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Evaluation of Disintegrant Potential of Carboxymethyl Starch Derived from *Cyperus esculentus (Cyperaceae)* Tubers

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ABSTRACT

Starch is an important excipient in the pharmaceutical industry. Pharmaceutical grade starch is mostly obtained from food sources and rarely from unconventional sources. The native starch has limited applications; these can be improved by modification. Native starch obtained from *Cyperus esculentus* tubers- an unconventional source was modified by carboxymethylation and evaluated for its disintegrant potentials in metronidazole tablet formulation.

Extraction of starch from *Cyperus esculentus* tubers was carried out using sodium metabisulphite. Chemical modification of the native starch by carboxymethylation was achieved using monochloroacetic acid (MCA). The physicochemical properties of the carboxymethylated starches were determined including their compatibility with metronidazole powder. The modified starches were also employed as a disintegrant at different concentrations (2.5%, 5% and 7.5%) in formulation of metronidazole tablets and compared with sodium starch glycolate (SSG), a commercial brand.

Two batches of *Cyperus esculentus* carboxymethyl starch with degree of substitution of 0.13 (CES1) and 0.47 (CES2) were obtained from the native starch (CES0). The chemical modification of the *Cyperus esculentus* native starch led to desirable physicochemical and micromeritics properties (especially increase in hydration capacity and flow potentials). The tabletting properties of metronidazole tablets formulated with the CES1 as disintegrant were comparable to the standard, SSG. At concentrations of 5% and 7.5%, there were no significant differences in the disintegration times of metronidazole tablets formulated with CES1 and SSG.

Carboxymethyl *Cyperus esculentus* starch possess improved flow properties and could be potential disintegrant in tablet formulations.

Keywords: carboxymethyl starch, *Cyperus esculentus*, disintegrant, metronidazole, carboxymethylation.

Introduction

Starch is one of the traditional excipients that possess a wide range of application in the pharmaceutical industry.[1] It is used as fillers, binders, disintegrants and anti-adhesives in tablet manufacture, as thickener in oral liquid, gelling agents in gels among other uses in biopolymer industries.[1] It is cost effective, readily available and accessible; it is a major carbohydrate reserve in plants. Starch consists of two naturally occurring high molecular weight polymers: mostly linear insoluble amylose and branched soluble amylopectin; both of which consist of repeating units of D-glucose joined via glycosidic bonds.[2] Depending on the botanical source, starch contains 20-25% amylose and 75-80% amylopectin.

Starches obtained from plant sources in their raw form are called 'native starch' or 'unmodified starch'. Native starch can be obtained either from conventional sources (such as banana, corn, maize, potato, cassava, rice, wheat and barley) or unconventional sources (sugar cane, soursop, lentil, breadfruit, tiger nut, ginger, turmeric, grass pea, chestnut, lablab bean, apple, borassus, white yam, broad bean, cowpea, jack bean, jackfruit seeds and kudzu).[3-6] Over the years, commercial starch is often obtained from conventional sources; starch derived from unconventional sources are often obtained during the isolation of bioactive compounds from raw materials and have been treated as waste, hence, these raw materials are underutilized.[1] Native starches possess limited industrial applications due to their poor flow properties and aqueous solubility, reduced viscosity, high gelatinization temperature, low shear resistance and tendency to recrystallize.[3] To obtain starch of high quality and improved functional applicability, native starch isolated from the various vegetable sources can be modified using physical, chemical, enzymatic and genetic methods.[7-9]

Carboxymethyl starch (CMS) is a chemically modified starch obtained by replacing the hydroxyl group on the anhydro glucose unit with carboxymethyl group;[7] the addition of bulky hydrophilic groups to polysaccharide chains results in reduced starch tendency to retrogradation (recrystallization), lower gelatinization temperature and improved cold-water solubility.[5,10] In the pharmaceutical industry, among other uses, carboxymethylated starch is used as disintegrant in tablets, [5] and as osmotic agents for adjusting the toxicity of drugs especially medicinal solutions for parenteral administration based on the swelling and solubility properties.[11]

Cyperus esculentus (Tiger nut) is a perennial herb that produces rhizomes and spherical nuts. It is a common weed in many parts of Nigeria, although some varieties are cultivated. The yellow variety yields more starch, with lower fat, higher protein, and more nutritional

