Physicochemical Characterization of Sucrose And Formaldehyde Modified-Starches From Maize, Wheat And Rice For Pharmaceutical Use

Ifeanyi Justin Okeke
University of Nigeria
Angus Nnamdi Oli
Nnamdi Azikiwe University
Chioma Miracle Ojiako (miracleojiako@gmail.com)
Federal University Oye-Ekiti
Emmanuel Chinedum Ibezim
University of Nigeria
Jude N. Okoyeh
Neumann University

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Abstract

Background: Starches have been shown to be important across various disciplines such as the pharmaceutical industries, food industries and also paper industries. Starch is basically a mixture of polymers consisting of a-D-glucose as the monomeric unit. The goal of this study is to modify the native starches which are gotten from *Zea mays, Triticum estivum*, and *Oriza sativa* through cross-linking using sucrose and formaldehyde at different concentrations, and assessing the utilisabilty of the modified starches as potential excipients [binder] for tabletting of Paracetamol tablets.

Method: Starch was extracted from Maize, Wheat and Rice grains and defatted. A confirmatory test was carried out on the extracted starch. The starches were treated with ethanol and crosslinked with varied concentrations of sucrose and formaldehyde. Further characterizations were carried out such as the determination of moisture content, bulk and tapped densities, effect of electrolyte on swelling behavior, viscosity and pH .

Results: Maize and rice starches cross linked with 2.5 % sucrose gave the least percentage moisture content. The batches cross-linked with 40% formaldehyde showed the highest moisture content. The densities (bulk and tapped) of maize wheat and rice starches showed a reduction with the increasing concentration of the cross-linking agent for sucrose, which is the reverse case for formaldehyde. The different concentrations of sucrose and formaldehyde cross-maize, wheat and rice starches had pH values between 4.50 and 5.52. The onset and end set of the glass transition temperatures were varied for all the starches modified with formaldehyde. The melting peak temperatures obtained indicated that the formaldehyde-modified rice starch had significantly lower melting temperature than those of wheat and maize starches.

Conclusion: The result of all the studies carried out shows that the different concentrations of sucrose and formaldehyde had effects on the various qualities of the native starches used and that the chemical agents used also had effects on the original molecular conformations of the native samples though the amorphous and crystalline structures were still present. Cross linking agents made the starch molecule more surfaces active by causing a change in conformation of the molecules at the interface hence an increase in viscosity. The starches were denatured by the cross-linking agents and this could improve their suitability for human consumption as food, cosmetic materials and even drug [as excipients].

Background

Starches and their pharmaceutical uses have been studied extensively by many researchers. Starch is found in just about all green plants in the form of a carbohydrate reserve. It is a natural polymer which is generated from carbon dioxide and water by the photosynthesis in plants [Jankovi, 2010].Starch is the chemical form of storage of solar energy [Kolawole *et al*., 2011]. It is basically a mixture of polymers which consists of α-D-glucose as the monomeric unit. Two types of starch polymers exist: a mixture of linear polymers, referred to as amylose and a mixture of branched polymers called amylopectin. These polysaccharides exist in the plant as granules that are insoluble in cold water [Perez & Bertoft, 2010]. The major intermolecular forces giving rise to the structure and integrity of the starch system are hydrogen bonds between these units and water. Starch is highly present in staple foods e.g potatoes, maize, wheat, rice and cassava [Umida-Khodjaeva,2013] as it is the commonest carbohydrate form in human diet.

Starches, especially modified starches have widespread use in pharmaceutical, food and paper industries and they contribute to the quality, appearance and structure of the food item [Hoover *et al*., 2010; Agyepong & Barimah, 2018]. Some of their pharmaceutical uses include as binder and diluents. Starches are also used in paper industries as binder for laminates and in the corrugating process, as surface sizing and coating agents. In food industries, starches and their modified forms have been used in canned, hot-filled, dry mix, baked or frozen foods, pet and infant foods, snacks and breakfast cereals, meats, dairy products, etc [BeMiller & Whistler, 2009]. Degradation of starch can be done by pre-gelatinization [Alabi *et al*., 2018]. Gelatinization employs the application of heat and water to disrupt the granular and crystalline structures of starch [Adetunji, 2019].

