Preliminary Evaluation of *Brachystegia eurycoma* Seed Mucilage as Tablet Binder

Olubunmi Olayemi*, Oremeyi Jacob

*Department of Pharmaceutics and Pharmaceutical Microbiology, Ahmadu Bello University, Zaria

ABSTRACT

Brachystegia eurycoma seed mucilage was evaluated for use as a tablet binder in metronidazole formulations in comparison with gelatin. The granules were formulated by the wet granulation method using the extracted mucilage and gelatin as binder at 1, 2, 4, 6%w/w concentrations. The granules were found to possess good flow property as indicated by the angle of repose, Hausner's ratio and Carr's index. The formulated tablets were evaluated for uniformity of weight, thickness, tablet hardness, friability, disintegration times, drug assay and dissolution profile. Generally, the tablets formulated from *Brachystegia eurycoma* seed mucilage were softer than those of gelatin, had good uniformity of weight and disintegrated within the official specified times for uncoated tablets. The tablets had a rapid dissolution rate which indicates the efficacy of *Brachystegia eurycoma* seed mucilage as a binder where fast release of a drug is desired.

Keywords: *Brachystegia eurycoma* seed mucilage, binder, wet granulation method, dissolution rate, metronidazole

INTRODUCTION

Drug substances are usually not administered as they are in their pure state, but rather as part of a dosage form where they are usually combined with other agents (excipients), which could be non-medicinal. These excipients include starches, celluloses, gums etc. which could be from natural or synthetic sources. The natural-plant based materials posses these advantages over the synthetic: they represent truly renewable sources which are biodegradable, most of these plant materials are carbohydrates comprising of monosaccharide units, so, they are non-toxic and biocompatible, they are cheaper since they are from natural sources and their production is also cheaper compared to the synthetic materials. They are also environmentally friendly and are locally available[1]. An example of a natural-plant based excipient is the "gums" although they could be natural, semi-synthetic or synthetic.

In Nigeria, the quest for local raw materials of pharmaceutical products to substitute the imported ones has led to the processing, purification and sourcing of many local gums. The usefulness of these locally available natural gums cuts across the various dosage forms and favorably competes with the conventionally imported ones. There has been a lot of investigations into the use of these local gums in various industries like paper, textile, food, ink, cosmetics, petroleum and frequently used in pharmaceuticals as thickeners, binders, disintegrants, suspending and stabilizing agents, emulsifiers, matrix formers and coating materials in micro encapsulation[2].

Brachystegia eurycoma Harms (synonym *B. spiceaformis*) family *leguminosae-caesalpinioideae* is a woody plant mostly found in the forest zone. The tree is about 35m tall, with bole of 2m diameter. It is vaguely buttressed, has low branching, large, flat crown common on river banks of the forest zone in southern Nigeria and Cameroun. It is also a very popular plant in the Eastern part of Nigeria. The sap wood is white, not durable and quickly rotting on exposure. It may be readily recognized by its large size, irregular bole and huge twisted spreading branches and by the rough fibrous bark which peels off in untidy patches and often exudes a brownish buttery gum. In Nigeria, it is commonly called Achi (Igbo), Akalado or Eku (Yoruba), Akpakpa or Apaupan (Ijaw), Dewen (Bini), Okwen (Edo), Okung (Efik)[3]. The seeds often have a hard coat with hourglass-shaped cells, and sometimes bear a U-shaped line called pleurogram (Carr). The seed has been said to contain 10.47% protein and total carbohydrate content of 71.94%. Products from the tree bark have found application as fibres, food wrappers and have been used to make containers. The timber products are used as building materials in carpentry and related applications. The seed is used in food majorly in soup making as a soup condiment, flavouring agent and for soup thickening

***Corresponding author:**
Email: olubunmibiala@yahoo.co.uk

(for emulsification and stabilization of soup) in south eastern Nigeria. The seeds are a good source of bioactive compounds comprising flavonoids, alkaloids, phenolic compounds, saponins and tannins, protein, carbohydrate, lipids and fiber. The seeds are also a good source of water soluble vitamins (ascorbic acid, thiamine, riboflavin and niacin) and minerals such as Ca, P, K, Mg, Na, Zn, Fe and Cu (but does not contain Pb and Co) therefore playing a major role in the nutritional status of consumers[4]. *Brachystegia eurycoma* seed gel has been investigated for the treatment of wounds in combination with snail mucin and honey[5] but the use of this gum as a pharmaceutical tablet binder has not been exploited.

