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EVALUATION OF THE DISINTEGRANT PROPERTIES OF *DIGITALIS EXILIS* (ACHA) STARCH IN METRONIDAZOLE TABLET FORMULATION

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ABSTRACT

Background: *Digitalis exilis* (acha) is one of the ancient cereals that are indigenous to West Africa. The species is the most important of a diverse group of wild and domesticated Digitaria species that are found in Nigeria where it has been harvested for decades. It's nutritional value and the critical roles played in food security were unprecedented. However, despite its exceptional dietary value, *Digitalis exilis* has received limited research and development.

Aim: Therefore, this work aimed to study the suitability of acha starch as a disintegrant in metronidazole tablet formulation.

Methods: Acha starch was extracted from the grains of *digitalis exilis*and used as disintegrant in metronidazole tablets formulation at 5% and 10% concentration. The physicochemical properties of the acha starch and the tablet properties of the tablets produced were analyzed.

Results: The result showed that Acha has a percentage starch yield of 53%. The starch was non-acidic, satisfactory moisture content (≥20%), excellent flow property and compatible with the drug. Furthermore, Acha starch concentration at 5% and 10% demonstrated good friability, average weight, crushing strength, and disintegration time comparable to maize starch.

Conclusion: The study showed that acha starch can be used as a disintegration agent.

Keywords: Native acha Starch; maize starch; metronidazole; wet granulation; disintegrants

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INTRODUCTION

In 1500 BCE the earliest oral solid dosage form, known as pills, came into existence. In 1844 the first compressed tablets were believed to be made and those tablets produced were very hard without any reference to their solubility or disintegration time. Fast forward, the idea of incorporating other materials such as: disintegrants, diluents, binders, and lubricants to improve the quality of tablets formulations where developed [1].

Disintegrants are agents which facilitate the breakdown of tablets when placed in an aqueous environment, they release their active ingredient or drug for dissolution and absorption from the gastro-intestinal tract by increasing the surface area of the tablet. Several mechanisms of action that have been proposed to rationalize the action of disintegrants are porosity, capillary action, water absorption, swelling, gas release, melting, enzymatic action, heat of wetting and lysis of physicochemical bond [2, 3]. Understanding the performance of formulations containing poorly soluble, lipophilic compounds is crucial, considering that approximately 40% of drugs available in the market and nearly 90 % of drug candidates in the development pipelines are poorly soluble [4]. However, tablet hydrophobicity is known to have a negative effect on disintegration due to poor wettability.

With the advancement of technology and realisation of solid-state pharmaceutics, the art of tablet formulation has been evolving and numerous researches have been conducted in identifying cheaper and efficient disintegrating agent. Starches from natural plants sources have been in use as disintegrant for ages in tablet formulation with corn starch as a traditional disintegrant [5]. Starches are widely distributed in different parts of plants, constituting 50 – 65 % of dry weight of cereal seeds and as much as 80 % of dry matter of tubers. It is a polysaccharide consisting mainly of two polysaccharides known as linear amylose and branched amylopectin and has been used extensively as a filler, binder and disintegrant in tablet formulations [6]. The two structural components are responsible for its inherent properties [7]. However, the botanical sources of starch greatly influence its composition, granule arrangement in the tissues, its shapes, size and structure [8]. Hence, it is crucial to investigate other sources of starch for tableting purpose.

Acha- *Digitalis exilis*, popularly known as hungry rice or millet belongs to the family Poaceae. It is an annual small yellowish-brown seed and it is grown throughout the savannah zone of West Africa as cereal. It contains high percentage of carbohydrate up to 81% and less percentage of fat, protein and fiber (< 1 %). This is an indication of a high purity level (98.6 – 98.9 % w/w) compared to official corn starch [9]. The high content of starch in acha and its cheap cost have made them a highly sourced raw material to be used as excipients by pharmaceutical industries. Considering a study carried out on material

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and compaction properties of native and acid modified form of fonio and sweet potato starches that indicated potential usefulness of using starch as disintegrants in tablet formulation [10]. And another study carried out on the disintegrant properties of Native and modified forms of fonio and sweet potato starches showing it efficacy in comparison to corn starch [11, 12].We therefore, investigate the disintegration properties of aches starch using hydrophobic metronidazole as a model drug to exploit the potential of *Digitalis exilis* starch to be used as disintegrating agent for poorly soluble drugs in pharmaceutical industries.

MATERIALS AND METHODS

Materials

Metronidazole powder BP (May and Baker Nig. Plc), Maize starch BP (May and Baker Ltd. Dagerham –England), Talc (BDH Chemical Ltd, Poole. England), Magnesium stearate (Hopkin and Williams Ltd. Chadwell Health Essex. England), grains of acha (purchased from kasuwanmata, Sabon gari market, Zaria, Nigeria), samples were identified at the Department of Biological Sciences, Ahmadu Bello University, Zaria.

