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EVALUATION OF *BORASSUS AETHIOPUM* STARCH AS A BINDER IN CHLOROQUINE TABLET FORMULATIONS

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ABSTRACT

This study was made to evaluate the binding property of Borassus aethiopum starch (BAS). The starch was extracted by blending the peeled, boiled and cooled tubers of the plant. Distilled water was added and the starch was recovered using a white calico cloth. Chloroquine tablets were formulated with BAS and maize starch B.P (MS) at binder concentrations of 2.5, 5.0 and 7.5 % w/v. The granules were evaluated for: loss on drying, angle of repose, flow rate, Carr's index and Hausner's ratio; and the tablets were evaluated for: weight uniformity, thickness, diameter, crushing strength, friability, disintegration time and dissolution rate. All the binder concentrations formed granules with good flow. The crushing strength, friability and disintegration time of tablets containing BAS and MS were comparable at all binder concentrations with MS having slightly better dissolution rate. As a binder, Borassus aethiopum starch can be reserved as a substitute for maize starch B.P.

Keywords:- *binding property, Borassus aethiopum, starch.*

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INTRODUCTION

Binders are agents added to powdered materials to impart cohesive qualities. They impart cohesiveness to the tablet formulation in order to improve the flow qualities by the formation of granules of desired hardness and size as well as ensuring that the tablet remains intact after compression [1]. Binders can be added to powders in three different ways. It can be added as dry powder to other ingredients before wet agglomeration [2]. It can also be added as binder solution to the powdered materials [3]. Alternatively, it can be mixed as powder with other ingredients followed by direct compression [4].

Starches, natural gums, gelatin, sugar solutions, modified, natural and synthetic polymers have been employed as binders with considerable success [5]. Many starches obtained from different food crops have shown sufficient potentials as binders in tablet formations [6]. Maize and potato starches have been in common use and recently

cassava starch appeared in British Pharmacopoeia as an official starch for use as binder [5]. Wheat and rice have also been shown to possess good binding property and hence suitable for pharmaceutical use [3]. Also, according to Ibezim *et al.* [5], ginger and gelatin showed comparative effectiveness as binders in paracetamol tablet formulations.

Borassus aethiopum (Family: *Palmae*) is an unbranched palm growing up to 20 m tall, characterized by a crown up to 8 m wide. The bark is pale grey and the leaves are very large, fan-shaped and bluish-green in colour. The tuber is a large underground fruit containing three woody kernels [7]. It gives a starch yield of 6.25 % w/w. Physicochemical characterization of the starch showed that it has hydration capacity of 2.92, swelling capacity of 2.75 and moisture sorption capacity of 24.50 % w/w. It also has better flow properties compared to maize starch B.P [8] .

With increasing search for starches for use in pharmaceutical industries, this work was aimed at evaluating the binding properties of starch obtained from the tubers of the African fan palm, *Borassus aethiopum* in comparison with maize starch B.P. in chloroquine tablet formulations.

MATERIALS AND METHOD

Materials

Borassus aethiopum tubers obtained from African fan palm grown in Zaria town of Kaduna State, Nigeria was used as the starch source. Maize starch B.P, magnesium stearate and talc were all obtained from BDH chemicals, Poole - England; while chloroquine phosphate powder was obtained from May and Baker, Lagos - Nigeria.

Collection and identification of *Borassus aethiopum* tuber

Borassus aethiopum tuber was obtained from African fan palm grown at Shika, Zaria town of Kaduna State, Nigeria. It was collected in mid - October. The plant material was identified, authenticated and assigned a voucher number 3081 by the taxonomist in the herbarium section of the Department of Biological Sciences, Ahmadu Bello University, Zaria - Nigeria.

Extraction of starch

The tubers were peeled to remove the unwanted parts. The peeled tubers weighing 8 kg were boiled for 2 h, allowed to cool and the kernels were removed. Size reduction was carried out by milling using a blender (Mouline, type 242, France). A slurry of the starch was made by adding 16 L of distilled water and sieving was carried out using a calico cloth. The starch suspension was allowed to settle for 24 h. The supernatant layer was decanted and the upper brown layer of the sediment was scrapped off leaving the lower off-white layer which was dried at 40 ^{O}C for 1 h in an oven (BS size 3, Philip Harris Ltd., England). The dried starch was pulverized using a blender (Mouline, type 242, France) and then stored in airtight container [8].

