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Original Research

The Swelling Properties of *Adansonia digitata* Mucilage: A Super Gel Forming Polymer

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ABSTRACT

The swelling properties of *Adansonia digitata* mucilage (ADM), a naturally occurring mucilage from the leaves of *Adansonia digitata* were investigated. ADM compacts were exposed to simulated intestinal fluid (SIF), simulated gastric fluid (SGF), phosphate buffer solution (PBS) and deionised water (DW). The effect of pH on the equilibrium swelling capacities of ADM was also investigated. The relationship between the amount of water uptake by the mucilage and time was investigated by fitting the data into the Korsenmayer and Pepas power equation as well as the Ofner and Schot second order equation. Linear correlation was obtained only with the Ofner and Schot equation. The equilibrium swelling capacities and the initial rate of swelling was estimated from the linear curve obtained. ADM showed variable swelling capacities in the various fluids. The equilibrium-swelling ratio of ADM in SIF and SGF was found to be 1.2 and 0.5 respectively. ADM compacts also showed a significant sensitivity to pH changes. The difference in the equilibrium swelling capacities of ADM in SIF and in SGF makes it a predictable candidate polymer for the controlled or targeted delivery of bioactive agents.

Key Words: *Adansonia digitata*, Mucilage, Swelling, Korsenmayer and Pepas power equation, Ofner and Schot second order equation

INTRODUCTION

Swellable polymers from both natural and synthetic origins have been extensively used for effecting the controlled release of bioactive agents (1). An important property that has made polysaccharides a material of choice in matrix systems is the ability of such polysaccharides to swell in aqueous media. The process of water transport into hydrophilic matrices and the corresponding structural changes that occur have a major influence on the profile of drug release from such matrices (2, 3, 4). Thus an understanding and characterization of the various aspects that may affect the hydration of the polymers becomes important as this will give the necessary information required for tailoring of drug release from formulations containing them (5).

Adansonia digitata mucilage (ADM) is a gelling, naturally occurring, hydrophilic polymer obtained from the leaves of *Adansonia digitata, a* tree plant that is found growing in most parts of Northern Nigeria as well as in parts of north and east Africa (6). Preliminary studies have shown that ADM is only slightly soluble in water absorbing several times its weight of water (7).

The purpose of this work is to investigate the swelling characteristics of ADM in the main physiological fluids of the gastro intestinal tract. To describe the swelling kinetics of ADM the time dependent uptake of water from SIF, SGF, DW and PBS would be fitted into two kinetic equations, Peppas and Korsenmayer power equation (8,9,10) and Ofner and Schott second order equation (11).

Vervoort *et al* (10) in evaluating the swelling kinetic of inulin hydrogels applied Eq 1.

$$M_t / M_\alpha = Kt^n \quad \text{-----} 1$$

where M_t is the amount of water uptake with time t and M_α is the equilibrium swelling capacity, n is the diffusion exponent which is indicative of the mechanism of solvent transport in the polymer system and K is a constant incorporating characteristic of the polymer system.

Ofner and Schott (11) adapted the linear expression proposed Robinson (12) in a one-dimensional measurement of the thickness of gelatin films by replacing change in thickness by a change in weight W of fluid absorbed per gram of gelatin as a function of time t. The linear equation is given by Eq 2.

$$t/W = A + Bt \quad \text{------} (2)$$

where A and B are constants. Rearranging and differentiating result in:

$$dW/dt = A/(A + Bt)^2 \text{ - - - - - -}(3)$$

For $t \rightarrow 0$, the initial rate of swelling is 1/A the reciprocal of the intercept in plot of t/W versus t according to equation 2. The reciprocal of the slope, 1/B, equals W_α , the maximum equilibrium uptake, because at long time Bt >> A (11).

MATERIALS AND METHOD

Materials: Sodium hydroxide (Sigma, Germany) HCl (BDH, England), Sodium chloride (BDH, England), Potassium dihydrogen phosphate (Aldrich, Germany), were used in the study. ADM was obtained in our laboratory as described below. The SIF, SGF and the various buffers of pH 1.2, 2, 6, 8 and10 were prepared in our laboratory as prescribed in United States Pharmacopoeia (13), PBS was prepared as prescribed in the British Pharmacopoeia (14).

Methods

Extraction and Purification of ADM

The method described by Adikwu *et al* (15) was adopted with some modification. Fresh leaves of *A. digitata* were washed and blended in a homogenizer (Bruan type 4142, Germany). The slimy mass was passed through a muslin cloth to separate mucilage from plant fiber. The mucilage extract was then centrifuged at 4,500 rpm for 1h (Beckman GS – 15, Germany) to remove any trace of solid matter and then precipitated with large volumes of acetone. The precipitate was washed several times with acetone to remove chlorophyll and other coloring matter. The mucilage was then re-dispersed in 0.1N Hcl to remove alkaloids (16) and re-precipitated with excess acetone. The precipitate was again dispersed in de-ionized water and re-precipitated with of acetone. The solid mass was then air-dried, pulverized and passed through sieve No. 100 with a sieve shaker (Retsch AS 200, Germany) and stored in an airtight container until used.

