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APPLICATION OF A HYDROPHILIC BIOPOLYMER OBTAINED FROM *PENNISETUM GLAUCUM* SEED FIBRE AS BINDER IN ALBENDAZOLE CHEWABLE TABLET FORMULATION

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ABSTRACT

Natural polymers with enhanced binding properties in tablet formulation continue to be highly sought over synthetic materials. This study aims to evaluate the binding properties of a hydrophilic biopolymer derived from the modification of the seed fibre of *Pennisetum glaucum* (TP) in the manufacture of albendazole chewable tablets. Dry TP seeds were steeped in water for 24h, washed, wet milled, and the fibre separated from the starch by washing slurry with water through a muslin cloth. Fibre of TP was dried at 60°C, screened through 180µm sieve (TP-NF). An 800 g of TP-NF was dispersed in 3.0L of 3.5% w/v sodium hypochlorite for 30 min, washed with distilled water to neutral pH, dispersed in 90% v/v ethanol for 10 min and dried at 60°C (TP-MC). The fibre was classified (180µm) and characterised using standard methods. Albendazole tablets were formulated using 5, 7.5, 10 and 15% w/w of the biopolymers by wet granulation. Avicel PH 101 was used as comparing standard binder. The dried albendazole granules were micromeritically evaluated while tablets made from the granules were evaluated for their physical properties, assay and dissolution studies. TP-MC powder flowed and compressed better than TP-NF, while albendazole granules had better flow and compressibility than TP-NF and TP-MC. The albendazole tablets were fairly strong and varied minimally in weight. Friability was <1%, and > 80% of albendazole was released from the tablets within 15 min. TP-MC served more effectively than TP-NF and compared favourably with Avicel PH 101 as binder in the formulation of albendazole tablets.

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INTRODUCTION

Active Pharmaceutical Ingredients (APIs) or drugs whether in their natural or synthesized form are deliberately formulated into dosage forms to aid delivery of reproducible accurate doses of efficacious, stable and safe dosage forms which that should elicit similar or reproducible therapeutic effects [1-3]. Different formulation variables such as the quantity of API and excipient used, processing steps can easily affect the physical integrity, pharmacological activity or therapeutic outcome of the formulation [4, 5]. The degree of mechanical strength permitted would depend on some factors such as the type of tablet and its intended use [6]. Conventional release tablets are meant to have such mechanical strength that would not only cause the tablets to be intact and not crumble under some permitted stress conditions but would also permit the complete disintegration of the tablets within a specified period of time in order to release the API content for dissolution and

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absorption. However, chewable tablets do not undergo disintegration as they are masticated in the mouth and swallowed as divided fragments or particles. Chewable tablets are formulated for children who may be unable to swallow tablets or for such drug formulations where a quick dissolution, absorption and onset of action is required [7-9]. Amongst the different pharmaceutical excipients that are required to aid in the formulation of a robust pharmaceutical tablet that contains the desired amount of the API, as well as possess good physical integrity, are binders.

Pharmaceutical binders act as an adhesive that can bind or glue together particles of powdered materials to form aggregates, granules, or cause other dry materials that are used in tablet formulation to come together and impart on the powders good flowability, compressibility and the necessary mechanical strength that is desirable in the product [10, 11]. Binders can be used in the dry form or as solutions or dispersions of the polymer in the necessary solvent. The quantity used and the method of addition of binders during the processing step in formulations greatly influences the degree of hardness that would be acquired by the tablet besides the compression pressure applied during compaction. Binders are polymeric materials that are available either in the synthetic or natural form. They must possess a non-toxic property and also be quite compatible with other excipients in the drug formulation. Examples of synthetic binders include polyvinylpyrrolidone (PVP), hydroxypropylmethylcellulose (HPMC), ethylcellulose, sodium carboxymethylcellulose, etc. while natural binders include gelatin, guar gum, acacia, tragacanth, starch, etc. [12]. Most natural binders are obtained from plant sources and they have the advantage of being cheap, abundant in nature, easily processed, good compatibility with other ingredients of the tablet formulation, eco-friendliness and biodegradability [11, 13, 14]. Binders can be extracted from different parts of the plant such as seeds, stem and roots.

Pennisetum glaucum (Family: Poaceae) is a millet and this terminology is often used to describe seeds belonging to several taxonomically diverse species of grass [15]. Millets serve as staple food in arid and semiarid regions of the world such as Germany, Russia, India, China, Burkina Faso, Mali, Nigeria, Ethiopia and Uganda [16]. In addition to its use as food by man, it is also used as a grazing forage crop where the leaves are harvested before the maturity of the plant and used to feed sheep and cattle because of their high fibre content.

Albendazole is an orally administered broad-spectrum anthelmintic. Currently it is mostly used in the treatment of soil transmitted helminthes disease, hydatidosis and neurocysticercosis caused by *Taenia solium* [17]. Albendazole is a benzimidazole derivative that has been widely used in the treatment of worm infestations in both humans and animals. The drug has low water solubility, limiting its oral absorption and resulting in a lower bioavailability [13, 18].

Although, reports of formulations of chewable albendazole tablets by some other researchers exist [9, 17-19], the desire to develop cheaper, more ecofriendly polymers from the local biomass which can favourably compete with or perform better than the imported commercially existing excipients/polymers is laudable. Increase in local content of materials used in the pharmaceutical sector would boost the economy of the nation by reducing the cost of importation of foreign materials for similar purposes. This study aims at extracting and modifying the seed fibre of *Pennisetum glaucum* and its application as a binding agent in the formulation of albendazole chewable tablets.

