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PREPARATION AND EVALUATION OF DISINTEGRANT PROPERTIES OF CROSS-LINKED SORGHUM (*SORGHUM ARUNDINACEUM*) STARCH IN METRONIDAZOLE TABLET FORMULATIONS

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ABSTRACT

Starch is one of the most versatile excipients used in this process due to its multifunctional properties. In its native form, it is commonly employed as a disintegrant in tablet formulations. However, several limitations that affect its stability on storage, compressibility, and flowability have led to its modification to obtain starch derivatives with better physicochemical and physicochemical properties. In the present study, native sorghum starch (NSS) and its cross-linked derivative were tested as a disintegrant in metronidazole tablets. NSS was cross-linked with phosphorus oxychloride ($POCl_3$), 0.3 %v/v, to obtain cross-linked sorghum starch (CSS). Both starches were evaluated for their physicochemical and micrometric properties and evidence of crosslinking and compatibility with the model drug was determined using Fourier Transform Infrared (FTIR) spectroscopy. Metronidazole tablets were formulated using both the wet granulation and direct compression methods, and the tablets were evaluated using standard pharmacopeia methods. FTIR revealed the presence of phosphorus-bound symmetry in CSS at 1273.06 cm^{-1} and 995.30 cm^{-1}. An improvement in the flow properties of CSS over NSS was achieved. Generally, the tablets had friability values of less than 1%, irrespective of the method of preparation. Also, tablets made by direct compression showed higher crushing strengths and DER but lower disintegration times for both NSS and CSS. All the tablets disintegrated and released 75 % of their drug content in less than 15 min, with slower release rates seen with CSS. The two starches perform well in both wet granulation and direct compression; however, the CSS formulation had longer disintegration time compared to those formulations of NSS and MSBP when used in both wet granulation and direct compression.

Keywords: Cross-linking, Disintegrant, Phosphorus oxychloride, Sorghum, starch

INTRODUCTION

Convenience, ease of administration, and suitability for systemic drug delivery make tablets the most accepted dosage form (Kailash *et al.,* 2022). Tablets of different types, sizes, and shapes can be made by directly compressing the powders or formulating the granules containing medicinal ingredients with or without diluents (Kanchan & Gaykar, 2023). Advancements in tablet technology have led to the development of modified dosage formulations to enhance drug efficacy, patient compliance, and ease of administration (Danae *et al.,* 2021).

Pharmaceutical excipients are crucial components of dosage forms, constituting the largest portion of the final product (Santhni *et al.,* 2023). These excipients, once considered inactive, it now plays essential roles in enhancing drug stability, bioavailability, appearance, taste, and administration processes (Zinan, 2023).

Starch is the most common pharmaceutical excipient owing to its compatibility, low cost, and wide availability. It serves various functions in tablet formulations, such as a binder, disintegrating agent, bulking agent, and film former in drug delivery systems (Marc-André *et al.,* 2023). Starch can be modified through physical, chemical, enzymatic, and genetic methods to enhance its properties for pharmaceutical applications (Aliyu *et al.,* 2022). A disintegrant is a substance or a mixture of substances added to a tablet or granules to facilitate its breakup after administration to allow rapid dissolution and absorption (Trisopon and Kittipongpatana, 2019).

Crosslinking is one of the most popular methods to alter the behaviour of biodegradable starch polymers, and it involves the interconnection of linear or branched chains in a polymer. Ether or ester bonds are formed when the reagents react with the hydroxyl groups in the starch molecules. This increases the polymer's rigidity by forming a three-dimensional network, making it soluble in organic solvents. Several agents are used to crosslink native starch: sodium trimetaphosphate (STMP), sodium tripolyphosphate (STPP), epichlorohydrin (ECH), and phosphoryl chloride ($POCl_3$), etc. (Gerezgihar and Szabo, 2022). Several techniques are employed to determine the degree of Crosslinking/Phosphorylation, among which are swelling, peak viscosity, amylose-amylopectin content determination, and phosphorus content (in the case of phosphorylation) (Kou and Gao, 2018).

Starch's use now enjoys applications in diverse industries, such as pharmaceutical, cosmetics, food, paper, and paint (Ahmad *et al.,* 2021). This research was designed to develop a crosslinked starch with practical application as a disintegrant in tablet formulations.

Phosphorus oxychloride ($POCL_3$) is extensively utilised as a crosslinking agent in starch modification processes to create crosslinked porous starch. This enhances molecular weight, reduces viscosity fluctuations, increases setting volume, and improves stability against heat, acid, and shearing forces (Abdussalam *et al.,* 2018).

