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An investigation of the direct compression properties of pre-gelatinized African bitter yam and cassava starches in acetylsalicylic acid tablet formulations

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ABSTRACT: The direct compression ability of pre-gelatinized African bitter yam and cassava starches in acetylsalicylic acid tablet formulation was investigated. Starches from the African bitter yam and cassava tubers were extracted following standard procedures. The starch powders were subjected to some physicochemical evaluations and pre-gelatinized. Batches of acetylsalicylic acid granules and tablets were formulated with the native and pre-gelatinized forms of both the test and maize starches and microcrystalline cellulose at 5.0 and 10 %w/w by direct compression. Granules were evaluated for their flow properties and drug-excipient compatibility using DSC and FTIR while the tablets were investigated for their tablet parameters. The extracted starches were off-white to white in colour, insoluble in water, smooth in texture with particle sizes ranging from 5.0-10 µm that are oval to elliptical in shapes. The powders showed a swelling capacity ≤ 2.15, hydration capacity ≥ 1.20 and a moisture content ≤ 14.3 %. The granules exhibited good to fair flowability. Only tablets formulated with 10 %w/w of the pre-gelatinized starches and MCC met compendial requirements in their crushing strengths and friability. All the tablets disintegrated within 15 min with the pre-gelatinized cassava starches giving the shortest times of < 1.0 min. The 10 %w/w pre-gelatinized starches tablets compared favourably with MCC in their drug release profiles. Compatibility studies revealed no interaction between drug and excipients. The study show that the pre-gelatinized test starches compared favourably with MCC, a known direct compression excipient in their direct compression ability and drug release profiles especially at a concentration of 10 %w/w.

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Keywords: bitter yam, cassava, starches, pre-gelatinized, drug formulation

A tablet is composed of an active or therapeutic ingredient(s) and a number of inert materials known as excipients or additives. These excipients may be classified either as materials that help to impart satisfactory processing and compression characteristics to the tablet formulation such as diluents, binders, glidant and lubricants or as materials that help to give additional desirable physical characteristics to the finished tablet such as disintegrants, colours, flavours and sweetening agents (Rudnic and Schwartz, 2006). There are also excipients that play two or more roles in a tablet formulation. Example of such multifunctional excipients is a direct compression excipient which may play the role of a diluent, binder and disintegrant in a formulation.

Starches are polysaccharides which serve as energy storage for most green plants. Apart from being a common carbohydrate in diets, it is also widely used in the pharmaceutical industries as excipients in tablet formulation as disintegrants, binders or lubricants. These roles of starch in tablet formulations have initiated a search for newer starches of natural origin and their modified improved varieties (Kottke *et al*., 1992; Odeku *et al*., 2009; Eraga *et al*., 2016). Native forms of starches are modified physically, enzymatically or chemically to improve the utility properties of the starch powder (Gotlieb and Capelle, 2005). Modified starches have been reported to improve tablet properties such as compressibility and dissolution characteristics in pharmaceutical preparations (Mostafa, 2004; Okunlola and Akingbala, 2013; Lawal *et al*., 2015; Akin-Ajani *et al*., 2016).

African bitter yam (*Discorea dumetorum*) is a root crop that grows in various parts of West Africa and it is popular in the south eastern part of Nigeria. It is cultivated in times of food scarcity or famine as a result of scarcity of other varieties of yam. It also grows in the wild and the wild specie is toxic (Kay, 1987). The yams are normally soaked in salt water before consumption in order to detoxify and remove the bitter components.
Cassava (*Manihot esculenta*) is a woody shrub cultivated annually in the tropical and sub-tropical regions for its edible starchy tuberous root, a major source of carbohydrate. It is called tapioca when dried and crushed to a powdery substance; its fermented, fried granular version is named "garri". Cassava is the third largest source of food carbohydrate in the tropics, after rice and maize. It is a major staple food in the developing world.

This study is aimed at investigating the direct compression property of pre-gelatinized starches sourced from African bitter yam and cassava for direct compression of acetylsalicylic acid tablets.

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MATERIALS AND METHODS

Materials: Acetylsalicylic acid crystals, microcrystalline cellulose and n-hexane (BDH Chemical Ltd., Poole, England), lactose (Sigma Chemicals, St. Louis, USA), maize starch BP (Roquette Freres, France), magnesium stearate (A.H.A. International Co. Ltd, China), talc (Chemic Laboratory Reagents & Fine Chemicals, France), 3.5 %w/v sodium hypochlorite (Reckitt and Coleman Nig. Ltd) were used as received. African bitter yam (*Discorea dumetorum)* and cassava (*Manihot esculenta)* tubers were purchased locally and processed in our laboratory. All sieves were BSS (Endecotts Ltd. London, England) and water was double distilled.

