Original Article

Evaluation of the Matrix-forming Ability of *Chrysophyllum albidum* Linn Fruit Gum in Sustained-release Tablet Formulations

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Abstract

Background: Plant gums are extensively being exploited as pharmaceutical excipients due to the ease of availability, biodegradability, and reduced costs. **Aim:** This study investigated the application of the fruit gum of *Crysophyllum albidum* (CFG) as a matrix former in the formulation of chlorpheniramine maleate and theophylline hydrochloride tablets. **Materials and Methods:** The gum was extracted using acetone and evaluated for flow, swelling, and hydration capacity. Effects of temperature on CFG and drug compatibility were evaluated using differential scanning calorimetry (DSC). Granules containing CFG at 10, 20, and 30% w/w were prepared using the wet granulation method and evaluated for flow properties. Compressed tablets were evaluated for uniformity of weight, hardness, friability, and drug content. *In vitro* drug release studies were carried out in simulated gastric (pH 1.2) and simulated intestinal (pH 6.8) fluids. Pearson's similarity correlations were used to analyze results. **Results:** CFG had a swelling capacity of 22% and hydration capacity of 1.44 with an angle of repose of 30° and Carr's index of 7.6 signifying good flow. DSC thermogram returned an endothermic glass transition peak at 72.1°C with no appreciable shifts in the peak when CFG was incorporated into the drug. Tablet hardness and friability were concentration dependent with values of 6.5–8.5 kg F and 0.04–0.4%, respectively; drug content was within official specifications. Formulations containing 30%w/w CFG sustained drug release for over 12 h and showed better ability to control drug release than HPMC at same concentration. **Conclusion:** This study shows the propensity of CFG to be used in the formulation of sustained-release tablet formulations.

Keywords: *Crysophyllum albidum, fruit gum, matrix-former, sustained release, tablet properties*

Introduction

Excipients are materials that impart several functionality to a dosage form such as modulating drug solubility, imparting cohesiveness on the drug particles, imparting color and taste, maintaining the stability of a formulation, etc. Examples of such excipients used in the pharmaceutical, cosmetics, and food industries range from starch to alginates, sugars, celluloses, gelatin, pectin, among others.

Many of these plant-derived materials are natural polymers and are exploited as excipients[1] because of their benefits. They are a renewable source, biodegradable, biocompatible, and relatively less toxic than synthetic materials. They are available in most localities and are thus cheap, and some of them are edible and readily acceptable more than their synthetic counterparts.[2,3] Although they are prone to microbial contamination, loss of viscous property upon storage, and batch to batch variation,[3] they are highly malleable to fit different formulation needs, thus they can compete with the available synthetic excipients.[4]

The plant *Chrysophyllum albidum* Linn. (Family; Sapotaceae), also known as the African star apple, is widely distributed in tropical West Africa and other African countries such as Ghana, Nigeria, Kenya, Sierra Leone, Sudan, and Uganda. In Nigeria, the plant is called "Agbalumo" by the Yorubas, "Ehya" by the Igalas, "Udara" by the Igbos, and "Agwaluma" by the Hausas.[5,6] The most popular part is the fleshy, juicy fruit which is often a source of agricultural waste due to poor storage, especially during the ripening season. Therefore, exploitation of these wastes as a suitable excipient in the tablet formulation could be a means to addressing the menace while improving its economic value.

C. albidum gum has been exploited as a dry compression excipient at optimum concentrations of 2 and 6% w/w.[7] The gum also demonstrated a faster onset of plastic

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deformation and a higher amount of total plastic deformation than methylcellulose when incorporated into paracetamol tablet formulations.[8] On the other hand, mucilage from the plant seed was found to be effective as a tablet binder at high concentrations (10%w/w) in comparison with acacia gum.[9] The cross-linked fruit gum has also revealed improved physicochemical characteristics over the native gum.[10]

Natural polymers have been exploited as drug release modifiers that reduce dosing frequency, improve patient compliance, and improve bioavailability and is attracting the interest of scientists and clinicians.

Chlorpheniramine maleate is an antihistamine used to relieve symptoms of common cold and allergies. It is a water-soluble drug that undergoes considerable first-pass metabolism and is about 70% bound to plasma proteins.[11] It is thus administered – two to three times daily to afford the patient its optimum benefit. Theophylline is a xanthine alkaloid that is used to effect relaxation of air passages in the lungs in asthma and related diseases but it has a narrow therapeutic index.[12,13] The peculiar properties of these drugs make them suitable candidates for development into controlled release systems to reduce the burden of frequent dosing and its associated adverse effects.

In this study, our aim was to develop sustained-release tablet formulations of chlorpheniramine maleate and theophylline hydrochloride using the extracted gum from the fruit pulp of *C. albidum* as a matrix-former.

Materials

The materials used are as follows: chlorpheniramine maleate powder (BDH Chemicals Ltd., Poole, England), theophylline powder (Sigma-Aldrich Laborchemikalien GmbH, Germany), hydroxypropyl methylcellulose powder (Sigma-Aldrich Laborchemikalien GmbH), acetone (Sigma-Aldrich Laborchemikalien GmbH), concentrated hydrochloric acid (Sigma-Aldrich Laborchemikalien GmbH, Germany), microcrystalline cellulose (BDH Chemicals Ltd., Poole, England). *C. albidum* fruit gum (CFG) was extracted in the Pharmaceutics Laboratory of Ahmadu Bello University, Zaria, Nigeria. All other chemicals used were of analytical grade.

Methods

Collection and extraction of CFG

Fresh fruits of *C. albidum* were obtained from the local market in Zaria, Nigeria, washed thoroughly, and identified at the Herbarium of the Department of Biological Science, Ahmadu Bello University. The pulp was obtained by peeling the fruit and removing the seeds. Extraction was carried out according to an earlier method with slight modifications.[14] The pulp was macerated in water for 24 h and filtered using a calico cloth. The gum was precipitated from the filtrate using acetone in a ratio of 1:2 (gum:acetone) and washed with the same until a cotton-like mass appeared; CFG was obtained. This was air-dried for 12 h and then oven-dried at 50°C for 4 h.

