Trop J Nat Prod Res, March 2022; 6(3):408-415

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Material and Excipient Properties of *Ceiba pentandra* Mucilage in Diclofenac Matrix Tablets

John O. Ayorinde*, Emmanuel O. Okonye, Oladapo A. Adetunji, Michael A. Odeniyi

Department of Pharmaceutics and Industrial Pharmacy, University of Ibadan, Ibadan, Nigeria

ARTICLE INFO

Article history:
Received 26 January 2022
Revised 28 February 2022
Accepted 10 February 2022
Published online 05 April 2022

ABSTRACT

Ceiba pentandra (CP) is a useful native plant with desirable therapeutic properties. However, its potentials as pharmaceutical excipient have not been extensively reported. In this study, mucilage from leaves of CP was evaluated with the aim of comparing its material and release properties with that of sodium starch glycolate (SSG), as disintegrants in diclofenac tablet formulations. Mucilage was extracted from the dried leaves of *Ceiba pentandra*, using standard method. Characterization of mucilage was carried out using angle of repose, Carr's index, XRD, Hausner's ratio, density measurements, viscosity, swelling index, photomicrography, pH, and moisture content. Mucilage and SSG were incorporated as exodisintegrant and endodisintegrant in diclofenac tablet formulations using wet granulation method. Mechanical and release properties of tablets were determined. Mucilage had good swelling capacity, poor flow and high viscosity; the viscosity reduced with increasing temperature. Photomicrographs showed that the mucilage had larger, translucent particles which were well spaced. X-ray diffractometry revealed that mucilage is amorphous. Tablet properties showed that formulations made with CP mucilage had higher crushing strength and lower friability than formulations that contained SSG. Dissolution profile showed that mucilage had better drug release property than SSG and that mucilage is capable of sustaining release of the API for 9 hours with drug release of 95–98%. The formulations had their drug released by swelling and diffusion. Mucilage of *Ceiba pentandra* possessed desirable physicochemical and release properties. The mucilage compares well as a disintegrant with SSG, has a longer disintegration time and better release profile when applied as endodisintegrant.

Keywords: *Ceiba pentandra*, Endodisintegrant, Exodisintegrant, Diclofenac tablets, Polymer

Introduction

Polymers have been used extensively as pharmaceutical excipients. The role of polymers in drug formulation and indeed tablet production can be described to be an indispensable one. The range of their application is quite vast, from material packaging to design of the drug matrix. Polymers can be classified into two, based on their origin:

1. Synthetic Polymers
2. Natural Polymers

In the last few decades, a number of synthetic polymers have been used as excipients in drug production. These synthetic polymers offer many advantages, which include the ability to alter characteristics (solubility), release properties of the formulations. However, synthetic polymers however have been found to be non-biodegradable and such materials, if used in drug delivery systems may have to be removed surgically after they release the drug at the target site.[1] Examples of synthetic polymers include poly acrylic acid, poly ethylene oxide, poly ethylene glycol, poly vinyl pyrrolidone, polyvinyl alcohol, poly isopropyl acrylamide. Natural polysaccharides and their derivatives are widely used in pharmaceutical formulations as excipients. In several cases, their presence may determine the mechanism and rate of drug release from the dosage form.[2]

*Corresponding author. E mail: shogo205@yahoo.com
Tel: +234 805 321 3650

Citation: Ayorinde JO, Okonye EO, Adetunji OA, Odeniyi MA. Material and Excipient Properties of *Ceiba pentandra* Mucilage in Diclofenac Matrix Tablets. Trop J Nat Prod Res. 2022; 6(3):408-415. doi.org/10.26538/tjnpr/v6i3.18

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

In solid, liquid and semisolid dosage forms, they may play roles such as disintegrants, binders, film formers, matrix formers, release modifiers, thickeners or viscosity enhancers, stabilizers, emulsifiers, suspending agents and muco adhesives.[3] Natural polymers have also been used more specifically as solid monolithic matrix system, implants, film, beads, micro particles, nano particles, inhalable and injectables systems as well as viscous liquid formulation.[4] The growing interest in the use of natural polymers in the pharmaceutical industry is because they are biodegradable, toxicologically harmless and have low cost.[5] They are also relatively abundant and possess renewable properties which confer the ability to offer a constant supply if cultivated or harvested properly.[6]

Natural polymers are of different origin, which include polysaccharides of the plant cell wall, seaweed polysaccharides, microbial polysaccharides, animal polysaccharides, mucilage exudates from plants, inulin and starches.[7-10]

The plant *Ceiba pentandra* is a very large, deciduous tree up to 60 m tall, with roots spreading quite horizontally, 10 m or longer, in the upper 40–80cm of the soil. Extracts of the stem bark of *Ceiba pentandra* tree have been the most investigated for their pharmacological activity. In a study conducted by Nwachukwu *et al*., 2008, [11] the alcohol and water extract of the plant was tested for its antifungal properties, using disc diffusion and agar dilution methods. The alcohol extract of the plant was found to be more effective against *Epidermophyton flocosum, Microsporum canis, Trichopyton rubrum* and *Candida albicas* than the water extract. This antifungal activity was attributed to the presence of saponins and phenols in the extract.[11] The phytochemical screening of the methanol extract showed that it contained saponins, flavonoids, tannins, terpenes, resins and carbonhydrates and the extract was found to have antidiarrhoeal activity.[12] The protective activity of the ethyl acetate fraction of the methanol extract of the stem bark, against paracetamol-induced liver

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

damage in rats, was reported in 2011 by Bairwa *et al.*[13] The hepatoprotective properties of this fraction was demonstrated by a reduction in serum enzymes GOT(ALT), aspartate transferase(AST), GPT alkaline phosphatase (ALP), total bilirubin content and histopathological screening, following hepatotoxicity induced by the administration of paracetamol (3mg/kg) to the rats.[13]

A study conducted based on ethnobotanical literature, claimed the plant had activity against worms, diarrhea and/or abdominal pain. The plant extracts were prepared using 90% ethanol and tested for potential antihelminthic activities using the larva of *Haemonchus contortus.* The result suggested that the bark, leaf and roots have wound healing and diarrhea disorders.[14]

The leaves of *Ceiba pentandra* have been used for soup and condiments. The blended leaves swell in water and it is a delicacy in the southern part of Kwara state, Nigeria.

