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Characterization of Cucumis sativus (Linnaeus) Mucilage and its Excipient Potentials in Metronidazole Tablet Formulation

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ABSTRACT

The objective was to characterize *Cucumis sativus* mucilage (CSM) and evaluate its binding potentials in metronidazole tablet formulation.

Characterization was done using proximate, elemental, material and rheological properties including FTIR. Tablets were produced by wet granulation with CSM, corn starch or acacia as binder (1-4%$^{w}/_{w}$) and evaluated using mechanical and release properties.

Generally, the properties of CSM showed that it can be used for oral formulations and it has significantly higher swelling index. The mechanical properties of metronidazole tablets as described by crushing strength–friability ratio ranked acacia > corn starch > CSM. An increase in the concentration of CSM produced faster disintegration for all tablets as opposed to corn starch and acacia which led to slower disintegration. The dissolution profiles of the tablets from CSM (4%$^{w}/_{w}$) showed highest similarity (f2=61.60) to those of acacia at 2%$^{w}/_{w}$.

CSM has excipient potentials that can be further developed for tablet production.

Keywords: *Cucumis sativus* mucilage, binding potential, metronidazole tablet.

INTRODUCTION

Excipient development is a research area that leads to discovery of new materials that may have assets similar to existing ones or sometimes offer improved properties to a dosage form. More so, development from locally available raw materials lowers manufacturing costs and boosts national status by creating jobs in different areas like planting, harvesting and storage systems[1]. In addition, the need to search for newer materials cannot be overemphasized especial-

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ly in oral drug delivery systems. Despite diverse advances in oral drug delivery systems, tablets remain tangible due to its being compact, simple and easy to use; offers opportunity for mass production, variability of designs can also be prepared compared to liquid dosage forms. Tablets also accounts for over 60% of solid dosage forms because of its high patient acceptance, compliance and adherence to medication.

Excipients used in tablet formulation include diluents, lubricants, glidants, sweetners, disintegrants and binders. Binders are agents which may be added in wet or dry form to assist the cohesiveness of powders thus ensuring the formation of intact tablets[2]. It has been estimated that less than 20 percent of active pharmaceutical materials can be compressed directly into tablets, the rest requires the use of binders either for direct compression or wet granulation. The use of natural polymers such as starches, gums and mucilages as pharmaceutical excipients grants several benefits such as biological compatibility, ready availability, non-toxicity, low cost and ease of chemical modification to suit diverse formulation requirements in comparison to synthetic ones[3].

Cucumis sativus Linnaeus (Family Cucurbitaceae) is commonly known as cucumber and was originally cultivated in Southern Asia, but now grows in most continents thriving both in temperate and tropical regions. Cucumber is a frost-sensitive annual plant whose heat requirement is greater than that for most common vegetables. It has a hairy climbing, trailing, or creeping stem, and is often grown on frames or trellises. The leaves are hairy and have 3–5 lobes; branched tendrils at leaf axes which support climbing or creeping. The plant bears cylindrical edible fruit when ripe with skins which can be smooth and thin, or thick and rough.

Jyoti and colleagues[4] studied the proximate and antimicrobial properties of cucumber extract and concluded that it has nutritional ingredients with considerable antimicrobial properties. Cucumber fruit has high water content, low calories, potential antidiabetic, lipid lowering and antioxidant activity[5]. Furthermore, several bioactive compounds have been isolated from cucumber including cucurbitacins, cucumegastigmanes I and II, cucumerin A and B, vitexin and orientin[5]. The medicinal properties of this valuable crop have been widely studied, and different parts of it have been acclaimed useful.

Cucumis sativus fruit has mucilage inside which helps the seeds to attach to the pulp and the excipient potentials of this mucilage is largely unharnessed. In our first study of this novel mucilage, the emulsifying properties in olive oil and liquid paraffin emulsions was assessed and the outcome showed that *Cucumis sativus* mucilage (CSM) may be used as a primary emulsifying agent for o/w emul-

sions[6]. To further increase the application of CSM, there is need to characterize it and evaluate its excipient properties in tablet formulation. In the present study therefore, an attempt was made to characterize the mucilage and its excipient potentials in metronidazole tablet formulation were evaluated in comparison with acacia and corn starch. The main finding showed that *Cucumis sativus* mucilage could be further developed for excipient use in tablet formulations.

METHODOLOGY

Materials

The materials used include Metronidazole, corn starch, lactose and xylene all obtained from BDH Laboratories (London, UK). Ethanol and diethyl ether were procured from Sigma (St Louis, MO, USA). Fruits of *Cucumis sativus* were purchased from Eleyele market, Ibadan town, South-west, Nigeria. All other chemicals and reagents were of analytical grade.

Methods

Extraction and purification of *Cucumis sativus* mucilage

The fruits of cucumber were cut open and the internal part was scooped out and hydrated for 72 h in chloroform-water DS (double strength) with intermittent stirring. The extraneous materials were removed by straining through a muslin cloth. To the filtrate, absolute ethanol (96%$^{v}/_{v}$) was added to precipitate the polymeric material. The precipitated mucilage was filtered, washed with diethyl ether, dried in a hot air oven (Laboratory oven TT-9083; Techmel and Techmel, TX, USA) at 40 ^{o}C, milled and sieved with 250 μm sieve and stored in airtight containers[7].

