ORIGINAL ARTICLE

Isolation, characterization and formulation properties of a new plant gum obtained from *Cissus refescence*

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This study elucidated the physical, thermal, sorption and functional properties of a gum obtained from the stem of *Cissus refescence* (CRG). Scanning electron microscopy (SEM), Particle size analysis, X-ray powder diffraction (XPRD), Thermo gravimetric analysis (TGA), Differential scanning colorimetry (DSC), Fourier transmittance infra red (FTIR), and Elemental analysis were used to characterize the gum sample. Tablets were prepared by incorporating an anti asthmatic drug; theophylline. *In vitro* drug release was carried out in simulated gastric and intestinal conditions. Effect of gum concentration on release kinetics was evaluated. CRG had a glass transition (Tg) and melting peak of 233.5 and 270°C respectively. This material showed a 10.59 % loss in weight at 195°C. The sample had very strong peaks at approximately 14°, 15°, 23°, 24°, and 29°2θ degrees of 2-theta (θ) in the X-Ray Powder Diffraction pattern. Elemental analysis showed that CRG contains 44.1, 7.1, 48.5, and 0.3% Carbon, Hydrogen, Oxygen and Nitrogen respectively. Release of theophylline under simulated biologic conditions varied between 2 to 12 hours depending on the concentration of the gum used in formulation. Drug release was found to be erosion-controlled initially (i.e. in SGF), but at later stage, it became swelling -controlled (i.e. in SIF). The results obtained in this study establish the fundamental characteristics of CRG. The matrices were pH sensitive and can potentially be used for intestinal drug delivery.

Key words: Characterization, *Cissus refescence* gum, sustained released tablets, theophylline

INTRODUCTION

Excipients are additives used to convert active pharmaceutical ingredients into dosage forms suitable for administration to patients.[1] New and modified excipients continue to emerge with better drug delivery performance. Synthetic polymers offer a broad range of properties that can be reasonably well "built-in" by design and modified by altering polymer characteristics. Excipients of natural origin are of particular interest to us for reasons of reliability, sustainability and avoiding reliance upon materials derived from fossil fuels.[2] Plant products are therefore attractive alternatives to synthetic products because of biocompatibility, low toxicity, environmental "friendliness", and low price compared to synthetic products. Excipients from natural products are also generally non-polluting renewable sources for the sustainable supply of cheaper pharmaceutical products.[1,2]

Natural gums obtained from plants have diverse applications in drug delivery as disintegrant,[3] emulsifying[4] suspending agents[5] and as binders.[6] They have also been found useful in formulating immediate and sustained release preparations.[7]

The plant *Cissus refescence* F. *Amphelidaceae* is a climbing stem widely distributed in many parts of Nigeria, especially within the guinea savannah region of Anambra, Kogi and Benue states. The Igala and Idoma ethnic groups refer to this plant as Okoho and use the mucilage from the stem as thickeners in soup.[3,8] Although the gum obtained from *Cissus refescence* has been evaluated for its potential use as a dispersant in pharmaceutical liquid systems,[3] literature survey reveals that comprehensive physicochemical characterization of the gum has not been done. The objective of this study therefore was to isolate and undertake a multiscale characterization of the gum. We have also assessed the *in vitro* performance of the gum on the release profile of theophylline from tablet matrices as a model of sustained release of a drug from a formulation matrix.

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MATERIALS AND METHODS

Materials

Tragacanth powder (Sigma, UK), *Cissus refescence* gum (CRG), sodium carboxymethylcellulose (Nacmc), Theophylline (Wako, Japan). All other chemicals and reagents used were of analytical grade.

Method

Isolation of gum

CRG was extracted and purified as previously described by Wang *et al*., 2006.[3]

Physicochemical Characterization of the Gum

Solubility test

The separated gum was evaluated for solubility in water, acetone, chloroform and ethanol in accordance with the British pharmacopoeia specifications.[9]

Swelling index

The method of Ohwoavworhua and Adelakun 2005[10] was used; 1.0 g each of the sample was placed in each of 15 ml plastic centrifuge tubes and the volume occupied was noted.10 ml of distilled water was added from a 10 ml measuring cylinder and stoppered. The contents were mixed on a vortex mixer (Vortex Gennie Scientific, USA) for 2 min. The mixture was allowed to stand for 10min and immediately centrifuged at 1000 rpm for 10 min on a bench centrifuge (GallenKamp, England). The supernatant was carefully decanted and the volume of sediment measured. The swelling index was computed using the equation:

$S = V_2/V_1$.

Where; S = Swelling index

V_1 = Volume occupied by the gum prior to hydration

V_2 = Volume occupied by the gum after to hydration

The data presented here is for triplicate determinations.