This study therefore aims at evaluating the properties of the powdered leaves of *Ceiba pentandra* and its mucilage. Further, the potentials of the mucilage as exo-disintegrant and endo-disintegrant in tablet formulations will be studied, using Diclofenac, a non-steroidal anti-inflammatory drug (NSAID) as the model drug.

Materials and Methods

Materials

The following materials were used in the study; leaves of *Ceiba pentandra* (obtained from Rore, Irepodun Local Government Area, Kwara State, Nigeria), Diclofenac (BASF, Ludwigshafen, Germany), gelatin, sodium starch glycolate and All other reagents used were of analytical grade.

Methods

Collection, authentification and extraction of Ceiba pentandra leaves

The leaves of *Ceiba pentandra* were collected during the early dry season (February, 2020) from Rore in Irepodun local government area of Kwara State, Nigeria. The collected leaf sample was authenticated at the herbarium of Botany Department, University of Ibadan and was allocated the voucher number UIH- 22406.

The leaves were sundried and pulverized. The powdered leaf (approximately 5 g) was soaked in a mixture of chloroform/water (0.5/95.5% V/V) for 24 hours to hydrate it, stirring from time to time; enough volume of the chloroform/water mixture to submerge the powdered leaf was used. The resultant mucilage was strained through a clean calico cloth to remove unwanted materials. The mucilage was then precipitated from solution with absolute ethanol. The precipitated mucilage was filtered, washed with diethyl ether and then dried in hot air oven at 40 °C. The mucilage was milled using a domestic blender (Panasonic Mixer Grinder, MX-AC400, India) and the powder obtained was sieved using a sieve of mesh size 0.50 mm. The powder was then stored in an air-tight container.

Characterization of Ceiba pentandra leaf powder

Swelling index

About 1 g each of the crude leaf powder and the mucilage were each weighed into measuring cylinders. The initial volume (Sa) of each of the powder type was determined and recorded. Distilled water was added and the mixture was stirred for even dispersion. The volume was made up to 50 mL using distilled water and left to stand for 24hours. The volume of the sediment (Sb) was measured and recorded and the swelling index was calculated using the equation: [15]

$$\text{Swelling Capacity} = \frac{sb}{sa} \quad \text{---------- (1)}$$

Where Sa = initial volume
Sb = volume of sediment after 24 hours

Angle of repose

About 10 g each of crude *Ceiba pentandra* leaf powder and the mucilage were poured through a short stem funnel clamped on a retort stand into an open-ended glass cylinder, whose lower end was resting on the base of a round cork of equivalent radius (r). Removing the cylinder vertically allowed the powder to flow out and cascade into a heap. The slanting height (side) of the cone formed an angle with the horizontal base known as angle of repose (Θ). The height of the cone was measured using a pair of dividers and a ruler. The Angle of repose is calculated thus:

$$\text{Tan } \Theta = \frac{h}{r} \quad \text{---------- (2)}$$

Where h = height of conical powder heap
r = radius of circular base (1.15cm)
Angle of repose, Θ was calculated from the mean value of three determinations.

Density measurements

The bulk density, tapped density, Carr's compressibility index, and Hausner's ratio of the mucilages were determined, using the Tap Density Tester (USP) ELECTROLAB ETD1020. The tapped density was determined using 250 taps at USP1 mode.

The particle density was determined on the True Density Meter SMART PYCNO 30. Determinations were carried out in triplicates.

Viscosity

The Viscosity of a 1% w/v aqueous slurry of each of the crude *Ceiba pentandra* leaf and the mucilage was determined using Brookfield Rheometer (DV-III+ Model, Brookfield Engineering, USA), at 50 and 100 rpm with spindle 5. Effect of temperature on the viscosity was determined by varying the temperatures. Determinations were carried out in duplicates.

Photomicrography

This was carried out to determine the particle shape and size of the materials. Photomicrographs were taken at x40, x100 and x400 magnifications using a digital microscope (VJ-2005 DN Model Bio-Microscope, China).

pH determination

The pH of 1% w/v aqueous slurry of each of the crude *Ceiba pentandra* leaf powder and the mucilage was determined using a pH meter (720A, Thermo Electron Corporation, MA, USA).

Flow rate

The flow rate of the crude *Ceiba pentandra* leaf powder and the mucilage was determined by weighing 5g of the powder into a short stem funnel, closed off with a stopper and measuring the time taken for the powder to flow out of the funnel (t). The flow rate was calculated using the formula:

$$\text{Flow Rate} = \frac{Weight\ of\ powder}{Flow\ time} \quad \text{---------- (3)}$$

Moisture content

The moisture content of the crude *Ceiba pentandra* leaf powder and the mucilage was determined by weighing 1 g of the powder on a white tile and placing in a hot air oven (Gallenkamp BS Oven 250,Leicestershire, U.K.) at 50 °C for 60 minutes. The powder was weighed at intervals of 2, 5, 8, 12, 15, 18, 24, 30, 35, 40 and 60 minutes to check for a reduction in weight. The moisture content was determined using the equation:

$$\text{Moisture content (\%)} = \frac{Initial\ weight - Final\ weight}{Initial\ weight} X\ 100 \quad \text{------ (4)}$$

Powder X-ray diffractometry (XRD)

The powder X-ray diffraction of the mucilage was carried out on a powder X-ray diffractometer (Rigaku Miniflex 600, Tokyo, Japan). Determination was carried out under the following conditions: a slit-detector Cu Kα radiation source (30kV, 15mA, λ = 0.15418nm), 2ɵ scan range was 3-350 and a scan rate of 40/min under ambient temperature.[16]

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

FT-IR spectroscopy
Possibility of interaction between the mucilage and API was studied using the Fourier transform infrared spectroscopy (FTIR). Spectra of diclofenac, the mucilage and the formulations were recorded on the FT-IR spectroscope (Model 2000 Perkin Elmer Spectroscopy, USA apparatus). Samples were prepared in KBr discs -1 (1%w/w). A scanning range of 1000 - 4500cm was used.

