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Characterization and Evaluation of the Suspending Potentials *of Corchorus olitorius* Mucilage in Pharmaceutical Suspensions

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ABSTRACT

The study was aimed at extraction, characterization and evaluation of suspending potentials of *Corchorus olitorius* mucilage (COM) in comparison with acacia BP (ACG) in pharmaceutical suspensions. *Corchorus olitorius* mucilage was extracted from its dried leaves decoction by differential precipitation with acetone, dried and micronized into powder. The powdered mucilage was screened and subjected to physico-chemical and flow properties analyses with acacia BP powder using standard methods. Functional groups elucidation and thermal analysis of the test mucilage was done using Fourier transform infrared spectroscopy (FTIR) and differential scanning calorimetry (DSC) respectively. Paracetamol suspensions were formulated using various concentrations of COM and ACG (1.0 - 3.0 %w/v) and assessed for their sedimentation volume, redispersibility, degree of flocculation, flow rate, particle size, pH, viscosity, drug content and *in-vitro* release profile. Drug-excipients compatibility was also assessed. The phytochemical tests revealed the presence of mucilage and carbohydrates and absence of starch and enzymes in the dried mucilage. COM powders had lower pH, percentage moisture content and bulk and tapped densities than ACG powders. The true density, porosity, angle of repose, Carr's index, Hausner's ratio and microbial load of COM powders were higher than those of ACG. Formulation containing 1.5 %w/v COM had a comparable suspending property to formulation containing 2.5 %w/v ACG. Results of accelerated stability studies showed no significant change in pH, viscosity, sedimentation volume and degree of flocculation of formulated suspensions. *Corchorus olitorius* mucilage at the low concentration of 1.5 %w/v could be employed as a suspending agent for formulation of pharmaceutical suspensions.

Introduction

Polymer compounds derived from plants have acquired diverse pharmaceutical applications over the years. Such applications include their use as protective colloids in suspensions, diluent, binder or disintegrant in tablets, thickeners in oral liquids, gelling agents in gels, bases in suppository and matrices for sustained or controlled release drugs[1,2]. Polymers such as natural gums and mucilages are readily available, inexpensive and biocompatible. Nowadays, they are preferred to semi-synthetic and synthetic excipients because of their availability, low cost, soothing action, non-irritant nature and relatively low toxicity [1,3].

Development of new and improved natural excipients has been necessitated by the cost, safety and biodegradability issues related to synthetic excipients. Bahadur *et al*. stated that newer excipients provide the means for simplifying formulation development as well as improving overall operational costs [4].

Mucilages are polymers made up of mainly water-soluble polysaccharides, commonly used as additives in the manufacturing of different pharmaceutical dosage forms. They are employed in pharmaceutical formulations largely due to their non-toxicity, low cost, high water-swellability and ready availability [5]. They possess a wide range of pharmaceutical applications, which include disintegrating, suspending, emulsifying, coating and mucoadhesives potentials at different concentrations in different pharmaceutical dosage forms [5,6].

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Suspending and emulsifying activities of mucilages are achieved via interfacial adsorption and formation of condensed films of high tensile strength that resist coalescence of the droplets [5]. Increase in the tensile strength of the hydration layer formed around the suspended particles is attributed to hydrogen bonding and molecular interactions [5].

Mucilages being hydrophilic colloids, form dispersion when in contact with water, increasing the dispersion of continuous phase thereby allowing the solid particles to remain suspended in the continuous phase for a sufficient length of time to measure a uniform dose.

Corchorus olitorius Linn (Tiliaceae), also known as jute plant is native to tropical Africa and Asia. Jute leaves are consumed in various parts of the world especially in West Africa. The leaves (either dried or fresh) are cooked into a thick viscous soup or added to stew that is very rich in vitamins and minerals [7]. The leaf extract of the plant is also employed in folklore medicine in the treatment of various ailments such as diarrhea, dysentery, cystitis, etc. [8-10].

The suspending potentials of mucilages obtained from various parts of some plants in formulations have been evaluated [11-13]. However, little or no knowledge exist on the suspending property of *Corchorus olitorius* leaf mucilage in the formulation of suspension dosage form.

Due to increasing demand on acacia and other natural gums, there is need to search for newer sources of natural bio-materials that are cost-effective and readily available. This study is aimed at investigating the suspending property of *Corchorus olitorius* leaf mucilage in the formulation of paracetamol suspension in comparison with a commercial suspending agent, acacia BP.

Materials and Methods

Paracetamol powder (Reference Standard) was a gift from Phamatex Nigeria Ltd. Lagos, Nigeria. Acacia, chloroform, ethanol and acetone, all of BDH Chemicals, Poole England and all other reagents were of analytical grades and were used as received from their suppliers.

Corchorus olitorius leaves were purchased in the month of September 2016 from a local market in Lagos, Nigeria. They were identified and authenticated in the Department of Botany, University of Lagos, Nigeria; voucher specimen number 7450 was assigned and a sample deposited in the departmental herbarium.