Loss on drying

The method adopted was that specified in the B.P 2004 for acacia.[9] 1.0 g of the sample was transferred into each of several Petri dishes and then dried in an oven at 105°C until a constant weight was obtained. The moisture content was then determined as the ratio of weight of moisture loss to weight of sample expressed as a percentage. The data presented here is for triplicate determinations.

Total ash and acid insoluble ash determination

Ash content was estimated by the measurement of the residue left after combustion in a furnace at 450°C.[10] The ash obtained from the determination of the ash was boiled with 25 ml of 2M hydrochloric acid solution for 5 minutes and the insoluble matter was filtered and washed with hot water and ignited and the subsequent weight was determined. The percent acid insoluble ash was calculated.[10] The data presented here is for triplicate determinations.

pH determination

This was done by shaking a 1%w/v dispersion of the sample in water for 5 min and the pH determined using a pH meter (Corning, model 10 England).[11] The data presented here is for triplicate determinations.

Angle of repose

The static angle of repose, a, was measured according to the fixed funnel and free standing cone method.[10] A funnel was clamped with its tip 2 cm above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The mean diameters of the base of the powder cones were determined and the tangent of the angle of repose calculated using the equation:

$\tan a = 2h/D$.

The data presented here is for triplicate determinations.

Bulk and tap densities

2.0 g quantity each of the powder sample was placed in a 10ml measuring cylinder and the volume, V_0, occupied by each of the samples without tapping was noted. After 100 taps on the table, the occupied volume V_{100} was read. The bulk and tap densities were calculated as the ratio of weight to volume (V_0 and V_{100} respectively). The data presented here is for triplicate determinations.

Hausners index

This was calculated as the ratio of tapped density to bulk density of the samples.

Compressibility index (C%)

This was calculated using the equation:

Compressibility = (Tapped density − bulk density)/Tapped density × 100.

Thermogravimetric Analyses

Thermogravimetric analyses were performed in a TG apparatus (Shimadzu, Japan). Sample (1.78 mg) was heated at a rate of 10°C/min from ambient temperature to 200°C. Nitrogen was used as the purge gas at a flow rate of 20 ml/ min.

Differential Scanning Calorimetry (DSC) Analyses

Thermal properties of CRG were characterized using a Netzsch DSC 204 F1 Phoenix (Netzsch, Germany). Nitrogen,

at the rate of 20 ml/min, was used as purge gas; 2.7 mg of powdered material were sealed in aluminium pan and heated from 30°C up to 400°C at the rate of 10°C/min, followed by a cooling cycle back to 30°C at the same rate.

Fourier Transform Infra Red (FT-IR)

The FT-IR spectrum of the sample was recorded in an IR spectrometer (Nicolet Magna 4R 560, MN, USA), using potassium bromide (KBr) discs prepared from powdered samples mixed with dry KBr in the ratio 1 : 200. Triplicate measurements were made, and the spectrum with the clearest identifiable peaks was chosen.

X-ray Powder Diffraction (XRPD)

X-ray diffraction patterns of the gum were analyzed using a Siemens D5000 X-ray diffractometer (Siemens, Munich, Germany). Powder sample, packed in rectangular aluminium cells, illuminated using CuKα radiation (λ = 1.54056 Å) at 45 kV and 40 mA. Samples were scanned between diffraction angles of 5° to 40°C 2θ. Scan steps of 0.1 were used and the dwell time was 15.0 s. A nickel filter was used to reduce the Kβ contribution to the X-ray signal. The'd' spacings were computed according to Bragg's law of diffraction. Triplicate measurements were made at ambient temperature.

Microstructure Studies by SEM

The morphological features of the gum were studied with a JSM-5600 LV scanning electron microscope of JEOL, Tokyo, Japan. The dried sample was mounted on a metal stub and sputtered with gold in order to make the sample conductive, and the images were taken at an accelerating voltage of 10kV with magnifications of ×1000, ×2000 and ×10,000. The samples providing most meaningful information for purposes of our analysis were obtained at ×2000 magnification.

Elemental Analysis

Elemental analysis of carbon, hydrogen and nitrogen was carried using a Leco CHN-2000 determinator. A Perkin-Elmer Elemental Analyzer was used for the determination of oxygen.

