ORIGINAL PAPER

Nig. J. Pharm. Res. 2018, 14 (1) pp 1-13
ISSN 0189-8434 **Available online at http://www.nigjpharmres.com**

Evaluation of Physico-Mechanical and Mucoadhesive Properties of Biopolymer Films From *Cola Acuminata* Gum

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background: Applications of film-forming materials in coating technology and drug delivery systems has led to several investigations into the film-forming potential of different polymers. A good film-forming material must possess good mechanical strength, wetting and adhesive properties

Objective: This study investigated the physico-mechanical and bioadhesive properties of biopolymer films from *Cola accuminata* pods, *obi* (Yoruba), *oji* (Ibo) and *gworo* (Hausa).

Methodology: The *Cola acuminata* gum (CAG) was extracted by soaking the sliced pods in distilled water and precipitating with acetone. Plasticizer-free CAG mucilage (10% w/v) was prepared using aqueous dispersion method. Similar batches of CAG mucilage containing plasticizers - propylene glycol (PPG) or glycerin (G) at concentrations of 1 - 3% v/v of the mucilage were also prepared using the same method. The mucilage samples were cast into films on Petri dishes by drying at 60^{o} C for 12 hours. Films with satisfactory texture were subjected to various physical tests. The mechanical properties of the films were assessed with Instron Universal Tester instrument (Model 3369) followed by folding endurance test. *Ex-vivo* mucoadhesive evaluation of the films was also conducted using Instron Probe Tack Tester (Model 5569).

Results: All the films were brown and odourless. The plasticizer-free film (F1) was dry and brittle, while F4 - F6 remained wet and tacky. Films containing 1% and 2% v/v of PPG (F2) and (F3) respectively were smooth, flexible, hydrophillic in nature and exhibited pH dependent mucoadhesion and swelling properties in aqueous medium. Swelling index increased with increase in PPG concentration but reduced the mucoadhesive strength of the films.

Conclusion: The CAG possessed good film-forming and mucoadhesive properties. It can be used as a coating agent for sustained release, pH dependent and mucoadhesive and topical drug delivery system.

Keywords: Mucoadhesive, Plasticizers, *Ex vivo*, Film - forming

INTRODUCTION

Polymers with film-forming properties have been employed in tablet coating, nano/microencapsulation, dermal and other drug delivery systems. Several film-forming polymers have been employed as coating agents for aesthetic, protective and control of drug delivery (Reddy and Shurwaika, 2000; Derar, *et al*., 2004; Akhgari, *et al*., 2006; Felton, 2013). The use of film forming materials as coating on medicines, in controlled drug delivery and as packaging materials has stimulated several studies towards the evaluation of the film - forming potential of many polymers (Morkhade, *et al*., 2007; Panda *et al*., 2008; Umeka and Yeole, 2008). The general properties of film-forming materials include; good wetting and binding of the particles to be dispersed in the film and good surface adhesion. It should also exhibit rapid drying in a thin layer within a few minutes to 24 hr at 15° – 200°C, form strong moisture - and gas-resistant films with good mechanical strength and must be able to withstand stress and prolonged action on the surface applied. In many cases, these properties are obtained by combining two or more film-forming materials or by the introduction of plasticizers (Gol'dberg, 2010; Panda, *et al.,* 2014). Natural (biopolymers) and synthetic polymers have wide applications in pharmaceutical sciences ranging from the preparation of simple dosage formulations to the design of complex drug delivery systems (Wu, *et al*., 2005; Onishi, *et al*., 2007; Carien, *et al*., 2009). Biopolymers have gained attention and are often preferred over synthetic polymers because they are less expensive, non-toxic, readily available, biocompatible, biodegradable and amenable to chemical modification to provide tailor-made materials for drug delivery system (Bharadwaj, *et al*., 2000, Varshosaz, *et al*., 2006; Kumal, 2008).

Many plant - derived biopolymers such as inulin, pectin, copal gum, *Moringa oliefera* gum and rosins have been evaluated for their film-forming potential and possible application in drug delivery systems (Satturwar, *et al*., 2003; Akhgari, *et al*., 2006; Shurwaika, *et al*., 2008; Ravi, *et al*., 2008; Panda, *et al*., 2008). As a contribution to the research in the field of plant derived biopolymers, an attempt was made to evaluate the film-forming and mucoadhesive properties of a novel biopolymer gum obtained from the pods of *Cola accuminata*, otherwise known as *obi* (Yoruba), o*ji* (Ibo) and *gworo* (Hausa).