MATERIALS AND METHOD

Materials

The following materials were used as procured: Absolute ethanol, n-hexane (JHD, China), 3.5 % w/v sodium hypochlorite solution (Multipros, Nigeria), albendazole powder (donated by Emzor Pharm. Ind. Ltd., Nigeria), *Pennisetum glaucum* seed (Rumuokoro market, Port Harcourt), distilled water. (Pharmaceutical Technology Laboratory, University of Port Harcourt).

Methods

Procurement and Processing of Sample

The *Pennisetum glaucum* seeds were purchased from the Rumuokoro market, Obio-Akpor Local Government Area, Rivers State. Dr. Oladele, A.T. of the Department of Forestry and Wildlife management, University of Port Harcourt identified and authenticated the sample. A specimen was deposited in the departmental herbarium and assigned voucher number FHUPH-101. The seeds were separately steeped in water for 24 h, wet milled with distilled water and the slurry washed through a muslin cloth with water until the starch was completely separated from the fibre (cellulose). The fibre was dried at 60 °C in an oven (Memmert, England), milled and screened through a 250 µm sieve (Retsch, Germany) and labelled as TP-NF. A quantity of 500 g each of TP-NF were steeped in 4.5 L of 3.5 % w/v sodium hypochlorite for 30 min with intermittent stirring, after which the sodium hypochlorite was washed off with water until a neutral pH was obtained. The water was removed by squeezing through a muslin cloth and the wet cellulose dispersed in 4.0 L of 95 % v/v ethanol for 15 min. The alcohol was squeezed off and the wet mass dried at 60 ° C and screened through a 180 µm sieve (Retsch, Germany). The modified cellulose obtained from TP-NF was labeled TP-MC.

Determination of Physicochemical Properties

Identification Test

The TP-NF and TP-MC (0.5 g) powders were singly placed in a porcelain crucible and treated with a few drops of iodine solution.—A blue black color would indicate the presence of starch.

pH and Viscosity
The pH of 2 % w/v aqueous dispersion of TP-NF and TP-MC was determined using a pH meter (Corning, model 10, England) while the viscosity was determined with the aid of a model Dv2 Brookfield viscometer (Brookfield Engineering Laboratories, Massachusetts, USA) using Lv-02 (number 62) spindle set to rotate at 12 rotations per minute (rpm) speed, at a temperature of 29.5 ± 0.5 °C.

Ash Content Determination
The ash profiling of TP-NF and TP-MC was done using standard methods [20].

Bulk and Tapped Densities
A 20 g quantity of TP-NF and TP-MC was employed in the determination of bulk and tapped densities using the Stampfvolumeter (STAV 2003JEF, Germany). The bulk and tapped densities were calculated using equations 1 and 2 respectively:

$$\text{Bulk density} = \frac{\text{mass}}{\text{bulk volume}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

$$\text{Tapped density} = \frac{\text{mass}}{\text{tapped volume}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

Particle Density
The particle density of TP-NF and TP-MC was determined by solvent displacement method using n-hexane as non-solvent. An empty 25 ml pycnometer was weighed (W). It was filled with n-hexane and weighed (W1). The difference between (W1) and W was calculated as W2. A 0.50 g quantity of the powder was weighed (W3) and carefully transferred into the pycnometer, the excess fluid was wiped off and the bottle was weighed again (W4). Three replicate determinations were carried out. Particle density, Pt was calculated according to equation 3:

$$\text{Pt} = \frac{\text{W2} \times \text{W3}}{\text{V}(\text{W3} - \text{W4} + \text{W2} + \text{W})} \ldots\ldots\ldots\ldots (3).$$

where: V is the volume of pycnometer. W = weight of empty pycnometer, W2 = weight of n-hexane only, W3 = weight of sample powder (0.50 g) and W4 = weight of pycnometer + sample + n-hexane.

Powder Porosity
The porosity of the powders was calculated using the respective values of the bulk and particle density determined for the powder. This was calculated using equation 4:

$$\text{Porosity (\%)} = \left\{1 - \left[\frac{\text{bulk density}}{\text{particle density}}\right]\right\} \times 100 \ldots(.4)$$

Flow Rate and Angle of Repose
A 20 g quantity each of the respective powders was used to determine flow rate using the funnel method. Three replicate determinations were carried out and data obtained was fitted into equation 5. The angle of repose of TP-NF and TP-MC was determined by pouring the powder into a cylindrical plastic roll fixed on to a flat base whose diameter is known and is the same as the internal diameter of the cylinder. The cylinder was slowly pulled out vertically so as to form a cone of powder on the base. The height of the cone was measured. The diameter of the circumference of heap formed was measured. Three replicate determinations were carried out. Calculations were made using equation 5 and 6 respectively:

$$\text{Flow rate} = \text{Mass of powder} / \text{Time} \ldots\ldots\ldots\ldots (5)$$

$$\text{Angle of repose } \theta = \tan -1 \frac{2\text{h}}{\text{d}} \ldots\ldots\ldots\ldots\ldots (6)$$

where θ is the angle of repose, *h* is the height of heap of powder, *d* is the diameter of heap of powder.

Hausner's Ratio
This was calculated as the ratio of tapped density to bulk density of TP-NF and TP-MC using equation 7.

$$\text{Hausner's quotient} = \frac{\text{tapped density}}{\text{bulk density}} \ldots\ldots\ldots\ldots\ldots (7)$$

Carr's Compressibility Index (CI)
This was calculated using bulk and tap densities of TP-NF and TP-MC when fitted into equation 8:

$$\text{CI} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100 \ldots\ldots\ldots (8)$$

Moisture Content
An empty crucible was weighed and the weight recorded. One gram each of TP-NF and TP-MC was transferred to the crucible and weighed. The crucible was placed in the oven at 105°C until a constant weight was reached. This was carried out in triplicate and the mean and standard deviation determined [21].