Evaluation of CFG

Angle of repose

The funnel method was used; 20 g each of CFG was allowed to flow through a funnel clamped at a fixed height from a flat surface. The height (h) and radius (r) of the powder heap were measured and the angle of repose (A) was calculated as

$$A = \tan -1 \frac{h}{r} \quad (1)$$

Bulk and tapped densities

The volume occupied by 20 g of CFG in a graduated measuring cylinder was noted and the bulk density (in g/mL) was calculated as a ratio of the powder weight to the volume occupied in the cylinder. Similarly, the tapped density (in g/mL) was computed as the ratio of powder weight to the volume it occupied after tapping the measuring cylinder 100 times.

Carr's compressibility index (CI) and Hausner ratio (HR)

The Carr's index (CI) was calculated using the following formula:

$$\text{CI} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100 \quad (2)$$

Hausner ratio (HR) was computed using the following formula:

$$\text{HR} = \frac{\text{tapped density}}{\text{bulk density}} \quad (3)$$

Determination of pH

The pH of a 5%w/v suspension of the gum in distilled water was determined at room temperature (28°C) using the Oakton pH meter (Series 1100, Singapore). Triplicate determinations were made and the mean was computed.

Hydration capacity

One gram of CFG was placed in a pre-weighed centrifuge tube, distilled water (10 mL) was incorporated into the tube, and the mixture was shaken for 2 min,and allowed to stand for 10 min. The tube was centrifuged at 3000 rpm for 10 min and the supernatant was decanted. The weight of the swollen mass was determined and hydration capacity was computed as the ratio of the weight swollen CFG and the initial dried weight.

Moisture sorption capacity

Two grams of CFG were placed in an evaporating dish and weighed; this was transferred into a desiccator containing water at a relative humidity of 33% using saturated salt solutions as shown in Table 1. The weight of the dish and its content was recorded daily for 5 days and the amount of moisture absorbed was calculated as the ratio of the difference between

the final and initial weight to the initial weight expressed as a percentage. The method was repeated for a relative humidity of 53, 75, and 84%.[15]

Determination of swelling index

The volume occupied by 5 g of CFG in a measuring cylinder after tapping was noted, water was poured into the measuring cylinder, and the volume occupied by the swollen mass after 24 h was noted. Swelling capacity was computed as the ratio of the initial to the final volume and expressed in percentage.

Determination of swelling characteristics of gum compact

Compacts of the gum (500 mg) were made using the Erweka Single Punch Tableting Machine (Type EKO-400, Erweka-Apparatebau). The compact was placed in a beaker containing phosphate buffer (7.4) and the weight was determined at intervals (0, 0.5, 1, 2, and 3 h) according to an earlier method.[16]

Differential scanning calorimetry

This was determined using the Mettler TA 3000 Controller and DSC 821e (Switzerland) differential scanning calorimeter. CFG (5 mg) was placed in the sealed aluminum pan which was heated at a rate of 5 K/min and flushed with 80 mL of N_2/min.

Preparation of granules using CFG

The wet granulation method of massing and screening was employed. Appropriate quantities of the drug, the diluents and microcrystalline cellulose, as presented in Table 2, were mixed in a mortar. The matrix-former (CFG) was incorporated as dry powder into the contents of the mortar and distilled water was added to obtain a wet coherent mass. The wet mass was screened through a sieve (1.7 mm) to obtain uniform granule sizes and dried in the oven at 40°C for 30 min; it was screened again then dried in the oven (40°C) for another 30 min to obtain dried granules. This procedure was repeated for all the batches as presented in Table 2.

Table 1: Composition of saturated salt solutions

Name of salt	Humidity (%)	Weight of salt (g)	Amount of water (mL)
Magnesium chloride	33	200	25
Magnesium nitrate	53	200	30
Sodium chloride	75	200	60

Evaluation of chlorpheniramine and theophylline granules containing CFG

The flow parameters such as angle of repose, Carr's index, and Hausner ratio of the prepared granules were evaluated using the methods previously described.

Preparation of tablets

The granules were lubricated with magnesium stearate [Table 2] in a tumble mixer (Erweka-Apparatebau) for 5 min and compressed at a compression pressure of 7 kg F in the Single Punch Tabletting unit (Type EKO, Erweka-Apparatebau) fitted with 8 mm punch and die set. The tablets were kept for 24 h after ejection to allow for elastic recovery before tablet evaluation was carried out.

Evaluation of tablet properties

Uniformity of weight

Twenty tablets were randomly selected and weighed, and the mean was calculated.

Hardness

The hardness of six randomly selected tablets was determined using the Monsanto hardness tester (Monsanto Chemicals, USA), and the mean was calculated.

Friability test

Ten tablets were randomly selected and weighed, and they were placed in the Erweka Tablet Friability Tester (Type TA3R) and set to rotate at 25 rpm for 4 min. The tablets were collected, dusted, and weighed again. The difference in weight was determined and the loss was expressed as a percentage.

