British Journal of Pharmaceutical Research
6(3): 155-165, 2015, Article no.BJPR.2015.058
ISSN: 2231-2919

SCIENCEDOMAIN *international*
www.sciencedomain.org

Derivatisation of Cashew Gum by Esterification Using Citric Acid and Glycerol

A. Abdulsamad[1*], A. R. Oyi[1], A. B. Isah[1] and I. Odidi[2]

[1]Department of Pharmaceutics and Pharmaceutical Microbiology, Ahmadu Bello University, Samaru Zaria, Nigeria.
[2]Research and Development Unit, Intelli Pharmaceutics Int. Corp, 30 Worcester Road Toronto, Ontario, M9W 5X2, Canada.

Authors' contributions

This work was carried out in collaboration between all authors. Author ARO designed the study and 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.

Article Information

DOI: 10.9734/BJPR/2015/16022
Editor(s):
(1) Syed A. A. Rizvi, Department of Pharmaceutical Sciences, College of Pharmacy, Nova Southeastern University, USA.
(2) Alyautdin Renad N, Department of Pharmacology (Pharmaceutical Faculty), I. M. Sechenov MSMU, Moscow, Russia.
Reviewers:
(1) Anonymous, Thailand.
(2) Sophia Wan-Pyo Hong, Biology Dept., School of Natural Sciences, Chungbuk National University (CBNU), South Korea.
(3) Anonymous, Romania.
(4) Anonymous, India.
(5) Syed Umer Jan, Faculty of Pharmacy, University of Balochistan, Quetta, Pakistan.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=984&id=14&aid=8322

Original Research Article

Received 31st December 2014
Accepted 18th February 2015
Published 3rd March 2015

ABSTRACT

Citric acid and glycerol were used to derivatise cashew gum via cross-linking. A dispersion of the purified gum, the acid, glycerol 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/170ºC for 30 min for the cross-linking to take place. The cross-linking was demonstrated using DSC, FT-IR and NMR spectral data and the esterified derivative (tagged CrosCCG) was characterized by determination of the solubility, water content, swelling and water holding capacity, moisture sorption and desorption, particle flow properties The results obtained indicated that the cross-linked product differed from the parent gum and from cashew gum cross-linked using citric acid alone, by displaying greater swelling ratios, water sorption and water holding capacities. This

**Corresponding author: Email: aabdulsamad@abu.edu.ng, abdulbnabdul@yahoo.com;*

product may find use as swellable device in controlling drug release or as disintegrant in pharmaceutical and biomedical applications.

Keywords: Cashew gum; citric acid; glycerol; derivatisation; cross-linking; cross-linking agent; characterization.

1. INTRODUCTION

Gums are naturally occurring polymeric materials of plant or animal origin. Abundance, sustainability, biodegradability and biosafety had made the polysaccharide gums a subject of intensive research in industrial raw material development [1-5]. These materials had found use in their putative forms as binders or disintegrants in tablets, as suspending or emulsifying agents [1], albeit when used in relatively high concentrations [4].

Structural modifications of these polymeric materials commonly via grafting or cross-linking using varying agents have given rise to derivatives with improved functionality [4,6]. Cross-linking has been used to make three-dimensional networks of water insoluble but swellable materials for use as swellable devices in controlling drug release or as disintegrants in pharmaceutical and biomedical applications [7-10].

Gums with free alcoholic (-OH) groups seem to be good candidates for modification by cross-linking [4]. Hydrogen bond formation between the –OH and –COOH molecules of the reacting substances aids cross-linking process [4,11], while covalent bonds are principally responsible for holding the polymers together. The search for relatively inexpensive, safe, environmental friendly cross-linking agents from renewable sources is highly relevant at this point in raw material research for pharmaceutical and biomedical processing.

Citric acid (CTA), a safe and relatively inexpensive cross-linking agent has been used to successfully cross-link cashew gum (CG) in a related study that is yet to be published. The cross-linked product showed better swelling, water sorption and water holding capacities and showed some drug release enhancing ability compared to the uncross-linked gum. A combination of CTA and glycerol (GLY) have not been used together to derivatise a gum via cross-linking, though the combination had been used to develop a biodegradable thermoset polymer by esterification [12].

Copolymerization has generally been utilized to enhance the mechanical properties of hydrogels for use in pharmaceutical formulations [7]. Copolymerisation of –COOH containing molecules with those carrying –OH may possibly enhance the polymerization yield and functionality of polymers.

In this study, cashew gum is considered for cross-linking using two cross-linking agents, CTA and GLY to develop a cross-linked derivative with enhanced properties that may find relevance in drug delivery and other biomedical applications.

2. MATERIALS AND METHODS

2.1 Materials

- Dichlorodimethyl silane, Dimethyl-formamide, 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, (Caledon Laboratories Ltd, Canada).
- Cashew gum/ CrosCCG were as purified/synthesized in the laboratory (IntelliPharmaceutics Inc., Canada).

