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Screening of A Variety of Nigerian Maize for The Production of Pharmaceutical Grade Tablet Excipient

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ABSTRACT

Aim: Maize starch is widely used in tablet production, considering the cost of importing pharmaceutical grade of corn starch, it becomes imperative to have a laboratory extract of the maize starch and compare the functionality of the extracted starch to Corn starch B. P as a pharmaceutical excipient. Also we investigated the mechanical properties and dissolution profile of tablets when corn starch is used as a binder and as a disintegrant in the same tablet formulation.

Method: Corn was extracted in the laboratory by the process of wet milling, Characterization of lab. extracted corn and Maize starch Bp powders were done, phytochemical analysis to determine the presence of starch was carried out. The both powders were used as binders and disintegrants in same formulation to formulate metronidazole tablets in 2 batches. With batch A containing lab. extracted corn powder and batch B tablets containing Maize starch B.P. Thereafter quality control tests and organoleptic tests were carried out on the 2 batches of tablets.

Result : Microscopic evaluation showed the 2 powders having the same morphology, Iodine test showed the presence of starch. Characterisation of lab. extracted maize starch and Maize starch B.P. powders gave the following results respectively: moisture content (10.52%, 8.24%), tapped density (0.659 g/ml, 0.661 g/ml), bulk density (0.432,0.449), Carr's indices (34.324,32.027),Hausner's ratio (1.524,1.471), Swelling capacity(1.214,1.167), Angle of repose (46.15°C, 45.06°C), moisture content (10.600,8.193), hydration capacity(1.880,1.677), moisture sorption capacity(17%,16%). For the lab. extracted maize starch and Maize starch B.P. powders Maize starch B.P. granules we had respectively; tapped density (0.583,0.593), bulk density (0.527,0.533), Carr's indices (9.951,9.949), Hausner's ratio (1.111,1.111), Angle of repose (36.699,36.511), Flow rate (10.857,13.650), Percentage fines (24.320,16.270). For the quality control tests of the tablets, batch A and batch B respectively; hardness (7.21KgF,8.39KgF), Friability (0.74%,0.67%), Weight uniformity(500mg,511.40mg), Disintegration time(1.19mins,2.45mins),Dissolution rate(96% in 5 mins, 94% in 5mins)

Conclusion: The lab. extracted maize starch can always be used in place of the Maize starch B.P. in tablet formulation. Also when maize starch is used in a tablet formulation, as both a binder and a disintegrant, the tablets have a good bioavailability.

KEYWORDS Maize starch, Binder, Disintegrant, Excipients

INTRODUCTION

When formulating tablets, the choice of excipients is extremely critical. It must fulfill certain requirements such as compressibility, good binding functionality, powder crystallinity, flowability and acceptable moisture content. Also, it is essential to have a well designed particle size distribution for favorable mixing conditions with drugs (Alanazi *et al*, 2008). Starch is used mainly as binders, dinsintegrants, fillers, glidants, or lubricants in the pharmaceutical industry (Owolabi *et al*, 2010). Starch constitutes the main form of carbohydrate reserve in green plants and is found especially in seeds, & underground organs. The green parts of plant exposed to sunlight contain granules of traditional starch which arise from photosynthesis (Evans; 2009). Starch is the major carbohydrate reserve in plant tubers and seed endosperm where it is found as granules. It contains mainly two types of polymer molecules; several million of highly branched amylopectin molecules (normally 70-80%) accompanied by a higher number of largely linear amylase molecules (normally 20-30%) (Alanazi *et al*, 2008). Cereal starches are the most abundant sources of starches and these are found in the grains or seeds of cereals such as maize, rice, wheat, oats, rye, barley, waxy maize, waxy rice, waxy sorghum, millets and high amylose corn. Root starches include tapioca, arrow root, canna, sweet potato, curcuma and zamia starches. Among these starches the most popular are maize, rice, wheat, and potato starches used for many official purposes. Maize or corn (Zea mays) is a plant belonging to the family of grasses (Poaceae). It is cultivated globally being one of the most important cereal crops worldwide. Maize is not only an important human nutrient, but also a basic element of animal feed and raw material for manufacture of many industrial products. The products include corn starch, maltodextrins, corn oil, corn syrup and products of fermentation and distillation industries. It is also being recently used as biofuel (biology of maize).

Many researches have been carried out on the use of corn starch as a pharmaceutical excipient in different areas e.g Alanzi *et al* 2008, Kottke et al, 1992, Ji et al, 2004 and so many others. But this research bases on extracting starch from maize in the lab and checking its functionality compared with maize starch B.P also finding out the behavior of tablets when corn starch is used both as a binder and disintegrant in same tablet formulation using metronidazole as the active pharmaceutical ingredient.

