample of metronidazole powder (24 g) was weighed and transferred into a clean mortar. A 3.6 g sample of maize starch was weighed and added (half of the required disintegrant). A 7.5 g of lactose was weighed and added. A sample of *Grewia gum* was converted into mucilage by dissolving 0.5 g of gum in sufficient quantity of hot water(0.5% w/w) and used to knead the powder blend in the mortar to form a wet mass. This was passed through a 1.18 mm sieve and dried in a hot air oven at 60 ± 0.5^{o}C for 2 h. The dried mass was passed through a 710 µm sieve to form the required granules. Other sets of granules were prepared using 0.75% w/w, 1% w/w, 1.25% w/w and 1.5% w/w of *grewia gum* and 0.5% w/w, 0.75% w/w, 1% w/w, 1.25% w/w and 1.5% w/w of *acacia gum.* All sets of granules were characterized and stored in air-tight container for further studies.

2.2.4 Characterization of metronidazole granules

(i) Flow rate and angle of repose: A 15 g sample of granules from each batch was weighed and poured into a glass funnel plugged at the orifice and suspended at a height of 7.5 cm above a flat surface. The plug was removed from the tip of the funnel and the time taken for the granules to completely flow through the funnel orifice was recorded. The height of the heap formed by the granules and the diameter of the heap base were also measured and recorded [12]. The flow rate was calculated using Equation 2 below:

$$\mathrm{FR} = \frac{Wt}{t} \ldots . (2)$$

Where FR = flow rate (g/s), Wt = weight of granules, t = time of flow (s)

$$Angle\ of\ Repose, \theta = arc\ Tan \frac{2H}{D} \ldots . (3)$$

Where H = height of heap of granule and D = diameter of granules heap.

(ii) Packing properties: These were established through measurement of the bulk and tapped densities using methods described previously by Avbunudiogba*et al.* [13]. In these methods, known weight (30 g) of the granules was weighed and transferred into cylinder of a Jolting volumeter. The volume occupied by the granules was recorded V_0. The volumeter was powered and allowed to make 100 taps, the new volume was recorded as V_{100}. The bulk and tapped densities were computed from Equations 4 and 5; while compressibility index (Carr's index) was computed from Equation 6:

$$Bulk\ density\ = \frac{(Wt)}{(V_0)} \ldots . (4)$$

$$Tapped\ density\ = \frac{(Wt)}{(V_{100})} \ldots . (5)$$

$$Carr^{'}s\ index\ (CI)\ = \frac{Td - Bd}{Td} * \frac{100}{1} \ldots . (6)$$

Where *Wt* is the weight of granules, V_0 and V_{100} is the volume occupied before and after 100 taps respectively. *Td* is the tapped density, while *Bd* is the bulk density.

(iii). Particle size analysis: A 40 g portion of the granules was weighed using a top loading balance (TX4202L model, Shimadzu Philippines) and transferred into the top most sieve of a set of sieves of decreasing apertures (500 µm to125 µm). The sieve shaker (Endecott Ltd, UK) was operated for a period of 5 min. The quantity of granules retained in each sieve were weighed to determine the size distribution. Mean particle size was computed with the formula:

$$\ddot{X} = \frac{\Sigma fX}{\Sigma f} \ldots . (7)$$

Where $\ddot{X}$is mean particle size, *f* is the frequency of size *X*.

2.2.5 Compression of metronidazole granules to tablets

A sample of the formulated metronidazole granules (35.1 g) was mixed with corn starch sample (3.6 g, 2nd half of disintegrant), 1% w/w talc and 1% w/w magnesium stearate before compression to tablets with the aid of multiple punch tablet press (Manesty machine Ltd, B3B, Liverpool, England) at 26 arbitrary units on the load scale.

2.2.6 Evaluation of tablets

(a) Thickness and diameter: Ten (10) tablets were selected at random from each batch and the diameter and thickness were measured using a multiple digital tablet hardness test apparatus (Veego Instruments Corporation Mumbai - 400099 India. Model NO: VDIGITAB – 1. Sr. NO: 04-1112) and the mean values recorded [14,15].