2.2 Methods

2.2.1 Extraction/purification of CG

The gum was extracted and purifies as described [13].

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 solution. One liter portion of the acetone was gradually poured into the beaker containing the mucilage while stirring to precipitate 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:

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

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

2.2.2 Cross-linking CG using CTA and GLY

Appropriate quantities of CG, CTA, GLY and sodium dihydrogenphosphate (NaH_2PO_4) (as catalyst) as presented in Table 1 were weighed and mixed with 100 ml of DI water contained in a beaker. The mixture was rendered homogenous by stirring over a boiling water bath and thereafter made to volume with more DI water. The homogenous mixture was transferred into a culture dish and concentrated by heating at 40ºC for 18 h. The solid mass was heated at 140 or 170ºC for 30 min for the cross-linking to take place, and thereafter the polymer was recovered and thoroughly washed using DI water to remove unattached cross-linking agents and catalyst [14]. The now fibrous looking material was transferred onto a mesh, lined with fine muslin cloth, and percolated with DI water. The material was soaked in DI water for 24 h and further rinsed with more DI water before the water was strained off 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. The yield was determined using the following equation:

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

Where W1 is the weight of CG, W2 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 study the degradation temperatures of the cross-linked polymer and also to demonstrate the cross-linking of CG. These were done using a method described [13].

About 10 mg samples of the CG and CrosCCG 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.

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 CrosCCG 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 [15,16].

2.2.5 Solid State ^{13}C Nuclear Magnetic Resonance (SS ^{13}C NMR)

The solid state ^{13}C MAS NMR experiments on CrosCCG were performed on a Bruker AVANCE, 400 spectrometer, equipped with a magic angle-spinning (MAS) inclined at 57.4º. The sample (about 5 mg) was spun at 8.0 kHz in a 4.0 mm outer diameter zirconia ceramic rotor spinner. The proton decoupling was applied. The recycle delay time was set to 5 ms. ^{13}C chemical shifts were referenced to tetramethylsilane (TMS) using solid adamantine as a secondary standard.

2.2.6 Determination of moisture sorption/desorption over saturated salt solutions

Saturated salt solutions of magnesium chloride, magnesium nitrate, potassium chloride and sodium chloride were prepared to provide controlled changes in relative humidity [17,18].

This was achieved by changing the type of salt solution after a 7 day period of exposure as shown in Scheme 1. Three sample dishes containing 2 g weights of dried uncross-linked CG, CG cross-linked with CTA alone (CrosCC) and CrosCCG respectively were prepared. An assembly of sample and the saturated salt solution all contained in a desiccator was made such that, the salt solution is placed at the bottom while the samples contained in tarred dishes were placed on top of the separator plate. The assembly was allowed to stand for 7 days during which the dishes containing the powders were brought out and weighed daily, to monitor the mass change as a function of time. Care was taken to avoid over exposure of the material to outside humidity. No attempt was made at controlling the temperature and the prevailing temperature was 22±2ºC.

2.2.7 Other physicochemical determinations

Swelling Ratio and level of insolubility of CrosCCG were evaluated using methods described in a related study [13], while moisture loss on drying (MLD), water content, sulphated ash and powder flow properties were determined using methods described in a related study [19].

2.2.8 Water holding capacity (WHC)

The method described [20] 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:

$$\%\, WHC = \left(\frac{W2-W1}{W2}\right) x\, 100 \quad (3)$$

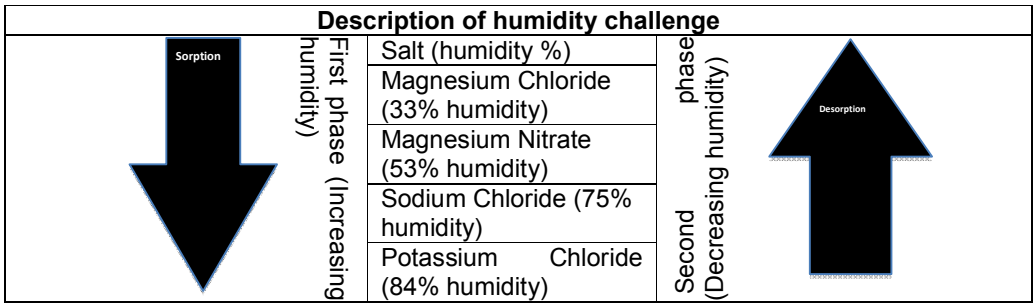
Where W_1 and W_2 were weights of dry and hydrated samples, respectively.

2.2.9 Statistical analysis

Results obtained that require statistical analysis were analyzed using GraphPad Prism software package. Results were expressed as mean ± SD and differences between means were considered significant at $P<0.05$ using the analysis of variance (ANOVA) or student's t test.