Preparation of Theophylline Matrix Tablets

Matrix tablets of theophylline were prepared by a wet granulation method. Lactose was used as diluent and magnesium stearate was used as lubricant. CRG gum was included in the formulations in various proportions. The composition of different formulations used in the study containing 100 mg of theophylline in each case is shown in Table 1. In all the formulations, CRG gum was sieved (<500 μm) separately before use and mixed with theophylline (<150 μm) and lactose (<150 μm) in a blender (Braun, Germany). The powder mixtures were mixed for 10 minutes using a tumbler mixer (Karl kolb, D. 6072 Dreieich, Germany) and granulated with water for 5 minutes using a granulator (Erweka, GMbH, Germany) fitted with a 1.6 mm mesh screen. After passage through the screen, granules were dried at 50°C for 2 h in a hot air oven (Salvis, Switzerland). The dried granules were rescreened through a 1.7 mm sieve and lubricated with 1.0 % magnesium stearate for 5 minutes using the tumbler mixer. The final blend was compressed using a single station tablet press (THP Shanghai, Tianxiang ad Chentai Pharmaceutical Machinery Co. ltd, China) equipped with 10.5 mm punch and die set. The tablet weight was adjusted to contain 100 mg of theophylline per matrix tablet. Tablets weighing 300 mg each and containing 100 mg theophylline were compressed at 23.75 kN and dwell time of 60 seconds. The tablets were tested for their hardness (n = 10), drug content (n = 10) and drug release (n = 4) characteristics.

Micromeritic Properties of Granules

The bulk and tapped densities for granulated powders was

Table 1: Some physicochemical properties of *cissus refescence* gum and tragacanth powder

Parameters		Results
Cissus refescence		
Solubility		Slightly soluble in water. Practically insoluble in ethanol, acetone and chloroform.
Swelling ratio	In 0.1N HCL	4.0
	In phosphate buffer 7.4	5.0
	In water	6.0
Loss on drying		0.71%
Total ash		2.0%
Acid insoluble ash		1.0%
True density		1.6g/dl±0.02
Density of powder	Bulk density (g/cc)	0.58
	Tapped density (g/cc)	0.71
Compressibility index		18.31%
Hausners quotient		0.13
Angle of repose		23.75º
pH		7.7
Tragacanth		
Solubility		Slightly soluble in water. Practically insoluble in ethanol, acetone and chloroform.
Swelling ratio	In 0.1N HCL	6.0
	In phosphate buffer 7.4	3.4
	In water	5.8
Loss on drying		0.67%
Total ash		3.0%
Acid insoluble ash		0%
Density of powder	Bulk density (g/cc)	0.76
	Tapped density (g/cc)	0.77
Compressibility index		1.30%
Hausners quotient		1.01
Angle of repose		20.31
pH		5.3

determined using standard methods.[12] Compressibility and Hausner' indices were calculated using the method of Carr 1965. The data presented here is for triplicate determinations.

Tablet Thickness and Tensile Strength

Tablet thickness and crushing strength were determined using the apparatus Pharmatest model PTB-311, Germany. Crushing strength was examined by placing a tablet between a stationary and moving spindle. Force was applied by turning the moving spindle until the tablet cracked diametrically. Tablet tensile strength was calculated according to the method reported by Emeje *et al*.[12] Friability of the compacts was evaluated from the mass loss of 10 tablets tumbled for 100 revolutions (25 rpm for 4 minutes) using a friabilator (Erweka, Germany). The data presented here is for triplicate determinations.

Determination of Drug Content

Theophylline matrix tablets were tested for their drug content. Ten tablets were finely powdered; 300 mg of the powder was accurately weighed and transferred into a 100 ml volumetric flask. 50 ml of distilled water was added and shaken on a vortex mixer for 10 minutes. The content of the flask was made up to 100 ml mark with more distilled water and allowed to stand for 2 h with intermittent sonication to ensure complete solubility of the drug. The mixture was centrifuged at 2000 rpm for 10 minutes and the content of theophylline in the supernatant liquid was analyzed spectrophotometrically at 272 nm.

***In vitro* Drug Release Studies**

The ability of CRG matrix tablets of theophylline to remain intact in the physiological environment of the stomach and small intestine was assessed by conducting drug release studies under conditions mimicking mouth to intestinal transit. Drug release studies were carried out using USP dissolution rate apparatus (Apparatus 1, 100 rpm, 37°C) for the first 2 h in pH 1.2 simulated gastric fluid (SGF) without enzymes (900 ml). Then the dissolution medium was changed to pH 7.4 simulated intestinal fluid (SIF) without enzymes (900 ml) and tested for drug release for the remaining 6 h. 5 ml aliquots of the dissolution medium were withdrawn at hourly intervals up to at least 8 h. The withdrawn amount was replaced with an equal volume of fresh dissolution medium kept at 37°C. The withdrawn samples were analyzed at 272 nm for theophylline content using a Shimadzu UV Spectrophotometer (Shimadzu, Japan). The data presented here is for quadruplicate determinations. For each dissolution profile, the release data was analyzed by fitting in the power law equation to elucidate the release mechanism.

