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Effect of pH and ionic strength on the bioadhesive properties of *Prosopis africana* gum

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Abstract

Prosopis gum (PG) extracted from *Prosopis africana* was investigated for bioadhesive properties as affected by pH and ionic strength. The bioadhesive properties were evaluated using the adhesion of gum dispersion-coated glass beads on the antrum region of the porcine gastrointestinal tract and Lecomte Du Nouy tensiometer. Results obtained indicated that prosopis gum is highly bioadhesive and that increase in both ionic strength and pH favour bioadhesion. By implication, PG can be used to target drugs intended to release in the small intestine and that way drugs sensitive to acidic pH, enzymatic attacks in the stomach or those that cause unbearable gastric irritation may be good candidates for bioadhesive drug delivery using *Prosopis africana* as the bioadhesive material.

Keywords: Bioadhesion; Ionic strength, pH, *Prosopis africana* gum.

Introduction

Most biological tissues contain mucosal epithelia covered by mucus. This makes it possible for bioadhesive polymers to interact with such tissues producing the phenomenon of bioadhesion. Glycoproteins present in the mucus are believed to be responsible for interaction between mucus and biopolymers (Nnamani, 2004). However, many factors play a role in bioadhesion (Attama *et al.*, 2003). Many in vitro methods are used to evaluate bioadhesion (Nnamani, 2004) but in vivo evaluation remains the most informative. Indeed, the method of evaluation is generally formulation-specific and many biopolymers have been evaluated for bioadhesive drug delivery (Attama *et al.*, 2000). However, applicability depends on the target area and the physiochemical properties of the candidate polymer. Some physicochemical properties of Prosopis gum (PG) were evaluated to determine their effects on PG bioadhesion. Gums are made up of highly branched polysaccharides with chain structure formed when monosaccharides condense with the elimination of water molecule(s). PG is a natural polysaccharide consisting chiefly of glucose, fructose, galactose and xylose as the monosaccharide units, as determined by thin layer chromatography and complete acid hydrolysis analysis (Attama *et al.*, 2000).

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In recent times, interest has been shown in the use of bioadhesives as controlled release systems for the release of drugs in the buccal or nasal cavity, the intestine or rectum and the urinary bladder (Nnamani, 2004). Bioadhesives could be used to target genetically engineered macromolecules, e.g. growth hormone and interferon used in tumors; also for drugs used to treat glaucoma and motion sickness; for contraceptives and narcotic antagonists; for insulin delivery and immunization (Nnamani, 2004). Semi-solid mucoadhesive dosage forms have been found suitable for the treatment of mouth ulcers because they can be spread as a thin pellicle over a large portion of the mucosa.

Experimental

Materials. Acetone and ethane (M & B, England), Hydrochloric acid, calcium chloride (Merck, Germany) were used without further purification. All other reagent solvents were of analytical grade and were used as supplied. Distilled water was obtained from a glass still while PG was obtained from a batch processed in our laboratory.

Preparation of PG. PG was extracted from the seeds of *Prosopis africana* using the method described in an earlier study (Adikwu, 1994).

Evaluation of the Bioadhesive strength of PG: Use of Coated glass beads. Solutions of increasing concentrations of PG were used to coat glass beads with an average diameter of 3 mm and average weight of 56 mg. The beads were coated to an average weight of 65 mg, by successive dipping in one polymer solution, air-drying and storage in a desiccator until use. Concentrations of PG solutions used for the Study were 3, 5, 8, and 10% w/v. The apparatus designed and used in this study consists of separating funnel clamped to a retort stand with a rubber tube attached at the end of the funnel. A metal support was used to position a plastic support at an angle of 30°. Freshly excised hog jejunum (1.7 x 15.0 cm) was pinned onto the plastic support, and a beaker was placed directly under the plastic support to collect the detached beads. Before coating the glass beads, they were thoroughly cleaned with distilled water and then with acetone to maximize the roughness factor (Attama *et al.*, 1999). Twenty coated glass beads were placed on the exposed mucus surface of the tissue. Mucus-gum interaction and gum hydration was allowed to take place over a period of 15 min. Simulated intestinal fluid (SIF) without pancreatin (250 ml) at pH 7.2, contained in the separating funnel, was allowed to flow over the beads at a rate of 30 ml per min until the whole volume (250ml) was finished (8-9 min). The number of undetached beads was noted and used as a measure of bioadhesion. The experiment was repeated five times and the average value recorded.

