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Formulation and development of metformin-loaded microspheres using *Khaya senegalensis* (Meliaceae) gum as co-polymer

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Abstract

Background: Khaya gum is a bark exudate from *Khaya senegalensis* (Maliaecae) that has drug carrier potential. This study aimed to formulate and comparatively evaluate metformin-loaded microspheres using blends of khaya gum and sodium alginate. Khaya gum was extracted and subjected to preformulation studies using established protocols while three formulations (FA; FB and FC) of metformin (1% w/v)-loaded microspheres were prepared by the ionic gelation method using 5% zinc chloride solution as the cross-linker. The formulations contained 2% w/v blends of khaya gum and sodium alginate in the ratios of 2:3, 9:11, and 1:1, respectively. The microspheres were evaluated by scanning electron microscopy, Fourier transform-infrared spectroscopy, differential scanning calorimetry, entrapment efficiency, swelling index, and in vitro release studies.

Results: Yield of 28.48%, pH of 4.00 ± 0.05, moisture content (14.59% ± 0.50), and fair flow properties (Carr's index 23.68 ± 1.91 and Hausner's ratio 1.31 ± 0.03) of the khaya gum were obtained. FTIR analyses showed no significant interaction between pure metformin hydrochloride with excipients. Discrete spherical microspheres with sizes ranging from 1200 to 1420 μm were obtained. Drug entrapment efficiency of the microspheres ranged from 65.6 to 81.5%. The release of the drug from microspheres was sustained for the 9 h of the study as the cumulative release was 62% (FA), 73% (FB), and 80% (FC). The release kinetics followed Korsmeyer-Peppas model with super case-ll transport mechanism.

Conclusion: Blends of *Khaya senegalensis* gum and sodium alginate are promising polymer combination for the preparation of controlled-release formulations. The blend of the khaya gum and sodium alginate produced microspheres with controlled release properties. However, the formulation containing 2:3 ratio of khaya gum and sodium alginate respectively produced microspheres with comparable controlled release profiles to the commercial brand metformin tablet.

Keywords: *Khaya senegalensis* gum, Microspheres, Metformin, Ionic gelation, Controlled release

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Background

Natural polymers are attractive, primarily because they are inexpensive, biodegradable, biocompatible, readily available, and non-toxic [1, 2]. These polymers have functional groups that make them able to be chemically modified to obtain products with desirable physicochemical properties. These qualities of natural polymers have attracted researches towards their widespread applications.

Khaya gum is obtained as exudates from the incised trunks of trees from the Genus, Khaya including the species: *Khaya grandifolia*, *Khaya senegalensis*, *Khaya ivorensis* (Family: *Meliaceae*) [3]. Khaya gum has been evaluated for several industrial applications such as binder [4], film coating [5], disintegrant [6], controlled release polymer [7].

Metformin (dimethylbiguanide) is majorly used in the management of type 2 diabetes mellitus. It acts by decreasing peripheral insulin resistance and hepatic glucose output. Metformin could be used in the management and treatment of steatohepatitis [8, 9], polycystic ovarian syndrome [10]. With absolute oral bioavailability of 40–60% and a mean plasma elimination half-life of 6 h, the frequency of administration is two to three times daily [11]. Controlled release formulations are needed to prolong its duration of action and to improve patient compliance.

Microspheres are microparticles made up of a polymeric matrix containing the drug which is dispersed at macroscopic or molecular level [12, 13]. Microspheres have the following advantages: sustained release properties, higher concentration of the active pharmaceutical ingredient at the target tissue, and increased bioavailability.

Synthetic polymers used in the production of marketed sustained release metformin tablets increase the cost of these medicines especially in low- and middle-income economies. Therefore, utilising readily available natural polymers will reduce cost and provide easier access to essential medicines. Although, different studies have been carried out on several industrial applications of *Khaya senegalensis* gum and other related gums [4–7], to the best of the authors' knowledge, there is no report on the use of khaya gum as a copolymer in the formulation of metformin-loaded microspheres.

This research aims to develop metformin-loaded microspheres using *Khaya senegalensis* gum as co-polymer by employing ionic gelation technique and to modulate release of the drug thereby reducing the frequency of its administration.

Materials

Khaya senegalensis plant was identified and authenticated. Voucher specimen number LUH 8582 was assigned and sample was deposited in the herbarium. Metformin hydrochloride powder (IOL Chemicals and Pharmaceuticals, India), sodium alginate (Loba Chemie, India), zinc chloride (Shanghai Chemex, China), absolute ethanol (BDH, Poole, England), chloroform (May and Baker reagent, England), and diethyl ether (Fisher Scientific, UK) were used in the study. All other reagents used were of analytical grade.

Methods

Extraction and purification of *Khaya senegalensis* gum

The method of Ofori-Kwakye et al. [14] was used in the extraction of the khaya gum. Briefly, one kilogram of dried crude *Khaya senegalensis* exudate was reduced and macerated in chloroform-water double strength and allowed to stand for 120 h with intermittent stirring. The gum mucilage was then strained with a muslin cloth to remove any insoluble impurities. Absolute ethanol was used to precipitate the mucilage. The mucilage was then collected and washed twice with diethyl ether and dried in hot air oven (Uniscope SM9053, England) at 40 °C for 24 h. The extracted gum was dried at 40 °C for 24 h. The dried gum was then pulverized using pestle and mortar and the powdered gum was passed through a sieve with mesh size of 210 μm. Thereafter, it was stored in an air-tight container until needed.