Proximate and elemental composition of *Cucumis sativus* mucilage

The ash, crude fat and crude fibre contents were determined using the Association of Official Analytical Chemists (AOAC) methods[8]**.** The protein content was calculated from the nitrogen content determined by elemental analysis using Atomic Absorption Spectrophotometer (AAS, Model 2500 Torontech Inc., Toronto, ON, Canada) using a conversion factor of 6.25. All determinations were done in triplicate and results were presented as mean and standard deviation.

Furthermore, elemental composition for cucumber mucilage was obtained by digesting an accurately weighed amount (2 g) of the sample to obtain a solution. The solution thus obtained was analysed for heavy metals using Atomic Absorption Spectrophotometer (AAS, Model 2500 Torontech Inc., Toronto, ON, Canada). The instrument was calibrated using manually prepared standard solutions of respective metals.

Density measurements

The loose bulk volume of the CSM or the granules was determined by pouring 30 g of powder at an angle of 45 ° through a funnel into a 50 mL glass measuring cylinder and the height was measured. The density was calculated from the ratio of the mass to the volume. The tapped volume was measured by applying 100 taps to 30 g of CSM or granules in a graduated glass cylinder at a standardized rate of 38 taps per min[9]. The particle density was measured using a 50 mL liquid pycnometer bottle with xylene as the displacement fluid[10].

Hausner's ratio and Carr's index determination

The Hausner's ratio was determined as the ratio of the initial bulk volume to the tapped volume.

The Carr's index was calculated from the results obtained from the bulk and tapped densities by using the equation below:

$$\text{Carr's index (\%)} = \frac{\text{Tapped density-Bulk density}}{\text{Tapped density}} \text{ x 100} \quad (1)$$

Swelling index

The swelling index of the excipients was determined using a standard method[11]. Excipient (2.5 g) sample was poured into a 100 mL measuring cylinder (v_1) and distilled water (40 mL) was added. The dispersion was well shaken for 5 min, made up to 50 mL with distilled water and allowed to stand for 24 h before sedimentation volume was obtained (v_2). The swelling power was then calculated as follows:

$$\text{Swelling index} = {}^{V_2}/_{V_1} \quad (2)$$

Solubility

The solubility of the CSM was determined using the method of Leach *et al* [12]. CSM (1 g) sample (w) was weighed into a conical flask; distilled water (15 mL) was then added and shaken slowly for 5 min. This was then transferred into a pre-weighed centrifuge tube; distilled water (7.5 mL) was added and centrifuged at 2200 rpm for 20 min. The supernatant was carefully decanted into a pre-weighed dish (W_2), dried at 100 °C to constant weight (W_3) and cooled for 30 min. The solubility was determined using the equation:

$$\text{Solubility (\%)} = \{[W_2\text{-}W_3]\}/w \text{ x } 100 \quad (3)$$

Water absorption capacity

The water absorption capacity (WAC) was determined using the method of Solsulski[13]. CSM (2.5 g) was added into a pre-weighed 50 mL centrifuge tube, distilled water (15 mL) was added and agitated on a vortex mixer for 2 min. The

mixture was centrifuged at 400 rpm for 20 min and the supernatant was decanted. The residue was weighed (W_1) and the absorbed water was removed by drying the residue at 60 °C to constant weight (w_2) in an oven. WAC was then expressed as:

$$WAC = \{(W_1 - W_2)/2.5\} \times 100 \quad (4)$$

Determination of Rheological profiles

The rheological profiles of the excipients were obtained using a heating and cooling viscometer coupled with Thermocline Windows Software (Rapid Viscosity Analyzer series 3 RVA, Newport Scientific Pty Ltd. Warriewood, Australia). Excipient (3 g), was weighed into the canister, distilled water (25 mL) was added and the slurry was heated under constant rate of shear. The increase in viscosity of the material was measured as torque on the spindle and the viscoamylographs obtained.

Microscopy of particles

The particle size and shape of the excipients were determined by optical microscopy on approximately 100 particles for each. The particles of each excipient sample was thinly spread over glass slides and observed under a light microscope (Olympus BX40 Research Microscope, New York Microscope Company, NewYork, USA) and photomicrographs were taken using an attached Digital Camera (Cannon EOS SL1, Cannon Inc, Tokyo, Japan).

Fourier Transform Infrared (FTIR) Spectroscopy

Sample (2 mg) was mixed with 100 mg of KBr and compressed into pellets in a hydraulic press. The pellet was placed in the light path and the spectrum was recorded in the wavelength region of 4000- 350cm^{-1} using FTIR Spectrophotometer (BXV5.3.1, PerkinElmer Inc., Massachusets□, U.S.A). The details of functional groups and assignment obtained from the FTIR spectroscopy were done using a Table-driven Infrared application (FTIR-Interpret software IR Pal, Version 2.0).