Use of the Tensiometer.

Preparation of mucin: The mucin solution used for the study was prepared as described elsewhere (Attama *et al.*, 1999).

Bioadhesion experiment: This was performed using a tensiometer (A kruss, Model No. Nr 3124, Germany) adapted to measure bioadhesive strength. The same PG concentrations used in the above-coated experiment were used. A 2 ml volume of the prepared mucin solution was poured into a watch glass, which was placed on a platform of the zeroed tensiometer. The plate on which the aqueous gum dispersion was coated to 2 mm thickness was dried for 5 h in a desiccator and then hung on the lever arm of the tensiometer and the platform gradually moved to establish contact with the coated plate. A 15 min contact time between the gum coat and the mucin was allowed to ensure proper interaction. The glass plate was raised by means of a screw until it just detached from the surface of the mucin. The force required to remove the glass plate from the surface of the mucin was read off from the microform

balance in degrees and conversion of this to tension was done using Equation 1 (Attama *et al.*, 2003). In each case, an average of the determinations was taken.

$$T = MgF/2L \quad \text{----------} \quad (1)$$

[T = tension equivalent to bioadhesive strength; M = mass required to return the lever pointer to its original position; L = perimeter of the plate, F = constant dependent on the perimeter and, g = acceleration due to gravity].

Effect of pH on bioadhesion of PG dispersion. Solutions of pH 2, 4, 8 and 10 were differently prepared using 0.1 N HCl and NaOH solutions. PG dispersion of 3, 5, 8, and 10 % w/v were prepared with these media and allowed to hydrate for 24 h. The various gum dispersions were each coated on glass plate to a thickness of 2 mm. A 2 ml volume of the prepared mucin solution was poured into a watch glass, which was placed on the platform of the zeroed tensiometer. This was done as earlier described.

Effect of ionic strength on bioadhesion of PG dispersion. Different ionic strengths of 0.3, 0.5, 0.8 and 1.2 M % w/v of sodium chloride were prepared and used to make various dispersions of 3, 5, 8 and 10% w/v PG dispersions. These were allowed to hydrate for 24 h. The above procedure was carried out again using a tensiometer.

Results and Discussion

The result of the bioadhesion studies using coated glass beads is shown in Table 1. The bioadhesive concentration is the concentration of gum at which no glass beads detached after having been washed with simulated intestinal fluid (SIF) without pancreatin. Based on that, the bioadhesive concentrations of PG was attained at 8% w/v. The differing values of resistance to washing of the coated glass beads may be due to differences in the strengths of the gel network of the gum dispersion (Attama *et al.*, 1999). Bioadhesive materials have been identified as being hydrophilic macromolecules containing numerous hydrogen bond- forming groups, hence favouring bioadhesion (Attama *et al.*, 2003). However, the mechanism of gum-mucus interaction may be due to mechanical interlocking or penetration of the mucus via a viscous flow into the microdefects of the gum surface.

The result of the tensiometric determination of the bioadhesive interaction confirmed those of the bioadhesion assay using coated glass beads (Table 1). PG dispersions showed very high bioadhesive strength. This may be due to long contact time between the gum and the mucus since increase in contact time favours bioadhesion provided excessive swelling leading to over-hydration does not occur (Adikwu *et al.*, 2005). The pH determines solubility, stability, viscosity and the ease of absorption of drugs from the gastrointestinal tract into the blood. However, as the pH increased from 8 to 10, an increase in bioadhesive strength was observed (Fig. 1). This implies that PG can be used as a pH sensitive polymer to coat drugs that are favoured by alkaline pH (Attama *et al.*, 2000). Thus, the polymer hydrates after passing the stomach to allow the bioadhesion to take place, a process similar to the disintegration of capsule shell in microencapsulation. PG can, therefore, be used as the bioadhesive material for entero-bound drugs that are sensitive to acidic pH, enzymatic attack in the stomach or those that cause unbearable gastric irritation or erosion provided the physicochemical properties of the intended drug allow for these conditions. Fig. 1 also reveals a direct relationship between bioadhesive strength and ionic strength. The correlation coefficient was unity approximately. The change in the concentration of ions inside the polymer and the change in swelling that preceded bioadhesion were highest in the 10 %w/v dispersion and least in that of 3 %w/v. One of