Table 1. Composition of metronidazole tablets

Ingredients / Batches	A1	A2	A3	A4	A5	B1	B2	B3	B4	B5
Metronidazole (mg)	400	400	400	400	400	400	400	400	400	400
Grewia gum (mg/%)	3(0.5)	4.5(0.75)	6(1)	7.5(1.25)	9(1.5)	-	-	-	-	-
Acacia gum (mg/%)						3(0.5)	4.5(0.75)	6(1)	7.5(1.25)	9(1.5)
Corn starch (mg)	60	60	60	60	60	60	60	60	60	60
Magnesium stearate (mg)	6	6	6	6	6	6	6	6	6	6
Lactose (mg)	125	123.5	122	120.5	119	125	123.5	122	120.5	119
Talc (mg)	6	6	6	6	6	6	6	6	6	6
Total (mg)	600	600	600	600	600	600	600	600	600	600

(b). Hardness test: The crushing strength (kg/m^2) of six tablets selected at random from each batch were determined using multiple digital hardness test apparatus and the mean values recorded.

(c). Friability test: Ten (10) tablets from each formulation were weighed and placed in a friabilator (Erweka friabilator). The apparatus was rotated at 25 rpm for 4 min; the tablets was removed, dedusted and reweighed. The percentage weight loss was calculated and taken as the measure of friability [16]. Friability was determined using Equation 8

$$Friability\ \% = \frac{W_L}{W_I} * \frac{100}{1} \ldots . (8)$$

Where $W_L$is lost in weight, $W_I$is the initial weight

(d). Disintegration test: The test was performed according to the method described in the British pharmacopoeia [17]. The test was done using a Manesty disintegration apparatus (model: TD29T176, Manesty machines LTD, England), which consists of six (6) baskets oscillating up and down. Water was use as the disintegration medium with temperature maintained at 37^{o}C ± 0.5^{o}C. Six (6) tablets were selected at random from each formulation and placed in the basket. The disintegration apparatus was operated until the tablets break and pass completely through the mesh and the average time was recorded as the disintegration time).

(e). Content uniformity: Five tablets each from different batch were separately crushed in a mortar, 0.150 g of the crushed tablet was dissolved in 0.1N HCL in a 100 ml beaker and made to the 100 mL mark and filtered through a filter paper. Six (6) aliquots were prepared using the stock solution and the absorbance of these aliquots were measured using a UV spectrophotometer (PG Instrument, USA) at a wavelength of 278 nm and the drug content was calculated using the equation of the calibration curve of the drug in 0.1N HCL and subsequently their percentage content were determined.

(f). In vitro drug release study: Granules dissolution test was carried out using the rotating basket method (USP apparatus one). The apparatus consists of a Pyrex glass vessel containing 900 ml of 0.1 N hydrochloric acid maintained at 37 ± 1^{o}C and a cylindrical basket made of stainless steel wire mesh (aperture size, 425 µm). A tablet from each batch was place in the basket and rotated at a speed of 100 rev. per min in the dissolution medium 5 ml samples were withdrawn from the dissolution medium at 5, 10, 15, 30, 45, 60 and 90 min. The sample were filtered with Whatman filter paper and the withdrawn volume replaced with an equal volume of 0.1N HCL maintained at the same temperature. The filtered samples were then analysed using a UV spectrophotometer (PG Instrument, USA) at a wavelength of 278 nm [16].

(g). Fourier transforms infrared (FTIR) spectroscopy): The Spectrum (Fourier Transform Infrared, FTIR) of metronidazole powder, was recorded with Perkin Elmer RXI spectrophotometer (Connecticut, USA). The powder drug was mixed with potassium bromide (KBr) and compressed into pellets. The spectrum was obtained by scanning between 1000 and 3500 /cm. This same procedure was used to record the FTIR spectra of batch A3 formulated with 1% *grewia specie* gum and that of batch B3 formulated with 1% acacia gum [18].

2.3 Data Analysis

All data were expressed as mean ± SD of three determinations. Differences between means were determined with one way analysis of variance (ANOVA) at $P < 0.05$.

