



## EVALUATION OF DISINTEGRANT PROPERTIES OF *Neorautanenia mitis* STARCH

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### ABSTRACT

*Neorautanenia mitis* is a leguminous sub-shrubby climbing plant with a tuberous root which could be exploited as a potential source of pharmaceutical grade starch. This study aims to determine the suitability of *Neorautanenia mitis* starch (NMS) as a disintegrant in tablet formulation. Its physicochemical properties such as solubility, acidity, pH, hydration capacity, swelling capacity, content of amylose and amylopectin and flow properties were determined. The starch (NMS) was employed as a disintegrant in the preparation of paracetamol granules at concentrations of 7.5, 10 and 15 % and evaluated. The granules were compressed into tablets at 0.5, 0.75, 1.00 and 1.25 MT and tablet properties were evaluated. The physicochemical properties showed NMS has good flow, lower amylose content and higher swelling power than maize starch BP (MS). Tablet formulations containing NMS had similar hardness with those containing MS at 0.5 MT while hardness was observed to increase with increase in compression pressure. Tablets containing NMS were found to elicit faster tablet disintegration than those containing maize starch BP and also had higher  $t_{75}$  values. Furthermore, increasing the compression pressure was found to decrease the rate of drug release.

**Keywords:** *Neorautanenia mitis* starch, disintegrant, compression pressure, paracetamol tablets

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### INTRODUCTION

Tablets which are the most common type of oral solid dosage forms consist of the active pharmaceutical ingredients (APIs) and excipients.

Disintegrants ensure tablet breakup when introduced into an aqueous medium by increasing surface area, leading to more rapid release of the API from the tablet matrix and thus influence the bioavailability of the drug.

When included in tablet formulations *via* the granulation process they are reported to be more effective when used intra-and extra-granularly [1]. Tablet disintegration and dissolution increases with increase in the particle size of disintegrants while the presence of moisture and impact of compression force have been shown to influence their compressibility [2].

Swelling is the most generally accepted mechanism of action of disintegrants [3]. It is



dependent on the degree of cross-linking and chemical structure of the disintegrants used; the porosity of the tablet matrix [4] and the pH of the disintegration medium [5]. Wicking or capillary action which involves the entry of fluid by capillary action into the voids of the tablet matrices is another mechanism of tablet disintegration. While it is generally believed that this mechanism is incapable of fully explaining tablet disintegration without factors like swelling [6], water uptake by tablets due to wicking or other means is considered as a major step in disintegration [7]. The disruption of the particle-particle bonds that exist in a tablet matrix due to the destruction of intermolecular forces between the bonds in the presence of an aqueous fluid has also been suggested as a major contribution to tablet break-up. It is however considered secondary to wicking [8].

The recovery of deformed powder particles in a tablet and the subsequent return to their original shape once the tablet comes in contact with an aqueous medium through a reversible viscoelastic process can result in tablet disintegration. This is due to the pressure generated during the process and the rapid influx of fluid into the particulate pores of the matrix [9]. Studies suggest that this mechanism is typical for starch particles [10] and superdisintegrants like croscarmellose sodium and crosspovidone [11].

Starches are polysaccharides composed of many monosaccharide units connected by glycosidic linkages and are widely used as tablet disintegrants. Starch has two structural components which are responsible for its inherent properties, the amylose and amylopectin in proportions of 20 – 30 % and 70 – 80 % respectively [12]. It can be isolated from relatively cheap sources such as tubers, cereals, fruits, legumes and roots [13]. The botanical source of starch influences its composition, granule arrangement in the tissues, its shape, size and structure [14].

Starch is widely utilized in pharmaceutical formulations as an excipient especially as binders and disintegrants. Reports have shown

that the source of starches can influence performance in pharmaceutical formulations. For example, corn starch from Saudi was found to have better disintegrating property than maize starch BP [15]. A comparison of the binding effects of wheat, rice and maize starches showed that wheat starch had the least swelling capacity which resulted in greater particle-particle bonding leading to tablets with high bond strength [16]. Manek *et al* [17] found that *Cyperus esculentus* starch had lower swelling power than maize or potato starch and when incorporated into metronidazole tablet formulations at 10 %, had better binding property than the other starches. *Dioscorea rotundata* (white yam) starch has been reported to be a better binder than maize starch BP in paracetamol tablet formulations [18]. When compared with microcrystalline cellulose (MCC) the disintegrant properties of banana and potato starches were found to be better [19].