MATERIALS

Corn Starch B.P (BDH Chemicals, Poole, England), Maize. Botanical name: Zea mays.(Variety: Zea mays indendata, Dent corn-Bendel variety, Colour-White corn). Hydrous lactose (Burgoyne, India), Metronidazole (Evans Pharmaceuticals, England), Magnesium stearate, Hydrochloric acid (Sigma, Germany), Sulphurous acid (Sigma, Germany), Xylene (BDH, England), hot air oven (Ceward medical equipment England, model No LDHG-9101-ISA), Tableting Machine (Cadmag, India), Monsanto Hardness Tester (Thermonik, China), Friabulator (Erweka, Germany), Disintegration test apparatus (Chemiscience Co. Nigeria Limited), Analytical Balance (OHAUS, China), UV spectrophotometer (UV 2100 Spectrophotometer UNICO ™, China).

METHOD

Extraction of Corn Starch

Using the procedure modified from Corn Refiners Association (2006) and Evans (2009). The corn grains were cleaned, and 1kg of corn was accurately weighed and steeped in hot water containing 0.2% sulphur dioxide for 24 hours, with the liquid being occasionally changed. The corn grains were then washed repeatedly with water to remove any trace of dirt of debris that were not removed initially, after which the mass was coarsely wet milled and mixed with water. The oil rich germs (which would float) were then skimmed off. The remainders of the grains were then fine milled resulting to a pulp rich in corn starch which was then collected and screened for starch using fine sieve that were doubled in order to prevent fibres from passing through the sieve pores. During the extraction process, water was repeatedly added to the pulp in order to facilitate extraction. The mixture of starch and water obtained was allowed to stand undisturbed for about 4 hours. The brownish supernatant layer was decanted. The sediment of corn starch was then washed repeated using 0.1N hydrochloric acid so as to remove impurities such as gluten (Starch is insoluble in dilute acids whereas gluten is soluble). The mixture was allowed to settle and the supernatant decanted off. The sediment was repeatedly washed with distilled water following decantation of the supernatant and subsequent redispersion of the sediment in distilled water. The sediment was then dried in an oven at a temperature of 60°C. The extract was pulverized and passed through sieve no. 100. The yield was calculated and recorded.

Characterization of Starch Powders

To confirm that the product contained starch, the sample was tested using iodine solution. Observations were made and results recorded. The morphology of the powders was observed under the microscope and results were recorded. The following characterization was done for the processed maize starch alongside a standard, Corn starch B.P.

Moisture Content

Loss on drying was used in determining the moisture content .5g of powder sample was transferred each into a Petri dish and then dried in an oven at 105°C until a constant weight was obtained. The % moisture content was then determined using the formula below (Alanzi *et al,* 2008).

$$\%\text{moisture} = \frac{\text{weight of sample used} - \text{weight of dried sample}}{\text{weight of sample used}} \times 100 \quad \ldots\ldots\ldots 1$$

This was carried out in triplicates. Maize starch B.P was used as standard for all the tests.

Tapped density and Bulk density

This was done using 50g of accurately weighed powder sample. This was then poured through a short stemmed funnel into a 250ml graduated cylinder. The volume occupied by the sample was the bulk volume. The powders were tapped on a wooden surface for 500 times, at a height of 7 inches until no further change in volume was observed (Olayemi et al, 2008). This volume was the tapped volume. The bulk and tapped densities were computed using the formula.

$$\rho b = \frac{\text{mass of powder}}{\text{bulk volume}} \quad \ldots\ldots\ldots 2$$

$$\rho t = \frac{\text{mass of powder}}{\text{tapped volume (T500)}} \quad \ldots\ldots\ldots 3$$

Where ρ_b = Bulk density and ρ_t = Tapped density

The same procedure above was repeated for the standard.

Carr's index and Hausner's ratio

The Carr's index (CI) and Hausner's Ratio(HR) were computed from the determined bulk and tapped densities as follows (Olayemi et al, 2008) :

$$\text{Hausner's Ratio} = \frac{\textit{Tapped density}}{\textit{Bulk density}} \quad \ldots\ldots 4$$

$$\text{CI} = \frac{(\rho t - \rho b)}{\rho t} \times 100 \quad \ldots\ldots\ldots 5$$

Where ρ_b = bulk density and ρ_t =tapped density

Determination of flow rate

Flow rate was determined as described by **(** Ohwoavworhua *et al,* 2009). Fifty grams (50g) of the starch powder from each batch was placed in a funnel with orifice diameter of 1.4cm and efflux tube length of 4.5cm. The powders were allowed to flow through the funnel orifice. The time taken for the powder to flow the orifice (t) was noted and the flow rate computed as:

$$\text{Flow Rate (F.R)} = \frac{\text{weight of powder (g)}}{\text{time of flow (s)}} \quad \ldots\ldots\ldots 6$$

This was done in triplicates for each powder and the mean calculated.