3. RESULTS AND DISCUSSION

3.1 Physical Properties of Granules

The physical properties of granules formulated with Grewiaspp gum and acacia gum such as: bulk and tapped densities, angles of repose and Carr's compressibility index etc. are shown in Table 2. No significant difference in densities among the various batches i.e. batches A1 to A5 and B1 to B5conventional granules (BF10 - BF13). Though slight variations were observed physically, but, these were not significant when subjected to statistical analysis (P > 0.05). However there is significant difference between the tapped and bulk densities of either granules prepared,*Grewia*and acacia gums (i.e. tapped density is greater than bulk density). The flow rate ranged from 5.37 g/s to 6.08 g/s for formulations with *grewia* gum (A1-A5) and 3.35 g/s to 3.88 g/s for formulations with acacia gum (B1-B5).These indicate that both sets of granules had good flow rate. However the granules prepared with *grewia species* gum flow faster

than those prepared with acacia gum.This may be because even though granules produced by both gums have relatively similar flow parameters like angle of repose, Carr's index and Hausner ratio, the tapped and bulk densities vary. As shown in Table 2, granules produced using Grewia gum have bigger tapped densities than those produced using acacia, therefore for same mass of granules, the volume of granules from Grewia gum will be smaller and will tend flow out completely from the funnel before that from acacia gum.

The angle of repose ranged from 29.75° to 31.97° for batches A1-A5 and 29.36° to 33.41° for B1-B5 which were below 35° showing that all sets of granules had a good flow property.

The carr's index were in the range of 16.22% to 20.00% for batches A1-A5 and 12.74% to 20.31% for batches B1-B5; Hausner's ratio were within the range of 1.19 to 1.25 for batches A1-A5 and 1.15 to 1.25 for batches B1-B5; indicating fairly good flow suitable for compression into tablet [19,20, 21].

3.2 Results of Particle Size Analysis of the Formulated Granules

The particle size distribution of the metronidazole granules of batches A1-A4 and B1-B4 is shown in Fig. 1. For all batches of metronidazole tablets, the sizes ranged from 125 µm to 850 µm. The most frequent sizes are 355 µm and 455 µm. Varying particle size distributions in a powder bed affect some tablets mechanical properties. There is a greater degree of consolidation of compacts formed from larger granules than smaller ones as a result of plastic deformation and fragmentation[22]. Thus, particle size should be controlled during tableting and encapsulation

Table 2. Micrometric values of formulated granules: Batch A1-A5 and B1-B5

Batches	Flow Rate (g/s)mean± SD	Bulk density (g/cm^3)mean± SD	Tapped density (g/cm^3) mean±SD	Angle of repose(°) mean±SD	Carr's index(%) mean±SD	Hausner's ratio mean±SD
A1	6.08±0.07	0.60± 0.02	0.73±0.02	30.72±2.14	17.81±1.24	1.21±0.02
A2	5.38±0.05	0.62±0.01	0.74±0.02	30.65±0.64	16.22±1.48	1.19±0.03
A3	7.14±0.26	0.67±0.00	0.81±0.01	30.97±0.37	17.28±0.57	1.21±0.01
A4	5.95±0.32	0.61±0.01	0.73±0.02	30.44±1.74	16.44±0.65	1.20±0.01
A5	5.37±0.16	0.60±0.01	0.75±0.02	29.75±1.52	20.00±0.32	1.25±0.00
B1	3.88±0.16	0.53±0.02	0.65±0.01	29.36±0.16	18.46±1.78	1.23±0.03
B2	3.35±0.05	0.48±0.12	0.52±0.01	32.74±0.09	12.74±0.91	1.15±0.01
B3	3.53±0.14	0.49±0.02	0.60±0.03	33.01±0.51	18.33±1.34	1.22±0.02
B4	3.68±0.03	0.54±0.02	0.65±0.02	32.14±0.38	16.92±0.94	1.20±0.02
B5	3.69±0.06	0.51±0.01	0.64±0.00	33.41±0.10	20.31±2.75	1.25±0.05