Characterization of gum sample

Moisture content

The moisture content of the gum sample was determined using a moisture analyser (Sartorius AG, Germany). Two grams of the gum powder was placed into the moisture balance and evenly spread on the tray. The readings were recorded at 15 min.

pH

A 5.0% w/v dispersion of the gum powder was made with distilled water and the pH measured using a pH meter (Hanna instruments, USA).

Ash value

A 2 g weight of gum powder sample was poured into a nickel crucible which was initially heated at 105 °C in a furnace (Carbolite, Germany) to a constant weight. The temperature was then increased to 600 °C and heated for 6 h. The sample temperature was allowed to cool to 100 °C and removed from the furnace, cooled in a desiccator over silica gel and reweighed using an analytical balance (Adventurer-Pro, Ohaus, USA). The weight of the residues (carbon-free ash) was determined and expressed as percentage of the initial sample.

For determination of the acid-insoluble ash content of the gum sample, the ash obtained from the above experiment was boiled with 25 mL of 2M HCl for 5 min. The insoluble residue was separated by centrifugation at 2000 rpm for 10 min using a centrifuge (Thermo

Scientific, Germany). The sediment obtained was re-suspended in hot water and evaporated to dryness in a tarred crucible. The weight of the residue was expressed as a percentage of the initial weight of the sample.

Phytochemical analysis
Phytochemical analyses were carried out to test for the presence of secondary plant metabolites in the gum powder. Secondary metabolites are various chemical compounds produced by plants from the materials derived from primary metabolites. Molisch's test, Fehling's test, frothing test, lead acetate test, ferric chloride test, Shinoda test, Keller-Kiliani test, Borntrager's test, Salkowski's test, Liebermann-Burchard test, and Dragendorff's test were carried out using methods reported in previous studies to determine the presence of carbohydrates, reducing sugar, saponin, phenolic compounds, tannin, flavonoid, cardiac glycoside, anthraquinone, steroid, terpenoid, and alkaloid, respectively [15, 16].

Elemental analysis
Chromium (Cr), cadmium (Cd), copper (Cu), lead (Pb), nickel (Ni), and cobalt (Co) contents in the gum sample were determined using an Atomic Absorption Spectrometer (iCE 3000, Thermo Fisher). Five grams of oven dried samples were weighed into a crucible and placed in an incinerator at 600 °C and left to ash for 2 h and then cooled to 105 °C and the gum powder weighed. This process was repeated until a constant weight was obtained. The ashed samples (0.5 g) were weighed and transferred into the digestion tube. The ashed sample was mixed in the digestion tube with 5 mL each of distilled water, 1 M perchloric acid and concentrated HNO_3. The contents were digested on a heating mantle and the temperature was set at 150 °C for 120 min followed by the addition of 1 mL of 2 M H_2SO_4. Distilled water was added to the tube to make up to the mark, mixed, and filtered. The elements were determined by using an atomic absorption spectrophotometer (AAS) at an appropriate wavelength, temperature and lamp-current for the different elements.

Micromeritics and rheological properties
The bulk density, tapped density, Carr's index, and Hausner's ratio of the gum powder were determined according to the methods described by Azubuike et al. [17].

The viscosity of the gum powder was determined using a digital viscometer (DV-E, China). The viscosity values of 2%, 5%, and 10 % w/v aqueous dispersion of the gum were determined at 50 rpm and 25 °C. The swelling index of khaya gum was determined using the method employed by Ologunagba et al. [18].

Fourier-transform infrared spectroscopy (FTIR) analysis
A 5 mg quantity of khaya gum sample, metformin, and metformin-loaded microspheres were individually blended with 50 mg of solid KBr and compressed into discs. The scanned range was from 500 to 4000 cm^{-1} in FTIR spectroscopy (Cary 630, Agilent Technologies, USA) under dry air at room temperature.

Differential scanning calorimetry (DSC)
The thermal behaviour of the gum powder was determined using differential scanning calorimeter (Mettler Toledo, USA) as described by Sindhu and Khatkar [19]. The gum powder (6 mg) was weighed into 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 °C to 250 °C with an empty-sealed pan as a reference. The DSC studies were also carried out for the pure metformin powder and the different formulations of the microspheres.

Scanning electron microscopy (SEM)
The granule morphology of the gum powder was observed in a scanning electron microscope (Pro X, The Netherlands). The gum powder was mixed with ethanol to obtain a 1% suspension. The suspension (one drop) was then smeared on aluminium stub with double-sided adhesive tape and the sample gum powder was coated with gold powder to avoid charging under the electron beam when the acetone has volatilized. An accelerating potential (15 kV) was used during micrography [20].

Preparation of metformin hydrochloride microspheres
Polymer blends {khaya gum:sodium alginate (2:3, 9:11, and 1:1) respectively} consisting of the different ratios of khaya gum and sodium alginate were used. The choice of the ratio blends of the polymers were based on pre-formulation studies carried out. Microspheres embedded with metformin were prepared by the ionic gelation technique as described by Odeku et al. [21]. Briefly, appropriate quantities of metformin (2% w/v) were added and stirred continuously until a dispersion was obtained (2:1 ratio of polymer and drug respectively). The resulting dispersion was extruded into zinc chloride solution (5% w/v) using a 5 mL hypodermic syringe with a 23 G needle at a dropping rate of 2 mL/min and stirring speed of 300 rpm. The formed microspheres were allowed 30 min curing time and then left standing for 1 h to allow further cross-linking. The microspheres were collected by decantation, washed with distilled water, and then dried for 18 h in hot air oven at 40 °C. The microspheres were then stored in airtight containers until needed.