METHODS

Starch crosslinking with phosphorus oxychloride ($POCl_3$)

The method of Kim *et. al*. (2015) was employed in cross-linking sorghum starch with $POCl_3$ (Sigma Aldrich laborchemikalien GmbH). A 10 % w/v solution of Anhydrous sodium sulphate in double-distilled water was used as a reaction medium. A starch suspension (20 g, w/v) in the reaction medium, $POCl_3$ (0.3 ml), was added under rapid stirring with a magnetic stirrer. The pH was adjusted to 11.5 with 1 M NaOH. The reaction was allowed to proceed for 120 min at 45 °C, after which the medium was neutralised to a pH of 5.5 with 1 M HCl to stop the reaction. The polymer was separated and dried, and a cross-linked product was obtained.

Determination of the degree of starch crosslinking

The method of Kaur *et. al*. (2004) was adopted in determining the degree/extent of cross-linking. The viscosity of a 25 %

w/v starch suspension was used as the determining factor measured concerning the change in temperature in the viscometer. Based on peak viscosity, starch suspension in measured concentration was placed in the Brookfield viscometer (DV-I Prime, England), and the temperature of the starch solution was raised from 30 to 95 °C at a constant rate of 11 °C/min and held at 95 °C for 2 min. Then, the paste was allowed to cool down to 50 °C at 11 °C/min and finally kept at 50 °C for 2 min. During this total cycle, viscosity was measured continuously.

The degree of crosslinking was calculated using the equation below:

Degree of cross-linking = $\frac{(A-B)}{A} \times 100$ (Eq. 1)

Where A is the peak viscosity of the control sample (without a crosslinking agent), and B is the peak viscosity of the cross-linked starch.

Fourier transform infrared (FT-IR) spectral study

The Fourier transform infrared spectral study was conducted for each of the native starch and cross-linked starch to confirm whether crosslinking took place or not. It was run using an FTIR machine (CARY- 630, Agilent Technologies, California, USA) at 400-4000 cm^{-1} on the spectrophotometer, as described by Rao *et al.* (2016).

Hydration capacity

The method of Kornblum and Stoopak (1973) was employed with slight modification. A 1.0 g each of the native and cross-linked starches and maize starch BP was placed separately in 15 ml plastic centrifuge tubes to which 10 ml distilled water was added and stoppered. The content was mixed for 2 min and allowed to stand for 10 min. The mixture was centrifuged (Sorvall Serial 75061 80) at 1000 rpm for 10 min. After this, the supernatant was decanted, and the weight of the sediment was recorded. The hydration capacity was determined as the ratio of the weight of the sediment to the dry sample weight.

Swelling capacity

The method of Achor *et. al.* (2014) was employed. A tapped volume occupied by 10 g of each starch (*Vd)* in a 100 ml measuring cylinder was noted. The powder was then dispersed in 85 ml of distilled water, and the volume was made up to 100 ml with more water. After 18 h of standing, the volume of the sediment (*Vw)* was estimated, and the swelling capacity was computed as:

Swelling capacity *Vw – Vd (*Eq. 2)

Granule and Powder Blend Characterisation

Flow rate

A 10 g quantity of powder sample was poured into the funnel of the Erweka TA-3R flow meter. The apparatus started, and the time taken for the powder to flow through the orifice was recorded. The flow rate, which is the quantity of material (in grams) that passes through the orifice in one second, was thus determined. The reading was taken in triplicate, and the mean was determined.

Angle of repose

A 10 g sample of the granules and powder blends was poured into a plugged glass funnel with the tip 6.0 cm above the flat surface of the bench. The granules were allowed to flow freely through the orifice of the funnel to form a heap whose height and diameter were determined. The angle of repose was calculated using the equation:

$Tan\ \theta = \frac{h}{r}$ (Eq. 3)

Where h = height and r = radius of circular heap

Bulk density

A 10 g quantity of the granules and powder blends was weighed using an electronic weighing balance and slowly poured into a 100 ml capacity graduated measuring cylinder. The powder surface was levelled by slowly moving the cylinder, and finally, the occupied volume was observed and recorded to calculate the untapped bulk density using the equation below.

Bulk Density = weight in grams/occupied volume (Eq. 4)

Tapped density

A 10 g weight of each of the granules and powder blends was weighed and poured into a 100 ml measuring cylinder and tapped on a hard surface 30 times from about 2 cm height, and the volume was recorded, which was used to calculate the tapped density using the equation below:

$$Tapped\ Density\ (TD) = \frac{M}{V} \quad \text{(Eq. 5)}$$

Where M is the mass of the starch sample and V is the volume occupied by the starch

Carr's index (C.I.)

Carr's Index (%) was extrapolated using the relationship below:

$$C.I. = \left(\frac{TD-BD}{TD}\right) x\ 100 \quad \text{(Eq. 6)}$$

Where TD-Tapped density and BD- Bulk density

Hausner's ratio (H.R.)