Mucilage extraction

Corchorus olitorius leaves were separated from the stem and dried under shade. The dried leaves (1000 g) were milled and soaked in 15 L of water for 6 h and then boiled for 30 min and left to stand for 1 h. The liquid extract was separated from the marc using a multi-layer muslin cloth bag. Acetone (in the volume equal to the volume of the liquid extract) was added to the liquid extract to precipitate the mucilage and the precipitated mucilage was filtered and dried under shade. The dried mucilage was then collected, ground and passed through a 177 µm sieve. The powdered mucilage was subsequently stored in an air tight container [14].

Characterization of Corchorus olitorius mucilage

All the evaluated parameters were carried out for both *Corchorus olitorius* mucilage (COM) and acacia gum (ACG) except for the phytochemical screening, FTIR and SEM studies that were carried out for COM only.

Phytochemical screening

Some preliminary tests were carried out to confirm the nature of the mucilage obtained. The chemical tests conducted included Molisch, Ruthenium, iodine and enzyme tests [5].

Organoleptic and solubility tests

The colour, odour and taste of the extract were determined and compared to those of acacia. One gram of the sample was dissolved in 2 mL of each of cold distilled water, hot distilled water, acetone, ethanol, methanol, ether, carbon tetrachloride and chloroform solvents, for the determination of solubility profiles of the extract.

Moisture content

Three grams of the mucilage powder was placed in the moisture content analyser (Sartorius, Germany). The analyser was then set at 130°C for 5 min. The value of the moisture content of the gum powder was obtained and compared to that of acacia BP.

Ash value

A 2 g weight of the sample was placed in a clean crucible and placed in a furnace. The content was ashed at 650 °C for 10 h until a whitish grey matter was obtained. The sample was removed from the furnace, cooled and reweighed. The percentage (%) ash was calculated using Eq. 1.

$$\%\, Ash = \frac{Wa}{Ws} x\ 100 \text{.....Eq. 1}$$

where *Wa* is weight of ash obtained, *Ws* is weight of sample used.

Hydration capacity and swelling power

The methods used by Musa *et al*. [15] were adopted for the evaluations of the hydration capacity and swelling power.

Micromeritics properties

The true densities of the samples were determined by the liquid displacement method using xylene as the immersion fluid as described by Ohwoauvorhua *et al.* [16], while the methods detailed in an earlier study [17] were employed for bulk density, tapped density, Hausner's ratio, Carr's index, angle of repose and porosity.

Heavy metal analysis

The lead (Pb), cadmium (Cd), mercury (Hg) and arsenic (As) contents in the mucilage powders were determined. A 5 g weight of each of the samples was accurately transferred into a 100 mL beaker followed by 2 M H_2SO_4 and HNO_3. The mixture was digested on a heating mantle for two hours, and allowed to cool. Deionized water (50 mL) was added and filtered; the resultant filtrate was used for trace metal assay. Atomic absorption spectrophotometry (Fishers Scientific, USA) was used to determine the quantity of Pb present in the samples, while Cd, Hg and As were determined using inductively coupled plasma-optical emission spectrometry (Optima 8300 ICP-OES, PerkinElmer, Inc. Shelton, CT USA).

Microbial load

Ten grams weight of the powdered mucilage was dissolved in 90 mL of 3 % Tween^R 80 then 10 mL of this solution was put into a universal bottle containing 90 mL of 3% Tween^R 80. The diluted solution was plated and incubated and the numbers of colonies formed were counted. For detection of fungal growth (total yeasts / molds count) in the sample, Sabouraud dextrose agar medium was used. The plates were incubated at 25°C and observed daily for one week. Tryptone soy agar was used for the detection of the total plate count and the plates were incubated at 37°C for 72 h while eosin methylene blue agar (EMBA) was used for the detection of *Escherichia coli* [18].

SEM analysis

The micrograph of the *Corchorus olitorius* mucilage sample was captured using a Scanning electron microscope (Pro X, Netherlands). The mucilage powder was mixed with ethanol to obtain a 1% suspension. The suspension (one drop) was then smeared on aluminum stub with double-sided adhesive tape and the sample mucilage powder was coated with gold powder to avoid charging under the electron beam when the acetone volatilized. An accelerating potential (30 kV) was used during micrography.

Thermal analysis

The thermal properties of the *Corchorus olitorius* mucilage was analysed using Differential Scanning Calorimeter (Mettler Toledo, UK) according to the method employed by Sindhu and Khatar [19]. Six milligrams of the mucilage sample was weighed and placed in an aluminum pan. The pan was hermetically sealed and equilibrated at room temperature for 1 h, then heated at the rate of 10°C/min from 30 - 120°C with an empty sealed pan as reference. Parameters such as (T_0), peak (Tp), conclusion (Tc) temperature and enthalpy (ΔH) of gelatinization were determined.

FTIR analysis

Small amount (≈ 5 mg) *Corchorus olitorius* mucilage sample and paracetamol powder were individually blended with solid KBr (≈ 50 mg) and compressed into discs. Also physical mixtures (1:1) of COM and paracetamol powder (≈ 5 mg) were blended with solid KBr (≈ 50 mg) and compressed into disc for compatibility study. The spectra were scanned from 500-4000 cm^{-1} in FTIR spectrometer (Bruker, South Africa) under dry air at room temperature.