Preparation of granules

Different batches (100 g) of metronidazole granules with a basic formula containing Metronidazole (60%$^{w}/_{w}$), Corn starch (10%$^{w}/_{w}$) and Lactose (30%$^{w}/_{w}$) were prepared using the wet granulation method. The required quantities were weighed out and mixed in a mortar. Mucilage of 1, 2 and 4%$^{w}/_{w}$ concentration of the binding agent (CSM, acacia gum or corn starch) were prepared in distilled water and used to moisten the powder mixture. The wet masses obtained were then granulated by passing it through a 1400 μm mesh size and dried in a hot

air oven (Laboratory oven TT-9083: Techmel and Techmel, USA) at 50 °C. Dry-screening was done through a 1000 μm mesh sieve before being stored in an air tight container.

Tablet compression

The granules produced from the various batches of the formulation were compressed into tablets (400 mg) using a single punch Carver hydraulic hand press (Model C, Carver Inc., Menomonee Falls, Wisconsin, USA) at pre-determined pressures. Tablet compression was done for 30 sec using a die having diameter of 10.5 mm. A dispersion of magnesium stearate in acetone ($1\%^{w}/_{v}$) was used to lubricate the die and punch surfaces before compression. After compression of the tablets, they were stored over silica gel for 24 h.

Mechanical properties of the tablets

The crushing strength (Cs) of the tablets was determined using the tablet hardness tester (MHT-100, Model P&M 01, Pharma Alliance Group, California, USA). The tablet was placed between the anvil and the spindle of the tester. The force at which the tablet broke into two halves was then recorded.

Tablet friability (Fr) was determined using a DBK Friabilator (Model 40FTA01, DBK Instruments, Mumbai, India) at a speed of 25 rpm for 4 min. Five tablets were selected at random, weighed with an electronic balance and transferred into the drum of the Friabilator before it was switched on to begin its rotation. The tablets were then dusted and re-weighed from which the percentage loss was calculated.

The crushing strength-friability ratios (Cs/Fr) of the tablets were then calculated from the values of crushing strength and friability.

Release properties (Disintegration and dissolution) of the tablets

The disintegration time (Dt) of the tablets was determined in distilled water at 37 ± 0.5 °C using the DBK disintegration testing apparatus (Type 40TDA01, DBK Instruments, Mumbai, India). The time taken for the tablets to disintegrate and pass through the mesh was recorded. Determinations were made in triplicates.

The disintegration efficiency ratio (DER) for the tablets was calculated as a ratio of Cs, Fr and Dt. The DER, a measure of the balance between mechanical and disintegration property of tablets, was obtained using equation 5 where Cs is crushing strength, Fr is friability, and Dt is disintegration time.

$$DER = \frac{Cs/Fr}{Dt} \quad (5)$$

The dissolution profiles of the tablets were determined using the DBK dissolu-

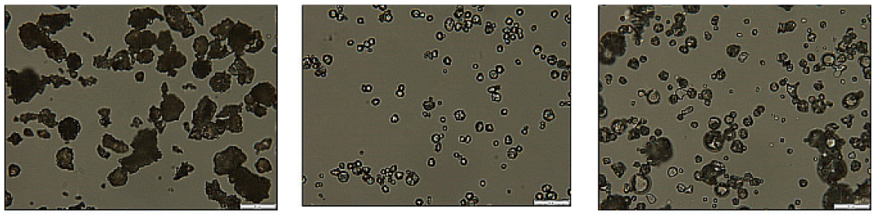
tion test apparatus (Type 40DRT01, DBK Instruments, Mumbai, India). Each tablet was placed in a cylindrical basket of stainless steel wire mesh which is attached to a rotor that can be regulated to varying speed and suspended in a glass vessel containing 900 mL of 0.1N HCl. The glass vessel was immersed in a water bath controlled at a temperature of 37 ± 0.5 °C. The apparatus was set to rotate at 50 rpm and 5 mL of the dissolution medium was removed from the glass vessel at specific time intervals and replaced simultaneously with an equal volume of fresh dissolution medium. The absorbance of the removed samples was measured at a wavelength of 277 nm and the drug concentration determined mathematically.

Data presentation and analysis

All experiments were performed using appropriate replicates and data were presented as mean ± standard deviation (SD) except for ratios. DD solver software was used to obtain dissolution times and compare the dissolution profiles by determining the similarity factor (f_2).

RESULTS AND DISCUSSION

The mucilage extracted from *Cucumis sativus* fruit was observed to be cream in colour, with a pleasant odour and a rough texture which is similar to *Chrysophyllum albidum* mucilage[14] and *Hibiscus esculenta* gum[15]. The photomicrographs of the excipients in Figure 1 showed that CSM particles are irregularly shaped and the surface is rough contrary to corn starch particles which are spherical. Acacia particles also have irregular shapes. The shape of the particles of a material is related to the botanical source of such materials and it affects how well such materials will pack in addition to other factors.



