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Rifampicin-loaded Silver-starch Nanocomposite for the Treatment of Multi-resistant Tuberculosis

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Abstract

Extraction, purification and synthesis of acetylated cassava starch was undertaken. The degree of modification for the acetylated (modified) starch was calculated to be 0.03. Physicochemical indices interrogated were all significantly ($P<0.05$) affected by the acetylation. Microstructural studies revealed starches that were predominantly polygonal in shape. The FTIR results confirmed introduction of an acetyl group with a new band at 1728 cm^{-1}. The results further show that, the modification did not degrade the granule morphology, but x-ray pattern showed increased crystallinity in the acetylated derivative. Thermogravimetric analysis and differential scanning calorimetry revealed 2 phase decomposition of both starches and improved gelation capacity with new peaks respectively. Rifampicin (RIF) loaded starch-stabilized silver nanoparticles yielded good mean particle size (248 nm), polydispersity index (0.276) and zeta potential (18.68 mV). There was a significant ($P<0.01$) sustained release of RIF from the nano formulations up to 14.0 h. Antimicrobial susceptibility tests show that, the nano formulation exhibited good antimicrobial activity. It is therefore concluded that, acetylated cassava starch could be a good stabilizer and vehicle for drug delivery.

Keywords: Cassava starch; Acetylation; Physicochemical properties; Nanoformulation; Rifampicin

Introduction

Cassava, *Manihot esculenta Crantz* is an important food crop in Nigeria, growing well in all upland conditions from the humid regions of the south to the semi-arid regions of the middle belt. Although Nigeria is the largest producer of cassava (an abundant source of starch) in the world [1], there is no scientifically acceptable processing technology, and the Pharmaceutical Industries in Nigeria still import 100% starch, implying lack of value addition to starch-based sources like cassava in Nigeria.

Starch and starch derivatives play very important roles in biopolymer industries [2]. This is because they are cheap, non-toxic, renewable and compatible with many other materials for industrial applications. Applications in food [3,4], environmental management [5,6], agriculture [7], pharmacy [8], biomedical engineering [9] and textiles [10] have been reported widely in the literature. Native starch are generally unsuitable for many industrial applications largely because they are not amenable to the harsh conditions [2]. To overcome this shortcoming, modifications are usually done to enhance or repress the inherent property of these native starches or to impact new properties to meet the requirements for specific applications. Processing technology has been reported to affect the biochemical properties of starches [2,11-14]. In a separate report, dry processing of Faba beans resulted in some cellulose and lignin being present in the starch [12], while the use of enzymes in the biosynthesis and isolation of starch from three varieties of maize hybrids has been reported to affect its biochemical properties [12,13]. As a matter of fact, we opine that, the significance of various modifications on starches of different origins which has been expounded in the literature [10,13,15-21], would only be more meaningful now if we start looking at the application of these derivatives in drug delivery, hence this study.

The therapeutic outcome of drug administration depends to a great extent on its effective and efficient release from its dosage form without which the disease may aggravate further [22]. A typical example of this is witnessed in the case of the first line drugs of tuberculosis. Tuberculosis (TB) patients are usually prescribed multiple oral administrations of the first line drugs (e.g., rifampicin) daily for at least six months. This makes patient adherence to the prescribed drugs difficult, thereby precluding effective treatment of the disease [22]. There is urgency therefore in not only discovering new drug molecules but also for developing new effective drug delivery systems [22]. Such a system should have sustained release property in order to facilitate the release of the drug over a longer period of time so that multiple daily administration of the drug is not required [22,23]. Starch based drug delivery systems [24-31] have been proposed with its implicit advantages of targeted delivery in enhancing its therapeutic value and sustained release minimizing frequent drug dosing [32].

Modified starches also have found useful applications in the pharmaceutical, food, paper and textile industries as binders, disintegrants, fillers, emulsion stabilizers, adhesives and are currently attracting the interest of researchers in this respect.

The aim of the work reported herein was to undertake a comprehensive investigation of the starch obtained from *Manihot esculentus*, secondly, to chemically modify the starch by acetylation and investigate the effect of the acetylation on the physicochemical and functional properties of the starch and finally to evaluate the ability of the acetylated starch to deliver rifampicin appropriately.

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Materials and Methods

Isolation, purification, modification and characterization of starch

Starch extraction and purification was carried out according to the method earlier reported by Kunle et al. [33], while the method of Sathe and Salunkhe [13] was adopted for the starch acetylation. Both native and modified starches were subjected to a comprehensive characterization such as degree of acetylation, total and acid insoluble ash, moisture content and pH, angle of repose, bulk and tapped densities, Hausner's, compressibility and solubility indices, amylose and amylopectin, foam, emulsion and water absorption capacities, gelatinization temperature, scanning electron microscopy (SEM), x-ray powder diffraction (XRD), Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC) and thermogravimetric Analyses (TGA) [34-37].