Formulation of paracetamol suspension using isolated mucilage

Ten formulations (F1-F10) of paracetamol suspensions were prepared containing different concentrations of COM (*Corchorus olitorius* mucilage) and ACG (acacia gum) as suspending agents (Table 1). The required quantity of the suspending agent and 2.5 g of paracetamol powder were triturated together with 10 mL of glycerin to form a smooth paste. Methyl paraben (0.2 mg) and 0.03 mg of propyl paraben were added to the mixture. Two millilitres of amaranth solution and 2 mL of raspberry syrup were introduced into the mixture gradually with constant stirring and then mixed with 25 mL of chloroform water B.P. The mixture was subsequently transferred into a tared amber bottle, made up to 100 mL volume with distilled water and then shaken vigorously for 2 min.

Evaluation of the paracetamol suspensions

The paracetamol suspensions were evaluated for pH, sedimentation volume, redispersibility, flow rate, viscosity, degree of flocculation, drug content as well as *in vitro* release and stability studies.

pH

The pH of a 1.0 %w/v of the formulations was measured using digital pH meter (Oakton pH Meter pH 1100 series, Singapore).

Sedimentation volume

The sedimentation volume (F) of each suspension was determined by measuring the volume of the sediments in the suspension placed in the measuring cylinders daily for 7 days. F was calculated using Eq. 2.

$$F = \frac{Hu}{Ho} \text{..... Eq. 2.}$$

where, Hu is final height of sediment of settled suspension while Ho is original height of suspension.

Redispersibility

A fixed volume of each suspension (50 mL) was kept in calibrated tubes and stored at room temperature. At various time intervals (1, 5, 10, 15, 20, 30, 45 days), a tube was removed and shaken vigorously to redisperse the sediment and the presence or absence of undispersed sediment was recorded.

Flow rate
For the flow rate, V, the time taken for 10 mL of suspension to flow through a 10 mL pipette was determined and the flow rate calculated using Eq. 3.

$$V = \frac{Volume\ of\ pipette\ (mL)}{Flow\ time\ (sec.)} \quad \text{.....Eq. 3.}$$

Viscosity
The viscosity of suspension samples at 25°C was determined using a digital viscometer (DV-E, China) at 20, 40, 60, 80 and 100 rpm. The procedure was repeated at 35 °C. All determinations were carried out in triplicates and results obtained expressed as the mean values.

Degree of flocculation
Degree of flocculation (β) was determined using Eq. 4.

$$\beta = \frac{(Vu)floc}{(Vu)defloc} \quad \text{.....Eq. 4.}$$

where, (Vu) floc is ultimate sedimentation volume in flocculated suspension and (Vu) defloc is ultimate sedimentation volume in deflocculated suspension.

Drug content
Ten millilitres of suspension (20 mg/mL) was accurately measured and transferred into 100 mL volumetric flask and the volume made up with 0.1 N HCl. One millilitre was withdrawn and added to a 10 mL flask, and made up to volume with 0.1 N HCl. Absorbance was measured using a spectrophotometer at λ max 280 nm. The drug content was calculated by using the equation obtained from a previously prepared standard plot of pure paracetamol.

Particle size measurement
Particle size determination was carried out by optical microscopy method using optical microscope (CX21FS2, Tokyo, Japan). Suspension was spread on a slide and observed under microscope. Diameters of 20 particles were measured.

In vitro release studies
The Erweka dissolution apparatus (DT 6R, Germany) was used to determine the release rate of the paracetamol from the different formulations using procedure stated by the British Pharmacopoeia [20]. The Basket stirrer type was used. The dissolution medium used was 900 mL 0.1M HCl thermostatically maintained at 37 ± 0.5°C. The basket which was adjusted 25 mm away from the base of the glass jar was set to rotate at 50 rpm. Ten millilitres of suspension was placed into each glass jar. Samples of the dissolution medium (5 mL) were then withdrawn at specific time interval of 5, 15, 30, and 45 min and spectrophotometrically analysed for paracetamol at 245.3 nm. After each withdrawal of the sample, same volume of the dissolution medium was replaced.

Stability studies
Accelerated stability testing was carried out as per ICH guidelines (40 ºC/75 %RH) [21]. Suspensions were packed in amber coloured bottles and kept in a stability chamber with set temperature and relative humidity. The suspensions were evaluated at 0 day, 3 months and 6 months for pH, particle size, viscosity, sedimentation volume and degree of flocculation.

Statistical analysis
Mean comparison with the standard was evaluated using one-way analysis of variance (ANOVA). Significant differences ($p < 0.05$) of mean values were determined by Tukey test. OriginPro 2016 (64-bit) software (OriginLab Corporation Northampton, MA 01060 USA) was used for statistical analysis.

