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Original Research Article

Assessment of the binding properties of methyl starch obtained from *Ipomoea batatas* in paracetamol tablet formulations

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Abstract

Purpose: The study assessed the binding property of methyl starch obtained from *Ipomoea batatas* starch compared to maize starch BP (MS).
Methods: *Ipomoea batatas* starch (IBS) was extracted and reacted with dimethyl sulphate to obtain methyl starch (IMS). The physicochemical and micromeritic properties of the starches were determined using standard methods prior to formulation of paracetamol tablets with the starches and maize starch BP as binder. The formulated tablets were assessed for their weight variation, crushing strength, friability, disintegration and drug release profile.
Results: The degree of substitution of IMS produced was 0.6 and the reaction efficiency was 20%. The swelling and hydration capacities of IMS and IBS were 34.52, 14.38% and 1.66, 1.88%, respectively. The micromeritic parameters; bulk density (0.53 g/mL), tapped density (0.55 g/mL), Carr's index (3.64%), Hausner's ratio (1.04), true density (2.11 g/mL) and powder porosity (2.30) of IMS were superior to those of IBS. The crushing strength and friabilityof the paracetamol tablets formulated with IMS were mechanically stronger than those of IBS and MS. Drug release from tablets formulated with IMS was however lower than those of IBS and MS.
Conclusion: The result of quality assessment of the tablets produced established IMS as suitable binder in comparison to IBS and MS in the formulation of paracetamol tablets in view of its improved crushing strength and reduced friability.

Keyword: Methyl starch, binder, tablet formulation, *Ipomoea batatas*

Indexing: Index Copernicus, African Index Medicus

Introduction

Pharmaceutical adjuncts or excipients such as binders, disintegrants, glidants, lubricants and colourants among others, are employed in the formulation of tablets in order to achieve the required bulk of a dosage form or serve as formulation aid. Binder is one of the six essential pharmaceutical adjuncts employed in the formulation of tablets, to impart cohesion to powder mix [1], ensuring intact tablets after formulation [2]. Some commonly used binders include starch, acacia, gums etc. Sweet potato (*Ipomoea batatas*) is a dicotyledonous plant that belongs to the bindweed or morning glory family, Convolvulaceae. Its large, starchy, sweet-tasting, tuberous roots [3]. *Ipomoea batatas* is native to the tropical regions in the Americas [4], but now it's widely grown and consumed in many part of Africa (including Nigeria), Latin America, Pacific Island and Asia.

Methyl starch is a modified starch that is prepared by chemical treatment of native starch in order to change its biometric and physicochemical properties. This process of modifying starch has been used in a range of industrial areas, particularly in drugs and food production due to its good filming properties and

excellent emulsion-stabilizing properties [5]. One of the most common procedure of chemical modification of native starch is by the methylation process, as it results in starch products with improved functionality and applications for various pharmaceutical and food processes. The process is carried out by substituting the OH group on the starch molecule with methyl group to produce methyl starch. The study is aimed at determining the binding property of methyl starch obtained from *Ipomoeae batatas* starch in paracetamol tablet formulations.

Materials And Methods

Materials

Ipomoea batatas tubers were purchased from the central market in Sokoto State, Nigeria. It was subsequently identified and authenticated by H. Mshelia of the Department of Pharmacognosy of Usmanu Danfodiyo University Sokoto. Magnesium stearate, talc, paracetamol, lactose and maize starch BP were gifts from Phamatex Industries Limited, Lagos, Nigeria). All other reagents used were of analytical grade.

Methods

Extraction of Ipomoea batatas starch

The procedure described by Alves *et al*. [6] was adopted with some modification. The tubers were peeled, washed and cut into pieces. The pieces were then soaked in 10 L of 0.075 %w/v of sodium metabisulphite solution overnight and then milled. The resulting paste was soaked in 20 L of water, stirred and filtered using double fold clean cheese cloth. The filtrate was allowed to settle for 3 h and the supernatant decanted. The starch sediment was centrifuged at 4000 rpm for 10min (Thermo Electron Co. IEC FL40R, France). The resultant starch was dried in a hot air oven at 45 °C for 6 h (Nurve FN055 Oven, Germany), pulverized (Super Master Co. Ltd. SMB-3377) and screened through Sethi standard sieves (250µm). The starch powder was then packed into an airtight container and stored at room temperature for further analysis.