Preparation of granules

Wet granulation method was utilized for the tablet production using the tablet formula in Table 1. Calculation was made for 100 tablets for each of the six batches. In each case, accurately weighed quantities of chloroquine phosphate and the intragranular disintegrant were mixed in a mortar and the binder mucilage added to obtain a damp coherent mass. The volume of the mucilage used was noted in order to ascertain the quantity of the binder used. The damp mass was sieved with 1.7 mm sieve and then dried at 50 ^{0}C for 1 h in an oven (BS size 3, Philip Harris Ltd., England). The dried granular mass was passed through a 1.6 mm sieve to obtain uniform-sized granules.

Evaluation of granules

The dried granules were subjected to the following evaluations:

Determination of loss on drying: Five gram sample of granules was heated in an oven (BS size 3, Philip Harris Ltd., England) at 105 ^{0}C and examined every h until a constant weight was obtained. The

percentage loss on drying was calculated relative to the initial weight of granules.

Determination of angle of repose : Twenty gram sample of granules was poured inside a funnel of orifice diameter 0.75 cm clamped at height 10 cm. It was then allowed to flow freely. The angle of repose θ was calculated using the equation :

$$\theta = \text{Tan}^{-1}(2h/D) \quad \text{.....(1)}$$

where h = height of heap and D is the diameter. It was repeated thrice and the average was calculated.

Determination of flow rate : Twenty gram sample of granules was placed in a flow rate meter. The time of flow was determined with the aid of a stop clock and the flow rate was calculated.

Determination of bulk and tapped densities *:* For the determination of bulk and tapped densities, 10 g of granules was placed in a 50 ml measuring cylinder and the bulk volume was noted. After 200 taps (raising to height of 15 cm above the table surface), the volume was noted again. The bulk density (B.D) and tapped density (T.D) were calculated as:

$$B.D = \frac{Weight}{Bulk\ volume} \quad \text{.....(2)}$$

$$T.D = \frac{Weight}{Tapped\ volume} \quad \text{.....(3)}$$

Determination of Carr's index and Hausner's ratio*:* The Carr's index (C.I) and Hausner's ratio (H.R) were calculated as:-

$$C.I = \frac{T.D - B.D}{T.D} X\ 100\ \% \quad \text{..... (4)}$$

$$H.R = \frac{T.D}{B.D} \quad \text{..... (5)}$$

Compression of granules

The different batches of granules were mixed with the accurately weighed extragranular disintegrant, magnesium stearate and talc and then compressed to tablet using a single punch tabletting machine (AR 400, Erweka Apparatebau, Germany) at compaction force of 55 KN.

Evaluation of tablets

A 24-h period was allowed for all the batches of tablet produced to undergo stress relaxation before subjecting them to quality control tests. The tests carried out include:

Uniformity of weight: Twenty tablets were weighed individually from each batch using analytical balance (WT Ltd. Birmingham U.K.). The mean weight was computed as total weight divided by 20. The standard deviation of the mean was calculated for the results obtained.

Thickness and diameter measurements*:* The thickness and diameter of 5 tablets per batch were measured using electronic caliper (Z540-1, U.S.A.). The mean diameter and mean thickness were subsequently calculated.

Crushing strength of tablets*:* The crushing strength of five tablets selected at random from each batch was determined using Monsanto hardness tester (Stokes Div. Pennwalt). The load was gradually increased until the tablet just fractured. The value of the load gave a measure of the crushing strength.

Friability test*:* Ten tablets were dusted, weighed together and then subjected to abrasion test in Roche frabilator operated at 25 rpm for 4 min. The tablets were then dusted properly and weighed again collectively. The difference in weight was determined and friability value was calculated.

Disintegration time studies*:* The disintegration time of the produced tablets was determined using disintegration tester (model ZT3, Erweka Apparatebau, GMBH Germany). Distilled water thermostatically maintained at 37 ± 0.5 ^{0}C was used as the disintegration medium. Six tablets were placed in the tubes of which lower end was fitted with a gauze disc made of rust-proof wire. The disintegration apparatus was calibrated to operate at thirty cycles per min. The time for each of the six tablets to disintegrate and pass through the mesh was determined using a stop clock. The mean disintegration time was subsequently calculated.