Preparation of granules
The formula for the granules of a 200 mg tablet formulation is as shown below:

Formula 1:	
Diclofenac (API)	50%
Ceiba pentandra mucilage	5%
Gelatin	4%
Lactose	41%
Formula 2:	
Diclofenac (API)	50%
Sodium Starch Glycolate	5%
Gelatin	4%
Lactose	41%

The mucilage and sodium starch glycolate were incorporated as endo- or exo- disintegrants.
The wet granulation method was used to prepare the granules using the formulae above. Either the *Ceiba pentandra* mucilage or sodium starch glycolate was incorporated into the granule formulations as endo-disintegrants and exo-disintegrants. All the constituents were incorporated using the physical mixing method. For the endo-disintegrants, sufficient quantities of materials for 40 tablets according to the formula were weighed and mixed gently in the mortar. Gelatin was formed into its gel state and added in drops until a lump that easily breaks when pressed with the thumb was formed. This wet mass formed was passed through a sieve of mesh size 1400um; it was then spread on a porcelain tile and dried in a hot air oven (Gallenkamp BS Oven 250, Leicestershire, U.K.) at 60^0C for 30 minutes. The exo-disintegrant preparations were made by forming the granules without the disntegrants, and then adding the disintegrants gently to the granules after they have been passed through a sieve of mesh size 1400um into a mortar. The granules were then dried in hot air oven (Gallenkamp BS Oven 250, Leicestershire, U.K.) at 60^0C for 30 minutes. The dried granules were then stored in air tight containers.

Granule size analysis
The sieves (1400 µm, 1180 µm, 1000 µm, 715 µm, 500 µm, 355 µm, 200 µm) were arranged vertically in decreasing mesh size with the receiver and lid attached. The dried granules (10 g) was then placed on the top sieve and covered with the lid. This was then subjected to shaking for 10 minutes, after which the sieves were disassembled and the granules retained in each sieve (including the receiver) were weighed.

Tablet production
The granules were compressed into tablets using Carver Hydraulic Hand Press machine (Model C, Carver Inc., Menomonee Falls, Wisconsin, USA). Tablets were compressed at different pressures of 2451.663, 4903.325, 9806.65 and 14709.98 N/m^2 for each batches of the formulations. The tablets were stored in appropriately labelled containers for at least 24 hours, to allow for elastic recovery and subsequently, their properties were evaluated.

Tablet properties
Weight uniformity
Ten tablets from each of the batches were weighed using the weighing balance (Scout Pro SPU402 Pine Brook, New Jersey, USA) and the average weight of the tablets was determined. Determinations were carried out in duplicates.

Thickness and diameter
Tablet thickness and diameter were determined using the micrometer screw gauge. Three tablets were picked from each batch. Each tablet was placed in between the spindle of the micrometer screw gauge and the reading was obtained in millimeters. The mean of duplicate determinations of tablet thickness and diameter, and their standard deviation were calculated respectively.

Crushing strength
The crushing strength of the tablets was determined using a hardness tester (DBK instruments, 400065, Model- EH 01; Mumbai, India). The results were taken from the tablets that split into two halves without any sign of lamination. The determination was carried out in duplicates.

Friability test
Friability test was used to determine how friable or fragile the tablets are. Ten tablets were weighed into the Friabillator (DBK Friability Test Apparatus 40FTA01, Woodvale, England) and allowed to undergo 100 revolutions. The weight of the tablets was taken, before and after undergoing fibrillations.

Release properties
Disintegration time test
The disintegration time of the tablets was determined in distilled water at 37 ± 2^0C using a Disintegrating Test Apparatus (DBK Disintegration Test Apparatus 40TDA01, Woodvale, England). The time taken for tablet to disintegrate and pass through the mesh was recorded with the determination made in triplicates.

Dissolution test
The dissolution test was carried out on the tablets using DBK Dissolution Apparatus 4ODRT01, Woodvale, England). The medium, 900 mL of 0.1M HCL, maintained at 37 ± 2^0C was used to carry out the test at 100 rpm. Volumes of 5 mL of the samples were drawn at 0, 5, 10, 15, 20, 25, 30, 60, 90 and 120 minutes and after each withdrawal, it was replaced with equal volume of 0.1M HCL. Each withdrawn sample was then analyzed spectrophotometrically at wavelength of 232nm for the concentration of Diclofenac released, using ultraviolet/visible spectrophotometer (LAMBDA 12 Perkin Elmer GmbH, Germany). A calibration curve was previously generated by measuring the absorbance values of pure Diclofenac at different concentrations.
To study the dissolution rate kinetics, the SolverDD, a Microsoft Excel add-in program was used. In order to determine the mechanism of drug release, the release data was fitted to several models including Zero order, First order, Higuchi and Korsemeyer-Peppas equations.[17]

$$Log\left(\frac{Mt}{Mf}\right) = LogK + nLogt \quad \text{---------- (5)}$$

This equation describes drug release behavior from polymeric systems. Mt is the amount of drug release at time t, Mf is the amount of drug release after infinite time; k is a release rate constant incorporating the structural and geometric characteristics of the dosage form and n is the diffusional exponent, which indicates the mechanism of drug release. For a cylinder-shaped matrix, the value of n = 0.45 indicates Fickian (case I) release; > 0.45 but < 0.89 for non-Fickian (anomalous) release; and > 0 indicates a super case II type of release. The case II mechanism refers to the erosion of the polymer and anomalous transport (non-Fickian) refers to a combination of both diffusion and erosion-controlled drug release.

Statistical analysis
The data obtained were analysed statistically using ANOVA, followed by posthoc Turley's test in cases where more than two sets of data were obtained, in order to determine the level of significance (p-values) of an effect or the difference between means. Significance at 95% confidence was considered significant or different at $p < 0.05$.