Hausner's ratio was calculated using the relationship below:

$$H.R. = \frac{TD}{BD} \quad \text{(Eq. 7)}$$

Where TD is Tapped density and BD is Bulk density

Tablet Formulation

Tablets were formulated using metronidazole as the model drug of choice. The Native and cross-linked sorghum starches were used to prepare tablets by wet granulation (Intra-Extra) and direct compression as a disintegrant and compared with commercially available MSBP. The granules and powder blend were compressed using a 12.5 mm punch and die set at a compression pressure of 6 KN using a single-stroke tablet press (Erweka, Type AR400, Germany). The target tablet weight was set at 400 mg, and a batch size of 100 tablets was prepared for each formulation. The tablet formulas are given in Tables 1 and 2 below.

Post-compression test on formulated tablets

Tablets weight variation test

From all the formulations, 20 tablets were sampled randomly and individually weighed using an electronic weighing balance. The variations in the tablet weight were determined and compared with USP standards as not to exceed ± 5 % (USP 32/NF 27-2011).

Crushing strength

From each formulation, 10 tablets were selected at random and individually placed between two anvils of the Erweka hardness tester. Force was applied to the anvils, and the crushing strength that caused the tablet to break was recorded as the tablet crushing strength.

Table 1.0: Tablet formula for metronidazole using NSS, CSS, and MSBP as disintegrant via wet granulation

Ingredient	F1	F2	F3
Metronidazole (%w/w)	50.0	50.0	50.0
Lactose (%w/w)	q.s	q.s	q.s
NSS/CSS/MSBP (%w/w)	5.0	5.0	5.0
Gelatin (%w/w)	5.0	5.0	5.0
Magnesium stearate (%w/w)	1.0	1.0	1.0
Talc (%w/w)	1.0	1.0	1.0
Total weight	**400 mg**	**400 mg**	**400 mg**

Key: NSS- Native sorghum starch; CSS- Cross-linked sorghum starch; MSBP- Maize starch BP; F1-NSS, F2-CSS, F3-MSBP.

Table 2.0: Tablet formula for metronidazole using NSS, CSS, and MSBP as disintegrant via direct compression

Ingredient	F4	F5	F6
Metronidazole (%w/w)	50.0	50.0	50.0
MCC	q.s	q.s	q.s
NSS/CSS/MSBP (%w/w)	5.0	5.0	5.0
Magnesium stearate (%w/w)	0.5	0.5	0.5
Talc (%w/w)	0.5	0.5	0.5
Total weight	400 mg	400 mg	400 mg

Key: MCC- Microcrystalline cellulose; NSS- Native sorghum starch; CSS- Cross-linked sorghum starch; MSBP- Maize starch BP; F4-NSS; F5-CSS; F6-MSBP.

Tablet thickness and diameter

The Vernier calliper (Fisher Scientific Company, USA) was used to measure the thickness and diameter of 10 tablets selected at random. Each tablet was placed between the two external jaws of the calliper.

Tablet friability

From each formulation, 10 tablets were selected at random, and their total weight was determined. The tablets were placed in a friabilator (Type TA3R Erweka, Germany) and made to rotate at 25 rpm for 4 min. The friability y was then extrapolated as the percentage of the difference in weight to the initial weight of the tablets.

Disintegration of tablets

The method described in B. P. (2002) was used. Six tablets selected at random were

used to conduct disintegration tests. Water thermostatically maintained at 37 ± 2 ºC was used as the medium. The time taken for each of the six tablets placed in each of the six tubes of the apparatus (Type ZT3, Erweka, Germany) to disintegrate and pass through the mesh was recorded as the tablet's disintegration time.

Dissolution test of tablets

This test was carried out according to the method specified in the B.P. (2002). One litre of 0.1 N Hydrochloric acid, thermostatically maintained at 37 ± 2 ºC, was used as the medium. The apparatus was set to rotate at a speed of 100 rpm. A tablet was placed in the clean, dried basket of the apparatus (Type DT, Erweka, Germany), which was afterwards immersed in the medium. A 10 mL sample was withdrawn every 5 min (with replacement of equivalent of the medium withdrawn), filtered, and I mL of the filtrate diluted to 10 mL (single dilution) and finally taken for UV VIS-Spectrophotometry at 257nm Wavelength to determine the absorbance of the drug (Metronidazole) from which the concentration of the dissolved drug can be extrapolated.

Statistical Analysis

Statistical Analysis was carried out using SPSS 15.0 Windows, a One-way ANOVA test, and a Turkey post hoc analysis to determine the level of significance.

RESULTS AND DISCUSSION

Starch is a versatile and sustainable biopolymer with extensive food and pharmaceutical applications (Sneh *et al.,* 2024). The innate hydrophilic behaviour of native starch due to the abundance of hydroxyl (OH) groups has presented challenges in developing starch-based materials. Hence, researchers have directed their efforts toward employing different chemical modifications to transform the numerous OH groups present in starch into different molecular structures (Shah *et al.,* 2016).