RESULTS AND DISCUSSION

Physicochemical Properties

Table 1 shows some of the physicochemical parameters of both the test and reference gums. The gum extracted from the stem of *Cissus refescence* is slightly soluble in water and a dispersion of it yielded a brown, slimy solution. The gum was practically insoluble in ethanol, acetone and chloroform. Tragacanth which was used as a reference sample gave a similar solubility profile.

The swelling characteristic of CRG was studied in different media; 0.1N hydrochloric acid, phosphate buffer (pH 7.4) and water. The swelling was highest in water followed by phosphate buffer and least in 0.1N HCl pH. Generally, the results show that CRG has high swelling index suggesting that the gum may perform well as binder/disintegrant/matrixing agent. The gum is a pH responsive polymer, it is therefore a "smart polymer," and may find application in controlled release dosage formulations.[13] The relatively higher swelling index obtained for CRG at pH 7.4 implies that unlike tragacanth, the gum may be useful as a matrix former in controlled drug release. Swelling is a primary mechanism in diffusion controlled release dosage form.[14]

The moisture content of CRG was low, suggesting its suitability in formulations containing moisture sensitive drugs. Given suitable temperature moisture will lead to the activation of enzymes and the proliferation of micro organisms, thereby affecting the shelf life of most routine formulations. It is important to investigate the moisture content of a material because the economic importance of an excipient for industrial application lies not only on the cheap and ready availability of the biomaterial but the optimization of production processes such as drying, packaging and storage.[15]

The total ash and acid insoluble ash value of CRG was found to be 2.0 and 1.0%w/w respectively. Ash values reflect the level of adulteration or handling of the drug. Adulteration by sand or earth is immediately detected as the total ash is normally composed of inorganic mixtures of carbonates, phosphates, silicates and silica. Therefore, the low values of total ash and acid insoluble ash obtained in this study indicate low levels of contamination during gathering and handling of crude *Cissus refescence*.[10]

The bulk and tapped densities give an insight on the packing and arrangement of the particles and the compaction profile of a material.[16] The compressibility index and angle of repose of CRG was 18.31% and 23.75° respectively, implying that the CRG has a good flow with moderate compressibility,

unlike tragacanth with a very poor compressibility index of 1.30% and an angle of repose 20.31°. This is important in scale up processes involving this material as an excipient in a pharmaceutical formulation. Modification of formulations containing this gum for the improvement of flow properties during process development will therefore be minimal compared to tragacanth (e.g., inclusion of glidants or agents to aid in feeding).

A 1% w/v suspension of CRG in water gave a pH of 7.7 while that of tragacanth was 5.3. The near neutral pH of CRG implies that when used in uncoated tablets, it may be less irritating to the gastrointestinal tract. It may also find useful application in formulation of acidic, basic and neutral drugs. Knowledge of the pH of an excipient is an important parameter in determining its suitability in formulations since the stability and physiological activity of most preparations depends on pH.[13]

Thermogravimetric Analyses

The thermogravimetric analysis (TGA) was used to determine the weight loss of the material on heating. Transitions involving mass changes are detected by TGA as a function of temperature and time.[17] The TG curve for the gum shown in Figure 1, showed a one stage weight loss corresponding to loss of water around 25-195°C. The curve shows that the gum did not decompose before 200°C. It has been reported[18] that water is formed by intra- and intermolecular condensation of polymeric hydroxyl groups which are the main product of decomposition at temperatures below 300°C. The gum underwent 10.59% weight loss at 195°C. This is low compared to weight loss reported for other polymers such as starch.[18] It implies that CRG has excellent thermal stability.

Differential Scanning Calorimetry

Differential scanning calorimetry (DSC) was used to measure the occurrence of exothermal or endothermal changes with increase in temperature. DSC, because of its sensitivity and accuracy, has been extensively used to study the phase transitions of polymers.[19,20,18,21] The thermogram for CRG is shown in Figure 2 and the corresponding parameters are tabulated in Table 2. It shows that the gum has both amorphous and crystalline portions. Glass transition (Tg) temperature occurred at 233.5°C while a melting peak was observed at about 270°C. Two exothermic peaks and one endothermic peak are exhibited by the sample corresponding to its glass transition, recrystallization and melting respectively. The onset, peak and conclusion temperatures of phase transition were observed to be very high [Table 2]. The continuous (broad) endothermic transition that followed the glass transition is indicative of crystallite melting occurring over the glass transition range.[22] The glass transition temperature (Tg) was also observed to be very high, indicating a high degree of crystallinity of the gum. This has been shown to provide structural stability and made granules more resistant to heat.[23,24] It has also been reported that materials of low Tg have low crystallinity.[25] The knowledge of Tg is essential in production processes and storage as Tg is affected by moisture and other additives, facilitating conversion to the rubbery state and hence facilitating crystallization through molecular rearrangement.[17] The gum was also observed to have low enthalpy, this is attributed to the presence of regular small and oval granules.[26]