Cross linking of starch is a highly popular method employed in polysaccharide chemistry [Ayoub & Rizvi, 2009]. A lot of biopolymers (such as starch) are hydrophilic and some are soluble in hot water. Native starch is incompatible with some hydrophobic polymers, hence cannot be used directly[Zhang *et al*., 2015]. Cross linking is a processing method in which small amounts of compounds that have the ability to react with more than one hydroxyl group are incorporated to starch polymers. Crosslinking has shown several effects on the physical properties of starch. Cross linking of starch varies its properties due to the fact that native starch doesn't usually possess the preferred properties [Shah *et al*.,2016; Ibezim *et al*.,2006].The use of highly cross linked starch amylose matrices has been described in formulation of controlled release oral solid dosage forms. Therefore, pharmaceutically, starch is a vital ingredient and no amount of study on its uses can be exhaustive. Changing starch so that it obtains the characteristics that deviate from the native starch is called modification and the products are called derivatives. The chemical modification of starch have proven to affect the digestion rate and level in the small intestine [Haub *et al*., 2010].There have been various modifications of starch granules such as blending [Neelam *et al*., 2012; Sapsfort *et al*.,2013].It does not matter whether or not change has come about in a physical or bio-chemical manner [Piriyaprasarth *et al*.,2010].

Excipients are defined as substances that are included in a drug delivery system (aside the active drug), and have been appropriately evaluated for safety. Pharmaceutical excipients are further explained as additives which are used in converting compounds which are pharmacologically active to pharmaceutical dosage forms which are appropriatefor administration to patients [Klevin, 2011; Mohammed, 2017]. Pharmaceutical excipients should be stable physically and chemically, non-toxic, available commercially, feasible economically and possess pleasant organoleptic properties [Allamnei & Suresh, 2014].

Starch is a commonly used excipient due to its relatively low cost and versatility [Muazu *et al*., 2012]. Native starches were used in solid dosage forms (as binders and disintegrants), but they have restricted utilization due to poor flowability. Nowadays, modified or cross-linked starches are mostly preferred e.g. pregelatined starch [Mohammed, 2017]. Modification of starch enhances the starch quality for use in pharmaceuticals as drug binders and disintegrants [Adjei *et al*., 2017]. Modified Rice starch, starch acetate, etc are now established in Pharmaceutical industries as multifunctional excipients. Different forms of modified starches have also been analyzed for maintaining the release of drug for improved compliances [Felton, 2005].Acid hydrolyzed modified starch of

Plectranthus esculentus have been reported to produce fillers/binders that can be directly compressed and can serve as alternatives for MCC PH 101 (microcrystalline cellulose) in modern tablet formulations [Khalid *et al*., 2016].

The aim of this study is to modify the native starches obtained from *Zea mays, Triticum estivum*, and *Oriza sativa* through cross-linking using sucrose and formaldehyde at different concentrations, and assessing the utilisabilty of the modified starches as potential excipients [binder] for tableting of Paracetamol tablets.

Method

Extraction of Starch

The maize [*Zea mays*], wheat [***Triticum estivum***], and rice [*Oriza sativa*] grains were procured from Nsukka central market and were stored in air tight containers prior to investigations. The grains were then washed and soaked in distilled water for 24 hours. After fermenting the grains, they were each grated with an aluminum grater and the resulting marsh was macerated for 24 h in distilled water, sieved with a fine nylon sieve, and the slurry allowed to stand undisturbed for ten hours [10 h]. The supernatant was then decanted and further washed with purified water to remove any soluble impurities that may be present. The final slurry was kept to stand for another 10 h, and then it was oven dried at 60^{o}C for two (2) hours and milled. This procedure was repeated for the three sources of starch.

All procedures were carried out in conformity with all applicable agricultural resource laws and guidelines of the National and international legislations.

Defatting of Starches

This was carried out with aqueous methanol [85%] using a soxhlet extractor. A 200 g quantity of *Z. mays* starch was extracted for 24 h in a soxhlet extractor using 85% v/v aqueous methanol as solvent. The defatted starch was oven dried, then pulverized to reduce its particle size with the aid of a pestle and mortar and the resulting powder stored in well dried plastic containers. The same procedure was repeated for *T. aestivum* and *O. sativa* starches respectively.