Hydration Capacity
The hydration (water retention) capacity of TP-NF and TP-MC powders was determined by the method of Ring [22] with modification. A 1 g quantity of each powder was placed in a 15 ml plastic centrifuge tube and 10 ml of water was added. The tube was shaken intermittently over a 2 h period and left to stand for 30 min. This was then centrifuged for 10 min at 3000 rotations per minute (rpm). The supernatant was decanted and the weight of the powder after water uptake and centrifugation, was determined. Triplicate determinations were carried out and mean values were calculated using equation 9.

$$HC = \frac{Wm}{Wd} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (9)$$

where: *Wm* is the weight of moist powder after centrifugation and *Wd* is the weight of dry powder.

Swelling Index

The swelling index of TP-NF and TP-MC was obtained by measuring the tapped volume occupied by 2 g of the powder sample, Vx, in a 50 ml glass graduated measuring cylinder. The powder was then dispersed in 35 ml of water and the volume made up to 50 ml with water. After 24 h of standing, the volume of the sediment, Vv, was estimated. Triplicate determinations were carried out. The swelling index (Sw. I) was computed using equation 10:

$$Sw.I = \frac{Vv}{Vx} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (10)$$

Moisture Sorption Profile

A quantity of 1 g each of TP-NF and TP-MC was weighed and transferred into a tarred empty boat. The boat was then placed in desiccators containing saturated solutions of magnesium nitrate, sodium chloride, potassium chloride, potassium sulphate and distilled water to simulate relative humidity (RH) of 52, 75, 84, 96 and 100 % at 25°C respectively. The weight gained by the exposed samples at the end of 5 days period was recorded and the amount absorbed was calculated from the difference in weight of each of the samples.

Fourier Transform Infrared Spectroscopy

The Fourier Transform Infrared Spectroscopy (FTIR) of TP-MC, albendazole, and TP-MC plus albendazole was carried out using FTIR equipment (Phenox Prox, Netherlands).

Formulation of Albendazole Granules and Tablets

Tablets containing 200 mg albendazole per tablet were formulated by the wet granulation method using the ingredients shown in Table 1. Each tablet was targeted to weigh 280 mg. The wet granulation method was used in the preparation of the granules. TP-NF, TP-MC and Avicel PH 101 (AV-MC) were used as binders at 5, 7.5, 10 and 15 % w/w. Dispersions of the binders made with hot water were used to moisten wet mass the intra granular ingredients powder blends of the formulation. The wet masses were passed through a 2 mm stainless steel sieve (Retsch, Germany), dried at 60 °C in an oven (Memmert, England) until sufficiently dried. Further screening of the granules was done using a 1 mm stainless steel sieve after which they were further dried to constant weight. Talc and magnesium stearate were added before compression into tablets using a 10 mm set of flat faced punches fitted to an automated single punch tableting machine, model NP 1 (Erweka, Germany) at a compression pressure of 1000 kg.

Evaluation of Tablets

The albendazole tablets were allowed a post compression relaxation period of 24 h before evaluation tests were carried out.

Weight Uniformity Test

Twenty tablets from each batch of the albendazole tablets were selected at random. The tablets were weighed individually and the mean and percentage coefficient of variation of each batch of tablet weight was calculated [23].

Crushing Strength Test

Ten tablets were randomly selected from each batch and tested using a Monsanto hardness tester. Each tablet was placed between the anvil and spindle of the tester and the knob screwed until the tablet was broken and the values were recorded in kgF units.

Height/tThickness

The height/thickness of the ten albendazole tablets that were randomly selected from each batch was measured using a micrometer screw gauge.

Friability Test

Ten (10) tablets from each batch were randomly selected, weighed and placed in the Erweka friabilator (D-63150 Heusenstamm, TAR 220, Germany) which was operated at 25 revolutions per minute (rpm) for 4 min. The tablets were removed, dusted and reweighed. Friability of the tablets was calculated using equation 11.

$$B = 100\left(1 - \frac{W}{Wo}\right) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (11)$$

where

B is friability, W is the final weight of the tablet after it has passed through the friabilator and Wo is weight of initial tablet.

Standard Calibration Curve

A quantity of 90 mg of albendazole powder was transferred accurately to a 250 ml volumetric flask. Ten (10) ml of acidified methanol was added and the flask was agitated to dissolve the powder and 0.1 N HCl (hydrochloric acid) was used to make up the preparation to the required volume while mixing. A 5 ml of the solution was transferred to a 200 ml volumetric flask and made up to volume with 0.1 N sodium hydroxide solution. It was shaken to mix well [23].

Serial dilutions of the stock were done to enable preparation of different concentrations of the albendazole solution. A scan of the serially diluted albendazole solution was done to determine the wavelength of maximum absorption. This was done using a spectrophotometer (model 6405, JENWAY, Germany) and was found to be 234 nm. The absorbance of the different diluted albendazole solutions were converted to concentrations and the standard calibration curve plotted.

Dissolution Test
The test was performed using the Erweka dissolution tester, (Model DT 600, Erwerka® Germany). A 900 ml volume of dissolution medium (0.1 N HCl) was measured into the 1 L beaker which was immersed into the bath of the dissolution equipment. The basket method was adopted and the dissolution medium and bath temperature were maintained at 37 ±1 ^{o}C. The speed of the basket was set at 50 revolutions per minute (rpm). A 5 ml sample of dissolution medium was withdrawn at 2, 5, 10, 15, 20 25, 30 min respectively. Replacement of withdrawn sample was done with the same volume of 0.1N HCl maintained at the same temperature [23]. The absorbance of each scanned solution was read in a UV/Vis spectrophotometer (Jenway, Model 6405, England) at a wavelength of 234 nm.