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factors. Tiger nut can be eaten raw, roasted, dried, baked, or made into a refreshing non-alcoholic beverage.[12] Tiger nut is an example of the unconventional sources of starch that is being underutilized. Although, tiger nut starch has been isolated and characterized,[12-14] to the best of our knowledge, its chemical modification by carboxymethylation and subsequent application as tablet excipient has not been reported. In this study, the tiger nut starch was modified by carboxymethylation and its disintegrant property in metronidazole tablet formulations were evaluated and compared with sodium starch glycolate (a commercially available modified starch).

Materials and Methods

Plant sample, Solvents and Reagents

Cyperus esculentus tubers (tiger nut) were obtained from Mushin, Lagos, Nigeria. The tubers were identified and authenticated at the Department of Botany of the University of Lagos, a voucher specimen number LUH 7591 was assigned and sample was deposited in the herbarium.

Metronidazole powder, sodium starch glycolate, lactose, acacia and talc were obtained as a gift from Phamatex Industry Ltd, Lagos, Nigeria. Absolute ethanol, n-hexane, glacial acetic acid, methanol, magnesium stearate all were product of BDH Chemicals, Poole England; all other reagents were of analytical grade and used as received.

Extraction and Carboxymethylation of Cyperus esculentus Starch

Tubers of *Cyperus esculentus* were sorted to remove damaged tubers, stones and other impurities. *Cyperus esculentus* starch (CESo) was isolated using a method employed in an earlier study with some modifications.[14] Briefly, the tubers of *Cyperus esculentus* were washed, pulverized and dried using B and T dryer (Greenfield-Oldham, England), at 100°C for 6 h. The pulverized tiger nut (3 kg, > 1 mm) was heated in ethanol (6 L) for 1 h and subsequently defatted using 6 litres n-hexane at 60°C. The defatted tiger nut was soaked in 0.075% w/v sodium metabisulphite for 96 h, the steeped water was changed every 24 h. After 96 h, it was stirred and passed through a muslin cloth of 150 µm pore to obtain the starch. The chaff was discarded, and the starch was allowed to stand for 24 h. The supernatant was decanted and the starch was washed in distilled water (2 L) and allowed to settle for 10 h. The water was decanted, and the resulting starch cake (CESo) was dried for 5 h at 50°C, pulverized and passed through a 250 µm mesh.

Carboxymethylation of *Cyperus esculentus* starch was achieved using the procedure reported by of Madu *et al*.[5] Briefly, carboxymethylation was carried out using monochloroacetic acid (MCA). Sodium hydroxide (0.5 M) was mixed with 80 ml of ethanol, then it was stirred until the NaOH completely dissolved. CESo (10%w/w) was then poured and stirred vigorously. After stirring, 5 g MCA was added and the reaction time was 1 h. After hydrolysis, the pH of the slurry was adjusted to 7 using 10–20 ml of glacial acetic acid to obtain carboxymethylated starch CES1. The same procedure was repeated using 2 M NaOH and reaction time of 2 h to obtain second batch of carboxymethylated starch (CES2).

Characterization of carboxymethyl Cyperus esculentus starch

All evaluation parameters were carried out on carboxymethyl modified starch CES1, CES2 and commercially available modified starch, sodium starch glycolate (SSG).

Degree of substitution

The degree of substitution (DS) was determined using back titration method as described by Stojanovic *et al*. [15]

Organoleptic and solubility test

The colour, odour and texture of native and modified starch were determined and compared to those of SSG. A 2 g weight of each starch sample was dissolved in 5 mL each of cold distilled water, hot distilled water and ethanol for the determination of solubility.

pH and moisture content determination

The pH of 2 g weight of each starch powder suspended in 20 mL distilled water was recorded using a pH meter (Metler Toledo/England).

Moisture content determination

Three grams of each of the starch powder was placed in the moisture content analyser (Sartorius AG, Germany). The analyser was then set at 130°C for 5 min and the value of the moisture content was obtained.