Viscosity is the measure of the resistance of a fluid/suspension material to deform at a given rate; it can also be used to optimize the concentration of the cross-linker required to obtain the desired level of cross-linking. The cross-linked starch showed a significantly higher peak viscosity throughout the temperature range than the native starch (Figure 1.0). Increased viscosity of the crosslinked starch may be due to the introduction of the new phosphorus bond linking the starch chains between the starch components (Amylose-Amylopectin or Amylopectin-Amylopectin) and consequent reduction in the loss of soluble component (Amylose), similar to the findings of Kou and Gao, (2018) when native starch was cross-linked with STMP/STPP. The increase in pasting viscosity is an indication of an increase in the structural network strength, making the suspension resistant to shear, which agrees with the findings of Shah *et al.* (2016) and Shen *et al.* (2019).

FT-IR spectroscopy is useful for compound identification of known/ unknown materials since no two molecular structures give the same FT-IR spectra (Stephen *et al.,* 2017). Comparative FT-IR spectra of native and crosslinked starches (Figure 2.0) showed that the broad peaks showing at 3410.26 cm^{-1} (O-H stretch band), 2924.18 – 2360.95 cm^{-1} (H-C-H asymmetric and symmetric stretch) and 1643.41 cm^{-1} (C-C=C symmetric stretch) in the native starch were replaced by the characteristic absorption peaks at 1273.06

cm^{-1} (P=O) and 995.30 cm^{-1} (P-O-C) in the crosslinked starch due to the presence of phosphorous bound symmetry, even though all the other major absorption bands were retained. This is in line with the findings of Ashwar *et al.* (2017) and Heo *et al.* (2017), who reported the appearance of new peaks of P=O at 1244-1266cm^{-1}, 1150-1400 cm^{-1}, and P-O-C at 995-1050 cm^{-1} respectively and Detduangchan *et al.* (2014), who reported P-O-C absorption peaks at 1035.75 cm^{-1} and 1261.38 cm^{-1} for P=O.

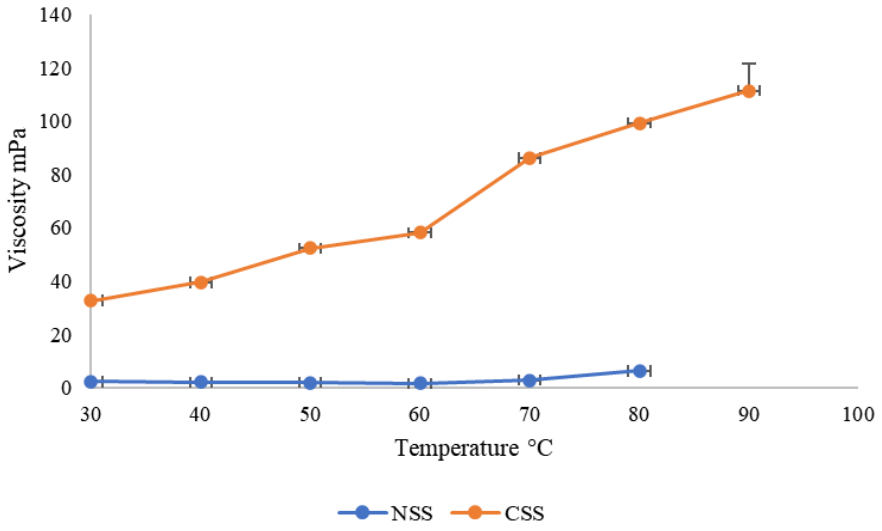

Figure 1.0: Rapid Viscosity analysis of Native and $POCl_3$-crosslinked Sorghum Starch