Table 2: Thermal properties of *Cissus refescence* gum

Parameter	*Cissus refescence* gum
Onset temperature (°C)	230.7
Peak temperature (°C)	239.3
Endset temperature (°C)	243.3
Delta Cp [J/(g*K)]	3.9
Melting point (°C)	270.1
Tg (°C)	233.5

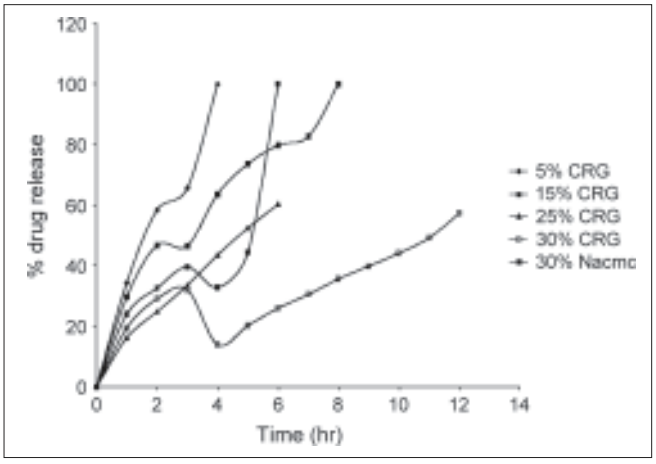

Figure 1: Effect of varying concentrations of *C. refescence* gum on the release profile of theophylline from tablet matrices

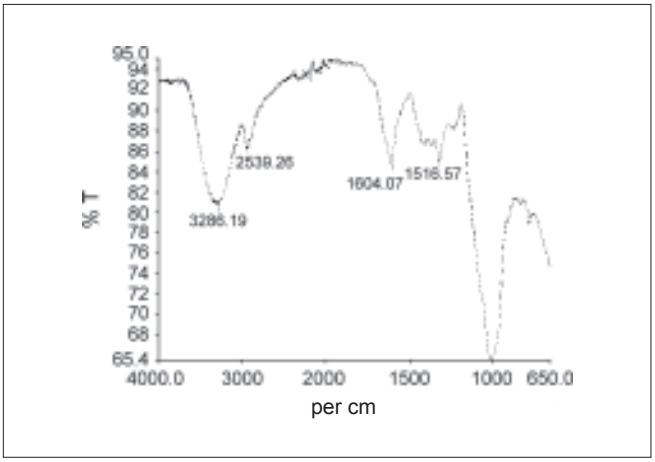

Figure 2: FT-IR spectrum of *C. refescence* powder

Fourier Transform Infra Red (FT-IR)

The IR spectrum is shown in Figure 3. The finger print region of the spectrum consists of two characteristic peaks between 700 and 1316 per cm, attributed to the C-O bond stretching.[27] The band at 1604 per cm was assigned to the O-H bending of water.[28] There are absorptions (weak) in the 1730 per cm area that indicate carbonyls. The absence of significant aromatic stretches in the 1660-1690 per cm region and the weakness of the stretches, imply that there is a modest amount of peptidic cross linking by amide bond formation. The sharp band at 2939 per cm is characteristic of methyl C-H stretching associated with aromatic rings. The broad band at 3286 cm^{-1} is due to the hydrogen-bonding that contributes to the complex vibrational stretches associated with free inter and intra-molecular bound hydroxyl groups which make up the gross structure of carbohydrates.[29] This is all consistent with a polysaccharide structure that is neither a starch nor a cellulose, but does have some peptide cross links and some amino-sugars. The essentially neutral pH of this material leads us to conclude that there can be very few free carboxyl groups to contribute to hydrogen bonding.

X-ray Powder Diffraction (XRPD)

The X-ray diffractogram of CRG is shown in Figure 4. The Bragg reflection angle, 2θ, along with the interplanar spacing, d, and the relative intensity of the peaks is listed in Table 3. The interplanar spacing has been calculated using Bragg's equation given as; $n\lambda = 2d \sin\theta$, where θ is one half the angle read from the diffractogram. As presented in Table 3, the sample shows strong peaks at approximately 14°, 15°, 24°, and 26° 2θ. However, other peaks between 16° and 23° 2θ, are very weak and unresolved or are shoulders on more intense peaks. The result of the XPRD corroborates that of the DSC which shows that, CRG is of low moisture and exhibit both amorphous and crystalline portions.