Angle of Repose

Angle of repose was measured for the batches of starch powders to observe the flow properties of the processed corn starch powder in comparison with maize starch B.P. The method employed a funnel secured with its tip at a given height, above a plane paper placed on a horizontal surface. The powders were poured through the funnel until the apex of the conical pile touched the funnel. (Alanazi et al, 2008)

The angle of repose was calculated using the following formula

$$\text{Tan } \emptyset = \frac{2(\text{Height of heap})}{\text{Diametrer of the heap}} \quad \ldots\ldots\ldots 7$$

This was done in triplicates for each batch of starch powder and the mean angle of repose calculated for each batch.

Swelling Capacity

The swelling of the coconut powder was determined by the method of Iwuagwu and Okoli, (1992). The tapped volume occupied by 5g of the powder Vx was noted. The powder was then dispersed in 85ml of distilled water and the volume made up to 100ml with more water. After 24hours of standing, the volume of sediment (Vv) was estimated and the swelling capacity computed as

$$\frac{Vv}{Vx} \quad \ldots\ldots\ldots 8$$

Where Vv= volume of sediment
Vx= tapped volume of 5g of powder

Hydration Capacity

The method of Kornbloom and Stoopak (1973) was used. A 1.0g of each of the samples was placed in each of the 13ml plastic centrifuge and 10ml distilled water was then added and stopped. The content of each centrifuge tube was vigor-

ously agitated for two minutes. The mixture was allowed to stand for 10minutes and immediately centrifuged at 3000rpm for 10 minutes on a bench centrifuge. The supernatant was carefully decanted and the sediment weighed. The hydration capacity was taken as the ratio of the weight of the sediment to the dry sample weight. This procedure was carried out in triplicates for each sample.

Starch True Density
The true densities (Dt) of the starch powders were determined by the liquid displacement method using xylene as the immersion fluid (Ohwoavworhua *et al,* 2009) and computed as:

Dt
=wp/((a+wp
-b)x SG……9

Where Wp is the weight of powder, SG is specific gravity of solvent, a is weight of bottle + solvent and b is weight of bottle + solvent + powder.

Powder Porosity
This was derived from the values of bulk and tap densities when fitted into the equation below (Ohwoavworhua *et al,* 2009);

$$E = \frac{\rho b}{Dt} \times 100 \quad \ldots\ldots 10$$

Where ρ_b is the bulk density, D_t is the true density and E is the porosity.

Moisture Sorption Capacity

The method of (Ohwoavworhua *et al,* 2004) was used. Two grams (W) of the sample material were accurately weighed and evenly distributed over the surface of a tarred Petri dish. The samples were then placed in a large desiccator containing distilled water in its reservoir at room temperature 25 and weight of the sample after a 5 day period was recorded (Wg) and the amount of water absorbed (Wa) was calculated as follows;

Wa
=Wg
-W……..11

PREPARATION AND CHARACTERIZATION OF GRANULES.
The preparation of granules for characterization and subsequent compression was done using the extracted corn starch alongside with the standard. Appropriate weight of lactose, metronidazole (the active ingredient) and corn starch were individually weighed and mixed in a porcelain mortar with pestle. The binder was prepared using the extracted corn starch at a concentration of 25%w/w. The starch powder was dispersed in 45ml of distilled water and heated over a water bath until a translucent paste was formed. The paste was gradually added to the powder mass in the mortar until the formation of a damp coherent mass. The damp mass was passed through a sieve with 2mm aperture and the damp granules were dried in an oven at a temperature of 60°C for two hours. The granules were passed through a 1.0mm aperture sieve such that the ratio of 2mm to 1mm granules were approximately 80 to 20 percent due to the punch size that was to be used in tablet compression. The same procedure was repeated using Corn starch B.P as standard. As such two batches of granules were obtained. Both batches were labeled for identification and characterized using the following parameters.

Tapped Density and Bulk Density

This was done using 50g (W_p) of accurately weighted granules (Olayemi et al, 2008). This was poured through a short stemmed glass funnel into a 100ml graduated cylinder. The volume occupied by the sample was the bulk volume. The powders were tapped on a wooden surface for 500 times, at a height of 7 inches until no further change in volume was observed. This volume was the tap volume. The bulk and tap density was computed using the formula;

$$\rho b = \frac{\text{mass of granules}}{\text{(bulk volume)}} \quad \ldots\ldots 12$$

$$\rho t = \frac{\text{mass of powder}}{\text{tapped volume (T500)}} \quad \ldots\ldots 13$$

Whereas ρ_b = Bulk density and ρ_t = Tap density. This was done in triplicates for both batches of granules.