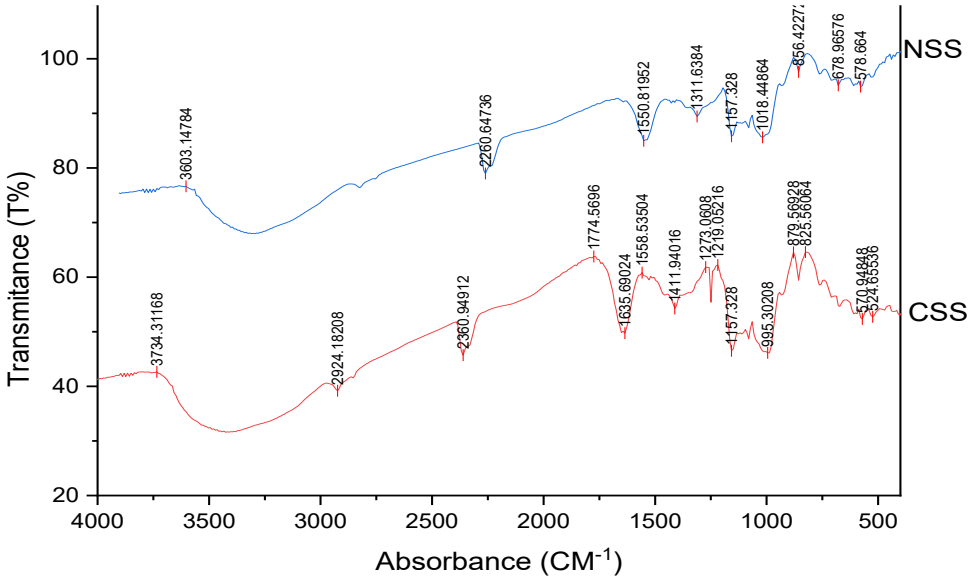

Figure 2.0 FTIR spectra of Native Sorghum starch and $POCl_3$-crosslinked sorghum starch

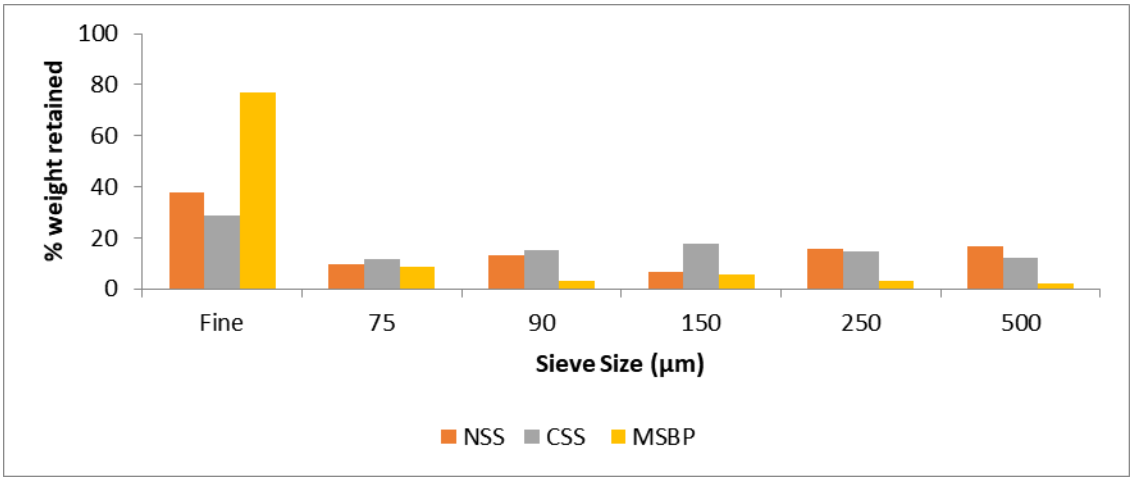

Figure 3.0 Particle size Distribution for the Native Sorghum Starch (NSS), Cross-linked Sorghum Starch and Maize Starch BP (MSBP)

One of the fundamental methods for the classification of powders is sieving, and it is the method of choice for determining the size distribution of coarse powders (Kale *et al.,* 2011). From the sieve analysis of the starches, the average particle size of the native and cross-linked (Table 3) starches was found to be similar, with CSS having an even distribution of the particles across the sizes of 75 µm and above when compared to NSS and MSBP. The NSS and MSBP, however, had a large percentage of fines, which is characteristic of all native starch powders. There was a general decrease in particle size after crosslinking, but the CSS had a better uniform distribution of mid-sized particles than the NSS. This ensured better packing geometry and compressibility of the cross-linked starch over the native and reference starches. This is in line with the findings of Malafaya *et al.* (2006), Hazarika and Sit (2016) and Desan *et al.* (2018), who reported a decrease in particle size as a result of crosslinking native starches. There was a marginal improvement in the flow characteristics of CSS compared to NSS, which could be a uniform distribution of fine and large-sized particles and probably spherical morphology of the crosslinked particles. The CSS had HR and CI comparable to that of MSBP (characteristic of fair flow and compressibility of material) and significantly better than NSS. This is in line with the findings of Rao *et al.* (2016), who reported a decrease in these values of psyllium seed starch cross-linked with STMP. Porosity is the space between the particles (Kale *et al.,* 2011). The CSS was less porous than NSS and MSBP, hence the better packing fraction exhibited by the crosslinked starch. This could probably be attributed to the even distribution of fine and large-sized particles in the crosslinked starch compared to the greater percentage of fines in the native starch.

Diverse functional properties of starches, like swelling power (SP), solubility, water absorption capacity (WAC) and oil absorption capacity (OAC), pasting attributes, etc., are affected by crosslinking (Sneh *et al.,* 2024). The cross-linked sorghum starch had significantly lower swelling power than the native and reference starch ($p\text{-}value \geq 0.05$). It is well known that cross-linking strengthens the bonding between starch chains, thus allowing them to resist swelling.