Confirmatory tests

This was done to identify/confirm the starches. A 1 mg quantity of each starch was boiled with 50 ml of distilled water and then cooled. Mucilage was formed, to which 1 ml of iodine solution was added and observed.

Cross-linking of maize starch

A 20 g of the dried maize starch was treated with 30 ml of ethanol to make it reactive. The slurry was then filtered to get back the starch residue. A slurry of the reactive starch was made in an alkaline medium using 0.5% NaOH and different concentrations of sucrose and formaldehyde used as the cross linking agents [2.5, 5,10,20,40%]. The mixture was kept at a temperature of 40^{o}C for 30 minutes with continuous stirring. Subsequently, the pH of the mixture was further adjusted to about 5.0 with 0.1N HCl after which it was washed and dried to recover the cross linked maize starch. After drying, the particle size of the maize starch was reduced by passing through a 0.17 mm mesh. This procedure was repeated for both *T. aestivum* and *O. sativa* starches.

Starch powder characterization

Moisture Content Determination

One-gram quantity of the starch was heated in an oven at 100^{o}C for 3 hours and the weight of the starch compared with the original weight, prior to heating. This process was continued till a constant weight was obtained. This final weight was noted and used to calculate the percentage moisture content.

The following equation was used to calculate the moisture content of the sample:

$$\text{Percentage of moisture in a sample} = \frac{100(\text{Wet sample weight} - \text{Dried sample weight})}{\text{dried sample weight}}$$

Bulk Density Determination

A 20 g of starch powders was poured through a short glass funnel into a 100ml graduated cylinder.

The volume occupied was then measured and the bulk density determined. The bulk density was taken for the average of three determinations. This was repeated with the two remaining starches.

Tapped density determination

A 20 g of the starch powder was poured into a graduated 100 ml measuring cylinder and then dropped twenty times from 2.5cm height onto a wooden bench. The final volume after “tapping” was recorded and was used to calculate the tapped density. This was repeated for the other two starches.

Determination of the Effect of Electrolyte [NaCl] on swelling behaviour

Ofner *et al*.[1986]'s method was used with a slight modification:

About five different concentrations of NaCl [2.0 N, 1.0 N, 0.5 N, and 0.1 N] were carefully added to the starch samples in a 10 ml measuring cylinder and the NaCl solution was allowed to get absorbed by the starch after which the unabsorbed solution was decanted. The product was left to stand at room temperature for 48 h. This was done for each of the cross linked starches which were prepared with varying concentrations of cross link agents [sucrose and formaldehyde]. The changes in volumes of the starches were recorded and the swelling extents calculated after 48h.

pH determination

This was done for the various batches formulated using a pH meter by inserting the pH meter into the slurry of the product and checking for the stabilization of the pH reading before taking the reading.

Viscosity

A 1% gel was prepared by dispersion of 1 g of starch in 20 ml of distilled water. The starch dispersion was heated using a water bath at a temperature of about 80 to 100^{o}C for 3 minutes while being continuously stirred to gelatinize. The gelatinized starch was raised up to 100 ml with distilled water and stirred for complete homogeneous mixture. A part of the starch solution was then poured into a U-tube viscometer and its viscosity determined. This test was done in triplicates and the results were recorded. The viscosity determination was carried out at room temperature.

Differential scanning calorimetry (DSC)

Investigations of the thermal transitions of the starch samples was done using a heat-flux calorimeter (DSC-204 F1 Phoenix®, NETZSCH, 6.240.10 apparatus, Germany) calibrated using an indium of high purity standard. A 1 mg starch sample was weighed into a high temperature Nimonic steel pan and a large quantity of water was added which yielded a starch/water ratio of approximately 1:3. The pan was sealed, equilibrated (for 3 h at 25 ^{o}C), and also heated at a rate of 3^{o}C/min, from 25 to 220 ^{o}C. The transition temperatures were the onset gelatinization temperature (To), peak temperature (Tp), and also the conclusion temperature (Tc). The Enthalpy of gelatinization was related to the dry mass of the sample.

Results

Yield of extractions

The percentage weight of starch extracted from *Zea mays* grain, *Triticuma estivum* and *Oryza sativa* are 48.3% w/w, 27.5% w/w and 17.3% w/w respectively.