Cola nut (cola spp), a genius of about 125 species (family *Sterculiaceae*), is native to the tropical rain forest of Africa, In Nigeria, *Cola accuminata* is a very common species usually cultivated in commercial quantity in the western part, widely chewed in the northern part and used for traditional ceremonies in the eastern part of the country. The seeds of *Cola acuminata* contain xanthine derivatives such as caffeine, theophylline and theobromine. The pharmacological effects of cola nut seeds include stimulation of central nervous system and gastric acid secretion. It is also a weak diuretic and possesses positive chronotropic, analeptic and lipolytic properties. Cola preparations were once used to treat migraine, neuralgia, nausea, physical and mental exhaustion. Cola pods (fruits) are the chambers that contain several cola nuts seeds; each of the pods can weigh up to 3 kg (Cleversley, 2002) While *Cola acuminata* seeds are of great economic value, the pods are obviously waste products usually thrown away after opening to remove the seeds. Information about the evaluation of biopolymer gum from the *Cola acuminata* pods have not been reported yet. Thus the objective of this study was to evaluate the physico-mechanical and mucoadhesive properties of films formed from the biopolymer gum for its potential application in mucoadhesive drug delivery systems.

METHODOLOGY

Materials

Two brands of commercially available uncoated, immediate release (IR) aspirin tablets were obtained from a retail pharmacy at Yenagoa, Bayelsa State, Nigeria. The tablets were within their shelf life and the labelled amount of drug substance for each brand is the same (300 mg). The primary and secondary packages were well examined to ensure the physical integrity of the products.The tablets were coded P (Plain aspirin tablet), S (Soluble aspirin tablet).

Twenty tablets from each brand were embedded in 3 g of freshly prepared food bolus (eba), a starchy staple food made from cassava flour and labelled PB (Plain aspirin tablet embedded in food bolus) and SB (Soluble aspirin embedded in food bolus).

Acetate buffer of pH 4.5 was used as the dissolution medium. The buffer solution was prepared by mixing 29.9 g of sodium acetate (Sigma-Aldrich, UK) with 16.6 mL of glacial acetic acid (Sigma-Aldrich, UK) and sufficient distilled water to produce 10 litres. Aspirin USP fine crystals (BDH, England) was dissolved in acetate buffer to make a series of solutions with different concentrations to develop a standard calibration graph using UV spectrophotometer (Spectronic 21, Milton Roy, USA) at 265 nm. All other materials used were of high analytical grade.

Materials and Method

Materials

The CAG was extracted from *Cola accuminata* pods. Cola nut pods containing cola nuts/seeds were purchased from the local market in Elele, Rivers State, Nigeria. The pods were cut open and the seeds were removed and identified in the Department of Pharmacognosy, Faculty of Pharmacy, Madonna University, Elele Campus, Rivers State and a voucher specimen was deposited in the Department. Analytical grade of glycerin (S.D. fine chemical, Mumbai), propylene glycol (Anglia Chemical, Suffolk), Acetone (BDH chemical ltd, England) and distilled water were obtained from suppliers and used without further modifications All other materials, solvents and reagents were of analytical grade and were used as such.

Method

Extraction of CAG

Freshly harvested cola nut pods were washed thoroughly with distilled water and then sliced into smaller pieces. A 2 kg quantity of the sliced pods was weighed and soaked in 5 liters of distilled water containing 0.1 % w/v sodium metabisulphite. The container was covered with a lid and left undisturbed for 24 hr after which the viscous mucilage produced was separated from the pods by passing it through a muslin cloth. Acetone was used to precipitate the cola gum from the viscous mucilage. The ratio of the quantity of acetone to gum mucilage is 3:1. The quantity of acetone used was to ensure complete extraction of the gum from the mucilage. The precipitated gum was washed repeatedly with more acetone to remove the remaining water until the gum became brittle. It was later dried at 60 ^{o}C for 1 hour. The dried mass was pulverized to fine powder and passed through sieve 150 µm and stored in an air tight amber coloured bottle.

Preparation of CAG Films

The CAG mucilage (10 % w/v) without plasticizer was prepared using aqueous dispersion method. Ten gram of the gum powder was dispersed in a small quantity of distilled water by trituration with the aid of mortar and pestle for 10 minutes. More distilled water was added gradually followed by trituration until the volume was made up to 100 mL The mucilage was allowed to equilibrate for a period of 24 hr. Twenty mL of the mucilage was transferred into a petri dish (diameter of 8.5 cm) to cast the film; it was allowed to dry in a hot air oven at 60 ^{o}C for 12 hr. Other batches of 10% w/v CAG mucilage (20 mL) containing plasticizers - PPG) or glycerin (G) at different concentration of 1 - 3% v/v of the mucilage as shown in Table 1 were also prepared using the same method.