Table 3 Elemental composition and X-ray powder diffraction data for *Cissus refescence* gum

Element	Composition (%)	Angle 2-θ (°)	d value (Å)	Intensity (%)
Carbon	44.0	14.7	6.0	100.0
		15.1	5.9	74.4
Hydrogen	7.1	23.3	3.9	68.1
		24.2	3.7	91.4
Oxygen	48.5	26.5	3.4	76.9
Nitrogen	0.3	29.9	3.0	68.5
		30.5	3.0	53.5
		31.3	2.9	50.9
		32.0	2.8	46.9

Morphology

The biological and botanical source of a pharmaceutical material serves as a determining factor in the granule shape, size and morphology. As a result, these characteristics not only help to differentiate between various materials but also give an indication of the processing parameters. The SEM of CRG is shown in Figure 5. It exhibits fairly regular, tiny granules and slightly elongated with rugged appearance. The mean particle size was 180 μm. Typical aspect ratio was calculated to be 3 : 2 : 2. The surface area as measured by BET analysis was 1.5 m^2/g. These properties could be of importance when considering applications based on surface characteristics, for example, use of granules as carrier particles.

Elemental Analyses

The quantitative elemental analysis is shown in Table 3. The results show the presence of carbon, hydrogen, oxygen and Nitrogen. The low level of nitrogen is suggestive of amino acid (peptide) crosslink in the sample. The ratio of carbon to hydrogen is just over 6 : 1 indicating, along with the ratio of carbon to oxygen, a good number of unsaturation due to aromatic rings and/or polysaccharide composition.