Results and Discussion

Phytochemical screening
The phytochemical screening of the *Ceiba pentandra* mucilage showed that it contained saponins, tannins, alkaloids, flavonoids and

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

coumarins (Table 1). The screening revealed that terpenoids, glycosides and steroids are absent in the leaves. The various metabolites contained in the mucilage possess specific physiological properties;[18-21] some of which may be useful both pharmacologically and in drug formulation. For instance, the presence of flavonoid, an antioxidant suggests the usefulness of the mucilage as a preservative as well as inhibiting the effects of free radicals on body cells.

Physicochemical properties

The mucilage extracted from *Ceiba pentandra* leaf possessed good organoleptic properties; they were found to be brown in colour, odourless and with bland taste.

The angle of repose of a powder is the angle to the horizontal at which a powder starts to slide upon itself. It is indicative of the flow properties of a powder and is dependent on the particle size and the frictional forces present between the particles of the powder. Powders with poor flow properties may cause poor flow properties for formulated granules, which in turn could lead to poor weight uniformity of the formulation.[22] An angle of repose of $< 25^{\circ}$ indicates a free flowing powder while an angle of repose of 40^{0} and above indicates a poor flow. Bothe the powdered leaf and extracted mucilage showed angle of repose of greater than 40^{0} (Table 2), indicating poor flow properties. Carr's index and Hausner's ratio are indices used to preview the degree of densification that would occur upon application of compaction force. Low values of Carr's index and Hausner's ratio indicate good flow and compression properties.[23] The mucilage had significantly lower values for the two parameters than the powdered leaf (Table 2); this therefore suggests that the mucilage possess better compressibility. The observed high values for both the angle of repose, Carrs' index and Hausner's ratio for the leaf is attributable to high moisture content, leading to increased friction between the particles. The bulk density and tapped density of a powder are indications of how closely packed the material is. The tapped density of a powder is affected by the particle size, electrostatic forces between the particles, the shape of the particle and the pressure applied. The bulk density is however dependent on the particle shape, size distribution of the particles and the cohesive forces between the powder particles.[24] From the results on Table 2 it is observed that the bulk density of the extracted mucilage is greater than that of the powdered leaf which implies that the mucilage had a larger volume reduction due to packing. However, the tapped density of the powdered leaf was greater than that of the mucilage which implies that the leaf had a higher maximum volume reduction compared to the mucilage. It means that the particles of the mucilage are more closely packed and would easily form a compact mass on application of compression pressure, which also agrees with the findings from the values of Carr's index and Hausner's ratio.

The swelling capacity of a powder describes its ability to absorb moisture. From Table 2 the swelling capacity of the powdered leaf was greater than that of the mucilage. This indicates that the crude leaf powder might be a better disintegrant compared to the mucilage, since swelling is a mechanism for disintegration.[25]

Both the mucilage and powdered leaf were found to be viscous. Viscosity is a measure of a fluid's resistance to gradual deformation by shear stress or tensile stress. The mucilage and the crude leaf powder showed thixotropy as their viscosity reduced with an increase in temperature.[26] Viscosity was also found to reduce with increase in shear rate (Figure 1) from shearing at 50 rpm to 100 rpm. This therefore suggests the suitability of the materials in the formulation of preparations where viscosity and thinning out are desired physicochemical properties.

The photomicrographs of the powdered leaf and extracted mucilage (Figures 2a and 2b) are similar; this indicates that the particles in the two materials are similar in morphology. However, the mucilage had larger, translucent particles which were well spaced out, compared to the more spherical, opaque particles of the crude leaf powder.

The X-ray diffractometry showed the mucilage to possess halo bands of amorphous materials (Figure 3). The sharp peaks observed could be attributed to the impurities still present with the mucilage. The amorphous nature is of importance in the formulation of insoluble and crystalline materials; this result suggests that *Ceiba pentandra*

Table 1: Phytochemical Screening of *Ceiba pentandra* leaves

Phytochemical	*Ceiba pentandra* Mucilage
Saponins	Present
Tannins	Present
Alkaloids	Present
Flavonoids	Present
Terpenoids	Absent
Glycosides	Absent
Coumarins	Present
Steroids	Absent

Table 2: Physicochemical Properties of the Powdered Leaf and Mucilage of *Ceiba pentandra*

Physicochemical Properties	Powdered Leaf	Mucilage
Angle of repose (˚)	48.50	43.73
Carr's index (%)	29.17	21.74
Hausner's ratio	1.41	1.28
Bulk density	0.42	0.43
Tapped density	0.59	0.56
Swelling index	3.00	2.00
pH at 28°C	7.16	7.67
Flow rate (g/sec)	1.47	1.00
Moisture content (%)	10.00	9.99
True density (gcm^{-3})	1.33	1.41

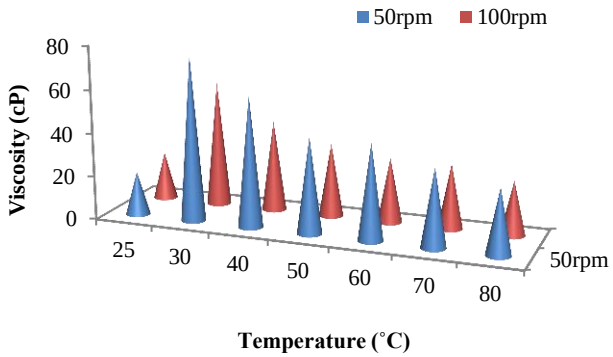

Figure 1: Viscosity of the mucilage at different temperatures

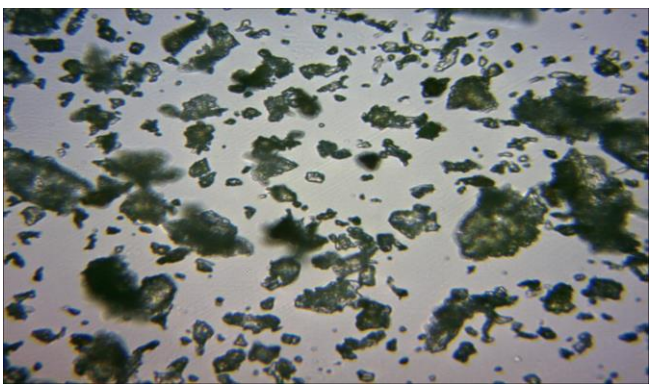

Figure 2a: Photomicrograph of *Ceiba pentandra* Powdered leaf (X 400)