Therefore, the reduced swelling power would be related to the formation of inter-molecular bridges by the residual phosphorus after the cross-linking reaction (Yusuf *et al.,* 2018; Abdrabuo *et al.,* 2020). This is similar to the findings of Abdrabuo *et al.* (2020), Sandhu *et al.* (2021), and Xiaofan *et al.* (2022), who reported that the swelling power of crosslinked starches was lower than that of the native starch at the same temperature.

Use of materials for tablet or capsule filling requires the material to have good flow, a property that necessitates granule formulation before tabletting and one of the properties that qualify the material used in direct compression. From the result of the micrometric properties after the addition of extra-granular excipients (Table 4), it can be seen that there was an improvement in the flow and compressibility indices from the initial results of Table 3 for the different starches. This is explained by the increase in size due to the granulation process and in these granules

.

Table 3.0: Physicochemical properties of the native and cross-linked starches compared to the reference standard MSBP

Parameters	NSS	CSS	MSBP
Mean particle size(µm)	180.74	167.54	93.72
Angle of repose (º)	32.80	34.50	36.10
Flow rate (g/sec)	4.48	3.66	2.04
Bulk density(g/ml)	0.54	0.59	0.53
Tapped density(g/ml)	0.71	0.71	0.67
Carr's index (%)	23.94	16.90	20.90
Hausner's ratio	1.32	1.20	1.26
Powder porosity (%)	37.40	34.45	38.21
Packing fraction	0.44	0.50	0.43
Hydration capacity (%)	1.45	1.47	1.33
Swelling Capacity (%)	3.03	2.00	2.20

Key: NSS- Native sorghum starch; CSS- Cross-linked sorghum starch; MSBP- Maize starch BP

Table 4.0: Micromeritic Properties of Metronidazole Granules Formulated Using Wet Granulation

Formulations	Angle of repose (◦)	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Hausner's Ratio
F1	24.60 ± 1.23	0.50 ± 0.01	0.58 ± 0.12	13.80 ± 0.35	1.16 ± 0.01
F2	28.90 ± 1.12	0.46 ± 0.02	0.53 ± 0.02	13.20 ± 0.40	1.15 ± 0.03
F3	24.00 ± 1.19	0.46 ± 0.01	0.56 ± 0.11	17.96 ± 0.41	1.22 ± 0.01

Key: NSS- Native sorghum starch; CSS- Cross-linked sorghum starch; MSBP- Maize Starch BP; F1-NSS; F2-CSS; F3-MSBP

The angle of repose for wet-granulated granules is considerably lower than for direct-compression blends, indicating better flowability. Carr's index and Hausner's ratio similarly show improved compressibility for the granules (Carr's index, Hausner's ratio compared to the powder blends (Carr's index, Hausner's ratio. These results are consistent with prior studies. Jubril *et al.* (2012) reported improved micromeretic properties for granules using a starch binder, indicating excellent flow. Wet granulation significantly improves the flow and compressibility properties of metronidazole formulations (Abdullahi *et al.,* 2024). The observed micromeritic properties in this study align well with the literature, confirming that granulation enhances powder behaviour crucial for tablet manufacturing compared to direct compression formulations.

The mechanical properties of pharmaceutical materials arise from how materials respond to applied mechanical forces **(**Stephen *et al.,* 2017). The mechanical strength of a tablet is associated with the resistance of the solid specimen to fracturing and attrition. An acceptable tablet must remain intact during handling at all stages (Alderbon, 2013). The crushing strength of compacts (Table 5.0) F2 gave tablet compacts with better crushing strength than F1, probably due to the improvement in the compressibility indices due to crosslinking and it agrees with the findings of Jubril *et al*. (2012), Rao *et al.* (2016) and Pachuau *et al.* (2018) that showed an enhancement of tablet hardness as a result of crosslinking native starches.

A disintegrant is any substance that is included in the formulation to ensure that the tablet, when in contact with a liquid, breaks up into small fragments, which promotes rapid drug dissolution (Alderbon, 2013). Disintegration time is one of the most important characteristics of a good excipient and, consequently, a good tablet. The disintegration of the F2 was slower than that of the F1 and reference F3 (Table 5.0), which could probably be linked to the effect that crosslinking has on the ability to imbibe and retain moisture (swelling index-table 3). According to the B.P., however, the disintegration time should be less than 15 min for uncoated tablets (Azubuike *et al.,* 2020). All the batches passed this test as they all disintegrated in less than 15 minutes.