Assay

Ten tablets of chlorpheniramine maleate tablet formulations were crushed in a glass mortar. Equivalent weight of 1 tablet was transferred into a volumetric flask containing 20 mL of hydrochloric acid (0.1 N). The flask was shaken for 10 min and the volume made up with hydrochloric acid (0.1 N) and the absorbance of the fluid was determined at the appropriate wavelength using the UV-Visible spectrophotometer (B. Bran, England). The same method was repeated for theophylline hydrochloride tablet formulations. The content of the drug

Table 2: Composition for the preparation of chlorpheniramine and theophylline granules using CGF as matrix-former

Ingredients (g)	CG 1	CG2	CG3	TG1	TG2	TG3	CG-H	TG-H
Chlorpheniramine maleate	0.8	0.8	0.8	–	–	–	0.8	–
Theophylline HCl	–	–	–	20	20	20	–	20
CFG	6	12	18	6	12	18	–	–
HPMC	–	–	–	–	–	–	18	18
Magnesium stearate	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Microcrystalline cellulose	qs	qs	qs	qs	qs	Qs	qs	qs
Total	60.0	60.0	60.0	60.0	60.0	60.0	60.0	60.0

Key: HPMC = hydroxypropyl methylcellulose, CG1, CG2, and CG3 = chlorpheniramine tablet formulations containing 10, 20, and 30% w/w CFG, respectively; TG1, TG2, and TG3 = theophylline tablet formulations containing 10, 20, and 30% w/w CFG, respectively; CFG = *C. albidum* fruit gum; CG-H and TG-H = chlorpheniramine HCl and theophylline tablet formulations containing 30% w/w HPMC

in each tablet formulation was computed from the individual standard calibration curves.

Swelling capacity

One tablet from each batch was weighed and placed in a beaker containing phosphate buffer 7.4 (100 mL). The tablets were removed from the fluid at intervals of 0, 0.5, 1, 2, and 3 h, dapped with tissue paper, and weighed again. The swelling capacity was computed as the ratio of the final weight to the initial weight and expressed as a percentage.

In vitro *drug release*

The calibration curve of chlorpheniramine maleate was prepared at concentrations between 0.0025 and 0.02 mg/mL. The corresponding absorbance was measured using a UV-Visible spectrophotometer (B. Bran, England) at a wavelength of 265 nm. Similarly, the calibration curve of theophylline hydrochloride was prepared at concentrations between 0.0025 and 0.02 mg/mL, and absorbance was measured at a wavelength of 275 nm using a UV-Visible spectrophotometer (B. Bran, England).

Dissolution was carried out using a Erweka dissolution test apparatus 1 (Type DT) at 50 rpm for 12 h. One tablet from chlorpheniramine maleate formulations was placed in the apparatus and lowered into the medium; simulated gastric fluid without pepsin (pH 1.2) maintained at 37 ± 2°C for the first 2 h, the tablet was removed and placed into the simulated intestinal fluid (pH 6.8) until the study elapsed. Aliquots of the medium (5 mL) were withdrawn every hour for 12 h and replaced with an equal volume of fresh medium. The absorbance of the withdrawn samples was measured at a wavelength of 265 nm using a UV-Visible spectrophotometer (B. Bran, England). The concentration of chlorpheniramine maleate was computed from its standard curve. Similarly, dissolution of theophylline hydrochloride tablet formulations was carried out as described above. The absorbance of the withdrawn samples was measured at a wavelength of 275 nm using a UV-Visible spectrophotometer (B. Bran, England). Consequently, concentration of theophylline was determined from its standard curve.

Drug release kinetics

Data from *in vitro* release studies were fitted kinetic models; zero-order, Higuchi, Hixson-Crowell, and Korsmeyer–Peppas.

Stability studies

The prepared tablets were stored in appropriate containers at room temperature (28°C) for 1 year and evaluated for parameters such as appearance, tablet weight, hardness, friability, drug content, and *in vitro* drug release.

Results

Organoleptic and physicochemical properties of CFG

The percentage yield of CFG was calculated as 18%. The organoleptic and some physicochemical properties of the extracted gum CFG are presented in Table 3.

Swelling profile of CFG compact

Swelling characteristics of the gum compact are presented in Figure 1 and were observed to increase with time.

Moisture sorption capacity

Moisture sorption characteristics of CFG were observed to increase as relative humidity increased and are presented in Table 4.

Differential scanning calorimetry

DSC thermograph of CFG shows an endothermic glass transition [Figure 2A]; thermograph of chlorpheniramine maleate shows endothermic peak [Figure 2B] and that of theophylline hydrochloride shows a sharp symmetrical glass transition peak [Figure 3A]. Thermographs of the combination of CFG with the chlorpheniramine maleate and with theophylline hydrochloride returned the individual characteristic peaks [Figures 2C and 3B respectively].

Flow properties of formulated tablets

Flow properties of chlorpheniramine maleate and theophylline HCl granules are displayed in Table 5.

Table 3: Organoleptic and physicochemical properties of CFG

Parameter	Result
Color	Brown
Taste	Tasteless
Odor	Odorless
Angle of repose (°)	30.0 ± 1.00
Flow rate (g/s)	8.0 ± 0.7
Carr's index	1.07
Hausner ratio	7.6
pH	6.0
Moisture content (%)	6.0
Hydration capacity (%)	1.44 ± 0.5
Swelling capacity (%)	22.0 ± 0.6