*Methods: Extraction of the starches***,** Tubers weighing about 5 kg were peeled, washed and chopped into smaller pieces. The pieces were milled into a paste using an electric grinder (Moulinex, France). The grounded material was slurried with 1 L of water containing 30 m1 of 3.5 %w/v sodium hypochlorite and allowed to stand overnight. After 16 h, the mixture was sieved using a muslin cloth to separate the starch from fibrous materials. Excess water was added to the resulting starch slurry, stirred and allowed to stand for about 4 h for the sedimentation of the starch. The supernatant water was decanted carefully and fresh excess water was added with continuous stirring. The supernatant water was again decanted after 3 h. This washing process was repeated several times until the supernatant tested neutral to pH test strip. The wet mass of the starch was air dried for 24 h and then oven dried at 60 °C for 1 h. The dried starch was milled into fine powder and stored in an airtight container until use.

Characterization of starch powders: Organoleptic properties, the taste, odour and colour of the starches were assessed by twelve individuals and a matching assessment result given by at least ten of the individuals was recorded.

*Solubility***:** About 100 mg of starch was placed in 2 ml of cold water in a test-tube and shaken. The dispersion was filtered and the residue air dried. The dried residue and the filter paper were weighed (KERRO BL3002, England) and the difference in weight was used as a measure of solubility of the starch powder.

*Chemical test***:** A 5 ml aliquot of the starch suspension was prepared and a few drops of 0.01 M iodine solution was added. The resulting colour change was recorded.

*Microscopy***:** The starch sample was thinly spread over a glass slide and viewed under a light microscope (Labo Microsystems GmbH, Germany) via a calibrated eyepiece and the sizes and shapes of the particles were recorded.

*Bulk density***:** A 30 g quantity of the starch powder was poured gently into a 100 ml graduated measure. The volume of the powder was read and the bulk density calculated.

Tapped density: The measure containing the 30 g of starch powder was tapped 100 times on a wooden platform to a constant volume. The volume was noted and used in calculating the tapped density.

Carr's index: The difference between the tapped and bulk density of the starch powder divided by the tapped density was calculated and the ratio expressed as percentage.

*Hausner's ratio***:** The ratio of the tapped density to the bulk density of the starch powder was calculated as the Hausner's quotient.

True density: A 25 ml specific gravity bottle (glass pycnometer) was filled with n-hexane, cleaned of any excess n-hexane and weighed (x). The bottle was emptied, rinsed with acetone and dried. About 1 g (y) of the starch powder was poured into the bottle and then filled with n-hexane. It was weighed (z) after cleaning off the excess n-hexane from the bottle. The various weights recorded were used to calculate the true density of the starch using Equation 1. All the tests were carried out for all the starches in replicates.

$$\rho = \frac{y}{[(x+y)-z]} \times S \qquad (1)$$

Where ρ is the particle density of the starch and S is the specific gravity of n-hexane

*Swelling capacity***:** A 10 g weight of the starch powder with a tapped volume (V_A) in a 100 ml measuring cylinder was dispersed with 85 ml of distilled water and thereafter made up to volume with more water. The dispersion was allowed to stand for 24 h and the volume of the sediment (V_B) noted. The swelling capacity was computed with Equation 2.

Swelling capacity = $V_B - V_A$ .... (2)

Where V_B and V_A are the volumes of the sediment and the tapped starch sample respectively

*Hydration capacity***:** A 1 g weight of the starch was introduced into a 15 ml centrifuge tube. The tube was covered after 10 ml of water was added and shaken for about 2 min. It was allowed to settle for 10 min and centrifuged at 2000 rpm for 10 min using a bench

centrifuge. The resulting supernatant was decanted and the sediment weighed. The hydration capacity was determined with Equation 3. This determination was carried out in quadruplicate.

$$\text{Hydration capacity} = \frac{W_B}{W_A} \qquad (3)$$

Where W_B and W_A are the weights of the sediment and the starch sample, respectively.

Moisture content: A 1 g quantity of the starch powder was dried in a hot air oven for 4 h at 105 ºC. The initial weight of the powder and the weight after drying were recorded and used to calculate the moisture content of the starch powder.

