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Evaluation of bioadhesive properties of natural and modified banana starches

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A study was carried out on banana (*Musa paradisiaca*) natural and modified starches (pregelatinised and acetylated), to determine the potential bioadhesive properties of the starches in 0.1M hydrochloric acid and phosphate buffer (pH 6.8) to simulate the stomach and small intestine conditions, respectively using the rotating cylinder method. Starches were characterized using particle size, swelling capacity, bulk density, particle density, angle of repose, viscosity, and fourier transform infra-red spectroscopy, while the mechanical properties were determined using the crushing strength. The bioadhesive property of the starches were not related to the viscosity as the pregelatinised starch which was the least viscous had the longest time of detachment in both media. Physical mixtures of starches with polyvinylpyrollidone increased adhesion time significantly. Pregelatinised banana starch could be useful in the formulation of drugs targeted to the stomach, which when mixed with polyvinylpyrollidone increases adhesion time.

Keywords: Banana starch, pregelatinised starch, acetylated starch, modification, bioadhesion

INTRODUCTION

Bioadhesion, in particular mucoadhesion has been of interest for the development of controlled drug delivery system to improve buccal, nasal and oral administration of drugs. Generally, bioadhesive polymers usually contain hyroxyl or carboxyl groups which help with the formation of hydrogen bonds with the mucosal surfaces. Polymers that have been investigated as bioadhesive drug carriers include polyacrylic acid (PAA) [1], polymethacrylic acid [2], cellulose derivatives [3], polyethylene oxide [4, 5], lectin and chitosan [6]. While PAA and its crosslinked commercial forms, Carbopol® and Polycarbophil®, exhibit strong bioadhesive properties [7], they were found to have severe mucosal irritation properties, which limits their use as bioadhesive drug carriers [8]. Hence there have been attempts in recent times to develop natural polymers as bioadhesive drug delivery systems [9].

Starch is the second most abundant renewable polymer in nature that is inexpensive, fully biodegradable and widely studied for many years in the field of materials. Starch (-$C_6H_{10}O_5$-)n, a combination of amylase and amylopectin, is the most familiar of the natural hydrophilic carbohydrate polymers. Starch may be commercially derived from a variety of common sources such as grain seeds (like maize (*Zea mays* L.), rice (*Oryza sativa* L.), wheat (*Triticum vulgare* L.), plant tubers (e.g. potato (*Solanum tuberosum* L.), cassava (*Manihot esculenta* Crantz)), and plant pith (e.g. sago of the Palmae family). The properties of the starch can vary with both the source and the method of processing.

Starches from various sources, banana inclusive have received extensive attention in relation, to structural and physicochemical properties [10]. Natural starch is a good texture stabilizer and regulator in food systems [11], but limitations such as low shear resistance, thermal resistance, thermal

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decomposition and high tendency towards retrogradation limit its use in some industrial food applications. Starch modification which involves the alteration of the physical and chemical characteristics of the natural starch to improve its functional characteristics can be used to tailor starch to specific food applications [12]. Starch modification is generally achieved through derivatization such as etherification, esterification, crosslinking grafting of starch decomposition (acid or enzymatic hydrolysis and oxidation of starch) or physical treatment of starch using heat or moisture. Chemical modification involves the introduction of functional groups into the starch molecule, resulting in markedly altered physicochemical properties such modification of natural granular starches profoundly alters their gelatinization, pasting and retrogradation behaviour [13].

The aim of this study was to evaluate the starch obtained from banana for bioadhesion and to determine the influence of thermal and chemical modification on bioadhesion properties.

MATERIALS AND METHODS

Natural banana starch was extracted from unripe banana (*Musa paradisiaca*) as desribed by Alves *et al.* [14]. The starch was further modified physically by pregelatinisation[15] and chemically by acetylation [16]. Briefly for pregelatinisation, 200g of natural starch sample was dispersed in 200 ml of distilled water and heated with slow mixing until a paste was obtained. The pregelatinized starch obtained was laid on ceramic tiles as a thin film and dried at 100 °C for 24 h. It was then milled into smaller particles and sieved through a mesh with size 0.315 mm and the resulting powder was stored in an air tight container.