Carr's Index and Hausner's Ratio
The Carr's index (CI) and Hausner's ratio (HR) were computed from the determined bulk and tapped densities of each granule sample as follows:

$$\text{Hausner's Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \quad \ldots\ldots 14$$

$$CI = \frac{(\rho t - \rho b)}{\rho t} \times 100 \quad \ldots\ldots 15$$

Where ρ_t = tapped density and ρ_b = bulk density

Determination of Flow Rate
Fifty grams (50g) (W) of the granules from each batch was placed in a funnel with internal diameter orifice diameter of 1.4cm and efflux tube length of 4.5cm. The granules were allowed to flow through the funnel orifice. The time taken for the granule to flow through the orifice (t) was noted and the flow rate computed as:

$$\text{Flow Rate (F.R)} = \frac{\text{weight of granule (g)}}{\text{time of flow (s)}} \quad \ldots\ldots 16$$

This was done in triplicates for each batch of granules and the mean calculated.

Angle of Repose
Angle of repose was measured for both bathes of granules to observe the flow properties of the granules produced using the processed maize starches as binders and maize starch B.P. The method employed a funnel secured with its tip at a given height (H), above a plane paper placed on a horizontal surface. The granules were poured through the funnel until the apex of the conical pile touched the funnel. The angle of repose was calculated using the following formula:

$$\text{Tan } \emptyset = \frac{2\text{Height of heap}}{\text{Diametrer of the heap}} \quad \ldots\ldots 17$$

This was done in triplicates for each batch of granules and the mean angle of repose calculated for each batch.

Percentage Fines
The percentage of fine in each batch was deduced by modifying the method described by Sanjay S. Patel &N atvarlal M. Patel (2009).Each batch of granules was passed through a 500um aperture sieve. The weight of fines and granules retained in the sieve were recorded and the percentage fines calculated using the formula;

$$\%F = \frac{f}{Tw} \times 100 \text{------} 17$$

Where f = weight of fines

Tw = total weight of granules.

ADDITION OF LUBRICANT AND COMPRESSION OF METRONIDAZOLE TABLETS

0.988g of magnesium stearate was weighed and mixed with the granules for each batch for about 3 minutes. The granules were then compressed into tablets using a Cadmag single punch tableting machine (India) using a punch size of 12.5cm in diameter. The first few tablets were used to adjust the die cavity to hold a granulation of 500g. The compressional pressure was adjusted to produce tablets with a hardness of 8kgf.

Table 5
FORMULATION USING PROCESSED CORN STARCH AS BINDER AND DISINTEGRANT IN COMPARISON WITH MAIZE STARCH B.P

INGREDIENT	PERCENTATE	PER TABLET (MG)	220 TABLETS (G)
Metronidazole	40%	200mg	44.00g
Corn starch as binder	25.640%	128.20mg	28.20g
Corn starch dry	1%	4.490mg	0.988g
Magnesium stearate	1%	4.490mg	0.988g
Lactose	32.564%	162.820mg	35.820g
Total	100%	500mg	110g

Formula adapted from Drug formulations Manual by Kohli and Shah, (2005), Third edition.

Quality Control Tests

Appropriate test methods and specifications have been developed which guarantee the quality of the tablets produced on a batch to batch basis. The parameter employed for such test methods include organoleptic tests, weight uniformity, hardness test, friability test, disintegration time test and dissolution rate test.

Organoleptic Test

The tablets within the different batches of each formulation were examined visually for variation in colour, nature of tablet surface and appearance of the tablet if any.

Hardness Test

The hardness of each batch of the prepared tablets was measured using the Mosanto tablet hardness tester (Thermonink, Chinda). Hardness is the breaking strength value of the tablet in kilograms (Chandrasekhar P *et al*, 2013). Ten tablets were used for each batch and the mean calculated.

Friability Test

The test was aimed at determining the wearing or abrasion of the tablets and was determined for each tablet batch. The friability (f) of the tablets was determined using the Erweka friabulator (Germany). 10 tablets were weighed (after dedusting with cotton wool) using an analytical weighing balance and the weight recorded. They were then placed in the friabulator by precisely removing and replacing the lid shaft. The machine was set to rotate at 25 rotations per minute for 4 minutes to give 100 revolutions. At the end of 4minutes, the tablets were retrieved by removing the lid shaft of the friabulator. The tablets were then dedusted again and reweighted using the analytical balance (Adventurer, China). The loss in weight was calculated as

$$\text{Friability} = \frac{dw\ 1 - w\ 0)}{w\ 0} \times 100 \quad \ldots\ldots\ldots\ldots\ldots\ldots 18$$

Where w_1 = final weight after 100 rotations

W_0 = initial weight of ten tablets.

(Ibezim *et al,* 2008)

This was done for the two batches of tablets and results were recorded.

Weight Uniformity Test

20 tablets were randomly selected in each batch and weighed individually using the analytical balance. The mean of twenty tablets, the percentage deviation were obtained. The uniformity in weight was tested for each tablet using the B.P 2011 method for tablets weight variation test.