Table 1: Components and Physical Features of Different Batches CAG films

Components of the films (ml)	CAG mucilage (10 %w/v)	Plasticizers (PPG)	Plasticizers (G)	Texture after drying	Colour	Odour	pH
F1	20	-	-	dry and brittle	brown	odourless	-
F2	20	0.2	-	smooth and flexible	brown	odourless	5.35 ± 0.15
F3	20	0.4	-	smooth and flexible	brown	odourless	5.39 ± 0.04
F4	20	0.6	-	wet and tacky	brown	odourless	-
F5	20	-	0.2	wet and tacky	brown	odourless	-
F6	20	-	0.4	wet and tacky	brown	odourless	-
F7	20	-	0.6	wet and tacky	brown	odourless	-

Evaluation of Physical Properties of CAG Films

Organoleptic and physical texture

After 24 hours of drying, the films were assessed for organoleptic properties (colour and odour) and physical texture such as smoothness, flexibility, crack and tackiness. Two batches of films; F2 and F3 (containing 1% v/v and 2% v/v of PPG respectively) showed satisfactory physical features of smooth appearance and flexibility without crack and tackiness. These two films were further subjected to other evaluation parameters.

Microscopic Study

Film F2 was placed on a glass slide and covered with a cover slip. The slide was mounted and made static on a Motic DMWB2-223 digital microscope fitted with 1/3 CCD camera imaging. A digital image of the film was captured using Motic Images 2000 (1.3 Version) image analysis software. The same procedure was repeated for F3.

Moisture sorption studies

The films were exposed to different relative humidity (RH) conditions at room temperature of 25 ^{o}C. The moisture contents of the films were determined to evaluate their sensitivity to moisture under different RH conditions. The method described by Mahmud, *et al.* (2008) was adopted. The films from batch F2 was cut into 2 cm x 2 cm strips and dried at 60 ^{o}C in a hot air oven for one hour and thereafter transferred into a glass desiccator containing calcium chloride at 40^{o} C for 24 hours. This was done to remove moisture from the films. The film strips were removed from the desiccator, the weight (W_1) was accurately measured. The strips were then placed over saturated sodium chloride solution in a glass desiccator to maintain high relative humidity condition (75 % RH) at the room temperature of 25 ^{o}C for a period of 5 days to enhance moisture gain by the films. The film strips were removed and the weight (W_2) was determined after the fifth day. Thereafter, the film strips were transferred into another desiccator containing activated silica gel (desiccant) to maintain dry relative humidity for another 5 days to facilitate the loss of moisture previously gained by the films. The samples were removed again and the new weight (W_3) was determined. Triplicate measurements were made and the average values recorded. The same procedure was repeated for F3 samples. Percent moisture absorbed (% M.A.) under various RH conditions was calculated using the following equations:

$$\% \text{ M.A. under 75\% RH} = \frac{W2 - W1}{W1} \times 100 \ldots\ldots (1)$$

$$\% \text{ M.A. under desiccant} = \frac{W3 - W1}{W1} \times 100 \ldots\ldots (2)$$

Surface pH of CAG films

The pH of the surface of film F2 was determined using an Oaklon pH meter (Model 1100). The method of Prabu, *et al*. (2011) was adapted. The pH meter was set to neutral (7.4) at a room temperature of 25 ^{o}C. The film was cut into 2 cm x 2 cm strips. Each strip was allowed to swell in a closed petri dish containing 10 mL of distilled water for 1 h. The swollen film was removed and placed directly under and in contact with the electrode of the pH meter and the surface pH of the film was determined at a room temperature of 25 ^{o}C. Triplicate measurements were

made and the average values recorded. The same procedure was repeated to determine the surface pH of film F3

Swelling property of CAG films

To investigate the swelling property, 2 cm x 2 cm film strip were cut from F2 and dried in an oven at 60 ^{o}C for 24 hours. The dried film was accurately weighed and immersed in a beaker containing 250 ml of buffer solution (pH 1.2) at 37$\pm$ 2 ^{o}C. The swollen film was withdrawn from the medium and weighed after removal of excess surface water by light blotting with Whatman paper. (Akhgari, *et al*., 2006; Rafiee –Tehrani, *et al*., 2007). Sampling was done at 15, 30 60, 90 and 120 and 150 minutes. The same procedure was repeated using phosphate buffer solutions of pH 7.2 and 9.2. The swelling index, Is (%) in various pH media was calculated as follows:

$$Is\ (\%) = \frac{Ws - Wd}{Wd} \times 100 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

W_d is the weight of dry film and W_s is the weight of film after swelling (Blanchon, *et al*., 1991). All experiments were carried out in triplicate and the average values recorded. The same procedure was repeated to determine the swelling index of film F3

Evaluation of Mechanical Properties of CAG Films

Stress-strain test

The method of Prabu, *et al.* (2011) was adapted to evaluate the films for stress-strain parameters using Instron Universal Tester instrument (Model 3369). The film F2 was cut into six strips of 2 cm x 5 cm and the thicknesses measured. All the strips employed for the test were free of any physical deformity. The film strips were mounted between the 2 clamps (grips) of the machine. The initial gauge length (distance of separation between the clamps) was set at 20 mm. The strips were pulled apart by moving the top clamp at cross head speed (CHS) of 10 mm / min at 50 % RH and 25 ^{o}C. The movement of the clamp continued until the film strips broke. At the break point, the stress - strain parameters such as tensile strength, percent (%) elongation and Young's modulus were determined for each film specimen. Only the results for the film strips that broke in between the clamps were considered while the results for the films that broke at the clamp grip site were rejected. The measurements were done in triplicate and the average values recorded. The same procedure was repeated for F3.