Micromeritic Properties of Theophylline Granules

All the granules irrespective of the concentration of the

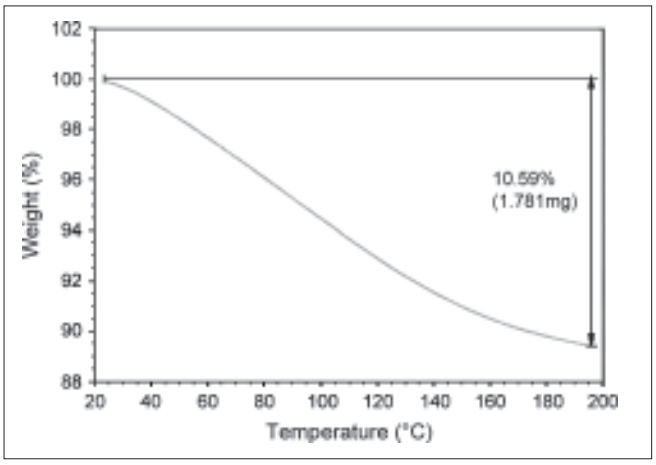

Figure 3: TG curve of *Cissus refescence* gum

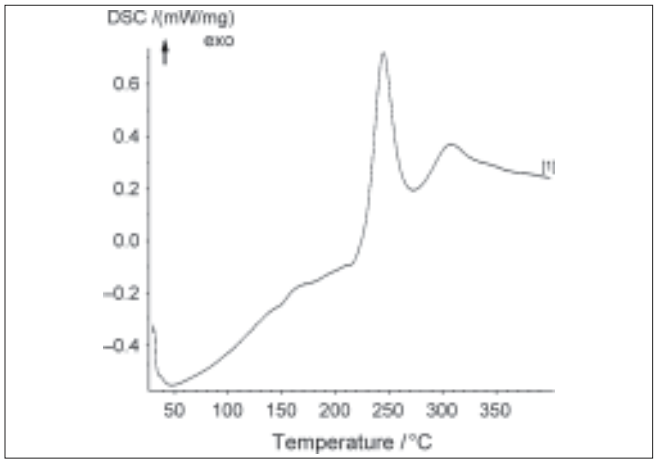

Figure 4: Differential scanning calorimetry curve of *Cissus refescence* gum

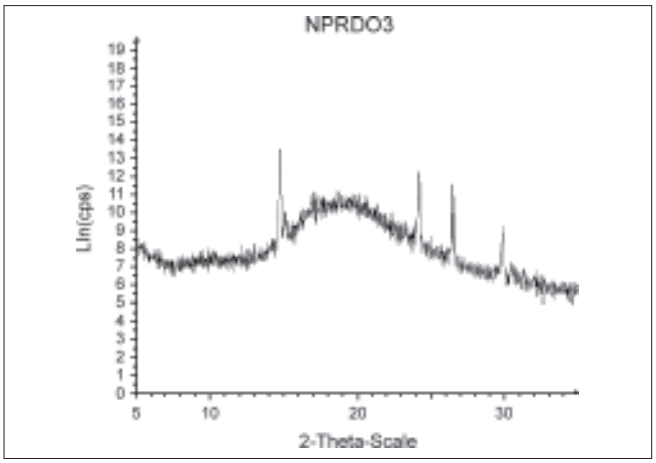

Figure 5: XRD pattern of *Cissus refescence* gum

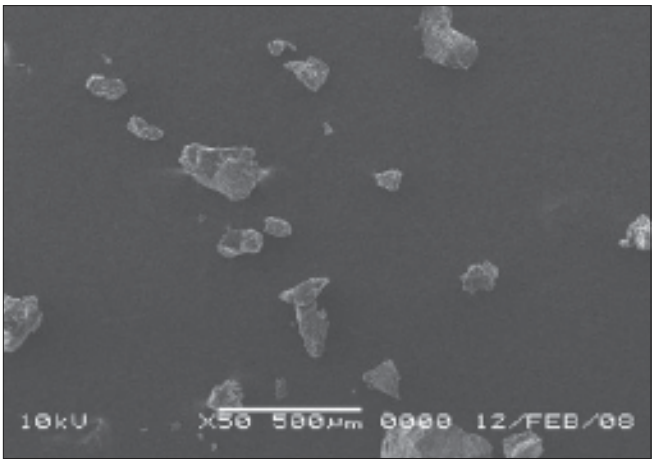

Figure 6: Scanning electron microscopy of *C. refescence* powder

gum used had good flow, as indicated by the values in Table 2. The values obtained did not follow any particular trend.

Properties of Theophylline Tablets

Generally, all the tablets had good pharmacotechnical properties, as none of the tablet s was friable and all the parameters investigated were comparable to that of the reference gum (30% Nacmc). The tensile strength was highest for 15% gum concentration and lowest for 20% gum concentration. It generally increased between 5 and 15%, but decreased between 20 and 25% gum concentration.

***In vitro* Release Studies**

Figure 6 shows the percent drug release versus time profiles of theophylline from matrix tablets. The time taken for 50 and 70% of drug to be released (t50% and t70% respectively) were taken as measure of polymer performance. Formulations containing 5% CRG had the lowest t50 of 1.46 h, while those containing 30% CRG had the highest t50 of 10.97 h [Table 4]. The formulations containing 30% Nacmc released 50% of the drug in 3.24 h, implying that 30% CRG has a better drug retarding property than Nacmc. All the formulations except those containing 25 and 30% CRG released 100% of the drug within the time of the dissolution study. In fact, these formulations retained their physical integrity for up to 24 h. Comparative evaluation of release from the matrix tablets using the student t test shows that CRG 5% was not significantly different from Nacmc 30%. However, drug release from 10, 15, 25 and 30% CRG differed significantly ($P < 0.05$) from the formulation containing 30% Nacmc.

Release Kinetics

Diffusional drug release can be classified as Fickian diffusion if $n \leq 0.5$, non Fickian if $0.5 < n < 1.0$, case II transport if $n = 1.0$ and super case II if $n > 1.0$.[30] Dissolution data which was analyzed using Peppas and Korsenmeyer equation

Table 4: Release parameters of Theophylline formulation containing *C. refescence* gum

Parameter	5% CRG	15% CRG	25% CRG	30% CRG	30% NaCMC
T50 (%)	1.46	5.05	4.49	10.97	3.24
T70 (%)	3.13	5.53	-	-	4.60
Cmax (%)	100.0	100.0	60.4	57.4	100.0

Table 5: Regression analysis and correlation coefficient values for dissolution data of Theophylline tablets using power law equation

Formulation	Power law equation	
	n	R
CRG 5%	0.71	0.98
CRG 15%	0.59	0.86
CRG 25%	0.75	0.99
CRG 30%	0.47	0.98
NaCMC 30%	0.56	0.97

above shows that the values of diffusional coefficient 'n' for all batches followed anomalous release mechanism except the batch containing 30% CRG which followed Fickian release mechanism [Table 5].

CONCLUSIONS

The results obtained in this study established for the first time, the fundamental characteristics of the gum obtained from the fresh stem of *Cissus refescence*. The gum performed better than sodium carboxymethylcellulose at 30% w/w as a sustained release excipient. It was also found to be pH sensitive and may therefore be useful in intestinal drug delivery.