Modification (methylation) of starch

A 50 g weight of starch powder was suspended in 200 mL of 0.1 M sodium hydoxide solution for 1 h at 40 °C. The mixture was filtered to remove excess sodium hydroxide and 50 mL of acetone and 20 mL of dimethyl sulphate were added to the mixture and allowed to react for 1 h at 40°C by shaking in a closed system. The mixtture was neutralized with 10% glacial acetic acid solution and filtered using a synthesized plate funnel. It was then washed with 3 successive portion of acetone and the final product was dried in an oven at 45°C for 6 h.

Determination of degree of substitution

About 0.5 g of the methyl starch was dispersed in 20 mL of 0.1 M NaOH and 80 mL of distlled water was added. The suspension (25 mL) was transferred to an Erlenmeyer flask and 75 mL of the distilled water was added. The excess of NaOH was back titrated with standard 0.2 M HCl using phenolpthalein as indicator. The titration was carried out three times and the average value of the HCl volume was used incalculating the degree of substitution (DS) employing Equations 1 and 2. A blank was also titrated.

$$A = \frac{BC - DE}{F} \quad (1)$$

$$DS = \frac{(0.162)\ X\ A}{1-(0.031\ X\ A)} \quad (2)$$

Where DS = Degree of substitution, A = Millilitre - equivalents of consumed acid per gram of specimen, B = Millilitre of added sodium hydroxide, C = Normal sodium hydroxide, D = Millilitre of consumed hydrochloric, E = Normal hydrochloric acid, F = Specimen gram used, 162 = Molecular weight of anhydrous glucose unit, 31 = Net increase in the anhydrous glucose unit for every substituted methoxyl group substituted.

Determination of reaction efficiency (RE)

Reaction efficiency was determine using Equation 3 as determined by Wurzburg [7].

$$RE\,\% = \frac{\%\ CH_3O\ \text{Substituted}}{\%\ Thepretical\ CH_3O\ Substituted} x\ 100 \quad (3)$$

Fourier transform infrared (FTIR)

The starch samples (5 mg) were individually blended with solid KBr (50 mg) and compressed into discs. The discswere scanned at400 - 4000 cm^{-1}using a FTIR spectrophotometer (Cary 630 Agilent technologies, USA).

Proximate analysis

Proximate analysis of *ipomoea batatas* starch is the determination of the major components of potato, which incude: moisture, lipid (fats), ash, protein, carbohydrates and fiber. The methods for proximate analysis were carried out according to standard procedure [8].

Hydration capacity

The method of Kromblum and Stopak [9] was used. A 1.0 g weight of the starch powders was placed in a 15 mL plastic centrifuge tube and 10 mL of distilled water was added and then stopped. The contents was mixed on a vortex mixer for 2 min. The mixture was then allowed to stand for 10 min and centrifuged. 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.

Swelling capacity

Using the method of Okhamafe *et al*. [10] the swelling capacity was computed using data from the hydration capacity test and Equation 4;

$$S = \frac{(V2-V1)}{V1} x\ 100\ \% \quad (4)$$

Where S is the % swelling capacity, V2 is the volume of hydration or swollen material and V1 is the tapped volume of the material prior to hydration.

Determination of pH

A 1.0 g quantity of the powder material was shaken with 50 mL of distilled water for 5 min and the pH of the supernatant liquid was determined using a pH meter (pH 1100 series, Singapore).

Moisture sorption

A 2.0 g of dried starch powder was weighed and evenly spread on a 90 mm wide Petri dish. The samples were then placed in a desicator containing distilled water in its reservoir (relative humidty ≥ 100 %) and kept at room temperature for 5 days. Weight gained by the exposed powders at the end of the period was recorded. The amount of water sorbed was calculated from the weight difference [11].