Micromeritics

The bulk density, tapped density, Carr's compressibility index, Hausner's ratio and angle of repose were determined using methods employed in an earlier study.[16]

Hydration Capacity

The method used by Jubril *et al* [17] was adopted with some slight modifications. Briefly, 1 g of each sample starch powder was weighed and transferred into centrifuge tubes. Distilled water (10 mL) was added, mixed for 2 min and centrifuged for 2 min at 5000 rpm. The supernatant obtained was decanted and the sediment weighed. Hydration capacity was determined using Eq 1.

$$Hydration\ capacity = \frac{Weight\ of\ the\ sediment\ formed}{Weight\ of\ the\ dry\ sample} \quad \text{---------- Eq 1}$$

Viscosity

The viscosity of a 2% w/v starch suspension was determined using a viscometer (DV-E/China) as described by Nattapulwat *et al*.[18]

FTIR Study

Fourier transform infrared (FTIR) spectra of native tiger nut starch and the carboxymethyl starches (CMS) were obtained using a FTIR spectrophotometer (Bruker, South Africa). Also compatibility of CES1 and CES2 powder with metronidazole powder was evaluated using FTIR spectrometer. Approximately 5 mg each of CES1, CES2 and metronidazole powder were individually blended with solid KBr (≈ 50 mg) and compressed into discs. Also, physical mixtures (1:1) of CES1: metronidazole, CES2: metronidazole powder and SSG: metronidazole (≈ 5 mg) were blended with solid KBr (≈ 50 mg) and compressed into disc for compatibility study. The spectra were scanned from 500-4000 cm^{-1} in FTIR spectrometer under dry air at room temperature.

Preparation of metronidazole granules and tablets

Granulation was carried out by wet method of massing and screening using modified method by Ofori-Kwakye *et al*.[19] Nine batches of metronidazole granules were prepared containing different concentrations of CES1, CES2 and SSG as disintegrants (Table 1). The various batches of granules obtained were mixed with 5% w/w of dry starch for 4 min, 1% w/w magnesium stearate and talc were added and mixed for 1 min in a tumbler mixer. The premixed blends were compressed using Single punch compression machine (Manesty Press/UK), all the batches were compressed under the same compression settings.

Evaluation of metronidazole tablets

All batches of the tablets were evaluated for uniformity of weight and dissolution using the methods reported in British Pharmacopeia.[20] The dissolution medium used was 900 ml of 0.1N HCL maintained at 37 °C ± 0.5 °C. Samples of the dissolution medium (5 mL) was withdrawn at 0, 5, 10, 15, 30, 45 and 60 min and filtered using a millipore filter 0.45µm, and were analysed for metronidazole by UV spectrophotometry at 277 nm. The friability and disintegration tests were carried out according to the method described by Bamiro *et al*. [21] The Vernier caliper was used to measure the diameter and thickness of the tablets. The mean value of five determinations was recorded in each case while hardness tester (Monsanto, Gupta Agencies, India) was used for measuring the tablet hardness.

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Statistical Analysis

Statistical analysis was carried out using ANOVA on a Graph Pad Prism 5.00.2.88. The limit of significance was set at $p<0.05$

Results and Discussion

Characterization of the starches

The degree of substitution obtained for the carboxymethyl starches (CES1, 0.13 and CES2, 0.47) indicates that an increase in concentration of NaOH and duration of treatment brought about an increase in the degree of substitution. The degree of substitution obtained is within the specified carboxymethyl substitution for starches,[7] at DS < 0.1, carboxymethyl starch can be used in food industries due to its texture, consistency and stability but at DS > 0.1 carboxymethyl starch can be used in pharmaceutical industries. [22]

The results obtained for other physicochemical properties are presented in Table 2. The percentage yield of the native starch (CES0) from the dried tubers of *Cyperus esculentus* was 20.08%, the yield could be improved upon by optimization of the extraction conditions. The colour of the starch samples (CES0, CES1, CES2 and SSG) ranges from off-white to white with a characteristic odor having fine to very fine texture. Iodine test is a general test for starch. All the four powders gave a positive result as a dark blue coloration was observed on the addition of Lugol's iodine, thus confirming the presence of starch in the samples. All starch samples had an odour characteristic of starch while the texture of CES0 and CES2 were fine, CES1 and SSG were finer.