Pre-gelatinization of the starches: A weighed quantity of starch was dispersed in 500 ml of water contained in a 1 L beaker. The dispersion was placed in a hot water bath, thermostated at 80 °C, the pre-gelatinization temperature of starch. The dispersion was stirred continuously until a slightly viscous gel was formed. The gel was then transferred to a flat stainless steel plate and oven dried (Gallenkamp, UK) into flakes at 60 °C for 24 h. Thereafter the flakes were powdered and passed through a 100 µm mesh screen and stored in an air tight container until evaluation. Maize starch BP was also subjected to pre-gelatinization for comparison with the test starches.

Preparation of granules by slugging: Using the formula shown in Table 1, a total of eleven (11) batches of acetylsalicylic acid powder blends were prepared using 5.0 or 10 %w/w of the native and pre-gelatinized forms of the test starches, maize starch BP and microcrystalline cellulose as the disintegrant/binder or direct compression agent. Each batch was prepared by dry mixing the required quantities of acetylsalicylic acid, lactose and the disintegrant/binder powders in a mixer for 10 min. The powder blend was compressed into large tablets (slugs) using a heavy duty tableting machine (Koln Niehi, Germany). The slugs were broken down into granules using a mortar and pestle and passed through an 850 µm sieve. The glidant (talc) and lubricant (magnesium stearate) were weighed and mixed in a mortar and then added to the granules in geometric proportion and mixed intimately. The granules were analysed and kept in an airtight container until compression.

Table 1: Formula of prepared acetylsalicylic acid tablets

Ingredients	Quantity/tablet (mg)
Acetylsalicylic acid	300
Lactose	82,67
Disintegrant/Binder* (5,10 %w/w)	15,30
Magnesium stearate	3
Talc	3
Total	**400**

*Disintegrant/Binder: African bitter yam starch (native; 5 %w/w, pre-gelatinized; 5 and 10 %w/w) or cassava starch (native; 5 %w/w, pre-gelatinized; 5 and 10 %w/w) or maize starch BP (native; 5 %w/w, pre-gelatinized; 5 and 10 %w/w) or microcrystalline cellulose (5 and 10 %w/w)

Analysis of granules: Micromeritic properties of prepared granules: The bulk and tapped densities of the granules were determined using the same methods as the starch powders and values obtained were used to compute the Carr's indices and Hausner's ratios of the various batches of the acetylsalicylic acid granules.

Angle of repose: The hollow tube method was used. A short hollow tube of 3 cm in internal diameter sitting on a circular horizontal surface of same diameter was filled with granules. The tube was vertically withdrawn and allowing excess granules to fall off the edge of the circular horizontal surface. The heap height was measured. The angle of repose, θ, was calculated using Equation 4.

$$\theta = tan^{-1}(h/r) \quad \ldots . \quad (4)$$

Where h is the height of the heap of granules and r is the radius of the circular base

Flow rate: The funnel method was employed. A glass funnel was clamped to a retort stand at a certain distance from a horizontal surface. Fifty grams of granules was poured into the funnel with its orifice blocked with a glass sheet. The glass sheet was withdrawn and the granules allowed to fall freely under the influence of gravity. The time taken for the entire granules to pass through the orifice was recorded. This was carried out in triplicate and the mean values and standard deviations recorded.

Drug-excipient interaction studies: In order to determine any interactions between acetylsalicylic acid and the pre-gelatinized forms of the starches, drug-excipients interaction studies were carried out on the granules prepared with the pre-gelatinized forms of the test starches and pure acetylsalicylic acid crystals using DSC and FTIR analyses. The DSC analysis was carried out using the Netzsch DSC 204F1 Phoenix apparatus (Netzsch, Germany). Four milligrams of the sample was weighed into an

aluminium pan. The seal of the pan was pierced and placed in the calorimeter previously calibrated with indium and nitrogen as the purge gas. Heating of the sample was carried out at the rate of 10 °C per min from 30 to 350 °C under nitrogen at a flow rate of 70 ml/min while the FTIR analysis was done using FTIR-4100 Spectrophotometer (Shimadzu Co. Japan). Five milligrams of the sample was blended with potassium bromide to give a 200 mg weight powder. The blended powder was compressed using a Sigma KBr press into a tablet, and then placed in the sample compartment of the spectrophotometer and scanned at a range of 4000 - 1000 cm^{-1}.