Drugs, organisms and reagents

Materials: The raw materials used in this study were native cassava starch (NCS), acetylated cassava starch (ACS) and Rifampicin (RIF) was a gift from Lupin Pharmaceutical, India, cassava starch was extracted and derivatized in our laboratories. *E. coli* (ATCC 35218), *S. aureus* (ATCC 29213), *P. aeruginosa* (ATCC 27853), two *M. tuberculosis* isolates; IEQ12 and MDR204 were used in the study. All other reagents were of analytical grade obtained from standard companies. Three clinical isolates; *K. pneumonia, S. paratyphi, C. albicans* were obtained from the Microbiology Laboratory of the University of Abuja Teaching hospital.

Microbiological procedure

For drug sensitivity testing, BACTEC MGIT 960 was used following manufacturers manual. Standard concentrations of streptomycin, rifampicin, Isoniazid and Ethambutol as well as the nanoformulations were prepared into the MGIT tube to obtain the following final drug concentrations in the medium: 1.0 ug/ml for Streptomycin, 0.1 ug/ml for Isoniazid, 1.0 ug/ml for Rifampicin, 5.0 ug/ml for Ethambutol, 40 and 80 ug/ml for ACS. The instrument did the final interpretation and reported the susceptibility results automatically.

Preparation of silver-drug-starch (Ag/drug/starch) nanocomposites

To gelatinized starch dispersion, 1 M $AgNO_3$ was added under constant stirring for 1 h, followed by the drug to obtain [Ag (drug/Starch)] $^{+}$. A 20 ml aliquot of a freshly prepared sodium borohydride ($NaBH_4$) was then added to the sol and the mixture was heated to 40 °C and was maintained at this temperature for 24 h. Then, obtained suspension of Ag/drug/Starch nanocomposites was lyophilized.

Effect of nanoparticles on Antimicrobial Activity

The disk inhibition zone assay was used to qualitatively evaluate the antimicrobial activity of the nanocomposites using the method of Pelissari et al. [38]. The optimized nanocomposite formulation with and without (control) RIF and silver nitrate were aseptically placed on plates containing Mueller-Hinton (MHA) agar which had been previously spread with 0.1 mL of inocula, each containing 10^8 CFU mL^{-1} of bacterial cultures, previously standardized using the McFarland scale. The plates were incubated at 37°C for 24 h. The diameter of the growth inhibition zones around the nanocomposites was measured using a pachymeter. The assay was repeated six times for the optimized formulation and six additional times on a different day with the formulation, to ensure reproducibility of results. The reported MIC correspond to at least three identical values out of six measurements. The RIF concentration in the optimized formulation used was 80 µg/ml.

Statistical analysis

Statistical analysis was carried out using analysis of variance (ANOVA) using GraphPad Prism® (GraphPad Software Inc. San Diego, USA). Tukey-Kramer's multiple comparison tests was used to compare the physicochemical parameters of the starches. At 95% confidence interval, P-values less than or equal to 0.05 were considered significant.

Results and Discussion

Table 1 shows the organoleptic properties of the starches. The color was generally off white and the powder had a gritty, non-sticky feel with bland taste. Generally, starch modification was found to reduce the physicochemical indices interrogated in this study. For example, the foam capacity of ACS was found to be 10.00%, which was lower than that of NCS (15.60%), while the emulsion capacity of ACS which was found to be 75.00% was higher than that of NCS (53.10%).

Microstructurally, there was no discernible differences between the native and acetylated starches (Figure 1). Similarly, as can be seen from Figure 2, the X-ray pattern of the native and acetylated starches are significantly similar. All the samples gave the characteristic A pattern with strong peaks at about 15, 17, 18, 19 and 23° θ. The DSC thermograms for NCS and ACS are shown in Figure 3 respectively and the corresponding parameters are tabulated in Table 2. Both starches showed two endothermic peaks and one enxothermic peak. The peaks however, became slightly sharper after acetylation. All these observations point to the fact that, this modification did not have destructive effect on the starch. The infrared spectra of the NCS and ACS are shown in Figure 4. The results of Thermo gravimetric analysis for NCS and ACS are presented in Figure 5. Acetylation was found to increase the swelling capacity of the starch significantly ($P<0.05$) implying that there was weakening of associative forces in the starch molecules. Similar observations have been reported in the literature including a previous study reported from our lab [2,22,39,40]. The degrees of crystallinity were 49.3 and 53.3% for NCS and ACS respectively, suggesting that, acetylation did not have any significant effect on the crystallinity of cassava starch. The To, Tp and Tc were respectively 90.6, 93.5 and 95.3°C for NCS, and 87.3, 88.1 and 90.1°C for ACS. The gelatinization enthalpies (δH) were 29.48 and 18.72 J/g for NCS and ACS respectively.

Antibiotic susceptibility tests for four first line drugs and the nanocomposites (NC) at concentrations of 40 µg/ml and 80 µg/

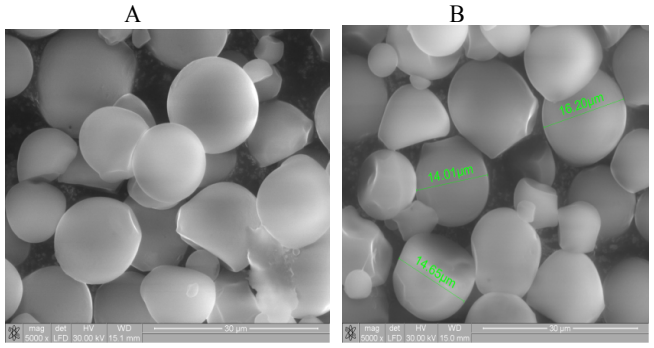

Figure 1: SEM of native (A) and acetylated (B) cassava starches.

