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Derivatisation of Cashew Gum via Cross-linking with Citric Acid: Characterisation and Preliminary Evaluation of Tableting Properties

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Authors' contributions

This work was carried out in collaboration between all authors. Author ARO designed the study, wrote the protocol. Author ABI managed the literature searches, analyses of the study performed the spectroscopy analysis. Author AA managed the experimental process and wrote the first draft of the manuscript and author IO provided the lab, research materials and participated in the experimental process. All authors read and approved the final manuscript.

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ABSTRACT

A polycarboxylic acid, citric acid, was used to derivatise cashew gum via cross-linking. A dispersion of the purified gum, the acid and sodium dihydrogen phosphate was made in deionised water and concentrated by heating at 40ºC for 18 h. The resulting solid mass was heated at 140ºC for 30 min for the cross-linking. The cross-linking was demonstrated using DSC and FT-IR, and the derivative was characterized by determination of the solubility, water content, swelling and water holding capacity, moisture sorption and desorption, particle flow properties and preliminary studies on drug release in tableting. The results obtained indicated that the cross-linked product differed from the parent gum. At 10 %w/w it retarded drug release while at 3 %w/w it enhanced drug release. The activity of the cross-linked gum in tableting is concentration dependent but could evidently find use as drug release modifier.

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1. INTRODUCTION

Polysaccharides from natural sources comprising of starches, gums and celluloses and their derivatives, represent a class of polymeric compounds largely used in pharmaceutical formulations and in systems for controlled drug delivery [1-3]. These classes of polysaccharides with varying physicochemical properties can be extracted from plants at relatively low cost and can be chemically modified to suit specific needs [4]. They are thus indispensable components in the manufacture of medicines for human or animal use, where they are employed to provide varied functions as dictated by the polymer's physicochemical properties.

Gums are now used as binders, drug release modifiers, disintegrants, emulsifiers, thickeners, viscosifiers etc. when employed in their natural forms or as derivatives after some structural modifications [5-8]. Structural modifications have been used to effect some changes that eventually tailor the properties of polysaccharides to suite a particular interest in pharmaceutical raw material development.

Epichlorohydrin (EPC), a powerful cross-linking agent, has found use in derivatisation processes involving starches, gums and celluloses [9-11]. It has been used to cross-link cashew gum (CG) and the derivative characterized [10], used as bioaffinity ligand [12] and recently used in enhancing Venlafaxine HCl release from tablets formulated with Hydroxyprophyl methylcellulose (HPMC ER K100)as binder [13]. A variety of factors, however, are considered in choosing a cross-linking agent needed for producing polymeric materials for use in foods and medicines such that, safety for use, handling concerns and environmental friendliness preclude the involvement of potential toxins/carcinogens during processing or manufacture.

As EPC was considered somewhat unsafe for production of polymers for pharmaceutical processing based on reports of its being a potential carcinogen, concerns for safety of use and handling [14-16], it became imperative to search for safer alternative cross-linking agents. The Polycarboxylic acids (PCAs) had been reported to be used in cross-linking cyclodextrins [15,17-18]. The low cost and effectiveness [19], safety and environmental friendliness [20] made the PCAs ready alternatives in cross-linking CG.

In this study, therefore, a derivative of CG was developed via cross-linking using citric acid (CTA). The derivative (tagged CrosCC) was characterised and subjected to preliminary studies to investigate its potentials in modifying drug release.

2. MATERIALS AND METHODS

2.1 Materials

- Succinic acid, Adipic acid, 1,2,3,4-Butanetetracarboxylic acid, Dichlorodimethylsilane, Dimethylformamide, Dimethylsulphoxide, Ethyl acetate, Toluene, Cyclo hexane, Sulphuric acid, Magnesium Chloride hexahydrate, Magnesium nitrate hexahydrate, (Sigma- Aldrich, USA)
- Acetone UN 1090, Citric acid, Sodium chloride, Potassium chloride, Aqualine™ Complete 5, (Fisher Scientific, USA)
- Sodium phosphate monobasic, Methanol UN 1230, (Caledon Laboratories Ltd, Canada)
- Venlafaxine HCl (Cadila Health Care Ltd., India)
- Hydroxypropylmethylcellulose- HPMC ER (K100) (Dow Chemicals, USA)
- Lactose anhydrous (Kerry Bioscience, USA)
- Silicone Dioxide (Evonik Industries, USA); Magnesium stearate, (Tycol Healthcare, USA)
- Cashew gum and CrosCC were as purified/synthesised in the laboratory (IntelliPharmaceutics Inc., Canada)

2.2 Methods

2.2.1 Extraction/Purification of CG

The gum was extracted using the method described by [21].

The dried latexes (CG) were plucked from the bark of cashew trees from a plantation in Likoro along Zaria - Kano road in Northern Nigeria. Five hundred (500) gram of the gum was weighed and stirred in 1.5 L of deionised (DI) water contained

in a 3 L beaker. The mucilage was filtered using suction through a fine muslin cloth to remove any extraneous matter.