Compression of granules: Batches of the granules were compressed into tablets using a single punch tableting machine (F-3 Manesty Machines, UK) at a compression pressure of 31 arbitrary units. The die volume was adjusted to compress tablets of uniform weight by using granules weighing 400 mg. The tablets made were then kept in air tight containers and stored in a desiccator until evaluation.

*Tablet evaluations***:** The following tests were carried out on the compressed tablets employing standard procedures: tablet weight uniformity, dimensions, crushing strength (hardness), friability, disintegration time and dissolution profile (BP, 2003).

Weight uniformity: The weight of each of 20 tablets was determined from each batch using an electronic balance (College B154, Mettler Toledo, Switzerland) and the mean weight and standard deviation were computed.

Dimensions: The thickness and diameter of 10 tablets from each of the batches were determined using the Gallenkamp micrometre screw gauge and the mean value and standard deviation were recorded.

Crushing strength: The crushing strength of each of ten tablets per batch was determined by diametric compression of the tablet until it breaks (Campbell Electronics, Model HT-30/50, India). The mean value and standard deviation were calculated.

*Friability test***:** The weight of 10 tablets was determined on the electronic balance and the tablets placed in the drum of a Roche friabilator (Erweka-ZT4 Heusenstamm, Germany). The apparatus was operated at a drum speed of 25 rpm for 4 min. The tablets were brought out, de-dusted and reweighed. The weight was recorded and friability calculated as percentage loss in weight.

*Disintegration time***:** The disintegration times of six tablets per batch of the tablets were determined in distilled water at 37 ± 0.5 °C using the disintegration apparatus (Veego, India). The time taken for each tablet to break down into its primary particles and pass through the mesh of the apparatus was recorded and used to calculate the average time and standard deviation.

Dissolution studies: In vitro dissolution profiles of the various batches of the acetylsalicylic acid tablets were determined using the USP Type II (paddle) method. A dissolution apparatus (Caleva ST7, UK) containing 900 ml of 0.1 M HCl solution maintained at 37 ± 0.5 °C with a paddle speed of 50 rpm was used. The apparatus was operated for 60 min and at various time intervals, a 5 ml volume of the dissolution fluid was withdrawn and replaced with an equivalent volume maintained at same temperature (37 ± 0.5 °C). The withdrawn samples were filtered and diluted with an equal volume of 0.1 M HCl and then hydrolyzed by heating at 90 °C for 2 h. About two drops 5 % ferric chloride was added to the sample solutions after cooling and their absorbances determined at λmax of 540 nm with a UV-VIS Spectrophotometer (Shimadzu, Japan). The concentration and the percentage of acetylsalicylic acid released at each time interval was determined using the equation from the standard calibration plot earlier obtained from the pure drug.

Statistical analysis: Descriptive statistics using Microsoft Excel (2007) was done for all data. Mean and standard deviations of replicate determinations were computed and reported. Differences between mean was determined using one-way ANOVA while $p < 0.05$ was considered significant.

RESULTS AND DISCUSSION

Starch powder properties: Some physical properties of the starch powders studied are shown in Table 2. The powder of the African bitter yam starch was off-white in colour while that of cassava starch was white. Both starches were odourless, tasteless and smooth in texture. They were insoluble in water and gave a blue black colouration with iodine solution. Microscopic examination of the starch particles showed an oval shape with a size range of 5.0 - 10 µm for the African bitter yam starch while the cassava starch was elliptical in shape with a particle size range of 7.0 - 10 µm.

Table 2: Some physicochemical properties of the starch powders studied

Properties		Starches	
		African bitter yam	**Cassava**
Organoleptic	Appearance	Off-white	White
	Taste	Tasteless	Tasteless
	Odour	Odourless	Odourless
	Texture	Smooth	Smooth
Chemical	Solubility (cold water)	Insoluble	Insoluble
	Test for starch	Positive	Positive
Microscopy	Size range	5.0 - 10 µm	7.0 - 10 µm
	Form	Oval	Elliptical
	Hilum	Stellate	Stellate
	Striations	Presence of striations	Presence of striations
Powder parameters	Bulk density (g/cm^3)	0.43	0.54
	Tapped density (g/cm^3)	0.76	0.86
	True density (g/cm^3)	1.25	1.52
	Carr's index (%)	43.42	37.21
	Hausner's ratio	1.76	1.59
	Swelling capacity	1.11	2.15
	Hydration capacity	1.20	1.50
	Moisture content (%)	14.3	14.1

The cassava starch powders exhibited comparable but higher densities than the African bitter yam starch and this result may be attributed to the particle shapes of the starch promoting an even packing resulting in fewer void spaces. The Carr's indices and Hausner's ratios of the test starch powders showed that the cassava starch was better flowing, but generally both starch powders had poor flow properties. Also the swelling and hydration capacities of the cassava starch powder were higher with the swelling capacity of cassava starch almost twice that of the bitter yam starch. This superior swelling ability of cassava starch would suggest that this starch would be a good candidate as a disintegrant.