Results and Discussion

Organoleptic, solubility and phytochemical tests
The percentage yield of the mucilage from the dried leaves of *Corchorus olitorius* (COM) was 24.54 %w/w. The colour of the extracted mucilage was green compared to acacia (ACG) which was pale yellow. Also, the texture of the extracted mucilage was fine while that of ACG was coarse. Both samples were practically insoluble in the organic solvents used in the test, swelled in cold distilled water but soluble in hot distilled water. The solubility profile of the COM was consistent with those reported for other mucilages [22]. The phytochemical tests revealed the presence of mucilage and carbohydrates and absence of starch and enzymes in the dried COM mucilage. The absence of these substances implies that the COM was not contaminated with the substances.

Physicochemical and micromeritics properties
The results of some physicochemical properties of COM and ACG powders are presented in Table 2. The results showed that there were significant differences ($p < 0.05$) between some of the physicochemical properties of COM and ACG powders. COM powders had lower pH, percentage moisture content and bulk and tapped densities than ACG powders. The true density, porosity, angle of repose, Carr's index, Hausner's ratio and microbial load of COM powders were higher than those of ACG.
The significantly lower bulk and tapped densities of COM might be due to the irregular shape of the COM powder particles, the fine nature and smaller particle size of COM. The small and fine particles of COM might fill the inter-particle void spaces when subjected to vibration or tapping. Knowledge of bulk and tapped densities as well as Hausner's ratio and Carr's index of powders gives an idea of the flow characteristics of the powder [17]. Accordingly, COM had a higher Carr's index signifying fair flow character while ACG had the Carr's index signifying good flow character. The findings from Hauser's ratio are consistent with that of Carr's index. Similarly, the data obtained for angle of repose which is a characteristic related to inter-particulate friction or resistance to movement between particles is consistent with those of Carr's index and Hausner's ratio as it showed that COM had fair flow property while ACG had good flow property.
Swelling can be assessed by the determination of hydration capacity, swelling capacity and moisture sorption profile [23]. COM had higher hydration capacity than ACG (Table 2). While COM was found to be capable of absorbing about one and a half times its own weight of water, ACG was found to be capable of absorbing less than its own weight. Similarly, the swelling capacity of COM was greater than that of ACG. Swelling capacity of a substance reflects the increase in volume of that substance following water absorption. The extensive swelling that COM exhibits in water could be indicative of its hydrogel nature which could be exploited in designing of sustained release dosage forms. Swelling could be a result of entanglement of the polysaccharide chains and development of intra- and inter-molecular hydrogen bonds between the polysaccharide and water causing more water to be entrapped within the macromolecular chains [24].

Table 1: Composition of the different batches of paracetamol suspension

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Paracetamol (g)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
COM (g)	1	1.5	2	2.5	3	-	-	-	-	-
Acacia (g)	-	-	-	-	-	1	1.5	2	2.5	3
Glycerin (mL)	10	10	10	10	10	10	10	10	10	10
Methyl paraben (g)	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Propyl paraben (g)	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Amaranth solution (mL)	2	2	2	2	2	2	2	2	2	2
Raspberry syrup (mL)	2	2	2	2	2	2	2	2	2	2
Chloroform water B.P (mL)	25	25	25	25	25	25	25	25	25	25
Distilled water to (mL)	100	100	100	100	100	100	100	100	100	100

In addition, the relatively higher hydration and swelling capacity values that were observed for COM compared to ACG could possibly be due to the powder porosity of COM which was found to be higher.

From the microbial limit test results (Table 2), there were bacterial and fungal growth seen on the samples of COM and ACG analysed. However, the total aerobic microbial count and total yeasts / molds count were below the 10^3 cfu/g and 10^2 cfu/g limit respectively, specified for substances for pharmaceutical uses in the USP [18]. Moreover, there was absence of *Escherichia coli* in the samples which is a requirement for both aqueous and non-aqueous preparations for oral use [18]. The microbial limit test results implied that both COM and ACG could be used successfully as excipients without affecting the shelf-life of the formulation.

The results for the heavy metal analysis showed that all the metals that were investigated were within the acceptable range specified by the USP [18] which is 0.5, 1.5, 0.5 and 1.5 µg for Pb, As, Cd and Hg, respectively. Hence, the COM passed the tested heavy metals' limit as specified by USP.

The result of SEM of COM (Figure 1) showed the irregular nature of the powder particles which might be responsible for the higher viscosity of COM formulations as irregular particles increases the chance of mechanical resistance to flow, which makes formulations of such particles to have high low shear viscosity.

The thermal properties of COM (Figure 2) showed that COM had an onset temperature of 62.25°C, peak temperature of 117.86°C, endset temperature of 132.48°C and enthalpy change (ΔH) of 990.69 J/g. This endotherm could be ascribed to the enthalpy relaxation of COM; no exothermic transition was observed. This implies that COM could be stable at temperature as high as 300°C since there was no evidence of degradation [25]. Figure 3 shows the FTIR spectra of COM, paracetamol and COM/paracetamol blend respectively, highlighting some major bands/peaks. Some major bands/peaks on the spectra were: - ≈ 3322.35cm^{-1} -H-bonded O-H stretching, ≈ 2922.57 cm^{-1} - –C-H stretching, and ≈ 1721.77 cm^{-1} – aldehyde/ketone –C=C- stretching. The spectral data of the extract confirmed the presence of functional groups such as hydroxyl, ester group and aldehyde group among others. For compatibility study, the FTIR spectrum of the COM/paracetamol blend was compared with that of paracetamol spectrum. The result showed that there was no disappearance or major shift of important peaks in the COM/paracetamol blend spectrum. This confirmed the absence of any chemical interaction between the drug and COM [26].