For acetylation, 200 g of the sample of the natural starch was weighed into a wide mouth container. Sodium hydroxide (60 ml of 50 %) was mixed into the powder and 100 ml of acetic anhydride added gradually into the mix with thorough mixing. After it had been thoroughly mixed, the mixture was spread on ceramic tiles and dried in the oven for 24 h at 100 °C. The dried lumps were blended, sieved through a sieve of mesh size 0.315 mm and stored in an air tight container.

Determination of the physicochemical properties of starch

Identification test

One gram each of the natural, pregelatinized and acetylated starch were weighed for the banana sample and mixed with 50 ml of water. This was then boiled for one minute and cooled. To 1ml of the mucilage obtained, iodine solution was added and the resultant colour observed.

Swelling capacity

Five grammes of each starch powder (natural, pregelatinized and acetylated) were weighed and transferred into a measuring cylinder. The tapped volume (V_a) occupied by the powders was determined and recorded.

To the 5 g portions, 50 ml distilled water was added and shaken for dispersion. The volume was then made up to 100 ml with distilled water. After 24 h of standing, the volume of the sediment (V_b) was determined and recorded.

The swelling capacity was estimated using the formula:

$$\text{Swelling capacity} = V_a/V_b$$

where, V_a = tapped volume, V_b = volume of sediment after 24 h

Particle size determination

The mean particle size of samples of the natural, pregelatinized and acetylated starch of banana were determined microscopically with the aid of a calibrated eyepiece. The particle size of each sample dispersed in glycerol was determined.

Angle of repose

This was used to measure the flow properties of the natural, pregelatinized and acetylated starch. For this purpose, 10 g of the different powders were poured into an open-ended glass cylinder with its bottom resting on a horizontal surface, the base. On raising the cylinder vertically, the granules flowed out and formed

a conical heap as a result of gravitational forces balancing the interparticulate forces. The side of the heap formed an angle with the horizontal base, known as angle of repose. The height of the cone was measured with the aid of a pair of dividers and a ruler. The angle of repose (θ) was calculated using the equation:

$$\theta = \tan^{-1}h/r$$

where, h= height of conical powder heap,

r= radius of the circular base.

Bulk density determination

The bulk density of the powder bed is simply the weight of the powder divided by the whole volume of the bed.

Ten grams each of the powders were poured inside a measuring cylinder made of glass through a funnel at zero pressure. The bulk volume (V_1) was recorded and the density determined in triplicate.

The bulk density (D_o) was determined using the following equation:

$$D_o = M/ V_1\pi r2h$$

where, M = weight of powder (g), V_1 = volume of powder bed, r = radius of the cylinder (cm), h = height of the powder

Determination of particle density

The particle density of the starch powders were determined by the generic liquid pycnometer method using xylene as the displacement fluid. A 50 ml capacity pycnometer was weighed empty (W), filled with the non-solvent (xylene) and the excess wiped off. The weight of the pycnometer with the non-solvent was determined (W_1). The difference in weight was calculated as W_2. A 2 g quantity of the sample was weighed (W_3) and quantitatively transferred into the pycnometer bottle. The excess non-solvent was wiped off and the pycnometer was weighed again (W_4). The particle density was calculated from the equation:

$$W_2W_3/50(W_3-W_4+W_2+W)\ gcm^{-3}$$

pH of 0.1% w/v solution

A 0.1% w/v solution of the three starches were made and their pH taken using a pH meter (F-21, Horiba Co. Ltd., Kyoto, Japan). The results were then recorded.

Determination of tablet crushing strength

The load required to break the tablet was determined at room temperature using a Newton tablet hardness tester, model EH01 (Mumbai, India). Five tablets, randomly selected, were used from each sample for the test.

Determination of viscosity

The viscosity profiles of the starch materials were obtained using a heating and cooling viscometer, series 3RVA (Rapid Visco Analyser) coupled with Thermocline for Windows software (Newport Scientific Pty. Ltd. Warriewood, NSW Australia). The test proceeded and terminated automatically. Heating of the slurry in the equipment was done uder a constant rate of shear and the increase in viscosity of material was measured as torque on the spindle and a curve was traced [17].

The peak viscosity (maximum viscosity of material) developed soon after the heating portion of the test. Trough viscosity is the lowest viscosity after the peak viscosity just before it begins to increase again. Final viscosity is the viscosity at the end of the test.