Characterization of microspheres
Size distribution of microspheres
The sizes of microspheres were determined using an optical microscope (Leica, Germany) fitted with an ocular micrometer. The mean diameter reported was obtained from a total of more than 100 microspheres.

Morphology of microspheres
The morphology of the microspheres was analysed by scanning electron microscopy. The microspheres were dusted onto double sided tape on an aluminium stub and coated with gold using a cold sputter coater to a thickness of 400 Å and then imaged using a 15 kV electron beam. Photographs were taken within a range of 190–250 magnifications [22].

Swelling index
A 100 mg quantity of microspheres was soaked in 20 mL of phosphate buffer, pH 6.8 for 3 h. After the 3 h, the microspheres were then removed and excess buffer was wiped using a dry filter paper and their final weights were determined. Swelling index was calculated by using equation (1).

$$swelling\ index\ (\%) = \frac{change\ in\ weight\ (mg)}{original\ weight\ (mg)} \times 100 \qquad (1)$$

Entrapment efficiency
Appropriate quantity of drug-loaded microspheres was crushed in a glass mortar with a pestle, weighed to obtain 100 mg (equivalent to 50 mg of metformin) and then suspended in 50 mL of phosphate buffer, pH 6.8. After 24 h, the solution was filtered and the filtrate was appropriately diluted with phosphate buffer, pH 6.8 and analysed using UV spectrophotometer (Biomate 3, USA) at 233 nm. The drug entrapment efficiency (E) was then calculated using equation (2).

Table 1 Physicochemical and pharmacopoeial properties of *Khaya senegalensis* gum

Parameter	Result
Yield (%)	28.48
Colour	Brown
Odour	Characteristic odour
Taste	Slightly bland
Texture	Slightly gritty
Moisture content (%)	14.59 ± 0.50
pH	4.00 ± 0.05
Total ash (% w/w)	5.25 ± 0.14
Acid insoluble ash (% w/w)	2.08 ± 0.09

Table 2 Elemental analysis of Khaya senegalensis gum powder

Metal	Content (ppm) ± SD
Chromium (Cr)	0.060 ± 0.008
Cadmium (Cd)	Not detected
Copper (Cu)	0.178 ± 0.062
Lead (Pb)	0.009 ± 0.006
Nickel (Ni)	0.024 ± 0.008
Cobalt (Co)	0.018 ± 0.004

$$E\ (\%) = \frac{practical\ drug\ content}{theoretical\ drug\ content} \times 100 \qquad (2)$$

In vitro dissolution studies and kinetic modelling of release profiles
The in vitro dissolution studies were carried out using the basket method USP type II rotated at 50 rpm in 900 mL of phosphate buffer, pH 6.8, maintained at 37 ± 0.5 °C. The microspheres equivalent to 500 mg of metformin was placed in the dissolution medium. Samples (5 mL) were withdrawn at 0, 30 min and then at 1 h intervals for 9 h and replaced each time with equal amounts of fresh medium. The samples withdrawn were filtered through a 0.45-micron membrane filter (Nunc, New Delhi, India). The amount of metformin released was determined after suitable dilution at wavelength of 233 nm, using a UV spectrophotometer (Biomate 3, USA). Dissolution test was also carried out using the same conditions for a sustained release marketed brand of metformin tablets (Panfor° SR 500 mg, Mega Lifesciences Pty. Ltd., Thailand).

Kinetic modelling of the release data for the three microspheres formulations was carried out by fitting to different kinetic equations. The results of drug release from the microsphere formulations was fitted into drug release kinetic models—zero order, first order, Higuchi, and Korsmeyer-Peppas. The model of best fit was identified by comparing the values of correlation coefficients.

Statistical analysis
All the tests were carried out in triplicates. All the values were expressed as mean ± standard deviation (SD).

Table 3 Micromeritics and rheological properties of *Khaya senegalensis* gum powder

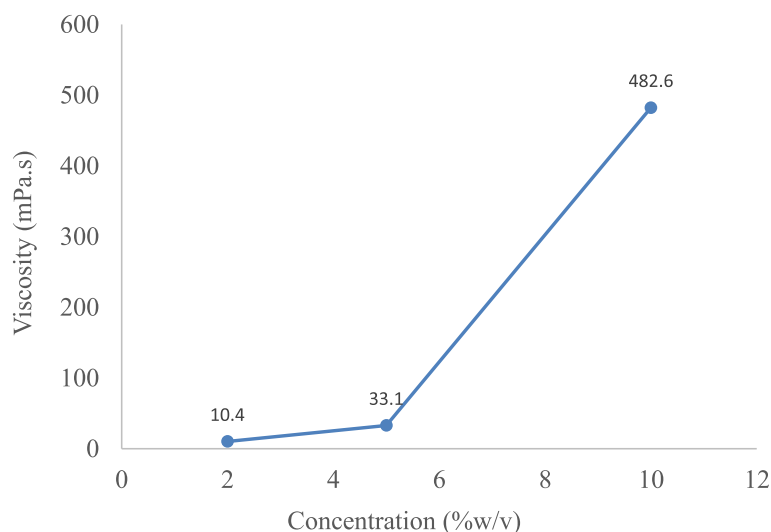| Parameter	Results ± SD
Bulk density (g/mL)	0.57 ± 0.01
Tapped density (g/mL)	0.75 ± 0.01
Angle of repose (°)	34.72 ± 0.97
Carr's index	23.68 ± 1.91
Hausner's ratio	1.31 ± 0.03
Swelling index	3.41 ± 0.01

Fig. 1 Viscosities of different concentrations of *Khaya senegalensis* gum

Differences with $p < 0.05$ were considered statistically significant. GraphPad Prism-7 software (GraphPad Software Inc., USA) was used for statistical analysis.