Physical properties of the suspensions

The results of some physical properties of the paracetamol suspensions formulated with COM and ACG as suspending agents are presented in Table 3. There were significant differences between some of the evaluated parameters for the formulations containing the two suspending agents. Generally, the result showed that concentration of suspending agent was inversely proportional to flow rate of the suspension and directly proportional to the degree of flocculation.

Table 2: Physicochemical and micromeritics properties of COM and ACG powders

Parameters	COM	ACG
True density (g/cm^3)	2.30±0.01	1.77±0.01
Bulk density (g/cm^3)	0.66±0.01	0.77±0.01
Tapped density (g/cm^3)	0.83±0.02	0.89±0.01
Porosity	1.47±0.01	1.30±0.01
Angle of repose (°)	36.70±0.98	28.40±0.12
Hydration capacity	1.36±0.01	0.77±0.05
Swelling capacity	67.37±3.40	36.9±1.35
Carr's index	20.13±1.34	14.17±0.61
Hausner's ratio	1.25±0.02	1.17±0.01
Moisture content (%)	4.85±0.26	6.59±0.52
pH	6.00±0.00	6.70±0.01
Ash value (%)	10.88±6.37	6.33±2.03
Total aerobic microbial count (cfu/g)	188.33 ±83.64	41.50±11.14
Total combined yeasts/molds count (cfu/g)	32.70±1.22	5.50±0.85
Pb (ppm)	0.100	0.001
As (ppm)	0.020	0.040
Cd (ppm)	0.020	0.020
Hg (ppm)	0.002	0.001

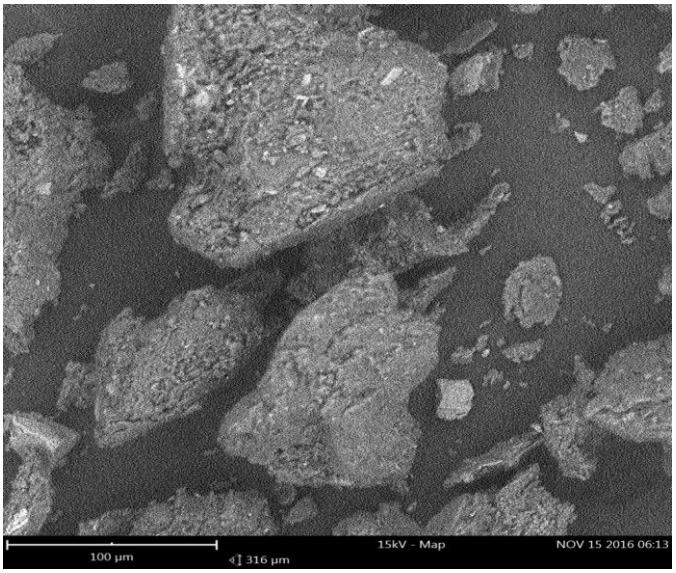

Figure 1: SEM photomicrographs of *Corchorus olitorius* sample

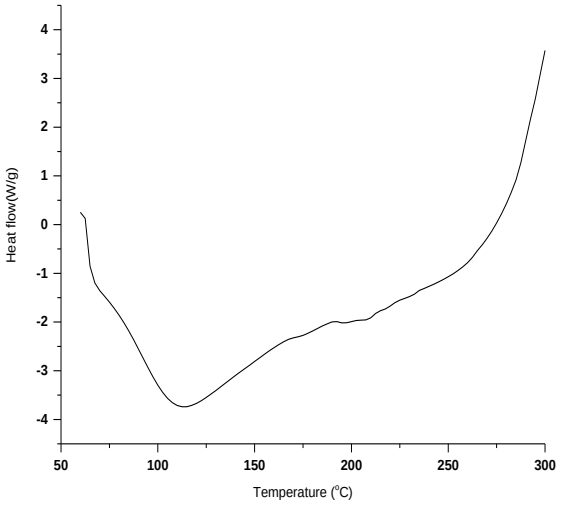

Figure 2: DSC thermogram of the *Corchorus olitorius* sample

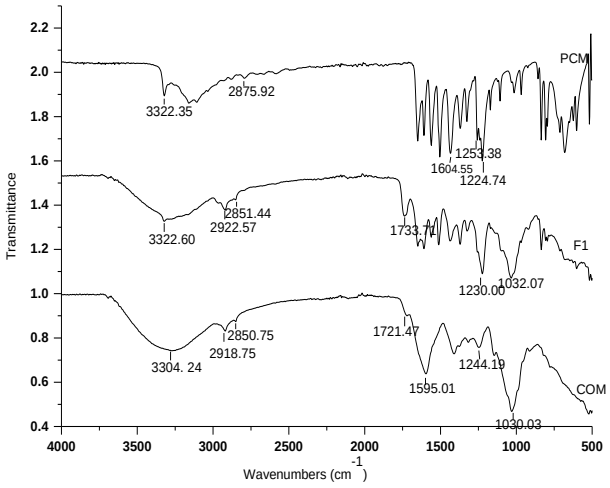

Figure 3: FTIR spectra of Paracetamol powder, *Corchorus olitorius* sample and F1 (Formulation containing Paracetamol and C*orchorus olitorius*) highlighting some major bands/peaks