Folding endurance test

Folding endurance was determined to evaluate the ability of the films to withstand folding stress. This was carried out using the method of Giradkar, *et al.* (2010). A strip of 5 cm x 5 cm was cut from film F2. This strip was manually folded repeatedly at the same place till it breaks or survives folding up to 300 times which is considered a satisfactory property for a good film. The films were conditioned at 50 % RH and 25 ^{o}C for 24 hours before testing. The same procedure was repeated for F3.

Evaluation of *Ex vivo* Mucoadhesion of CAG Films

The *ex vivo* mucoadhesive strength of CAG films was determined using Instron Probe Tack Tester (Model 5569). The instrument is made of a probe with an automated force gauge attached underneath. There is a moveable annular weight above the probe which controls the applied pressure when lowered on the probe. Freshly excised gastric and intestinal mucosal of sheep obtained from a local slaughter house were employed in this study. The gastric mucosal membrane was washed with distilled water and then with simulated gastric fluid (SGF) of pH 1.2 at 37 ^{o}C. The gastric mucosa was attached on the top of the flat surface of the probe (25 mm diameter) while the film F2 (5 cm x 5 cm) was attached to the lower part of the annular weight with cyanoacrylate glue. The exposed surface of the film was hydrated with SGF for 30 seconds to facilitate initial hydration and swelling. The annular weight was then slowly moved downwards so that the attached film at the lower part was brought in contact with the gastric mucosal membrane on the top of the probe. A preload of 5 g was applied by the annular weight for 5 minutes to achieve maximum contact area and adhesion between the film and the mucosa tissue. After the contact time of 5 minutes, the film was detached from the mucosa surface at the fixed velocity rate of 0.1 mm per second. The weight required to detach the probe from the film at the fixed velocity rate was recorded as tack and expressed in gram (g) on the automated force gauge attached to

the probe. The experiment was conducted in triplicate and the mean value was recorded. This experiment was similarly repeated using intestinal mucosal membrane and simulated intestinal fluid SIF (pH 7.4) as the hydrating fluid. The same procedure was repeated for F3.

The weight (g) required for detachment of the film from the mucosal membrane was taken as a measure of mucoadhesive strength. Consequently, the bond strength (weight of detachment per area) was calculated from the mucoadhesive strength, using the equation below:

Weight of detachment per area (g/cm^2) = Mucoadhesive strength (g)

Contact surface area (cm^2) ....……..… (4)

RESULTS AND DISCUSSION

Physical Properties of the CAG Films

Organoleptic and physical texture

As shown in Table 1, all the films were brown in colour and odourless. The plasticizer - free film F1 was dry and brittle, and broke when folded. Films F2 and F3 (containing 1% v/v and 2% v/v PPG respectively) showed satisfactory features of smooth appearance, flexibility without crack and tackiness. Other films such as F4 (containing 3% v/v PPG) and F5 – F7 (containing 1% v/v - 3% v/v glycerin respectively) remained wet and tacky. Therefore, films F2 and F3 with acceptable preliminary physical properties were subjected to further evaluation and characterization. The dryness of F1 might be as a result of inadequate quantity of the plasticizers, while excess quantity of plasticizers might account for the wetness and tackiness of F4 – F7. Optimum quantity of plasticizer is required in the formation of films with satisfactory physical textures (Gol'dberg, 2010; Prabu, *et al.*, 2011).

Microscopic Study

Photomicrographs of films F2 and F3 as shown in Figures 1 and 2 respectively, revealed the surface morphology of the two films to be smooth. It is an indication of uniform distribution of the polymer molecules in the films. This further substantiated the smooth appearance of the films as observed visually.