Confirmatory Test

The result of the starch identification test according to the British Pharmacopeia [2002], showed that product from *Zea mays, Triticuma estivum* and *Oryza sativa* were positive to iodine solution.

Properties of cross-linked starches

Percentage Moisture Contents: From the result in Table 1, maize and rice starches cross- linked with 2.5% of sucrose gave the least percentage moisture content. Wheat starch, combined with 10%, 20%, 40% sucrose and 2.5% formaldehyde also had 20% moisture content. While, in all the starches, the batches cross-linked with the 40% formaldehyde had the highest moisture content.

Table 1
The moisture content determination

Cross Linking Agent	Comparative % Moisture Content		
	Maize	Wheat	Rice
Native starch	30	35	25
2.5% sucrose	20	40	20
5% sucrose	40	40	40
10% sucrose	40	20	40
20% sucrose	40	20	40
40% sucrose	40	20	40
2.5% formaldehyde	40	20	40
5% formaldehyde	40	40	40
10% formaldehyde	40	40	40
20% formaldehyde	40	20	40
40% formaldehyde	50	40	40

Bulk and tapped density: The bulk and tapped densities of maize, wheat and rice starches, as presented in Table 2, showed a decrease with a rise in the concentration of the cross linking agent for sucrose, while in formaldehyde, reverse was the case in some cases. The bulk and tapped densities of maize

decreased as concentration of the cross linking agent for sucrose increases, while in formaldehyde, the reverse is the case. The sucrose cross-linked maize starch had greatest bulk and tapped density of 25 and 35g/ml respectively, while formaldehyde cross-linked also had highest bulk and tapped density of 27 and 40 g/ml. The 20% sucrose cross- linked maize starch has the highest Carr's index of 42.4 and Hausner's ratio of 1.74 while 40% formaldehyde cross-link had highest Carr's index of 32.5 and Hausner's ratio of 1.48 which showcase poor flowability of the starch powder.

The bulk and tapped densities of wheat starch reveals, that 40% sucrose cross-linked wheat starch powder had the highest bulk and tapped density of 37 g/ml and 55 g/ml respectively. Similarly, the 2.5% formaldehyde cross-linked wheat starch powder had the least bulk and tapped density of 9 g/ml and 13 g/ml. The bulk and tapped density of rice starch powder was significantly influenced by the moisture content as the bulk density reduced greatly with a rise in moisture content. The result revealed that, 40% sucrose rice cross-linked starch had the highest bulk density of 39.5 g/ml, and 10% formaldehyde cross-linked rice starch powder had better Carr's index of 11.8 and Hausner's ratio of 1.13. Also 5%, 10%, 20% and 40% formaldehyde cross-linked rice starch powder with Carr's indices 12.2, 11.8, 12.8 and 12.5 and Hausner's ratio of 1.14, 1.13, 1.15 and 1.14 respectively had good flowability.

From the results further physicochemical profiles of the different cross-linked starches are shown in Table 3. The percentage swelling of the native starches of maize, wheat and rice are higher than the cross-linked derivatives. The highest swelling for the cross-linked starches was observed in both sucrose and formaldehyde cross-linked rice starch, while the least swelling was observed in 5% and 40% sucrose cross-linked maize and wheat starches.

pH;The different concentrations of sucrose and formaldehyde cross- linked maize, wheat and rice starches had pH values between 4.50 and 5.52. The 5% formaldehyde cross-linked wheat starch had the highest pH of 5.53, while 20% formaldehyde sucrose cross-linked rice starch had the lowest pH of 4.5. The pH of almost all the concentrations of sucrose and formaldehyde cross-linked maize, wheat and rice starches with cross-linked maize and rice had pH above 5. While the exception of 10%, 20% and 40% formaldehyde cross-linked maize and rice starch had pH below 5 respectively. The sucrose and formaldehyde cross-linked maize, wheat and rice starches had acidic pH between of 4.50 and 5.55.