Results

Physicochemical and pharmacopoeial characterization of gum sample

Physicochemical and pharmacopoeial properties of *Khaya senegalensis* gum is presented in Table 1. The pH of khaya gum (4.00 ± 0.05) was slightly higher than the one (3.38 ± 0.00) reported by Olorunsola et al. [23]. The

moisture content reported for the khaya gum was within the moisture content limit (15.0% w/v) for natural gums [24]. The total ash content (% w/w) was 5.25 ± 0.14. The allowed limit according to the British Pharmacopoeia [25] is 4.00% w/w. This implies the presence of extraneous materials and impurities. Total ash content of *Khaya senegalensis* gum was lower (3.00 ± 0.15) in the findings of Akin-Ajani et al. [26].

Phytochemical screening showed that there was absence of some secondary plant metabolites in the gum powder, namely alkaloids, tannins, saponins, flavonoids, and amino acids. However, the gum sample contained
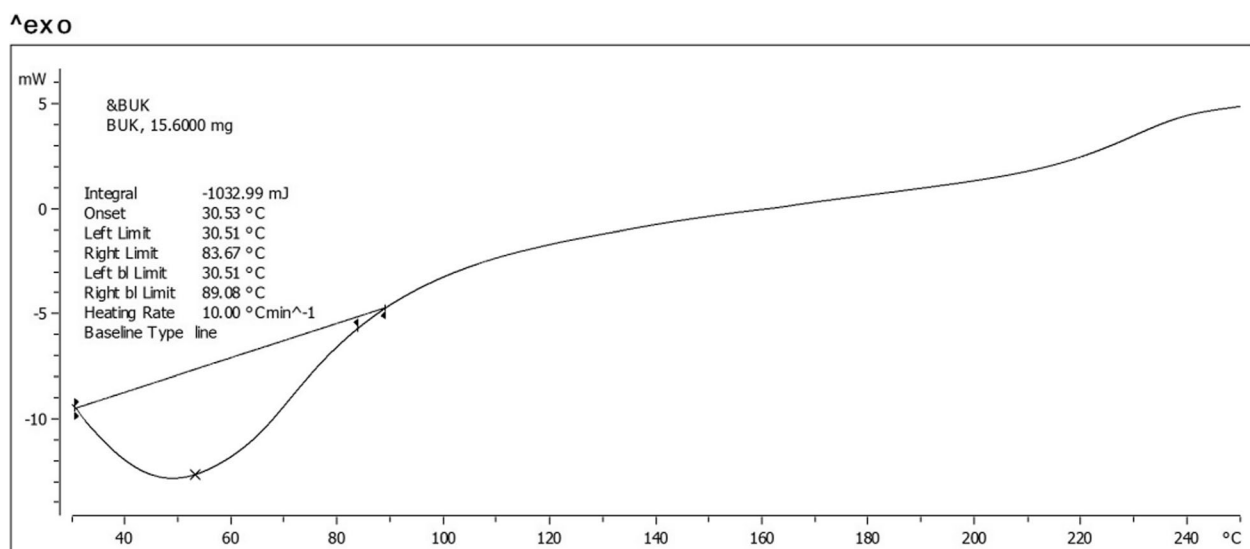
Fig. 2 DSC thermogram of *Khaya senegalensis* gum

reducing sugars and trace of anthraquinones. The presence of carbohydrates and reducing sugars implies the presence of chains of monosaccharides and polysaccharides. Secondary metabolites are various chemical compounds produced by plants from the materials derived from primary metabolites. These phytoconstituents have bioactivities. It was therefore pertinent that this was investigated for this gum which was used in the study as a sustained release carrier. Gums are expected not to have these phytoconstituents except monosaccharides/reducing sugars (carbohydrates) and hence inert and biodegradable. The reported trace amount of anthraquinone observed might be due to parts of Khaya bark which was not totally eliminated by the extraction process used.

Table 2 represents the elemental composition of the Khaya senegalensis gum for polyvalent and heavy metals. The values obtained for copper, chromium, nickel, and lead were found to be within the USP limit for heavy metals content in oral drug products [27].

Micromeritics and rheological properties
As shown in Table 3, the bulk and tapped densities (g/mL) of the gum powder were 0.57 ± 0.01 and 0.75 ± 0.01, respectively. The Carr's index was 23.68 ± 1.91. Carr's index values from 23 to 35 have been classified to have poor flow [28]. Hausner's ratio obtained from the experiment was 1.31 ± 0.03. Hausner's ratio from 1.26 to 1.34 has passable flow character [28].

As seen in Table 3, the swelling index of the gum powder was 3.41 ± 0.01. Khaya senegalensis gum is hydrophilic and it can hydrate in water to form a gel.

The swelling index of a gum (3.41 ± 0.01) demonstrates its hydrophilic nature and its ability to swell into a gel in an aqueous medium [18].

As shown in Fig. 1, the viscosity of the gum sample obtained at 2, 5 and 10% w/v were 10.4 ± 0.79, 33.1 ± 0.86, and 482.6 ± 1.96 mPaS, respectively. This showed that the viscosity of gum increased as the concentration of gum dispersions increased from 2 to 10% w/v.