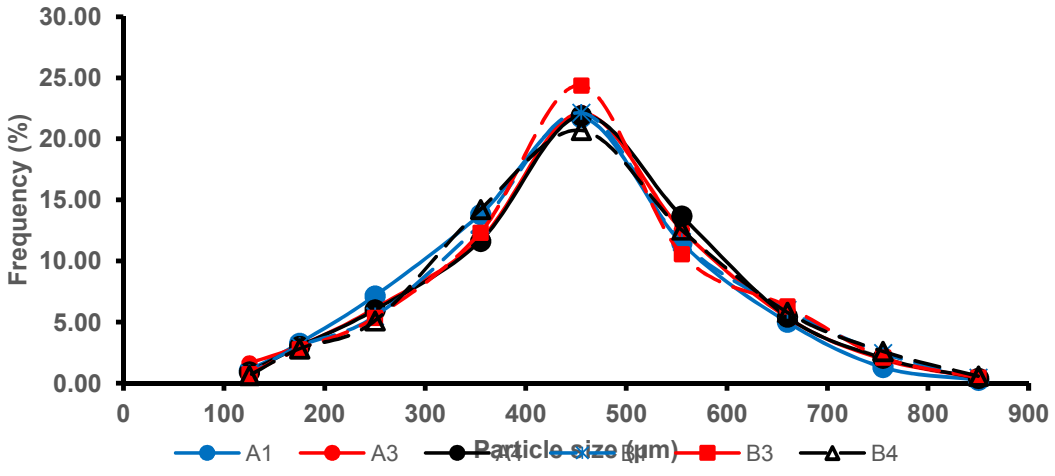


Fig. 1. Particles size distribution of conventional metronidazole granules formulated with Grewia gum (A1, A3 and A4) and that prepared with acacia gum (B1, B3 and B4)

3.3 Results of Tablets Evaluation

Post compression parameters are presented in Table 3. The hardness for batches A1-A5 ranges from 5.46 kgF to 7.87 kgF and 6.06 kgF to 8.20 kgF for batches B1-B5 which were above the minimum requirement (4 kgF) for satisfactory crushing strength. The % friability for batches A1-A5 ranges from 0.72% to 1.09% and 1.0% to 1.20% for batches B1-B5; only batches A3-A5 with values 1%, 0.9% and 0.72% respectively and batch B5 with a value of 1% met the standard requirement which according to the limit; no compressed tablet should have a friability value greater than 1.0% in order to withstand pressure or mechanical shock during packing, handling, packaging and transportation. These findings indicates that the higher the concentration of the binder, the greater the cohesive force and inter particulate bonding and the lower the friability. However the tablets formulated with acacia gum showed greater friability.

According to the British Pharmacopoeia 2012, the standard disintegration time for a conventionaltablet should be less than 15 minutes; all batches A1-A5 and B1-B5 disintegrated in less than 15 minutes except for A5 with a disintegration time of 19.56 minutes. The results indicate that increase concentration of the binder significantly increased the disintegration time of the formulated metronidazole tablets. This is because the higher the concentration of the binder, the higher the binding capacity as a result of higher interparticulate cohesive or binding force. This means the higher the force needed set the particles of the drug apart from themselves.Metronidazole tablets formulated with acacia gum generally disintegrated faster than those formulated with *grewia species* gum.This may be because the binding capacity of acacia gum is lower than that of grewia gum, which may result in weaker interparticulate force and subsequently, faster disintegration.

The British pharmacopoeia [17],specifications for the percentage content of metronidazole tablet ranges from 99-101%. All batches met this requirement except for batches A3, A5 and B2 with percentage content 104%, 98% and 98.94% respectively.

Results of *in-vitro* drug release study are presented in Fig. 2. At 45 minutes all the batches containing grewia gum (A1-A5) released up to 60% of the drug. At the end of 90 min dissolution study, the percentage drug release by formulations A1, A3, and A5 were found to be 93%, 78% and 75% respectively. Batch A1 with the lowest concentration of the binder gave the highest release which shows that increase concentration of the binder leads to a decrease in drug release. At 45 min all the batches containing acacia gum (B1-B5) released more than 76% of the drug as shown in Fig. 2. At the end of 90 minutes, the percentage drug release for batches B1, B3, B5 were 98%, 97%, and 95% respectively. Batch B1 with the lowest percentage of binder gave the highest release. From this study, the tablets formulated with *Grewia species* gum gave comparable drug released with tablets formulated with acacia gum.