Disintegration Time of the Prepared Tablets

Disintegration time for each batch of tablets was determined using the Disintegration Test Apparatus (Chemiscience Nigeria Co. Ltd). The B.P method was adopted. The woven stainless steel wire cloth had an aperture of 2mm. The immersion fluid used in this test was 500ml distilled water. Six tablets from each batch were used in this test. Each of the six tablets from a batch was placed in each of the 6 tubes of the basket and the disc put in place. The basket rack assembly was then immersed in the immersion fluid maintained at 37^0C and the apparatus switched on. The speed of rotation was set at 32 cycles per minute. The time taken for the tablets to disintegrate and pass completely through the sieve was noted. This was carried out for the two batches of the tablets in triplicates.

Complete disintegration is defined as that state in which any residence of the unit except fragments of insoluble coating or capsule shell, remaining on the screen of the apparatus is a soft mass having no palpable film core (British Pharmacopoeia 2011).

Dissolution Rate Test

The USP method was used and the apparatus was the Dissolution rate apparatus (Chemiscience Nigeria Co. Ltd). Dissolution medium- 900ml of 0.1N HCl was placed in each flask, and then placed in the glass tank of water thermostatistically maintained at 37^0C. When the dissolution medium reached 37^0C, a tablet from each batch was placed in each basket and the basket attached to the rotating shaft which was lowered to 2cm above the bottom of the flask. The speed of rotation was set at 100rpm. The apparatus was turned on and 10ml of the sample was withdrawn from the dissolution medium at 5 minutes intervals. An equivalent volume (10mls) of 0.1N HCL at 37^0C was added to the dissolution medium as replacement. Twelve reading were obtained that corresponded to 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60 minutes interval. The withdrawn samples were filtered using Whatmans filter paper and further diluted with the dissolution medium in a ratio of 1 to 10. Absorbance of the different samples at 278nm was measured using the UV spectrophotometer (UV 2100 Spectrophotometer UNICO™) connected to a PC. Using the values obtained from the Beer's calibration curve for metronidazole pure sample, the concentration in the dissolution medium at the different time intervals were calculated. The percentage of metronidazole released was plotted against the withdrawal time. This was done for the two tablet batches.

Active Drug Content (Assay)

This was carried out using the method outlined in Onyishi *et al*(2013). Five tablets were randomly selected collectively weighed, crushed and quantity equivalent to the mean weight dissolved with 0.1N Hcl and made up to 100ml with dilute acid. 1ml of the sample was withdrawn again and further diluted to 100ml. the sample was filtered and the absorbance of the filtrate read. The concentration of the active ingredient was determined from the standard Beer's plot obtained with the pure sample.

Statistical Analysis of Data

Data was analyzed using Excel software. The P values were used to assess if the difference between the respective means were statistically significant at a level of 0.05.

$P<0.05$ = statistically significant
$P>0.05$ = statistically insignificant.

RESULTS AND DISCUSSION

Percentage Yield

Weight of maize grains = 1kg

Weight of extracted starch = 0.425kg

percentage yield $= \frac{\text{weight of extract}}{\text{weight of raw material}} \times 100$

yield%= $\frac{0.425}{1.000} \times 100$

= 42.5%

Properties of the Starches
On testing the extracted starch with iodine, a blue colouration was obtained. This positive colour reaction is a confirmation that the sample contains starch.

Microscopic Study
When viewed under the microscope, the extracted starch showed similar results with the standard, Corn starch, B.P. The shape and size of the maize starches for both samples were similar. The granules were fairly uniform in size. They were polyhedral in shape with blunt edges. Some were rounded. Most of the granules occurred in clusters, but some occurred singly. The hilum was centrally placed with a triangular cleft. There were no striations. This is in line with official microscopical description of corn starch granules (Evans, 2009).

Starch Powder Characterization
Moisture content
From the results above, it is observed that sample B (Corn Starch B.P) had a moisture content of 8.24% which falls within acceptable limits. Sample A had a moisture content of 10:522. Sample A is seen to have a higher moisture content than sample B (Statistically significant, p value less than 0.05). However, both values fall within acceptable limits (<15% as stated in the British Pharmacopoeia).

Tapped density, Bulk density, Carr's index and Hausner's ratio
From the results of these parameters, it is observed that Sample A had a tapped density of 0.659g/ml, Sample B, 0.661g/ml. The Carrs indices and Hausner's ratio for sample A were also seen to be higher than sample B.

Carrs compressibility index and Hausner's ratio are related to the flowability of a powder or granule material. They are measures of the relative importance of interparticulate interactions. In a free flowing materials, the bulk and tapped densities will be closer in value. For poor flowing materials, there are frequently greater inter particulate interactions and a greater interactions between the bulk and tap densities will be observed (U.S Pharmacopoeia, 2009). The generally accepted scale of flowability is shown in the table below.

Table 3: Showing the relationship between Carr's Index, Hausner's quotient and flowability

Compressibility index	Flow character	Hausner's
<=10	Excellent	1.00-1-11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very Poor	1.46-1.59
>38	Very very poor	>1.60

Comparing the values obtained for these parameters with flowability scale above, it is seen that both samples have poor flow characteristics. Maize starch has been established to have poor flow (Rowe et al; 2006). As the values of the parameters above increases, the flowability of a powder sample usually decreases (Staniforth, 1996). Sample B would appear to have a better flow in comparison to A.