Bulk and tapped densities

A 10 g quantity of the powdered starch samples was placed in 50 mL measuring cylinder and the volume (V0) occupied by the sample without tapping determined. After 500 manuals taps, occupied volume (V500) was determined.The bulk and tapped densities was calculated as the ratio of the weight of volume (V0 and V500 respectively). The Carr's index and Hausner's ratio were determined from the values of the bulk and tapped densities results using Equation 5 and 6.

$$Carr's\ index = \frac{tapped\ density - bulk\ density}{tapped\ density} x\ 100\ \% \quad (5)$$

$$Hausner\ ratio = \frac{tapped\ density}{bulk\ density} \quad (6)$$

True density

The true density (Dt) of the starch powder were determined by the liquid displacement method as described by Ohwoavworhu [12] using xylene. Starch powder (0.5 g) was placed in a dry pre-weighed pycnometer and filled with 50 mL xylene. The weight of the pycnometer filled with only liquid (xylene) had previously been establsihed and the true density of the powder was computed according Equation 7:

$$Dt = \frac{w}{[(a+w)-b]} x\ SG \quad (7)$$

Where: W is the weight of the powder, SG is the gravity of solvent (SG 0.86), "a" is the weight of bottle + solvent and "b" is the weight of bottle + solvent + powder.

Powder porosity

This was derived from the values of the bulk and true densities of the starch powder using Equation 8.

$$e = \frac{1-PB}{Dt} x\ 10 \quad (8)$$

Where: PB is the bulk density,Dt is thetrue density and "e" is the porosity.

Formulation of paracetamol tablets

Thirteen batches of 200 mg paracetamol tablets were prepared by wet granulation method using various concentrations of the starches as binder and other excipients as indicated in Table 1. This was carried out in 5 stages. Stage 1 involves the blending of paracetamol powder, lactose and maize starch BP (internal disintegrant). Stage 2 involves the preparation of binder solution of

various concentrations as depicted in Table 1. Stage 3 involves the preparation of granules and stage 4 involves the mixing of the granules with maize starch BP (external disintegrant), talc and magnesium stearate. Finally, stage 5 involves granules compression and tablet formulation.

Table 1: Formula for paracetamol tablets formulation

Batches	Paracetamol Powder (mg)	Binders (mg)	Maize starch BP (ID) (mg)	Lactose (mg)	Maize starch BP (ED) (mg)	Talc (mg)	Mag stearate (mg)
F1	200.0	6.0	7.5	64.9	15.0	6.0	0.6
F2	200.0	12.0	7.5	58.9	15.0	6.0	0.6
F3	200.0	18.0	7.5	52.9	15.0	6.0	0.6
F4	200.0	24.0	7.5	46.9	15.0	6.0	0.6
F5	200.0	30.0	7.5	40.9	15.0	6.0	0.6
F6	200.0	6.0	7.5	64.9	15.0	6.0	0.6
F7	200.0	12.0	7.5	58.9	15.0	6.0	0.6
F8	200.0	18.0	7.5	52.9	15.0	6.0	0.6
F9	200.0	24.0	7.5	46.9	15.0	6.0	0.6
F10	200.0	30.0	7.5	40.9	15.0	6.0	0.6
F11	200.0	15.0	7.5	55.9	15.0	6.0	0.6
F12	200.0	30.0	7.5	40.9	15.0	6.0	0.6
F13	200.0	45.0	7.5	25.9	15.0	6.0	0.6

Key: ID = Internal Disintegrant, ED = External Disintegrant, F1-F5 = Native Starch as Binder (2, 4, 6, 8, and 10%), F6-F10 = Methyl Starch as Binder (2, 4, 6, 8, and 10%), F11-F13 = Maize Starch BP as Binder (5, 10, and 15%

Evaluation of formulated tablets

Weight variation

Twenty tablets (20) from each batch were weighed individually using an electronic weighing balance (Aw 320, Shimadzu, Japan), and the mean weight and the standard deviation were determine and recorded.

Disintegration time

Six tablets were randomly selected and placed individually in the six tubes of the disintegration test apparatus (Erweka, Germany) filled to the assigned level with distilled water whose temperature was thermostatically maintained at 37 ± 1 °C. The time taken for the complete disappearance of the tablet or its fragment through the 2mm mesh into the disintegrating medium was recorded for each batch.