Table 2
The bulk and tapped densities of cross-linked the three starches

Cross linked agent	Bulk Density[g/ml]			Tapped Density[g/ml]			Carr's Compressibility index [%]			Hausner's Ratio		
	Maize	Wheat	Rice	Maize	Wheat	Rice	Maize	Wheat	Rice	Maize	Wheat	Rice
Native Starch	38	47	28	44	52	43	13.6	9.6	34.9	1.16	1.12	1.54
2.5% sucrose	25	32	21.5	35	45	34	28.6	29	36.8	1.40	1.41	1.58
5% sucrose	21	19	27	30	23	35	30.0	17.4	22.9	1.43	1.21	1.30
10% sucrose	20	35	16	32	50	26	37.5	30	38.5	1.60	1.43	1.63
20% sucrose	23	24	29	40	32	35	42.5	25	17.1	1.74	1.33	1.21
40% sucrose	11	37	39.5	15	55	47	26.7	32.7	16	1.36	1.49	1.19
2.5% formaldehyde	18	9	19	22	13	24	18.2	30.8	20.8	1.22	1.44	1.26
5% formaldehyde	22	18	18	31	23	20.5	29.0	21.7	12.2	1.41	1.28	1.14
10% formaldehyde	20	20	15	24	25	17	16.7	20	11.8	1.20	1.25	1.13
20% formaldehyde	24	23	15	32	33	17.2	25.0	30.3	12.8	1.33	1.43	1.15
40% formaldehyde	27	25	14	40	37	16	32.5	32.4	12.5	1.48	1.48	1.14

Table 3
Further physicochemical profiles of the cross-linked maize, wheat and rice

Cross Linking Agent	% Swelling			pH			Viscosity [CP]		
	Maize powder	Wheat powder	Rice powder	Maize starch	Wheat starch	Rice starch	Maize starch	Wheat starch	Rice starch
Native starch	40	58.3	49.5	6.12	5.84	6.27	150.0	152.0	149.0
2.5% sucrose	42	44	71	5.47	5.40	5.01	143.2	145.3	150.0
5% sucrose	41	54	68	5.52	5.35	5.28	145.6	143.0	147.0
10% sucrose	47	44	72	5.12	5.41	5.23	146.0	146.0	148.0
20% sucrose	48	63	71	5.47	5.40	5.03	148.4	148.0	152.0
40% sucrose	42	42	72	5.50	5.47	5.13	152.0	149.0	149.7
2.5% formaldehyde	76	44	72	5.35	5.47	5.11	142.0	147.0	145.0
5% formaldehyde	66	62	72	5.05	5.53	5.10	146.5	147.5	147.0
10% formaldehyde	56	64	75	4.77	5.26	5.04	149.0	145.0	148.0
20% formaldehyde	48	43	70	5.18	5.50	4.50	151.0	150.0	146.5
40% formaldehyde	44	46	72	5.54	5.13	4.74	150.7	149.2	149.4

Table 4
Thermal properties of starches modified with formaldehyde

Parameter	Thermal property (value) per %						Thermal property (value) per %						Thermal pro	
	Wheat						Maize						Rice	
Concentration	2.5%	5%	10%	20%	25%	40%	2.5%	5%	10%	20%	25%	40%	2.5%	5%
Tg Onset temp (°C)	42.7	39.0	42.60	28.90	43.40	34.70	38.5	37.6	39.6	33.3	38.4	40.6	23.4	28
TgEndset temp (°C)	39.0	48.5	41.60	30.40	69.50	50.10	41.4	43.2	44.6	55.1	47.3	45.9	32.7	35
ΔH (Delta Cp) (J/(gk))	5.365	8.214	2.354	6.471	42.291	14.060	5.577	11.47	19.388	27.829	23.5	7.129	20.12	18
Melting/Endothermic Peak Temperature (°C)	300.1	304.5	310.6	299.50	284.30	297.10	291.1	297.6	302.3	297.6	298.8	298.2	173.2	18
Peak intensity (m/N/mg)	-0.3896	-0.119	-1.007	2.151	-1.43	0.1424	0.9706	1.02	1.037	0.3403	0.732	0.644	-4.968	-5.

Melting/Endothermic Peak temperature [°C]*Key: Tg = Glass Transition; ΔH = Energy change

Thermal properties of cross-linked starches

As observed in Table 4, the onset and end set of the glass transition temperatures [Tg] were varied for all the starches modified with formaldehyde. The energy changes [ΔH], for the glass transition were also varied at the various concentrations of formaldehyde used. At 2.5% formaldehyde concentration, the ΔHs were 5.365, and 5.577 J/[gk],for the wheat and maize starches, respectively. At 20% formaldehyde concentration, the ΔHs, were 6.471, 27.829 and 10.265 J/[gk] for the wheat, maize and rice starches, respectively. At 40%, the ΔHs were 14.060, 7.129 and 13.870 J/[gk] for the wheat, maize and rice starches, respectively.