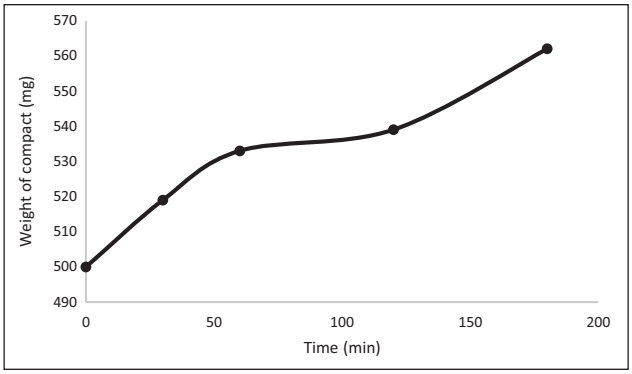

Figure 1: Swelling profile of CFG compact

Table 4: Moisture sorption of CFG

Relative humidity (RH %)	Moisture sorbed (%)
33	16
53	24
75	29
84	36

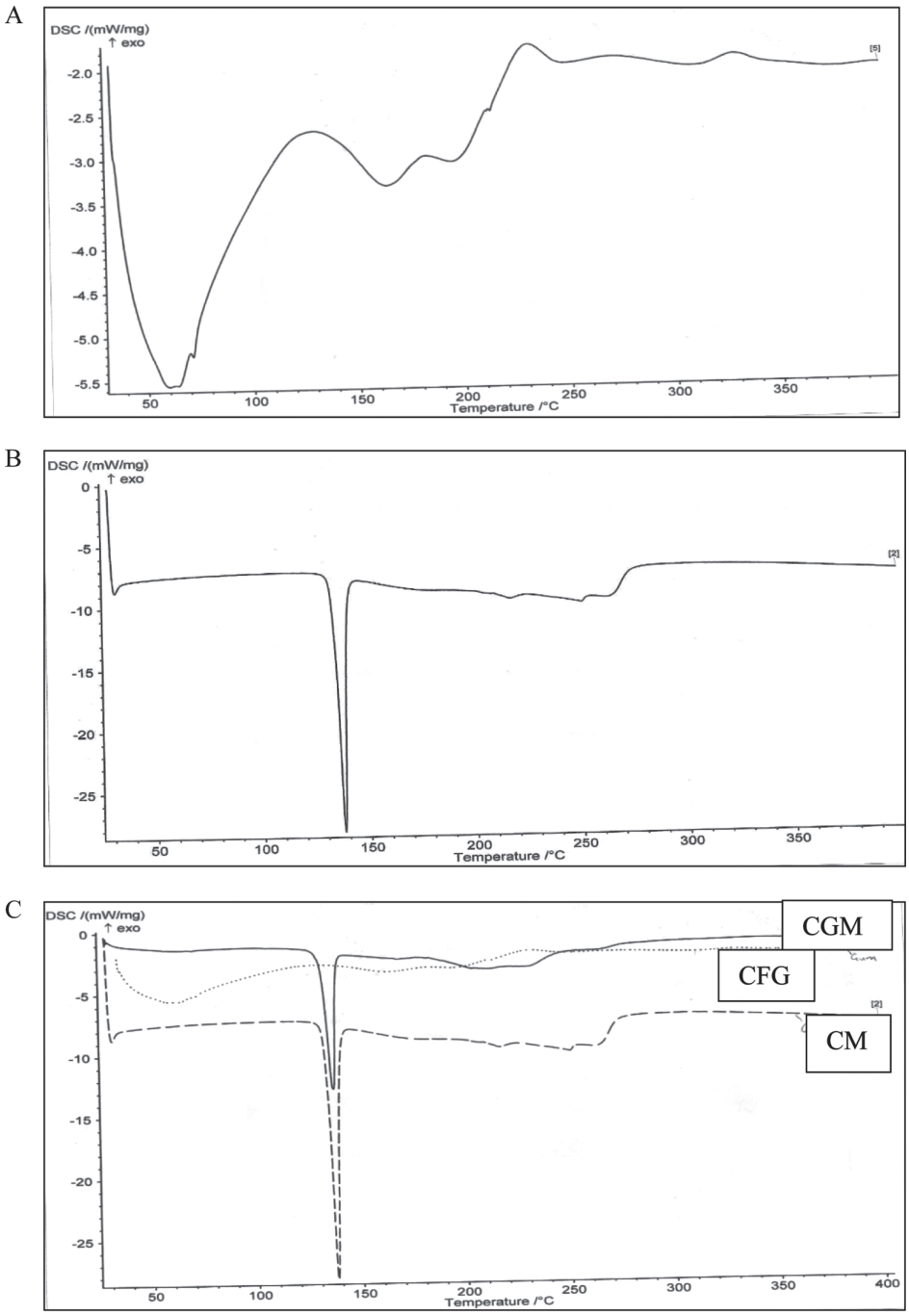

Figure 2: (A) Thermogram of CFG. (B) Thermogram of chlorpheniramine maleate. (C) Thermogram of chlorpheniramine maleate alone (CM), CFG, and the combination of chlorpheniramine maleate and CFG (CGM)

Table 5: Flow properties of tablets formulated with CFG

Parameter	CG1	CG2	CG3	TG1	TG2	TG3
Angle of repose (°C)	29.6	31.6	33.5	27.2	27.6	29.7
Flow rate (g/s)	4.15	3.89	3.67	3.11	4.05	3.88
Carr's index	23.3	24.4	23.4	33.0	26.9	24.4
Hausner ratio	1.30	1.32	1.31	1.40	1.37	1.30

Tablet parameters

Chlorpheniramine maleate and theophylline HCl tablet formulations prepared with CFG had uniform weights, were compact and non-friable, and contained specified quantities of the individual active ingredients. Dissolution efficiency showed that 50% drug release was achieved at 2, 6, and 12 h for the chlorpheniramine tablet formulations (CG1, CG2, and CG3, respectively) and at 2, 7, and

Table 6: Evaluation of tablets formulated with CFG

Parameter	CG1	CG2	CG3	TG1	TG2	TG3
Uniformity of weight (mg)	300 ± 9	300 ± 11	306 ± 3	298 ± 4	301 ± 7	301 ± 6
Diameter (mm)	8.00 ± 0.00	8.00 ± 0.00	8.00 ± 0.00	8.00 ± 0.00	8.00 ± 0.00	8.00 ± 0.00
Thickness (mm)	4.70 ± 0.02	4.50 ± 0.01	4.30 ± 0.03	4.00 ± 0.07	4.10 ± 0.01	4.10 ± 0.03
Hardness (kg F)	6.5	7.0	7.5	6.5	7.5	8.5
Friability (%)	0.4	0.2	0.1	0.4	0.2	0.04
Assay (%)	91.0 ± 0.31	100.0 ± 0.50	97.0 ± 0.92	101.0 ± 0.06	98.0 ± 0.07	102.0 ± 0.05
Dissolution efficiency ($t_{50\%}$)	2	6	12	2	7	>12