Drug Content/Assay of Tablets
Twenty tablets that were selected at random from each batch were weighed collectively and crushed, and a portion equal to the mean weight was weighed into a 100 ml volumetric flask where it was dispersed with 0.1N HCl to make a 100 ml dispersion. It was filtered using a Whatman filter paper and the filtrate scanned in the spectrophotometer at 234 nm. The absorbance readings were taken and converted to concentration using the standard calibration equation.

Statistical Analysis
The statistical analysis of the data obtained was done using one way analysis of variance (ANOVA) with the aid of an IBM SPSS version 21 software (IBM, Chicago, USA). Values were considered significant at 95 % confidence interval or $p < 0.05$.

RESULTS
The percentage yield of fibre TP-NF obtained from the dry seeds of PT was 13.05 % w/w. The TP-NF powder was rough, coarse, off white in color, bland tasting and odorless.

Physicochemical and Some Micromeritic Properties
The results of some physicochemical properties of the materials (TP-NF and TP-MC) such as iodine test, pH, viscosity, ash content are shown in Table 2 while some micromeritic properties are shown in Table 3.

Fourier Transform Infrared Spectroscopy
The FTIR spectra of albendazole, TP-MC and albendazole + TP-MC are shown in Figures 1-3. Sharp peaks depicting the existence of distinct functional groups were observed in all the figures.

Albendazole Granule Properties
The results of some of the micromeritic properties of albendazole granules containing TP-NF, TP-MC and Avicel PH 101 (AV-CL) are shown in Table 4. Parameters evaluated include the bulk and tapped densities, granule density, porosity, Hausner's quotient and Carr's compressibility index.

Albendazole Tablets
Some properties of the albendazole tablets such as uniformity of weight, crushing strength, friability, crushing strength-friability ratio (CS-FR), and content of Active Pharmaceutical Ingredient are shown in Table 5.

Dissolution Profile
The dissolution or drug release profiles of the different batches of the albendazole tablets are shown in Figures 4 and 5.

DISCUSSION
The ash content of the natural and modified fibres showed that the total ash values of the modified samples were generally higher than those of the raw fibres and this may be attributed to the introduction of inorganic materials to the fibre during the processing (modification process) stage [24]. The pH values were close to neutral which is good for the formulation of both basic and acidic drugs, the viscosity of TP-NF was low ($p > 0.05$), while TP-MC was higher and showed a significant difference in value ($p < 0.05$).
The FTIR spectra of the albendazole powder (Fig. 1) showed prominent sharp peaks at 3318.268 and 2999.008 cm^{-1} which were characteristic of non-aromatic compounds and can be attributed to a hydroxyl group (OH) stretch vibration. Other prominent not very sharp peaks were observed at 2793.077 cm^{-1} and 2507.842 cm^{-1} depicting $–CH_2$ and N=C bonding respectively. A peak was also observed at 1855.48 cm^{-1} indicative of carbonyl (C=O) vibrational mode. The spectra for the cellulose fibre TP-MC (Fig. 2) showed sharp peaks at 3008.940, 3244.790 and 3340.572 cm^{-1} which can be attributed to the presence of hydroxyl (OH) group. Sharp and narrow peaks were also noticed at 2738.813 and 2510.070 which could denote stretching bands implicated in $–CH_2$ and N=C bonding respectively. The FTIR spectra of the mixture of albendazole and TP-MC (Fig. 3) show peaks at 3374.020, 3290.166, 2993.138 cm^{-1} which could be attributed to retention of the hydroxyl groups. Similarly observed were sharp peaks at 2787.754 and 2694.855 cm^{-1} which can be attributed to $–CH_2$ and N=C bonding respectively. Thus, it can be inferred that there was no distinctive loss of the functional groups as a result of mixing of the polymer (TP-MC) and albendazole which implies that no untoward chemical reaction occurred and the products are expected to be stable on the shelf after their formulation.
The tapped density of TP-NF and TP-MC showed increase in the density of the powders upon tapping. Modification was found to increase the densities of the powders. The effect of quantified agitation of the powders led to increased densities [25]. Results of the particle densities of TP-NF and TP-MC powders show that the density of TP-MC was higher ($p<0.05$) than TP-NF which implied that modification possibly affected the structural arrangement and lattice structure (crystallinity) of the cellulose powders.

The porosity of TP-NF and TP-MC powders is shown in Table 2. The modified powder had higher porosity than the natural fibre. This implies that modified powder is more loosely packed and would have a better flow behaviour.

Results of the flow rate showed an interrupted discharge of the powders from the orifice of a funnel showing their poor flow property. The angle of repose of TP-NF was higher than that of TP-MC implying that modification enhanced the

Table 1: Formula for albendazole chewable tablets

Ingredients	**TPF-1**	**TPF-II**	**TPF-III**	**TPF-IV**	**TMC-I**	**TMC-II**	**TMC-III**	**TMC-IV**	**AVC-I**	**AVC-II**	**AVC-III**	**AVC-IV**
Albendazole (mg)	200.00	200.00	200.00	200.00	200.00	200.00	200.00	200.00	200.00	200.00	200.00	200.00
Mannitol (mg)	28.00	28.00	28.00	28.00	28.00	28.00	28.00	28.00	28.00	28.00	28.00	28.00
TP-NF	14.00	21.00	28.00	42.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
TP-MC	0.00	0.00	0.00	0.00	14.00	21.00	28.00	42.00	0.00	0.00	0.00	0.00
Avicel PH 101	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	14.00	21.00	28.00	42.00
Magnesium stearate (mg)	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40	1.40
Lactose (mg)	36.60	29.60	13.00	8.60	36.60	29.60	13.00	8.60	36.60	29.60	13.00	8.60
Total (mg)	**280**	**280**	**280**	**280**	**280**	**280**	**280**	**280**	**280**	**280**	**280**	**280**