Fourier transform infrared (FT-IR) spectral analysis

The Fourier transform infrared (FT-IR) spectra of the films were recorded on an IR Spectrometer (Perkin–Elmer, model 2000, California, USA) in the wavelength range 400–4000 cm^{-1}. To perform FT-IR measurement, 5 mg each of the completely dried powdered starch samples was weighed and then dispersed in 200 mg KBr. The signal averages were obtained at a resolution of 4 cm^{-1}.

Determination of the mucoadhesive properties of banana starch

The rotating cylinder method was used. For this test, the method which can be carried out with a slightly modified dissolution apparatus described in the USP [18]. An intestinal

segment is fixed on a stainless-steel cylinder, the basolateral side facing the cylinder. Then the tablets containing the mucoadhesive polymer are pressed on the apical side and the cylinder is put into a medium containing about 500 ml of buffer medium (pH 6.8) or 0.1N HCl. The rotation speed was about 50 rpm. The time the tablets detach from the mucosa is observed.

RESULTS AND DISCUSSION

The identification test carried out was to further confirm banana as a source of starch, and from the results obtained, a blue black colouration was observed for the natural and modified banana starches.

The swelling capacity test is used to evaluate the degree to which fluid can be held within the starch. From the results (Table 1) it was observed that the acetylated starch had the highest swelling capacity followed by natural starch while the pregelatinized starch had the least swelling capacity. Thus chemical modifications such as acetylation increase the swelling power of banana starch.

The results of the particle and bulk densities of the natural and modified starches are also presented in Table 1. Bulk density is a property of powders and granules and it is defined as the weight of the powder divided by the whole of the bed. From the results obtained, the natural starch had the greatest bulk density followed by acetylated starch and the pregelatinised starch had the least bulk density. Further, the particle density values show that the pregelatinised starch had the highest values and the natural starch lowest.

The angle of repose tests (powder flowability is not a fundamental parameter, unlike particle size or bulk density), is the maximum angle of a stable slope determined by friction. From the results obtained, the natural banana starch had the highest angle of repose, followed by the acetylated starch and the pregelatinised starch had the least angle of repose (Table 1). This implies that the pregelatinised starch is the most free flowing followed by the acetylated starch while the natural banana starch is the least.

The morphology and size distribution of natural and modified starches that were studied showed that the natural banana starch had the largest particle size followed by acetylated starch, while the pregelatized starch had the least particle size, this may be attributed to the effect of the modification. The particles of the starches were generally ovoid to spherical as shown in the photomicrograph presented in figure 1.

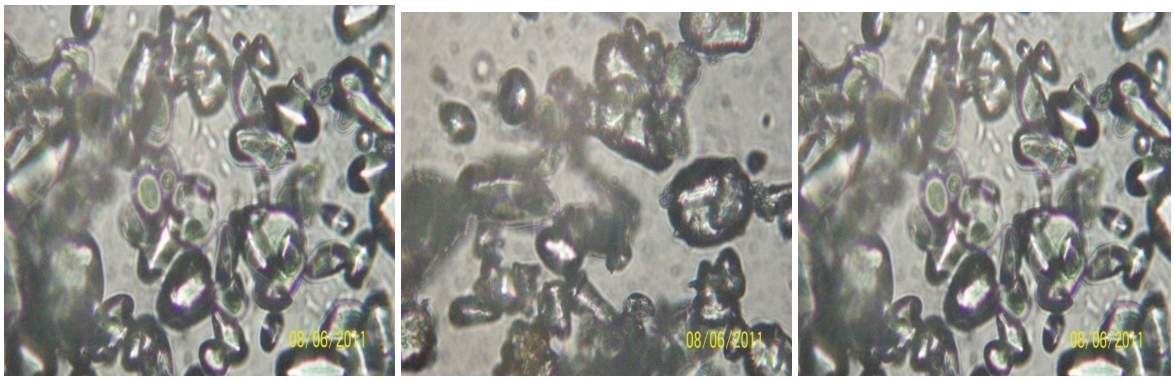
The results of the crushing strenght of the tablets obtained from each starch are given in Table 1. The term crushing strength is defined as the load required causing a solid to fail (or break) by fracture. The results obtained as the crushing strength of the tablets show that the pregelatinised banana had the highest value of 219.8 N followed by natural banana starch 36.5 N.