Dissolution test*:* The dissolution test was carried out on a tablet each from the batches containing 7.5 % w/v binder concentration using B.P method [9]. One L of 0.1 M hydrochloric acid thermostatically maintained at 37.0 ± 0.5 ^{0}C was the medium in the dissolution rate apparatus (Erweka Apparatebau, Germany). The tablet was placed in the dry basket and the apparatus was set to a rotational speed of 100 rpm. A 10 ml sample was taken out at 10 min interval with subsequent replacement with equal volume of 0.1 M HCl solution. Sample withdrawn was filtered and 1 ml of the filtrate was diluted to 10 ml. The absorbance of the resulting solution was taken at the maximum wavelength of 257 nm. A graph of percentage drug dissolved was plotted against time.

Data analysis

Statistical analysis was carried out to compare the properties of tablets containing *Borassus aethiopum* starch with those containing maize starch B.P using student's t – test. At 95 % confidence interval, *p* values less than 0.05 were considered significant.

RESULTS AND DISCUSSION

The physical properties of granules containing different binder concentrations are shown in Table 2. The binder concentration had no significant effect on moisture loss.

There was no significant difference in the angle of repose of the different granules. Similarly, there was no significant difference in their flow rate. The angle of repose which ranged from 31.00 to 32.06 corresponds to passable flow. A passable flow is one that can be improved by a glidant [10]. This will ensure good die-filling for the production of tablets of uniform weight.

The Carr's index (compressibility index) and Hausner's ratio express the difference between the bulk and tapped densities. According to Staniforth and Aulton [11], the lower the compressibility index, the better is the predicted flow of the granules. The Carr's index for all the batches indicates excellent flow. Also, the values of Hausner's ratio for all the granules correspond to excellent flow [11]. However, the two indices showed that granules containing BAS had better flow compared to those containing MS. All the binder concentrations produced granules with acceptable flow properties for tablet production.

The properties of tablets containing different binder concentrations are shown in Table 3.

The weight uniformity test showed that all the tablets had percentage deviation of not more than 5 %. This conforms to B.P specification [9]. There was no specific trend in the tablets' thickness and diameter. This could be due to inconsistent density of granules, inconsistent pressure applied during compression and/or non-uniform speed of compression [12].

Apart from the 2.5 % w/v binder concentration, maize starch B.P produced tablets with higher crushing strength compared to *Borassus aethiopum* starch. All the batches gave crushing strength of 6-8 kgf which is within the acceptable values [1]. The crushing strength generally increased with increase in binder concentration. As the concentration of binder increases, there is increase in plastic deformation leading to formation of more solid bonds with increase tablet strength [13].

The friability generally decreased with increase in binder concentration. The 2.5 and 5.0 % w/v binder concentrations produced tablets that failed friability test while 7.5 % w/v binder concentration produced tablets that passed the test for both maize starch B.P and *Borassus aethiopum* starch. As the binder concentration increased, there was formation of more solid bonds which conferred resistance to tablet fracture and abrasion [6].

The disintegration time increased significantly (P □ 0.05) with increase in binder concentration for both binders. As the binder concentration

increased, harder tablets were formed which became difficult to be penetrated by the disintegration medium [1]. All the tablets passed the B.P specification of DT which is 15 min maximum for uncoated tablets [9].

The crushing strength/friability index (CS-FR) is a better tool for measuring mechanical strength compared to either crushing strength or friability alone [14]. The value increased with increase in binder concentration for both starches. The higher the index, the higher was the mechanical strength of the tablet.

The crushing strength/friability/disintegration time index (CS–FR/DT) is a better tool for measuring tablet quality compared to CS–FR as it takes into consideration both the mechanical and release properties [15]. The value generally increased with increase in binder concentration; with maize starch B.P giving slightly higher values at all binder concentrations.

Batches containing 7.5 % w/v binder concentration were used for dissolution test because they were the only batches that passed all the other tests. The dissolution profile of tablets containing 7.5 % w/v binder concentration is as illustrated in Figure 1.

At $t_{45\ min}$, 77 % drug release was obtained for the batch containing maize starch B.P while 71 % was obtained for the batch containing *Borassus aethiopum* starch. According to B.P specification [9], a minimum of 70 % drug release must be obtained in 45 min. Therefore, both batches passed the test.