Assay of content

A samples of 20 paracetamol tablets were weighed and powdered. To a quantity of the powder containing 0.2g of paracetamol, 25 mL of distilled water and 50 mL of 0.1M NaOH solution was added until dissolution was effected. The mixture was agitated for 15 min and sufficient water was added to produce 100mL, mixed and subsequently filtered. 10 mLof the filterate was diluted to 100mL with water and labelled as the stock solution. Finally, 10mL of the stock solution was added to 10 mL of 0.1M NaOH solution and diluted to 100mL with distilled water and absorbance of the resulting solution taken at 257 nm.

Friability

Ten (10) tablets were randomly selected form each batch, dusted and weighed..The tablets were placed in a roche friabilator (Erweka Ambh, Germany) and subjected to tumblig action at 25 revolution per minutes for four minutes. The tablets were dusted again and reweighed. The percentage weight lost was calculated with Equation 9.

$$Friability\ (\%) = \frac{(w1-w2)}{w1} x\ 100 \qquad (9)$$

Where W1 = Initial weight, W2 = Final weight

Crushing strength

Sample tablets (5) of each batch were randomly selected, then placed between the anvil and spindle of the Erweka hardness tester machine and pressure was applied by turning the knurled knot just to hold the tablet in position. The pressure was uniformly increased until the tablet cracked and the pressure required to break the tablet was then recorded.

Dissolution test

A dissolution mediumof 900 mL 0.1 M HCl solution maitained at 37 ± 0.5 °C with a basket revolution of 25 rpm was used. A 5mL volume

of leaching fluid was withdrawn at various intervals (10, 20, 30, 40, 50 and 60 min) and replaced with an equivalent volume of 0.1 M HCl maintained at same temperature (37 ± 0.5 °C) of the dissolution medium.The absorbance of the resulting solutions were measured at λmax of 245 nm. The concentration and the percentage of drug released at each time interval was determined using equation from the standard calibration plot obtained from the pure drug.

Results

The degree of substitution and reaction efficiency of *Ipomoea batatas* Methyl starch (IMS) was 0.6 and 20% respectively (Table 2.0). There was an increase in swelling capacity of IMS (34.52 %) in comparison to *Ipomoea batatas* starch (IBS) (14.38%). Introduction of methyl group onto IMS was evident as shown in the FTIR spectra (Fig 1.0) with a prominent peak at 1012 cm^{-1} corresponding to OH bond stretching.

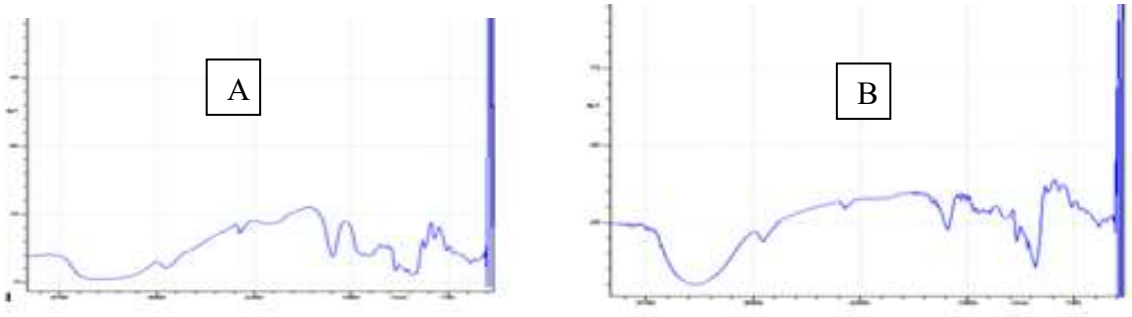

Figure 1: FTIR spectra of native (A) and methyl starch (B) obtained from *Ipomoea batatas*

There was no significant difference in the moisture (1.6 and 1.5%), nitrogen (0.084 and 0.070%), lipid (trace), fiber (trace) and carbohydrate (96.79 and 97.49%) contents of IBS and IMS respectively (Table 2.0). There was a significant increase in moisture sorption capacity (Fig. 2.0) for IMS (60.1%) as compared to the IBS (20.4%) after 5 days. A slight increase in bulk, tapped and true densities of IMS compared to IBS was also observed (Table 2.0) but with no appreciable increase in its flow characteristics as seen with the Carr's and Hausner's ratio.