The flow rates of suspensions containing COM were significantly ($p < 0.05$) lower than those containing ACG. The flow rate of the F5 formulation was the lowest while that of F1 was the highest amongst the formulation prepared using the extracted mucilage. Similarly, the flow rate of F10 formulation was the lowest while F6 was the highest for the formulations containing ACG. This showed that the flow rate of a suspension was inversely proportional to the concentration of the suspending agent incorporated into the formulation. Similar results were obtained when katira gum was evaluated for its suspending property [27]. This inverse relationship between concentration of suspending agent and the flow rate of the formulated suspension might be due to the increase in viscosity as the viscosity of the formulation generally increased with increase in concentration. Flow rate was used to determine the extent of pourability of the formulated suspension as an ideal suspension must be easily poured from its container during administration.

To evaluate the suspending properties of the extracted COM, paracetamol suspensions were prepared with varying concentrations (1.0, 1.5, 2.0, 2.5, and 3.0 %w/v) of the test mucilage as well as the commonly used suspending agent, gum acacia. The higher sedimentation volumes of formulations containing COM might be due to their higher viscosity which allowed the individual particles to sediment more slowly than formulations containing ACG which were less viscous. F5 exhibited the highest sedimentation volume throughout the period of evaluation. The sedimentation volumes of the formulation containing higher concentrations of the suspending agents were high while those containing lower concentrations were relatively lower (Figure 4).

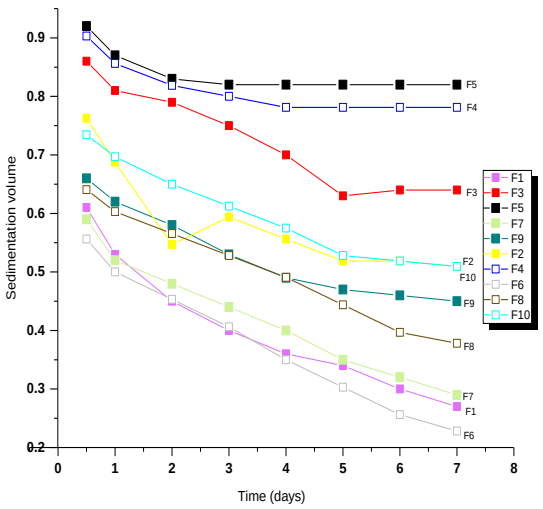

Figure 4: Sedimentation volume profiles of the paracetamol suspensions

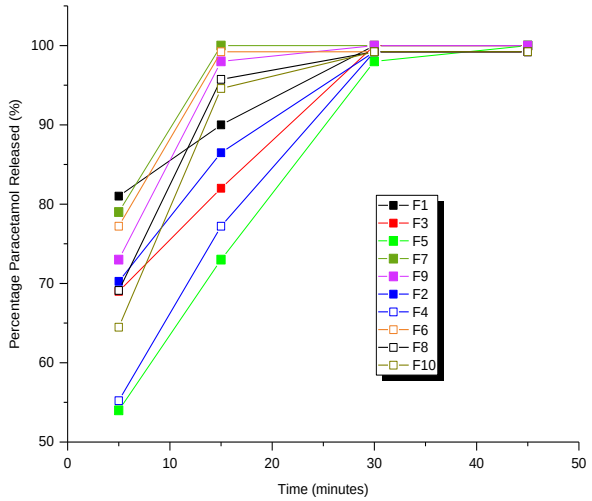

Figure 5: Drug release profiles of the formulated paracetamol suspensions

This was because the particles sedimented at a faster rate in suspension containing 1.0 %w/v of the suspending agents when compared with higher concentrations. Similar result was obtained when fenugreek seed mucilage was evaluated for its suspending property in comparison with tragacanth, gum acacia and bentonite [28]. Since the suspension produces sediment on storage it must be readily dispersible so as to ensure the uniformity of the dose. If sediment remains even after shaking vigorously for specified time, the system is described as caked [29].

The redispersibility of all formulated suspensions was studied and compared with each other (Table 3). All the suspensions were found to be easily redispersible after maximum 9 times shaking after 45 days. The redispersibility of the suspensions formulated with COM was found to require more shaking compared to the suspensions formulated with ACG as suspending agents. The redispersibility of the suspensions with lower concentration of suspending agents was easier than those of higher concentrations. This observation might be attributed to the higher viscosity of the formulations with higher concentrations of suspending agents [28]. In all the formulations, no caking occurred during the 45 days period that the formulations were stored before evaluation for redispersibility as they were all able to be redispersed with just few number of inversions.