Swelling capacity, Hydration capacity
From the figure in table 3, it is seen that Sample A recorded a higher swelling capacity (1.214) than B (1.167). The common feature of all theories of disintegration is that penetration of water (or liquid medium) must precede disintegration and this can be assessed by the swelling capacity and hydration capacity (Caramella, 1986). Swelling capacity of a powder is important in tablet disintegration. Maize Starch has a wide application as a tablet disintegrant. Its ability to swell when in contact with water and wicking mechanism is the proposed mechanism for its disintegrant properties. Therefore high swelling capacity would favour a more rapid disintegration when the starch is used as a disintegrant. The hydration capacity for sample A was also seen to be higher than the standard. The higher swelling capacity and hydration capacity of the processed maize starch would favour a more rapid disintegration when used in tablet formulation as a disintegrant.

Flow rate, Angle of repose Both samples were observed to have very poor flow characteristics. When the powders were poured through a funnel, poor flow was observed for all samples even with tapping it has been established in previous studies that Maize starch has very poor flow properties in comparison with other commercial sources of starches; wheat, potato and rice, (Olayemi et al, 2008).

Table 4: Results of Granules Properties

Parameters	A	B	P value
Tap density	0.583 ± 0.00	0.593≠0.01	0.053
Bulk density	0.527≠0.00	0.533≠0.00	0.06
Carr's compressibility index	9.951≠0.81	9.949≠0.57	0.99
Hausner's ratio	1.111≠0.01	1.111≠0.03	0.96
Angle of repose	36.699≠0.15	36.511≠0.53	0.5
Flow rate (g/sec)	10.857≠0.70	13.650≠0.00	0.02
Percentage fines	24.320%	16.270%	

Key: A = granules formulated using processed maize starch as binder and disintegrant. B=granules formulated using maize starch B.P. as binder and disintegrant.

Granules Properties
From table 4, it is seen that the granules for both tablet batches have excellent flowabilty based on their flow rate values, Carr's compressibility index and Hausner's ratio. The flowability of batch A granules is higher than batch A granule (Statistically significant, p<0.05). This is seen in the higher flow rate value for batch B granules. However, the bulk, tap densities, carr's indices, Hausner's ratio for both batches are similar (stastically insignificant, p value (0.05).

Batch A granule recorded higher percentage fines (24.320%) than batch B granules (16.27%). Hence it can be said that maize starch B.P has more binding capacity than the processed maize starch.

Organoleptic Test
The tablets were round, with flat surfaces. They were white, with a bitter taste due to the active ingredient, metronidazole. Chipping was observed in some of the tablets.

Chipping is defined as breaking of tablets edges, while the tablets leave the tablet press or during subsequent handling and coating operations. It could occur as a result of the nature and state of the tablets punches and dies, and improper setting of the tableting press.

Table 5: Hardness test results

S/N	Batch A (kgf)	Batch B (kgf)
1	7.30	8.00
2	7.80	9.00
3	8.10	8.40
4	6.60	7.00
5	7.20	8.50
6	6.50	7.50
7	6.60	8.00
8	7.00	10.00
9	7.20	9.00
10	7.80	8.50
Mean	7.21≠0.55	8.39≠0.84

Key: A = Tablet batch produced using processed maize starch as binder and disintegrant

B = Tablet produced using maize starch B.P as binder and disintegrant. P value 0.002.

Hardness Test

The resistance of a tablet to chipping, abrasion or breakage under conditions of storage, transportation, and handling before use depends on its hardness (Rudnic and Schwartz, 2005). Hardness of a tablet is expressed as the force required to break the tablet. It is essential that the hardness of a tablet be sufficient enough to resist handling during storage, and transportation. However the tablets should not be too hard or too soft. The hardness of all tablet batches were measured in kilogram force using Monsanto hardness tester and the result presented in table 5. The results showed that batch A tablets had lower hardness values compared to batch B tablets (statistically significant $p<0.05$). batch A tablets had a mean hardness of 7.21kgf, batch B tablets had a mean hardness of 8.39kgf. A force of about 4kgf is considered the minimum requirement for a satisfactory hardness. Batch Bwould have a higher resistance to breakage during handling, transportation, and shipping compared to A.

Table 6: Percentage friability of the tablet batches

Friability	A	B
1	0.735	0.685
2	0.753	0.686
3	0.739	0.665
Mean	0.742≠0.01	0.679≠0.01

P value 0.002

Friability Test

Tablet friability is related to the tendency of a tablet to crumble. It could be a function of tablet hardness. It is a measure of the abrasiveness or wearing properties of a tablet. It is usually measured by subjecting the tablets to rolling and repeated shocks resulting from free fall. The lower the friability, the higher the tablets resistance to abrasion during handling, shipment and packaging. A maximum weight loss of not more than 1% is generally acceptable (Allen et al, 2009).