3.4 FTIR Spectroscopy

The FTIR spectra of pure metronidazole powder and metronidazole tablets formulated with *Grewiaspp*gum are shown in Fig. 3.

Table 3. Post compressional properties of formulated metronidazole tablets

Batches	Thickness (mm)mean ±SD	Diameter (mm)mean± SD	Hardness (kgF)mean ±SD	% Friability (%) mean±SD	Disintegration time(min) mean±SD	% content (%) mean±SD
A1	3.58±0.15	13.05± 0.02	5.46±0.03	1.09±0.03	1.27±0.01	100.1±1.1
A2	3.64±0.07	13.05±0.02	6.11±0.61	1.05±0.02	2.01±0.28	99.0±0.6
A3	3.48±0.05	12.99±0.04	6.26±0.51	1.00±0.05	2.56±0.42	104.1±2.0
A4	3.52±0.04	13.02±0.02	7.26±0.34	0.90±0.01	14.39±0.26	100.6±1.0
A5	3.06±0.04	12.50±0.01	7.87±0.22	0.72±0.02	19.56±1.65	98.18±0.0
B1	3.70±0.07	13.11±0.02	6.06±0.39	1.20±0.07	0.45±0.03	99.12±0.6
B2	3.70±0.04	13.09±0.04	6.81±0.42	1.10±0.01	1.12±0.24	98.94±1.1
B3	3.70±0.04	13.15±0.04	7.40±0.31	1.09±0.02	1.49±0.21	100.3±1.5
B4	3.09±0.05	12.53±0.04	8.11±0.53	1.05±0.04	1.30±0.06	100.3±1.5
B5	2.995±0.02	12.50±0.02	8.20±0.26	1.00±0.03	3.09±0.52	100.3±1.4

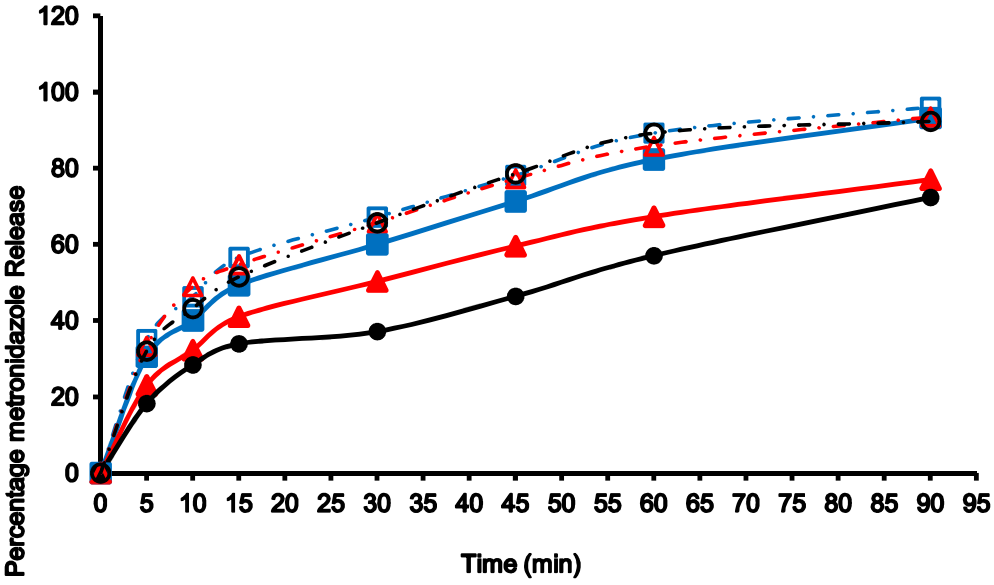
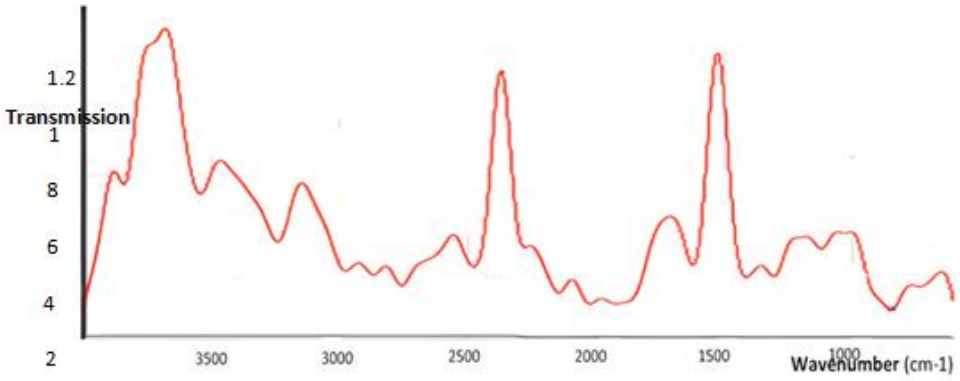