Table 2: Material, proximate and micromeritic properties of *Ipomoea batatas* methyl starch (IMS) and *Ipomoea batatas* starch (IBS)

Parameters	Native Starch	Methyl Starch
Degree of Substitution	-	0.60
Reaction efficiency	-	20.00
Hydration capacity (%)	1.88	1.66
Swelling capacity (%)	14.38	34.52
pH	7.00	7.20
Moisture Content (%)	1.60	1.50
Ash (%)	1.00	0.50
Nitrogen (%)	0.084	0.070
Crude Protein	0.53	0.44
Lipids (%)	Trace	Trace
Fiber (%)	Trace	Trace
Carbohydrate (%)	96.79	97.49
Bulk density (g/mL)	0.51±0.21	0.53±0.17
Tapped density (g/mL)	0.52±0.13	0.55±0.01
Carr's index (%)	3.44± 0.11	3.64± 0.23
Hausner's ratio	1.03± 0.02	1.04± 0.06
True density (g/mL)	1.97±0.01	2.11±0.05
Powder porosity	2.25±0.55	2.30±0.27

From Table 3.0, all tablets formulated with IBS (F1 - 5), IMS (F6 -10) and MS (F11 - 13) were within compendia specification for weight variations, disintegration time and percentage drug content (Assay). Generally, for these parameters, tablets formulated with IMS (F6 - 10) showed reduction in disintegration time as compared to its IBS form but with MS showing far less disintegration time as compared to both. Tablets formulated with IMS also showed improved percentage friability over the ranges of binder concentration used as compared to those formulated with both IBS and MS (Fig. 3.0). Both tablets formulated with IBS and IMS have acceptable crushing strength (> 4.0 kgF) as compared to those formulated with MS (Fig. 4.0) with tablet batch formulated with binder concentration above 8 % surpassing 6 kgF. Although, tablets formulated with MS has an excellent drug release property (< 10 min.), IMS and IBS has optimal release of drug within 20 min. (Fig. 5, 6 and 7).

Table 3: Physicochemical properties of the tablets formulated

Batches	Weight variation (%)	Mean disintegration time (min)	Drug content (%)
F1	0.93	7.92 ± 0.08	98.70
F2	1.55	7.50 ± 0.07	101.70
F3	0.86	8.26 ± 0.57	98.60
F4	2.39	8.05 ± 0.92	103.30
F5	1.77	8.41 ± 0.25	104.00
F6	2.68	0.54 ± 0.03	100.10
F7	1.09	1.23 ± 0.66	96.51
F8	1.03	1.53 ± 0.32	102.00
F9	1.76	1.64 ± 0.09	102.50
F10	0.35	1.35 ± 0.51	98.80
F11	1.86	0.34 ± 0.08	98.30
F12	1.43	0.33 ± 0.84	99.30
F13	2.15	0.78 ± 0.44	102.88