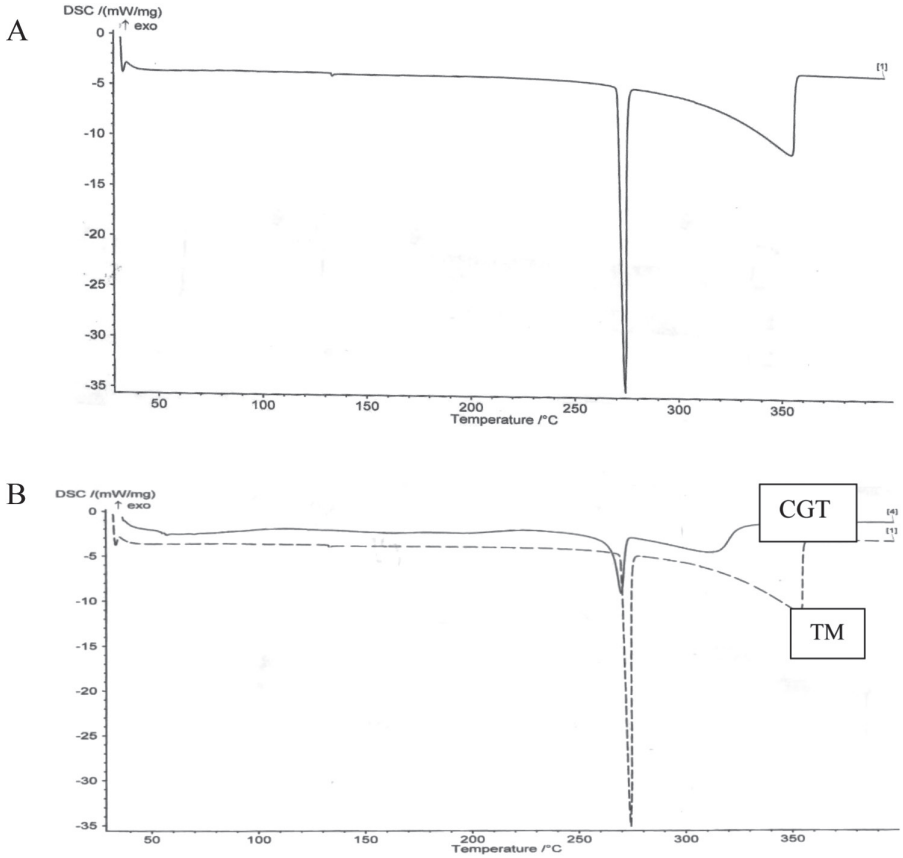

Figure 3: (A) Thermogram of theophylline HCL. (B) Thermogram of theophylline alone (TM) and the combination of theophylline and *chrysophyllum aibidum* fruit gum (CGT)

>12 h for theophylline tablet formulations (TG1, TG2, and TG3, respectively) as shown in Table 6.

In vitro dissolution studies

In vitro drug release profile shows drug release was concentration-dependent; drug release decreased with increased CFG concentration [Figure 4A]. Tablets prepared with CFG were found to provide better sustained release ability than those prepared with HPMC at corresponding concentrations [Figure 4B].

Kinetic model of drug release

In vitro drug release data from the formulated tablets fitted into zero-order, Higuchi and Hixson-Crowell, had varying regression values [Table 7]. The mechanism of drug release as determined by Korsmeyer–Peppas shows exponent values between 0.5 and 1.10.

Stability studies

Evaluation of some tablet parameters after 1 year of storage of the optimized formulations (CG3 and TG3) shows no significant changes in physical appearance and drug content. However, significant differences in tablet strength and *in vitro* drug release were observed [Table 8].

Discussion

The percentage yield of CFG obtained (18%) is different from 34% obtained from the mesocarp of the fruit[7] but similar to 15%[9] from the fruit seed. The low yield may be attributed to a limitation in the extraction method used; as such, it will be necessary to develop a more efficient extraction method to produce a better yield that would ultimately make this gum cost-effective. However, it is important to note that product yield from crude plant materials could vary as a result of differences in the