Using a heating and cooling viscometer, the viscosity of the starches was determined. The peak and breakdown viscosity values are measures of the stability of the starch materials showing the resistance to breakdown of their granules, while the final viscosity is a direct measure of the viscosity of the gel formed after retrogradation. The natural starch exhibited higher values than the modified starches. From the results obtained (Table 2), it was discovered that the natural banana starch had the highest viscosity. This implies that modification of banana starch decreases its viscosity with an increase in rotational speed thereby resulting in shear thinning behaviour [13].

The evidence of acetylation and pregelatinisation was verified by utilizing FT-IR. In the natural banana starch, pregelatinised banana starch and acetylated banana starch the following characteristic peaks; 1635.03 cm^{-1}, 1644.23 cm^{-1} and 1641.17 cm^{-1} (respectively) are attributed to C=0 bond stretching. Another strong broad band due to hydroxyl bond stretching appears at 3650-3200 cm^{-1} for the natural and modified starches. The thermal treatment of starch might have significant effect on the natural banana starch resulting in conformational change.

Table 1: Physical characteristics of natural, pregelatinized and acetylated banana starch

Starch (Banana)	Swelling capacity	Angle of repose (θ)	Bulk density (g/cm^3)	Particle density (g/cm^3)	pH	Crushing strength (N)
Natural	0.56	66.49°	0.538	1.67	5.44	36.5
Pregelatinised	0.42	62.58°	0.448	2.23	4.63	219.8
Acetylated	1.45	63.82°	0.459	1.83	6.13	58.3



(a)…….(b) (c)

Figure 1: Photomicrographs of natural (a), pregelatinised (b) and acetylated banana starches (c)