the most remarkable, and useful, features of a polymer's swelling ability manifests itself when that swelling can be triggered by a change in the environment surrounding the delivery system (Nnamani, 2004). Depending upon the polymer, the environmental change can involve pH, temperature, or ionic strength, and the system can either shrink or swell upon a change in any of these environmental factors. Because many of the potentially most useful pH-sensitive polymers swell at high pH values and collapse at low pH, the triggered drug delivery occurs upon an increase in the pH of the environment. Such materials are ideal for systems such as oral delivery, in which the drug is not released at low pH in the stomach but rather at high pH.

Conclusion

Prosopis gum has demonstrated good bioadhesive properties sensitive enough to the tested stimuli of pH and ionic strength which showed a direct relationship with each other. PG was more bioadhesive in alkaline pH which is suggestive of the fact that it can be a good bioadhesive polymer for drugs intended to release in the intestine.

Table 1: Bioadhesion test

Concentration (% w/v)	Percentage of glass beads undetached (mean ± S.D)	Bioadhesive strength (N M^{-1}) (Mean ± S.D)
3	90 ± 0.11	22.81 ± 0.71
5	90 ± 0.21	38. 51 ± 0.31
8	100.0	40.78 ± 0.20
10	100.0	42.50 ± 0.31

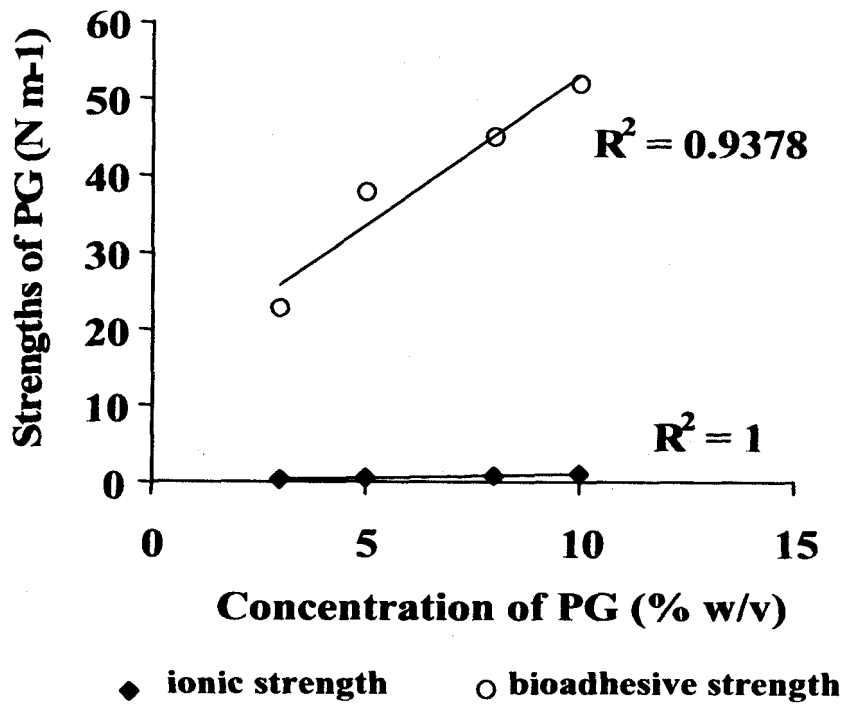

Fig 1: Relationship between ionic and bioadhesive strength of PG

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