Differential scanning calorimetry (DSC)
The thermal behaviour of Khaya senegalensis gum as represented in Fig. 2 showed that the gum had an onset temperature of 30.53 °C, peak temperature of approximately 53.00 °C, an endset temperature of 89.08 °C, and an enthalpy change of 1032.99 J/g. The thermogram signifies that the gum sample could be stable at temperatures as high as 250 °C since there was no evidence of degradation [23].

Scanning electron micrograph (SEM)
The SEM of the extracted gum powder is represented in Fig. 3. The shape and surface characteristics of the particles were generally granular and rough. Khaya senegalensis gum showed irregularly shaped particle. It thus revealed the amorphous nature of the gum sample.

Fourier transform-infrared spectroscopy (FTIR) study
The stacked FTIR spectra of extracted Khaya senegalensis gum powder, pure metformin, and metformin-loaded microspheres is presented in Fig. 4.
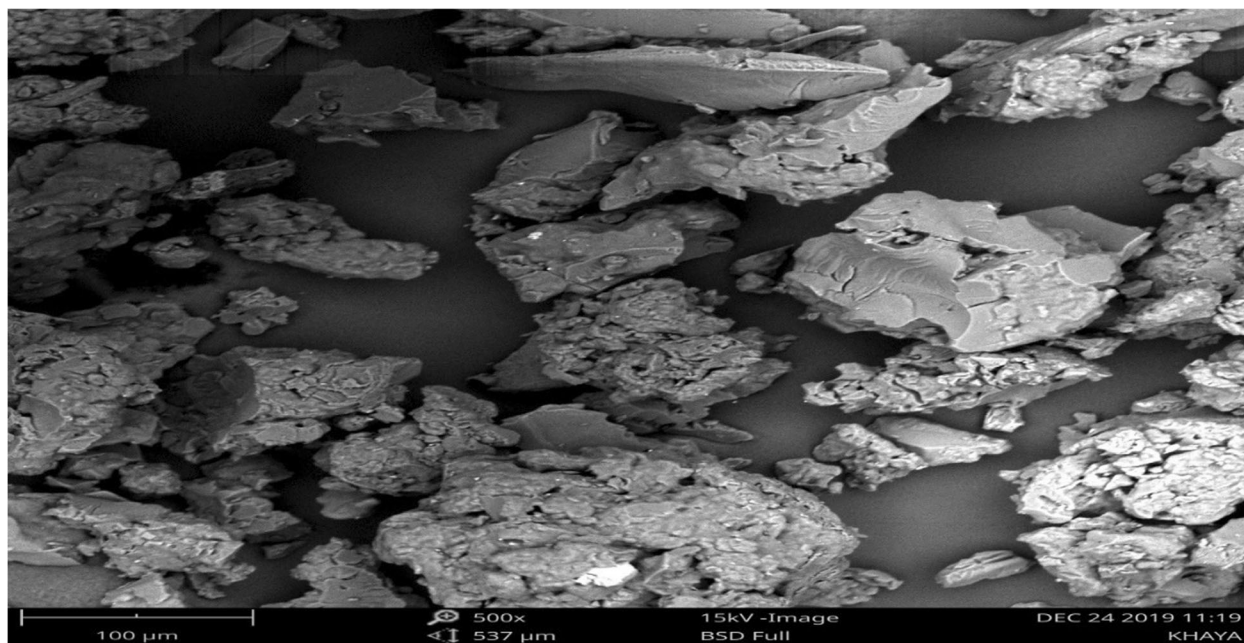

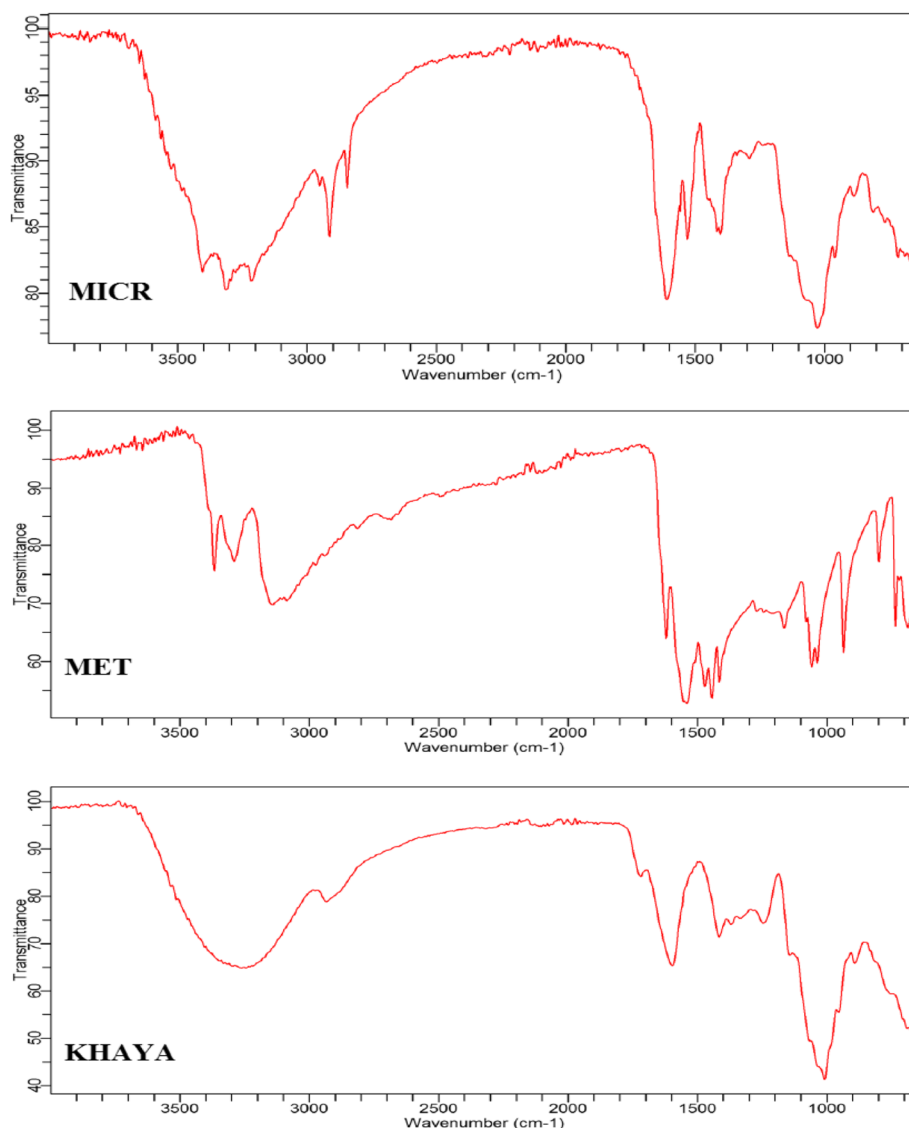**Fig. 3** SEM micrograph of Khaya senegalensis gum