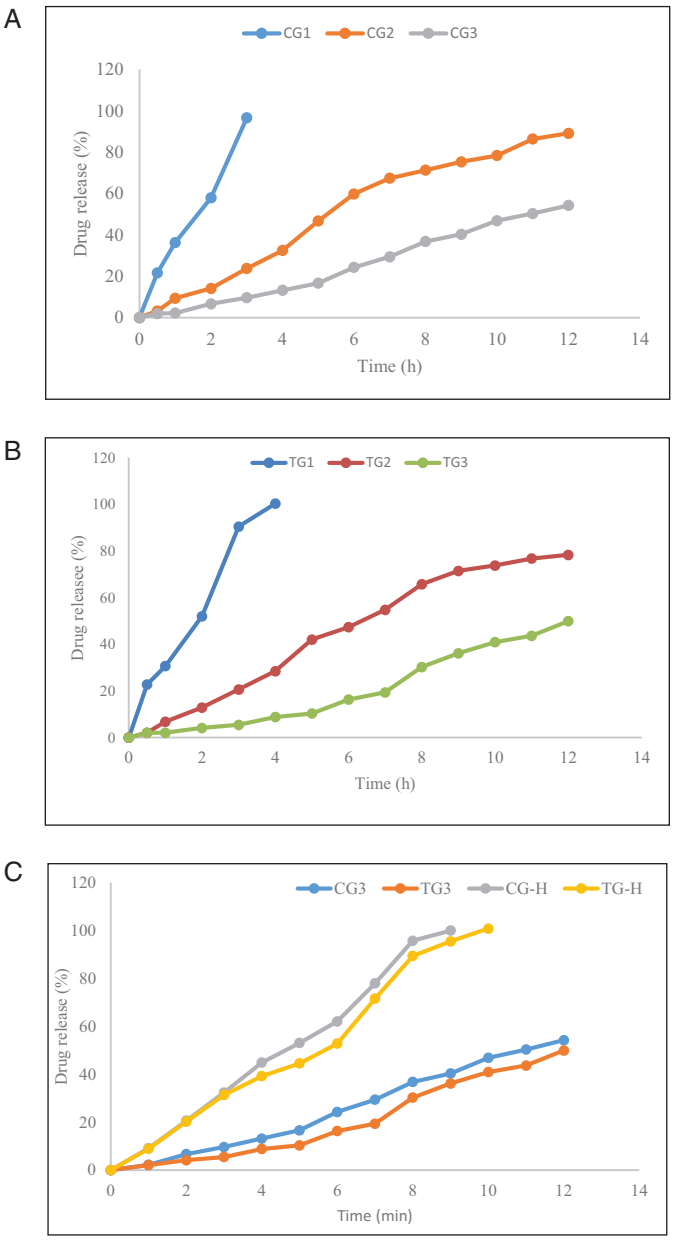

Figure 4: (A) Release profile of chlorpheniramine tablets formulated with 10, 20, and 30% w/w CFG. (B) Release profile of theophylline tablets formulated with 10, 20, and 30% w/w CFG. (C) Release profile of optimized formulations (CG3 and TG3) compared with release from tablet formulations containing 30% w/w hydroxyl methylcellulose (HPMC)

source of the crude material, environmental influences, solvent of extraction in addition to the method of extraction employed.[17]

The extracted CFG was observed to be brown in colorless, odorless, and tasteless [Table 3], portraying that it would not influence the palatability of the final product when used as an excipient.

Materials with a good flow are important in tablet formulation because good flow ensures adequate filling of the tablet die resulting in tablets with uniform weights.[18] The angle of repose is a parameter that shows the flowability of a material by measuring the internal friction of the heap created by the particles. Values between 23° and 35° reflect that the material has excellent flow, 31° and 35° shows good flow while 36° and 40° shows that the material has poor flow.[19] A value of 30° observed in this result [Table 3] shows that CFG has excellent flow. Carr's compressibility index expresses the propensity of a powder to deform under pressure and values below 10% are considered excellent, 11–15% is good while 16–25% is fair. Hausner ratio, however, portrays the cohesive nature of a material.[20] Carr's compressibility index of CFG was 7.6%, showing a good tendency to be compressed, while the Hausner ratio was 1.07 indicating that it is cohesive and would require lubrication during the process of tablet compression.

Swelling is an important parameter that shows the nature and determines the applicability of gums. The ability to swell in aqueous media shows the degree of hydration and water retention, which is an important feature that influences drug release from a formulation.[21] The result shows a swelling capacity of CFG is 22% [Table 3] and its compact showed about 12% increase in weight within the period of study [Figure 1] while hydration capacity was 1.44% [Table 3]. This infers that CFG could influence the manner and extent of drug release when incorporated in a formulation.

The pH of the aqueous suspension of CFG was 6.0 and shows that CFG can be used in the formulation of acidic as well as basic active pharmaceutical ingredients.

Materials to be used in pharmaceutical formulations are required to have a minimum amount of moisture because excess moisture causes degradation, aids decomposition, and chemical reactions like hydrolysis, and also encourages microbial growth. The presence of moisture or the ability of a material to absorb moisture

Table 7: Kinetics model for tablets formulated with CFG

Batch	Zero order (r^2)	Higuchi (r^2)	Hixson-Crowell (r^2)	Korsmeyer–Peppas (r^2)	*n*
CG1	0.952	0.952	0.988	0.971	0.5
CG2	0.973	0.973	0.916	0.979	1.02
CG3	0.977	0.977	0.943	0.993	1.05
TG1	0.959	0.959	0.962	0.978	0.5
TG2	0.977	0.977	0.901	0.988	1.02
TG3	0.934	0.934	0.969	0.967	1.10
CG-H	0.992	0.967	0.950	0.996	0.992
TG-H	0.981	0.984	0.959	0.989	0.991

Table 8: Tablet evaluation after storage

Parameter	CG3 (initial)	CG3 (after storage)	TG3 (initial)	TG3 (after storage)
Physical appearance	Smooth	Smooth	Smooth	Smooth
Uniformity of weight (mg)	306 ± 6.0	303 ± 2.0	303 ± 2.0	306 ± 6.0
Hardness (kgF)	7.5 ± 1.0	6.5 ± 1.0	8.5 ± 2.0	7.5 ± 1.0
Friability (%)	0.1	0.4	0.04	0.6
Drug content (%)	97 ± 0.9	97 ± 1.0	102 ± 0.1	99 ± 9.0
In vitro release; $t_{50\%}$ (h)	12	10	12	10

influences the design, packaging, and storage of products in which the material is incorporated. This consequently leads to problems of stability during the shelf life of the product. The fruit gum (CFG) absorb more moisture as humidity increased [Table 4] with 16, 24, 29, and 36% been sorbed, respectively, at 33, 53, 75, and 85% relative humidity. However, the moisture content of CFG 6% [Table 3] is within the limit official limit specified for gums used in both pharmaceutical and food industries.[22] This suggests that CFG and its products should be stored in air-tight containers to keep away from moisture.