A total 1.5 L of acetone was used to extract the gum from the aqueous dispersion. One liter portion of the acetone was gradually poured into the beaker containing the mucilage while stirring, to extract the gum. The water/acetone solution was decanted and the remaining 500 ml acetone was used to further wash the extracted gum. The gum was then separated from the acetone and spread on nonstick baking trays and dried in an oven (Memmert, Germany) at 40ºC for 5 h.

The extraction yield (%) was calculated using the relationship:

$$\% \text{ Yield} = \left(\frac{W1}{W2}\right) x\, 100 \quad (1)$$

Where W1 is weight of crude gum; W2 is weight of extracted (processed) gum.

2.2.2 Cross-linking of CG using PCAs

The methods for polymerization of cyclodextrins using PCAs as cross-linking agents described by [15,17,18] were followed with some modifications, to crosslink CG.

An appropriate quantity of the gum to make 10 %w/v mixture in deionised (DI) water was weighed into a beaker. Polycarboxylic acid [adipic acid (ADA), succinic acid (SCA), citric acid (CTA) or 1,2,3,4-Butanetetracarboxylic acid (BTCA)] and sodium dihydrogen phosphate (serving as catalyst) were weighed and mixed with the gum in proportions shown in Table 1. About 100 ml of DI water was added into the beaker while being stirred and the total volume made to 200 ml with DI water. The mixture was stirred over boiling water bath until homogenous.

The homogenous mixture was transferred into a culture dish and concentrated by heating at 40ºC for 18 h. The resulting solid mass was again heated at 140ºC for 30 min for the cross-linking process to take place. The material was thereafter allowed to cool and recovered by soaking in some quantity of DI water. The now fibrous looking material was transferred onto a mesh, lined with fine muslin cloth, and thoroughly percolated with DI water. The material was soaked in DI water for 24 h and further rinsed with DI water, the water drained off thereafter and the polymer spread on a non-stick, baking tray and dried at 40ºC for 5 h. The polymer was milled using a coffee bean mill (Bodum(R), China) and packed in a moisture free container. Cross-link yield was calculated using the following relationship:

$$\% \text{ Yield} = \left(\frac{W1}{W2}\right) x\, 100 \quad (2)$$

Where W_1 is the weight of the CG, W_2 is the weight of the cross-linked polymer

2.2.3 Thermal analysis using differential scanning calorimetry (DSC)

Heat flux DSC (NETZSCH-Geratebau, Germany) was used to obtain valuable information on the cross-link formation between CG and the PCAs. About 10 mg samples of the CG and CrosCC were respectively encapsulated in aluminium disposable pans. DSC scans were run to measure the energy changes associated with heating the samples to 500ºC at a scan rate of 10ºC/min using nitrogen as purge gas. Thermograms of the cross-linked polymer were laid over those of the uncross-linked CG and observed differences were noted. Appearance or disappearance of peak(s) suggests the formation of new bonds/structures [22].

2.2.4 Fourier transform infra red (FT-IR) studies

FT-IR spectra of CG and its cross-linked derivative were obtained using JASCO IR spectrophotometer (model 4200, Jasco Inc. Japan). The powdered samples were mixed with potassium bromide (KBr), compressed into pellets and analysed between 400 and 4000 cm^{-1}. The spectrum of CG and that of CrosCC were overlaid to reveal the presence or absence of IR absorption bands representative of respective functional groups of interest. Appearance, disappearance or broadening of absorption band(s) on the spectrum of the cross-linked polymer in comparison with that of CG was used to assess the cross-linking of CG [23-24].

2.2.5 Evaluating the level of insolubility of CrosCC

The method of evaluating solubility as described by [25] and modified by [13] was used to support the formation of an insoluble cross-linked product.

Table 1. Formulae for Cross-linking CG using PCAs (ADA, SCA, CTA or BTCA)

	Batch 1	Batch 2	Batch 3
Ingredient	**CG:PCA (2:1)**	**CG:PCA (1:1)**	**CG:PCA (1:2)**
CG (g)	20	20	20
PCA (g)	10	20	40
NaH_2PO_4 (g)	2	2	2
DI water to (ml)	200	200	200

2.2.6 Moisture loss on drying (MLD)

Two (2) g samples (W_1) of powders of CrosCC were dispersed into three tarred and conditioned evaporating dishes. A total drying time of 3 h attained by interrupted heating at temperatures of 105ºC and cooling in a desiccator brought the samples to constant weight. The MLD was determined using the following relationship:

$$\% \text{ MLD} = \frac{(W1-W2)\,100}{W1} \quad (3)$$

Where W_1 and W_2 are weights of CrosCC powders before and after drying, respectively.

2.2.7 Water content determination using Karl Fisher Titrimetry

Karl Fisher Titrator (Mettler Toledo DL38, Switzerland) was used to determine the percent water content of CrosCC as described by [26]. A 2 g sample of CrosCC was weighed out directly from the storage container (i.e. at ambient temperature and humidity) and a second 2 g sample was spread on tarred sample dish and stored over activated silica gel for a period of 7 days. Quantities weighing 150 mg of powders from the two samples were tested for percent water content. Karl Fisher volumetric reagent, Aqualine^{TM} Complete 5 and anhydrous methanol were used for the tests.