Table 1. Formulae for cross-linking CG using CTA and or GLY

Ingredient	CG:CTA (CrosCC)	CG:CTA:GLY (CrosCCG)		
Ratio (g)	1:1	1:1:1	1:1:2	2:2:1
CG (g)	20	20	20	20
CTA (g)	20	20	20	20
GLY (g)	-	20	40	10
NaH_2PO_4 (g)	2	2	2	2
DI water (ml) to	200	200	200	200



Scheme 1. Moisture sorption/desorption studies over some selected saturated salt solutions

3. RESULTS AND DISCUSSION

3.1 Percentage Yield of Cross-linking CG with CTR and GLY

Cross-linking CG with CTA or CG with CTA & GLY conducted at 140ºC for 30 min gave a cross-link yield (%) of 64.72±1.13 and 26.22±1.59 for cross-links of CG:CTA (1:1) and CG:CTA:GLY (1:1:1), respectively; while at 170ºC, yields (%) of 54.73±2.88 and 73.60±3.61 were obtained. Differences in yield between the two cross-link formulas or between the two temperatures were significant (*P*= .05). Maintaining weight ratios of CG and CTA but varying that of GLY (2:2:1 or 1:1:1 or 1:1:2) and heat treated at a temperature of 170ºC for 30 min gave respective yields (%) of 74.89±2.30, 75.1±2.80% and 75.3±3.80%. Differences in yield (%) was not statistically significant (*P*= .05).

Cross-linking CG with the two cross-linking agents CTA & GLY was found to give better overall yield when the reaction mixture was heat treated at 170ºC for 30 min. This combination also gave a polymer with superior qualities over that made using CTA alone as cross-linker. Copolymerization processes have been used to synthesise hydrophilic matrices as was demonstrated [21] when they prepared novel super absorbent by copolymerization process using CG, glycidylmethacrylate and acrylamide. [7] in a review on hydrogels in pharmaceutical formulations reported that copolymerization has generally been utilized to enhance the mechanical properties of hydrogels. Cross-linking via the incorporation of safe and environmentally friendly dual cross-linking agents CTA and GLY, was considered to improve the cross-linking of CG. GLY has been used to cross-link Carbopol in making hydrogels for buccal administration via ester formation between Carbopol carboxyl groups and glycerol hydroxyl groups [22]. Complexes formed between poly(acrylic acid) and poly(ethylene glycol) are held together by hydrogen bonding between the oxygen of the poly(ethylene glycol) and the carboxylic group of poly((meth)acrylic acid) [6]. Recently Halpern et al. [12] developed a biodegradable thermoset polymer by esterification of citric acid and glycerol.

Inclusion of GLY in the cross-linking mixture offers two approaches to the overall CG cross-linking process. One, is ester formation with the unreacted carboxyl group of CG:CTA polymer [23] and two, is the H- bond formation with the carboxyl group or –OH of sugar from the gum [6,11]. These claims could, however, not be verified in this study as the FT-IR spectral data could not be used to discern any increase in the ester or hydroxyl absorption peaks. What was obvious in the study was that inclusion of GLY imparted on the net cross-linking yield and swelling (Fig. 4) of the cross-linked CG polymer.

Temperature was found to influence the cross-linking of CG with the combination of CTA and GLY as cross-linkers. [24,25] reported on the influence of temperature on cross-linking β-CD with PCA, where water soluble or insoluble polymer fractions were obtained by varying the temperature. In this study, reaction temperature of 170ºC, a temperature beyond the flash point of GLY, was found to favor the cross-linking reaction when GLY was included in the reaction mixture. A significant (*P*= .05) increase in yield was noticed as the reaction temperature was changed from 140ºC to 170ºC in cross-linking CG with a combination of CTA and GLY. On the other hand a statistically significant (*P*= .05) decrease in cross-link yield of CG:CTA (1:1) was observed when the cross-linking temperature was changed from 140ºC for 30 min to 170ºC for 30 min.

3.2 Thermal Analysis by DSC

DSC thermograms of CrosCCG showed the disappearance of the 156.3ºC characteristic melting temperature of CTA suggesting its absence or “envelopment” in the cross-link structure. Disappearance of this peak was also noticed in a related study not yet published on cross-linking CG with CTA.

3.3 Fourier Transform Infrared (FT-IR) Spectral Studies

Fig. 1a is the FT-IR spectrum of CrosCCG showing the characteristic absorption bands associated with aromatic sugars of carbohydrates. The band with peak at 3421.1 cm^{-1} is H–bonded OH stretch band of aromatic compounds that has shifted from the 3388.32 cm^{-1} peak of the uncross-linked gum [15,19]. The 1735.62 cm^{-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} [26] and the carbonyl frequency of CTA noted in this study at 1728.87 cm^{-1}. Fig. 1b is the overlay of FT-IR spectra of CG and CrosCCG highlighting the

formation of the prominent peak at 1735 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 the binary mixture at 1727 cm^{-1} but not in the spectrum of the cross-linked polymer, where in its place appeared a strong band at 1735 cm^{-1}. A strong band around 1735 cm^{-1} (Fig. 1) 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 and or GLY.