DSC measures heat loss or gain that occurs consequently upon either physical or chemical changes within a sample. The effect of temperature on polymers displays the amorphous and crystalline arrangement within the lattice of the polymer, and this is an important feature that makes a material applicable for industrial processes. In addition, it also reveals possible interactions between drugs and polymers in formulations.[1] The DSC thermogram of CFG presented in Figure 2A shows an endothermic glass transition onset temperature of 44.4°C and an end temperature of 92.1°C. The thermogram of chlorpheniramine maleate alone shows a sharp peak at 137.9°C which is similar to the peak observed at 137.4°C in the thermogram of the mixture of CFG and chlorpheniramine maleate [Figure 2C]. This suggests that no interaction between the drug and CFG can lead to loss of the pharmacological activity of the drug. On the other hand, the thermogram of the mixture of theophylline and CFG [Figure 3B] showed a slight but non-appreciable shift in the peak (271.3°C) when compared with that of theophylline alone; 274.4°C [Figure 3A]. This also signifies that the inherent activity of the drug (theophylline) is not affected. DSC also demonstrates the relative purity of samples evidenced by sharp symmetric endotherms[23] as observed in these figures.

All the prepared granules were found to have good flow properties [Table 5]. The tablets were found to have uniform weights and similar thicknesses; tablet diameter was also uniform because the same punch size was used to compress all the tablets. The strength of a tablet indicates its ability to withstand the rigors of handling, shipping, storage, and use throughout its shelf life. Tablet hardness was found to increase with an increase in the concentration of CFG [Table 6]; this is attributable to the establishment of better particle–particle contact between the polymer and the drug resulting in stronger bridges and bonds.[24] Tablet friability is associated with hardness because the stronger the tablet, the better its resistance to fracture and abrasion.[25] Consequently, tablet friability that was between 0.04 and 0.4 decreased with an increase in tablet strength [Table 6].

Assay is a parameter that assures that the amount of active ingredient in a tablet is as specified by the manufacturer. The formulated tablets were observed to contain 91–100% of chlorpheniramine maleate and 98–102% of theophylline hydrochloride, which are all within official specifications.[26]

Drug release in all the formulations was observed to decrease with increase in CFG concentration. This is because hydration of a polymer in a matrix system results in the formation of a gelatinous layer around the matrix surface. This serves as a barrier for the penetration of fluid, consequently decreasing the rate at which the drug is leached out of the matrix.[27] Figure 4A shows that complete drug release (100%) from CG1 was achieved at about 3 h while only 89.13 and 54.24% of chlopheniramine was released from CG2 and CG3, respectively, at the end of the dissolution period (12 h). Meanwhile, complete drug release from TG1 was achieved at 4 h while only 78.31 and 49.92% of theophylline were released from TG2 and TG3, respectively, by the end of the study period [Figure 4B]. Drug release was found to be faster from either of the tablet formulations containing lower concentration of CFG, i.e., CG1 and TG1. Conversely, higher concentrations of CFG in both tablet formulations (CG3 and TG3) proved to provide steady drug release over each hour while also sustaining drug release with only 54.24 and 49.92%, respectively.

Drug release from formulations containing CFG at 30% (CG3 and TG3) was found to be about 50% by the end of 12 h and the release from these formulations was observed to be progressive even though at a slow rate over a long period of time. This suggests the feasibility of using 30% of CFG in preparation of a single daily dose tablet formulation. Comparison of 30% of CFG in both tablet formulations (CG3 and TG3) with the standard polymer (hydroxyl propylmethylcellulose; HPMC) at the same concentration showed that the former has better propensity to sustain drug release than the latter [Figure 4C]. This suggests the usefulness of CFG, a locally extracted and processed polymer as a better sustained release agent than HPMC.

The obtained *in vitro* release data were subjected to various models; Zero order, Higuchi, Hixson-Crowell, and Korsmeyer peppas, in order to predict the mechanism and kinetics of drug release. The model with the highest regression value (r^2) was chosen as the most appropriate model to describe the possible

mechanism and kinetics of release. Zero order was found to be the most predominate model [Table 7] to define the kinetics of release across the formulations, showing that drug release was independent of time. Although this type of release is ideal for controlled delivery systems because it can achieve drug release at a constant rate, its practicability, however, requires several manipulations to maintain the balance between the drug-depleted matrix surface and path length of drug travel which is time-dependent.[28] The release mechanism was confirmed by Korsmeyer–Peppas model. Values of exponent '*n*' ≥ 0.89 predict drug release that is swelling-controlled (super case II transport) while values between 0.45 and 0.89 (non-fickian diffusion) indicate drug release as a result of swelling and diffusion.[29] Drug release from hydrophilic matrices like these ones containing CFG is a complex interaction of swelling and diffusion from the hydrated gelatinous layer around the tablets, although, sometimes, mechanisms that control erosion also come to play.

Formulation CG1 and TG1 had '*n*' values of 0.5, each showing that drug release was non-fickian while CG2, CG3, TG2, and TG3 had values of 1.02, 1.05, 1.02, and 1.10, respectively, portraying that the release was swelling controlled. In addition, drug release from formulations containing the reference polymer (CG-H and TG-H) was found to be also swelling controlled with values of 0.992 and 0.991, respectively.

Stability studies show no significant change ($P > 0.05$) in tablet appearance, uniformity of weight, hardness and drug content of formulations CG3 and TG3 over the 1 year period of storage [Table 8]. However, friability and *in vitro* drug release were found to be significantly different ($P < 0.05$) from the results obtained at the beginning of the study although both parameters are still within the official stated limits. Thus, formulations containing CFG can be deemed to be stable within the limit of the parameters studied.

Conclusion

This study investigated the use of CFG as a matrix-polymer for sustained-release tablet formulations. The gum possesses good flow properties, high swelling capacity, and good compatibility. It has shown potential to be used as a matrix-former for sustained delivery of chlorpheniramine maleate and theophylline hydrochloride at an optimized concentration of 30% w/w. CFG also produced tablets that were stable over a period of 1 year. This suggests that CFG can be employed as a readily available and efficient alternative to the expensive synthetic polymers that are often used in sustained delivery systems.