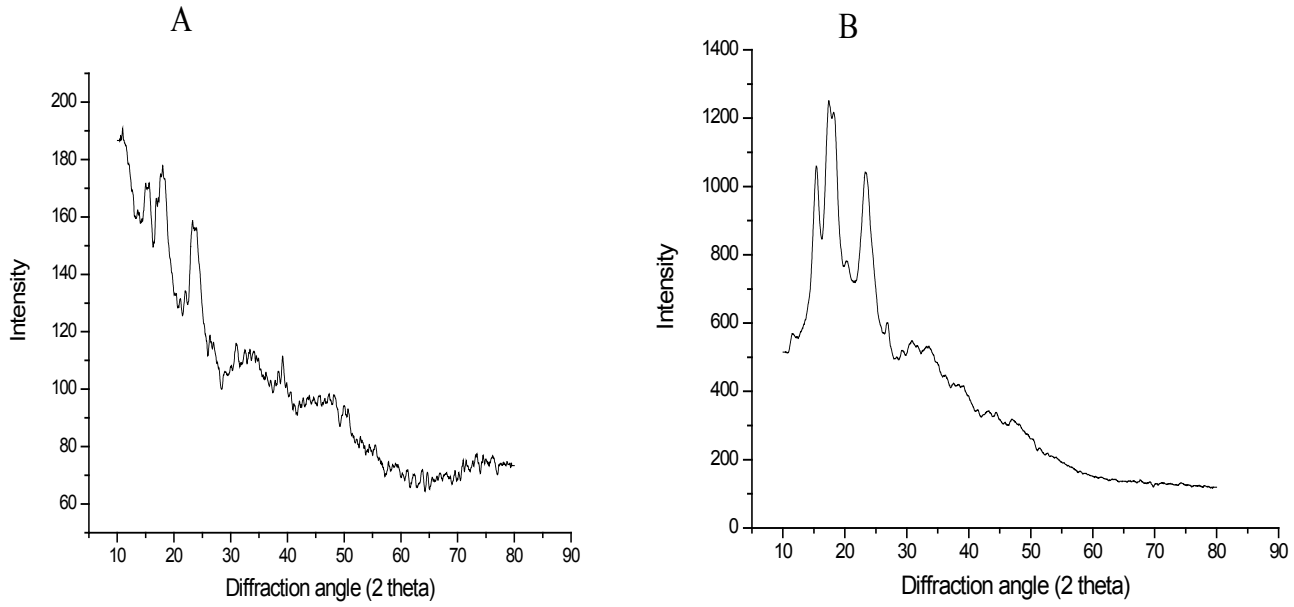

Figure 2: X-ray diffractogram of native (A) and acetylated (B) cassava starches.

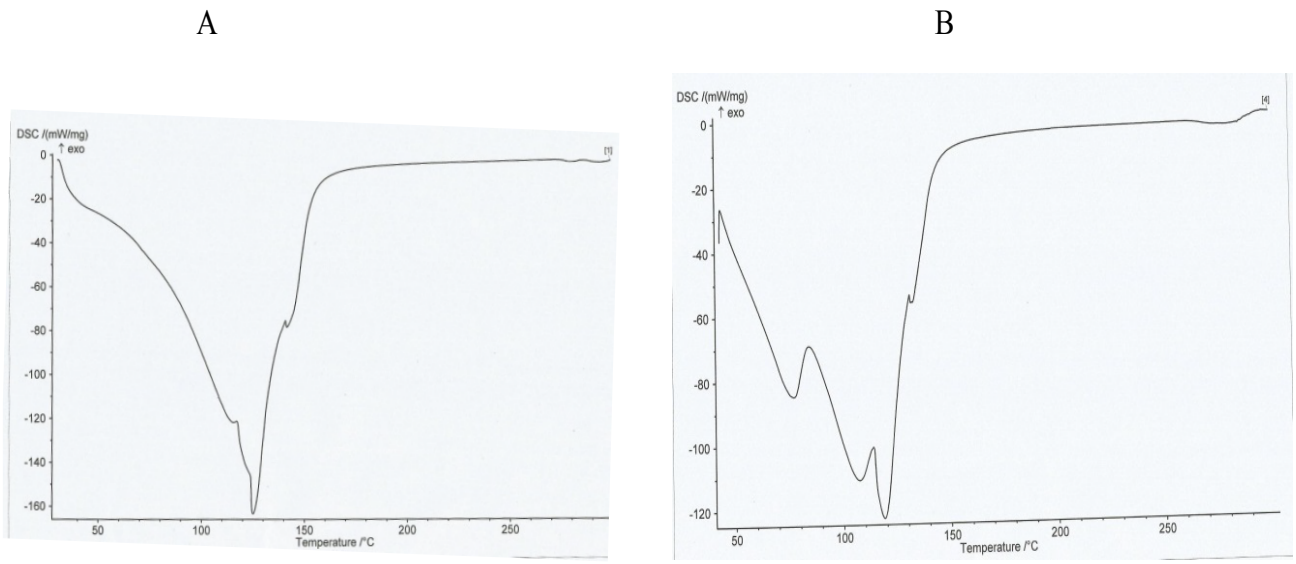

Figure 3: DSC thermograms of native (A) and acetylated (B) cassava starches.