Both starches showed similar moisture content values ≤ 14.3 %. These values were comparable to those obtained in a similar study involving different cultivars of cassava starch where values ranging from 9.4 - 13.3 % were recorded (Chitedze *et al*., 2012).

*Granule properties***:** The results of the flow properties of the acetylsalicylic acid granules are presented in Table 3

Table 3: Flow properties of the acetylsalicylic acid granules

Starch		Concentration (%w/w)	Batch	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner's ratio	Angle of repose (°)	Flow rate (g/sec)
African bitter yam	*Native*	5	A	0.86	1.05	18.01	1.26	33.64	18.18
	Pre-gelatinized	5	B	0.83	1.05	20.95	1.22	33.25	20.00
		10	C	0.80	1.11	27.00	1.32	33.08	19.38
Cassava	*Native*	5	D	0.86	1.04	20.00	1.25	33.69	14.29
	Pre-gelatinized	5	E	0.83	1.05	20.95	1.21	33.55	20.00
		10	F	0.86	1.05	18.09	1.22	33.51	18.18
Maize	*Native*	5	G	0.83	1.05	20.95	1.26	33.51	16.18
	Pre-gelatinized	5	H	0.80	0.91	12.08	1.14	33.73	19.54
		10	I	0.86	1.17	31.00	1.34	33.47	17.50
Microcrystalline cellulose		5	J	0.83	1.05	20.95	1.31	33.95	15.38
		10	K	0.80	1.00	20.00	1.25	33.64	20.00

The results show a lower bulk and tapped densities for the batches of granules prepared with the native starches when compared with those prepared with the pre-gelatinized starches at the same concentrations of 5.0 %w/w, which indicates that the batches of pre-gelatinized starch granules were more porous and free flowing as reflected in their Carr's indices, Hausner's ratios, angles of repose and flow rates (Chitedze *et al*., 2012). But the batches of granules produced with higher concentrations of the pre-gelatinized starches (10 %w/w) showed a decrease in granule porosity and consequently a reduction in their flow properties when compared with the 5.0 %w/w batches of granules. This observation suggests an increase in the cohesiveness and a resultant densification of the granule particles with increase in the concentration of the pre-gelatinized starches (Abdulsamad *et al*., 2008). The batches of granules produced with microcrystalline cellulose showed an increase in flow characteristics with increase in concentration. Generally, all the batches of granules were

comparable in their Carr's indices, Hausner's ratios, angles of repose and flow rates.

Compatibility studies: Thermal analysis; Thermograms from the DSC compatibility analysis are shown in Figure 1 (a-d). Pure acetylsalicylic acid crystal thermogram (Figure 1 (a)) showed a sharp endothermic trough corresponding to 175 °C on the temperature scale. The sharp trough appeared as a spike which is an indication of its crystallinity and purity. The thermograms of the granules containing the combination of acetylsalicylic acid and the pre-gelatinized starches of bitter yam (Figure 1 (b)), cassava (Figure 1 (c)) and maize (Figure 1 (d)) showed the characteristic trough of pure acetylsalicylic acid. This observation suggests no interaction between the drug and the pre-gelatinized starches.

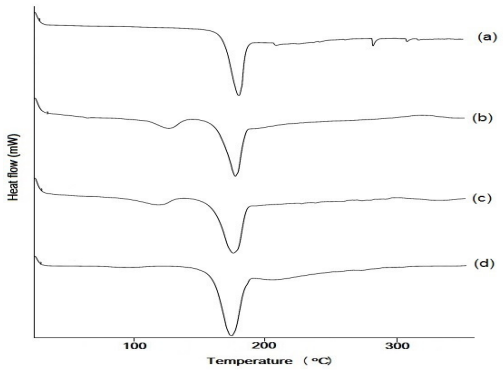

Fig 1: DSC thermograms of pure acetylsalicylic acid crystals (a) and the tablet granules prepared with pre-gelatinized starches of bitter yam (b), cassava (c) and maize (d)