The pH values (Table 2) of all starch powders fell within the range of 5.6 to 7.5. SSG had the highest pH value while native starch had the lowest value. CES2 and CES1 had comparable values. Hence, carboxymethyl modification increased the pH value of the starch thereby making it less acidic. Lesser acidic starches would be more preferable as excipients in oral formulation as they will not cause damage to the gastro intestinal tract.

The hydration capacity and viscosity (Table 2) increased upon modification and at higher DS. The higher hydration capacity makes the carboxymethyl starches good candidate for use as disintegrant. Hydration capacity increased with increase in DS, at higher degrees of substitution, more water can penetrate the starch granules due to the hydrophilicity of the carboxymethyl groups, resulting in swelling of the starch granule. Hence, the modified starches will be a better disintegrant when employed if formulations of tablets. [22]

The bulk and tapped densities (Table 2) decreased with an increase in DS, the higher the bulk density of an excipient, the more the amount of the excipient required for compression. [15] However, there was no statistically significant difference in the values of both densities with the standard starch, SSG ($p<0.05$). British Pharmacopoeia classified powders with Carr's index values of 16-20 and 21-25 to have fair and passable flow character respectively while those with Hausner ratio values of 1.19-1.25 and 1.26-1.34 have fair and passable flow character.[20] The values of Carr's index and Hausner's ratio (Table 2) imply that CES0 had a very poor flow property, upon modification to carboxymethyl starch, the flow properties improved. CES1 also had a better flow than CES2 and its value is comparable to that of the standard starch, SSG. However, the results of angle of repose (Table 2) are not fully consistent with those of Carr's index and Hausner's ratio. The results of angle of repose indicate that CES2 had a better flow than CES0, CES1 and SSG which had a fair flow.[23]

The FTIR spectra (Figure. 1) of CESO, CES1, CES2 and SSG samples showed general characteristic spectrum of starch however there were some minor differences in some signals and band intensities. [24] The band stretch around 3245 - 3279 cm^{-1} in the spectra of the four samples is attributed to hydrogen-bonded hydroxyls on the starch molecules. The absorption bands at 2912 cm^{-1}, 2914 cm^{-1}, 2922 cm^{-1} and 2914 cm^{-1} for the samples (CES0, CES1, CES2 and SSG respectively) are attributed to the C–H stretching vibrations. The absorption bands peak at 826 – 1258 cm^{-1} are attributed to **α**-glycosidic linkages between the sugars units, indicating that amylose residues forming the backbone of *Cyperus* starch were bonded by linkages and the presence of carbohydrate (C–O stretching in C– O–C and C–O–H in the glycosidic molecule of carboxymethyl starch.[4] The FTIR spectra of CES1 and CES2 show all typical peaks of starch with new additional peaks due to carboxymethylation reaction. The O-H stretching peak shifted to lower wavelength at 3245, 3276 and 3263 cm^{-1} for the carboxymethyl starches. This might be due to the interaction of OH group with $COO^{-}Na^{+}$. Intense absorption band at 1721 cm^{-1}, 1676 cm^{-1} and 1611 cm^{-1} indicated the substitution of $CH_2COO^{-}Na$ group on starch molecular chain during carboxymethylation while the native starch had band at 1634 cm^{-1} assigned to the scissoring of two O-H bonds of water molecules.

Compatibility studies

The compatibility of metronidazole with CES1 and CES2 were evaluated using FTIR spectroscopy. The FTIR spectra (Figure. 2) of the three mixtures of metronidazole and the starches show insignificant shift in the peaks/bands of the pure metronidazole hence CES1 and CES2 are compatible with metronidazole. The FTIR spectrum for pure metronidazole (Figure 2) displayed a broad peak at about 3200 cm^{-1} due to O-H stretching vibrations; the group, C=O (amide) is represented at 1717 cm^{-1} and C-N-H group is denominated at 1264 cm^{-1}. Similar peaks were observed for the samples containing mixtures the metronidazole and the starch samples, hence establishing compatibility.

Table 1: Composition of the different batches of Metronidazole granules.