Table 2: Physicochemical Properties of TP-NF and TP-MC

Parameter		**TP-NF**	**TP-MC**
Iodine test		Non blue black	Non blue black
pH*		4.94 ± 0.15	6.31 ± 0.11
Swelling index (%)*		173.33 ± 3.77	253.33 ± 5.77
Hydration capacity (%)*		391.31 ± 5.97	549.15 ± 7.24
Total insoluble ash		0.6	6.6
Acid insoluble ash		0.0	0.0
Water soluble ash		0.2	0.9
Sulphated ash		6.9	8.1
Ethanol extractive yield		0.0	4.0
Water extractive yield		0.0	0.0
*Moisture sorption	52%	7.00 ± 0.03	18.51 ± 1.12
	75%	14.09 ± 0.18	21.51 ± 1.02
	84%	14.68 ±1.23	25.14 ± 1.75
	96%	25.69 ± 1.42	63.22 ± 2.79

**Values are mean ± STD*

Table 3: Some micromeritic properties of TP-NF and TP-MC

Parameters	**TP-NF**	**TP-MC**
Bulk density (g/ml)	0.23 ± 0.00	0.22 ± 0.00
Tapped density (g/ml)	0.39 ± 0.02	0.30 ± 0.01
Particle density(g/ml)	1.40 ± 0.01	1.55 ± 0.01
Porosity (%)	82.82 ± 0.00	86.14 ± 0.15
Hausner's ratio	1.69 ± 0.11	1.36 ± 0.05
Carr's index (%)	41.03 ± 0.65	26.67 ± 0.04
Angle of repose (°)	80.51 ± 0.16	78.02 ± 1.64
Loss on drying (%)	7.71 ± 2.31	8.84 ± 0.51