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

mucilage has the potential of improving solubility of materials and reducing the crystallinity of active pharmaceutical ingredients.[27, 28]

Tablet evaluation

A crushing strength of 40 N is regarded as the minimum for a compressed tablet. The crushing strength and friability is used to measure the resistance of the tablet to mechanical stress. Formulated tablets would undergo a considerable amount of mechanical stress, especially during the transportation of the finished product to the ware house and up to when the tablets are used by the patients. The crushing strength is directly proportional to the strength of the tablet while the friability of a tablet is inversely proportional to the strength of the tablet.[29] The crushing strength depends on the amount of binder, the compression pressure, the weight and porosity of materials, as well as, the dimensions of the punch and die that used in the formulation process.[30] Results obtained (Tables 3a and 3b) show that the tablets containing the mucilage as endo-disintegrant possessed higher values of crushing strength than the tablets containing SSG as endo-disintegrant ($p < 0.05$). This suggests that the mucilage of CP is capable of producing stronger and more adhesive, intra- and inter-particulate bonding in the materials than SSG at the same concentration. However, both the mucilage and SSG produced tablets of lower values of crushing strength when they were both applied as exo-disintegrants ($p < 0.05$). This may be attributable to the possibility of more molecules of the polymers being made available for interaction at the sub-particle level than when the polymers were applied as exo-disintegrants.[31] Results further suggest that a lower concentration of the mucilage is required when applying it as endo-disintegrant.

Friability is defined as the percentage of weight loss of powder from the surface of tablets due to mechanical action; friability test is carried out to evaluate the weight loss during tablet handling and transportation. Tablets produced with the mucilage and SSG applied as either endo- or exo-disintegrant (Tables 3a and 3b) possessed acceptable friability values of not more than 1% .[30] This indicates the similarity between SSG and the mucilage as excipients in tablet production.

Release properties

Disintegration test is a measure of the time required under a given set of conditions for tablets to break into particles, through a mesh size of 10. A tablet passes the disintegration test if its disintegration time is < 15 minutes.[32] From the results (Tables 3a and 3b), all the tablets disintegrated in less than 15 minutes; suggesting that the tablets possess good disintegrating properties. Generally, the disintegration times for tablets containing the polymers as endo-disintegrant were longer than tablets containing exo-disintegrants. This is attributable to the fact that endo-disintegrant mode of application could lead to greater intra-particulate and inter-particulate interaction between the polymers and other materials in the formulation, which suggests that incorporating the mucilage as endo-disintegrant could impart greater mechanical strength on tablets. Furthermore, the disintegration times of preparations containing the mucilage were generally longer than those containing SSG ($p < 0.05$). During disintegration, water uptake by tablets depends on hydrophilicity of the API and /or excipients;[31] this result therefore suggests that the mucilage is more hydrophilic than SSG. The crushing strength-friability ratio (CSFR) is a parameter that is also used to measure the mechanical strength of a tablet.[34] The value gives an indication of the ability of the tablet to withstand the stress associated with mobility, storage and use by the patients. Generally, the higher the CSFR, the stronger the tablet. [35] From the values of the CSFR shown in Tables 3a and 3b, it was observed that there is a direct relationship between the compression pressure and the CSFR values of the tablets formulated using CP Mucilage as the disintegrants, with the mucilage incorporated as the endo disintegrants having higher values, thus indicating that more solid bonds were formed by these tablets. However, tablets that contained SSG showed an initial direct relationship between the compression pressure and the CSFR values at lower compression pressures and an inverse relationship was observed as the compression pressure approached 9806.65Nm^{-2}.

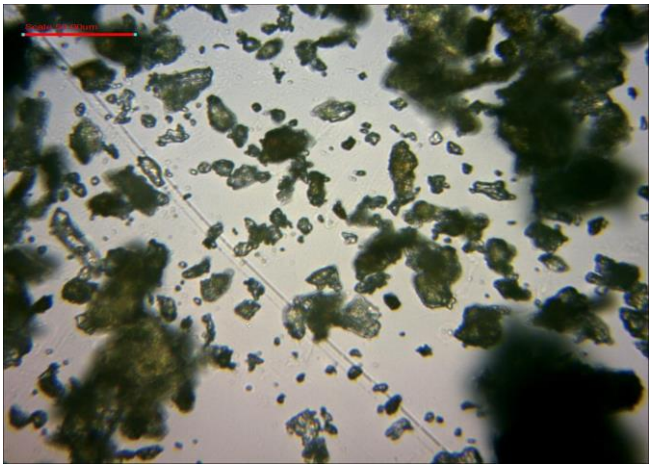

Figure 2b: Photomicrograph of *Ceiba pentandra* Mucilage (X 400)