Methods

Preparation of Acha Starch

The grains were properly cleaned to remove dirt and foreign seeds. It was then washed to remove sand and dust, then air dried in a clean environment. The grains were weighed and soaked in water for 24h, it was blended and sieved using 180 µm sieve size. The blended grains were rinsed multiple times with distilled water. Three drops of 0.1 N sodium hydroxide was added to neutralize the slightly acidic nature of the starch, the NaOH solution also assisted in separating the gluten from the starch. The resultant liquid was allowed to stand and decanted. Purified water was used to further wash it and allowed to stand and decanted several times. The wet mass was then dried in an oven at 70 ^{o}C for 12 h. The dried mass was size reduced to fine powder and passed through 180µm mesh sieve and stored in airtight container. The percentage starch yield was calculated using this formula:

$$\% \text{ starch yield} = \left[\left(\frac{weight\ of\ dried\ starch}{weight\ of\ wet\ starch}\right) x\ 100\right] \quad [1]$$

Solubility

0.5 g of the starch was weighed and poured into a 100 mL conical flask; 20 mL of cold water was added. In another 100 mL conical flask, 0.5 g of the starch was poured into the flask and 10 mL of 90 % alcohol was added. Both flasks were stirred and observed for evidence of solubility.

Identification Test

A suspension of 0.5 g of acha starch in 25 mL of water was boiled and cooled, the resultant mucilage was noted. 0. 1mL of 0.005 M iodine was mixed with 2 mL of the mucilage obtained and the color reaction was noted.

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Moisture content

5 g of acha starch was weighed and dried to constant weight at a temperature of 105 ^{o}C, the percentage loss in weight was then determined and expressed as percentage moisture content.

$$\% \text{ moisture content} = \frac{initial\ weight - final\ weight}{initial\ weight} x\ 100 \quad [2]$$

Flow rate

Acha starch 50 g was weighed and allowed to flow through the orifice of Erweka flowability tester, the time taken for the whole powder to flow through the orifice was noted and the flow rate calculated.

Angle of repose

Acha starch 50 g was allowed to flow through a funnel to form a heap on a clean flat surface from a distance of 10 cm from the flat base to the tip of the funnel. The angle of repose Q was calculated from tangent of the base radius r and height h.

$$\text{Tan Q} = \frac{h}{r} \quad [3]$$

Bulk and Tapped Density

Acha starch 10 g was weighed and poured into a 50 cm^3 measuring cylinder, this was gently tapped on a flat surface for 5, 25 and 50 taps and the final volume was noted. Carr's index and Hausner's ratio was calculated using the formula below.

$$\text{Bulk density} = \frac{weight\ of\ powder}{initial\ volume} \quad [4]$$

$$\text{Tapped density} = \frac{weight\ of\ powder}{final\ volume} \quad [5]$$

$$\text{Carr's index (\%)} = \frac{(Tapped\ density - Bulk\ density)}{Tapped\ density} X\ 100 \quad [6]$$

$$\text{Hausner's ratio} = \frac{Tapped\ density}{Bulk\ density} \quad [7]$$

Preparation of Binder

Maize starch B.P 1.25 g was weighed and poured in a beaker, 15 mL of distilled water was added and the mixture was continually stirred using stirring rod until a paste was obtained. Distilled water 20 mL was boiled and poured on the maize starch paste. The solution was placed on the hot plate and stirring continued until a jelly like mucilage was obtained which was allowed to cool.

Granulation

The granules were prepared using the processes of massing and screening of wet granulation. Metronidazole powder 20 g was weighed and added in a porcelain mortar, 5 and 10 % concentration of maize starch and acha starch (disintegrants) were added in to their respective mortar followed by 300 mL of the binder to each mortar. The powders were mixed using a spatula until a consistent wet mass was obtained, the wet mass was force screened through a 1.7 mm sieve after which the granules were dried in the hot oven at 40 ^{o}C for 50 min. The dried granules were

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then passed through 1.6 mm sieve to break up large granules and then dried for 20 min. Extra granular excipients were added, maize starch 7.8 % w/w, talc 2 % w/w, and magnesium stearate 0.2 %w/w. The granules were stored in airtight container for further analysis.

Analysis of Granules

Analysis of granules were carried out to evaluate the flow properties of the granules and hence its compressibility. Flow properties such as angle of repose, flow rate, bulk and tapped density were analyzed.

Compression of granules

After analyzing the lubricated granules, they were compressed into tablets using a single punch tableting machine DIAF A/S at the rate of 30 tablets per minutes for all the formulation.