Inclusion of GLY in the cross-link formula led to the production of a polymer, CrosCCG, characterized by greater (*P*=.05) swelling and water sorption/holding properties. GLY with its –OH groups is a good candidate for formation of ester linkages with the –COOH of CTA [27]. Addition of GLY therefore must have served an additive or synergistic contribution to the overall esterification process. Another possible contribution of GLY in increasing the water reactivity of CrosCCG is hydrogen bond formation with water. [28] opined that glycerol interacts favorably with water to strengthen the H-bond network of the solvent. This claim, however, could also not be substantiated using FT-IR as there was no corresponding broadening of the O-H stretching frequency. [16] suggested that hydrogen bonding is important, but the effect tends to be weaker than for the hydroxyl group, and the overall effect on the spectrum is slightly less pronounced. A band at 1040 cm^{-1} used for quantitative determination of glycerol [29] was found present in the spectra of both uncross-linked CG and CrosCCG, though with higher intensity in the latter.

3.4 ^{13}C NMR Spectral Analysis of CrosCCG Polymer

Fig. 2 is the solid state ^{13}C NMR spectrum of CrosCCG showing the various resonances associated with respective resonating carbons as interpreted in Table 2. The spectrum showed peaks corresponding to resonances of the carbon atoms of glucose, galactose, xylose, rhamnose and ribose sugars. These sugars are similar to those identified by [30] in an analysis of the acid hydrolyzed sample of CG similarly from Nigeria.

An interesting additional carbonyl peak at 204.0 ppm was noticed in the present study. This peak was not seen in some reported ^{13}C NMR spectra of CG not subjected to cross-linking process [21,31-32]. Presence of this carbonyl frequency further supports the claim of the cross-linking of CG with CTA and or GLY through esterification.

3.5 Moisture Sorption / Desorption Determination

Fig. 3 shows the moisture sorption/desorption isotherm of 2 g samples each of CG, CrosCC and CrosCCG subjected to humidity changes (Scheme 1). All the samples were found to sorp moisture commensurate to the degree of humidity. Cross-linking has significantly (*P*=.05) influenced the level of moisture sorbed by the polymers. On the first week of exposure (over magnesium chloride), CG sorbed only about 1% of its weight of water just as CrosCC and CrosCCG sorbed about 2.4% and 15% of their weights of water, respectively, over the same period. By the fourth week's exposure (over potassium chloride) the polymers respectively took about 6, 12 and 30% of their weights of water.

To monitor the interactions of water in solids, varying relative humidities are established by the respective use of saturated solutions of appropriate salts [17]. The rate and extent of moisture sorption were found to be almost equivalent to the rate and extent of moiture desorption following sample exposure to varying RHs. This is demonstrated by the shape of the isotherm or hysteresis loop [18], which is a measure of the interraction of the polymers with water; and specifically highlighting the reversibility of the process (Fig. 3). This figure also shows a relationship between the sample nature and the amount of moisture sorped. Cross-linking has been reported to increase the water uptake ability of polymeric materials [7,8,11]. The cross-linked polymers were found to sorp greater amounts of water than CG with CrosCCG, cross-linked using both cross-linking agents demonstrating greater (*P*=.05) water uptake compared to CrosCC.

3.6 Swelling Properties of CrosCCG Powder

Fig. 4 shows the swelling property of CG, CrosCC and CrosCCG. CG was not found to swell even though it absorbed some amount of

water as shown by the water sorption/desorption isotherm (Fig. 3). Cross-linking CG with CTA caused the material (CrosCC) to imbibe more water and most importantly, it imparted a remarkable swelling property on the polymer (*P*= .05). Cross-linking CG using a combination of CTA and GLY led to the formation of a cross-linked polymer, CrosCCG, characterized by a greater (*P*=.05) rate and extent of swelling (Omidian and Park, 2008) compared to the uncross-linked CG or CrosCC. Knowledge of the swelling characteristics of polymers is of great importance in pharmaceutical and biomedical applications [11].