ml as well as the formulations without the drug (nRIFForm) and silver (nAgForm) against drug resistant strains of *Mycobacterium tuberculosis* using BACTEC Mycobacteria Growth Indicator Tube (MGIT) 960 system is represented in Table 3. From the results, both isolates IEQ 12 and MDR 204 were susceptible to Rifampicin and the NC at the interrogated concentrations (40 µg/ml and 80 µg/ml). Both *M. tuberculosis* isolates were resistant to ethambutol, isoniazid and streptomycin as well as the formulations without drug and silver. The minimum inhibitory concentrations (µg/ml) of the NC against some pathogenic microorganism are shown in Table 4. The NC showed an MIC of 5000 µg/ml against *Klebsiella pneumonia*, *E. coli*, *S. aureus*, *C. albicans*, *S. paratyphi* and MIC of 2500 µg/ml against *P. aeruginosa*. Its MIC against *M. tuberculosis* was 3800 µg/ml. The formulations without drug and silver did not exhibit any zone of inhibition, hence was not measured.

Both NCS and ACS were dried under the same condition, therefore, the reduction in moisture content may be as a result of the substitution of the hydroxyl groups on the starch molecules as found also in other previous reports [2]. The reduction observed with the total and acid insoluble ash after acetylation may be attributed to the washing away of the mineral contents of the starches during acetylation [41]. The decrease in pH of cassava starch after acetylation was not unexpected as the introduction of acetyl groups on the starch molecules was expected to increase the acidity of starch molecules. The increase in

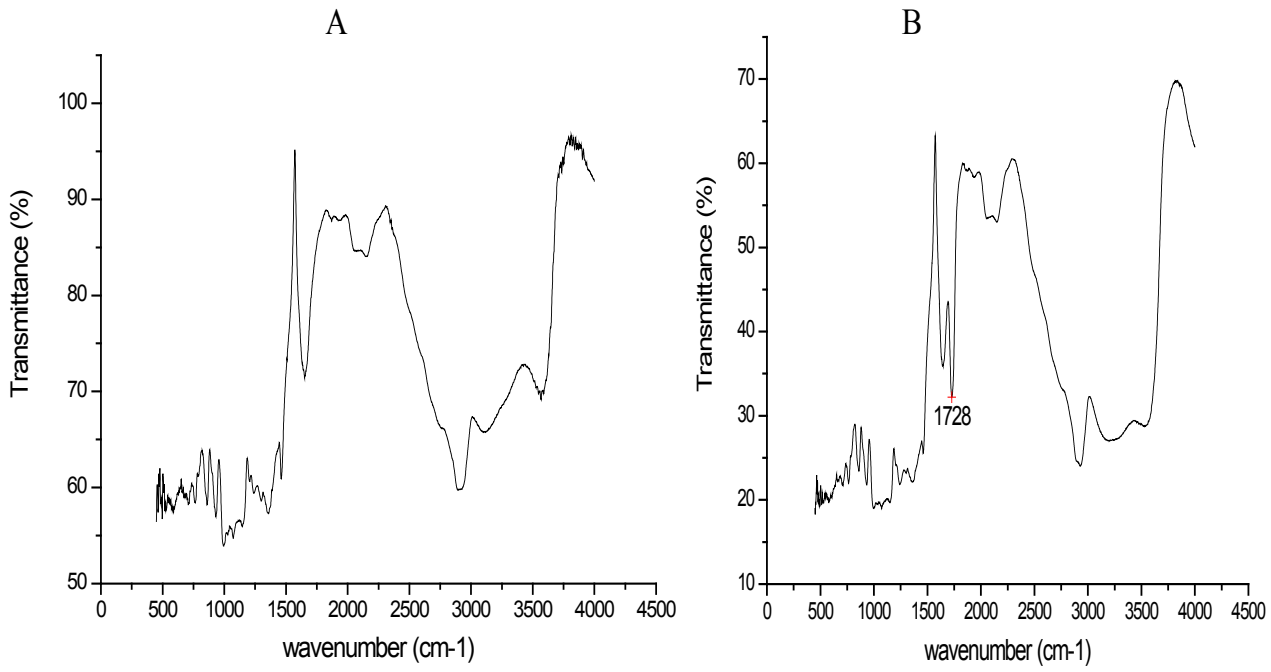

Figure 4: FTIR spectra of native (A) and acetylated (B) cassava starches.