Values are mean ± STD

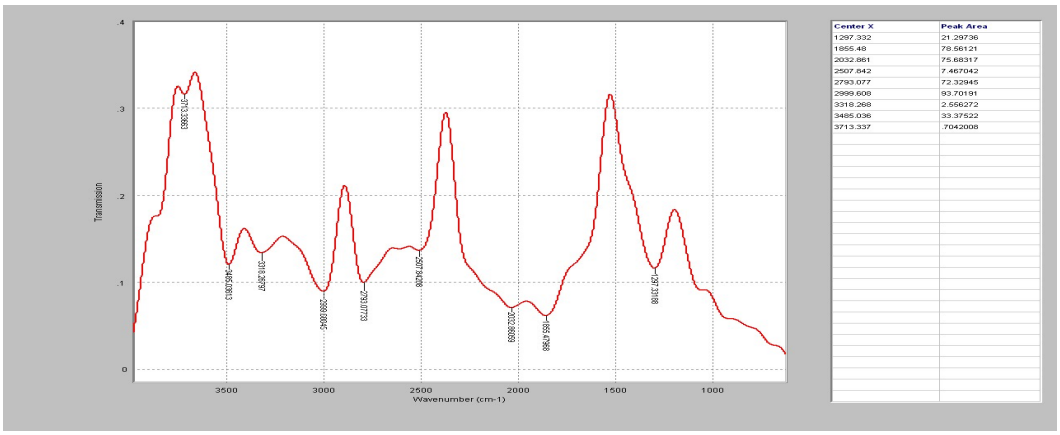

Fig. 1: FTIR of albendazole powder

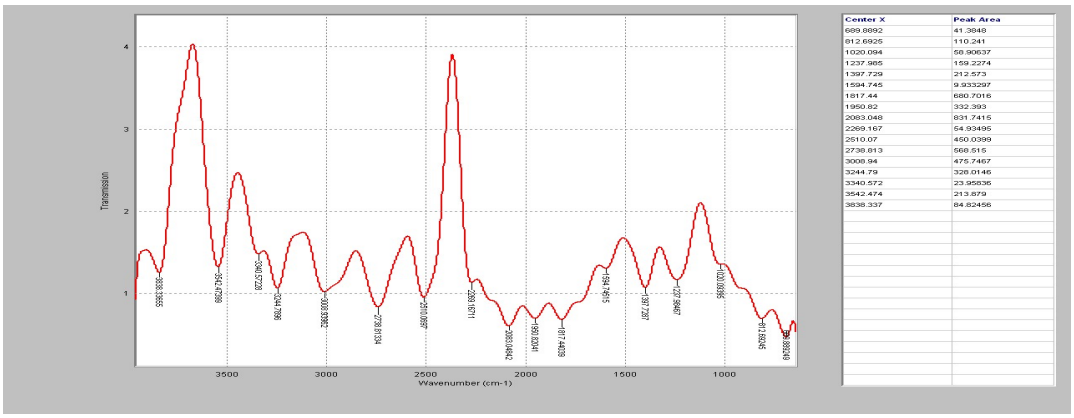

Fig. 2: FTIR of TP-MC

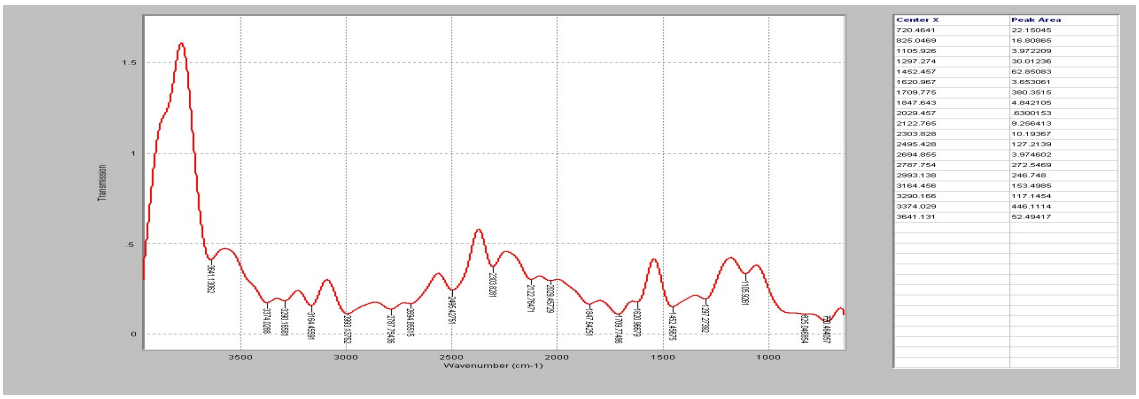

Fig. 3: FTIR of albendazole powder and TP-MC

Table 4: Some micromeritic properties of albendazole granule formulations

Parameter	Bulk density (g/ml)	Tapped Density (g/ml)	Granule Density (g/ml)	Porosity (%)	Hausner's Quotient	Carr's Index (%)	Angle of Repose (°)	Flow Rate (g/s)
TPF-1	0.50±0.01	0.57±0.01	2.01	75.01±0.01	1.14±0.02	12.28±1.38	27.14±0.25	4.21±1.05
TPF-II	0.48±0.00	0.55±0.01	2.16	77.78±0.01	1.15±0.02	12.73±1.06	26.35±0.76	5.19±1.04
TPF-III	0.46±0.01	0.54±0.01	2.23	79.37±0.60	1.16±0.03	14.81±1.34	27.31±0.17	5.96±0.49
TPF-IV	0.46±0.01	0.53±0.01	2.44	78.61±0.23	1.15±0.02	13.21±1.23	27.50±0.17	6.26±0.65
TMC-1	0.40±0.01	0.48±0.01	1.62	75.30±0.49	1.21±0.01	16.93±0.81	30.44±0.35	6.40±0.23
TMC-II	0.38±0.01	0.46±0.01	1.92	80.07±0.12	1.19±0.01	15.93±0.45	29.17±0.01	6.99±0.68
TMC-III	0.40±0.01	0.44±0.01	2.12	81.34±0.41	1.17±0.03	13.63±1.15	28.24±0.58	7.52±0.44
TMC-IV	0.35±0.01	0.43±0.01	2.23	84.25±0.27	1.21±0.02	16.36±0.55	29.45±0.01	8.99±0.25
AVL-I	0.43±0.01	0.50±0.01	1.42	70.01±0.01	1.18±0.02	15.60±1.20	29.75±0.01	6.66±0.07
AVL-II	0.44±0.01	0.52±0.01	1.67	73.94±0.01	1.12±0.01	16.54±0.39	28.34±0.01	NF
AVL-III	0.44±0.01	0.54±0.01	1.76	75.09±0.32	1.23±0.02	18.96±1.03	29.26±0.16	NF
AVL-IV	0.41±0.01	0.54±0.01	1.87	78.12±0.01	1.25±0.02	19.72±0.01	29.45±0.01	NF

Values are mean ± STD and NF represents 'no flow'

Table 5: Some properties of albendazole tablets

Parameter	Uniformity of weight (mg)	Crushing strength (kgF)	Friability (%)	Thickness (mm)	CS-FR	Content of active ingredient (%)
TMF-1	281.00±0.01	3.41 ±0.25	0.58±0.01	3.03±0.02	5.88	99.25 ±0.02
TMF-II	275.28±0.02	3.62 ±0.19	0.41±0.02	3.01±0.01	8.83	97.91 ±0.41
TMF-III	293.00±0.02	3.91 ±1.14	0.39±0.02	3.02±0.01	10.03	99.13 ±0.14
TMF-IV	282.00±0.02	4.34 ±1.07	0.28±0.01	3.00±0.02	15.50	98.12 ±1.15
TMC-1	285.22 ±0.02	4.74 ±0.29	0.12±0.02	3.05±0.03	39.50	98.79 ±1.75
TMC-II	282.53 ±0.02	4.93 ±0.29	0.06±0.01	3.03±0.00	82.16	98.05 ±2.01
TMC-III	293.68 ±0.02	5.11 ±0.44	0.05±0.00	3.05±0.01	102.20	97.24 ±0.19
TMC-IV	282.00 ±0.02	6.87 ±0.62	0.05±0.00	3.03±0.01	137.40	98.05 ±2.26
AVL-I	287.20 ±0.02	4.83 ±0.05	0.11±0.01	3.03±0.05	43.91	99.37 ±1.90
AVL-II	288.20 ±0.02	4.93 ±0.75	0.09±0.01	3.02±0.02	54.78	97.88 ±2.50
AVL-III	294.44 ±0.02	5.00 ±1.71	0.04±0.00	3.04±0.03	125.00	98.96 ±1.98
AVL-IV	290.24 ±0.01	5.34 ±1.07	0.04±0.01	3.04±0.01	133.50	100.02 ±0.88

Values are mean ± STD

flow properties. Generally, powder flow is known to be dependent on surface morphology, particle size and shape, surface charges on the particles/powder as well as the moisture content of the powders [26].