Cucumis sativus mucilage *Corn starch* *Acacia gum*

Figure 1. Photomicrographs of the particles of excipients (X 400)

The results obtained from the proximate analysis of CSM are presented in Table 1. It showed that CSM contains protein, fibre, ash, fat and carbohydrate in varying degrees. As expected, carbohydrate has the highest percentage (57.65%) indicating that CSM is a polysaccharide, protein content is much less than carbohydrate but, the content is important as well because gums and mucilages have

nitrogenous compounds. Generally, protein, fat and ash are part of the minor constituents of gums and mucilages and their presence influences the functional performance such as pasting and gelling behaviour[16]. The moisture content of *Cucumis sativus* mucilage was 11.23%$^{w}/_{w}$. Generally, gums and mucilages absorb moisture from the surrounding air and this usually depends on the properties of the material and the environmental humidity. According to Williams and Phillips[17], the moisture in a material should be moderate, otherwise enzymatic activation could set in motion the process of degradation.

Table 1. Proximate and elemental composition of *Cucumis sativus* mucilage

Proximate composition	Crude protein (%)		Crude Fibre (%)		Crude Ash (%)		Crude Fat (%)		Carbohydrate (%)		Moisture Content (%)	
	20.13		40.19		3.59		2.12		57.65		11.23	
Elements	Mg	K	Ca	Na	Fe	Cu	Co	Cd	Pb	Ni	Mn	Zn
(%)	0.11	1.18	0.14	38.11	9.01	2. 11	0.00	0.00	0.00	0.00	1.50	3.053

The results obtained from the elemental analysis is presented also in Table 1 and it showed that *Cucumis sativus* mucilage contained Calcium, Magnesium, Potassium, Sodium, Manganese, Iron, Copper, and Zinc which are not harmful to the body system while heavy metals such as Lead, Cadmium, Cobalt, Chromium and Nickel were found to be absent. This gives CSM an acceptable biological profile hence it may be useful as a food or drug additive.

Material properties

The material properties of CSM and the reference standards (corn starch and acacia gum) are presented in Table 2. The bulk and tapped densities of the excipients were in the order CSM <corn starch <acacia while particle density ranked- corn starch <CSM <acacia. In addition, particle size was in the order of corn starch <acacia <CSM. The particle arrangement, packing and the entire compaction profile of a material can be perceived by the bulk and tapped densities[18]. CSM showed lower values of these parameters thus indicating that acacia and corn starch have higher capacity in reducing die fill-volume during tablet compression. Furthermore, a high bulk density, that is a low porosity, will result in a low deformation potential, due to a lack of space for deformation during compression causing less intimate contact between the particles within the tablets ultimately resulting in weaker tablets[19,20]. There were no significant differences ($p>0.05$) between the particle density of acacia and CSM while that of corn starch was significantly ($p<0.05$) lower than for both. Generally, materials with higher particle density may require greater compression forces but usually produce tablets with improved mechanical strength[21]. The particle size of CSM was

significantly higher ($p<0.05$) than for corn starch and acacia. The dispersion of gums and mucilages has been reported to improve with increase in particle size though materials with lower particle sizes shows faster dissolution[22]. It implies therefore that where fast dissolution rate is not crucial, higher particle size may be of immense benefit.

Table 2. Material properties

Parameters	Cucumis sativus	Corn starch	Acacia
Bulk density (g/cm^3)	0.411 ± 0.023	0.468 ± 0.022	0.581 ± 0.335
Tapped density (g/cm^3)	0.563 ± 0.112	0.625 ± 0.113	0.778 ± 0.447
Particle density(g/cm^3)	1.349 ± 0.025	1.233 ± 0.039	1.374 ± 0.37
Particle size	64.871 ± 27.959	13.257 ± 3.298	32.058 ± 10.193
Carr's index (%)	26.998 ± 5.223	25.121 ± 6.004	25.310 ± 3.448
Hausner's ratio	1.420 ± 0.552	1.360 ± 0.235	1.339 ± 0.110
Angle of repose (^{0})	27.860 ± 2.443	30.591 ± 3.211	16.802 ± 4.009
Compressibility index (%)	26.998± 6.443	26.560 ± 4.335	25.311 ± 3.898
Swelling index (%)	310.091 ± 5.678	3.749 ± 0.113	128.314 ± 6.887
Solubility (%)	22.013 ± 8.321	6.029 ± 2.543	44.435 ± 6.237
Water absorption capacity (%)	80.002 ± 8.667	68.012 ± 7.532	58.956 ± 6.745

The results of Carr's index for the excipients ranked CSM > acacia > Corn starch without significant differences ($p>0.05$); Hausner's ratio also ranked CSM > Corn starch > acacia while angle of repose was in the order of corn starch > CSM >> acacia. There were no significant differences ($p>0.05$) between the Hausner's ratio and acacia yielded significantly lower ($p<0.05$) angle of repose in comparison with CSM and corn starch. The high values of Carr's index, Hausner's ratio and angle of repose for the excipients showed that they do not possess good flow properties[21]. The Carr's index is an expression of compressibility of a powdered material while Hausner's ratio describes the degree of densification that can occur due to feed hopper vibration during tableting procedures.

