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Design and Preliminary Characterization of Sweet Potato Starch – Urea-Borate Polymer

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background – Sweet potato (*Ipomoea batatas*) starch has been reported for its potential as a directly compressible and sustained-release polymer in its native and modified forms. Chemical modification by crosslinking with urea and borax to form starch urea-borate will enhance its drug release-retarding properties.

Objective – To design starch-urea-borate (SUB) polymer using sweet potato starch to produce a new, affordable biodegradable polymer, and carry out preliminary characterization of the polymer.

Method – Native starch was extracted from sweet potato tubers and crosslinked with urea and borax to form starch-urea borate (SUB) polymer. The native and modified starches were characterized for morphology (SEM), FT-IR, DSC, pH, densities, swelling, flow properties and viscosity.

Results – Modification yielded 96.66% w/w of SUB and disrupted the granular structure of the native starch, producing significantly larger ($p<0.01$) granules with irregular shapes. FTIR spectrum revealed a peak at 3369.05 cm^{-1} due to $–NH_2$ confirming the presence of a secondary amide resulting from the polymerization reaction between urea and starch in the presence of borate. A shift in the peak of DSC endotherm was observed for SUB. Modification yielded lower particle density but higher bulk and tapped densities. The swelling index increased significantly ($p<0.01$). Hausner's ratio (1.06± 0.00), Carr's index (6.33± 0.01%) and angle of repose (26.14±1.15º) showed good flow but reduction in compressibility of SUB. Viscosity revealed shear thickening or dilatant behaviour.

Conclusion- The material and physicochemical properties of SUB polymer showed its potential for application in drug delivery systems, possibly as a release retarding polymer.

Keywords: Flow properties, Sweet potato starch, Starch-urea-borate, Controlled release polymer

INTRODUCTION

Polymers used as release-retarding materials play a critical role in the design of controlled-release drug delivery systems. The effectiveness, availability and cost of different classes of polymers are important considerations in the formulation of controlled drug delivery (Uhrich *et al* 1999). Even though a wide range of release-retarding polymers are available, there is a continued need to develop new, more efficient and cost-effective polymers for controlled release (Adepu and Ramakrishna, 2021). Synthetic or semi-synthetic polymers such as hydroxypropyl methylcellulose (HPMC) appear to be popular choices for the formulation of matrix systems for controlled delivery. However, starch is also widely used owing to its availability, versatility, inert nature, cost-effectiveness, biodegradability, eco-friendly characteristics, and adaptability to various modifications (Yongsong *et al*, 2005; Compart *et a*l, 2023). Several studies have been reported to evaluate local, underutilized starches with high yield and

relatively low cost for pharmaceutical applications as polymers (Adeoye and Alebiowu, 2014; Okunlola and Ghomorai 2018; Adetunji, 2020).

Sweet potato (SP) (*Ipomoea batatas* Lam), family Convolvulaceae, is a low-cost and readily available vegetable crop that is cultivated extensively for its nutritious value in many regions of the world, including Nigeria. Sweet potato is among the most important versatile and underutilized food crops, grown mainly for its large, sweet-tasting, starchy tuberous roots (Tortoe, 2010). The tuber has a high percentage of starch (58 -76%w/w) with properties such as thickening, binding, and filling (Issa *et al*, 2016). Sweet potato starch in its native form has been evaluated as a diluent, binder and disintegrant in tablet formulations. The results established sweet potato starch as a more effective pharmaceutical diluent, binder and disintegrant, compared to the commercially available corn starch (Bayor *et al*, 2013). Acid-hydrolyzed sweet potato starch was also reported to impart good compaction properties in tablets and was found suitable as a directly compressible excipient. (Akin-Ajani *et al*, 2014). In another study, floating bilayer tablets of ambroxol hydrochloride were prepared and evaluated using native and acid-modified sweet potato starches as immediate and sustained-release polymers, respectively (Okunlola, 2022).