*Neorautanenia mitis* (A. Rich) Verdcourt (Fabaceae) [*karamin karara* in Hausa] is a leguminous sub-shrubby climbing plant with a tuberous root. It is widely distributed in Tropical Africa (North, West and Central) especially in grasslands, open lands and rocky soils [20]. *N. mitis* root is popular for its insecticide properties which are reported to be comparable to those of deltamethrin and cypermethrin against mosquito species like *Anopheles* [21]. The plant also has activity against infections such as syphilis and those associated with the skin like rashes and scabies [22, 23]. There have also been reports of the cytotoxic activity of the ethanolic extract of the plant [24].

However, there are no reports on the exploitation of starch from *N. mitis* tubers. The high demand for starch as a pharmaceutical excipient due to its low cost, wide availability and versatility makes it useful to continually search for new sources of pharmaceutical grade starch with potentially superior formulation properties or lower cost. This study seeks to evaluate the disintegrant property of starch extracted from *Neorautanenia mitis* tubers.



## MATERIALS AND METHODS

### Materials

Maize starch (BP), Paracetamol powder (BP), *Neorautanenia mitis* tubers purchased from Suleja, Niger state, Nigeria, Magnesium stearate (BDH), all the solvents used were of chemical and analytical grade. *Neorautanenia mitis* starch (NMS) was prepared as described below.

### Methods

#### Collection and isolation of starch

The tubers of *N. mitis* were peeled, washed with water, sliced into small pieces and then soaked in sodium metabisulphite solution (0.75 % w/v) for 2 h. The soaked pieces were then ground with the addition of water using a blender and sieved using a calico cloth; the suspension was allowed to stand overnight after which the supernatant was discarded and the sediment (starch) was washed with distilled water and then air dried for 24 h. The dried starch was pulverized in a mortar and then packaged for further analysis.

Physicochemical properties of *Neorautanenia mitis* starch (NMS)

**Morphology:** A small quantity of NMS was mounted on the microscope slide using a mixture of glycerin and water (1:1) and examined under the microscope (Leica CME) at a magnification x400. The photomicrograph of the starch was obtained and the diameter of the particles determined [25].

**pH determination:** The pH of a 5% slurry of *Neorautanenia mitis* starch was determined at room temperature (28 °C). Triplicate determinations were made and the mean determined.

**Solubility test:** One (1) gram of NMS was poured into a beaker containing 1 mL, 2 mL, 10 mL, 1 L, 10 L distilled water and 95 % ethanol at 28 °C and stirred. Solubility was qualitatively determined by visual assessment.

**Iodine test:** *N. mitis* starch (1 g) was boiled with 15 mL of water, allowed to cool and then 3 drops of 0.1 N iodine solution was added to 1

mL starch mucilage and the color change recorded [26].

**Acidity test:** 10 g of NMS was dispersed in ethanol (70 %v/v) and 2 drops of phenolphthalein solution was added as indicator. The mixture was shaken, filtered and the filtrate (50 mL) was titrated with 0.1 N NaOH, the volume of NaOH required to cause a color change was noted and recorded. The average of triplicate determinations was calculated.

**Hydration capacity:** The method of Kornblum and Stoopak [27] was employed, 1g of NMS was mixed with 10 mL distilled water in a stoppered centrifuge tube, shaken intermittently for 10 min and then allowed to stand for another 10 min. The suspension was then centrifuged at 1000 rpm for 10 min, the supernatant was discarded, weight of the starch after centrifugation was noted and the hydration capacity was calculated using the equation below

$$H (\%) = \frac{\text{weight of dry starch}}{\text{weight of starch sediment}} \times 100 \dots (1)$$

**Swelling capacity:** A 1 % w/v NMS slurry in distilled water was heated on a water bath at 50 °C for 30 min while stirring intermittently after which it was centrifuged at 1500 rpm for 20 min. The supernatant was discarded and the weight of wet starch was recorded. The swelling capacity was calculated as;

$$S (\%) = \frac{\text{weight of wet starch}}{\text{initial weight of dry starch}} \times 100 \dots (2)$$

**Moisture content:** 3g of NMS was placed in the oven at 105 °C for 3 h and weighed. Triplicate determinations were made, the mean was calculated then the ratio of the final weight to the initial weight was expressed as a percentage.