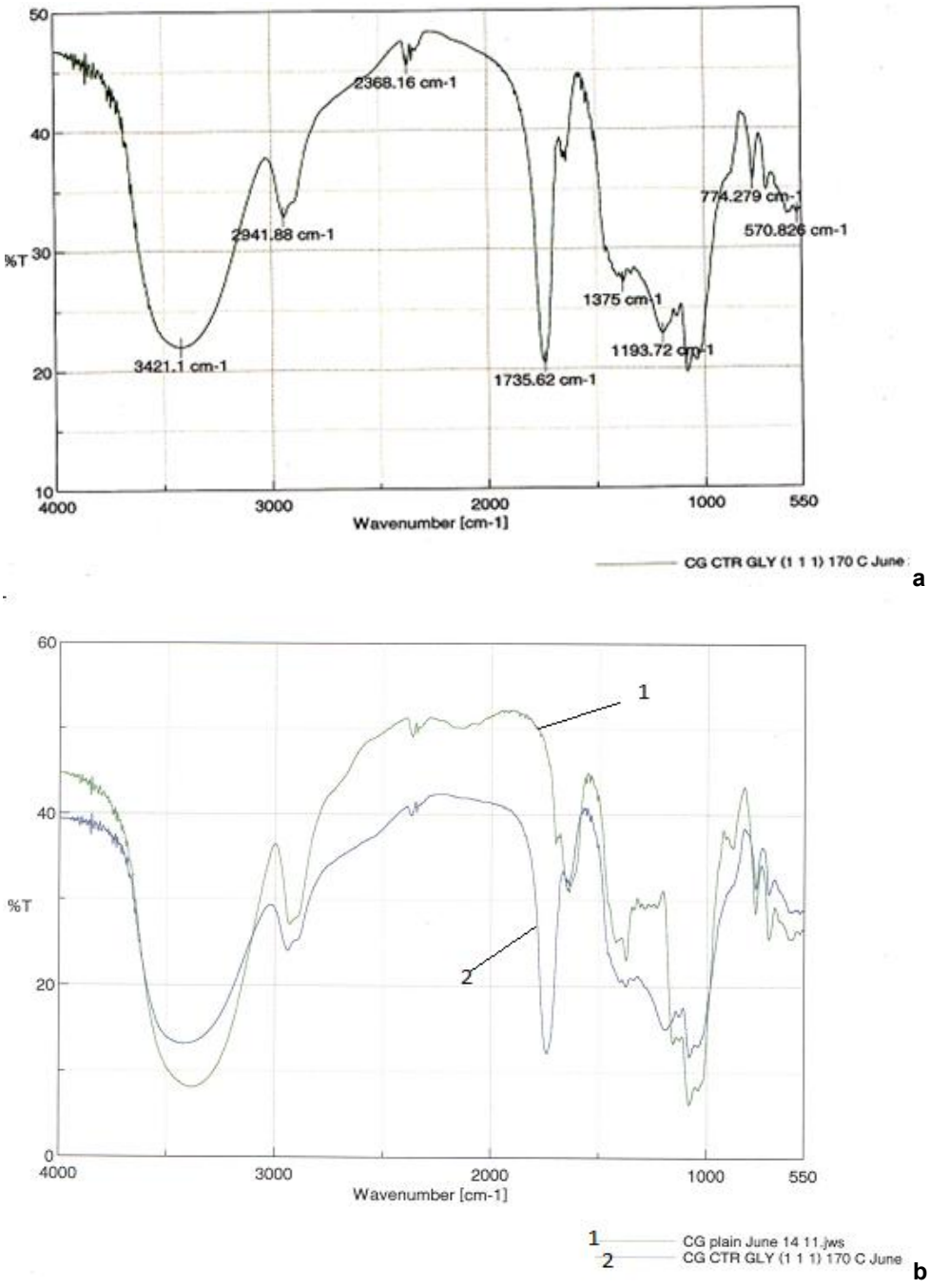


Fig. 1. FT-IR Spectrum of (a) CrosCCG and (b) overlay of CG and CrosCCG

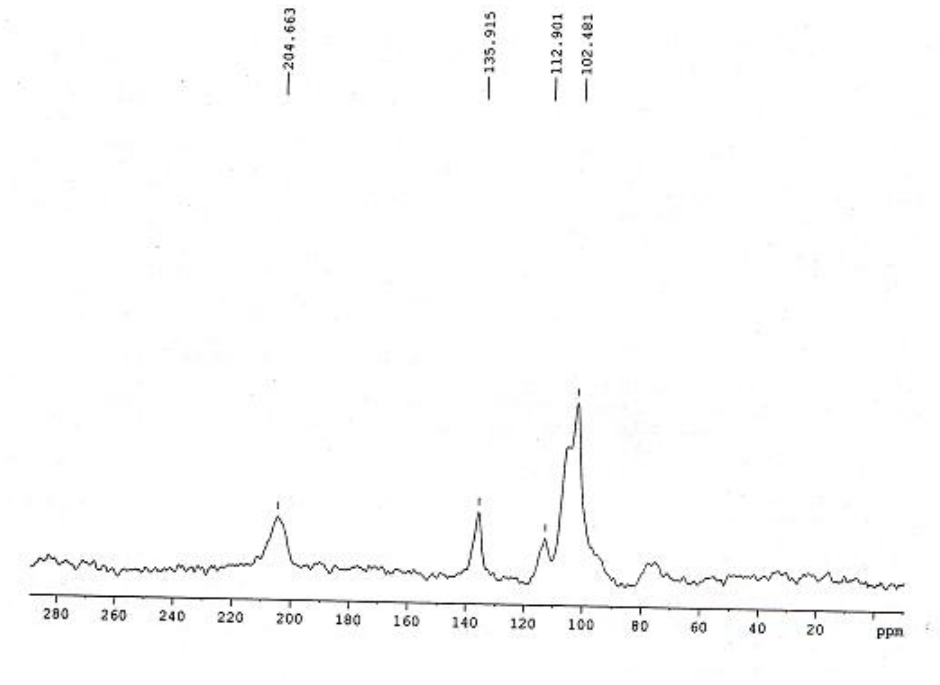


Fig. 2. Solid state ^{13}C nuclear magnetic resonance of CrosCCG

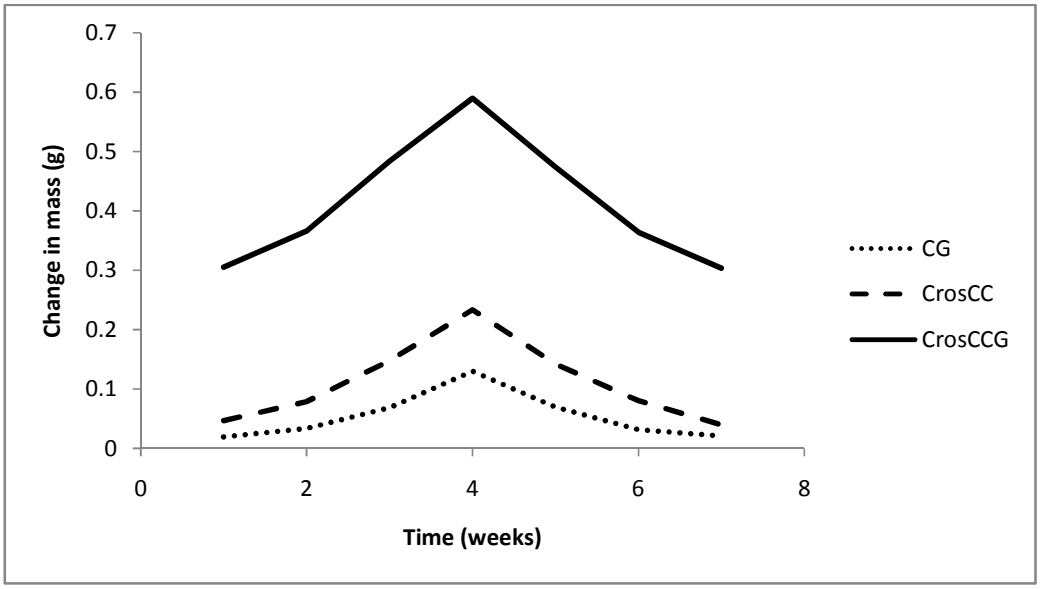


Fig. 3. Moisture sorption/desorption isotherm of CG, CrosCC and CrosCCG after subjection to varying humidity challenges

Table 3 reports on organoleptic and some physicochemical properties of CrosCCG. Cross-linking CG with the two cross-linking agents, CTA and GLY did not give a polymer that differs significantly from that cross-linked using CTA alone, in terms of organoleptic, insolubility and flow characteristics as determined in a related study reported by [13]. CrosCCG powder was found to be coarse, free flowing with particle size distribution skewed to the bigger size fraction. A significant difference (*P*=.05) was, however, noticed in WHC. The cross-linked polymer

derived via use of two cross-linking agents showed greater (*P*=.05) ability of retaining water in its folds. This finding agreed with the result of moisture sorption/desorption (Fig. 3) and swelling (Fig. 4) obtained for the polymer. Cross-linking could be seen to increase the water sorption and swellability of CG. The additive cross-linking has aided the entrapment of water in the macromolecular structure of the cross-linked polymer [7,8,11].

Table 2. Interpretation of the solid state ^{13}C nuclear magnetic resonance of CrosCCG

Resonance (PPM)	Responsible carbon
18.0	Methyl group of Rhamnose
73.0	C-2, C-4, C-5
102.5	Anomeric carbon resonance of glucose, galactose and xylose sugars
112.9	Anomeric carbon resonance of β-D ribofuranose
204.0	Carbonyl frequency