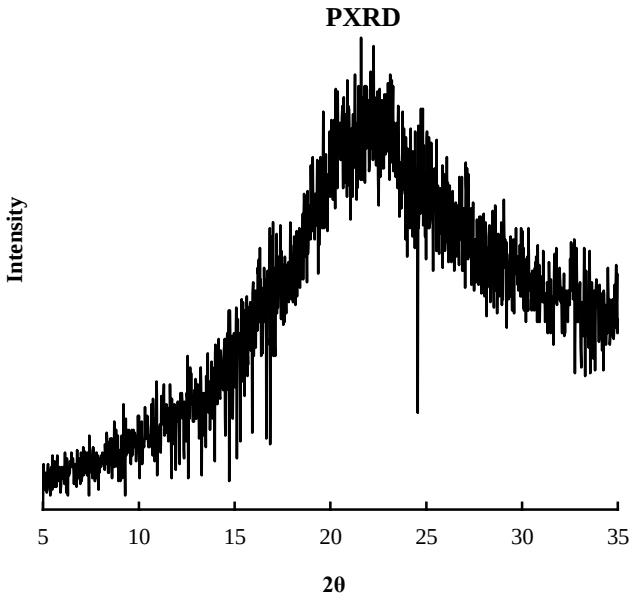

Figure 3: X-Ray Diffractogram of *Ceiba pentandra* Mucilage

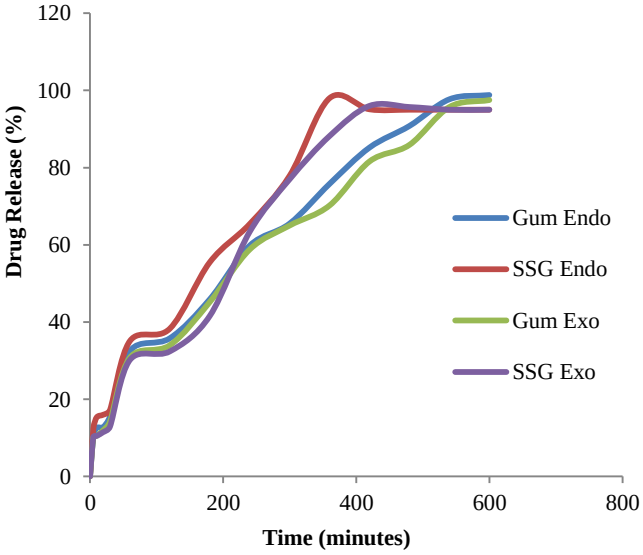

Figure 4: Drug Release Profile for Diclofenac Tablet Formulations

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Table 3a: Physical and Mechanical Properties of Diclofenac Tablets Prepared Using Sodium Starch Glycolate (SSG) and the *Ceiba pentandra* (CP) mucilage as Endo-Disintegrants

Disintegrant	Compression Pressure (N/M^2)	Friability (%)	Crushing Strength (N) mean ± SD, n = 2	Disintegration Time (minutes) mean ± SD, n = 2	CSFR	CSFR/DT
CP Mucilage (Endo)	2451.66	0.75	34.80 ± 1.55	13.98 ± 0.12	26.10	1.87
	4903.33	0.79	42.00 ± 1.56	12.60 ± 0.28	33.18	2.63
	9806.65	0.81	51.40 ± 2.55	9.92 ± 0.12	41.63	4.19
	14709.98	0.82	58.00 ± 1.69	12.65 ± 0.21	47.56	3.76
SSG (Endo)	2451.66	0.70	38.65 ± 0.35	14.00 ± 0.07	27.06	1.93
	4903.33	0.75	37.45 ± 0.64	11.83 ± 0.25	28.09	2.37
	9806.65	0.76	32.90 ± 1.27	11.27 ± 0.09	25.00	2.21
	14709.98	0.81	31.90 ± 0.42	9.04 ± 0.06	25.84	2.86

Table 3b: Physical and Mechanical Properties of Diclofenac Tablets Prepared Using Sodium Starch Glycolate (SSG) and the *Ceiba pentandra* (CP) mucilage as Exo-Disintegrants

Disintegrant	Compression Pressure (N/M^2)	Friability (%)	Crushing Strength (N) mean ± SD, n = 2	Disintegration Time (minutes) mean ± SD, n = 2	CSFR	CSFR/DT
CP Mucilage (Exo)	2451.66	0.85	34.60 ± 0.98	7.89 ± 0.16	29.41	3.73
	4903.33	0.88	36.85 ± 0.21	8.06 ± 0.08	32.43	4.02
	9806.65	0.92	40.80 ± 0.42	11.09 ± 0.12	37.54	3.39
	14709.98	0.95	42.75 ± 0.21	7.87 ± 1.75	40.61	5.16
SSG (Exo)	2451.66	0.81	39.75 ± 0.4	7.25 ± 0.21	32.19	4.44
	4903.33	0.86	39.10 ± 0.57	7.2 ± 0.38	33.63	4.67
	9806.65	0.92	20.45 ± 0.51	7.04 ± 0.18	18.81	2.67
	14709.98	0.94	22.15 ± 1.06	6.88 ± 0.11	20.82	3.03

Table 4: Correlation coefficients obtained for the formulations using different release models

Formulation	Zero Order			First Order			Korsmeyer-Peppas				Hixon-Crowel		
	R^2	T_{50} (min)	T_{90} (min)	R^2	T_{50} (min)	T_{90} (min)	R^2	T_{50} (min)	T_{90} (min)	n	R^2	T_{50} (min)	T_{90} (min)
Mucilage Endo	0.899	258.75	465.75	0.969	164.29	545.77	0.99	178.23	488.08	0.583	0.971	183.49	476.61
SSG Endo	0.796	242.62	436.71	0.965	129.08	428.79	0.97	136.69	437.44	0.505	0.965	144.84	376.19
Mucilage Exo	0.908	267.38	481.28	0.973	176.92	587.72	0.99	191.73	514.11	0.596	0.974	196.06	509.25
SSG Exo	0.878	249.01	448.22	0.965	149.51	496.66	0.97	170.06	454.84	0.597	0.975	165.50	429.88

This observation supports the ranking of the crushing strength and the friability values, where the tablets containing the endo-disintegrants had higher crushing strength values and higher resistance to surface abrasion (friability). This could be due to the innate binding properties of the mucilage reinforcing the adhesive characteristics of gelatin in the formulations.

The CSFR/DT ratio measures the tablet strength (crushing strength), weaknesses (friability) and the negative effects of these parameters on disintegration time; therefore, it is documented to be a better index of measuring tablet quality than the CSFR.[36] Generally, higher values of the CSFR/DT ratio indicate a better balance between binding and disintegration properties at different compression pressures.[36] The values obtained for the CSFR/DT ratio suggests that tablets containing CP Mucilage that were incorporated as endo or exo disintegrants at the high compression pressures employed had good balances of ingredient mix as indicated by the high values of CSFR/DT ratio, while at the lowest compression pressure employed in the study ($2451.66 Nm^{-2}$), the ranking of the tablets based on the constituent disintegrants was SSG (Exo) > CP Mucilage (Exo) > SSG (Endo) > CP Mucilage (Endo), thus suggesting that when low compression pressures are employed, disintegrants may be incorporated into the entire mixture prior to granulation.[35]