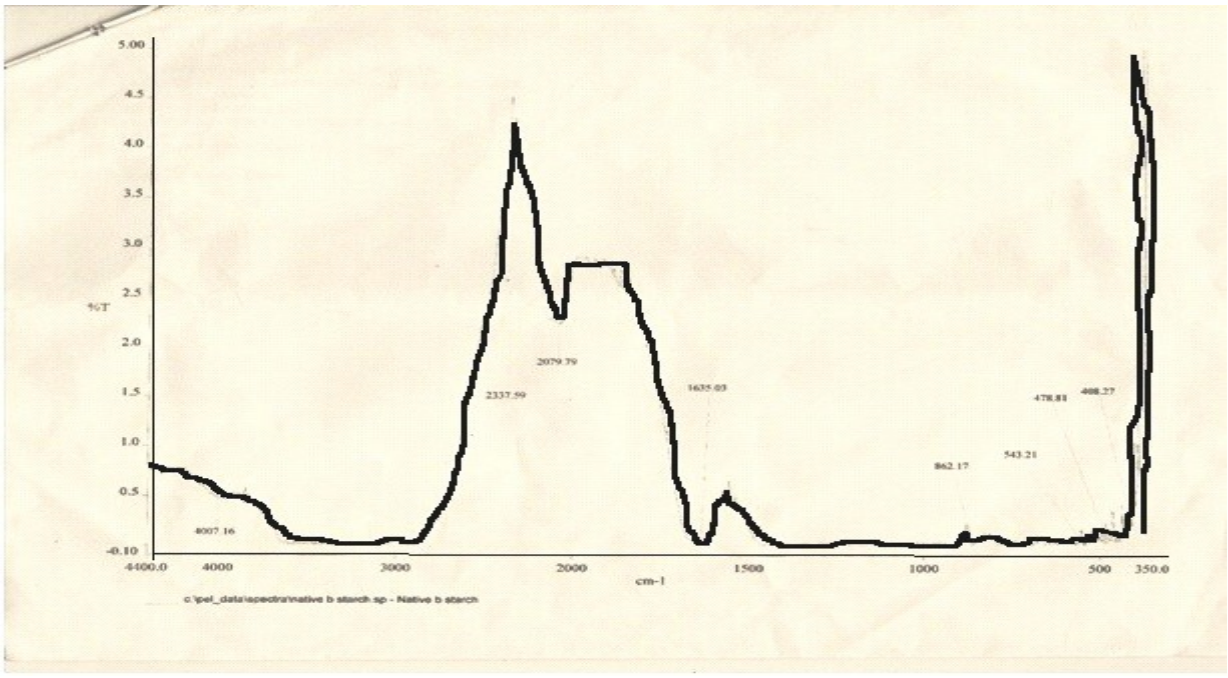


Figure 2: Infra red spectrum of natural banana starch

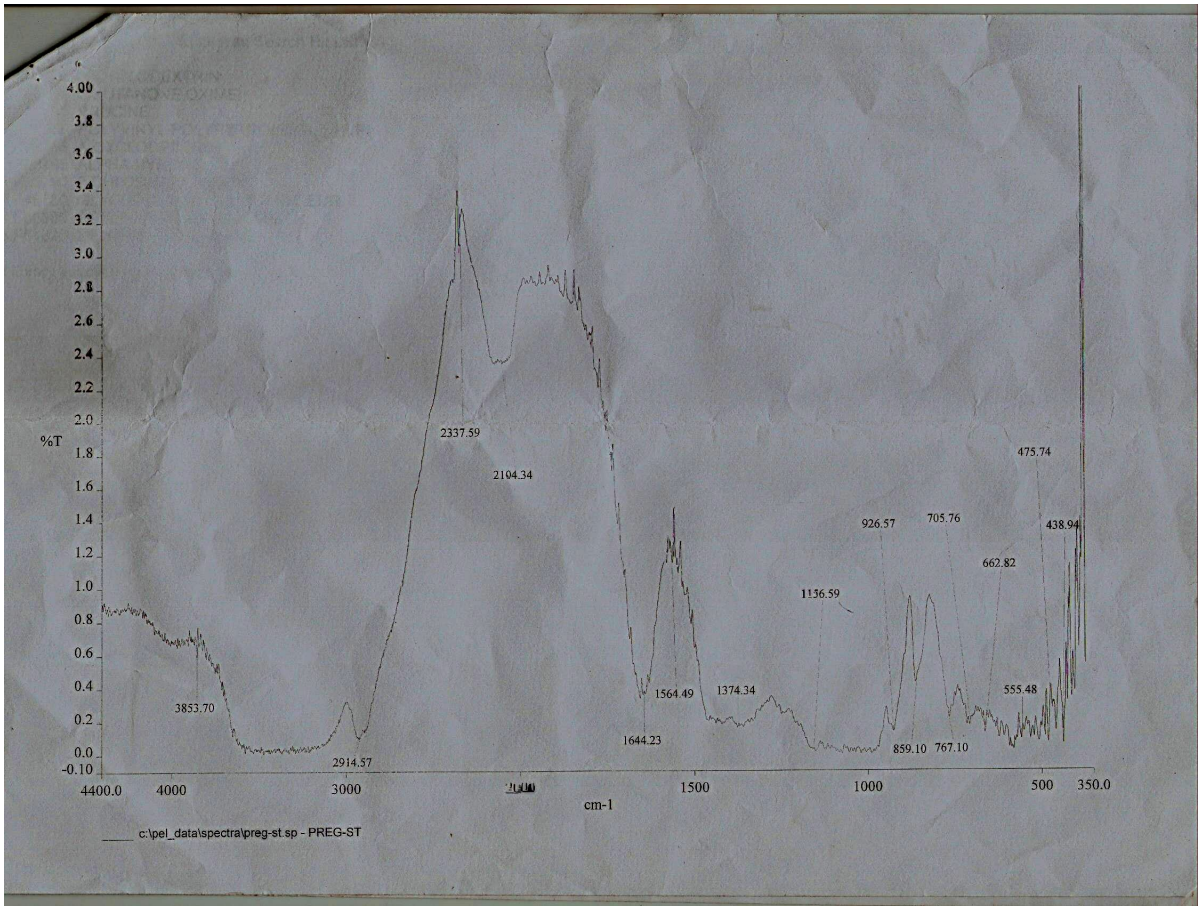


Figure 3: Infra red spectrum of pregelatinised banana starch

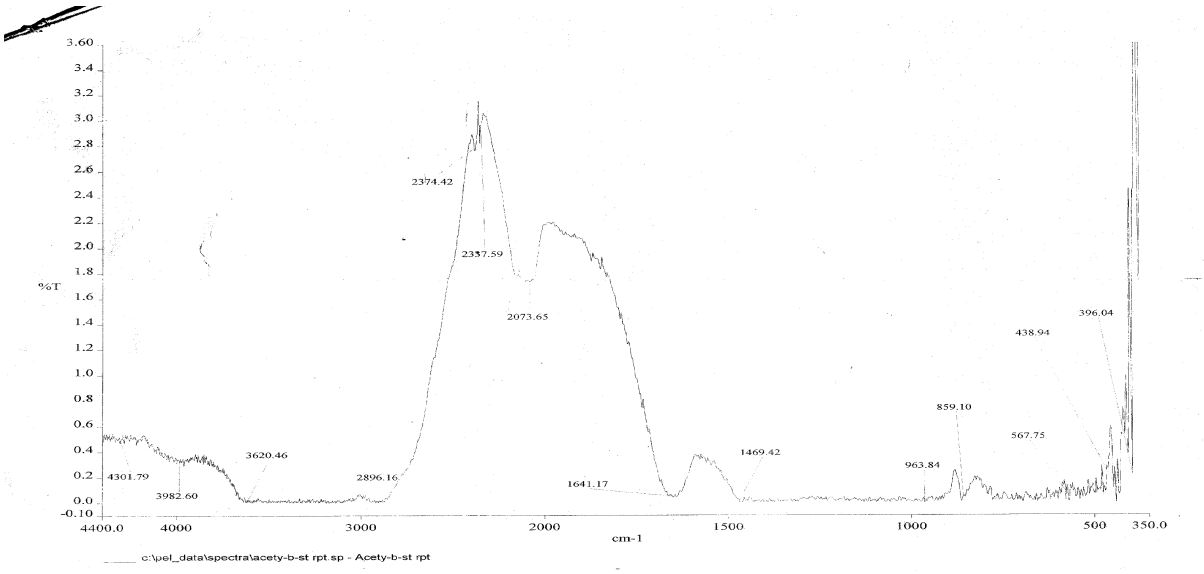


Figure 4: Infra red spectrum of acetylated banana starch

Table 2: Viscosity parameters of natural, pregelatinized and acetylated banana starches

Starch	Peak 1 viscosity	Trough 1	Breakdown viscosity	Final viscosity	Setback	Peak time	Pasting temperature
Natural	348.42	264.58	83.83	442.92	178.33	4.82	82.4
Pregelatinized	244.25	225.25	18.5	356.92	131.17	5.38	83.85
Acetylated	316.58	227.75	88.83	392.33	164.58	4.82	82.35