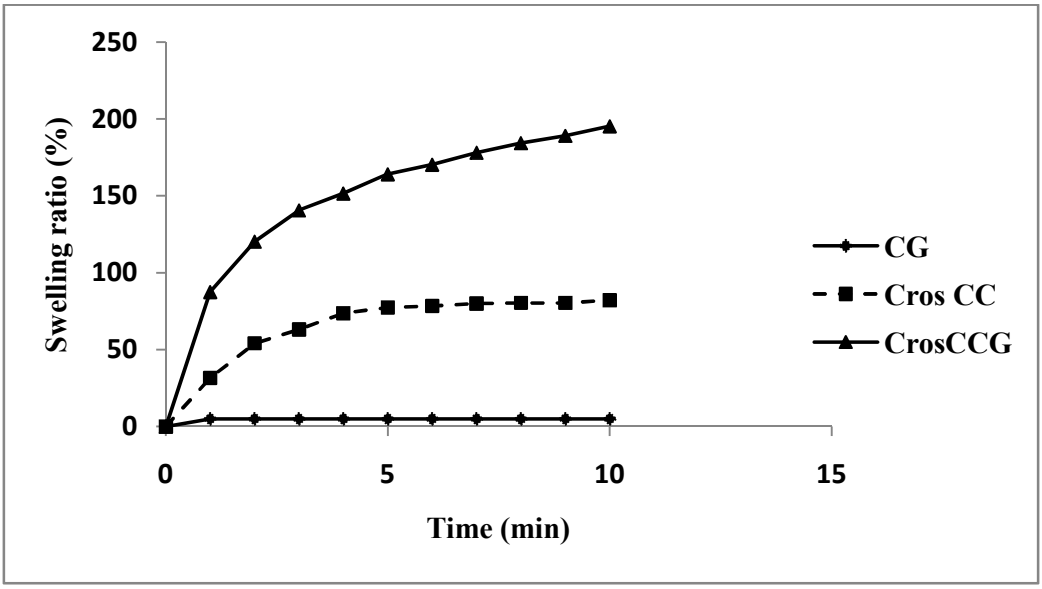


Fig. 4. The effect of cross-linking on percentage (%) swelling ratio of CG

Table 3. Organoleptic and some physicochemical properties of CrosCC powder

Parameter	Result
Color	Brown turned white (after bleaching)
Taste	Tasteless
Odour	Odourless
Solubility	Insoluble
Water holding capacity (%)	244±5.25
Moisture loss on drying (±SD)	7.39±3.81
Sulphated ash (±SD)	2.70±0.04
Flow rate (g/s)	12.5±0.07
Angle of repose (^{o})	29.24±1.94
Bulk density (g/ml)	0.549±2.16
Tap density (g/ml)	0.714±1.01
Compressibility index (%)	23.00±0.32
Hausner ratio	01.29±0.19
(%) Water content (Karl Fisher titration)	
At ambient temperature and humidity	7.04%,
After 7 day storage over activated silica gel	2.96%

4. CONCLUSION

Derivatisation of cashew gum via esterification using citric acid and glycerol has been found to produce a coarse, insoluble and free flowing polymer. This polymer showed greater abilities to absorb water and to swell compared to the polymer derived via cross-linking with citric acid alone. The polymer, as characterized, showed potentials for use as swellable device in controlling drug release or as disintegrant in pharmaceutical and biomedical applications.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the contributions of Ahmadu Bello University, Zaria, Nigeria for giving the permission and fellowship for the study; Education Trust Fund, Abuja Nigeria and STEP-B, Abuja Nigeria for providing the grant and Intellipharmaceutics Int. Corp. Toronto, Canada for providing the laboratory and research materials for the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Jani GK, Shah DP, Prajapati VD, Jain VC. Gums and mucilages: Versatile excipients for pharmaceutical formulations. Asian Journal of Pharmaceutical Sciences. 2009;4(5):309-323.
2. Singh AK, Shingala VK, Selvam RP, Sivakumar T. Evaluation of *Mangifera indica* gum as tablet binder. Indian Journal of Pharm Tech Research. 2010;2(3):2098-2100.
3. Amelia MA, Rakesh RD, Shilpa NS. Recent investigations of plant based natural gums, mucilages and resins in novel drug delivery systems. Indian Journal of Pharmaceutical Education and Research. 2011;45(1):86-99.
4. Rana V, Rai P, Tiwary AK, Singh RS, Kennedy JF, Knill CJ. Modified Gums: Approaches and Applications in Drug Delivery. Carbohydrate Polymers. 2011; 83:1031-1047.
5. Ogaji IJ, Nep EI, Audu-Peter JD. Advances in natural polymers as pharmaceutical excipients. Pharm Anal Acta. 2012;3(1):1-16.
6. Hennink WE, Van Nostrum CF. Novel crosslinking methods to design hydrogels. Advanced Drug Delivery Reviews. 2002;54:13-36.
7. Peppas NA, Bures P, Leobandung W, Ichikawa H. Hydrogels in pharmaceutical formulations. European Journal of Pharmaceutics and Biopharmaceutics. 2000;50:27-46.
8. Hoare TR, Kohane DS. Hydrogels in drug delivery: Progress and challenges. Polymer. 2008;49:1993-2007.
9. Omidian H, Park K. Swelling agents and devices in oral drug delivery. J. Drug Del. Sci. Tech. 2008;18(2):83-93.
10. Misra GP, Gil ES, Lowe TL. In the biomedical arena. In: Polymer grafting and cross-linking, Ed. Bhattacharya, A., Rawlins, J.W. and Ray, P., John Wiley & Sons, Inc. 2009;145-177.
11. Brannon-Peppas L. Preparation and characterisation of crosslinked hydrophylic networks, superabsorbent polymers: Science and technology; ACS Symposium Series 573; American Chemical Society, Washington, DC. 1994;1478-1481.
12. Halpern JM, Urbanski R, Weinstock AK, Iwig DF, Mathers RT, Von Recum HA. A biodegradable thermoset polymer made by esterification of citric acid and glycerol. Journal of Biomedical Materials Research Part A. 2013;102(5):1467-1477.
13. Abdulsamad A, Oyi AR, Isah AB, Odidi I. Cashew gum crosslinked with epichlorohydrin to enhance venlafaxine hydrochloride release from tablets formulated with HPMC as binder. Nigerian Journal of Pharmaceutical Sciences. 2014;13(1):43-53.
14. Reddy N, Yang Y. Citric acid cross-linking of starch films. Food Chemistry. 2010;118(3):702-711.
15. Hsu CPS. Infrared spectroscopy. In: Handbook of Instrumental Techniques for Analytical Chemistry. 1997;247-283.
16. Coates J. Interpretation of infrared spectra, a practical approach. In: Encyclopedia of Analytical Chemistry. Ed. Meyers, R.A.,