The Hausner's quotient and percentage Carr's compressibility index values obtained ranged from 1.36± 0.05 to 1.69 ± 0.01 to 26.67 ± 0.69 to 41.05 ± 0.65 % respectively. Both flow indices signify poor flow properties by the cellulose fibres [20,23]. However, modification improved the flowability of TP-MC as the flow values were better than TP-NF.

The results of the moisture studies such as the swelling index and hydration capacity of TP-NF and TP-MC were more than 100 % implying good swelling properties and possession of a good property that would enhance binding as well as disintegration when used in tablet formulation. However, TP-MC had higher swelling index and hydration capacity ($p<0.05$) than TP-NF. These show the ability of both materials to take up water into their structure causing the disentanglement of their polymeric chain. These would positively affect disintegration of the particles in the tablet formulation. The moisture sorption properties of TP-NF and TP-MC are contained in Table 2. Generally, the moisture sorption increased as the relative humidity of storage/test condition also increased. TP-MC had higher moisture sorption properties than TP-NF. At the same relative humidity conditions, TP-MC had consistently higher moisture sorption

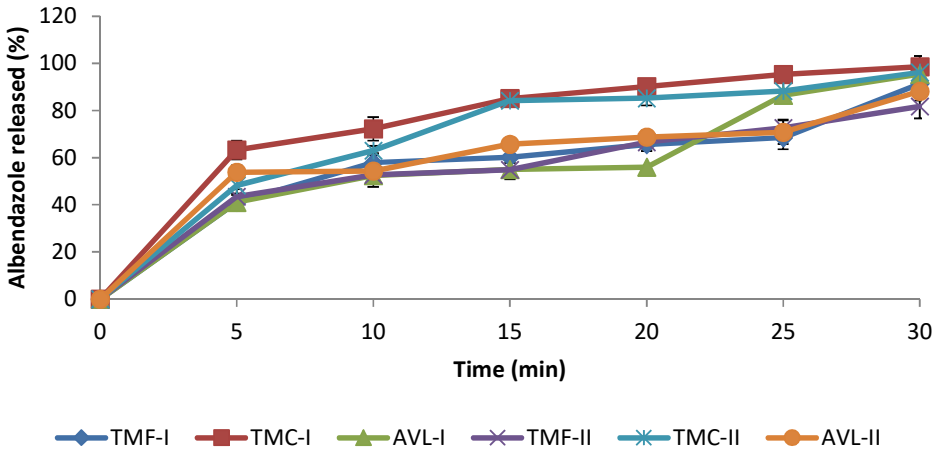

Fig.4: Dissolution profile of albendazole from TMF, TMC and AVL tablets at 5 and 7.5 % polymer concentrations

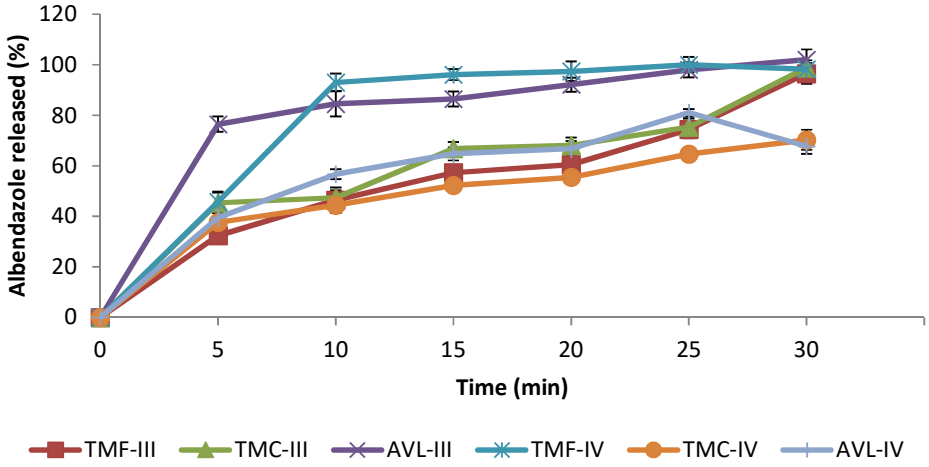

Fig.5: Dissolution profile of albendazole from TMF, TMC and AVL tablets at 10 and 15 % polymer concentrations

than TP-NF. This implies that tablet drug formulations containing the modified fibre would have the tendency to be more easily degraded in humid environments than those containing the natural fibre.

Some micromeritic properties of albendazole granules such as the bulk and tapped density of albendazole granules formulated with TP-NF (TPF-I to TPF IV) were higher than those formulated with AV-CL (AVL-I to AVL-IV) while those containing TP-MC (TMC-I to TMC-IV) were lower. Thus albendazole granules containing TP-NF would occupy a larger space in a container. The higher tapped density values obtained in each formulation shows that the powders are compressible. The particle density values for each of the binders also increased as the concentration of the binder that was used in each formulation increased.

Results of the flow rate and angle of repose of the albendazole granules containing TP-MC showed uninterrupted flow from the funnel. However, the flow rates increased with increase in the amount of TP-MC that was used in the formulation. Albendazole granules containing AV-CL behaved in a contrast manner. Formulation AVL-I (containing 5% AV-CL) had a good flow while the other formulations (AVL-II to AVL-IV) containing AV-CL at strengths greater than 5 % had interrupted flow. This is expected, since one of the short comings of AV-CL as a pharmaceutical excipient is poor flow. The Hausner's quotient of the granules containing TP-MC decreased as the concentration of TP-MC in the formulations increased. Generally, all the albendazole granules containing TP-MC had Hausner's quotient of < 1.25 which confers on them good flow property. The Hausner's quotient of albendazole formulations containing AV-CL were also less

than 1.25. However, the indices increased with increase in the quantity of AV-CL that was added to the formulation. The percentage Carr's index of the albendazole granule formulations containing both TP-MC and AV-CL followed the same trend that was observed for the Hausner's quotient. All the granules can be classified as having a good flow, although the TP-MC formulations had a better flow than the AV-CL formulations.