METHODOLOGY

Materials

Sweet potato tubers were obtained from local farmers in Ibadan, Oyo State, Nigeria. Borax was from Chem Private Limited, New Delhi while Urea was from EuroChem Zug, Switzerland. Xylene was from ACS Chemicals Sarkhej, Ahmedabad, India. All other reagents were of analytical grade.

Methods

Extraction of Sweet potato starch

Sweet potato tubers were washed with distilled water, peeled, rinsed again and then cut into small pieces. The small pieces were milled into a fine paste using a laboratory mill and the slurry was strained through a muslin cloth. The filtrate was left to settle. The supernatant was decanted at 12 h-interval and the starch slurry re-suspended in distilled water. The starch cake was collected and dried in a hot-air oven at 50ºC for 48 h. The dried mass was pulverized using a laboratory blender and then screened through a 125-µm mesh sieve (Okunlola, 2022).

It is known that starch reacts with urea to form starch carbamate, a starch–urea cross-linked polymer. Khalil *et al* (2002) investigated the reactions between starch and urea resulting in the formation of starch cross linked with urea. Starch, when cross-linked with urea using sodium borate as a catalyst, results in the formation of the polymer starch-urea borate (SUB). This new polymer has been utilized in the formulation of the pesticide acetamiprid for controlled release (Yongsong *et al*, 2005). In other studies, a polymer matrix made of starch, borax, and urea was used in formulating controlled-release tablets of diclofenac and gliclazide (Chowdary and Murali-Krishna, 2009) and to encapsulate the insecticide, deltamethrin, in a controlled-release formulation (Kumar and Chowdary, 2019). It appears from the literature search that no research work has been carried out on cross-linking sweet potato starch to form starch-borate -urea forms with a view to characterizing the material properties of the local starch and evaluate its potential as a sustained release polymer. Thus, this study aims to design starch-urea-borate polymer prepared with sweet potato starch (SUB) and carry out the preliminary characterization of SUB by determining some material and physicochemical properties of the native and modified starches.

Preparation of starch- urea- borate

Starch–urea–borate was synthesized by gelatinizing sweet potato starch in the presence of borax and urea (Kumar and Chowdary, 2019). Sweet potato starch (50 g) was dispersed in 100 mL of purified water to form starch slurry. Borax (10.0 g) and urea (15.0 g) were dissolved separately in 400 mL of purified water, and the urea and borax solutions were mixed and then heated to boiling. While boiling, the starch slurry was added to the mixture, and mixing was continued for 10 min while heating to gelatinize starch and form starch–urea–borate polymer. The mass formed was spread onto a stainless-steel plate and dried at 60°C for 6 – 8 h. The dried polymer was powdered and passed through a mesh of 250 µm. The percentage yield of the modified starch (%w/w) was determined from the quantity of dried SUB polymer obtained divided by the quantity of sweet potato starch powder (50 g) used in the modification.

Characterization of starches
Morphology

The morphology of the native starch and starch-urea-borate polymer were observed using a scanning electron microscope (Phenom-ProX desktop SEM, Phenom-World, Eindhoven, The Netherlands) at an accelerating potential of 15.0 kV. The mean particle size and shape of 300 starch granules were determined using an optical microscope (Olympus XSZ-107BN, Shinjuku, Japan.

Fourier Transform Infra-red (FT-IR) analysis

The starches were analyzed by Fourier Transform Infra-red FTIR spectroscopy (FTIR spectrum BX II by Perkin Elmer, USA) in transmission mode. Transmission spectra were recorded using at least 64 scans with 8 cm^{-1} resolution in the spectral range 4000-400 cm^{-1}

Differential Scanning Calorimetry (DSC)

DSC thermogram of starch – urea – borate was recorded on DSC 2, Mettler Toledo, Ohio, USA. Samples (2-5 mg) were sealed into aluminum pans and scanned at a heating rate of 10ºC min^{-1} over a temperature range of 35 – 350ºC.

pH

The pH of 1% w/v suspension of the samples was measured using a pH meter (Model 720 A, Thermo Electron Corporation, MA, USA) at 25°C.