Fig. 4 Stacked FTIR spectra of *Khaya senegalensis* gum (KHAYA), pure metformin powder (MET), and microsphere (MICR)

The FTIR spectrum for khaya gum highlights some major bands and peaks. The peak at 894.6 cm^{-1} could be assigned to aromatic C–H bending vibration while that at 2937.1 cm^{-1} could be attributed to C–H stretching vibrations in the substituted aromatic hydrocarbon. The peaks at 1371.7 cm^{-1} and 1416.4 cm^{-1} could be assigned to O–H bending of aromatic alcohol and carboxylic acids. The peak at 1718.3 cm^{-1} could be assigned to C=O stretching of ether, unsaturated ester while that of 3246 cm^{-1} could be assigned to O–H stretching of carboxylic acid.

Physicochemical properties of microspheres

The data for physicochemical properties of the metformin-loaded microspheres are presented in Table 4. The mean particle sizes of the microspheres (µm) ranged from 1200.7 ± 21.6 to 1420.5 ± 9.8. The SEM

Table 4 Physicochemical properties of microspheres

Formulation code	Polymer blend khaya:sodium alginate (%)	Microsphere size (µm)	Swelling index (%)	Entrapment efficiency (%)
FA	2:3	1360.2 ± 10.7	32.80 ± 2.67	65.6 ± 0.45
FB	9:11	1200.7 ± 21.6	61.33 ± 6.30	78.6 ± 1.32
FC	1:1	1420.5 ± 9.8	74.27 ± 6.54	81.5 ± 1.41

micrographs of drug-loaded microspheres are presented in Fig. 5 while the thermal curves of pure metformin and microspheres are shown in Fig. 6.

In vitro dissolution studies and kinetic modelling of release profiles

The result of in vitro dissolution studies of the metformin-loaded microspheres and marketed sustained release metformin tablets is presented in Fig. 7.

The correlation coefficients generated from the various release kinetic models are presented in Table 5. All the microsphere formulations fitted into the Korsmeyer-Peppas equation as they showed good linearity (r^2 = 0.9970–0.9994) and slope between 0.928 and 1.210.

Discussion

The yield (28.48% w/w) of gum obtained from *Khaya senegalensis* exudates was slightly higher than what was reported (25.00%) by Olorunsola et al. [23]. This variation could be because of a difference in botanical source, processing parameters and environmental conditions. The higher yield could also be attributed to the concentration of the precipitating agent employed in the extraction.

The pH of the extracted khaya gum was in the acidic range, indicating its applicability in pharmaceutical preparations. Incorporation of basic excipients into drug formulations promotes oxidation of susceptible drugs [23]. Hence, acidic and neutral gums are more widely used for pharmaceutical formulations [23].

The microspheres prepared with the highest concentration of khaya gum had the highest particle size of 1420 ±9.8 μm. The sizes of the formulations were statistically significant ($p < 0.05$). The swelling index of the microspheres (Table 4) increased as the concentration of khaya gum in the formulations increased. This might be attributed to the presence of pores and cavities present in the polymer as the concentration of khaya gum increased as indicated in the SEM micrographs of drug-loaded microspheres (Fig. 5). However, there was statistically significant difference ($p < 0.05$) in swelling indices between microsphere formulations.

Entrapment efficiency is an essential parameter for assessing drug loading of microspheres. In addition, it indicates the extent to which the drug is embedded in the polymer network. In this study, the entrapment efficiency ranged from 65.6% to 81.5% in the microspheres made from khaya:sodium alginate gum polymer blends indicating that the presence of *Khaya senegalensis* gum in the formulations improved drug loading. Entrapment efficiency increased with an increase in concentration of khaya gum in the polymer network in the order 2:3 < 9: 11 < 1:1. There was statistically significant difference ($p < 0.05$) in entrapment efficiencies between formulations.