MATERIALS AND METHODS

Materials

Metronidazole powder, magnesium stearate, talc powder, acetone (BDH chemicals Ltd, Poole, England), Gelatin (May and Baker Ltd, Dagenham, England) and *Brachystegia* gum (prepared in the department of Pharmaceutics, Ahmadu Bello university, Zaria).

Extraction method

Brachystegia eurycoma seeds were obtained from a local market in Enugu state. The seeds were sun-dried and then powdered. The extraction was carried out according to a known method with some modification[5]. Two hundred and fifty (250) grams of the powdered seeds of *Brachystegia eurycoma* was dispersed in 3000ml of distilled water for 24 hours (The dispersion was aided by stirring with a spatula). The mixture was centrifuged and the sediment was discarded while the supernatant portion was kept. Acetone was added to the supernatant portion in the ratio 1:1 to precipitate the gum. This was then centrifuged and the supernatant portion was discarded but the sediment kept as gum. The gum was further washed with Acetone in a ratio 1:1 and then dried at 40^0C in an oven for about 48hrs. The dry flakes were pulverized using a blender and stored in an air tight container.

Physicochemical properties of gum.

The powdered gum was evaluated for the following parameters; solubility, pH, viscosity, ash value, moisture sorption capacity. The flow indices also evaluated were;

The angle of repose was used to characterize a flow property of powder material and it was computed as

$$\tan^{-1}\frac{h}{r} \quad (1)$$

where h=height of heap and r=- radius of heap.

The bulk density was measured by putting the accurately weighed powder into a graduated cylinder and the volume was calculated as

$$\frac{weight\ of\ powder}{volume\ occupied\ by\ powder} \quad (2)$$

The cylinder was tapped until powder bed volume reached a constant value and the volume was recorded as tapped volume. Compressibility index was calculated as

$$\frac{tapped\ density - bulk\ density}{tapped\ density} \quad (3)$$

While the Hausner's ratio was calculated as

$$\frac{tapped\ density}{bulk\ density} \quad (4)$$

Preparation of Metronidazole granules

Granules containing 200mg metronidazole where prepared with *Brachystegia eurycoma* gum as binder at 1, 2, 4, 6%w/w (BE1, BE2, BE3, BE4 respectively) and gelatin was used as the reference binder. The wet granulation method of massing and screening was employed in the formulation of the granules. Metronidazole powder, lactose, *Brachystegia eurycoma* gum, maize starch were mixed appropriately and the resulting masses were screened through a 1.7mm mesh size, dried for 1 (one) hour at 40^oC in an oven and then screened again through a 1.6mm mesh size and finally dried to constant weight.

Granule analysis:

The granule analysis carried out were moisture content and flow indices determination (bulk, tapped densities, compressibility index, Hausner's ratio and angle of repose).

Compression of granules

The granules were then mixed with the appropriate quantities of extra-granular excipients (MS BP, talc and magnesium stearate) and compressed into tablets at 5metric tonnes using the Erweka type G. M B. H machine. Batches of 100 tablets were prepared according to the formula in Table 1. The tablets produced were stored for 24hours before the tablet evaluation.

Characterisation of tablets:

The tablets were evaluated for the following parameters after 24hours of production; uniformity of weights, thickness, crushing strength (hardness), friability and assay.