Swelling index

Sample (5 g) was placed into a 100-mL measuring cylinder and the volume occupied was noted (V1). Distilled water (90 mL) was added; the dispersion was shaken for 2 min and then made up to volume. The slurry was allowed to stand for 24 h before the sedimentation volume was read (V2). The swelling index was calculated as:

$$V2 \,/\, V1 \qquad (1)$$

Determinations were done in triplicate.

Particle density

A 50 mL pycnometer was weighed empty (W), filled with the non-solvent (xylene) and the excess wiped off. The weight of the pycnometer with the non-solvent was determined (w1). The difference in weight was calculated as W2. A 2 g quantity of the sample was weighed (W3) and quantitatively transferred into the pycnometer bottle. The excess non-solvent was wiped off the pycnometer and weighed again (W4). The particle density was calculated from the equation:

$$\frac{W2W3}{50(W3-W4+W2+W)} gcm^{-1} \qquad \ldots.(2)$$

The determination was done in duplicate.

Bulk and tapped densities

The bulk density of the starch powder at zero pressure (loose density) was determined by pouring 10 g of powder at an angle of 45º through a funnel into a glass measuring cylinder with a volume of 50 mL. The bulk density was measured as the ratio of mass to volume occupied by the starch. Determinations were done in triplicate. The tapped density was measured by applying 100 taps to 10 g of starch sample in a graduated cylinder) at a standardized rate of 30taps per minute. Determinations were done in triplicate.

Flowability

The flowability of the starches was evaluated with the Hausner's ratio and Carr's index using the values of bulk and tapped densities:

$$Hausner's\ ratio = \frac{Tapped\ density}{Bulk\ density} \qquad (3)$$

$$Carr's\ Index = \frac{Tapped\ density - Bulk\ density}{Tapped\ density}\ x100 \qquad (4)$$

Angle of repose

An open-ended cylinder was placed on a base of similar diameter. Sample (5 g) was allowed to flow freely through a funnel under gravity, to form a conical heap. The angle of repose was calculated from:

$$Tan\ \theta = h/r \qquad (5)$$

Where h is the height of the powder and r is the radius of the base of the cone. The angle of repose was calculated from the average of three determinations.

Viscosity

The viscosity of 1% w/v aqueous slurry of native and modified starches was determined at various shear rates 20, 50 and 100 rpm on Brookfield rheometer (DV-III + model, Brookfield Engineering, USA) using CPE 40. Spindle no 3.

RESULTS AND DISCUSSION

The yield of starch from sweet potato tubers was 23.50 %w/w. This was comparable with those reported in the literature, 15 – 28 %w/w on a dry weight basis (Wang, 1984). The yield is a function of species, soil and climatic environment. Starch derivatives are prepared by reacting some other components with the hydroxyl groups in the native starch molecules to produce modified starch with different physicochemical properties without compromising their biodegradability (Zang, 2001; Pareta and Edirisinghe, 2006). The yield of starch-urea-borate (SUB) obtained from the native starch was high at 96.66%, indicating the efficiency of the modification process. The starch–urea–borate polymer was characterized using microscopy, FTIR, DSC, pH and physicochemical properties and the results are discussed below:

Morphology

The scanning electron micrographs (SEM) of native and modified sweet potato starches are shown in Fig. 1. SEM of native sweet potato (NSP) starch revealed largely oval and polygonal granules with striations and mean particle size of 10.47±3.74 µm. The modification process resulted in disruption in the granular structure of the native starch producing significantly larger ($p < 0.01$) granules with irregular shapes of mean size of 29.99±3.05µm and rough and porous surfaces.