2.2.8 Swelling ratio determination

A simply assembled measuring device made using siliconised cylindrical tube as described by [13] was employed in determining polymer-swelling ratios.

2.2.9 Water holding capacity (WHC)

The method described by [27] was followed with some modifications. Two (2) g samples of CrosCC were placed in tarred siliconised 50 ml centrifuge tubes and weighed (W_1). DI water (30 ml) was added into the tubes, shaken and allowed to stand for 1 h. The samples were centrifuged using (Hanil Science Industrial Co. Ltd., Korea) at 5000 rpm for 25 min. The supernatant liquid was removed and the tubes were placed in a forced-draft air oven (Model 1370 F, VWR Scientific Products, USA) at an angle of 15–20º, allowed to dry at 50ºC for 25 min and then cooled in a desiccator for 30 min. The tubes with the dried samples were weighed (W_2) using AT 261 DeltaRange$^{(R)}$ Balance (Mettler Toledo, Switzerland). The WHC was calculated using the equation:

$$\% WHC = \left(\frac{W2-W1}{W2}\right) x\ 100 \quad (4)$$

Where W_1 and W_2 were weights of dry and hydrated samples, respectively.

2.2.10 Residue on Ignition/sulphated ash

The residue on ignition was determined as described by [21].

2.2.11 Evaluation of powder flow properties

Powder density measurements, flow rate, angle of repose and particle size distribution were determined as described by [21].

2.2.12 Preliminary evaluation of CrosCC as drug release modifier in Venlafaxine HCl tablets

Wet method of granulation was used to make granules containing venlafaxine hydrochloride (Ven. HCl) as active pharmaceutical agent, HPMC ER (K100) as tablet binder and CrosCC or pregelatinised starch (PGS) being drug release modifier as shown in Table 2. The granules were compressed into tablets using Betapress Manesty Machine (No. 74182, Manesty Machines Ltd., England).

2.3 Statistical Analysis

The results obtained that required statistical analysis were analyzed using GraphPad Prism software package. Results were expressed as mean ± SD and differences between means were considered significant at P=.05 using the analysis of variance (ANOVA) or student's t test.

Table 2. Ven. HCl Tablet Formulae Containing HPMC ER as Binder and CrosCC or PGS as Release modifier

Ingredient	Batch number/Quantity (%)		
	G1	G2	G3
Venlafaxine HCl	30	30	30
Lactose DT	51.5	51.5	58.5
HPMC ER	7.5	7.5	7.5
CrosCC	10	-	3
PGS	-	10	-
Silicone dioxide	0.5	0.5	0.5
Magnesium stearate	0.5	0.5	0.5
Total	100	100	100

3. RESULTS AND DISCUSSION

3.1 Percentage Yield of Cross-linking CG with PCAs

The dicarboxylic acids, ADA and SCA, gave a cross-link yield only when used at a CG:PCA weight ratio of 2:1. At this ratio, the yields obtained for the cross-linked products CG:ADA and CG:SCA were 32.13 % and 34.81 %, respectively. At 1:1 and 1:2 weight ratios, neither ADA nor SCA was found to be effective in cross-linking CG.

CTA and BTCA cross-linked CG at all the three ratios tested. The yields recorded for CG:CTA weight ratios of 2:1, 1:1 and 1:2 in order of increasing cross-linker concentration, were 51.11, 57.61 and 57.95 % respectively. BTCA on the other hand gave a yield of 54.84, 56.99 and 69.89 respectively for the CG:BTCA weight ratios of 2:1, 1:1 and 1:2.

It has been reported that the dicarboxylic acid, Adipic acid, has been used in derivatisation of carboxymethylated polysaccharides [28] and Succinic acid was used to cross-link cotton cellulose [29] while [30] used it as cross-linking agent to attach titanium dioxide to cotton. Both acids, however, showed dismal performances in cross-linking CG in this study. Similar unsuccessful use of the dicarboxylic acids in polycondensation reactions of cyclodextrins was reported by [15]. At higher concentrations of the dicarboxylic acids, formation of monolithic crystals [31] was found to reduce the effective concentration of the acid for the cross-linking reaction.

PCAs having greater than two carboxyl groups, CTA and BTCA, were found to be effective agents in cross-linking CG. It has been observed that the more the number of carboxyl groups in the PCA, the better the cross-link yield [15]. This was reflected in better yields obtained with BTCA over CTA. This may be attributed to greater number of cross-linking points occasioned by increased availability of the cross-linking COOH moiety. Nonetheless, high cost of BTCA [32-33] informed the choice of CTA over BTCA to cross-link CG in this study.

Cross-linking condition of 140ºC for 30 min was found to favour formation of CrosCC with a yield of 64.5% as against 54.5% when the condition was 170ºC for 30 min.