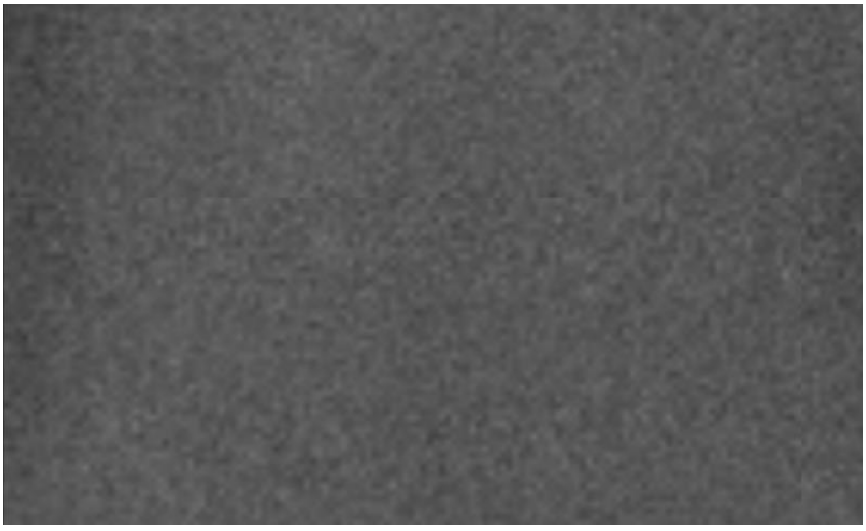

Fig 1: Photomicrograph of film F2 containing 1% v/v PPG

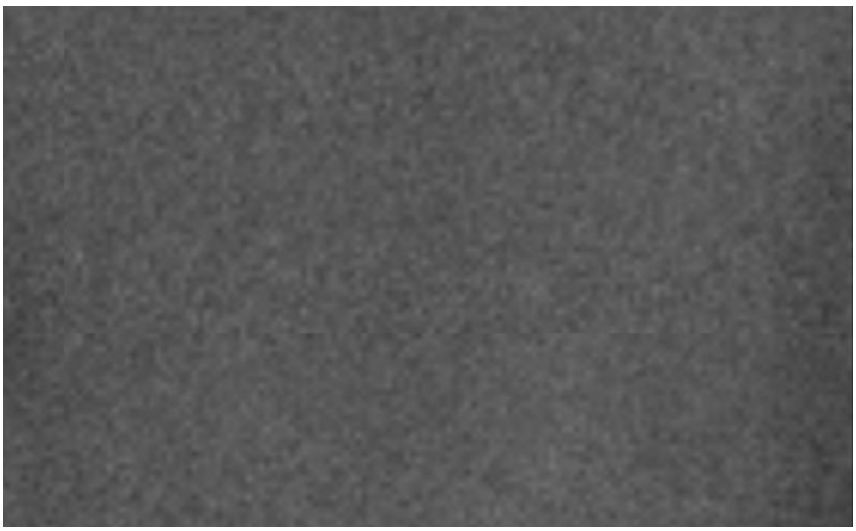

Fig 2: Photomicrograph of film F3 containing 2% v/v PPG

Moisture sorption

According to Table 2, the films absorbed appreciable quantity of moisture when exposed to high relative humidity (RH 75%) and lost the moisture absorbed when transferred to a desiccant environment. Even though there were moisture gain and loss by the films under different RH conditions, there was no significant change in the physical appearances of the films. Moisture absorption of the films indicated the hydrophilic nature of the CAG. Increase in the amount of propylene glycol – a hydrophillic plasticizer in F3 increased the moisture absorption capacity of the film. It can then be assumed that the nature of cola gum and the amount of the plasticizer contributed to the moisture absorption capacity of the films. Therefore, CAG films or any dosage form containing the gum should be well kept in air tight containers to preserve its quality and integrity, just like other hydrophilic natural gums. The result obtained is similar to other study where it was observed that hydrophilic plasticizer – polyethylene glycol 400 enhanced moisture absorption of film from *Moringa oleifera* gum. (Panda, *et al*., 2008).

Surface pH and skin irritation

The surface pH of CAG films was determined in order to evaluate the compatibility of the films with the skin; this is to avoid the potential of causing any irritation when used in the formulation of dermatological preparations. A substance with acidic or alkaline pH may cause irritation to the skin. It is assumed that product with a pH similar to that of healthy skin will be safe and most comfortable to the skin. The pH of human skin has a broad range from pH 4.0 to 7.0 (Lamber, *et al.*, 2006). The pH of CAG F2 and F3 were found to be 5.35 $\pm$ 0.15 and 5.39 $\pm$ 0.04 respectively which are within the acceptable pH range for human skin and therefore, may be considered suitable in the formulation of dermal patches (Parsons, *et al.*, 2005).

Swelling Index CAG films

Structurally, hydrogel polymers can be divided into two major groups: ionic and non-ionic. Ionic polymers can be categorized into anionic or cationic. Unlike non-ionic polymers, the physicochemical properties of ionic polymers such as swelling index, viscosity and bioadhesion are greatly and significantly affected by the pH (ionic strength) of the environment in which such polymers are subjected.The swelling of the ionic hydrogels is hindered when exposed to an unfavourable pH environment where the entropy-driven swelling process and ionization is hindered. In a favourable pH environment, ionization occurs leading to increase in the osmotic and electrostatic forces within the hydrogel structure thus, making the ionic hydrogel to swell appreciably and occupy more space of the surrounding. This makes some ionic hydrogels to be suitable for pH dependent drug delivery systems. (Florence and Attwood, 2006; Omidian and Park, 2008). The swelling and viscosity of anionic

hydrogels increase when the pH of the medium changes from acidic to alkaline. (Soppimath, *et al*., 2001).