Ingredients (%w/w)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Metronidazole(%w/w)	30	30	30	30	30	30	30	30	30
SSG	2.5	5.0	7.5	-	-	-	-	-	-
CES1	-	-	-	2.5	5.0	7.5	-	-	-
CES2	-	-	-	-	-	-	2.5	5.0	7.5
Acacia	4	4	4	4	4	4	4	4	4
Lactose	60.5	58	55.5	60.5	58	55.5	60.5	58	55.5
Magnesium stearate	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2

Formulations F1, F2 and F3 contain 2.5%, 5% and 7.5% SSG as disintegrant, F4, F5 and F6 contain 2.5%, 5% and 7.5% CES1 while F7, F8 and F9 contain 2.5%, 5% and 7.5% CES2 as disintegrant.

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Evaluation of compressed tablets

The results of the quality assessment of the formulated tablets are presented in Table 3. The thickness for all the tablet was 1.1 mm. There was no statistical difference in the thicknesses of the tablets for the nine batches.

Weight uniformity of compressed tablets is important because it helps to guard against overdose or under dose. There are acceptable values of percentage deviation upon which the tablet weights are acceptable. For tablets weighing 250 mg and above, the value of percentage deviation should not be more that 5 % [20]. The average weight of the compressed metronidazole tablets varied from 666 – 671 mg. From the study, it was observed that all the tablets passed the weight uniformity test except formulation F9 containing 7.5% CES2 as disintegrant.

The crushing strengths of formulated tablets (Table 3) ranged from 9.33 to 10,33 kg. A force of about 4 kg is considered the minimum requirement for a satisfactory tablet. [25] All the nine batches of the metronidazole tablets had crushing strength above the minimum requirement. Friability is a measure of the tablet's ability to withstand mechanical stress of handling, packaging and transportation with little or no loss in the drug content. The acceptable friability value for tablets is < 1.0.[20] It was observed that the compressed metronidazole tablets had friability values between 0.10 – 0.79%, hence, all tablets passed the friability test. At a higher concentration (5%), a reduction in friability was observed for metronidazole tablets containing CES1 and SSG. Increasing the concentration to 7.5% brought about an increase in the friability when compared with the initial concentration of 2.5%. However, for CES2 metronidazole tablets, higher disintegrant concentration produced a successive decrease in friability.

The release of a drug from its dosage form is very important in drug absorption, before any drug can be released, it must first be broken down into fragments to aid absorption. The British Pharmacopoeia states that the disintegration time for uncoated tablets should not exceed 15 min. [20] The higher the concentration of disintegrant, the lower the disintegration time observed in each of CES1, CES2 and SSG metronidazole tablets, therefore, the faster the drug release. With exception of F8 (containing 5% of CES2), all the metronidazole tablets formulations containing 5 or 7.5% of the starch disintegrant disintegrated within the specified time for uncoated tablets (Table 3). Generally, at the same concentration of disintegrant, tablets formulated with CES2 had longer disintegration times, this could be because of the formation of viscous gel mass after contact with water due to increased degree of substitution. Disintegration does not however imply complete dissolution of the tablet or its active pharmaceutical ingredient (API), it is an intrinsic parameter which links the first in a series of steps to drug release from the dosage form prior to dissolution.

Table 2: Organoleptic and physicochemical properties of native starch (CES0), modified starches (CES1 and CES2) and sodium starch glycolate (SSG)

Parameters	**CES0**	**CES1**	**CES2**	**SSG**
Iodine Test	Positive	Positive	Positive	Positive
Odour	Characteristic	Characteristic	Characteristic	Characteristic
Colour	Off-white	Off-white	Off-white	Off-white
Texture	Fine	Very fine	Fine	Very fine
pH	5.76 ± 0.2	6.15 ± 0.13	6.18 ± 0.15	7.5 ± 0.15
Moisture content (%)	14.87 ± 0.2	15.67 ± 0.2	16.54 ± 0.2	15.85 ± 0.2
Solubility – cold water	Insoluble	Insoluble	Insoluble	Insoluble
Hot water	Soluble	Soluble	Soluble	Soluble
Alcohol	Insoluble	Insoluble	Insoluble	Insoluble
Viscosity (mPa.s)	82.4 ± 0.3	87.5 ± 0.3	93.7 ± 0.1	90.2 ± 0.2
Hydration capacity	2.5 ± 0.3	4.6 ± 0.1	5.3 ± 0.3	6.5 ± 0.5
Bulk density (g/ cm^3)	0.35 ± 0.03	0.32 ± 0.09	0.29 ± 0.02	0.50 ± 0.02
Tapped density (g/ cm^3)	0.56 ± 0.09	0.44 ± 0.04	0.44 ± 0.02	0.63 ± 0.25
Carr's index	37.5 ± 0.5	27.2 ± 0.2	34.0 ± 2.0	15.0 ± 2.0
Hausner ratio	1.60 ± 0.2	1.38 ± 0.08	1.52 ± 0.02	1.35 ± 0.05
Angle of repose (θ°)	40.90 ± 0.2	46.25 ± 11.07	24.55 ± 0.05	31.6 ± 0.2