Table 5 shows the effect of the thermal [DSC] treatment of the defatted and undefatted wheat, maize and rice starches as analysed. For the defatted starch, the onset temperatures of the Tg were of the order: wheat › rice › maize while that of the end set were: wheat › maize › rice. However, there was no significant difference between the end set temperatures of the defatted wheat and maize starches. The ΔHs, obtained for the defatted starches were of the order: maize › wheat › rice with significant differences between the values obtained. However, the melting peaks were recorded at 292.9°C, 285.2°C and 287.5°C for the defatted wheat, maize and rice starches, respectively, showing only slight differences. Considering the maize starch, both the onset and end set temperatures of the glass [Tg] as well as the energy change [ΔH] recorded were higher for the undefatted than the defatted.

Table 5
Thermal properties of defatted and undefatted starches

Thermal properties	Defatted starches			Undefatted starches		
	Wheat	Maize	Rice	Wheat	Maize	Rice
Tg Onset temp [°C]	40.3	31.0	36.4	37.2	35.6	31.8
TgEndset temp [°C]	49.7	48.8	41.3	28.5	56.6	49.4
ΔH [Delta Cp][J/[gk]]	13.226	22.604	10.125	32.42	29.6	16.865
*Peak Temperature	292.9	285.2	287.5	279.5	284.7	282.2
Peak intensity [m/N/mg]	0.8362	0.9534	0.1582	1.041	1.041	1.256

Melting/Endothermic Peak temperature [°C]

*Key: Tg = Glass Transition

ΔH = Energy change

Discussion

Native starch cannot be used in a vast range of starch applications due to the fact it cannot exhibit the desired properties. The desired properties can be obtained by the modification of native starch. Most commonly used method is the chemical modification of starch molecules. More so, by using specific moisture and temperature conditions, there can be alterations in the physicochemical properties of starch since a lot of physical modifications involve the use of water and heat [Senanayake *et al*., 2013]

Cross- linked maize and rice starch had the highest pore sizes that trap the highest amount of water resulting to the highest moisture content. At 40% formaldehyde concentration, the moisture content of maize when treated with 40% formaldehyde is the highest as compared to wheat and rice. This shows that treatment with formaldehyde has a direct proportional effect on maize starch i.e., the percentage moisture contents varied but generally increased with increase in level of cross-linker [Oladunmoye *et al*.,2014; Belibi *et al*.,2014]. However, the variation in the concentration of formaldehyde treatment on rice showed a constant effect on moisture content. In all the starches, the batches cross-linked with the 40% formaldehyde had the highest moisture content.2.5% sucrose gave a decrease in the moisture content of maize and rice, while 10, 20 and 40% sucrose gave a reduced effect in wheat starch. This shows that a raise in the concentration of sucrose gave an inversely proportionate effect on the moisture content of wheat starch. High moisture content may lead to enzyme activation and microbial proliferation. Low moisture content usually shows a high level of stability during storage, protecting starches from growth of moulds, and giving a high yield of dry weight [Jubril, 2012]. Percentage moisture contents close to 12% and above will provide enough moisture for drug degradation and microbial activities [Odeku *et al*., 2005].