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REFERENCES

1. Patel DM, Prajapat DG, Patel NM. Seed mucilage from Ocimum americanum as disintegrant in tablets: Separation and evaluation. Indian J Pharm Sci 2007;69:431-4.
2. Liu M, Fan J, Wang K, He Z. Synthesis, characterization and evaluation of phosphated cross linked konjac glucomannan hydrogels for colon targeted drug delivery. Drug Deliv 2007;14:397:402.
3. Alfa J, Chukwu A, Udeala OK. Cissus stem gum as potential dispersant in Pharmaceutical liquid systems, rheological characterization. Boll Chim Farm 1999;140:20-7.
4. Nasipuri RN, Igwilo CI, Brown SA, Kunle OO. Mucilage from Abelmoschus escelentus (okra) Fruit- A potential pharmaceutical raw material part II- Emulsifying properties. J Phytomed Ther 1999;2:27-34.
5. Nasipuri RN, Igwilo CI, Brown SA, Kunle OO. Mucilage from Abelmoschus escelentus (okra) Fruit: A potential pharmaceutical raw material; part II- Suspending properties. J Phytomed Ther 1999;1:22-88.
6. Sinha VR, Kumria R. Binders for colon specific drug delivery: An *in vitro* evaluation. Int J Pharm 2002;249:23-31.
7. Ibrahim MA, Dawes VH, Bangudu AB. Evaluation of cissus populnea polymer as a matrix former for controlled drug release. J Phytomed Ther 2002;5:23-32.
8. Burkill HM. The useful plants of West Tropical Africa Vol. 5. 2000.
9. Shengjum C, Jiabi Z, Fengquin M, Qun F. Preparation and characterization of solid dispersion of dipyridamole with a carrier copolyvidonun plasdone® S-630. Drug Dev Ind Pharmacy 2007;33:888-9.
10. The British Pharmacopoeia. Her Majesty's Stationary Office, London: 2004.
11. Ohwoavworhua FO, Adelakun TA. Some physical characteristics of microcrystalline cellulose obtained from raw cotton of cochlospermum planchonii. Trop J Pharm Res 2005;4:1-7.
12. Emeje MO, Kunle OO, Ofoefule SI. Effect of the molecular size of carboxymethylcellulose and some polymers on the sustained release of theophylline from a hydrophilic matrix. Acta Pharm 2006;56:325-35.
13. Nasipuri RN, Igwilo CI, Brown SA, Kunle OO. Mucilage from Abelmoschus esculentus (okra) Fruit: A potential pharmaceutical raw material; Part 1; Physicochemical properties. J Phytomed Ther 1996;1:22-88.
14. Jain SK, Rai G, Saraf DK, Agrawal GP. The preparation and evaluation of albendazole microspheres for colonic delivery. Pharmaceutical Tech 2004;12:66-71.
15. Emeje MO, Nwabunike PI, Isimi CY, Kunle OO, Ofoefule SI. Hydro-alcoholic media: An emerging tool for predicting dose dumping from controlled release matrices. J Pharm Toxicol 2008;3:84-92.
16. World Health Organization: Quality control methods for medicinal plants materials. 1998;28:S29.
17. J, Lantz J. Pharmaceutical dosage forms (Chapter 3) 2005;2:166-7.
18. Giron D. Thermal analysis of drugs and drug products. Encyclopedia Pharma Technol 2002;3:2766-93.
19. Krueger BR, Knutson CA, Inglett GE, Walker CE. A differential scanning calorimetry study on the effect of annealing on gelatinization behavior of corn starch. J food Sci 1987;52:715-8.
20. Hover R. Composition, molecular structure, and physicochemical properties of tuber and root starches: A review. Carbohydr Polym 2001;45:253-67.
21. Manek RV, Kunle OO, Emeje MO, Builders PF, Rama Roa GV, Lopez GP, *et al*. Physical, Thermal and Sorption Profile of starch obtained from Tacca leontopetaloides Starch/Starke 2005;57:1-7.
22. Donovan JW. Phase transitions of the starch water system. Biopolymers 1979;18:263.
23. Barichello V, Yada RY, Coffin RH, Stanley DW. Low temperature sweetening in susceptible and resistant potatoes: Starch structure and composition. J Food Sci 1990;55:1054-9.
24. Singh N, Singh J, Kaur L, Sodhi NS, Gill BS. Morphological, thermal and rheological properties of starches from different botanical sources: A review. Food Chem 2003;79:1-13.
25. Ezekiel R, Rana G, Singh N, Singh S. Physicochemical, thermal and pasting properties of starch separated from γ-irradiated and stored potatoes. Food Chem 2007;105:1420-9.
26. Mathew S, Abraham TE. Physico-chemical characterization of starch ferulates of different degrees of substitution. Food Chem 2007;105:579-89.
27. Goheen SM, Wool RP. Degradation of polyethylene-starch blends in soil. J Appl Polymer Sci 1991;42:2691-701.
28. Mano JF, Koniarova D, Reis RL. Thermal properties of thermoplastic starch/synthetic polymer blends with potential biomedical applicability. J Mat Sci Mater Med 2003;14:127-35.
29. Fang JM, Fowler PA, Tomkinson J, Hill CA. The preparation and characterization of a series of chemically modified potato starches. Carbohydrate Polymers 2002;47:245-52.
30. Sood A, Panchagnula R. Release evaluation of diltiazem CR preparations. Int J Pharm 1998;175:95-107.

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