Table 1: Evaluation of Disintegration Property of 5 % and 10 % Acha and Maize Starch in Metronidazole Tableting

	Batch I	Batch II	Batch III	Batch IV
Metronidazole (g)	200	200	200	200
Disintegrants 5% Maize starch (g)	1	-	2	-
Disintegrants 5 % acha starch (g)	-	1	-	2
Binder 5 % Maize starch (mL)	300	300	300	300
Extra Granular Excipient				
Maize starch 7.8 % w/w	0.879	0.803	0.916	0.887
Talc 2 % w/w	0.225	0.206	0.235	0.227
Magnesium stearate 0.2 % w/w	0.023	0.021	0.024	0.023

Evaluation of Tablet Properties

The tablets were evaluated to assess the performance of the tablets made with acha starch as disintegrants and compared with those made with standard maize starch.

Tablet Weight Variation Test

Twenty (20) tablets were picked from each batch and weighed collectively using electric balance and the mean calculated. The tablets were also weighed individually and the percentage deviation from the mean calculated for each batc.

Hardness Test

Four (4) tablets were taken from each batch and crushed using the Monsanto tablet hardness tester to determine their crushing strength. The result was recorded in kg.

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Friability test

Ten (10) tablets were weighed and subjected to abrasion using the Roche friabilator (Erweka. TA-3R, ErwekaApparatebau, GmbH; West Germany) after which the tablets were then dusted to remove clipped off particles and weighed collectively again. The difference in weight was determined and expressed as percentage.

Disintegration Test

The disintegration of the tablets was determined using Erweka disintegration apparatus. Distilled water was used as the disintegrating medium and it was thermostatically maintained at $37^oC \pm 0.5^oC$. Six (6) tablets were each placed in the six tubes of the apparatus and the time taken for each of the tablet to disintegrate and pass through the mesh of the tube was recorded using a stop clock.

Thickness test

Four (4) tablets from each batch were used to carry out this test and their thicknesses were determined using the micrometer screw gauge (ErwekaApparatebau. G.m.b.H, West Germany).

RESULTS AND DISCUSSION

Table 2 shows the physicochemical properties of acha starch studied. The starch was insoluble in water and alcohol, it gave a dark blue colour when iodine was added and this indicated that it was starch. It had a percentage yield of 53.8 % and this is above average. Moisture content of 4.6 % which follows the official specification of ≤15 % [13, 14]. The moisture content of pharmaceutical excipients affects its microbiological stability and storage, agglomeration and flow properties [15]. Acha starch has a polygonal shape with mean particle size of 7µm.

Table 2: Physicochemical Properties of Acha Starch

Parameters	Result
Solubility – cold water	Insoluble
Solubility - 90 % alcohol	Insoluble
Iodine test	Dark black
Percentage yield (g %)	53.8
Moisture content (%)	4.6
Flow rate (g/sec)	16.5
Bulk density (g/cm^3)	0.42
Microscopic characters	Shape – polygonal Helium – present, central Striation-absent
Particle size (µm)	3.32 – 13.32 Mean – 7
Acidity test	Not acidic

Table 3 represents some tableting properties of the metronidazole tablet produced with acha starch as disintegrants. The value obtained for the average weight (217 -231) for all the batches are within the acceptable limit of the official book. The United State Pharmacopoeia (1980) states that the batch would have passed the test if no more than 10% of the samples are outside the

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percentage limit and no tablet should differ by more than twice the percentage limit [16]. This therefore implies that there was uniform filling of the die as a result of good flow characteristics of the granules of drugs made from both starches. Disintegration is the time taken for the tablet to break up into small, discrete particles to enable dissolution at the gastrointestinal tract. All the tablets produced from both batches dissolved within the stipulated standard time of ≤ 15min for uncoated tablets. The crushing strength increased with increase in the concentration of the disintegrants. The results obtained for the hardness tests are within the acceptable standard of between 4 – 8 kgF [17], 10 % concentration of maize starch BP and acha starch shows comparable and higher crushing strength than those of 5 % concentration. Friability is the measure of interparticulate cohesiveness in tablets. The results obtained for % friability is between 0.5 – 1 which is within the official limit of 1 % [18]. Thickness (mm) is measured using the micrometer screw gauge, the results obtained from tablets made acha starch correspond with that obtained from maize starch BP, thus implies that acha starch is effective as a disintegrant.

Table 3: Tablet Properties of Metronidazole Tablets Produced using Different Concentration of Maize and Acha Starch as Disintegrants

Batch	Average Weight (mg)	Disintegration Time (sec)	Friability (%)	Thickness (mm)	Hardness (kgF)
I	227	30	0.6	5.09	3.45
II	217	49	0.8	4.63	2.00
III	231	50	0.5	5.27	3.93
IV	227	49	1	4.68	3.88

Key: Batch I: 5 % Maize starch as disintegrant
Batch II: 5 % Acha starch as disintegrant
Batch III: 10 % Maize starch as disintegrant
Batch IV: 10 % Acha starch as disintegrant

CONCLUSIONS

From the parameters obtained in this study, acha starch has been found to have similar and comparable physicochemical and tableting properties tomaize starch BP. The result confirmed its suitability as disintegrant in metronidazole tablet formulations and can be use as maize starch substitute in pharmaceutical industries.

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