Drug and excipients compatibility studies were studied by FTIR and DSC. FTIR technique is employed to study the changes in functional groups of host and guest molecules [29]. The study the FTIR spectrum of the microspheres (Fig. 4) showed that the major bands and peaks of metformin were retained. The additional bands and peaks that appeared in the spectrum of the microspheres might be attributed to the other excipients employed in the formulation.
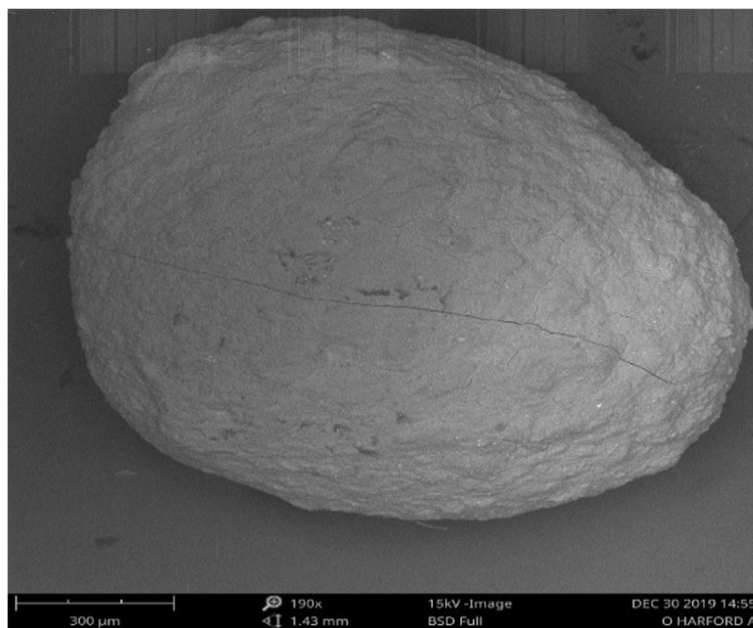

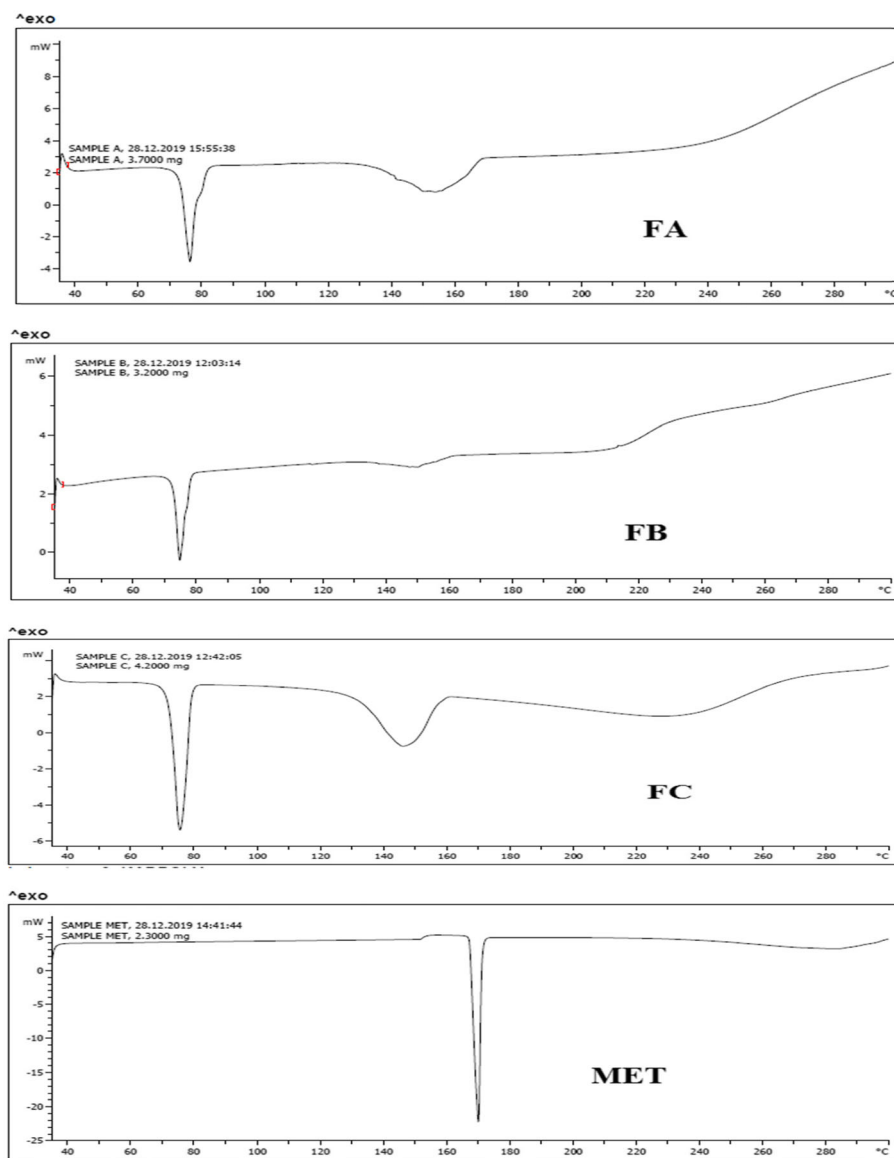**Fig. 5** SEM micrograph of metformin-loaded microsphere

Fig. 6 Differential scanning calorimetry thermograms of pure metformin (MET) and microspheres (FA, FB, and FC)

The thermal curve of pure metformin (MET) exhibited an initial flat profile followed by a sharp endothermic peak at 170.27 °C (representing the melting point of metformin) and an associated fusion enthalpy of 661.29 J/g indicating its crystalline state. The DSC thermograms of the microspheres showed a shift in the endothermic peak observed in metformin. The endothermic peaks of the microspheres (FA, FB, and FC) were observed at 77.11 °C, 75.51 °C, and 77.98 °C, respectively. Therefore, the thermal curve of the formulations and pure metformin maintained an initial flat profile but the incorporation of excipients in the formulations increased the melting points of the formulations. It has been observed that the differences

in DSC thermograms do not always indicate incompatibilities between the samples [30].