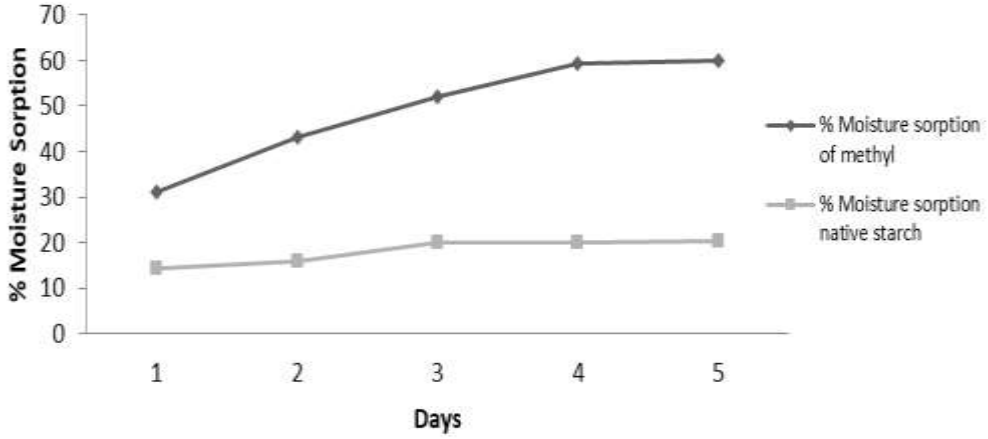

Figure 2: Moisture sorption capacity of IMS and IBS

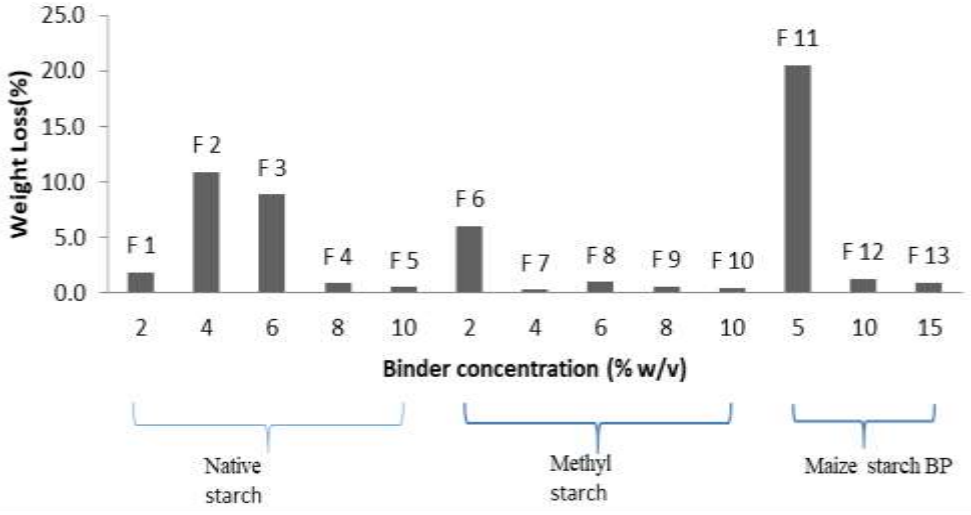

Figure 3: Friability (%) of the formulated paracetamol tablets

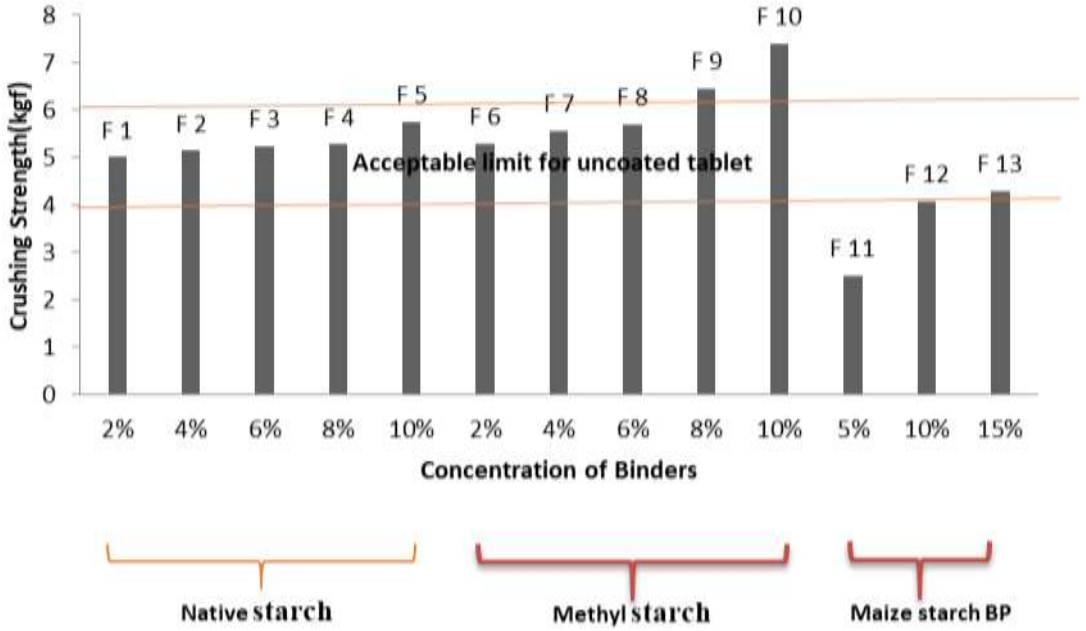

Figure 4: Crushing strength against binder concentration of the formulated paracetamol tablets (F1-F13).