Table 3: Evaluation of the compressed metronidazole tablets

Sample	Weight uniformity (mg)	Thickness (mm)	Crushing Strength (kg)	Friability (%)	Disintegration time (min)
F1	666.0 ± 1.0	1.1 ± 0.00	10.33 ± 0.57	0.45 ± 0.45	21.0 ± 2.0
F2	668.0 ± 2.0	1.1 ± 0.00	9.66 ± 1.15	0.10 ± 0.14	11.0 ± 4.0
F3	666.3 ± 1.2	1.1 ± 0.00	10.00 ± 0.00	0.79 ± 0.79	10.0 ± 1.0
F4	669.0.7 ± 3.2	1.1 ± 0.00	9.33 ± 0.57	0.54 ± 0.54	28.0 ± 9.0
F5	668.0.3 ± 1.5	1.1 ± 0.00	10.00 ± 0.00	0.24 ± 0.24	11.0 ± 1.1
F6	667.0 ± 0.0	1.1 ± 0.00	10'00 ± 1.00	0.58 ± 0.57	8.0 ± 5.0
F7	670.0 ± 3.0	1.1 ± 0.00	10;00 ± 0.00	0.57 ± 0.57	43.0 ± 9.0
F8	667.7 ± 2.1	1.1 ± 0.00	9.50 ± 0.57	0.36 ± 0.36	29.0 ± 8.0
F9	671.3 ± 7.6	1.1 ± 0.00	10.33 ± 0.57	0.32 ± 0.33	15.0 ± 6.0

F1, F2, F3 contain 2.5%, 5%, 7.5% SSG respectively, F4, F5, F6 contain 2.5%, 5%, 7.5% CES1 respectively while F7, F8, F9 contain 2.5%, 5%, 7.5% CES2, respectively.

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There were variations in the dissolution profiles of the different batches of the metronidazole tablets (Figures 3 and 4). At 30 min, about 70% of metronidazole in formulations containing CES1, 60-80% in CES2 formulations and about 80% in SSG formulated tablets had been released. The rate of dissolution helps to determine the amount of the API that is released when the tablet goes into solvation and subsequently, the rate and extent of absorption and therapeutic outcome of a drug. The factors that affect dissolution include type and concentration of binder, hardness, surface area, solubility of the drug, manufacturing process (wet granulation or direct compression) and diluents [26]. According to BP, compressed uncoated tablet should release at least 70 % of the active content within 30 min [20]. The percentage of drug release for all formulations was greater than 70% after 30 min, therefore, all formulations passed the dissolution test.

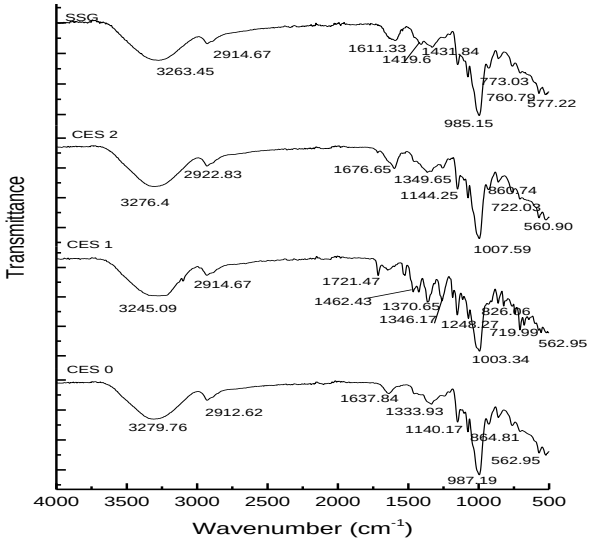

Figure1: Stacked FTIR spectra of native starch (CES0), modified starches (CES1 and CES2) and sodium starch glycolate (SSG).