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Conflicts of interest

There are no conflicts of interest.

References

1. Kumar PG, Gangarao B, Kotha NS, Raju L. Isolation and evaluation of tamarind seed polysaccharides being used as a polymer in pharmaceutical dosage form. Res J Pharm Bio Chem Sci 2011;2:2.
2. Anekant J, Yashwant G, Sanjay K. Perspectives of biodegradable natural polysaccharides for site-specific drug delivery to the colon. J Pharm Pharm Sci 2007;10:86-128.
3. Goswami S, Naik S. Natural gums and its pharmaceutical application. J Sci Innov Res 2014;3:112-21.
4. Avachat AM, Dash RR, Shrotriya SN. Recent investigations of plant based natural gums, mucilages and resins in novel drug delivery systems. Ind J Pharm Educ Res 2011;45:86-9.
5. Amusa NA, Ashaye OA, Oladapo MO. Biodeterioration of African star apple (*Chrysophylum albidum*) in storage and the effect on its food value. Afr J Biotechnol 2013;2:56-9.
6. Florence AB, Adiaha AH. Storage effects and the postharvest quality of African star apple fruits (*Chrysophyllum africanum*) under ambient conditions. Afr J Food Sci Tech 2015;6:35-43.
7. Okoye EI, Ndiwe I. Characterization of *Chrysophyllum albidum* and *Anacardium occidentale* gums as wet and dry binders in ciprofloxacin tablets. Marmara Pharm J 2016;20:122-30.
8. Ajala TO, Akin-Ajani OD, Ihuoma-Chidi C, Odeku OA. *Chrysophyllum albidum* mucilage as a binding agent in Paracetamol tablet formulations. J Pharm Investig 2016;46:565-73.
9. Ologunagba MO, Azubuike CP, Sadiku OR, Silva BO. Evaluation of the binding potential of *Chrysophyllum albidum* seed gum in paracetamol tablet formulation. Trop J Nat Prod Res 2018;2:136-9.
10. Bakre LG, Akinsanya KE. Crosslinking of *Chrysophyllum albidum* gum with calcium chloride to enhance its physicochemical, compressional and tableting properties. Res Pharm 2019;23:415-25.
11. Rumore MM. Clinical pharmacokinetics of chlorpheniramine. Drug Intell Clin Pharm 1984;18:701-7.
12. Ojoe E, MitieMiyauchi E, Kaneko TM, ValériaRolbes MV, Consiglieri VO. Influence of cellulose polymers type on in vitro controlled release tablets containing theophylline. Brazilian J Pharm Sci 2007;43:571-9.
13. Raja ST, Palanichamy S, Shanmuganathan S, Tamilvanan S, Thanga TA. Formulation and evaluation of theophylline controlled release matrix tablets using guar gum. ARS Pharmaceutica 2010;51:28-38.
14. Tavakoli N, Ghasseni DN, Teimouri R, Heimishehkar H. Characterization and evaluation of OKRA gum as tablet binder. Jundishapur J Nat Pharm Prodts 2008;3:33-8.
15. Ofokansi KC, Kenechukwu FC, Isah AB, Allagh TS, Anumeka OO. Formulation and evaluation of solid dispersions based on Eudragit RS 100 and PEG 8000 for improved delivery of trandolapril. Afr J Pharm Res Dev 2012;4:38-42.
16. Okafor IS, Chukwu A, Udeala K. Some physicochemical properties of grewia gum. Nig J Poly Sci Tech 2001;2:161-7.
17. Olayemi OJ, Mahmud HS, Apeji Y. Effect of concentration on the release property of khaya senegalensis gum in chloroquine phosphate tablet formulation. Int J Appl Pharm 2010;2:22-6.
18. Staniforth JN, Aulton ME. Powder flow. In: Aulton ME, editor. Aulton's Pharmaceutics: The Design and Manufacture of Medicines, 3rd ed. London: Churchill Livingstone Elsevier, Chapter 13; 2007.
19. Davies P. Oral solid dosage forms. In: Gibson M, editor. Pharmaceutical Preformulation and Formulation. 2nd ed. USA: Informa Healthcare; 2009.
20. Carr RL. Evaluating flow properties of solids. Chem Eng 1965;72:163-8.
21. Omidian H, Park K. Swelling agents and devices in oral drug delivery. J Drug Del Sci Tech 2008;18:83-93.
22. British Pharmacopoeia (BP). Vol. I and II. London: Her Majesty's Stationery Office; 2009.

23. Vippagunta SR, Brittain HG, Grant DJW. Chrystalline solids. Adv Drug Del Rev 2001;48:3-26.
24. Reza E, Mohammed A, Fadakar Y. Assessment of ferula *gummuosa* as a binding agent in tablet formulation. Acta Poloniae Pharm Drug Res 2012;69:291-8.
25. Itiola OA, Odeniyi MA, Adetunji OA. Compression, mechanical and release properties of chloroquine phosphate tablets containing corn and trifoliate yam starches as binders. Trop J Pharm Res 2006;5:589-96.
26. United States Pharmacopoeia. USP 31–NF 26. Rockville, MD: U.S. Pharmacopoeial Convention; 2008.
27. Singh PK, Shukla TS, Easwari TS, Kumar S, Chudhary R. Formulation development and evaluation of mucoadhesive oral dosage form containing clarithromycin using different muco-adhesive polymers. Int J Pharm Sci Health Care 2012;2:159-71.
28. Turner S, Federici C, Hite M, Fassihi R. Formulation development and human in vitro-in vivo correlation for a novel, monolithic controlled-release matrix system of high load and highly water-soluble drug niacin. Drug Dev Ind Pharm 2004;30:797-807.
29. Siepmann J, Streubel A, Peppas NA. Understanding and predicting drug delivery from hydrophilic matrix tablets using the "sequential layer" model. Pharm Res 2002;19:306-14.