DSC thermogram (Fig. 1) revealed that the 156.3ºC characteristic melting temperature peak of CTA shifted to 158.6ºC when thermogravimetric analysis of binary mixture of the acid and CG were made. This figure also highlighted the complete disappearance of the CTA melting peak when analysis of the cross-linked product was conducted, apparently in consequence to the changes undergone by both the gum and the acid in forming the new derivative. The decomposition temperature of the binary mixture was found to be 313.8ºC while that of the derivative was 309.4ºC.

CTA has a prominent characteristic endothermic peak at 156.3ºC caused by the melting of anhydrous citric acid [34]. Thermogram of a 50/50 physical mixture of the CG and CTA (Fig. 1) reflects that the characteristic melting temperature of CTA remained with the peak slightly shifted to 158.6ºC and the peak height shortened. Slight changes in peak heights and sharpness may be caused by presence of impurities [35], with CG possibly being identified as the impurity in this case. After the cross-linking, the peak representing the melting temperature of CTA was completely missing, with the thermogram taking a shape similar to that of CG as depicted in the Figure. Apparently, the COOH of CTA may have been completely used up in the cross-link formation or any unattached COOH (see scheme 1) may have been “enveloped” between strands of the cross-linked polymer. And so, the absence of the melting temperature peak of CTA in the cross-linked polymer is suggestive of the formation of a new material with a structure that may not be so different from the parent material, CG [17]. The decomposition temperature of both the binary

mixture (313.8ºC) and the cross-linked polymer (309.4ºC) did not differ significantly with that of the uncross-linked CG (311.6ºC) found in a related study [21]. This shows that, and as the name connotes, cross-linking did not tamper with the structural framework of the CG but simply linked strands of the polymer. Cross-linking CG with epichlorohydrin, however, showed larger differences in decomposition temperatures [10,13].

3.2 Fourier Transform Infrared (FT-IR) Spectral Studies

Fig. 2a is the FT-IR spectrum of CrosCC showing the H–bonded OH stretch band of aromatic compounds that has shifted slightly up from the 3388.32 cm^{-1}peak of the uncross-linked gum [21, 23] to 3422.06 $cm^{-}1$. The 1734.66cm^{-1} is a carbonyl frequency of an ester group, formed in consequence to the cross-linking process. The peak differs from the characteristic stretch carbonyl frequency of carboxylic acids at 1726 cm^{-1} [31] and the carbonyl frequency of CTA noted in this study at 1728.87 cm^{-1}. Fig. 2b is the overlay of FT-IR spectra of CG and CrosCC highlighting the formation of the prominent peak at 1734.66 cm^{-1} assigned to a newly formed ester molecule.

A spectrum of a 50/50 binary mixture of CTA and CG showed peaks that can be likened to peaks in the spectrum of CTA or CG. Of interest, however, was the observation that a peak 1729 cm^{-1} seen in spectrum of CTA was also noticed in the spectrum of a binary mixture of CG and CTA but not in the spectrum of the cross-linked polymer, where in its place appeared a strong band at 1734.66 cm^{-1}.This band was indicative of the formation of an ester bond between –OH from the sugar of the gum and –COOH of the cross-linking agent, CTA [23].