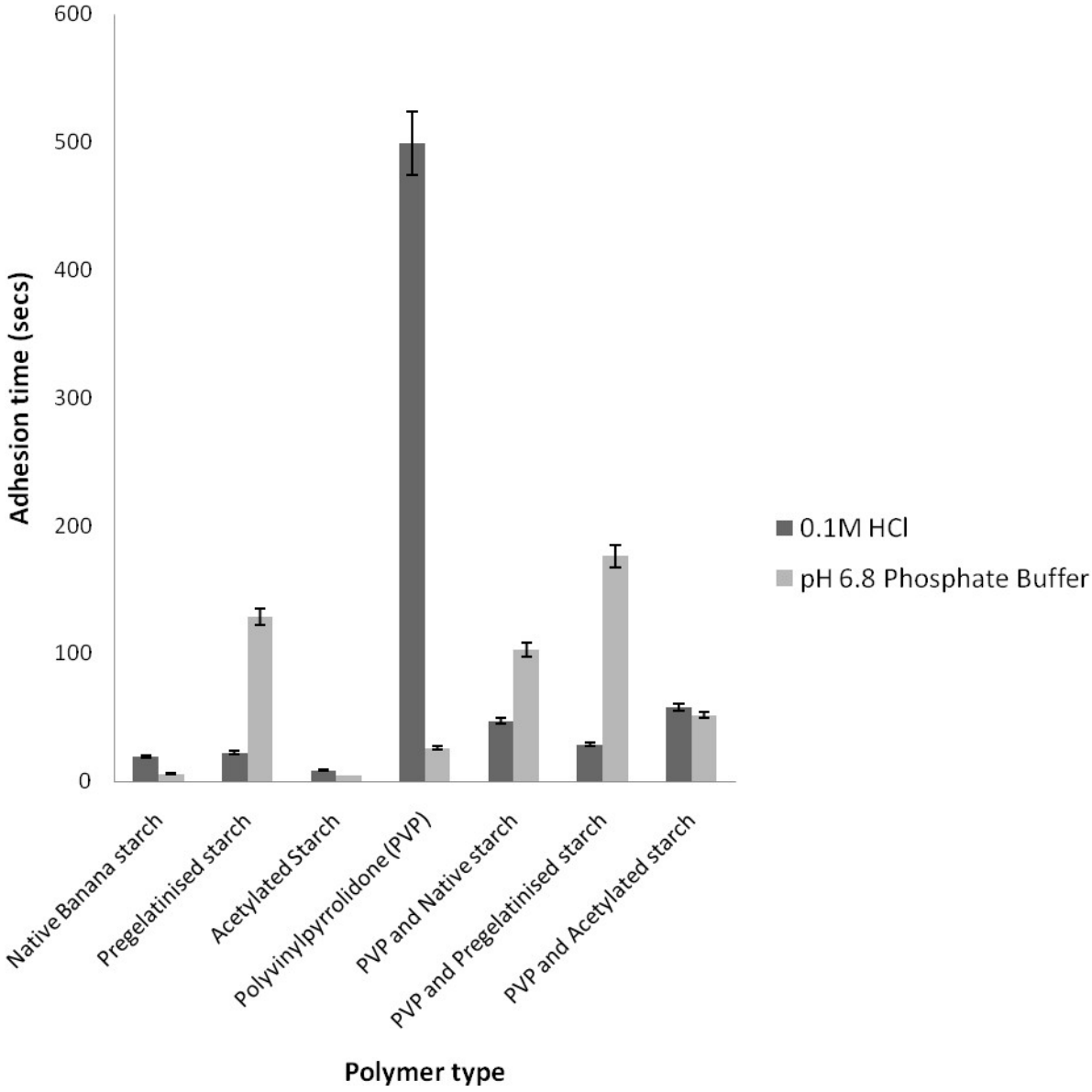


Figure 5: Adhesion time for polymer and polymer combinations in 0.1M HCl and phosphate buffer (pH 6.8).

In the case of the acetylated banana starch, the etherification of the natural starch could be responsible for an increase in the number of the characteristic peaks due to C=O functional group. Overall, the spectra have similar profiles.

The results from the bioadhesive study are given in figure 5. The test carried out shows that in 0.1M HCl solution, the rank order for time of detachment for unmixed polymers was polyvinylpyrollidone (PVP)>> pregelatinised starch > natural starch > acetylated starch. It was observed that the synthetic polymers had the longest time of detachment. In order to prolong the adhesion time for the starches, mixtures of the starches with PVP at 1:1 ratio gave the adhesion rank order PVP/acetylated starch > PVP/natural starch > PVP/pregelatinised starch. The rank order for the time of detachment from the pig's ileum for the unmixed polymers in the pH 6.8 phosphate buffer was pregelatinised starch >> PVP > natural starch > acetylated starch. Further, the rank order for the similarly mixed starches with PVP gave the rank order for time of detachment in phosphate buffer as PVP/pregelatinised starch > PVP/natural starch > PVP/acetylated starch.

A synergistic effect was observed in acid medium where the time of detachment for the mixed PVP and pregelatinized starch had significantly longer time of detachment than polymers had singly (Figure 5). This could have been due to the specificity conferred by the starch combined with the longer adhesion time imparted by the synthetic polymer. This implies great potential for the use of the PVP-pregelatinized banana starch in the targeted delivery of drugs into the stomach with bioadhesion possibilities. Further modification in ratio of polymers could yield a more specific polymer combination.

The rate of detachment also varies with media used, the tablet of the PVP which took the longest time to detach from the 0.1M HCl, displayed quite a short time of detachment in the phosphate buffer. The values obtained for tablets of acetylated banana starch in both media was quite close but tablets of the natural and pregelatinised banana starches were far from each other in both media. The variability of the starches in both media may be attributed to their pH with the phosphate buffer almost at neutral pH and the 0.1M HCl at acidic pH value.

The rate of detachment of the tablets may not be attributed to the viscosity parameters of the starches because the pregelatinised banana starch which is the least viscous had the longest time of detachment

CONCLUSION

The bioadhesive properties showed selectivity of the different modifications of the starch in the different media used. The difference in bioadhesive properties of the starches could be better attributed to the swelling power of the starches and the pH of the media they were used in. Thus both the swelling power of the starches and the pH of the media affects the bioadhesive properties of the starches.

Hence, the pregelatinized banana starch adhered longest to the pig's ileum in both the 0.1M HCl and phosphate buffer (pH 6.8) media, which are *in-vitro* representation of the stomach and intestines, respectively. This shows that the drugs can be incorporated into the pregelatinized banana starch when the stomach or the intestine is the target site for the targeting and controlled release of such drugs in the stomach and small intestine.

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