Fourier Transform Infra-red (FT-IR) analysis

The FTIR spectra of native starch and SUB are presented in Fig. 2. The spectrum of the native starch showed the characteristic broad absorption bands of O-H stretching at 3430.45- 3333.30 cm^{-1} as in Figure 2a. In addition, the bands at 1675.09- 1593.81 cm^{-1} are attributed to characteristic C=C stretching on the anhydroglucose ring which is present in both native and modified starch. In Figure 2b, SUB has different peaks at 405.14cm^{-1},1462.74cm^{-1}(C=C), and 1593.21cm^{-1} (C=C). The peaks at 2925.84 cm^{-1} (O=C stretch) and 1271.99 cm^{-1} (fingerprint region) indicate the presence of α- amylose. The presence of IR absorption peaks at 3301.8 cm^{-1} due to –N-H and at 1668.72 cm^{-1} due to – C = O and 996.21 cm^{-1} due to NH_2 stretch indicated the presence of urea in the polymer. These peaks show the presence of secondary amide in the SUB sample. In a secondary amide, the amido-group (nitrogen) is directly bonded to two carbon atoms. This secondary amide was produced during a polymerization reaction between urea and starch in the presence of borate (Jin *et al*, 2010).

Differential Scanning Calorimetry (DSC)

The DSC endotherm peaks of native sweet potato starch appeared between 62 and 98.5°C (Fig 3). The difference in gelatinization temperatures among starches has been attributed to the interplay of three factors: the molecular structure of amylopectin, the starch composition and their granular architecture. On the other hand, the gelatinization range is dependent on differences in the degree of heterogeneity of crystallites within the starch granules (Gunaratne and Hoover, 2002). A melting peak was observed for SUB at 66.5ºC which corresponds to the melting of urea present in the polymer, confirming the modification of the starch (Kumar and Chowdary, 2019).

Physicochemical and material properties

The physicochemical and material properties of the native and modified starches are presented in Table 1.

pH

The pH of the SUB polymer was 7.4, higher than the acidic pH of the native starch. The SUB polymer, like most polymers with higher pH, will have appeal in drug delivery because they display good biocompatibility while being able to interact with drug molecules to enhance wettability, adsorption and adhesion, which can control drug release from delivery systems. Polymers used in drug delivery systems may swell, collapse or change, depending on the pH of their environment. The pH-sensitivity of cationic polymers makes them suitable to mask the

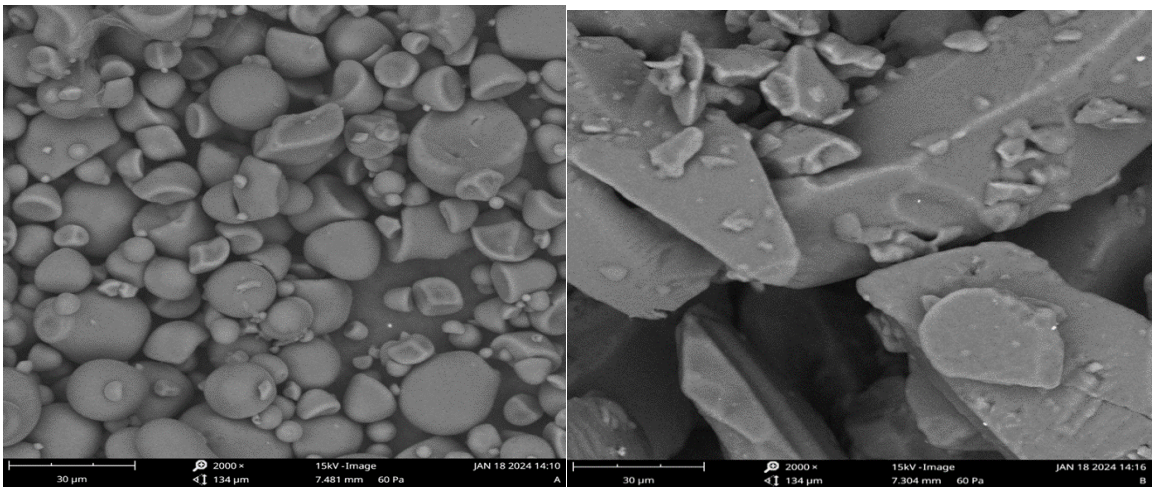
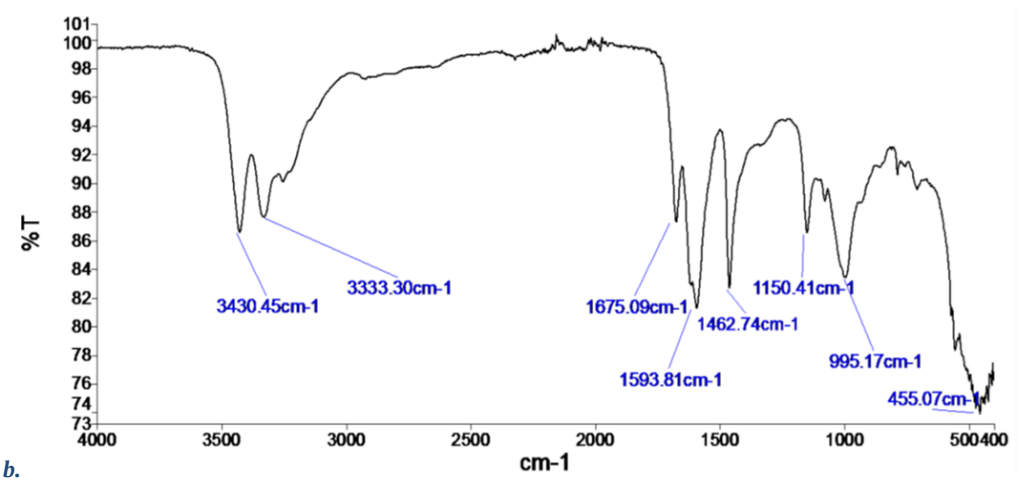