The viscosities of the suspensions containing COM (Table 3) were significantly higher than those suspensions containing gum acacia. The viscosity of the suspension containing low concentration of COM was low and so sedimentation was fast. This could be attributed to the fact that at higher solid content, (higher concentration), particles would tend to meet each other more frequently and have a higher chance of interaction which could result in particle aggregation. The effect of increased interaction and aggregation caused the viscosity of the suspension to rise. When under no or low shear conditions, the intermolecular forces holding the particles of an aggregate together are strong enough not to be overcome by the weak shear forces [24].

As shear rate was increased from 30 - 60 rpm, the viscosity was seen to decrease and this might be attributed to the fact that as shear rates increased, the individual particles of the aggregate lost their intermolecular forces, broke apart and aligned in the direction of increased shear. This loss or decline in resistance to flow results in a decreased viscosity of the fluid. This shear-thinning behavior of a fluid is referred to as pseudoplasticity [24]. Also, as temperature was increased from 25 to 35^{0}C, the viscosity decreased, this could be attributed to the increase in the kinetic energy of the individual particles making it easier for them to move past each other.

The degree of flocculation (β) is the ratio of ultimate sedimentation volume in the flocculated and deflocculated system [30]. The degree of flocculation of the formulated suspensions using 1.5, 2.0, 2.5 and 3.0 %w/v COM as suspending agent showed significantly higher values than those of the suspensions using 1.0, 1.5, 2.0, 2.5 and 3.0 %w/v of ACG as suspending agents (Table 3). Again, the degree of flocculation of suspensions using 2.0 %w/v COM exhibited significantly higher values than those of the suspensions using 1.0, 1.5, 2.0, 2.5 and 3.0 %w/v ACG as suspending agents. Among all the suspensions, the suspension formulated using 3.0 %w/v COM showed significantly higher value than that of the other suspensions. These observations showed that the test mucilage (COM) might be a better suspending agent than gum acacia (ACG).

The results of drug content analysis showed that the paracetamol content in all the formulations were within the range of 98.67-104.33 %. This is within the acceptable limit of (90-110 %) as specified by the USP [18].

The pH values of the formulated suspensions were within the neutral to slightly acidic pH range (6.02-6.89), and this implies that they would not cause any damage to the gastro-intestinal tract after administration.

The bioavailability of a suspension is determined by the extent of absorption of the contained drug through the GIT which can be affected by wettability, viscosity and effect of suspending agent on the suspension [31]. The drug release profile of the formulated paracetamol suspensions (Figure 5) showed a steep rise in the first five minutes. This initial upsurge in drug release might be due to large surface area of the fine drug particles immediately exposed to the dissolution medium. It was found that the drug release followed a biphasic dissolution profile consisting of an initial (0-5 min) upsurge followed by (5-45 min) sustained release characteristics. The release rate of paracetamol was instantaneous for suspensions formulated using the two suspending agents. The release profile of the drug from suspensions formulated using ACG was rapid while it was more gradual from suspensions formulated with COM. However, all the suspensions released more than 80% of their drug content within 30 min which met the USP requirement [18].

It is evident from the stability test results (Tables 4a, 4b and 4c) that there was no significant change in pH, particle size, and degree of flocculation of any batch of the prepared suspensions. However, a concentration dependent increase in sedimentation volume was observed in all the prepared batches of suspension.

Table 3: Physical properties of the paracetamol suspensions

Sample Code	Flow rate (mL/s)	pH	Degree of flocculation	Redispersibility	Particle size (µg)	% Drug content	Viscosity at 30rpm, 25°C (cp)	Viscosity at 60rpm, 25°C (cp)
F1	0.36±0.04	6.02±0.02	2.19±0.01	2.33±0.58	5.33±2.51	98.67±3.06	118.00±0.00	71.00±3.61
F2	0.22±0.02	6.08±0.03	2.89±0.02	3.67±0.58	8.00±4.00	100.67±3.79	140.00±4.36	73.67±1.15
F3	0.13±0.00	6.11±0.03	3.09±0.01	6.00±0.00	8.67±6.66	100.33±1.53	260.00±2.00	142.67±3.51
F4	0.09±0.00	6.20±0.03	3.35±0.01	7.67±0.58	23.67±11.50	104.33±3.21	324.00±3.46	173.33±2.52
F5	0.07±0.00	6.3±0.04	3.54±0.02	9.00±1.00	22.67±18.50	101.33±2.89	570.00±11.14	299.67±4.16
F6	0.81±0.04	6.73±0.00	2.04±0.02	2.00±0.00	3.00±1.00	103.33±3.21	123.00±2.00	60.67±2.52
F7	0.75±0.01	6.76±0.03	2.34±0.02	2.33±0.58	4.00±1.00	100.67±3.79	128.00±1.73	67.33±1.15
F8	0.74±0.01	6.81±0.01	2.56±0.02	2.00±0.00	9.00±4.00	101.00±3.00	131.00±1.73	67.67±0.58
F9	0.71±0.01	6.84±0.00	2.64±0.01	3.33±0.58	21.67±5.51	102.00±2.65	140.67±1.15	74.67±1.15
F10	0.66±0.01	6.89±0.01	2.87±0.02	4.33±1.15	19±7.21	100.00±1.73	150.33±3.21	77.00±1.73