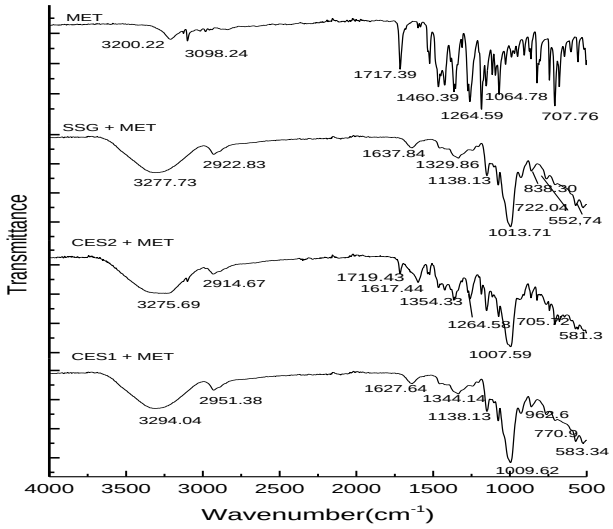

Figure 2: Stacked FTIR spectra for compatibility studies of metronidazole with modified starch samples (CES1 and CES) and sodium starch glycolate.

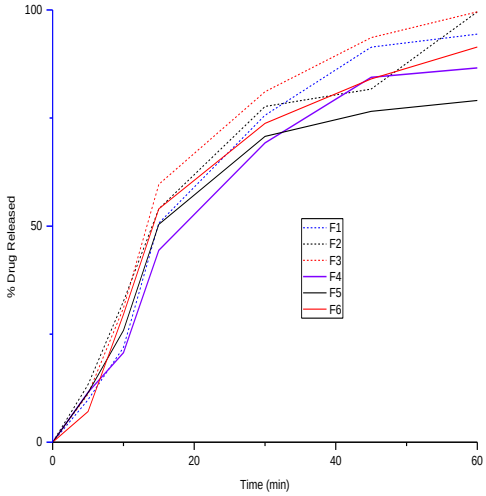

Figure 3: Dissolution profile of the different batches of metronidazole tablets using different concentration of starch samples as disintegrant. *F1, F2, F3 contain 2.5%, 5%, 7.5% SSG respectively while F4, F5 and F6 contain 2.5%, 5%, 7.5% CES1, respectively.*

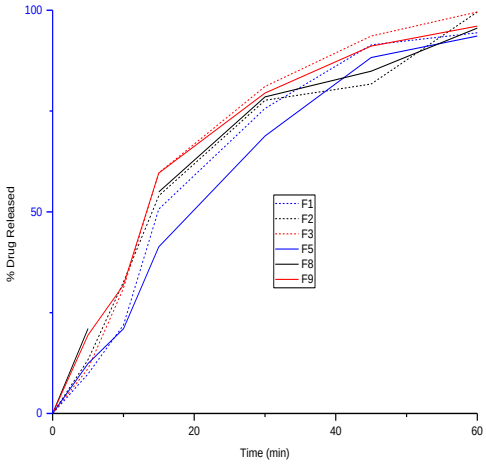

Figure 4: Dissolution profile of the different batches of metronidazole tablets using different concentration of starch samples as disintegrant. *F1, F2, F3 contain 2.5%, 5%, 7.5% SSG respectively while F7, F8, F9 contain 2.5%, 5%, 7.5% CES2, respectively.*

Conclusion

Carboxymethylation of native *Cyperus* nut starch led to production starch with increased hydration capacity, improved flow and disintegrant potentials. The physical properties of metronidazole tablets formulated *Cyperus* carboxymethyl starch with low degree of substitution (0.13) as disintegrant was comparable to that of commercial brand sodium starch glycolate. *Cyperus* carboxymethyl starch could be employed as an alternative disintegrant for tablet formulations.

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Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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