The swelling indices of the materials were in the order of CSM > acacia >> corn starch with significant ($p<0.001$) differences. The swelling index of an excipient is crucial in tablet formulation as it impacts on disintegration properties of the tablet. Materials with high swelling index may confer faster disintegration compared to those with lower values[23]. Furthermore, the solubility ranked acacia>CSM>corn starch while water absorption capacities were in the order of CSM>corn starch>acacia. The differences thus observed in these properties may be attributed to divergent intensities of molecular association forces inside the particles. Higher water absorption capacity has been ascribed to loose structure

of the polymer particles while low values imply firmness. Generally, the materials are from different botanical sources hence there is variation in their material properties.

The parameters obtained from the viscoamylographs of the excipients are presented in Table 3. The peak viscosity ranked corn starch>CSM>>acacia. The peak viscosity of corn starch was significantly higher than for CSM and acacia because the materials were subjected to heating and starches gelatinize when subjected to heating. Generally, viscosity properties of excipients become useful when agglomeration of particles is required during tableting procedures. Materials with moderate to high viscosity may demonstrate superior binding properties during granulation compared to those with low values. The high peak temperature shows that the materials are not going to be adversely affected by the heat generated during tablet compression. Materials with low peak temperature are sensitive to heat and may thus form gel or paste which is not desired during tablet compression[24].

Table 3. Parameters obtained from viscoamylography of the excipients

Parameter	Cucumis sativus mucilage	Corn starch	Acacia gum
Peak viscosity (cp)	135.50	200.57	14.50
Trough viscosity	110.00	151.75	11.50
Breakdown viscosity (cP)	25.50	51.88	44.00
Final viscosity (cP)	201.00	192.67	18.00
Setback from trough (cp)	91.00	41.75	7.00
Peak temperature (^{0}C)	97.00	90.97	60.00
Peak time (min)	7.00	6.03	1.60

Fourier Transform Infrared Spectroscopy

The Fourier transform infrared spectroscopy (FTIR) of the excipients is shown in Figure 2. The FTIR interpret software used to analyze the spectra showed different functional groups depending on the material involved. For *Cucumis sativus* and acacia, the functional groups shown are alcohols, alkane, alkenes, amides, carboxylic acids, amines and alkyl halides. The FTIR of corn starch also revealed the presence of carboxylic acid, alkanes, alkenes, amides, aromatic compounds and alkyl halides. In general, the functional groups thus identified showed that these materials are polymeric in nature.

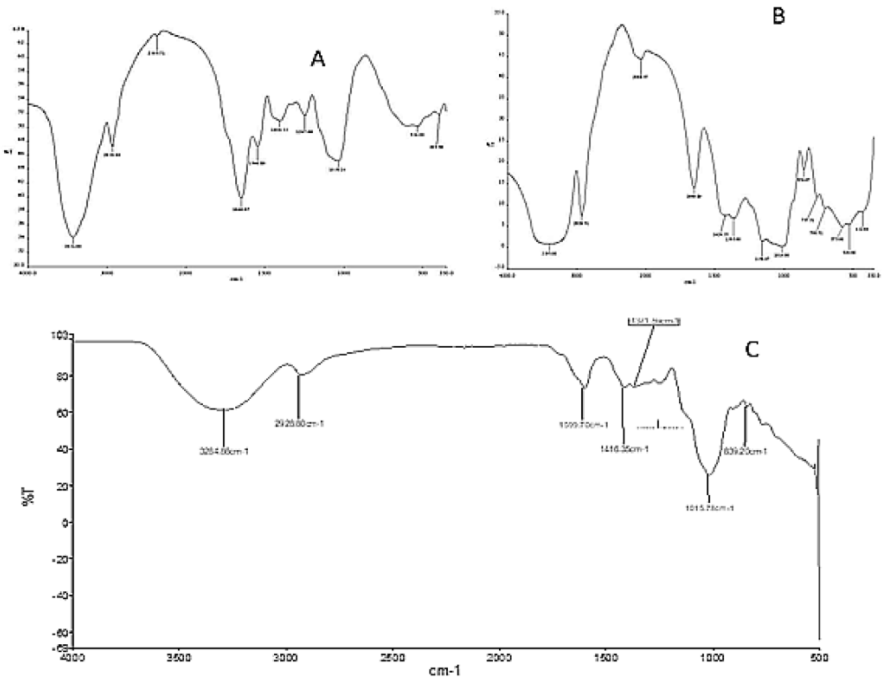


Figure 2. FTIR spectroscopy of the excipients (A-CSM, B-Corn starch, C-Acacia)

Mechanical properties of tablet

Tables 4, 5 and 6 shows the mechanical (Cs, Fr & Cs/Fr) properties of tablets prepared using the excipients (CSM, corn starch and acacia) as binding agents. The Cs of tablets prepared using the excipients generally increased with increase in binder concentration and compression pressure. The Cs were significantly ($p<0.05$) lower at every pressure for tablets prepared without a binder although the Cs for all the tablets were observed to be somehow small for tablets containing CSM. Tablets prepared using corn starch mucilage as binder had significantly higher Cs in comparison to those prepared using CSM. Generally, Cs values ranked CSM<corn starch<acacia.