Table 2: Moisture sorption studies CAG films at 75 % RH and desiccant environments

CAG films	% moisture absorbed at 75 % R.H. and desiccant conditions (n = 3± SD)	
	75% RH	Desiccant
F2	80.60 ± 5.02	0.00
F3	85.15 ± 3.53	0.00

Note: F2 is CAG film with 1 % v/v PPG, F3 is CAG film with 2 % v/v PPG

Many polysaccharides are neutral but most plant gums are acidic, because they are essentially, polyuronides consisting of sugar and uronic acid (Choudhary and Pawar, 2014). The pH of CAG films (5.35± 0.15 and 5.39± 0.04) is slightly acidic in nature as shown in Table 1. Slightly acidic polymers such as xanthan, pectin, alginic acid, polyacrylic acid are anionic polymers that ionize in alkaline pH to become negatively charged. (Reza, *et al*., 2003; Andrew, 2009). The swelling property of CAG films in different phosphate buffer media are presented in Fig 3. The swelling index was pH dependent and followed the order of pH 1.2 < pH 7.2 < pH 9.2. In this case, ionization of CAG was hindered in acidic medium while alkaline medium favoured its ionization thereby enhancing its swelling in higher pH media. The higher the degree of ionization the higher the swelling profile, this may be the reason why the films have the highest swelling profiles in pH 9.2. The possible mechanism of drug release from CAG film may be swelling dependent. Therefore, CAG film may have the potential to be used as a coating for pH dependent, enteric and colon targeted drug delivery system. Copal gum, another plant derived natural polymeric gum investigated had shown a similar characteristic (Umeka and Yeole, 2008). Furthermore, increase in the concentration of the plasticizer from 1 % v/v to 2 % v/v increased the swelling property of the films because of its hydrophilic nature which can facilitate water uptake into the film to enhance its swelling ability.

Mechanical Properties

The results of the mechanical properties of the films evaluated are presented in Table 3. The films were conditioned at 50 % RH which is the optimum (controlled) RH and 25 ^{o}C for stress-strain and folding endurance tests. This is because of the sensitivity of the films to moisture in order to prevent loss or gain of moisture by the films and to maintain the physical integrity for accurate results.

Stress-strain test

The thickness of F3 (0.15 mm) was slightly but not significantly higher ($p > 0.05$) than that of F2 (0.17 mm), indicating that difference in the plasticizer's concentration did not have a significant impact on the film thickness (Table 3).

Tensile strength is the maximum stress that is applied to a point at which the films breaks Panda, et al., 2014. Tensile strength is an indicator for hardness of a substance while percent elongation and Young's modulus are indicators for its flexibility and elasticity. The tensile strength of F2 (0.49 MNm^{-2}) was significantly higher ($p < 0.05$) than the value for F3 (0.29 MNm^{-2}) Similarly, the % elongation (36.60) and Young's Modulus (0.307) for F2 were significantly lower ($p < 0.05$) than the values for F3 (63.56 and 0.523 respectively). Therefore concentration of plasticizer significantly influenced the mechanical properties of the two films. This shows that increase in the plasticizer content led to an increase in film flexibility with a corresponding decrease in hardness.