John Wiley & Sons Ltd. Chichester. 2000;10815-10837.
17. Greenspan L. Humidity fixed points of binary saturated aqueous solutions. Journal of Research of the National Bureau of Standards – A, Physics and Chemistry. 1977;81A(1):89-96.
18. Airaksinen S. Moisture sorption isotherm, In: Role of excipients in moisture sorption and physical stability of solid pharmaceutical formulations. Academic Dissertation, Faculty of Pharmacy of the University of Helsinki, Finland. 2005;12-13.
19. Abdulsamad A, Oyi AR, Isah AB, Odidi I. Characterisation and studies on binding properties of Cashew Gum and its Mixtures with Microcrystalline Cellulose in Venlafaxine Hydrochloride Tablet Formulations. Nigerian Journal of Pharmaceutical Sciences. 2012;2(2):9-20.
20. Vittadini E, Vodovotz Y. Changes in physicochemical properties of wheat- and Soy-containing breads during storage as studied by thermal analyses. Journal of Food Science. 2003;68(6):2022-2027.
21. Guilherme MR, Reis AV, Takahashi SH, Rubira AF, Feitosa JPA, Muniz EC. Sythesis of a novel superabsorbent hydrogel by copolymerization of acrylamide and cashew gum modified with glycidyl methacrylate. Carbohydrate Polymers. 2005;61:464-471.
22. Gonzalez NG, Kellaway IW, Fuente HB, Igea SA, Charro BD, Espinar FJO, Mendez JB. Influence of glycerol concentration and carbopol molecular weight on swelling and drug release characteristics of metoclopramide hydrogels. International Journal of Pharmaceutics. 1994;104:107-113.
23. Ducoroy L, Martel B, Bacquet B, Morcellet M. Cation exchange finishing of nonwoven polyester with polycarboxylic acids and cyclodextrins. Journal of Applied Polymer Science. 2007a;103:3730-3738.
24. Martel B, Ruffin D, Weltrowski M, Lekchiri Y, Morcellet M. Water-soluble polymers and gels from the polycondensation between cyclodextrins and Poly(carboxylic acid)s: A study of the preparation parameters. Journal of Applied Polymer Science. 2005;97:433-442.
25. Ducoroy L, Martel B, Bacquet B, Morcellet M. Ion exchange textiles from the finishing of PET fabrics with cyclodextrins and citric acid for the sorption of metallic cations in water. J Incl Phenom Macrocycl Chem. 2007b;57:271-277.
26. United States Pharmacopoeia (USP) 34 NF 29. Adipic acid NF Monograph. 2011; 1425.
27. Garcia PS, Grossmann MVE, Yamashita EF. Citric acid as multifunctional agent in blowing films of starch/PBAT. Quim. Nova. 2011;34(9):1507-1510.
28. Dashnau JL, Nucci NV, Sharp KA, Vanderkooi JM. Hydrogen bonding and the cryoprotective properties of glycerol/water mixtures. J. Phys. Chem. B. 2006;110(27):13670-13677.
29. Gorinstein S, Kitov S, Deutsch J. Spectroscopic determination of glycerol, polyphenols, and nitrogenous compounds in beer and wine. MBAA Technical Quaterly. 1980;17(3):156-159.
30. Abdulsamad A, Bhatia PG, Ojile JE. Phytochemical, toxicological and rheological properties of cashew gum and its dispersions. Nigerian Journal of Pharmaceutical Research. 2006;5(1):85-90.
31. De Paula RCM, Heatly F, Budd PM. Characterisation of *Anacardium occidentale* exudates polysaccharide. Polymer International. 1998;45(1):27-35.
32. Silva DA, Feitosa JPA, Maciel JS, Paula HCB, de Paula RCM. Characterisation of Crosslinked Cashew Gum Derivatives. Carbohydrate Polymers. 2006;66:16-26.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=984&id=14&aid=8322