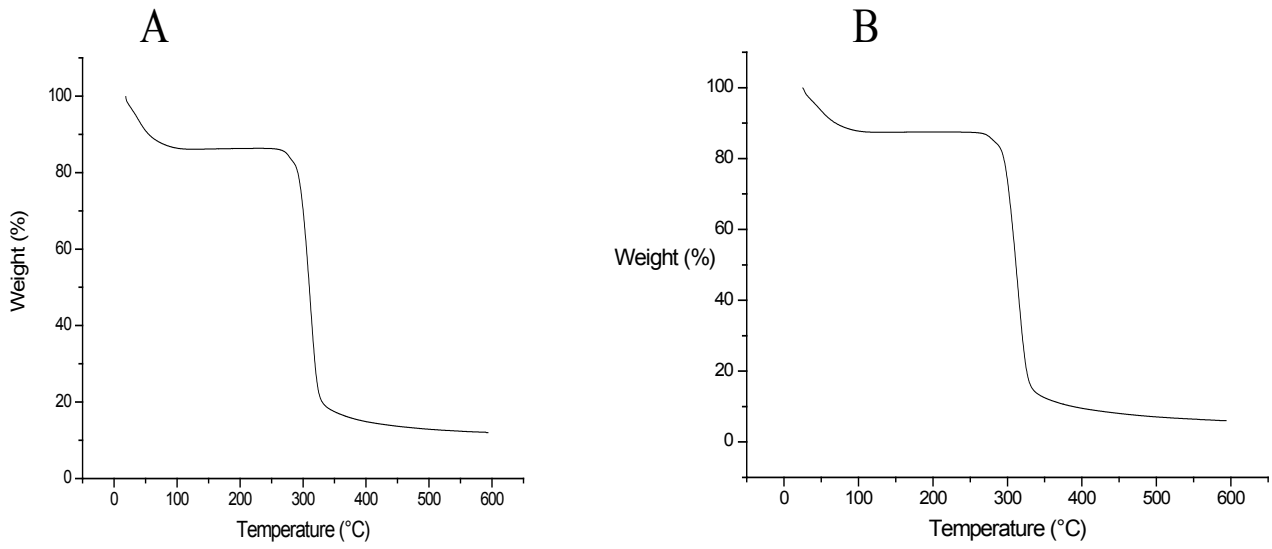

Figure 5: TG thermograms of native (A) and acetylated (B) cassava starches.

swelling introduced after acetylation is very important especially in the application of this starch as a vehicle in drug delivery, while the enhanced emulsion capacity of ACS suggests that the acetylated starch could find application as an emulsifier in the food and pharmaceutical industries [42].

Microstructural studies

The botanical and biological origin of starch serves as a determining factor in the granule shape, size and morphology. Different types of starches have been reported to have different morphologies ranging from oval, spherical, polygonal to irregular shapes [2,33,42-45]. Figure 1 shows the SEM for NCS and ACS respectively. In our investigation, no obvious differences were observed in the morphology of the native and acetylated starch. The physiology and/or degree of starch modification have been suggested as factors responsible for such observation. Worthy of note too is the fact that, we have equally reported a similar observation in our lab [2,41].

The thermograms for NCS and ACS are shown in Figure 3 and the corresponding parameters are tabulated in Table 2. The results in Figure 3 suggests some increase in crystallinity [43,46]. The additional endothermic peaks noticed in ACS samples is indicative of granule swelling and crystallite melting occurring over the gelatinization range

S/N	Parameters	Native Cassava Starch	Acetylated Cassava Starch
1	Total ash (%)	0.30 ± 1.21	0.10 ± 2.10
2	Water-soluble ash (%)	0.00 ± 0.00	0.00 ± 0.00
3	Acid insoluble ash (%)	0.05 ± 0.00	0.00 ± 0.00
4	True density (g/ml)	1.74 ± 0.02	1.54 ± 0.01
5	Amylose: amylopectin ratio (%)	20.32 ± 1.20	18.11 ± 0.66
6	Angle of repose (o)	ND	19.67 ± 5.19
7	Degree of substitution	NA	0.03 ± 0.02
8	pH	6.96 ± 0.64	6.65 ± 0.22
9	Bulk density (g/ml)	0.50 ± 0.00	0.67 ± 0.01
10	Tapped density (g/ml)	0.70 ± 0.00	0.84 ± 0.00
11	Moisture content (%)	14.00 ± 0.40	8.00 ± 0.01
12	Gelatinization temperature (°C)	125.1	77.2
13	Foam capacity (%)	15.60 ± 0.00	10.00 ± 0.00
14	Emulsion capacity (%)	53.10 ± 0.18	75.00 ± 0.10
15	Water absorption capacity (%)	120.00 ± 3.11	870.40 ± 5.00
ND; could not be determined, NA; not applicable. NCS; native cassava starch, ACS; acetylated cassava starch			

Table 1: Some physicochemical properties of NCS and ACS starches.

Parameter	NCS	ACS
Onset temperature (T_0) (°C)	123.7	65.4
Peak temperature (Tp) (°C)	125.1	77.2;107.5;118.8
Conclusion temperature (Tc) (°C)	124.6	71.8
Enthalpy of Gelatinization [J/(g*K)]	228.46	16.5
ΔT (Tc-T_0)	0.9	6.4
Peak Height Index (PHI)	0.64	0.54,0.15,0.12
NCS: Native Cassava Starch, ACS: Acetylated Cassava Starch.		