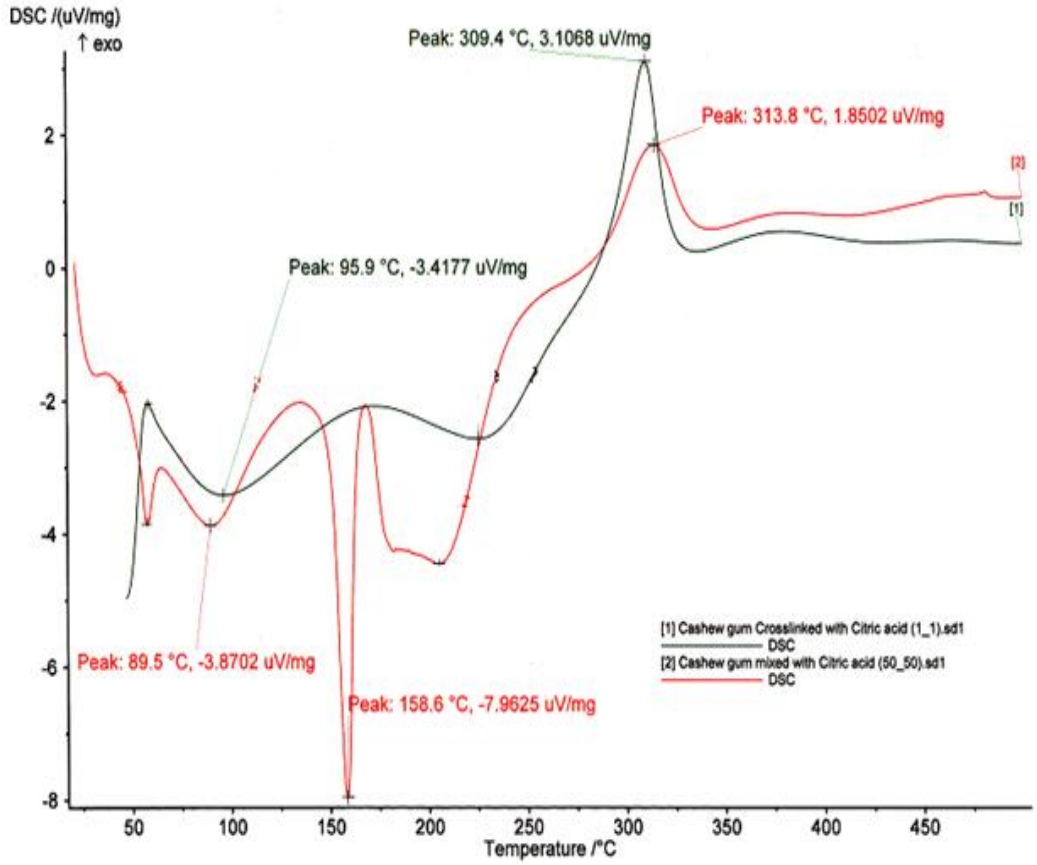
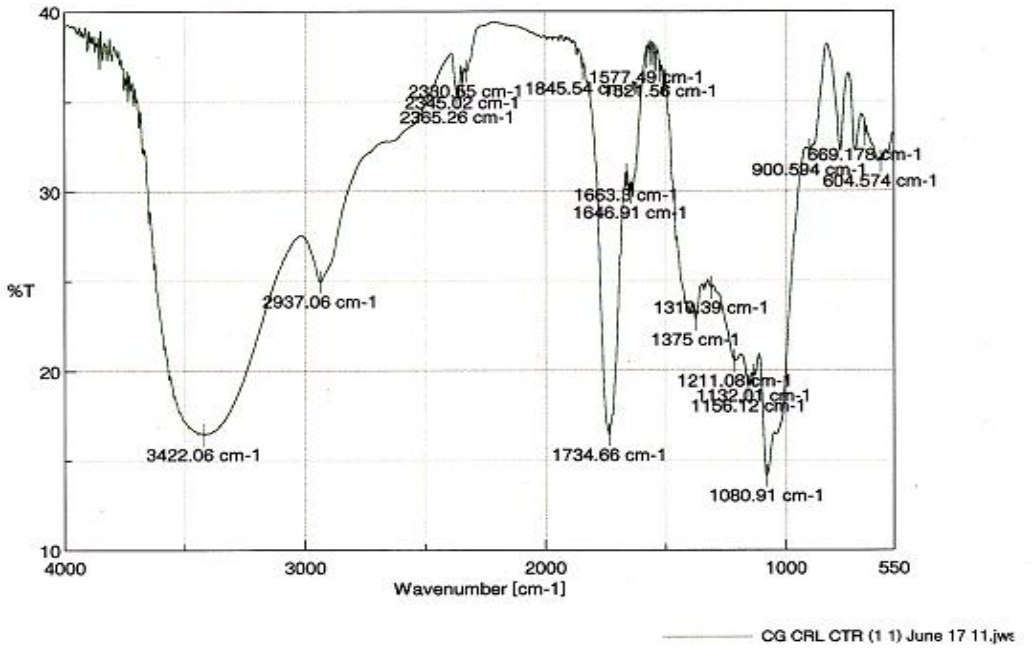
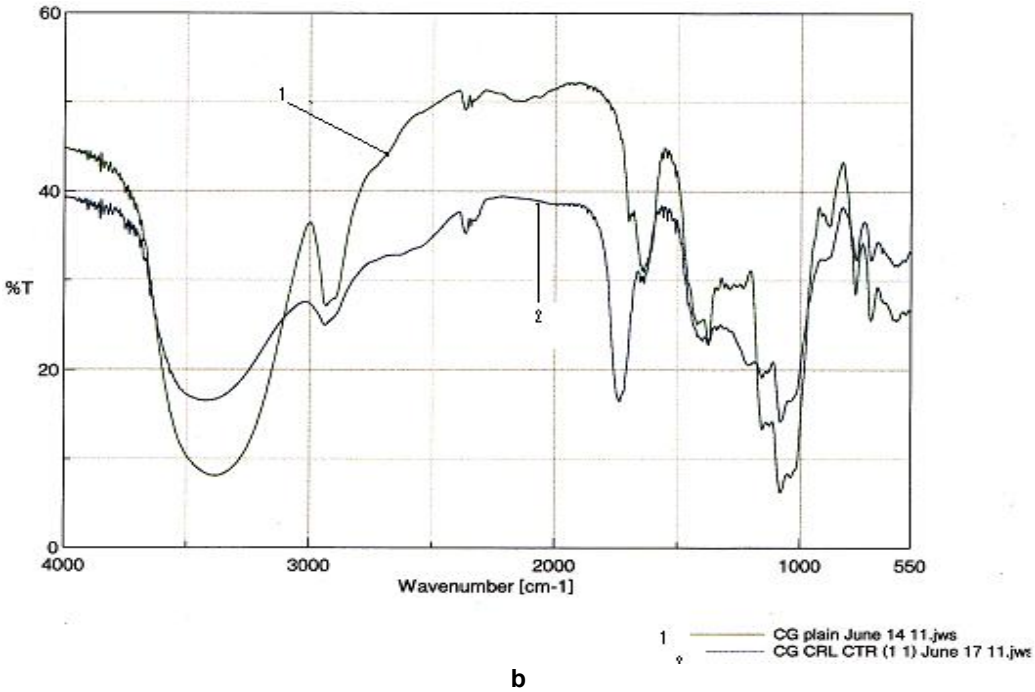