The percentage weight loss after the test was calculated as the friability.

Batch A tablets had a mean friability of 0.742% and batch B 0.67%. Both values are within acceptable standard as stated in the U.S.P.

It is essential that a tablet possess enough hardness to be able to resist abrasiveness or wearing otherwise it crumbles or forms unacceptable powdered tablets. Therefore it can be said that these two parameters tablet hardness and friability accesses the binding capacity of the starches used as binder in the tablet formulation. A low concentration or amount of binder would produce tablets that are soft and tend to crumble (Allen et al, 2009).

Weight Uniformity Test

The quantity of fill in the die of a tablet press determines the weight of the tablet (Loyd et al, 2009). The volume of fill is adjusted with the first few tablets to yield the desired weight and content. Small variations in weight of individual tablets during compression are inevitable and admissible. Accordingly, accepted limits are usually stated for uncoated tablets in official texts. The British Pharmacopeia states acceptable limits for weight variation for uncoated tablets. A tablet passes if not more than 2 of the tablets deviate from the average weight by more than the percentage deviation stated and non-deviates by more than twice that percentage. For tablets weighing greater than 250mg, the acceptable percentage deviation is 5% of the mean weight. Both tablet batches passed the British Pharmacopeia standard for weight uniformity. It is observed from the above table that 2 tablets in batch B fell outside the 5% percent deviation stated in the B.P, but no tablet deviates by twice that percentage. Weight uniformity is highly related to content uniformity. The smaller the variation in weight within a tablet batch, the more likelihood of content uniformity of the active ingredient in a tablet batch.

Table 8: Weight Uniformity of Tablet batches A and B

	A		B	
	Weight of individual tablets randomly selected	Percentage deviation (%)	Weight of individual tablets randomly selected	Percentage deviation (%)
	519	8.52	500	2.29
	489	2.39	501	2.07
	522	4.08	515	0.69
	497	0.74	535	4.41
	511	2.02	512	0.11
	505	0.85	518	1.29
	500	0.17	554	7.69
	497	0.74	474	7.89
	502	0.26	489	4.58
	503	0.46	498	2.69
	514	2.59	494	3.52
	498	0.54	534	4.23
	497	0.76	497	2.90
	488	2.60	489	4.58
	488	2.60	522	2.03
	497	0.74	518	1.27
	494	1.36	533	4.05
	503	0.46	536	4.50
	485	8.23	511	0.05
	505	0.85	518	1.27
Mean weight (x)	**500.70**		**511.40**	

Table 9: Disintegration time of the tablet batches.

S/N	Disintegration time in minutes	
	Batch B	Batch A
1	2.46	1.17
2	2.50	1.23
3	2.40	1.18
MEAN	2.45≠0.05	1.19≠0.03

P value of 0.000043, statistically significant.

Disintegration Time

For the medicinal agent in a tablet to be fully become available for absorption, the tablet must first disintegrate and dis-

charge the drug to the body fluid for dissolution.

From the result of the disintegration time test, batch A tablets had a mean disintegration time of 1.19minutes, batch B 2.45minutes. Batch A tablets were formulated using the processed maize starch as binder and disintegrant in the same formulation. From the results above, it can therefore be said that the processed maize starch is a more efficient disintegrant than maize starch B.P.

These tablet batches are more likely to release the active ingredient into the gastrointestinal tract than batch B tablets when the drugs are administered in vivo. The shorter disintegration time observed with batch A tablets is supported by the higher swelling capacity and hydration capacity of the processed starch as against maize starch B.P.

British Pharmacopeia states that for uncoated tablets, tablets selected from each batch must disintegrate within 15minutes. This is to ensure that the active ingredient be released from the tablet into the gastro intestinal fluid in order for it to exert it therapeutic effect.

Dissolution Rate Test

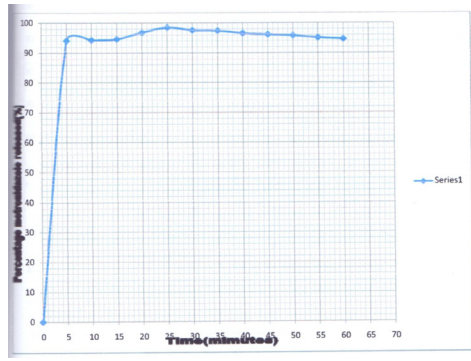
Clinical scientists rely on dissolution tests to establish *in-vitro/invivo* correlations between release of drug from the dosage form and drug absorption (Dressman J *et al,* 1998). Rapid disintegration of a tablet is no indication that the active ingredient would be released completely into the physiological fluid. Drug disintegration precedes dissolution and subsequently bioavailability. The dissolution process has been shown to be a function of the physicochemical characteristics of the tablet formulation. Many factors affects the dissolution rate of tablets and they include effects of solid characteristics such as specific surface, particle size distribution and shape, solvent effects, temperature, viscosity.