Table 2: Thermal properties of NCS and ACS starches.

[43]. The gelatinization values are consistent with those reported for other starches [43,47,48]. The onset, peak, and conclusion temperatures of gelatinization of ACS were observed to be lower than that of NCS. The results obtained from the X-ray diffraction studies indicated that the degree of crystallinity of NCS increased after acetylation (Figure 2) corroborating the DSC (Table 2) results which showed the introduction of two new endothermic peaks (Figure 3). Thus it was concluded that acetylation may have increased the crystalline regions of the starch, confer thermal and structural stability and at the same time, conferring faster gelatinization on the starch. The results from XRD and TGA studies substantiated the fact that the associative forces, which stabilize the granule structure in NCS were weak, but strengthened following the modification.

Infrared spectrometry

Figure 4 shows the infrared spectra for NCS and ACS. The band stretch around 3420-3538 cm^{-1} is attributed to hydrogen-bonded hydroxyls on the starch molecules. The band at 2929-2931 cm^{-1} is attributed to CH_2 symmetrical stretching vibrations. In the native cassava starch, the band at 1648 cm^{-1} is assigned to scissoring of two O–H bonds of absorbed water molecules. The bands at 856 and 764 cm^{-1} are due to skeletal stretching vibrations of starch. In the acetylated starch, the weak peak at 2379 cm^{-1} describes the -NH- in the starch molecule, the sharp band displayed at about 1648 cm^{-1} may be due to the stretching vibration of carbonyl group. The new band introduced at 1728 cm^{-1} confirms that acetylation took place on the starch molecules [49].

Thermal stability

In our case, two step thermograms were noticed in both the native and acetylated starches (Figure 5). The ACS showed decompositions to be 10 and 75% successively. The studies indicate that the maximum degradation occurred within the range 100-350°C. Successive decompositions for NCS were 10 and 70%. Similarly, the range of maximum decomposition was within 100-350°C. The TGA result showed that there was a slight decrease in the thermal stability of the modified starch and this corroborates our DSC results. The difference in the decomposition pattern of the two starches was not significant as about 75% of the acetylated starch decomposed within the similar range where 70% of the native starch decomposed. The reason for the slightly higher IDT of ACS is the heterogeneity that results after modification [41]. Although increase in thermal stability after acetylation has been reported for other polysaccharides such as hemicelluloses [50], the result obtained showed that, the degree of acetylation of starch may be responsible for the extent of thermal stability conferred. "The main decomposition mechanism of starch is the dehydration reaction between starch hydroxyls; this suggests that the smaller the amount of hydroxyl group left on the starch, the more stable it becomes. This position was corroborated in the higher thermal stability of methylcellulose compared with the unmodified cellulose" [50].

Synthesis of silver nanoparticles and preparation of nanocomposites

Silver nanoparticles was synthesized rapidly within 15 min of incubation period. The aqueous silver nitrate solution turned to deep brown color within 15 min, with the addition of $NaBH_4$ (Figure 6). The intensity of the brown color increased gradually from about 5 to 15 min incubation period. This behavior has been attributed to the excitation of surface plasmon resonance (SPR) effect and reduction of $AgNO_3$ [51]. The characteristic absorption peak at 400 nm in UV–vis spectrum (Figure 7) confirmed the formation of silver nanoparticles. "The SPR patterns which is characteristics of metal nanoparticles strongly depend on particle size, stabilizing molecules or the surface adsorbed particles and the dielectric constant of the medium" [51]. It was observed that, the single SPR band in the early stages of synthesis corresponding to the absorption spectra of spherical nanoparticles was more pronounced in formulations containing the acetylated starch than the native starch (Figure 7), implying that, the modified starch had little or no inhibitory effect on the synthesis, therefore a better additive in this preparation. The nanocomposites prepared with ACS yielded mean particle size of 248 nm, polydispersity index of 0.276 and zeta potential value of 18.68 mV. The corresponding values for nanocomposites prepared with NCS

Drugs	Isolate	
	IE Q12	MDR 204
Streptomycin	R	R
Isoniazid	R	R
Rifampicin	S	S
Ethambutol	R	R
NCS	R	R
nRIFForm	R	R
nAgForm	R	R
NC 40µg/ml	S	S
NC 80µg/ml	S	S
nRIFForm: Formulation without Drug, nAgForm: Formulation without Silver, NC: Nanocomposite, NCS: Native Cassava Starch		

Table 3: Susceptibility of M. tuberculosis isolates as determined by the BACTEC MGIT 960 system.