Fig. 1. DSC overlay of croscc and 50:50 binary mixture of CG and CTR



a



b

Fig. 2. FT-IR Spectrum of (a) CrosCC and (b) overlay of CG and CrosCC

3.3 Proposal on the CG and CTA Reaction Scheme

Scheme 1 shows the proposed mechanism of formation of CrosCC resulting from cross-linking CG with CTA. The scheme depicts a molar ratio reaction components involved in the synthesis of CrosCC. Two (2) moles of the CG reacted with 1 mole of CTA to give 1 mole of CrosCC. The attachment of the sugar molecules was stepwise with one attached before the other and in each case 1 mole of water is eliminated. Steric hindrance may have prevented the attachment of the third sugar molecule onto the third and

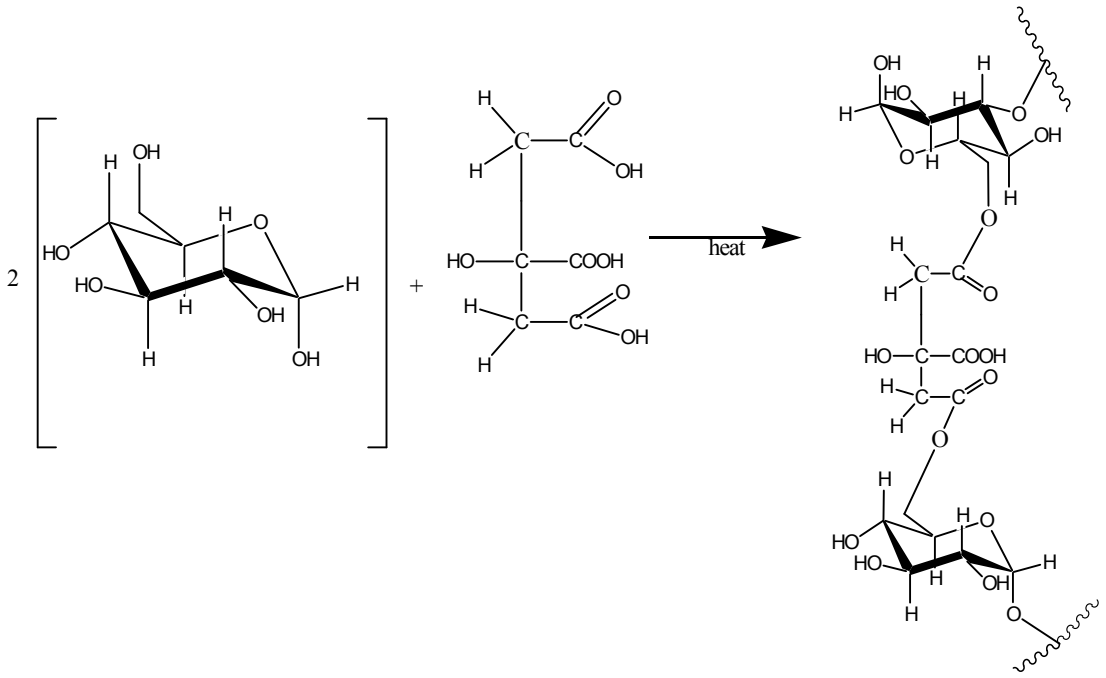
unreacted carboxyl group situated at the center of the structure.

The DSC and FT-IR spectra obtained in this study and the presence of an ester carbonyl frequency in a Solid State ^{13}C Nuclear Magnetic Resonance (NMR) of CrosCCG, a cross-linked polymer developed in a similar study yet to be published, led to the suggestion of a possible mechanism for the synthesis of CrosCC as shown in Scheme 1. Identification of ester group in FT-IR and the presence of an ester carbonyl absorption peak in the ^{13}C NMR were indicative of the nature of the bond formed during the cross-linking process. Esterification involving the –COOH of the CTA and the –OH of sugar from the gum led to the cross-linking of CG to form an insoluble but swellable CrosCC. Similar mechanism was attributed to the cross-linking of cyclodextrins with the PCAs containing at least three carboxylic groups [15, 17-18].

Table 3 shows the organoleptic and some physicochemical properties of CrosCC. The cross-linked product was brown in colour when first obtained with the intensity of the colour dependent on the amount of the cross-linker used; the more the proportion of the cross-linker, the darker the colour. Colour, odour and taste of a material when not appealing, may pose problems to the use of such material in foods and pharmaceutical formulations. The cross-linked product was found to be bleached white with hypochlorite solution.