Other factors include starch content, compression pressure, tablet density and age. Dissolution rate tests are usually carried out under conditions that simulate the gastric fluid. This is to provide as far as possible a reasonable correlation with the products in vivo bioavailability. The dissolution rates results of the different tablet batches is seen in appendix 13. From the dissolution test result carried out, it can be observed that more than 90 percent of the active ingredient was released within 5 minutes for both tablet batches with batch A tablets having a somewhat slower dissolution rate compared to batch B tablets. This could be explained as being due to the adsorption of the active ingredient by impurities such as fats.

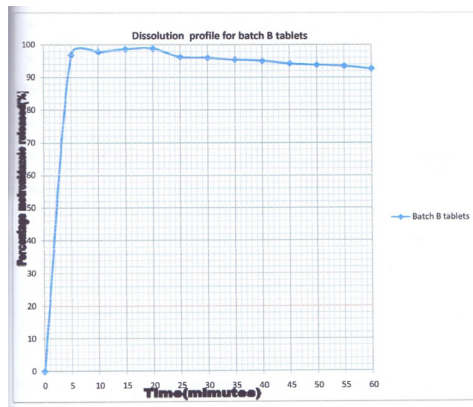
Despite faster disintegration observed in tablet batch A, batch B had a somewhat faster dissolution rate (94 percent released at 5 minutes for batch A tablets as compared to 96 percent released at 5miuntes for batch B tablets). This is in line with the fact that rapid disintegration is no indication that the active ingredient in a tablet would go into the physiological fluid. Despite the hardness of the tablet batches ad the high binder concentrations in both batches, it did not hinder the release of the active ingredient from the tablet matrix. Hence when these drugs are administered in vivo a very rapid onset of action is likely to be observed since more than 90 percent of the drug would go into solution within 5 minutes in the gastrointestinal fluid. However both tablet batches conform to USP specification for dissolution rate of metronidazole tablets which states 85 percent release within 60 minutes.

The findings observed in the dissolution rate results strongly suggests that the use of maize starch as the only binder and disintegrant in the same tablet formulation produces tablets with rapid drug release profiles due to the efficiency of maize starch as a tablet disintegrant.

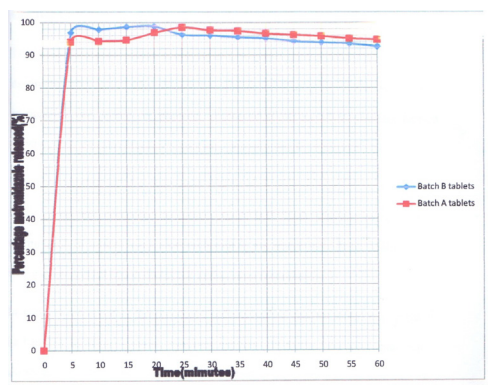
Graph 1: Dissolution profile for metronidazole tablets batch A produced using extracted maize starch.



Graph 2: Dissolution profile for metronidazole tablets batch B produced using extracted maize starch B.P.



Graph 3: Comparison of the dissolution profile of tablets batch A and B maize starch.



Key: Batch A = Tablet batch produced using processed maize starch as binder and disintegrant.,

Batch B = Tablet batch produced using maize starch B.P as binder and disintegrant.

T90 = time taken for 90 percent of the active ingredient to be released = 4.5 minutes for both tablet batches.

CONCLUSION

In view of the result of the physical characterization, the processed maize starch had higher moisture content, swelling capacity, hydration capacity than maize starch B.P. these higher swelling and hydration capacity may suggest that the extracted starch would be a better disintegrant than the standard starch.

The processed starch also had higher values for Carrs index, Hauser's ratio and angle of repose compared to the standard. This indicates poorer flow ability in comparison with maize starch .B.P.

Also the formed granules produced from both starches were

characterized and compressed into tablets. It can be concluded the maize starch B.P has superior binding capacity than the processed maize starch. This is reflected in the lower Percentage fines, higher hardness and lower friability values seen in batch B tablets as against batch a tablets.

However the locally produced maize starch had superior disintegrating ability to the standard, maize starch B.P the dissolution profiles of both tablets batches were however similar. More that 90 percent of the active ingredient as released within 5 minutes for both tablet batches with batch A tablets having a somewhat slower dissolution rate in comparison to batch B tablets. This is a confirmation that rapid disintegration does not necessarily mean rapid and complete dissolution.

It can also be concluded that when maize starch is used as a binder (in the absence of any other binding agent) and disintegrant in the same formulation, the tablets would have a somewhat short disintegration time and fast dissolution rate despite high hardness values. This is reflected in the rapid released of the medicinal agent from the tablets matrix despite high compression pressures and tablets hardness seen in both tablet batches.

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