The dissolution test is done to evaluate the release profile of the drug from the pharmaceutical formulation. It is a method that simulates the physiological system *in-vitro*, giving an estimate of the bioavailability of the drug.[37] Generally, the formulations containing *Ceiba pentandra* mucilage showed slightly higher drug release ($p > 0.05$) than formulations containing SSG. All the formulations had initial burst at about one hour and drug release was sustained for up to 9 hours; a general drug release of 95 – 98% was obtained (Figure 4). Results therefore indicate that the mucilage is capable of sustaining release of the API for up to 9 hours which suggests suitability for sustained release delivery.[38,39] Formulations containing the mucilage showed significantly higher drug release of 97.5 to 98.8% than formulations containing SSG. The difference between the drug release profiles among formulations containing the same polymer (either the mucilage or SSG) was not significant; however, a slightly higher percentage drug release was obtained when the mucilage was applied as endo-

disintegrant. This suggests that application of ceiba mucilage as endo-disintegrant would give better drug release rate than SSG.
The percentage drug release of the formulations was fitted into various kinetic mathematical models; the best fit kinetic model was Korsmeyer-Peppas. The Korsmeyer-Peppas model of kinetic release describes a drug release from a polymeric system equation.[40]

$M_t / M_\infty = Kt^n$ ---------- (6)

Where M_t / M_∞ is a fraction of drug released at time t,
K is the release constant,
n is the release exponent.
In the Korsmeyer-Peppas' model, the release exponent is used to characterize the release mechanism of drug.[41] The value of $n \leq 0.43$ indicates a classical Fickian diffusion-controlled release, when n = 0.89, it means the mechanism of release is by swelling, and when the value of n is between 0.43 and 0.85, it indicates that release is by both swelling and diffusion.[41, 42]
The Fick's law of diffusion states that rate of change of concentration of dissolved material with time is directly proportional to concentration difference between two sides of diffusion barrier. The law basically explains that drug diffuses from a region of higher concentration to a region of lower concentration until equilibrium is attained. The release profiles showed that all the formulations had a release exponent (n) greater than 0.43 and less than 0.85 (Table 4). This indicates that the formulations had their drug release by the combined mechanisms of swelling and diffusion. [43, 38]

Conclusion

Mucilage extracted from the leaves of *Ceiba pentandra* possessed desirable physicochemical properties and produced tablets of good qualities. Physicochemical properties of the mucilage compared well with that of sodium starch glycolate, when employed as tablet disintegrants. Application of the mucilage as endo-disintegrant produced tablets with better mechanical and release properties than when used as exo-disintegrant.

Conflict of Interest

The authors hereby declare that they do not have any conflict of interest.

Authors' Declaration

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

References

1. Debotton N and Dahan A. Applications of Polymers as Pharmaceutical Excipients in Solid Oral Dosage Forms. Med Res Rev. 2017; 37(1):52-97.
2. Beneke CV and Hamman J. Polymeric Plant Derived Excipients In Drug Delivery. Molecule. 2009; 14:2602-2620.
3. Guo J, Skinner G, Harcum W, Barnum P. Pharmaceutical Applications of Natuirally Occuring Water Soluble Polymers. Plasm Sourc Sci Technol. 1998; 1:254-261.
4. Pandey R and Khuller G. Polymer Based Drug Delivery System for Mycobacterial Infections. Curr Drug Deliv. 2004; 1:195-201.
5. Verbeken D, Dierckx S, Dewettinck K. Exudate Gums: Occurence, Production and Application. Appl Microbial Biotechnol. 2003; 63:10-21.
6. Perepelkin K. Polymeric Materials of the Future Based on Renewable Plant Resources and Biotechnologies. Fibre Chem. 2005; 37:417-430.
7. Parija S, Misra M, Mohanty A. Studies of Natural Gum Adhesive Extracts-An Overview. Polymer Reviews. 2001; 4:175-197.
8. Bhardwaj T, Kanwar M, Lal R, Gupta A. Natural Gums and Modified Natural Gums as Sustained-Release Carriers. Drug Dev Ind Pharm. 2000; 26:1025-1038.
9. Gupta V, Hariharan M, Wheatley T, Price J. Controlled-release tablets from carrageenans: effect of formulation, storage and dissolution factors. Eur J Pharm Biopharm. 2001; 51:241-248.
10. Mohamadnia Z, Zohuriaan-Mehr M, Kabiri K, Jamshidi A, Mobedi H. Ionically Crosslinked Carrageenan-Alginate Hydrogel Beads. J Biomater Sci Polym. 2008; 19:47-59.
11. Nwachukwu I, Allison L, Chinakwe EN. Studies on the Effects of *Cymbopogon citratus*, *Ceiba pentandra* and *Loranthus bengwelensis* Extracts on Species of Dermatophytes. The J Am Sci. 2008; 4(4):58-67.
12. Sule M, Njinga N, Musa A, Magaji M, Abdullahi. Phytochemical and Antidiarrhoeal studies of the Stem Bark of *Ceiba pentandra* (bombacaceae). Nig J Pharm Sci. 2001; 8(1):143-148.
13. Bairwa N, Sethiya K, Mishra S. Protective Effect of Stem Bark of *Ceiba pentandra* Linn Against Paracetamol-induced Hepatotoxicity in rats. Phcog Res. 2011; 2:26-30.
14. Diehla M, Kamanzi A, Betschart B. Prospect for Anthelmintic Plants in the Ivory Coast Using Ethnobotanical Criteria. J Ethnopharmacol. 2011; 95(2-3):277-284.
15. Ayorinde JO and Odeniyi MA. Solid State Characterization of Two Novel Gums from *Cedrela odorata* and *Enterolobium cyclocarpum*. J Pharm Invest. 2017; 48(4):487-496.
16. Kadota K, Senda A, Tagishi H, Ayorinde JO, Tozuka Y. Evaluation of Highly Branched Cyclic Dextrin in Inhalable Particles of Combined Antibiotics for the Pulmonary Delivery of Anti-tuberculosis Drugs. Int J Pharm. 2017; 517:8-18.
17. Samia, EA, Babitar EM, Karamalla A. Analytical studies on gum exudates of *Angeissus leiocarpus*. Pak Nutr. 2009; 8(6):782-786.
18. Moumita C, Abhijit S, Lopamudra D, Sumana C. Role of Mucilage as Pharmaceutical Additives and Cytoprotective Agents. J Innov Pharm Biol Sci. 2017; 4(2):46-52.
19. Friday ET, James O, Olusegun O. Gabriel A. Investigations on the nutritional and medicinal potentials of *Ceiba pentandra* leaf: A common vegetable in Nigeria. Int J Plant Physiol Biochem. 2011; 3:95-101.
20. Kubmarawal D, Ajoku GA, Eniverem N, Okorie D. Preliminary Phytochemical and Anti-microbial Screening of fifty Medicinal Plants from Nig. Afr J Biotechnol. 2007; 6(14):1690-1696.
21. Akaneme F. Identification and Preliminary Phytochemical Analysis of Herbs that can Arrest Threatened Miscarriages in Orba and Nsukka towns of Enugu State. Afr J Biotechnol. 2008; 7(I):006–011.
22. Wang C and Fang J. Pharmaceutical Powders Flow Properties Characterization: Methods and Applications. Chinese J New Drug. 2013; 22(7):809-813.
23. Ayorinde JO, Balogun-Agbaje O, Odeniyi MA. Formulation and Evaluation of Oral Dissolving Films of Amlodipine Besylate Using Blends of Starches with Hydroxypropyl methyl cellulose. Polym Med. 2016; 46(1):45–51.
24. Momoh M, Brown S, Onunkwo G, Chime S, Adedokun M, Akpabio E. Effect of Hydrophilic and Hydrophobic Binders on the Physico-Chemical Properties of Sodium Salicylate Tablet Formulation. J Pharm Res. 2012; 5(4):2045-2048.
25. Singh A, Selvam R, Shivkumar T. Isolation and Characterization and Formulation Properties of Natural