Crushing strength is a measure of the bond strength and ability of tablets to withstand the stress of packaging, transportation and handling. It is dependent on the amount of binder solution used, compression pressure and also the tablet dimensions. It is also a function of the weight, density and porosity of materials used and the space between the upper and the lower punches at the moment of compression. Generally, an increase in the concentration of a binding agent has been shown to cause an increased particle–particle contact points resulting in the creation of more solid bonds; resulting in tablets with more resistance to fracture and abrasion[25]. It is not surprising therefore that the Cs of tablets containing

higher concentrations of the binders was improved. The effect of compression pressure on the Cs of the tablets was also expected because as forces are increased during compression, an increase occurs in the packing fraction of the granulation leading to a decrease in intra and inter-granular voids thus creating more contact points hence an increase in the degree of bonding between the particles[26].

The friability of all tablets is shown in Tables 4, 5 and 6. The results revealed that tablets prepared without using a binding agent were extremely friable with significant differences ($p<0.01$) in comparison to those with binders. Generally, the friability of all tablets reduced with increased compression pressure and concentration of binder. The ranking of friability among tablets produced with the different binders was CSM>acacia>corn starch showing that corn starch and acacia produced stronger tablets than CSM. Friability is a mechanical property of tablets with compendial specification of not more than 1%[27]. Most tablets in this study did not comply with official specification for friability and it could be that higher binder concentrations would be preferable. Generally, binders could be used up to 10% but lower concentrations have been used in a previous work[15] after which this study was patterned. While crushing strength is considered as a bulk deformation of tablets, friability is related to surface deformation which may be enhanced by tablet morphology[28]. Tablets with rough surfaces are usually more friable than smooth ones. Ideally, friability should decrease with increase in compression pressure and binder concentration[28]. This is the pattern followed by the tablets produced in this study, if higher binder concentrations were used however, the tablet friability would likely reduce significantly.

Table 4. Mechanical (Cs, Fr & Cs/Fr) and release (Dt & DER) properties of metronidazole tablets prepared using *Cucumis sativus* mucilage as excipient

Binder concentration ($\%^{w}/_{w}$)	Compression pressure (MN/m^2)	Cs (N)	Fr (%)	Cs/Fr	Dt (min)	DER
0.0 (No binder)	56.660	1.467 ± 0.462	93.550	0.016	0.142 ± 0.019	0.113
	84.840	5.067 ± 0.231	62.231	0.081	0.754 ± 0.120	0.107
	113.130	9.567 ± 0.611	27.320	0.552	0.787 ± 0.093	0.701
1.00	56.660	8.823 ± 0.042	31.232	0.283	0.471 ± 0.468	0.601
	84.840	10.931 ± 0.611	25.743	0.425	0.547 ± 0.024	0.777
	113.130	13.684 ±1.058	20.662	0.662	0.693 ± 0.019	0.955
2.00	56.660	10.870 ± 0.231	38.811	0.280	0.241 ± 0.072	1.162
	84.840	13.233 ± 0.401	26.090	0.507	0.614 ± 0.521	0.826
	113.130	18.623 ±1.058	18.440	1.010	0.680 ± 0.431	1.485
4.00	56.660	19.353 ± 1.007	15.501	1.249	0.193 ± 0.051	6.472
	84.840	19.977 ± 1.888	11.820	1.690	0.271 ± 0.093	6.236
	113.130	21.763 ± 3.274	4.000	5.441	0.390 ± 0.037	13.951

Table 5. Mechanical (Cs, Fr & Cs/Fr) and release (Dt, DER) properties for metronidazole tablets prepared using Corn starch as excipient

Binder concentration (%w/w)	Compression pressure (MN/m²)	Cs (N)	Fr (%)	Cs/Fr	Dt (min)	DER
0.0 (No binder)	56.660	1.467 ± 0.462	93.550	0.016	0.142 ± 0.019	0.113
	84.840	5.067 ± 0.231	62.231	0.081	0.754 ± 0.120	0.107
	113.130	9.567 ± 0.611	27.320	0.552	0.787 ± 0.093	0.701
1.00	56.660	15.901 ± 1.670	2.101	7.572	1.226 ± 0.072	6.176
	84.840	17.402 ± 1.210	1.569	11.091	1.472 ± 0.017	7.535
	113.130	20.900 ± 3.02	1.927	10.846	2.203 ± 0.300	4.923
2.00	56.660	17.10 ± 0.523	1.677	10.197	1.222 ± 0.210	8.345
	84.840	18.980 ± 2.433	1.469	12.920	1.567 ± 0.170	8.245
	113.130	24.903 ± 5.410	1.227	20.296	2.623 ± 0.038	7.738
4.00	56.660	23.374 ± 1.661	1.366	17.111	2.244 ± 0.032	7.625
	84.840	29.030 ± 0.231	1.213	23.932	3.293 ± 0.017	7.268
	113.130	32.431 ± 4.452	1.070	30.309	4.334 ± 0.108	6.993