**Amylose/amylopectin content:** The method of Onah and Bristol [28] was adopted. NMS (2 g) was dispersed in 50 mL boiling distilled water, the solvent mixture of butanol and water (1:9) was added to the boiling suspension and allowed to cool in a cold water bath. The resultant supernatant was decanted and the precipitate formed was washed repeatedly with the solvent



mix, dried in the oven at 70 °C and then weighed. Triplicate determinations were made and the average weight was noted as amount of amylose. The decanted supernatant was precipitated with excess methanol after which the precipitate was dried and the weight recorded as amount of amylopectin. The ratio of amylose to amylopectin content was then determined.

**Angle of repose:** The funnel method was used; the height (h) and radius (r) of the starch heap were measured and the angle of repose was calculated using the formula below;

$$A = \tan^{-1} \frac{h}{r} \dots \dots \dots (3)$$

**Flow rate:** *N. mitis* starch (50 g) was poured into the funnel of the Erweka flow tester and the time taken for the powder to flow through the orifice was noted and the average of three determinations was used to compute the flow rate

**Bulk and tapped densities:** The volume occupied by 20 g of NMS in a graduated measuring cylinder was noted and the bulk density (g/mL) was calculated as a ratio of the starch weight to its volume. Similarly the tapped density (g/mL) was computed as the ratio of starch weight to the volume it occupied after 50 taps.

**Carr's index and Hausner ratio:** The Carr's index (CI %) was computed using the formula below;

$$\frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100 \dots (4)$$

Hausner ratio was calculated as ratio between the tapped and bulk densities.

**Determination of true density:** The liquid displacement method was adopted. The pycnometer bottle was cleaned, filled with xylene (displacement fluid) and the note was noted (a), the bottle was emptied and cleaned then NMS (2 g) was put into it. The bottle was filled with xylene, stirred with a glass rod, allowed to stand for the bubbles to be released and weighed again (b). The true density was then computed as;

$$\frac{P_w}{(a + P_w) - b} \times SG \dots \dots \dots (5)$$

Where Pw = weight of powder  
 a = weight of pycnometer bottle and fluid  
 b = weight of pycnometer, fluid and powder  
 SG = specific gravity of xylene (0.855)

**Preparation of granules**

Paracetamol granules were prepared by the massing and screening method of wet granulation. Quantities of paracetamol powder (25 g) and the starches (7.5, 10 and 12.5 %w/w) as indicated in Table 1 were geometrically mixed in a porcelain mortar, massed together with 7.5 % w/v binder mucilage which was added to the powder mix in aliquots. The damp mass was passed through a sieve of 7 mm mesh size, allowed to dry in the oven at 60 °C for 1 h and then screened again before it was dried in the oven and packaged for further analysis.

**Table 1: Formula for preparing 50 tablets of paracetamol**

Ingredients/Batches	N1	N2	N3	M1	M2	M3	F1	F2	F3	F4	F5	F6
Paracetamol (g)	25	25	25	25	25	25	25	25	25	25	25	25
NMS (% w/v)	7.5	10	12.5	-	-	-	10	10	10	-	-	-
MS (% w/v)	-	-	-	7.5	10	12.5	-	-	-	10	10	10

**Key:**

N1, N2 and N3 - tablets containing 7.5, 10 and 12.5 % *Neorautanenia mitis* starch respectively and compressed at 0.5 MT



M1, M2 and M3 - batches containing 7.5, 10 and 12.5 % Maize starch BP respectively and compressed at 0.5 MT

F1, F2 and F3 - batches containing 10 % *Neorautanenia mitis* starch and compressed at 0.75, 1.00 and 1.25 MT respectively

F4, F5 and F6 - batches containing 10 % Maize starch BP and compressed at 0.75, 1.00 and 1.25 MT respectively

### Granule properties

The flow properties of the granules were evaluated using flow rate, angle of repose, bulk and tapped densities, Carr's index and Hausner ratio as earlier described.