Table 5.0: Micromeritic properties of the powder blend for direct compression of metronidazole tablets

Formulations	Angle of repose (◦)	Bulk density (g/ml)	Tapped density (g/ml)	Carr's index (%)	Hausner's Ratio
F4	38.60 ± 2.19	0.46 ± 0.03	0.66 ± 0.02	29.36 ± 2.20	1.42 ± 0.02
F5	38.79 ± 3.25	0.48 ± 0.01	0.64 ± 0.02	24.57 ± 2.18	1.33 ± 0.00
F6	33.39 ± 2.32	0.49 ± 0.01	0.66 ± 0.01	24.96 ± 2.20	1.33 ± 0.00

Key: NSS- Native sorghum starch; CSS- Cross-linked sorghum starch; MSBP- Maize Starch BP; F4-NSS; F5-CSS; F6-MSBP

Table 6.0: Properties of metronidazole tablets formulated via wet granulation using NSS, CSS and MSBP as disintegrants

Formulations	WV (gm)	DM (mm)	TK (mm)	CS (Kg/F)	DT (min)	FR (%)	DER
F1	0.41 ±0.00	12.06 ±0.00	3.55 ±0.02	3.89 ±0.60	3.60 ±2.40	1.65	1.78
F2	0.41 ±0.00	12.05 ±0.00	3.65 ±0.01	5.80 ±0.67	13.26 ±0.10	0.78	0.34
F3	0.41 ±0.00	12.05 ±0.00	3.54 ±0.02	6.30 ±0.03	2.13 ±0.08	0.82	2.43
	±5	**-**	**±5%**	**At least 5KgF**	**≤15min**	**≤1%**	

Key: NSS- Native sorghum starch; CSS- Cross-linked sorghum starch; MSBP- Maize Starch BP; DER- Disintegration efficiency ratio; WV- Weight variation, TK= Thickness; DM= Diameter; CS= Crushing strength; DT= Disintegration time; FR= Friability; F1-NSS, F2-CSS, F3-MSBP containing formulations

Table 7.0: Properties of metronidazole tablets formulated via direct compression using NSS, CSS and MSBP as disintegrants

Formulations	Weight (mg)	TK (mm)	DM (mm)	FR (%)	CS (Kg/F)	DT (min)	DER
F4	390 ±0.01	3.43 ±0.14	12.06 ±0.02	0.84	6.20 ±1.26	0.32	16.28
F5	390 ±0.01	3.14 ±0.04	12.06 ±0.01	0.86	9.30 ±1.25	0.43	18.60
F6	400 ±0.01	3.37 ±0.02	12.06 ±0.02	0.80	5.60 ±1.95	0.39	11.49
USP limits 32/NF27	**±5%**	**±5%**	**-**	**≤1%**	**At least 5KgF**	**≤15min**	

Key: NSS- Native sorghum starch; CSS- Cross-linked sorghum starch; MSBP- Maize Starch BP; DER- Disintegration efficiency ratio; TK= Thickness; DM= Diameter; CS= Crushing strength; DT= Disintegration time; FR Friability; F4-NSS; F5-CSS; F6-MSBP

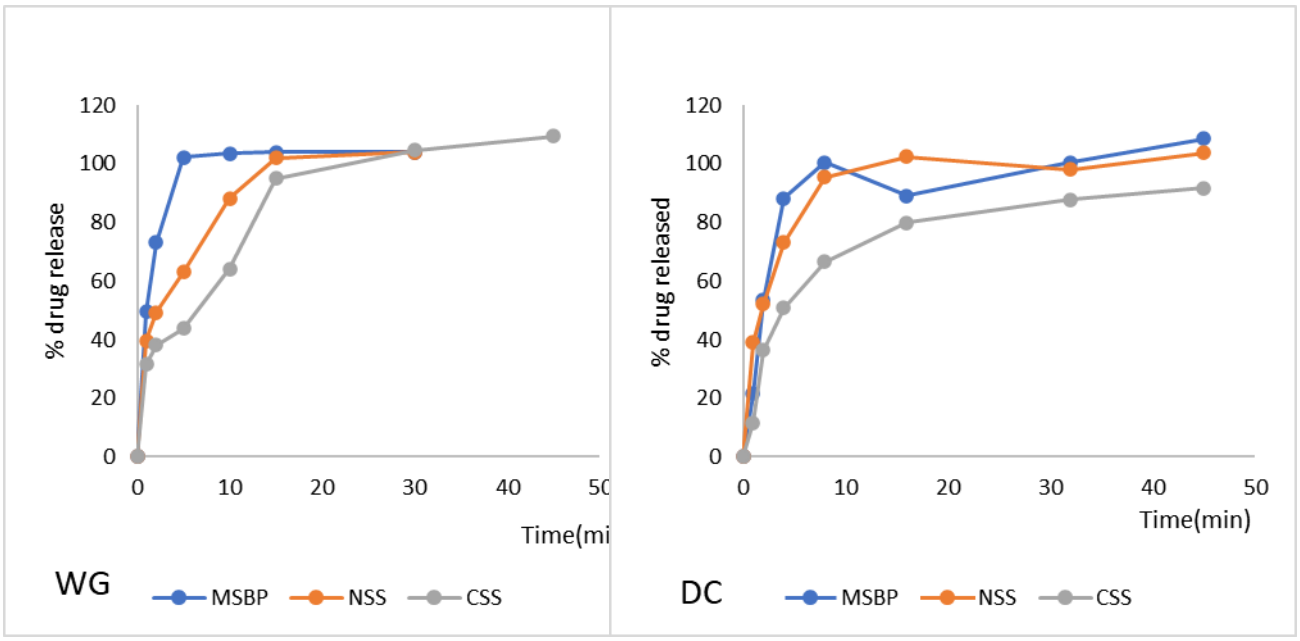

Figure 4.0: Dissolution Profile for the 5 % NSS, CSS, And MSBP As Disintegrant Formulated