CONCLUSION

The *Borassus aethiopum* starch and maize starch B.P have comparable binding effects. Therefore, as a binder, *Borassus aethiopum* starch can be reserved as a substitute for maize starch B.P.

Table 1. Tablet formula for chloroquine phosphate tablets

Ingredient	**Qty/tablet (mg)**
Chloroquine phosphate (active drug)	250
Maize starch B.P (intragranular disintegrant)	25
*Binder	q.s
Talc (glidant)	5.5
Maize starch B.P (extragranular disintegrant)	17.5
Magnesium stearate (lubricant)	0.5

Binder *

BAS – *Borassus aethiopum* starch (2.5, 5.0, 7.5) % w/v.

MS – Maize starch B.P (2.5, 5.0, 7.5) % w/v.

Table 2. The physical properties of granules containing different binder concentrations

Properties	***Borassus aethiopum* Starch**			**Maize starch B.P**		
Binder concentration (% w/v)	2.50	5.00	7.50	2.50	5.00	7.50
Loss on drying (%)	5.00	4.00	5.00	4.00	4.00	5.00
Angle of repose (^{O})	31.10	31.00	31.18	31.50	32.06	31.86
Flow rate (g/sec)	2.29	2.37	2.50	2.47	2.22	2.30
Bulk density (g/cm^3)	0.49	0.50	0.51	0.49	0.47	0.47
Tapped density (g/cm^3)	0.52	0.53	0.56	0.53	0.54	0.54
Hausner's ratio	1.06	1.06	1.10	1.08	1.15	1.15
Carr's index (%)	5.77	5.66	8.93	7.55	12.96	12.96

Table 3. Properties of tablets containing different binder concentrations

Properties	*Borassus aethiopum* Starch			Maize starch B.P		
Binder concentration (%w/v)	2.50	5.00	7.50	2.50	5.00	7.50
Mean weight ± S.D (mg)	302 (10.33)	306 (11.74)	304 (8.43)	300 (6.67)	307 (8.23)	307 (10.59)
Thickness (mg)	3.02	2.91	2.83	2.51	2.83	2.85
Diameter (mg)	10.66	10.68	10.64	10.67	10.65	10.64
Crushing strength (kgf)	6.64	6.70	7.60	6.46	7.90	8.00
Friability (%)	1.28	1.28	0.97	1.31	1.28	0.66
Disintegration time (min)	1.99	2.01	2.73	1.75	2.10	3.23
CS-FR	5.19	5.24	7.83	4.93	6.17	12.12
CS-FR/DT	2.61	2.61	2.87	2.82	2.94	3.75
t_{45min}			71.00			77.00

Key
CS-FR = Crushing strength/friability index
CS-FR/DT = Crushing strength/friability/disintegration time index
t_{45min} = Drug release in 45 min

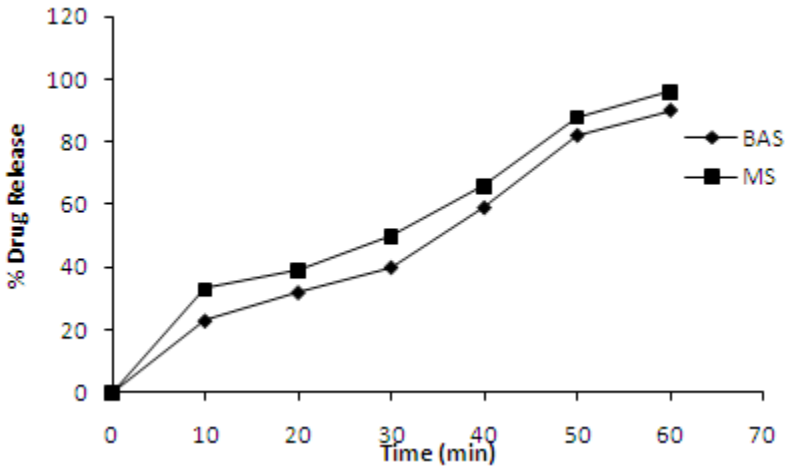

Figure 1 Dissolution profile of chloroquine tablets containing 7.5 % w/v binder concentration.

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