### Compression of granules

The granules were compressed at 0.5, 0.75, 1.00 and 1.25 MT on a Carver hydraulic hand press (Carver, USA) using the 10.5 mm punch and die set. The surface of the punches and die were lightly lubricated with talc/magnesium stearate using a brush before filling with granules. After ejection of the tablets, they were stored over silica gel for 24 h to allow for elastic recovery.

### Tablet evaluation

**Uniformity of weight:** Twenty (20) randomly selected tablets were weighed and the average weight was calculated.

**Tablet hardness:** Five (5) tablets were randomly selected and the hardness ( $\text{Kg/cm}^3$ ) was determined by the Monsanto hardness tester and the mean was calculated.

**Friability test:** Ten (10) tablets were collectively weighed and transferred into the Roche frabilator to rotate at 25 rpm for 4 min after

which the tablets were re-weighed. Friability (%) was expressed as;

$$F (\%) = \frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} \times 100 \dots (6)$$

**Disintegration test:** Six tablets were placed in each of the disintegration tester compartment containing distilled water at  $37 \pm 0.5$  °C. The time taken for all the particles of the tablets to pass through the wire mesh of the compartment was recorded and the average was calculated.

**Dissolution test:** The dissolution rate of the tablets was determined using the dissolution apparatus; the tablet was placed in the cylindrical stainless steel basket and lowered into the glass vessel containing 900 mL of 0.1M HCl thermostated at  $37.0 \pm 0.5$  °C. The apparatus was set to rotate at 100 rpm for 60 min; aliquots of 5mL were withdrawn from the vessel at 5, 10, 15, 20, 30, 40, 50 and 60 min and replaced with the same volume of fresh medium. The absorbance of the samples was obtained using a UV spectrophotometer (Shimadzu UV240A) at 243 nm and the drug concentration determined using the calibration curve.

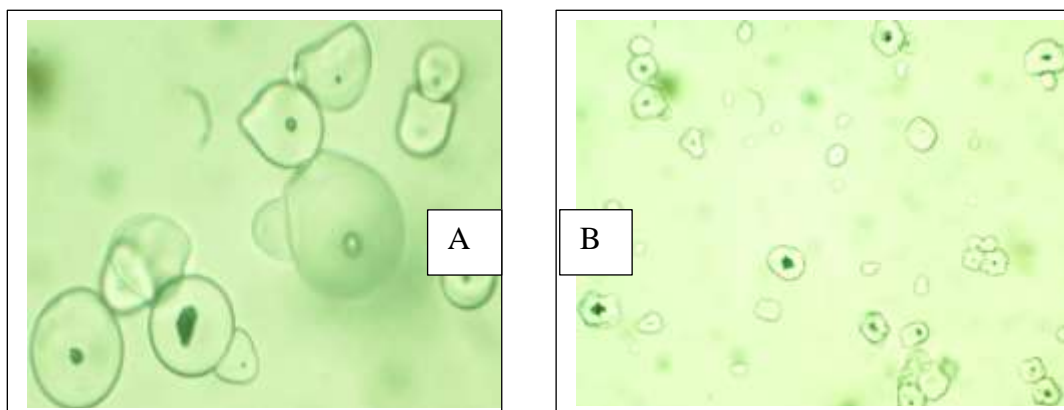
**RESULTS AND DISCUSSION**

**Table 2: Physicochemical properties of *Neorautanenia mitis* starch (NMS)**

Parameter	NMS	Maize Starch BP (MS)
Solubility- water	Insoluble	Insoluble
- 95 % ethanol	Insoluble	Insoluble
Iodine test	Blue-black color	Blue-black color
Acidity test (mL)	1.65	1.56
pH	7.3	7.1
Hydration capacity	1.9	1.2
Swelling power (%)	27	23
Moisture content (%)	11.46	9.26
Microscopic properties	Hilum; absent Striation; absent Size; 20 - 60 µm Shape; spherical	Hilum; triangular, central Striation; absent Size; 10 - 30 µm Shape; polyhedral
Amylose ratio (%)	19	20.5
Amylopectin ratio (%)	81	79.5