The flow properties of powders are important in assessing the adequacy of a material as a direct compression excipient. Hausner index and Carr's percent compressibility are regarded as indirect ways of measuring the flow property of powder. The Hausner index reflects inter-particle friction, while the Carr's index shows the ability of a material to reduce in volume. Hausner ratio which is higher than 2.5% signifies poor flow, Carr's index less than 16% signifies good flowability while values more than 35% signifies cohesiveness. As the value of these indexes increase, there is a reduction in the flow of the powder and this increases the likelihood of producing tablets with more weights variation [Okunola & Odeku, 2011]. All starches from all the sources had an Hausner's ratio less than 2 and Carr's index greater than 16% (except for 10%, 20% and 40% formaldehyde treated starches). Wheat cross-linked with 5% sucrose, had a good flow ability with Carr's index of 17.4 which indicates low flowability and chances of producing tablets with weight variation [Jubril, 2012].Bulk, tapped and true densities are the usually measured density values which are used to analyses the major properties of powders. Bulk density gives details on the volume occupied by the inter-granular spaces, inner and external pores of the solids. Bulk density indicates the overall degree of packing in a specific volume. Tapped density is referred to as the density after tapping or vibration. The bulk densities of maize reduced with a rise in the concentration of sucrose and increased with an increase in concentration of formaldehyde. Wheat and rice showed a slight irregularity at 10% and 40% sucrose, and decreased with an increase in the concentration of formaldehyde. The tapped densities showed an irregular/wavy effect at different concentrations of sucrose and formaldehyde. This shows that the rise in concentration of the cross-linking agents enhances the bulk and tapped density of the starch powder.

Swelling is widely accepted as an assessment of tablet disintegration ability. From the results obtained for swelling profile of different cross-linked starches in Table 3. The percentage swelling of the native starches of maize, wheat and rice are higher than the cross-linked derivatives, and could be attributed to the fact that cross linked starches experienced granule modification that decreased the hydration capacity. Increase in concentration of cross linking agent led to an increase in the amount of cross-links and this confers a greater stability on the starch granule. Therefore, the water absorption reduction was more pronounced at higher concentrations of the cross-linkers. Presumably, cross linking has an effect on the easy access of water to the starch. This in turn causes a reduction in the swelling properties of the cross linked polymer [Yu *et al*., 2016]. Porosity determines the swelling ability of starch. The higher the porosity, the more the inter-particulate spaces where water could be absorbed [Carmona-Garcia *et al*., 2009]. The increase in the ionic strength of the cross-linked starch decreased the osmotic pressure inside the charged paste and a reduction in its swelling. Cross-linking caused a high elastic contraction of polymer network which counteracted the swelling process. Hydration which leads to swelling is dependent on the type and number of hydrophilic groups in the polymer structure. The highest swelling for the cross-linked starches was observed in both sucrose and formaldehyde cross-linked rice starch, while the least swelling was observed in 5% and 40% sucrose cross-linked maize and wheat starches. Swelling power is a parameter that is analysed in theory of

disintegration, which must be preceded by water penetration, therefore the high percentage swelling of sucrose and formaldehyde cross-linked rice starches to compare with the native starch will enhance disintegrating properties of tablets formulated with, more than others in this studies.

All cross-linked starches showed an overall slight reduction in their pH as compared with the native starch. The pH of almost all the concentrations of sucrose and formaldehyde cross-linked maize, wheat and rice starches with cross-linked maize and rice had pH above 5. While the exception of 10%, 20% and 40% formaldehyde cross-linked maize and rice starch had pH bellow 5 respectively.

Swelling and Viscosity of cross linked are the very important and useful features of assessing the level of cross-linking. Table 3 also illustrates the dependence of viscosity of starch on the concentration and type of cross-linkers. It is observed that the viscosity of the cross-linked wheat and rice decreased as the concentration of the cross-linker increases for the two cross-linkers except for maize which showed a slight increase at 40% sucrose and formaldehyde. Also the viscosities of the cross-linked starches were generally different from those of the non-cross-linked (Native) ones. In general, the viscosities of the native starches were more than those of the cross linked starches. This is in conjunction with Shah *et al*., [2016], that the degree of peak viscosities of cross-linked starches is inversely proportional to the concentration of crosslinking agent. Starch with a greater crosslinking level will show a lesser peak viscosity as compared with starch with lesser crosslinking levels.

The thermal properties of the defatted and undefatted wheat, maize and rice starches were also analysed as shown in Table 5. For maize starch, both the onset and end set temperatures of the glass (Tg) as well as the energy change (ΔH), recorded were higher for the undefatted than the defatted. This shows that the process of defatting probably lowered the intermolecular forces within the starch sample leading to the requirement of less energy for the Tg process. Except for the onset temperature, similar trend was observed for the rice starch. There were no significant differences between the melting peaks recorded for the undefatted and defatted starches.