The porosity of albendazole granule showed that the least concentration of the binder had the least porosity while increase in porosity was noticed as the concentration of the binder increased. This pattern was consistent in the three formulations containing both the test binder materials as well as the standard. The order of porosity was TMC > TPF > AVL albendazole granule formulations

In terms of weight variation of the albendazole tablets, all the albendazole tablet formulations showed a minimal variation in weight irrespective of the type and concentration of the polymer that was used in the formulation. They complied with the acceptance specifications of both the British Pharmacopoeia and United States Pharmacopoeia for uncoated tablets weighing 280 mg [20,23].

Results of the crushing strength of the albendazole tablets showed that there was a general increase in the crushing strength of the albendazole tablets as the binder concentration applied in the formulation increased. All the tablets had crushing strength greater than 4 kgF except for formulations containing the natural fibre at 5, 7.5 and 10 % w/v (TMF-I – TMF-III). Albendazole tablets containing the modified fibre (TMC tablets) were mechanically stronger than those containing the natural fibre (TMF tablets) and avicel PH 101 (AVL tablets) (Table 4). Thus tablets (TMF-I – TMF-III) failed the crushing strength test while TMF-IV, TMC-I – TMC-IV, and AVL-I –AVL-IV) passed [20,23] and can be considered strong enough to withstand the necessary stresses of packaging, handling and transportation.

All the formulations had friability of less than 1% irrespective of the type of polymer used as binder. They passed the friability test and are expected to withstand the abrasive stresses that the tablets could be exposed to in the processes of handling and transportation. Both the British Pharmacopoeia and the United States Pharmacopoeia stipulate an upper limit of not more than 1 % for uncoated tablets [20,23] With regards to thickness, the albendazole tablets had thickness in the range of 3.00 ± 0.02 – 3.00 ± 0.03. There was no statistical difference ($p > 0.05$) in the thickness of the tablets which implied a uniform die filling and compression pressure of the granules when the tablets were being compressed.

The results of the crushing strength friability ratio (CS-FR) show that TMF tablets had CS-FR that was consistently lower ($p < 0.05$) than obtainable with TMC and AVL tablets at similar binder concentrations. The crushing strength friability ratio (CS-FR) of the different tablet formulations is a parameter used to establish mechanical strength of the tablet formulations not only on the bond or bridges built when the tablets were compressed but also on the effect that abrasive stress could have on such tablets.

With regards to the content of active ingredient, all the albendazole tablet formulations contained albendazole in quantities that ranged from 97.24 ± 0.19 - 100.02 ± 0.88 %. Their albendazole content met with specifications given in the pharmacopoeia for albendazole tablets [20,23].

Concerning drug release, the quantity of drug (albendazole) release from the tablets containing the polymers at 5 and 7.5 % w/w over a 30 min. period showed that albendazole release was generally gradual but consistently increased with time (Figures 5 and 6). There were significant differences ($p < 0.05$) in drug release for each polymer at the different sampling times. TMC-I was most released, followed by TMC-II, while AVL-I was least released up to 20 min. All the tablets released up to 80 % of their albendazole content within 30 min and were found to comply with Pharmacopoeia specifications for uncoated tablets [20,23]. Modification seems to have enhanced the release behavior of albendazole from the tablets ($p<0.05$). The dissolution profile of albendazole release from tablets containing 10 and 12.5 % w/w of the polymers (TMF-III, TMC-III, AVL-III, TMF-IV, TMC-IV and AVL-IV) show that all the tablets released more than 80 % of their albendazole content within 30 min. TMF-IV had the highest release of drug within 30 min and was followed by AVL-IV ($p < 0.05$). TMC-IV had the least release although it released more than 80 % of albendazole within 30 min and therefore passed the dissolution test and complied with the BP and USP set limits for dissolution of albendazole tablets. The higher release rates observed with the natural fibres can be related to the reduced binding effect as the concentration used increased when compared to the concentration of the modified cellulose binder. This correlates with the crushing strength of tablets produced from these polymers at different concentrations. The modified fibres had prominent binding properties and ensured good drug release at concentrations of 5 % and 7.5 % as shown in Figure 4.

CONCLUSION

The hydrophilic cellulosic biopolymer (TP-MC) obtained from the modification through oxidation of the fibre (cellulose) from the seed of TP had enhanced properties with regards to flow, compressibility, swelling capacity, hydration capacity. Albendazole granules formed from it had better flow properties than the natural fibre (TP-NF). In addition the albendazole tablets formed there from had good physical attributes as well as good release of albendazole during dissolution. These good physical properties and drug release conform to standards of the British and United States Pharmacopoeias. The results compared favorably with the standard polymer (AV-MC) suggesting that TP-MC can be used effectively in the formulation of albendazole tablets as binder.

CONFLICT OF INTEREST

The authors declare no conflict of interest in this work. The financing of this work was entirely borne by the authors.

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 us.

AUTHOR'S CONTRIBUTIONS

The work was designed by Nwachukwu, N. The bench work, literature search, data collection and analysis, and the write up of the manuscript were done by both authors.

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