Table 2 shows the physicochemical properties of NMS compared with those of maize starch BP (MS). Like MS, *Neorautanenia mitis* starch was insoluble in water and alcohol while it tested positive to the iodine test for starch. The test also had higher porosity (Table 3). High porosity has been linked to fast disintegration [29], as

starch passed the acidity test [26] and its pH of 7.3 was similar to that of MS. The NMS granules were spherical in shape with a size range of 20-60 µm which is larger than that of maize starch BP (10 -30 µm) as in Figure 1; they such, NMS as disintegrant would be expected to effect tablet break-up faster than MS.



**Figure 1: Photomicrographs of *Neorautanenia mitis* starch (A) and Maize starch (B) grains**



The amylose content of NMS was lower than that of maize starch BP (Table 2). Swelling is dependent on the ratio of amylose to amylopectin content because high amylose content causes initial hindrance to particle swelling which could progress rapidly once the amylose content has been leached [30, 31]. NMS would therefore be expected to swell better in

comparison to MS when immersed in water. As expected, the hydration and swelling capacities of NMS were higher than for maize starch (Table 2). Polysaccharides imbibe water (swell) once exposed to an aqueous medium with the degree of such swelling being an indication of the extent to which the polysaccharide can imbibe and retain water.

**Table 3: Flow Properties of NMS and MS**

Parameters	NMS	MS
Flow rate (g/sec)	0.61	0.56
Angle of repose (bulk density (g/mL)	38.60	40.30
Bulk density (g/mL)	0.58	0.46
Tapped density (g/mL)	0.72	0.60
Carr's index (%)	20.54	22.96
Hausner ratio	1.26	1.30
True density	1.41	1.43
Porosity (%)	40.85	32.02

The flow rate, angle of repose, bulk and tapped densities evaluated shows that NMS has better flow than MS (Table 3). Hausner ratio (HR) is an indication of the degree of densification of a powdered material; this index assesses the cohesive nature of the material. Compressibility index (CI) on the other hand, assesses the ability of a material to deform under pressure [32].

Materials with  $HR \leq 1.11$  and  $CI \leq 10$  are reflective of materials with lower cohesiveness and excellent flow, those with  $HR 1.12 - 1.2$  and  $CI 16 - 20$  % indicate moderate flow while  $HR$  of  $1.26 - 1.34$  and  $CI 21 - 25$  are considered fair flowing [33, 34, 35]. The results (Table 3) show that NMS has moderate flow.

**Table 4: Flow properties of Paracetamol granules**

Ingredients/Batches	N1	N2	N3	M1	M2	M3	F1	F2	F3	F4	F5	F6
Flow rate (g/s)	10	10	10	10	10	10	10	10	10	10	10	10
Angle of repose (°)	29.90	29.59	29.42	28.95	27.69	28.22	31.68	28.70	27.41	27.70	27.69	28.81
Bulk density (g/mL)	0.35	0.38	0.36	0.34	0.35	0.38	0.38	0.38	0.38	0.35	0.34	0.36
Tapped density (g/mL)	0.36	0.39	0.41	0.40	0.42	0.38	0.39	0.37	0.40	0.42	0.42	0.41
Carr's index (%)	6.77	10.51	5.78	12.23	7.70	7.15	10.5	6.23	10.73	7.7	7.7	7.5
Hausner ratio	1.07	1.12	1.06	1.14	1.08	1.07	1.12	1.07	1.12	1.08	1.08	1.08

Although all the granules had good flow properties irrespective of the type of starch used as disintegrant, those containing NMS were

found to have lower compressibility index across the concentrations used than those containing MS. This shows that these granules



would produce good compacts when pressure is applied during tablet compression.