Figure 1: Scanning electron micrographs (SEM) of (a) native sweet potato starch and (b) SUB (mg x 2000)

a.



b.

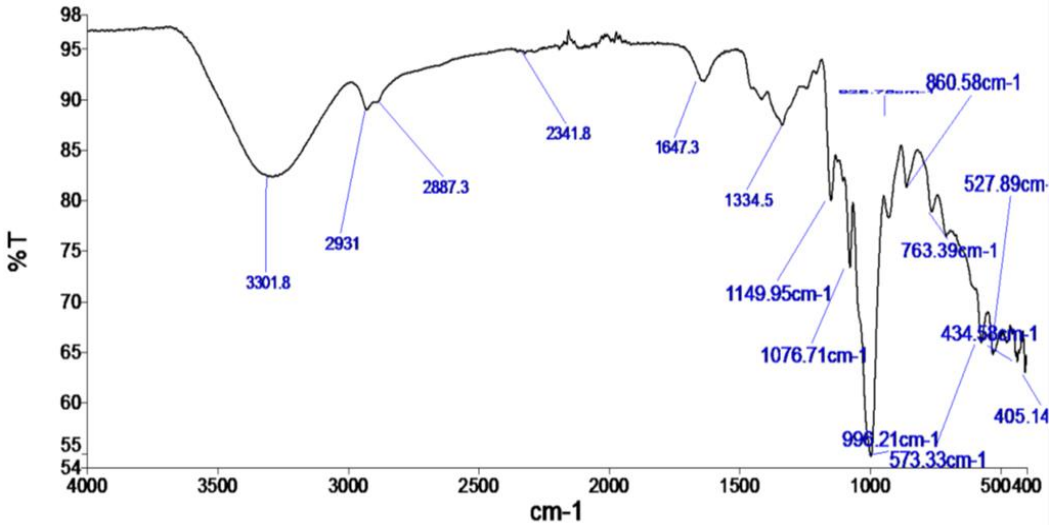
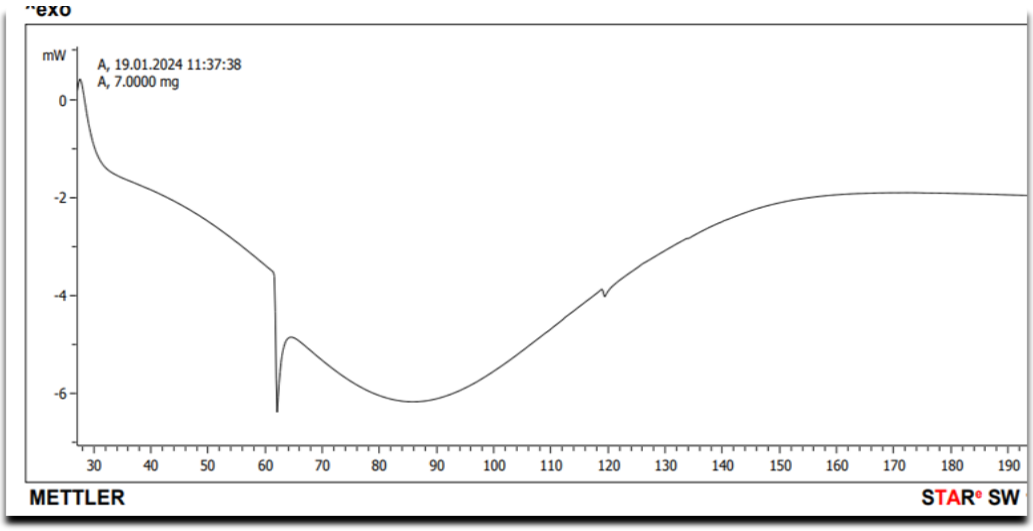