Table 6. Mechanical (Cs, Fr & Cs/Fr) and release (Dt, DER) properties for metronidazole tablets prepared using acacia gum as excipient

Binder concentration (%w/w)	Compression pressure (MN/m²)	Cs (N)	Fr (%)	Cs/Fr	Dt (min)	DER
0.0 (No binder)	56.660	1.467 ± 0.462	93.550	0.016	0.142 ± 0.019	0.113
	84.840	5.067 ± 0.231	62.231	0.081	0.754 ± 0.120	0.107
	113.130	9.567 ± 0.611	27.320	0.552	0.787 ± 0.093	0.701
1.00	56.660	19.800± 0.67	3.298	6.004	0.588 ± 0.032	10.211
	84.840	24.740± 2.021	2.683	9.221	1.347 ± 0.034	6.846
	113.130	29.430± 2.402	2.212	13.305	1.453 ± 0.076	9.157
2.00	56.660	26.410 ± 0.952	2.434	10.850	1.082 ± 0.023	10.028
	84.840	29.950 ± 3.143	2.353	12.728	1.256 ± 0.062	10.134
	113.130	34.510 ± 3.241	1.542	22.380	1.372 ± 0.103	16.312
4.00	56.660	27.537 ± 3.006	1.793	15.358	1.734 ± 0.204	8.857
	84.840	35.283 ± 4.423	1.451	24.316	2.309 ± 0.107	10.531
	113.130	56.453 ± 5.045	1.184	47.680	2.937 ± 0.440	16.234

The mechanical strength of tablets can also be measured by the crushing strength – friability ratio (Cs/Fr). The Cs/Fr is a stronger parameter for determining the mechanical strength of tablets and the higher the Cs/Fr, the stronger the tablet since it provides a balance between tablet weakness and strength[25].

The Cs/Fr for the tablets was also presented in Tables 4, 5 and 6. Generally, the results showed that Cs/Fr increased with increase in compression pressure and

binder concentration with tablets prepared from acacia having the highest values. The ranking of Cs/Fr was acacia>corn starch> CSM. Tablets produced without using binding agents had significantly ($p<0.05$) low Cs/Fr compared to the others showing the usefulness of the binders for optimum mechanical properties.

Release properties of tablets

The release properties-Disintegration time (Dt) and Disintegration efficiency ratio (DER) of the tablet formulations prepared using the different binding agents are also shown in Tables 4, 5 and 6. Generally, all tablets prepared with the excipients passed the disintegration time test with values much less than the 15 min stipulated in the official compendia. In addition, the disintegration times increased with increase in compression pressure. It was observed also, that an increase in the concentration of CSM produced faster disintegration for all tablets compressed at the same pressure while an increase in the concentration of corn starch and acacia led to increased Dt. The disintegration for all the tablets could have been fast because of the high friability values, while the reduced disintegration time as CSM concentration increased could be a pointer to potential disintegration property of the excipient. Swelling has been reported as the most accepted mechanism for tablet disintegration[29]. In swelling, there is dimensional increase in size of particles in an omni-directional pattern and this pushes apart the adjoining components, thereby instigating break-up of the tablet matrix[30]. It is possible therefore since CSM has a high swelling index, this property may cause it to potentiate the effect of the disintegrant in the formulation.

Disintegration efficiency ratio (DER) otherwise known as Cs/Fr/Dt has been reported as a superior index for assessing tablet quality[31]. This parameter simultaneously evaluates tablet strength (crushing strength) and weakness (friability). In addition, DER also evaluates the negative effects of friability on Dt and the overall usefulness of a binder in a formulation[31]. In general, a higher value of DER suggests an enhanced balance between binding and disintegration properties[32]. The DER of tablets produced with CSM increased with increase in compression pressure and excipient concentration showing that tablets produced with 4% binder concentration and a compression pressure of 113.13MN/m2 were optimal. Generally, tablets without any binder had the least DER with significant differences ($p<0.001$) in comparison to all the tablets with binding agent showing a poor balance of mechanical and disintegration properties.

Dissolution is a significant parameter in tablet evaluation as tablets must dissolve before absorption can occur and may also be a rate-limiting step in drug bioavailability. Since drug absorption depends on amount dissolved, it is therefore imperative that tablets demonstrate acceptable dissolution characteristics.

Drugs having poor dissolution profile may fail to elicit its therapeutic action since availability of such drug in the systemic circulation cannot be guaranteed. Representative drug dissolution profiles for tablets produced with 2 and 4%$^{w}/_{w}$ of the excipients and compression pressure of 113.13 MN/m² are shown in Figure 3. The choice was based on the general outlook of the disintegration efficiency ratio. The higher the DER, the optimal the balance of mechanical and release properties of tablets. The amount of drug dissolved was observed to increase with time and formulations containing lower amount of binding excipient also released faster than those with higher concentration. From the plots, dissolution times - t_{50} and t_{80} (the time required for 50 and 80% of the drug to be released) were determined and the values are presented in Table 7. The dissolution times increased with increase in the concentration of the binding agent in the order- Corn starch <CSM<acacia implying that corn starch showed faster release than the other excipients.