The results of tablet evaluation are presented in Table 4. The tablets had average weights between 479 and 490 mg which were within the official specification [26]. Disintegrant type did not have a significant effect on the hardness of tablets produced as all the tablets compressed at 0.5 MT (N1 - N3 and M1 - M3) had low values between 2 and 2.3 Kgcm<sup>3</sup> irrespective of the starch used (Table 5). However, significantly higher hardness (3 - 10 Kgcm<sup>-3</sup>) was observed with increasing compression pressure (0.75, 1.00 and 1.25 MT). High compression pressures are

known to force particles into available voids thus increasing the area of contact between particles; this brings about particle densification which in turn causes particle-particle interaction and consequent formation of strong bonds leading to higher hardness [36]. There was no significant difference in the hardness of tablets containing NMS (F1, F2 and F3) and those containing MS (F3, F4 and F5) with increasing compression pressure. A hardness of 4 - 8 Kgcm<sup>-3</sup> is considered satisfactory for uncoated tablets [37] although this value is largely dependent on the type and concentration of additives incorporated into the tablet formulation.

**Table 5: Effect of disintegrant concentration on physical properties Paracetamol tablets**

Batches/ Ingredients	Mean weight (mg)	Hardness (Kg/cm)	Friability (%)	Disintegration time (sec)	Dissolution efficiency	
					T <sub>50</sub> (min)	T <sub>75</sub>
N1	479.3±0.01	2	4.25	1.07	7.5	13
N2	481.9±0.02	2.2	6.87	0.87	7.5	10
N3	482.0±0.01	2.2	9.26	0.69	9	NA
M1	489.8 ± 0.01	2.2	7.38	1.20	8	12.5
M2	485.0 ± 0.01	2.2	8.10	0.96	7.5	9
M3	484.1 ± 0.01	2.3	8.51	0.88	7.5	10
F1	481.9 ± 0.02	3.8	0.8	3.78	10	NA
F2	481.9 ± 0.02	4.3	0.61	13.82	NA	NA
F3	481.9 ± 0.02	10.5	0.40	42.52	NA	NA
F4	481.9 ± 0.02	3.6	0.7	4.45	9.5	NA
F5	481.9 ± 0.02	4.3	0.61	14.87	NA	NA
F6	481.9 ± 0.02	10	0.42	46.62	NA	NA

Key: NA = not attained

The friability of tablets compressed at 0.5 MT (N1, N2, N3, M1, M2 and M3) was found to be between 4 and 9 % which is well above the official limit of 1 % [25]. This can be attributed to the low hardness values (Table 5) since friability is inversely related to hardness. Increasing the concentration of both starches (NMS and MS) as disintegrant at a compression pressure of 0.5 MT resulted in tablets with high friability because the tablets produced had low mechanical strength. Increasing the compression

pressure significantly decreased friability due to formation of more solid bonds between the particles which would increase tablet resistance to shock and abrasion [38]. There was no difference in the friability of tablets containing NMS (F1, F2 and F3) and those containing maize starch (F4, F5 and F6).

Increasing the concentration of disintegrant in formulations compressed at 0.5 MT (N1 - N3 and M1 - M3) decreased tablet disintegration time because of consequent increase in swelling power in the presence of more starch particles. This is similar to earlier reports by Nattapuluwa

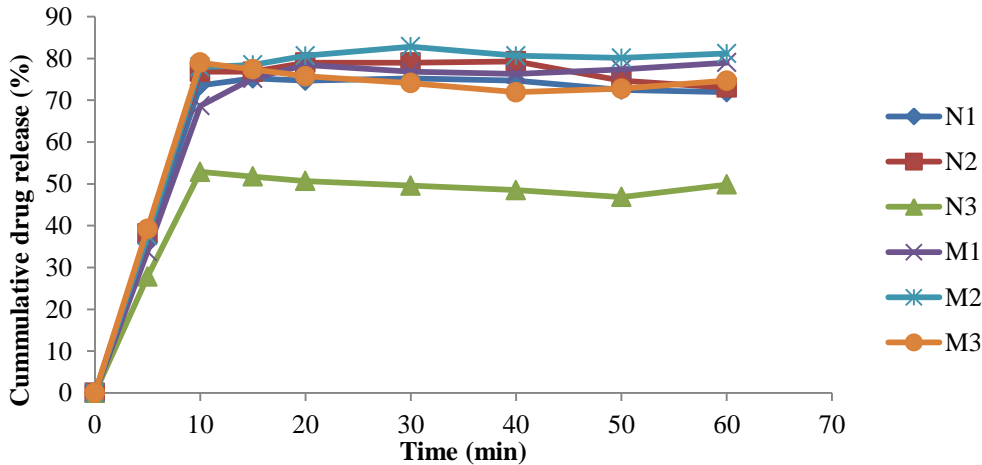


*et al* [39]. However, disintegration time was found to increase with increase in compression pressure in formulations F1 – F6 due to higher hardness which would have resulted in increased resistance to the penetration of disintegration medium thus prolonging the time for tablet break-up.