Fig. 2. Drug release profiles of conventional metronidazole tablets prepared with *Grewia*gum (A1 —■—, A3—▲—, A5 —●—) and acacia gum (B1 ▪▪▪□▪▪▪, B3▪▪▪Δ▪▪▪, B5 ▪▪▪O▪▪▪)

A



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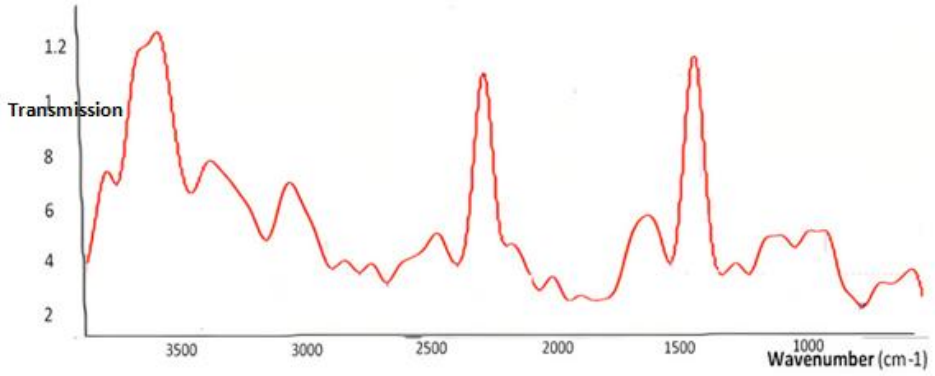

Fig. 3. FTIR spectra of pure metronidazole powder (A) and metronidazole tablet prepared with 1%$^{w}/_{w}$*grewia species* gum (B)

The basic peaks which is characteristic of metronidazole was found atwavelengths of 3,800, 2,400 and 1500 cm^{-1}. These peaks were presentinpure metronidazole powder and the formulations. The basic functional groups of metronidazole remain intact in all the formulations. This observation implies that there was no chemical interaction between the metronidazole, the gum and the different excipients in the formulated tablets

4. CONCLUSION

Conventional metronidazole tablets were formulated using *Grewiaspp* gum extracted from fresh *Grewia species* pods as binder via wet granulation techniques. Tablets so formed were evaluated and compared with tablets formulated with the well-established natural gum – *Acacia.* Flow and packing properties of granules and post-compression parameters of tablets so formed compared adequately with those prepared with acacia gum. FTIR spectra of metronidazole and that of formulated tablets shows no interaction. Thus gums from *Grewia species* can be employed in place of acacia in metronidazole tablets formulation.

CONSENT

By the nature of this research, this is not applicable.