*FTIR***:** The FTIR spectrum of pure acetylsalicylic acid (Figure 2 (a)) crystals showed characteristic absorption bands at 918.50, 1195.00, 1300.91, 1688.26, 1759.81 and 3010.00 cm^{-1}. These bands observed for acetylsalicylic acid remained unchanged when compared with the spectral data of the granules containing the combination of acetylsalicylic acid and the pre-gelatinized starches of bitter yam (Figure 2 (b)), cassava (Figure 2 (c)) and maize (Figure 2 (d)) starches. This observation ruled out the possibility of chemical interaction and complex formation between acetylsalicylic acid and the pre-gelatinized starches during the mixing process.

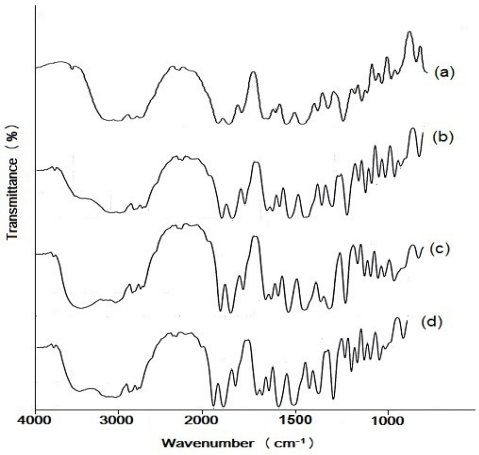

Fig 2: FTIR spectra of pure acetylsalicylic acid crystals (a) and the tablet granules prepared with pre-gelatinized starches of bitter yam (b), cassava (c) and maize (d)

Tablet properties: The results from the evaluation of the various batches of the directly compressed acetylsalicylic acid tablets are outlined in Table 4. The tablet weight uniformity results showed that the mean weight of the tablets prepared with the test starches, maize starch BP and microcrystalline cellulose met the British Pharmacopoeia (BP 2009) specification of not more than two of the individual weights of tablets deviating from the average weight by more than ± 5 % and none should deviate by more than ± 10 %.

Table 4: Some physicochemical characteristics of the paracetamol tablet

Starch	Batch	Tablet weight (mg)	Tablet dimensions (mm)		Crushing strength (kp)	Friability (%)	Disintegration time (sec)
			Diameter	Thickness			
African bitter yam	A	405 ± 0.32	12.56 ± 0.04	2.31 ± 0.09	3.72 ± 0.1	1.6 ± 0.5	480 ± 4.0
	B	402 ± 0.11	12.45 ± 0.06	2.23 ± 0.04	3.60 ± 0.1	1.4 ± 0.3	420 ± 2.0
	C	401 ± 0.14	12.53 ± 0.03	2.46 ± 0.02	4.20 ± 0.2	0.9 ± 0.2	180 ± 1.0
Cassava	D	404 ± 0.55	12.63 ± 0.07	2.99 ± 0.07	3.52 ± 0.1	1.6 ± 0.6	48 ± 4.0
	E	404 ± 0.16	12.98 ± 0.09	2.32 ± 0.03	3.20 ± 0.1	1.0 ± 0.2	47 ± 5.0
	F	402 ± 0.40	12.02 ± 0.05	2.64 ± 0.03	4.09 ± 0.8	0.9 ± 0.2	33 ± 4.0
Maize	G	407 ± 0.20	12.53 ± 0.03	2.23 ± 0.04	3.70 ± 0.1	2.0 ± 0.4	180 ± 1.0
	H	401 ± 0.44	12.57 ± 0.05	2.95 ±0.05	3.10 ± 0.1	1.7 ± 0.2	77 ± 2.0
	I	401 ± 0.42	12.59 ± 0.06	2.95 ± 0.05	4.00 ± 0.1	1.9 ± 0.2	73 ± 3.0
Microcrystalline cellulose	J	408 ± 0.32	12.45 ± 0.06	2.35 ± 0.09	4.00 ± 0.1	2.0 ± 0.4	160 ± 1.0
	K	413 ± 0.10	12.56 ± 0.04	2.46 ± 0.02	4.30 ± 0.2	0.9 ± 0.1	110 ± 2.0

± Standard deviation

Table 5: ANOVA results for tablet crushing strength, friability and disintegration time