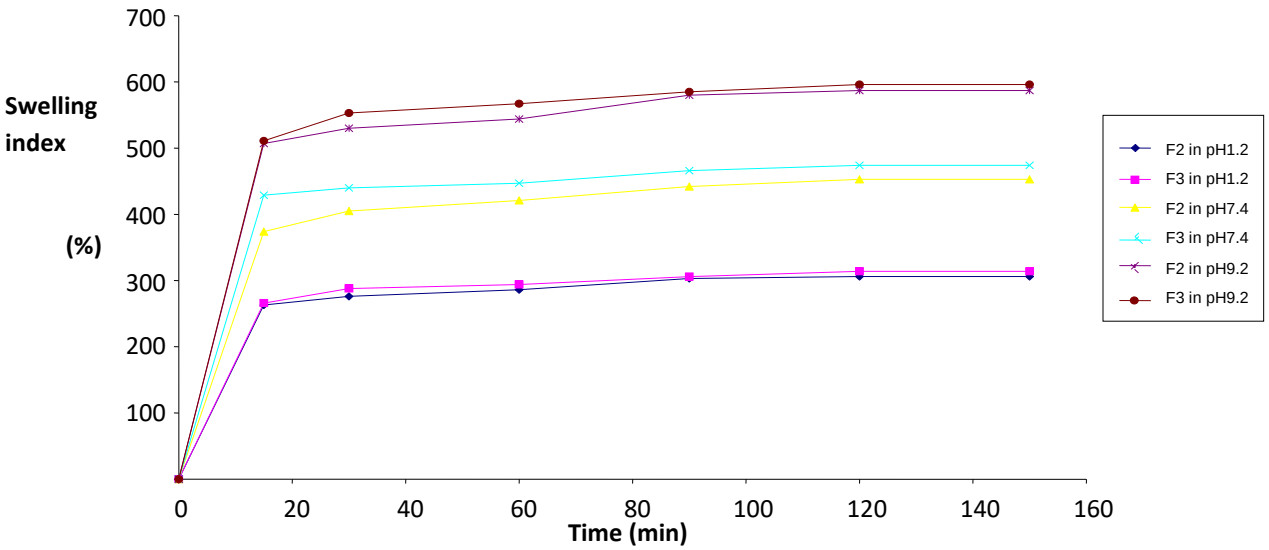

Fig 3: Swelling index profiles of CAG films in different pH media
Note: F2 is CAG film with 1 % v/v of PPG; F3 is CAG film with 2 % v/v of PPG

Polymeric films used as a coating material must possess acceptable tensile strength that can withstand stress to prevent breaking during manufacturing, transportation and storage. It must also be flexible and elastic to provide smooth and effective coating devoid of cracks around the coated drug (Gol'dberg, 2010; Panda, et al., 2014). The two films F2 and F3 exhibited acceptable mechanical properties in terms of smoothness, hardness, elasticity and flexibility required of a coating material necessary for both oral and topical dosage formulations. These results obtained are comparable with that of other polymeric films already investigated (Umekar and Yeole, 2008; Panda, *et al*., 2008).

Folding Endurance

The number of times a film can be folded at the same place without breaking gives a value of the folding endurance (Giradkar, *et al*., 2010). The result shown in Table 3 confirmed that the two films did not break or show any crack even after repeated folding for more than 300 times, this is an indication of good flexibility and malleability. It is a further confirmation of acceptable requirements necessary for films that can be apply as a coating material. This observation was comparable with other polymers with excellent film forming ability (Morkhade, *et al*., 2007; Giradkar, *et al*., 2010). Films with good folding endurance property will not crack when applied as coating on tablets. Moreover such films will be able to withstand frictional stress and absorb energy without abrasion when applied as a dermatological patch for drug delivery on skin (Prabu *et al.*, 2011).

***Ex vivo* Mucoadhesive strength of CAG films**

The use of mucoadhesive films in drug delivery systems is quite important because their attachment to mucosal membranes leads to prolonged retention at the site of application, providing controlled drug release, enhanced absorption and increased concentration of the drug to be delivered to its site of action to elicit improved therapeutic effect. Mucoadhesive performance of a dosage form is multifactorial. Apart from the condition of the mucosal tissue, various physicochemical properties of the polymeric formulation such as molecular weight, viscosity and concentration of the polymer affect the mucoadhesion of a dosage form. The nature, flexibility and spatial conformation of the polymer chain are also essential mucoadhesive factors. Moreover, the degree of ionization of the

polymer, optimum medium pH, optimum hydration of the polymer, formation of hydrogen-bond are also some of the basic properties which a polymer must have to show a good mucoadhesive profile (Roy, 2009; Shaikh, *et al.*, 2011).

Table 3: Mechanical Properties of CAG films

Mechanical Properties	F2 (n = 3+ SD)	F3 (n = 3+ SD)
Thickness (mm)	0.15 + 0.01	0.17 + 0.06
Tensile strength (MNm-2)	0.49 + 0.05	0.29 + 0.03
Elongation (%)	36.60 + 2.03	63.56 + 4.13
Young's Modulus	0.307 + 0.08	0.523 + 0.07
Folding Endurance	> 300	> 300

Note: F2 is CAG film with 1% v/v PPG; F3 is CAG film with 2% v/v PPG

Other factors that may affect mucoadhesion may include the initial force of application. Higher forces lead to enhanced interpenetration and high bioadhesive strength. In addition, the greater the initial contact time between bioadhesive and substrate, the greater the hydration leading to increased swelling and subsequent interpenetration of polymer chains. Based on these factors, mucoadhesive property of a polymer can be tailored by changing the parameters which have the capacity to alter the interaction between the polymer and the mucosal layer (Smart, 2005; Roy, 2009).