ETHICAL APPROVAL

By the nature of this research, this is not applicable.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Hussain A, Qureshi F, Abbas N, Arshad MS and Ali E. An Evaluation of the Binding Strength of Okra Gum and the Drug Release Characteristics of Tablets Prepared from It. Pharmaceutics. 2017; 9(2):20.
2. Ghatage SL, Patil SV, Navale SS, Mujawar NK. Natural binders in tablet formulation. Int J PharmTech Res. 2014;6(3):1070-1073
3. Okoye EI, Onyekweli AO, Kunle OO. Okra gum-an economic choice for the amelioration of capping and lamination in tablets. Ann. Biol. Res. 2014;2(2):30-42
4. Karmakar K. Application of natural gum as binder in modern drug delivery. J Anal Pharm Res. 2016;3(4): 00061. DOI: 10. 15406/japlr.2016.03.00061.
5. Amiri MS, Mohammadzadeh V, Yazdi MET, Barani M, Rahdar A, and Kyzas GZ. Plant-Based Gums and Mucilages Applications in Pharmacology and Nanomedicine: A Review. Molecules. 2021;26:1770. Available:https://doi.org/10.3390/molecules 26061770
6. Goswami S and Naik S. Natural gums and its pharmaceutical application. J. Sci. Innov Res. 2021;3(1):112-121.
7. Avbunudiogba JA, Okuntarami MD, Adjene JO. Evaluation of the emulsifying properties of *Grewia spp.* J Bio Innov. 2020;9(5):910-919
8. Leitsch D. A review on metronidazole: an old warhorse in antimicrobial chemotherapy. Parasitology; 2017. Available:https://doi.org/10.1017/S0031182 017002025.
9. Cosar C, Julou L. The activity of 1-(2-hydroxyethyl)-2-methyl-5-nitroimidazole (R. P. 8823) against experimental Trichomonasvaginalis infections. Annales d l'Inststitut Pasteur. 1959;96:238–241.
10. Holmes AH, Moore LS, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, Guerin PJ and Piddock LJ. Understanding the

mechanisms and drivers of antimicrobial resistance. 2016;Lancet 387:176–187
11. Okafo SE, Chukwu A. Studies on *Sidaacuta* hydrogel I: processing and physicochemical properties of the derived hydrogel obtained from South East Nigeria. Int. J. Pharm. Pharm. Sci. 2017;9(6):5-11.
12. Patil BS, Raokin KU, Khalids and Korwar PG. Properties of *Zingniberofficinale* starch as a novel tablet binder. Int J Pharm Sci. 2010;2(3):717-723.
13. Avbunudiogba JA, Okor RS, Uhumwangho MU and Arhewoh MI. Melt granulation of aspirin powder as alternative to slugging: Implication for compressibility and dissolution rate. Nig. J Pharma Sci. 2012; 11:32 – 40.
14. Ashford M, Fell J, Attwood D. Studies on pectin formulations for colonic drug delivery. J Control Release. 1994;30:225–232.
15. Turkoglu M, Ugurlu T. In vitro evaluation of pectin-HPMC compression coated 5-aminosalicylic acid tablets for colonic delivery. Eur. J. Pharm Biopharm. 2002; 53:65–73.
16. Kapoor D, Rajora A, Saini V. Formulation development and dissolution enhancement of Compeba-400 (Metronidazole-400) tablet. Asian J. Biomed Pharm Sci. 2011; 1(2):25-31.
17. British pharmacopoeia. Her Majesty's stationary office, London; 2012.
18. Bamiro OA, Duro-Emanuel AJ. Factorial analysis of the binding property of acetylated ginger starch in metronidazole formulations. Int J Pharm. Investig. 2017; 7(1):18-24.
19. Staniforth JN, Aulton ME. Powder flow. In Aulton ME, editor. Aulton's Pharmaceutics: The Design and Manufacture of Medicines. 3rd ed. Philadelphia: Churchill Livingstone Elsevier; 2007.
20. Yuksel N, Turkmen B, Kurdogglu AH, Barsaran B, Erkin J, Baykara T. Lubricant efficacy of magnesium stearate in direct compressible powder mixtures comprising cellactose® 80 and pyridoxine hydrochloride. FABAD J. Pharm. Sci. 2007;32:173-183.
21. Chime SA, Attama AA, Agubata CO, Ogbonna JD, Onunkwo GC. Micrometric and anti-nociceptive properties of lyophilized indomethacin-based SLMs based on solidified reverse micellar solutions. J. Pharm. Sci. 2012;5(6):3410-3416.
22. Eichie FE, Kudehinbu AO. Effect of particle size of granules on some mechanical properties of paracetamol tablets. Afr. J. Biotechnol. 2009;8(21):5913-5916.

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