Table 1: Formula for preparing metronidazole granules

Ingredients (g)/ Batches	BE1	BE2	BE3	BE4	GE1	GE2	GE3	GE4
Binder Concentration (w/w)	1	2	4	6	1	2	4	6
Metronidazole	20	20	20	20	20	20	20	20
Lactose	25	24.5	23.5	22.5	25	24.5	23.5	22.5
BE gum	0.5	1	2	3	-	-	-	-
Gelatin	-	-	-	-	0.5	1	2	3
MS BP	3.9	3.9	3.9	3.9	3.9	3.9	3.9	3.9
Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Magnesium stearate	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Total weight	**50**	**50**	**50**	**50**	**50**	**50**	**50**	**50**

***In-vitro* drug release 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.

A Beer Lambert's calibration curve for metronidazole was plotted. This was done by serially diluting metronidazole powder in 0.1N HCL then, the absorbance of the dilutions were taken at 277nm wavelength in a UV spectrophotometer. The concentrations obtained from the Beer's plot were plotted against the absorbance to give the calibration curve with regression equation y = 0.0351x and R^2 value of 0.9818.

RESULTS AND DISCUSSION

From the organoleptic properties of this gum shown in Table 2, the extracted gum powder was brown in colour, moderately coarse in texture with a bland taste and a cocoa-like smell. The powder formed a cloudy-dispersion in hot water but was insoluble in cold water, acetone, chloroform and ethanol. It is because it has been said that organic solvents precipitate gums[6]. The total ash value was found to be 2% and this indicates low levels of contamination during gathering, processing, and handling of the crude *Brachystegia eurycoma* seed gum[7]. The moisture sorption studies indicated that when the gum is stored in damp environment, the gum quickly gets hydrated but has the ability to rapidly loose such water molecules in the presence of desiccants. This property makes the gum susceptible to microbial and physicochemical deterioration. *Brachystegia eurycoma* gum was found to possess good flow property as seen from its low angle of repose (25.91^o) and moderate compressibility (20.69%). It is important to know these properties of the gum so as to help with the scaling up processes in further formulations.

Table 2: Organoleptic and physicochemical properties of *brachystegia eurycoma* seed gum

PARAMETERS	BE GUM
Yield (%)	18.46
Colour	Brown
Odour	Cocoa smell
Taste	Bland
Texture	Moderately coarse
Solubility:	
Acetone	Insoluble
Chloroform	Insoluble
Ethanol	Insoluble
Hot water	Soluble
pH at 28ºC	5.55
Viscosity (mPas)	3.6
Loss on drying (%)	16
Moisture sorption (g)	1.22
Ash value (%)	2
Mean particle size (µm)	163.76
Angle of repose (^{0})	25.91
Flow rate (g/sec)	6.46
Bulk density (g/ml)	0.69
Tapped density (g/ml)	0.87
Hausner's ratio	1.26
Carr's index	20.69

Table 3: Physico-chemical properties of granules

BATCHES / PARAMETERS	BE1	BE2	BE3	BE4	GEL1	GEL2	GEL3	GEL4
Binder concentration (%w/w)	1	2	4	6	1	2	4	6
Moisture content (%)	4	5	5	4	6	4	4	5
Angle of repose (º)	28.10	31.60	34.00	34.90	36.30	33.40	33.80	34.20
Flow rate (g/sec)	4.56	4.13	4.95	3.93	4.11	3.79	4.29	3.33
Bulk density (g/ml)	0.53	0.50	0.59	0.53	0.48	0.47	0.53	0.50
Tapped density (g/ml)	0.63	0.59	0.69	0.63	0.56	0.56	0.61	0.57
Hausner's ratio	1.19	1.18	1.17	1.19	1.17	1.19	1.15	1.14
Carr's index	15.87	15.25	14.49	15.87	14.29	16.07	13.11	12.28

The flow properties of the granules (Table 3) were good as indicated by the angles of repose which were below 40^{o} and has been said to be indicative of good flow property[8]. The compressibility of granules are usually determined to know the ability of the granules to form compact (which will produce strong tablets) and decrease in volume under applied pressure. Compressibility index is known to be an indication for good flow properties of granules with values of below 15% and the Hausner's quotient is said to relate to the cohesiveness of the granules with values below 1.25[9]. The Carr's indices were between 14 and 16 while the Hausner's quotient were less than 1.25, these show that generally the formulated granules possessed good flow properties and this should translate to production of tablets with minimal weight variation.