Sample	MIC (µg/ml)						
	K. pneumonia	*E. coli*	*S. aureus*	*P. aeruginosa*	*S. paratyphi*	*C. albicans*	*M. tuberculosis*
NC	5000	5000	5000	2500	5000	5000	3800
Ciprofloxacin	1.0	0.5	0.5	1.0	0.5	-	-
nAgForm	NM	NM	NM	NM	NM	NM	NM
nRIFForm	NM	NM	NM	NM	NM	NM	NM
Fluconazole	-	-	-	-	-	2.0	-
Rifampicin	-	-	-	-	-	-	0.625

nRIFForm: Formulation without Drug, nAgForm: Formulation without Silver, NC: Nanocomposite, NM: Not Measured because, there was no Zone of Inhibition. The activity of pure Fluconazole and RIF were reported for comparison. MIC values (micrograms per milliliter) were calculated based on the actual RIF concentration in the sample. Incubation time: 24 h

Table 4: Minimum inhibitory concentration (MIC) of the optimized NC against some pathogenic microorganisms.

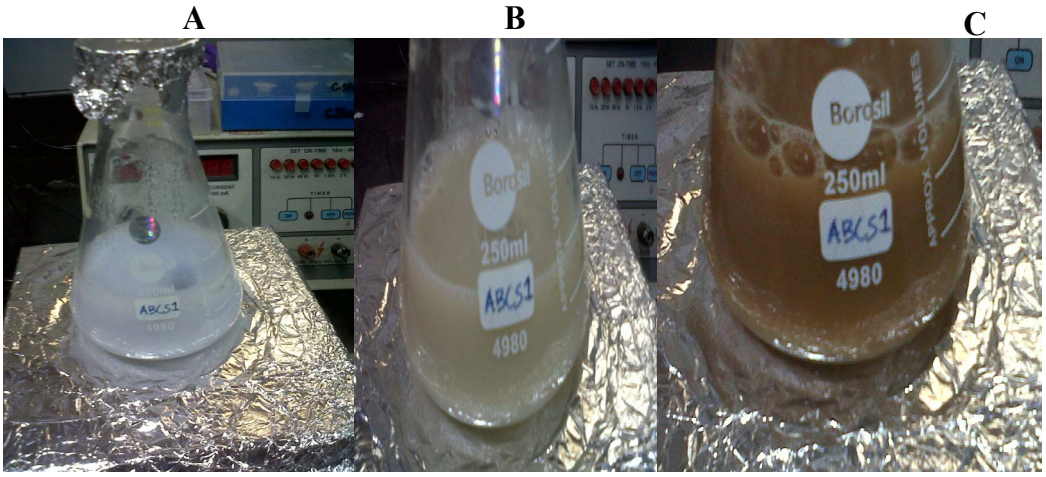

Figure 6: Stepwise preparation of Ag/drug/starch nanocomposites (A; starch suspension, B; starch suspension with drug/silver nitrate/$NaBH_4$ at 2 min, C; starch suspension with drug/silver nitrate/$NaBH_4$ at 15 min).

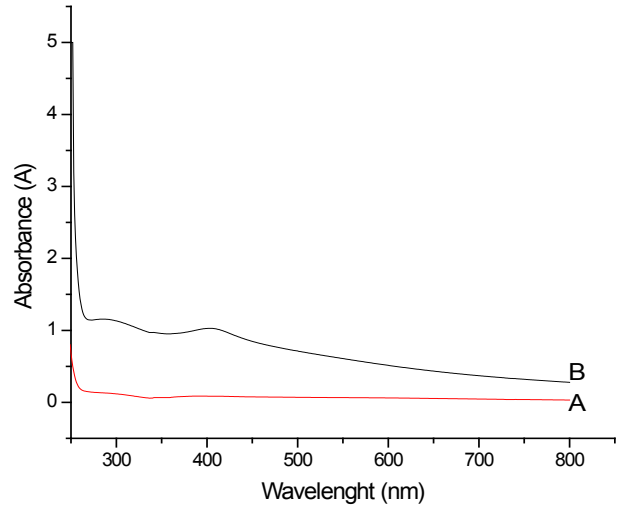

Figure 7: UV-visible absorption spectra of silver – starch – drug nanocomposites suspension (A) native starch (B) Acetylated starch.

were 390 nm, 0.229 and 4.88 mV respectively. There was no significant change in these values after 28 days, confirming the increased stability of the ACS nanoformulation.

Drug resistance in tuberculosis is no doubt a global problem and a major threat to the wellbeing of humans and in the opinion of Lange et al. [52], the emergence and alarming increase in the proliferation and spread of multidrug-resistant (MDR) strains of *Mycobacterium tuberculosis* (*M. tuberculosis*) is substantially challenging the goal of elimination of TB in the 21st century. Determination of *M. tuberculosis* susceptibility to anti tuberculosis drugs is therefore considered a key step in laboratory diagnosis of the disease [53]. In this study the multidrug resistant isolates of *M. tuberculosis* were susceptible to the nanocomposites at a concentration of 40-80 µg/mL, implying that, the formulation retained its anti-tuberculous properties. The study also revealed the antimicrobial properties of the formulation on common pathogenic microorganisms implicated in infection of humans. The NC showed a broad spectrum of antimicrobial activity, with effect on Gram positive and Gram negative bacteria as well as yeast. The inhibitory action of the NC was strongest on *Pseudomonas aeruginosa* with MIC of 2500 µg/mL. *Pseudomonas aeruginosa* has been reported as the most common cause of infections of burn injuries and of the external ear alongside *S. aureus* [54]. *Candida albicans* has been the most prevalent pathogens in systemic fungal infection. They are implicated in superficial and systemic diseases in immunocompromised patients [55]. None of the formulations without drug or silver exhibited antimicrobial effects on any of the tested organisms. The enhanced antimicrobial property of the NC in addition to its traditional antimycobacterial effect may be attributed to the synergistic effect of the silver nanoparticles. The antimicrobial properties of silver nanoparticles even when present as part of a complex composite has been previously reported in literature [56-58]. As expected, the antimicrobial reference standards used for comparison; ciprofloxacin and fluconazole consistently displayed superior potency when compared with the NC.