Table 4a: Accelerated stability testing data (viscosity) of formulated paracetamol suspensions

Batch	Viscosity at 25°C (cp)					
	30 rpm			60 rpm		
	Months			Months		
	0	3	6	0	3	6
F1	118.00±0.00	117.33±1.15	116.00±1.00	71.00±3.61	70.67±0.58	70.00±0.00
F2	140.00±4.36	141.33±1.53	140.67±0.58	73.67±1.15	73.00±0.00	71.00±1.73
F3	260.00±2.00	260.00±0.00	259.67±2.52	142.67±3.51	141.00±1.00	140.33±0.58
F4	324.00±3.46	322.67±1.15	320.67±1.15	173.33±2.52	172.00±1.00	169.33±2.52
F5	570.00±11.14	570.00±0.00	567.67±2.08	299.67±4.16	297.33±2.08	293.00±3.61
F6	123.00±2.00	120.00±2.65	10..00±0.00	60.67±2.52	62.67±2.52	61.00±1.00
F7	128.00±1.73	125.67±2.08	125.67±0.58	67.33±1.15	65.00±3.46	65.00±0.00
F8	313.00±1.73	129.67±1.53	129.00±0.00	67.67±0.58	67.00±0.00	65.33±1.53
F9	140.67±1.15	138.00±2.08	136.67±1.15	74.67±1.15	73.67±0.58	72.67±0.58
F10	150.33±3.21	148.00±2.00	147.33±0.58	77.00±1.73	75.33±1.53	75.00±0.00

Table 4b: Accelerated stability testing data (pH and particle size) of formulated paracetamol suspensions

Batch	Parameters (Months)					
	pH			Particle size (µm)		
	0	3	6	0	3	6
F1	6.02±0.02	6.07±0.06	6.07±0.02	5.33±2.51	5.45±0.03	6.5±0.3
F2	6.08±0.03	6.1±0.03	6.11±0.04	8.00±4.00	9.14±0.04	9.39±0.44
F3	6.11±0.03	6.12±0.01	6.17±0.03	8.67±6.66	12.6±0.03	12.31±0.41
F4	6.20±0.03	6.21±0.02	6.25±0.04	23.67±11.50	17.58±0.04	24.62±0.03
F5	6.3±0.04	6.32±0.02	6.36±0.04	22.67±18.50	24.09±0.03	25.17±0.03
F6	6.73±0.00	6.77±0.01	6.82±0.03	3.00±1.00	2.99±0.07	4.26±0.03
F7	6.76±0.03	6.77±0.01	6.85±0.04	4.00±1.00	4.79±0.15	4.03±0.08
F8	6.81±0.01	6.85±0.03	6.89±0.08	9.00±4.00	7.74±0.04	8.65±0.03
F9	6.84±0.00	6.87±0.02	6.89±0.09	21.67±5.51	19.32±0.04	21.22±0.09
F10	6.89±0.01	6.96±0.04	6.95±0.02	19±7.21	22.55±0.03	22.93±0.03

Table 4c: Accelerated stability testing data (sedimentation volume and degree of flocculation) of formulated paracetamol suspensions

	Parameters (Months)					
Batch	**Sedimentation volume**			**Degree of flocculation**		
	0	3	6	0	3	6
F1	1±0.00	0.23±0.01	0.21±0.00	2.19±0.01	2.17±0.03	2.11±0.04
F2	1±0.00	0.44±0.01	0.43±0.01	2.89±0.02	2.85±0.02	2.84±0.04
F3	1±0.00	0.53±0.01	0.54±0.02	3.09±0.01	3.05±0.04	2.96±0.08
F4	1±0.00	0.66±0.02	0.65±0.01	3.35±0.01	3.33±0.02	3.28±0.03
F5	1±0.00	0.77±0.03	0.75±0.02	3.54±0.02	3.51±0.03	3.4±0.02
F6	1±0.00	0.16±0.01	0.15±0.01	2.04±0.02	2.01±0.03	1.99±0.01
F7	1±0.00	0.25±0.00	0.23±0.01	2.34±0.02	2.25±0.04	2.22±0.02
F8	1±0.00	0.29±0.01	0.27±0.00	2.56±0.02	2.55±0.01	2.50±0.05
F9	1±0.00	0.38±0.01	0.35±0.01	2.64±0.01	2.61±0.02	2.62±0.03
F10	1±0.00	0.42±0.00	0.39±0.01	2.87±0.02	2.81±0.06	2.77±0.03

Conclusions

Corchorus olitorius mucilage at low concentration (1.5 %w/v) had comparable suspending potentials to 2.5 %w/v of acacia gum and also desirable physicochemical properties, hence *Corchorus olitorius* mucilage could be a potential cheaper alternative suspending agent in the formulation of suspensions.

Conflict of interest

The authors declare no conflict of interest.

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