Evaluation of the tablets showed that the tablets had uniform weights which were within the range of the official specification. The specification states that for tablets of weights above 324mg, not more than two tablets should deviate from the average by more than 5%[10]. This implies that the granules had good flow and thus, filled the compression die uniformly. The thicknesses of the formulated tablets were between 3.77 - 4.16mm. Although tablet thickness is said to vary with no change in weight due to differences in the density of the granules, the pressure applied to the tablets, as well as the speed of tablet compression[11], wide variations in tablet weights and thickness has been said to affect the disintegration and dissolution of the tablets [12].

The tablet strength as indicated by the crushing strength (hardness) of the tablets was seen to increase with increase in concentration of the binder (Table 4). This increase in tablet hardness with increase in binder concentration could be attributed to more particle-particle contact points of the binding agents as well as the drug particles which help to create more solid bonds and also due to the formation of thicker adhesive coats around the particles. Although the BE-formulated tablets were generally softer than the GEL-formulated tablets, the tablets passed the minimum requirement of 4kg for satisfactory mechanical strength of tablets[13]. The friability test is designed to evaluate the ability of the tablets to withstand abrasion in packaging, handling, and transportation. From the results obtained, the friability of the tablets was observed to decrease with an increase in binder concentration. This could be due to formation of more solid bonds within the tablets due to increase in binder concentration which conferred resistance to tablet fracture and abrasion[14]. It was also observed that tablets formulated with the extracted gum were more friable than those of gelatin and only formulations with higher concentrations of the binder fell within the official specification of friability values not exceeding 1%[10]. Since the resistance of a tablet to chipping, abrasion, or breakage under conditions of storage, transportation and handling before use has been said to depend on its hardness[11] and the BE-formulated tablets were observed to be softer than the GEL-formulations, this could explain the friable nature of the BE-formulations.

Disintegration time is the time required under a given set of conditions for a group of tablets to disintegrate or break up into smaller particles and it is a crucial step in release of drugs from immediate release dosage forms. It was observed that the disintegration times of all the formulated tablets increased with an increase in binder concentration this could be due to the formation of a thick film of gum mucilage as the tablet comes into contact with the disintegrating fluid with the film being converted into a mucilaginous viscous barrier[15].

Table 4: Tablet properties

PARAMETERS	BE 1	BE 2	BE 3	BE 4	GEL 1	GEL 2	GEL 3	GEL 4
Average weight (mg)	501.2 (± 0.010)	495.75 (± 0.004)	506.85 (± 0.003)	506.6 (± 0.009)	498.95 (± 0.004)	496.45 (± 0.003)	499.1 (± 0.004)	499 (± 0.003)
Uniformity of thickness (mm)	3.94 (± 0.14)	3.86 (± 0.10)	4.16 (± 0.03)	3.97 (± 0.16)	3.78 (± 0.10)	3.83 (± 0.12)	3.85 (± 0.06)	3.77 (± 0.11)
Uniformity of diameter (mm)	12	12	12	12	12	12	12	12
Crushing strength (kgF)	5 (± 0.55)	6 (± 0.27)	7.5 (± 0.55)	8 (± 0.42)	9 (± 0.89)	11 (± 1.75)	12 (± 0.00)	11.5 (± 0.55)
Friability (%)	11.02	8.08	2.45	1.01	1.92	1.43	0.99	0.65
Disintegration times (mins)	0.83	3.06	6.06	11	1.04	4.38	8.43	10.81
Drug content (%)	99.36	98.64	95.50	96.69	93.22	96.86	96.69	97.47