Figure 2: FT-IR spectra of (a) native sweet potatoes (b) sweet potatoes -urea-borate

a



b

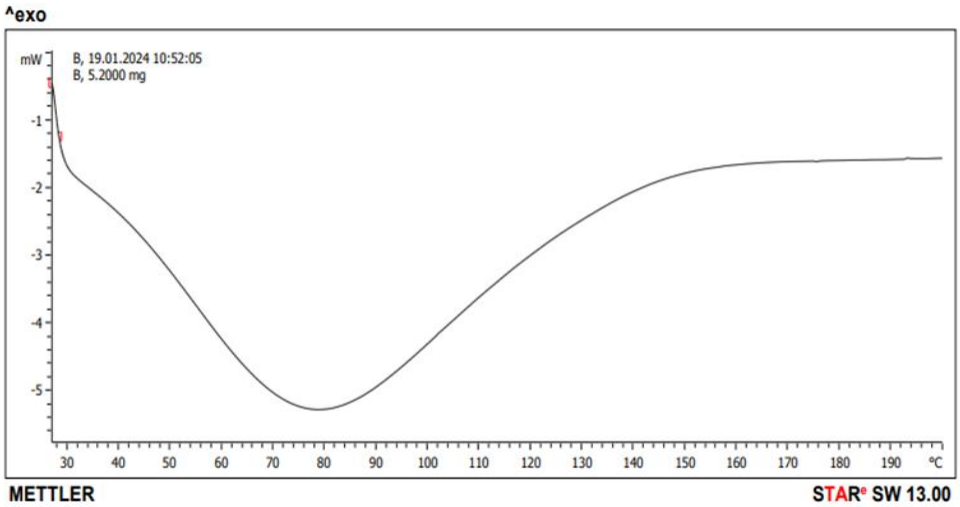


Figure 3: DSC endotherms of (a) native sweet potato starch and (b) SUB

Table 1: Material properties of the native sweet potato starch and sweet potato starch-urea-borate polymer (SUB)

Starch	pH	Particle density gcm^{-3}	Bulk density gcm^{-3}	Tapped density gcm^{-3}	Hausner's ratio	Carr's Index %	Angle of repose °	Swelling Index	Viscosity cP		
									30 rpm	50 rpm	100 rpm
Native	6.5	1.37±0.02	0.69±0.01	0.80±0.01	1.15	13.75	30.70°±1.25	1.50±0.00	3300	5000	9000
SUB	7.4	1.19 ±0.03	0.74 ±0.01	0.79±0.01	1.06	6.33	26.14°±1.15	3.91±0.24	3300	4000	7000

mean ± SD, n=3

obnoxious taste of drugs and release drugs in the low pH of the stomach. Anionic polymers responsive to intestinal high pH are used for preventing gastric degradation of drugs, colon drug delivery and achieving high bioavailability of weak basic drugs (Yoshida *et al*, 2013).