	Source of Variation	SS	df	MS	F	P-value	F crit
Crushing Strength	Between Groups	4.819084848	10	0.481908485	484.8469512	2.14435E-23	2.296695957
	Within Groups	0.021866667	22	0.000993939			
	Total	4.840951515	32				
Friability	Between Groups	5.592121212	10	0.559212121	22.9156836	2.27573E-09	2.296695957
	Within Groups	0.536866667	22	0.02440303			
	Total	6.128987879	32				
Disintegration time	Between Groups	688713.8788	10	68871.38788	5398.469834	6.98569E-35	2.296695957
	Within Groups	280.6666667	22	12.75757576			
	Total	688994.5455	32				

SS = sum of squares; df = degree of freedom; MS = mean square; F = calculated F-value

Whereas there were variations in the crushing strengths, friability and disintegration times of the formulated batches of tablets as confirmed in the significant differences ($p < 0.05$) between their mean values shown by the analysis of variance in Table 5. All the batches of tablets showed crushing strength values > 3.0 kp. Only those batches of tablets prepared with microcrystalline cellulose and 10 %w/w of the pre-gelatinized starches of both the test starches and maize starch BP gave satisfactory crushing strength values ≥ 4 kp. The friability test results of the tablets revealed values ≤ 2.0 % with only tablet batches prepared with 10 %w/w of both microcrystalline cellulose and the test starches meeting the British Pharmacopoeia (BP 2009) specification of 0.8 - 1.0 %. The acceptable crushing strength and friability results of the tablet batches prepared with 10 %w/w of the pre-gelatinized starches can be attributed to their granule properties. Though their granules exhibited fair flowability, their higher particle consolidation must have ensured better compaction properties by promoting increased inter-particulate bonding upon compression (Oyi *et al*., 2009All the formulated tablets disintegrated within 15 min as specified by British Pharmacopoeia (BP 2009) for uncoated tablets, but the results showed a decrease in the disintegration time with the pre-gelatinized starches and also with increase in the concentration of the pre-gelatinized starches. The decrease in the disintegration times of the tablets formulated with the pre-gelatinized starches could be as a result of the higher swelling ability of the pre-gelatinized starches. Starch pre-gelatinization has been reported to increase the swelling ability of the starches and consequently decrease the disintegration times of tablets prepared with them by facilitating the absorption of large quantities of water into the tablet mass and the subsequent generation of a higher swelling force which would initiate the active mechanism of disintegration at a faster rate than the natural starch disintegrants (Guyot-Herman, 1992; Alebiowu and Itiola, 2003; Abdallah *et al*., 2016).

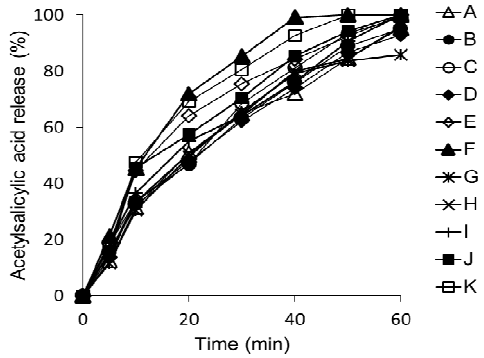

Fig 3: Dissolution profiles of the different batches of the acetylsalicylic acid tablets (A-K)

Results from the dissolution studies of the tablet batches showed a dissolution rate that is in direct correlation to the disintegration times of the tablets (Figure 3). There was an increase in dissolution rate with decrease in the disintegration times of the tablets. This is in line with the findings of some researchers who have maintained that disintegration times and dissolution are directly correlated as shorter disintegration times will invariably lead to faster and increased rate of dissolution (Rubeinstein and Wells 1997; Iwuagwu *et al*., 2001). Tablets prepared with the pre-gelatinized cassava starch were comparable in their release profiles with those containing microcrystalline cellulose. Also, all the batches of the

tablets formulated achieved almost 100 % drug release within 60 min with all the batches of tablets passing the British Pharmacopoeia (BP 2003) dissolution test for tablets, which specifies that at least 70 % of the drug should be in solution after 45 min.

*Conclusion***:** This study has shown that tablets prepared with the pre-gelatinized forms of the test starches were superior in some important tablet properties to those prepared with their native counterparts. Also the pre-gelatinized test starches compared favourably with microcrystalline cellulose, a known direct compression agent in their direct compression ability and drug release profiles especially at the concentration of 10 %w/w.

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