NB: Standard deviations in parenthesis

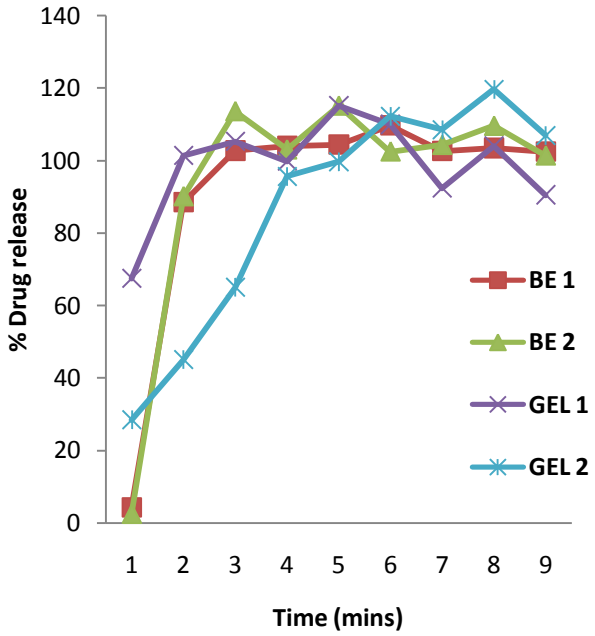

Figure 1: Dissolution profile of metronidazole tablets formulated with 1% and 2% binders.

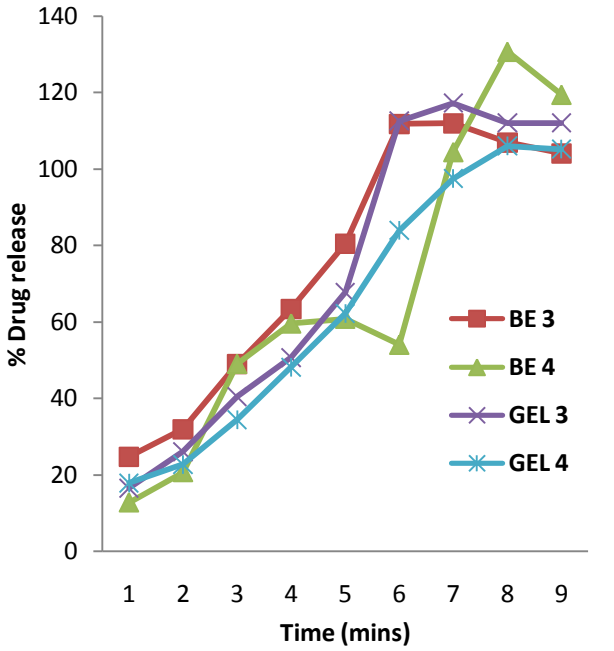

Figure 2: Dissolution profile of metronidazole tablets formulated with 4% and 6% binders.

The disintegration times of BE-formulations were comparable with those of the GEL-formulations and all the formulated tablets met the[10] specifications for disintegration of uncoated tablets within 15minutes.

The formulated tablets were assayed for the amount of metronidazole in them and were found to meet the USP specification which states that the tablets contain not less than 90% and not more than 110%.

Dissolution plays an important role in the bio-availability and therapeutic efficacy of a drug in the body. The factors that affect the dissolution rate include type and concentration of binder, hardness, solubility of the drug and manufacturing process (either wet or dry granulation or direct compression). From figures 1 and 2, the drug release profiles of the BE-formulated tablets were observed to be more comparable to GEL-formulations at 4% than at the other concentrations used (i.e. BE 3). The BE-formulations were observed to release a higher

amount of the drug and at a faster rate (at 5minutes) than the GEL-formulations. This rapid dissolution rate shows that *Brachystegia eurycoma* gum could be suitable for use as a binder in conventional tablets where fast release of the drug is desired. All the formulated tablets met the [10] specification for tablets which states that at least 70% of the drug should be released in 30 minutes.