The results of mucoadhesion (weight of detachment in g/cm^2) of the films in both media of pH 1.2 and 7.4 are shown in Fig 4. The mucoadhesion of the CAG films in pH 1.2 shows that F2 (3.10 $\pm$ 0.80) was not significantly ($p > 0.05$) higher than F3 (2.72 $\pm$ 0.45). Similarly, the mucoadhesion of the films in pH 7.4 showed no significant difference between F2 (6.38 $\pm$ 1.05) and F3 (5.46 $\pm$ 0.25). However, it was observed that mucoadhesion of the films was pH dependent with values range obtained at pH (7.4) significantly higher ($p < 0.05$) than values obtained in pH (1.2).
Mucoadhesive property of ionic hydrogels is dependent on the presence of functional groups which can ionize. The ionization of the functional group influences the swelling property of the hydrogel depending on the pH of the external medium. (Roy, 2009). Consequently, a direct relationship exists between swelling and bioadhesion of polymers; adhesion occurs shortly after the beginning of swelling. Bioadhesive polymers are able to adhere to or bond with biological tissues by the help of the surface tension and forces that exist at the site of contact but the bond formed between mucosal layer and polymer is not very strong (Giradkar, *et al.*, 2010). Increase in swelling of hydrophilic polymers allows maximal exposure of potential adhesive sites on the polymer necessary for binding with biological tissues. In addition, swelling of polymers leads to polymer chain relaxation leading to increased chain flexibility which is essential for efficient diffusion and penetration of the polymer chain across the interface into the mucosal substrate (Aidoo, 1997; Shaikh, 2009; Soppimath, *et al.*, 2001). The intermingling and entanglement of the chains between the polymer and the biological tissues leads to formation of interpenetrating network of semi-permanent bond. The strength of these bonds depends on the degree of penetration between the polymer and the tissues. The adhesion will increase with increase in hydration until a point where over hydration leads to abrupt drop in adhesive strength due to disentanglement at the polymer/tissue interface (Smart, 2005; Andrew, *et al.*, 2009).

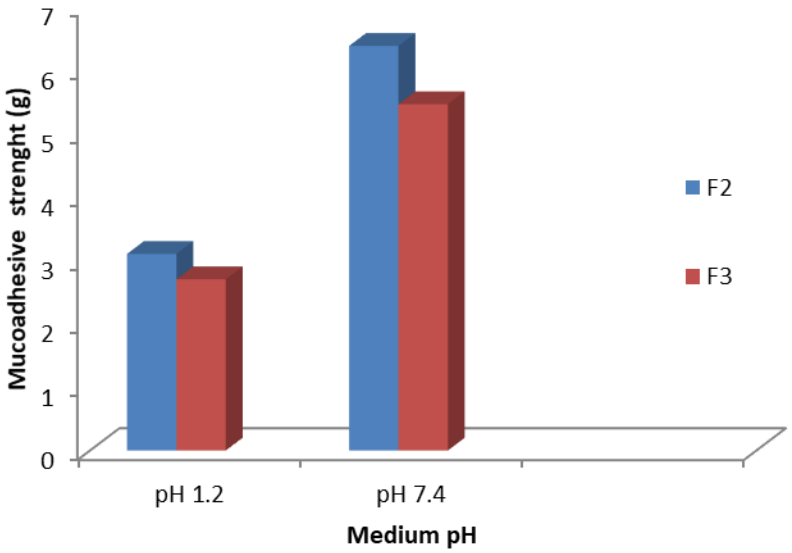

Fig 4: Mucoadhesion of CAG films in pH 1.2 and pH 7.4
Note: F2 is CAG film with 1% v/v PPG; F3 is CAG film with 2% v/v PPG

Since the swelling profiles for the two films are significantly higher in pH 7.4 than in 1.2, therefore, the surface tension, and interfacial adhesion, penetration of polymer chains, formation of interpenetrating network bond and bioadhesion of the matrix tablets will be greater in pH 7.4 than in 1.2. This may be the reason for the pH dependent mucoadhesive property displayed by CAG films. More so, the mucoadhesion values obtained for F3 were slightly but insignificant ($p > 0.05$) lower than the values obtained for F2. The hydrophilicity of propylene glycol used as plasticizer enhanced the rate of hydration. Increase in the amount of propylene glycol in F3 modified its mechanical properties (tensile strength and % elongation) and kinetics of swelling. This phenomenon may contribute to slight decrease in adhesive strength of F3 due to over hydration and decrease in adhesive strength leading to disentanglement at the polymer/tissue interface as a result of erosion of the polymer component (Smart, 2005; Andrew, et al., 2009). Increase in bioadhesion of the films in pH 7.4 can lead to prolong attachment of the CAG films to the intestinal mucosal thereby facilitating enhanced absorption and increased concentration of the drug to be delivered to its site of action to elicit improved therapeutic effect. This positions CAG film as a good coating material suitable for pH dependent drug delivery systems.

CONCLUSION

The CAG films possessed good physical, mechanical and mucoadhesive properties. It may be useful as a coating and encapsulating agent for sustained release, pH dependent, mucoadhesive drug delivery system and as a dermal patch for topical delivery of drugs

RECOMMENDATION

Further works exploiting the use of CAG films as a dermal patch for topical drug delivery and other drug delivery systems may need to be carried out.

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Conflict of Interest: None declared

Received: 10 October, 2017

Accepted: 08 January, 2018