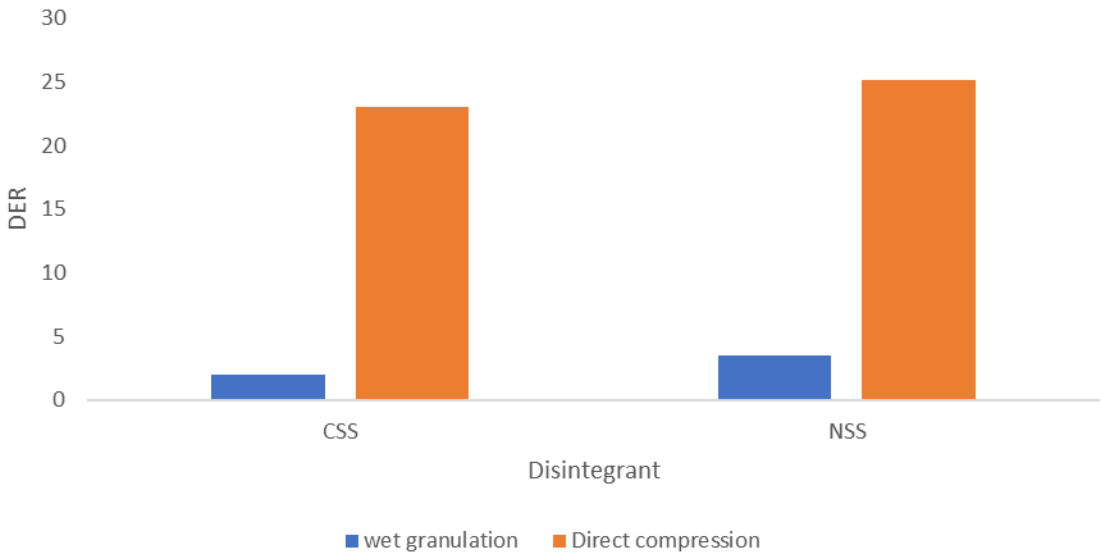

Figure 5.0: DER Profile of the Tablets Containing 5.0 % NSS And CSS Disintegrant Concentration Prepared By Wet Granulation And Direct Compression

The tendency of a tablet to chip, crumble or break during the process of packing, transit or during patient handling is termed tablet friability. Friability has an allowable limit of ≤1.0 %. The formulations F2 and F3 produced had passed the friability test, whilst the F1 did not.

The direct compression method of tablet production is a method of directly compressing the powder blend without any prior processing (Lawal *et al.,* 2019). Evaluation of the tablets produced via DC shows that the friability values of all the formulations (Table 7) were within the pharmacopeial limit of less than 1.0 % (USP, 2011). The crushing strength of a tablet measures the amount of force required to just break the tablet; it is a measure of the strength of the tablet. It was observed that the crushing strength of F5 is better than that of F4, and the two formulations had better crushing strength than the reference F6 ($p \geq 0.05$). The disintegration times for the three formulations were within the acceptable Pharmacopeial limit of <15 min for uncoated tablets. British Pharmacopoeia (2002) specification has it that 70 % of the drug is expected to be released within 45 minutes of drug dissolution for immediate release dosage forms. The time taken for 50 % and 80 % of the drug released by all the excipients was extrapolated from the plot (Figure 3 A & B) and all the batches were released in less than 15 minutes in the order of F3/F6>F1/F4>F2/F5 (MSS>NSS>CSS) in both wet granulation and direct compression.

Generally, formulations perform better in direct compression than in wet granulation methods. The crosslinked starch had a better balance between its mechanical strength and ability to break (disintegration time) than the native starch, considering the DER values (Figure 6.0). The cross-linked starch also performed better when used as a directly compressible excipient than in wet granulation.

CONCLUSION

Cross-linking of *Sorghum arundinaceum* starch was intended as a modification tool to improve the functionality of the native starch. Its suitability as a disintegrant in the formulation of immediate-release Metronidazole tablets by wet granulation and direct compression was investigated, and it was observed that the cross-linked starch had good disintegrant properties. The cross-linked starch also performed better when used as a directly compressible excipient than in wet granulation.

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