The results obtained from this work show that the formulated granules had good flowability and the tablets had good uniformity of weight, thickness, increasing the concentration of the mucilage increased tablet disintegration time and decreased tablet friability. The dissolution profile shows that *Brachystegia eurycoma* mucilage could be used where fast release of a drug is required. Therefore, the dried gum of *Brachystegia eurycoma* seed which is a natural agent can be used as a pharmaceutical tablet binder for immediate release of uncoated tablets.

REFERENCES

1. Girish, K. J., P.S. Dhiren, D.P. Vipul and C.J. Vineet, 2009. Gums and mucilages *Asian Journal of Pharmaceutical Sciences*, 4 (5): 309-323
2. Mahesh, V.C., 2006. Excipient development for Pharmaceutical, Biotechnology and Drug delivery system, Edited by Ashok Katdare, pp. 109-124
3. Ikegwu, O.J., P.E. Okechukwu and E.O. Ekumankana, 2010. Physico-chemical and pasting characteristics of flour and starch from Achi; *Brachystegia eurycoma* seed. *Journal of food technology,* 8(2): 58-66
4. Uhegbu, F.Q., C.C. Onwuchekwa, E.J. Iweala and I. Kanu, 2009. Effect of processing methods on nutritive and antinutritive properties of seeds of *Brachystegia eurycoma* and *Detarium microcarpum* from Nigeria. *Pakistan Journal of Nut*rition, 8: 316-320
5. Adikwu, M.U. and T.C. Enebeke, 2007. Evaluation of snail mucin dispersed in *Brachystegia eurycoma* gum gel as a wound healing agent. *Animal research international*, 4(2): 685-697
6. Sarah, L.V., B.W. Singer, S.M. Hitchen and J.H. Townsend, 1998. The development and initial application of a gas chromatographic method for the characterization of gum media. *Journal of the American Institute for Conservation* 37: 295-311
7. Singh, K.A., R.P. Selvam and t. Sivakumar, 2010, Isolation, characterisation and formulation properties of a new plant gum obtained from *mangifera indic*a, *International Journal of Pharmaceutical Biomedical Research*, *1*(2): 35-41
8. Reddy, K., S. Mutalik, and S. Reddy, 2003. Once-daily sustained-release matrix tablets of nicorandil: Formulation and in vitro evaluation. *AAPS Pharmaceutical Science Technology*, 4(4): 480-488
9. Mohammadi, M.S. and N. Harnby, 1997. Bulk density modelling as a means of typifying the microstructure and flow characteristics of cohesive powders. Powder Technology, 92(1): 1-8
10. British Pharmacopoeia 2002, Vol I and II: Her Majesty's Stationery Office, University Press, Cambridge
11. Remington, 2006. The science and practice of pharmacy. 21st Ed. US: Lippincott.Williams and Wilkus. pp 672-688, 889-918.
12. Ngwuluka, N.C., B.A. Idiakhoa, E.I. Nep, I. Ogaji, and I.S. Okafor, 2010. Formulation and evaluation of paracetamol tablets manufactured using the dried fruit of *Phoenix dactylifera* Linn as an excipient, Research In Pharmaceutical Biotechnology, 2(3): 25-32
13. Allen, L.V, N.G. Popovich, and H.C. Ansel, 2004. Ansel's pharmaceutical dosage forms and drug delivery systems" in, 8th Edition edn, Lippincott Williams and Wilkins, Philadelphia. pp. 236
14. Itiola, O.A., M.A. Odeniyi, and O.A. Adetunji, 2006. Compression,mechanical and release properties of chloroquine phosphate tablets containing corn and trifoliate yam starches as binders. *Tropical journal of pharmaceutical research*, 5 (2): 589-596
15. Adetogun, G.E. and G. Alebiowu, 2009. Properties of *delonix regia* seed gum as a novel tablet binder Acta Poloniae Pharmaceutica ñ Drug Research, 66(4): 433 and 438