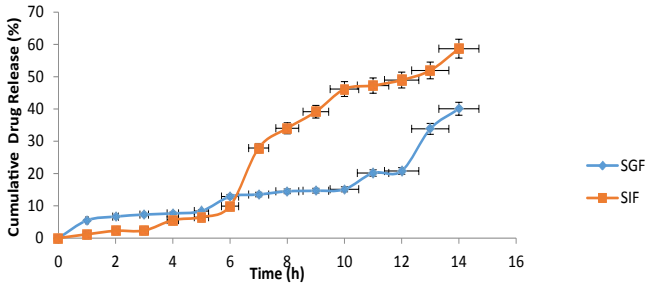

Figure 8: *In vitro* drug release profile of rifampicin from the nanocomposite in simulated gastric fluid (SGF) and simulated intestinal fluid (SIF). (n=3, error bars=SD).

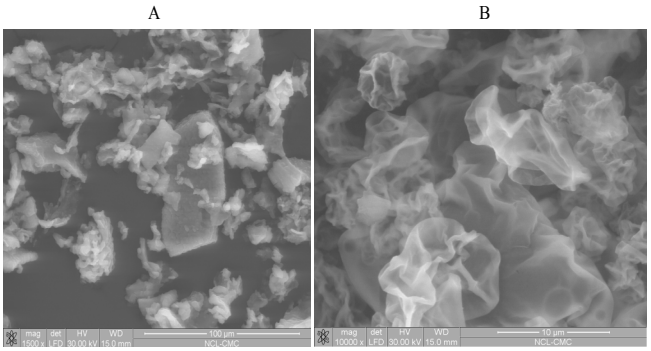

Figure 9: (A) Rifampicin-loaded native starch nanocomposite (B) Rifampicin-loaded modified starch nanocomposite.

In vitro drug release studies

Figure 8 shows the *in vitro* release parameters from the nanocomposite preparation. The values for the time for 10 and 50% of the drug to be released (T_{10} and T_{50} respectively) as well as the maximum cumulative drug released (C_{max}) were used to characterize the nanocomposite release performance [58]. The time for 10% of rifampicin to be released in simulated gastric fluid (SGF) was 5.5 h. The corresponding T_{10} value was found to be 6.0 h in simulated intestinal fluid (SIF). Drug release was initially faster in the acidic medium of SGF for about 6 h, but rapidly changed after this time with release becoming faster in the alkaline SIF. Drug release from SIF was two-fold that of SGF after 6 h. The maximum cumulative drug released after 14 h was 40 and 60% for SGF and SIF respectively. From this result, the nanocomposite is less stable in acidic environment of the dissolution medium than in the alkaline SIF. Although the RIF is generally known to be highly soluble at low pH of SGF if the temperature is maintained at 37°C, its stability is however erratic at this pH as it may convert to its quinone [57,58]. The observed behavior of the drug from the nanocomposite in both SGF and SIF, i.e. the retarded dissolution rate observed at the acidic medium of the SGF and the enhanced released at the alkaline medium of the SIF may not be connected to the inherent property of the drug alone, but rather, due to a combination of factors; complex interaction between the polymer, metallic nanoparticles of silver and the drug, pH of the dissolution medium and solubility of the polymer as well as the drug in the dissolution medium. In fact, the scanning electron micrograph (Figure 9B) with a spongy-like network shows that, a new gel network capable of immobilizing a drug has been formed, unlike the discrete mass in Figure 9A, which could allow a faster drug release. The drug may also have had an increased solubility in SIF and therefore resulted in higher quantities of the drug diffusing into the dissolution medium. There was a significant ($P<0.01$) sustained release of RIF from the nanoformulation up to 14 h. The cumulative drug released at 14 h was 40 and 60% in SGF and SIF respectively and this surely corroborates the higher release rate noticed in SIF due to faster rate of diffusion of drug from the nanocomposite.

Conclusions

Starch obtained from *Manihot esculentus* was subjected to modification by acetylation and some physicochemical properties of both the native and modified starches determined. Acetylation had a very significant effect on the water absorption capacity and solubility of the starch, suggesting that the acetylated cassava starch may be a potential disintegrant in solid dosage formulations in the pharmaceutical industry. The modified starch was used as a stabilizer in Rifampicin nano drug delivery with significant extended release profile and antimicrobial activity.

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