Cross-linking tampered with the solubility of CG. While CG forms mucilaginous dispersions in water [12,36], the cross-linked product, CrosCC failed to dissolve or disperse in any of the solvents used for the study, in spite of the deliberate use of solvents with varied polarity. Cross-linking reduces solubility [37] or even renders a hitherto soluble material insoluble, especially when established by covalent bond formation [38-39].

Moisture loss on drying (LOD) for CrosCC was found to be 7.21%. The method of drying 2 g ground sample at 105 ^{o}C for 2 h appears to be an optimum condition ensuring most of the water in the sample is given off [40] and is sensitive for determinations both in materials with high or low moisture content [41]. CG was found to have relatively more water content than the cross-linked product of the gum as reported in a related study [21] and as was equally observed by [10]. Official recommendations have specified values for some polymeric materials evaluated for LOD e.g. acacia ≤ 15.0 %; starch ≤ 15 %; HPMC ≤ 10 [42]. It can thus be seen that CG and the derivative have moisture contents within the limits specified for similar polymers.



Scheme 1. Proposed Structural Representation of CrosCC Synthesis

Table 3. Organoleptic and some physicochemical properties of CrosCC Powder

Parameter	Result
Colour	Brown turned white (after bleaching)
Taste	Tasteless
Odour	Odourless
Texture	Granular
Solubility (non-polar, polar aprotic, polar protic solvents)	Insoluble
Water holding capacity (%)	143
Swelling ratio (%)	84.2
Water content (Karl Fisher titration)	
At ambient temperature and humidity (%)	7.12
After 7-day storage over activated silica gel (%)	3.15
Moisture loss on drying (%) (±SD)	7.21 ±2.10
Sulphated ash (±SD)	1.91 ±0.04
Flow rate (g/s)	12.5
Angle of repose (^{o})	30.11
Bulk density (g/ml)	0.556
Tap density (g/ml)	0.739
Compressibility index (%)	21.92
Hausner ratio	01.26

Karl Fisher titration has been described as an appropriate method of determining water contents of both solid and liquid samples [43-44]. At ambient temperature and humidity, samples collected from sealed storage containers showed a 7.12% water content for CrosCC while storage for one week over activated silica gel contained in a desiccator reduced the water content to 3.15%. The cross-linked polymer, which was relatively hygroscopic for pharmaceutical concerns, was found to lose water at lower humidity. It therefore shows that including a pack of desiccant in its container can allay fears on the gum's spoilage due to its hygroscopic nature.

Swelling potentials of CG was found to increase following the derivatisation process.CG has been found to sorp some amounts of water but this did not make it swell to an appreciable level. CrosCC, sequel to the cross-linking was found to have a swelling ratio 0.0 % at 0.0 min, 31.6 % at 1 min, 54.2 % at 2 min and 82.2 % after 10 min contact with water. Cross-linking CG with CTA caused the material to imbibe more water and most importantly, it imparted a remarkable swelling property on the polymer. CrosCC, a cross-linked derivative of CG was thus found to swell to a greater height (*P*=.05) compared to the uncross-linked variety, when made to contact water. The swelling rate was more pronounced during the first 4 min after which the curve almost flattens out, signaling less and less swelling taking place. One of the very important features of hydrogel swelling is the rate of swelling or swelling kinetics [45].

Water holding capacity of 143 % was found for CrosCC powder. Determination of the WHC of a hydrogel made from carbohydrate polymers for use in foods and pharmaceuticals is required to provide information on the storage and handling precautions to be adopted to avoid spoilage of the product [46,47].

Ash values can serve as parameters for the determination of the purity of gums [48] and other polymeric materials. Gums, like other plant based materials, present with varied ash values necessitating the recommendation of limits for some commercially available polymeric materials e.g. acacia ≤ 5 %; tragacanth ≤ 5 %; starch ≤ 0.5 %; propylene glycol ≤ 0.01 %; cellulose acetate phthalate ≤ 0.1 % [42]. CrosCC with sulphated ash value 1.91 can be categorized along with acacia and tragacanth powders; and can be said to have low sulphated ash values.

The powder of CrosCC was found to be coarse with particle size distribution that appeared skewed to the larger particle size fraction. The powder was also free flowing with over 70 % of the particles having sizes greater than 250 µm, and particles with this size are free flowing [49].

Table 4 and Fig. 3 show the properties of tablets of Ven. HCl formulated with HPMC ER as binder at 7.5 %w/v concentration and CrosCC or PGS as drug release modifiers. The results showed all the batches to have passed the prescribed tests with slight inter-batch variations. CrosCC at low concentration (T2) was found to enhance (*P*=.05) Ven. HCl release with the release becoming more pronounced within the first 15 min of *in vitro* dissolution time. Almost 40 % of the drug was released within this time against 35 % released in the batch not containing CrosCC (T1). CG cross-linked with EPC was also reported to enhance drug release [13].Cross-linked polymers have been used to facilitate drug-release from tablets [50]. $T_{50\%}$ and $T_{80\%}$ were however similar

for both T1 and T2. At higher concentration of CrosCC (T3), there was delayed release of the drug with a $T_{80\%}$ of 120 min; this concentration, however, also produced tablets with reduced crushing strength. In general, derivatisation of the natural polymers had availed the pharmaceutical industries of better performing or multifunctional biomaterials for use in drug delivery [8, 38-39, 51]. CrosCC may possibly be a multifunctional polymer that showed superior property of enhancing drug release over PGS.