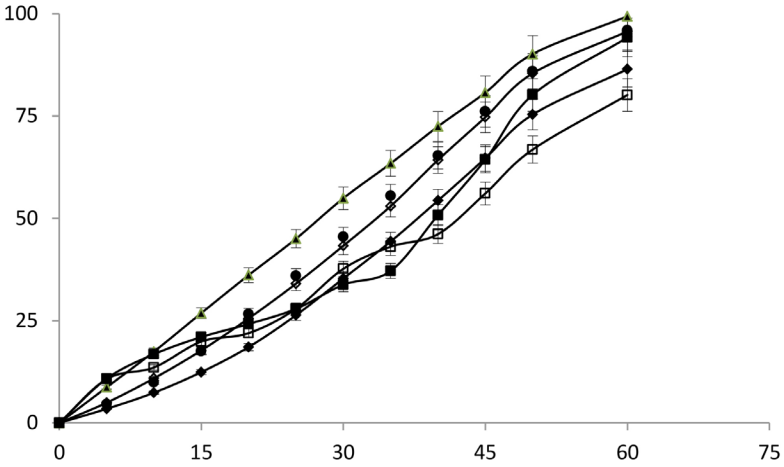


Figure 3. Dissolution profiles of the tablet formulations (2% Cucumis sativus ◊, 4% Cucumis sativus ♦, 2% Corn starch ▲, 4% Corn starch ●, 2% acacia ■, 4% acacia □).

Table 7. Dissolution times for tablets prepared with the excipients

Excipient	t_{50} (min)	t_{80} (min)
CSM (2%)	30.389	48.623
CSM (4%)	34.727	55.623
Corn starch (2%)	27.705	44.328
Corn starch (4%)	29.994	47.991
Acacia (2%)	35.524	56.838
Acacia (4%)	39.412	63.060

Since the dissolution profiles from the formulations visually looked similar, there was a need to conduct further verification. A model independent mathematical

approach (similarity factor, f2) proposed by Moore and Flanner[33] was employed to compare the dissolution profiles using pairwise procedures on DDSolver. The f_2 is a mathematical treatment that uses the mean dissolution values from the curves at each time point. When the f_2 value is 100 then the profiles are identical, when it is 50, it indicates that there is an average difference of 10% at all measured points. Generally, an f_2 value between 50 and 100 designates sameness or equivalence of the dissolution profiles[34]. The use of f_2 is widely emphasized by the Food and Drug Administration in various documents except when the products are rapidly dissolving (more than 85% in 15 min). The similarity factor for the dissolution profiles are presented in Table 8. None of the formulations showed identical profile i.e f_2=100. However, there were similarities between formulations containing 2% of CSM and that of corn starch or acacia ($f_2 > 50$), in addition, 4% CSM and corn starch or acacia also yielded $f_2 >50$. The highest f_2 in the groups was between 4% CSM and 2% acacia ($f_2 = 61.60$) showing superior similarity. This may imply that where 2% acacia is needed for acceptable release, as much as 4% of CSM will be required. Other formulations as shown on the table were dissimilar in dissolution profiles. In this study, the dissolution profile similarity between acacia and CSM was stronger (higher f_2 values) than for corn starch. This is to be expected as gums and mucilages have relative resemblance than starches. These results indicate that *Cucumis sativus* mucilage have excipient potential worthy of further development.

Table 8. Similarity factors for the dissolution profiles

Dissolution profiles compared	Similarity factor (f_2)
2% CSM and 2% corn starch	54.84
2% CSM and 2% acacia	54.51
4% CSM and 4% corn starch	53.28
4% CSM and 4% acacia	61.04
4% CSM and 2% acacia	61.60
4% CSM and 2% corn starch	41.09
2% corn starch and 2% acacia	42.08
2% corn starch and 4% acacia	38.36

CONCLUSION

Cucumis sativus mucilage was successfully extracted, characterized and its binding properties evaluated in a poorly compressible drug-metronidazole. Generally, CSM properties showed that it can be used as an excipient for oral formulations; its swelling index was significantly higher compared to corn starch and acacia.

Tablets obtained using the new excipient had low crushing strength showing that it may be more useful when soft tablets are required or a higher concentra-

tion may be needed to achieve stronger tablets. The mechanical properties of metronidazole tablets as described by Cs/Fr ranked acacia>corn starch> CSM. It was observed also, that an increase in the concentration of CSM produced faster disintegration for all tablets compressed at the same pressure as opposed to corn starch and acacia which led to slower disintegration. This may be a pointer to potential disintegrant properties of CSM due to its high swelling index and the less than 1 min disintegration time for all tablets produced using it. The dissolution profiles of the tablets from CSM (4%$^{w}/_{w}$) showed highest similarity (f2=61.60) to those of acacia at 2%$^{w}/_{w}$. These results showed that CSM could be further developed for excipient use in tablet formulations.

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