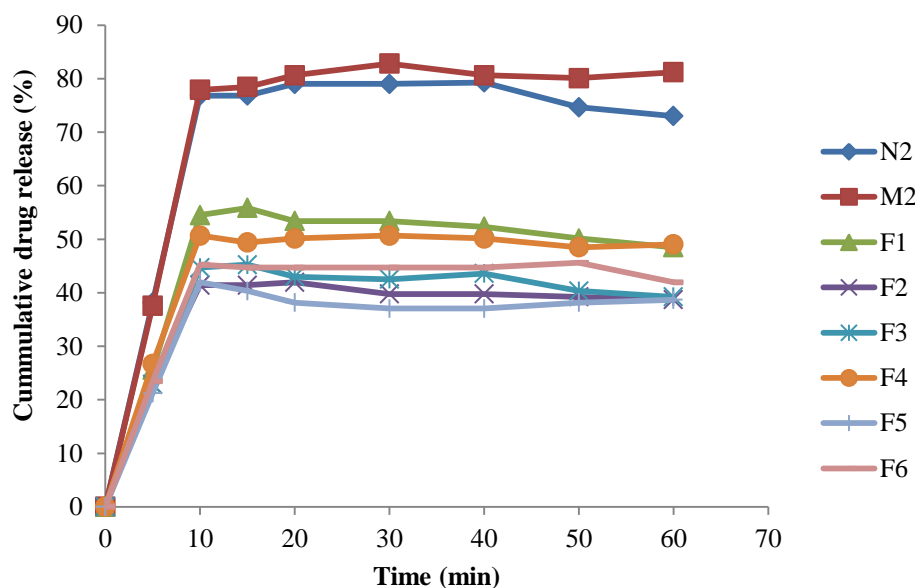
All the tablet formulations except those compressed at 1.25 MT (F3 and F6 respectively) met the official specification for disintegration of < 15 min for uncoated tablets [26]. Formulation F3 (10 % NMS compressed at 1.25 MT) had a shorter disintegration time than formulation F6 (10 % MS compressed at 1.25 MT). This could be due to the higher swelling and hydration capacities of NMS (Table 2); it could also be related to the lower amylose content of NMS [40].

Dissolution efficiency ( $T_{50}$  and  $T_{75}$ ) which indicates the time taken for 50 and 75 % of the drug to go into solution was similar for formulations containing NMS and MS compressed at 0.5 MT (Table 6).

None of the tablets compressed at pressures higher than 0.5 MT released up to 75 % of the drug at 60 mins irrespective of the starch used. This shows a direct correlation between hardness, disintegration time and dissolution rate since increasing the compression pressure ultimately led to lower dissolution rates. The time taken for 75 % of the drug to be released ( $t_{75}$ ) increased with increase in disintegrant concentration (Table 5); however, formulations N1 – N3 (which contained NMS) had higher  $T_{75}$  values than those containing MS (M1 –M3). Increasing the compression pressure decreased the rate of drug release (Figure 3). Although some studies have shown that compression pressure does not influence the rate of drug release [41, 42], the results in this study which agrees with the reports of some other workers [43, 44] shows that it plays a role.



**Figure 2: Dissolution profile of paracetamol tablets containing NMS and MS**



**Figure 3: Dissolution profile of paracetamol tablets formulated at different compression pressures**

### Conclusion

This study has highlighted the potential of an underutilized tuber as a renewable source of starch. *Neorautanenia mitis* starch has similar physicochemical properties and comparable disintegrant properties to maize starch suggesting its suitability as a substitute for maize starch BP as a tablet disintegrant.

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