PGS at 10 %w/w can act either as tablet binder or disintegrant [42] and the result obtained (T4) for crushing strength, friability and drug release seem to support the tablet binder action of PGS over the disintegrant action. The tablets were found to be harder and less friable and the dissolution profile showing a $T_{80\%}$of 105 min against $T_{80\%}$ of 90 min for T1.

Table 4. Properties of Ven. HCl tablets containing HPMC (ER) as binder and CrosCC or PGS As release modifier

	Batches			
Parameter	T1	T2	T3	T4
Weight variation (mg ± SD)	166.23 ± 1.97	169.43 ±3.10	167.13 ± 1.71	168.90 ± 1.77
Crushing Strength (KN ± SD)	5.63 ±1.31	5.88 ±0.52	4.57 ± 1.01	6.72 ±0.73
Friability (%)	0.12	0.2	0.29	0.06
Content of active ingredient (%)	101.56	98.08	100.32	101.24
$T_{80\%}$ (min)	90	90	120.0	105.0
Diameter (mm ± SD)	7.040 ± 0.007	7.040 ±0.006	7.040 ± 0.007	7.040 ± 0.005

Key: HPMC ER 7.5 % alone (T1); Plus CrosCC 3% (T2); CrosCC 10% (T3); PGS 10% (T4);

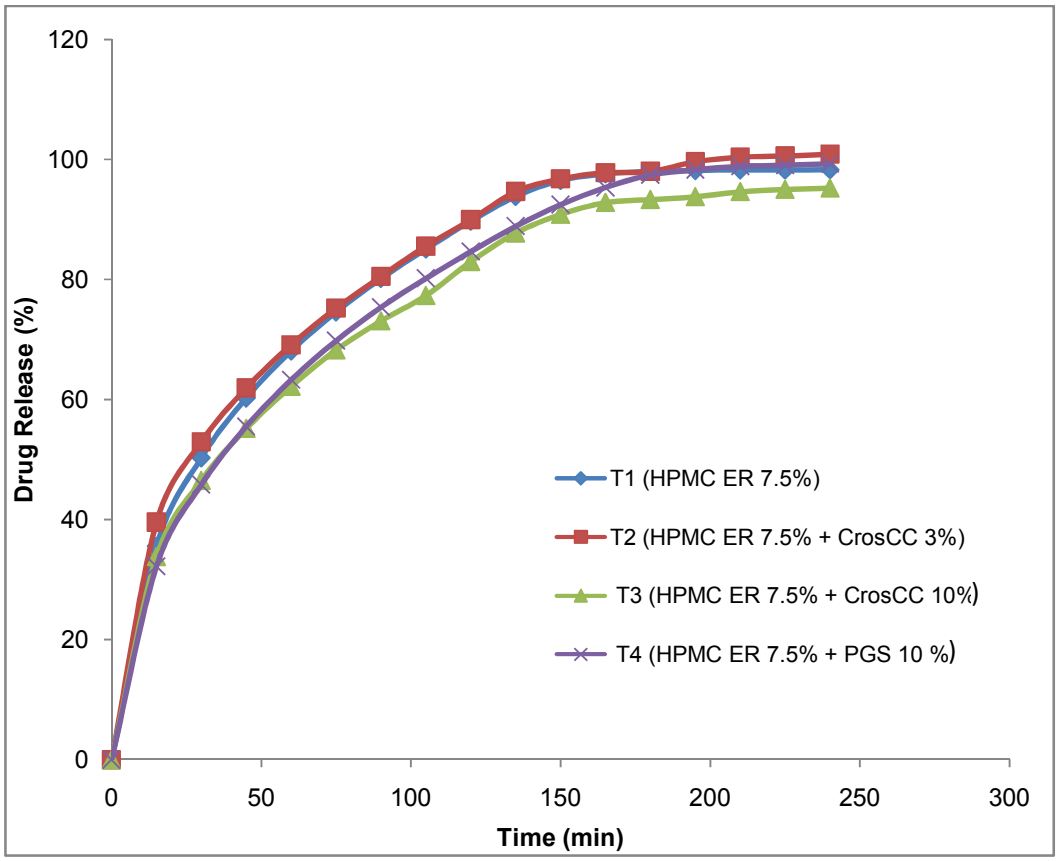


Fig. 3. Effect of CrosCC or PGS on Ven. HCl Release from Tablets Formulated with HPMC ER at 7.5 %w/w as Binder

4. CONCLUSION

Cashew gum can be derivatised by cross-linking using a polycarboxylic acid with more than two carboxyl groups. The derivative obtained using citric acid as cross-linking agent was found to be a free flowing coarse powder with pronounced water reactivity. The polymer imbibes water and swells to an appreciable level. The use of this polymer as adjunct in tablets showed it to have potentials in enhancing drug release at low concentrations and delaying the release at higher concentration.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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