Considering the thermal parameters of the defatted and formaldehyde – modified wheat starches, it was shown that the Tg took place at lower temperatures for the samples treated with 2.5–20% formaldehyde. However, with increased formaldehyde concentrations up to 25–40%, the Tg occurred at much higher temperatures. Similar trend was observed for the ΔHs involved in the transitions. The melting peaks generally occurred at slightly elevated temperatures for the formaldehyde-modified wheat starch samples. These observations indicate that the chemical modification resulted to wheat starch of a more ordered (crystalline) molecular conformation than the natural moiety. In comparison with the sucrose-modified wheat starch, the end set temperature of the Tg as well as the ΔH were significantly higher than for the formaldehyde – modified sample. However, the melting endotherm was higher for the formaldehyde – modified wheat starch than for the sucrose-modified sample.

For the formaldehyde-modified maize- starch, the onset temperatures of the Tg were obviously greater than that of the defatted maize starch for the various range of concentrations tested. The end set temperatures were however lower except at 20% formaldehyde concentration. Similarly, the ΔH for the Tg of the defatted maize starch was higher than those of the formaldehyde – modified except at 20% formaldehyde concentration. The melting peaks of the formaldehyde-modified maize starch were greater than for the untreated defatted sample. In comparison with the sucrose-modified maize starch, the onset temperatures were also higher than for the untreated and defatted samples. The onset of transition occurred at approximately similar temperature except at 10% sucrose concentration where it was significantly much higher. The results showed that the ΔHs for the Tg were generally higher for the formaldehyde than the sucrose – modified maize starches except at 20% chemical agent concentration where the latter had significantly higher value. The melting peaks generally occurred at higher temperatures for the formaldehyde-modified maize starch than the sucrose – modified except at 2.5% chemical agent concentration where the reverse was the case.

Both the onset and end set temperatures of the Tg for the formaldehyde-modified rice starch were greater than for the untreated and defatted sample. However, the ΔHs for the Tg of the crosslinked rice starch samples were higher than for the untreated sample. On the other hand, the melting peaks of the formaldehyde-treated rice starch samples occurred at really lesser temperatures compared to the untreated sample.

For the sucrose-modified rice starch, the onset and end set Tg occurred at higher temperatures, at 2.5% sucrose concentration than for the untreated but defatted sample. However, the onset and end set Tg occurred at lower temperatures when the sucrose concentration was increased to 5%. The ΔHs for the Tg were also higher for the sucrose-modified rice starch than for the untreated sample. However, the melting peak of the untreated but defatted rice starch was significantly higher than for the sucrose-modified samples. In comparison with the formaldehyde-modified rice starch, the sucrose-modified had higher onset and end set temperatures for the Tgs. Varied results were obtained for the ΔHs and the melting peak temperatures. The overall results obtained for the various modified starches showed that the chemical (cross-linking) agents used had effects on their original molecular conformations of the native samples though the amorphous and crystalline structures were still present as indicated by the glass and melting transitions. The changes were due to the cross-linking of the starch moieties by the functional groups in the chemical agents used. The extent of changes might partly be attributed to the level of amorphosity and crystallinity of the original starch molecules. The resultant effect is that new starch motifs were produced with perhaps improved or new functionalities as pharmaceutical excipients.

Conclusion

The result of all the studies carried out shows that the different concentrations of sucrose and formaldehyde had effects on the various qualities of the native starches used and that the chemical agents used also had effects on the original molecular conformations of the native samples though the amorphous and crystalline structures were still present. Cross linking agents made the starch molecule more surfaces active by causing a change in conformation of the molecules at the interface hence an increase in viscosity. The starches were denatured by the cross-linking agents and this could improve their suitability for human consumption as food, cosmetic materials and even in drug formulation as excipients [fillers/binders].

Declarations

ABBREVIATIONS

- DSC

DECLARATION OF INTEREST

NONE

Additional Information

Ethics Approval and consent to participate

Not Applicable

Consent for publication

Not Applicable

Availability of data and material

All data and material are available in the manuscript

Conflict of Interest

The Authors declare that they have no conflicting interest

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Author's contribution

ECI conceived and designed the work. IJO participated in the design, laboratory work and data collection. ANO and CMO drafted the manuscript. JNO read the work for intellectual content. All authors have read and approved the manuscript.

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