The in vitro dissolution study showed that as the viscosity of the polymer matrix increased, there was a resultant resistance to polymer erosion and drug diffusion [31]. This indicates that the rate of release of drugs from microspheres is influenced by the drug/polymer ratio used in the formulation. The dissolution studies graph (Fig. 7) showed that formulations FA, FB, and FC released about 27%, 22%, and 30% of metformin respectively after 2 h while the commercial brand sustained release metformin tablet (FM) (Panfor® SR 500 mg, Mega Lifesciences Pty. Ltd., Thailand) released about 25%. After 9 h, the amount of drug released by the
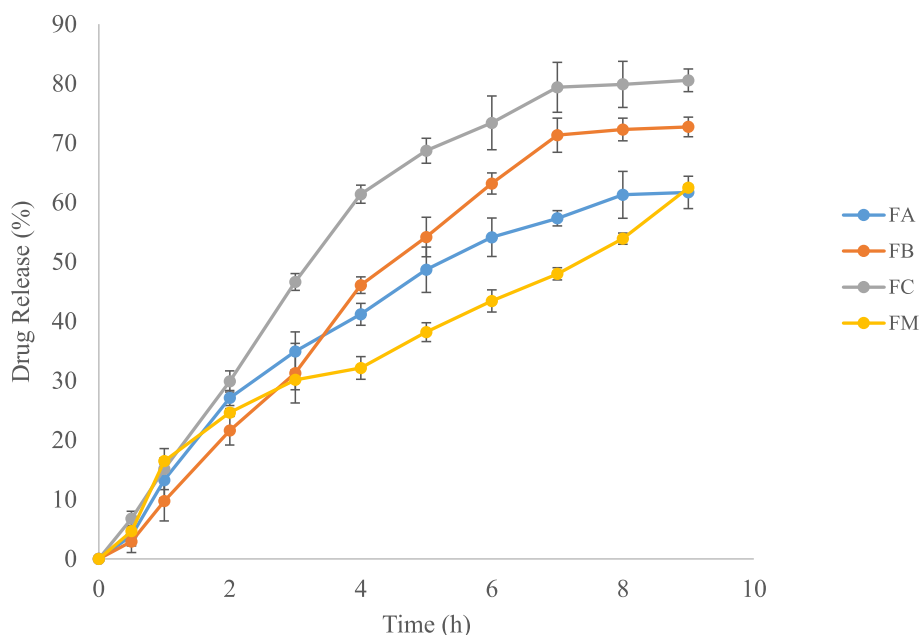
Fig. 7 In vitro release profile of microspheres and marketed metformin tablets

microspheres were about 62%, 73%, and 80%, respectively while the commercial brand metformin tablet released about 63%. Although, the metformin-loaded microspheres and the commercial brand metformin tablet seemed to show similar release patterns, there were significant differences in their release properties. Apart from formulation FC, all the formulations released less than 5% of metformin at 30 min. This is of great significant for formulations that are intended for sustained release. Burst release which has been designated as the release of more than 15% of the drug in the first 1 h is not desirable. In the study, the microspheres including the sustained release metformin tablet released approximately 15% of the drug or less which is desirable for sustained release formulations thus suggesting effective entrapment [26]. Among the three microsphere formulations, FA had more comparable release profile to that of the commercial brand metformin tablet (FM).

To determine the kinetics and mechanism of drug release from the microspheres, data obtained from in vitro release studies were fitted into kinetic models such as zero order, first order, Higuchi, and Korsmeyer-Peppas. The data were analysed by the regression coefficient method,

and regression coefficient value (r^2) of the microsphere formulations (Table 5). To confirm the release mechanism, the data were fitted into the Korsmeyer-Peppas equation as they showed good linearity (r^2 = 0.9970–0.9994) with slope (n) between 0.928 and 1.210) which indicates that the release of the drug followed a super case II transport system (occurs when sorption is controlled by stress-induced relaxations in swellable matrix systems) [32].

Conclusion

The extracted *Khaya senegalensis* gum had desirable pharmacopoeial and physicochemical properties and is a good candidate for potential applications as pharmaceutical excipient. The blend of the khaya gum and sodium alginate produced microspheres with controlled release properties. The ratio of drug to polymer influences drug release from the microspheres. Korsmeyer-Peppas was the best model to describe its release mechanism. Formulations containing 2:3 ratio of khaya gum and sodium alginate (FA) produced microspheres with comparable controlled release profiles to the commercial brand metformin tablet.

Table 5 In vitro release kinetic parameters of metformin from the microspheres

Formulation code	Zero order		First order		Higuchi		Korsmeyer-Peppas		
	r^2	K	r^2	K	r^2	k	r^2	k	n
FA	0.9594	32.85	0.8308	0.11	0.9552	171.47	0.9970	1.53	0.928
FB	0.9736	43.70	0.8657	0.13	0.9389	189.65	0.9990	1.70	1.210
FC	0.9417	44.11	0.8553	0.11	0.9538	232.20	0.9994	1.50	1.020

Abbreviations

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Authors' contributions

CPA conceived the study. CII and MOO helped design and coordinate the study. CHO and SST carried out the experimental studies. CHO, CPA, MOO, and SST drafted the manuscript. All authors have read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interest.

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