Swelling

The swelling index of the native and modified starches is presented in Table 1. Modification of the starch significantly enhanced its cold-water swellabilty owing to the disrupted and loosened structure of the SUB polymer (Singh *et al*, 2011). Most swellable, biodegradable polymers are used to modify drug release. The swelling increases the aqueous solvent content within the drug formulation as well as the polymer mesh size, enabling the drug to diffuse through the swollen network into the external environment (Adepu, and Ramakrishna 2021).

Densities

Particle density has been observed to affect the compaction behavior of powders since dense and stiff powders require higher compression pressure to produce formulations with improved mechanical strength and cohesive impact (Mbang *et al*, 2015). Modification of sweet potato starch resulted in lower particle density for SUB as presented in Table 1. The decrease in densities observed after modification may be closely related to a decrease in the cohesiveness of the powders. The bulk density of a starch powder describes its packing behavior while the tapped density indicates the rate and extent of packing that would be experienced by the material when subjected to low pressure. The bulk and tapped densities of SUB were less than the density of water, suggesting its potential usefulness as a polymer in the formulation of floating drug delivery systems.

Flow properties

The values of the Carr's index and Hausner's ratio were obtained from the bulk and tapped densities. The Carr's index and Hausner's ratio measure compressibility and flowability of the powder. The lower the Carr's index the better the flowability but the poorer the compressibility. Carr's index of 5-10, 12-16, 18-21 and 23-28 represent excellent, good, fair and poor flow properties, respectively (Carr, 1965). The Carr's index of SUB was lower than that of the native starch, implying better flow properties. Hausner's ratio indicates the degree of densification that could result from the vibration of the feed hopper, for example, during tableting. Hausner's ratio ≥1.35 to ≥1.12 indicates poor flow properties and good flow properties respectively. The SUB had lower values of Hausner's ratio indicating that upon modification, the flowability was improved and compressibility reduced.

The angle of repose of a powder is also an important qualitative measurement in determining powder flow properties. It has been used in qualitative measures of cohesiveness or the tendency of powdered or granulated materials to resist flow. The angle of repose of NSP was 30.70°±1.25 while that of SUB was 26.14°±1.15. These results further confirm that modification of native sweet potato starch into SUB improved flow properties and minimized cohesiveness, suggesting SUB can be suitable as an excipient in the formulation of tablets and other solid dosage forms such as microspheres in the controlled delivery of drugs.

Viscosity

Viscosity is an important property of starches that may determine their utility in various industrial applications (Gryszkin *et al*, 2014). The viscosity of a fluid is a measure of its resistance to gradual deformation by shear stress or tensile stress. In the formulation of controlled release delivery systems viscosity increased with speed suggesting shear thickening or dilatant materials. At similar speed, cross-linking of native starch with urea (in the presence of borax) reduced the starch's sensitivity to water by minimizing water uptake, resulting in lower viscosity for the aqueous slurry of SUB. Drug release has been reported to be somewhat influenced by the

such as microspheres, the viscosity of the polymer solution or dispersion is known to influence the drug release properties of the delivery system (Obeidat and Price, 2003; Maderuelo *et al*, 2011). The viscosity values of both native and modified starches at different speeds are presented in Table 1 It was observed that

viscosity of the polymer (Bettini *et al*,1994). Lower viscosity of a formulation permits the active drug substance diffuse more easily than high viscosity because of the inverse relation between viscosity and drug release property (Velissaratou and Papaioannou 1989).

CONCLUSION

Sweet potato starch was thermally processed with urea and borate to form starch-urea-borate polymer (SUB). The presence of urea and borate in the starch

dispersion altered the physicochemical and material properties of the final product (SUB). FTIR spectra confirmed modification to SUB, showing a new peak

at 996.21 cm^{-1} that indicated the presence of secondary amide produced during the polymerization reaction between urea and starch in the presence of borate. SUB had larger granules, higher pH that suggest biocompatibility, enhanced swelling and flow properties, suggesting its potential usefulness as a polymer in drug delivery systems. Future research following the design and preliminary characterization of this new starch-based polymer will employ sweet potato starch-urea-borate polymer in gastro- retentive floating microspheres of an antihypertensive agent and evaluate it for controlled delivery of the drug.

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