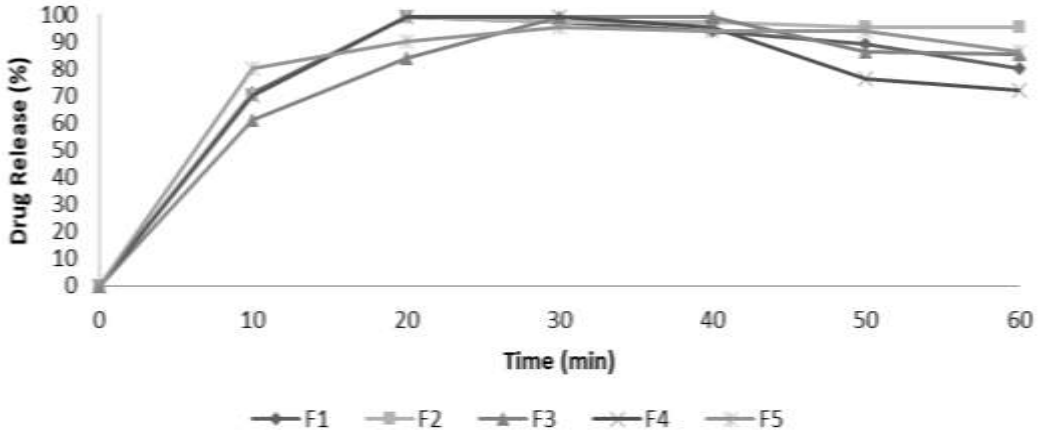

Figure 5: Percentage release of paracetamol tablet prepared using Native starch (F1-F5) against time (mins)

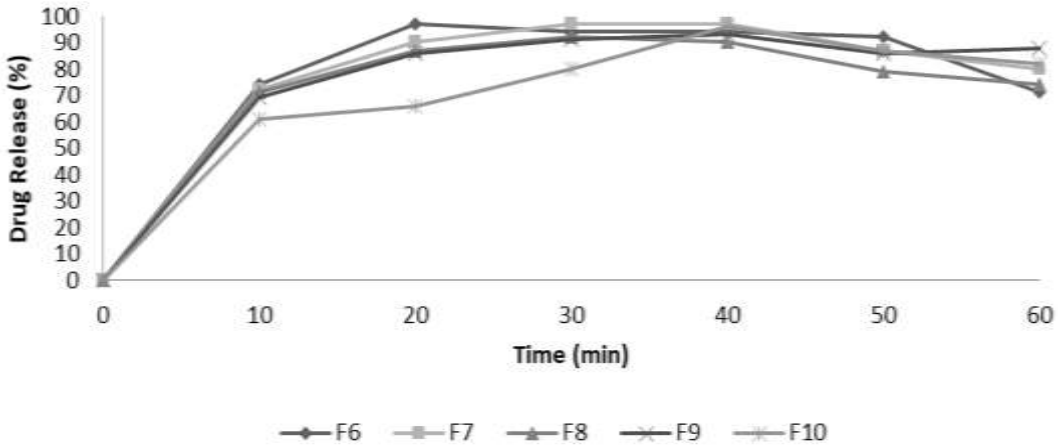

Figure 6: Graph of percentage release of paracetamol tablet prepared using methyl starch (F6-F10) against time (mins)