Gum Obtained From Mangifera indica. Int J Pharm Biomed Res. 2010; 1(2):35-41.
26. Quanquan M, Huaishi J, Lei G, Yujie C J, Xiaoting F, Xin G. Rheological Prperties of Five Plant Gums. Am J Anal Chem. 2018; 9:210-223.
27. Tiwari M, Chawla G, Bansal AK. Quantification of Olanzapine Polymorphs Using Powder X-ray Diffraction Technique. J Pharm Biomed Anal. 2007; 43(3):865-872.
28. Ayorinde JO and Odeniyi MA. Physicochemical and Release Properties of Ibuprofen Formulations Prepared with Two Native Starches and Different Processing Techniques. West Afr J Pharm. 2019; 30(1):119-133.
29. Ayorinde JO, Odeniyi MA, Itiola OA. Evaluation of Pharmaceutical and Chemical Equivalence of Selected Brands of Diclofenac Sodium Tablets. East and Central Afr J Pharm Sci. 2012; 15:3-9.
30. Adeleye OA, Femi-Oyewo MN, Odeniyi MA. Effect of compression pressure on mechanical and release properties of tramadol matrix tablets. Curr Iss Pharm Med Sci. 2015; 28(2):120-125.
31. Bala R, Pawar P, Khanna S, Arora S. Orally Dissolving Strips: A New Approach to Oral Drug Delivery System. Int J Pharm Invest. 2013; 3(1):67-73.
32. Odeniyi MA and Ayorinde JO. Effects of Modification and Incorporation Techniques on Disintegrant properties of Wheat (*Triticum aestivum*) Starch in Metronidazole Tablet Formulations. Polym Med. 2014; 44(3):147-155.
33. Pahwa R and Gupta N. Superdisintegrants in the Development of Orally Disintegrating Tablets: A review. Int J Pharm Sci Res. 2011; 2:2767-2780.
34. Adetunji OA, Odeniyi MA, Itiola OA. Compression, Mechanical and Release Properties of Chloroquine Phosphate Tablets Containing Corn and Trifoliate Yam Starch as Binders. Trop J Pharm Res. 2006; 9(2):55-59.
35. Njega EK, Maru SM, Tirop LJ. The Binder Effect of Povidone on the Mechanical Properties of Paracetamol Containing Tablets. East and Central Afr J Pharm Sci. 2018; 21:3-9.
36. Adetunji OA and Odeniyi MA. Material and Compression Properties of *Cedrela odorata* Gum Co-Processed with Plantain Starch and Microcrystalline Cellulose. Polym Med. 2016; 46(1):35-43.
37. Martin PG and Grey AV. Selection of Dissolution Medium for QC Testing of Drug Products. J Valid Tech. 2011; 16:7-11.
38. Ayorinde JO, Odeniyi MA, Bansal AK. Evaluation of Two Novel Plant Gums for Bioadhesive Microsphere and Sustained-release Formulations of Metformin Hydrochloride. Polym Med. 2017; 47(1):13-23.
39. Adeleye AO, Odeniyi MA, Jaiyeoba KT. The Influence of Cissus Gum on the Mechanical and Release Properties of Paracetamol Tablets – A factorial Analysis. J Bas Appl Pharm Sci. 2010; 31(2):131-136.
40. Korsmeyer RW, Gurny RE, Doelker EP, Buri NA, Peppas NA. Mechanisms of Solute Release from Porous Hydrophilic Polymers. Int J Pharm. 1983; 15:25-35.
41. Rippi M, Antikainem O, Niskanen T, Yiruusi J. The Effect of Compression Force on Surface Structure, Crushing Strength, Friability and Disintegration Time of Erythromycin Acistrate Tablets. Eur J Pharm Biopharm. 1998; 46(3):339-345.
42. Hixson AW and Crowell JH. Dependence of Reaction Velocity Upon Surface and Agitation. J Ind Eng and Chem. 1931; 23:923-931.
43. Sharma N, Kulkarn GT, Sharma A, Bhatnagar, A., Kumar N. Natural Mucoadhesive Microspheres of *Abelmoschus esculentus* Polysaccharide as a New Carrier for Nasal Drug Delivery. J Microencapsul. 2013; 30(6):589-598.