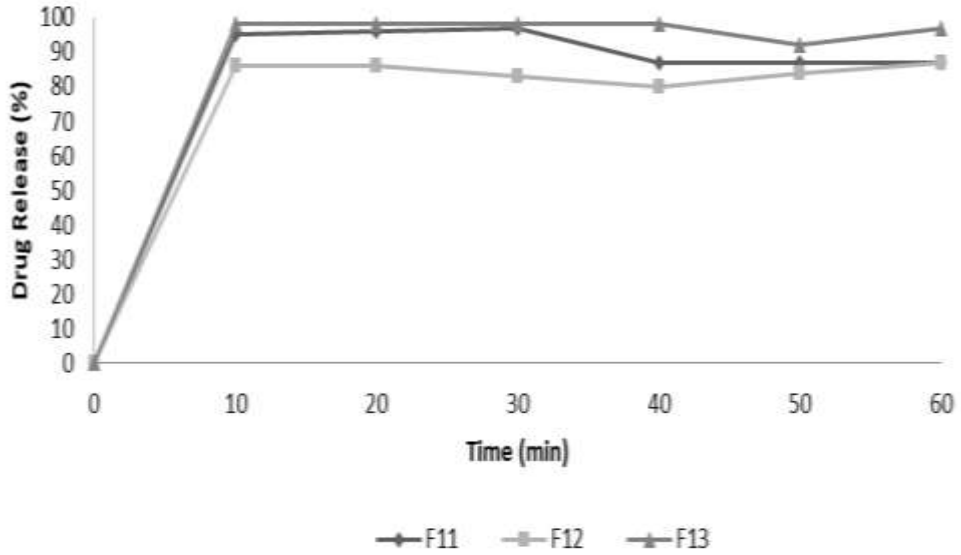

Figure 7: Graph of percentage release of paracetamol tablet prepared using maize starch (F11-F13) against time (mins)

Discussion

Methylation of granular starch in an aqueous suspension using dimethyl sulfate takes place preferably at the branched regions of amylopectin. However, the linear regions of amylopectin are substituted more heterogeneously than the branched regions [13].

Thus, low-amylose starches like rice starch are able to undergo better substitution than high-amylose starches [14] like *Ipomoea batatas* with a DS of 0.6. Increase in swelling capacity of methylated starch as compared to *Ipomoea batatas* starch (IBS) was expected due to the methyl group attached, which enhances water uptake in most polymers and hydrocolloids. Infrared spectroscopy (FTIR) was used for rapid characterization of the methylated starch sample. It can detect intermolecular interactions, especially hydrogen bonding interactions. This molecular interaction plays a crucial role in determining the tertiary structure of starch as seen with a prominent peak at 1012 cm^{-1}.

There was no significant difference in the moisture, nitrogen, lipid, fiber and carbohydrate contents between both starches and are generally within limits of these substances expected in starches [15]. Optimal level of moisture in starch (5-10%) have been shown to be essential in producing compact with high tensile strength and low friability. Low protein starch content (< 0.2%) is recommended as high protein content can influence their functional properties and result in false characterization [16]. Carbohydrate is an indirect measure of purity. A good starch for pharmaceutical application should contain more than 96 %w/w starch and as much as possible devoid of other plant component such as fiber,protein and lipid [16].

Increase in moisture sorption capacity for IMS as compared to the IBS could be as a result of increase hydrophilicity and water retention attributes of methylated hydrocolloids. High moisture sorption by material may improve the flow, compression characteristics, and hardness of granules, it may however cause materials with adhesive properties to stick to punch surface. The stability of moisture sensitive active pharmaceutical ingredient (APIS) would be adversely affected leading to reduced product shelf life [17].

A slight increase in bulk, tapped and true densities of modified starch may result to high diluents power as they substantially reduce powder bulk or volume while improving consolidation and flow [18].

Binders are added to tablet formulation to impart plasticity and thus increase the inter particulate bonding strength within the tablet [19]. By promoting plastic deformation, binders increase the degree of consolidation or compactions while

decreasing the brittle fracture tendency (capping and lamination) during tableting [20]. The resultant cohesiveness ensures that the tablet remains intact after compression [21]. The quantity of binders used has a considerable influence on the characteristics of the compressed tablets [22,23]. Increasing the binder concentration invariably raises the disintegration times [24] as can be seen with IBS and IMS. The uniformity of the tablet's features depends on the quality of the binder added to the formulation. A high concentration of binder can cause hard granulation, whilst insufficient quantity of the binder would result to fragile granulation.

Tablets formulated with MS, IMS and IBS had optimal release of drug within 20 min. The dissolution test is related directly to drug absorption and bioavailabilityand not less than 70% of the drug should be released in 30mins [15]. The rate of dissolution determines the rate and extent of absorption and subsequent therapeutic outcome of a drug.

Conclusion

In view of the improved physico-chemical, material and tableting properties of methyl starch obtained from *Ipomoea batatas*, it could serve as an alternative binder to maize starch BP in uncoated tablet formulations.

Conflict of Interest

There is no conflict of interest associated with this work.

Contribution of Authors

“We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors”. Both authors contributed to the conception, design, critical review of the article and final approval of article.

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