Preparation of ADM compacts

A 100 mg quantity of ADM was compressed into circular disc in a single punch tableting machine fitted with a 6 mm punch and die set at a compression load of 23.6 KN. The compacts were stored in a desiccator for 72 h for further drying. The residual moisture content of the compacts was determined using a moisture balance (Ultra X, Germany).

Swelling studies

The method of Moussa *et al* (5) was adopted. The dry ADM compacts of known weight (W_d) were immersed in the various fluids (SIF, SGF, DW, and PBS) maintained at 32 °C in a mesh in such a way that swelling could occur three dimensionally with fluid penetrating into all sides of the tablet. At 1h intervals each ADM compact was removed from the hydration fluid and patted briefly with a lint free tissue to remove excess water and the weight (W_s) determined on a balance (Mettler-Toledo, Switzaland). The equilibrium-swelling ratio of ADM compacts was also determined in buffer solutions of pH 2, 6, 8 and 10. The swelling assessment was carried out for 48 h. All swelling assessment was done in triplicate. Fig. 1 was obtained by plotting swelling time (t) in hours/ water uptake in gram against time.

Water uptake = weight of water swollen compact after time t, - Dry weight of compact.

The swelling ratio (Q) used for the plots of Fig. 2 and 3 was calculated according to Eq 4 (10).

$$Q = W_s / W_d \text{ ---- } (4)$$

DISCUSSION

The ADM compact were light brown, glossy tablets with average weight of 100 mg. The compacts were maintained at a moisture content of 2% before introduced into the various fluids, this is to prevent the residual moisture from interfering with the water intake of the compact.

The swelling isotherm (Fig. 1) is characterized by an initial steep portion, which corresponds to the initial rapid water uptake followed by an almost horizontal portion corresponding to a near equilibrium or polymer saturation. The compacts exhibited the highest swelling within the first 1 h of introduction into the various fluids. The least swelling within the first hour of exposure to excess fluid was in SGF and the highest was in PBS (Table. 1).

Table 1. Some properties of ADM compact in the various fluids

	SGF	SIF	PBS	DW
% Swelling within first 1 h	0.091 g ± 0.006	0.156 g ± 0.012	0.204 ± 0.015	0.164 ± 0.026
Equilibrium swelling capacity by actual swelling experiment (g)	0.543 ± 0.013	1.069 ± 0.011	–	–
Equilibrium swelling capacity from swelling curve 1/B (g)	0.545	1.289	1.125	0.950
Linear regression equation	W = 10.47 + 1.8366t	W = 6.046 + 0.7757t	W = 4.34 + 0.889t	W = 5.2 + 1.02t
Linear correlation of coefficient (r)	0.9999 (n = 24)	0.9834 (n = 22)	0.997 (n = 7)	0.9992 (n = 7)

Initial swelling rate 1/A (g/h)	0.095	0.165	0.230	0.192

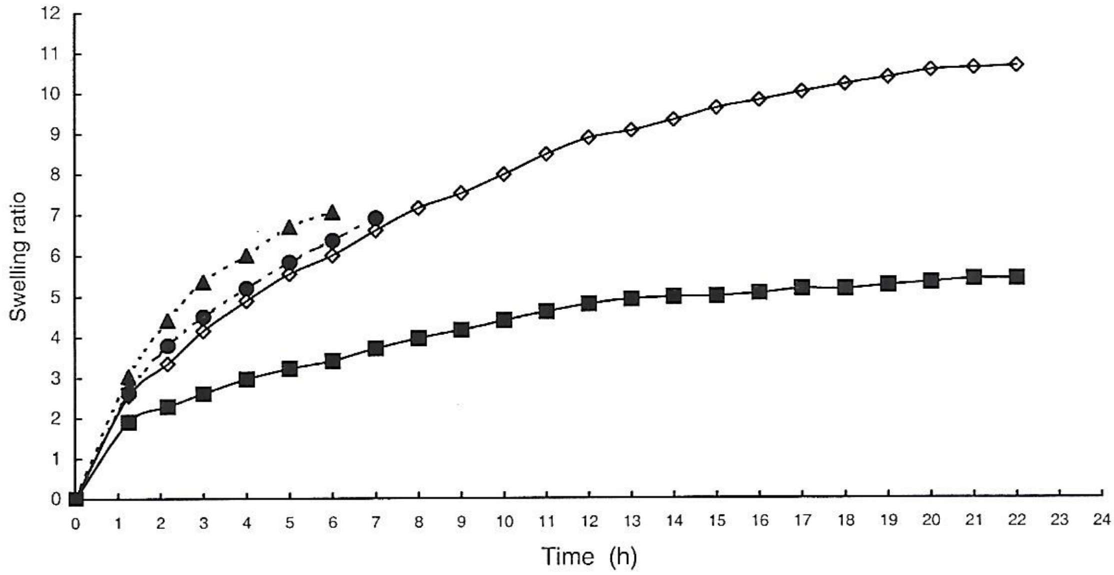


Fig. 1 Swelling isotherm for ADM in SIF, SGF, PBS and DW

—◇— Swelling ratio (SIF) —■— Swelling ratio (SGF)
- - ▲ - - Swelling ratio (PBS) — ● — Swelling ratio (DW)

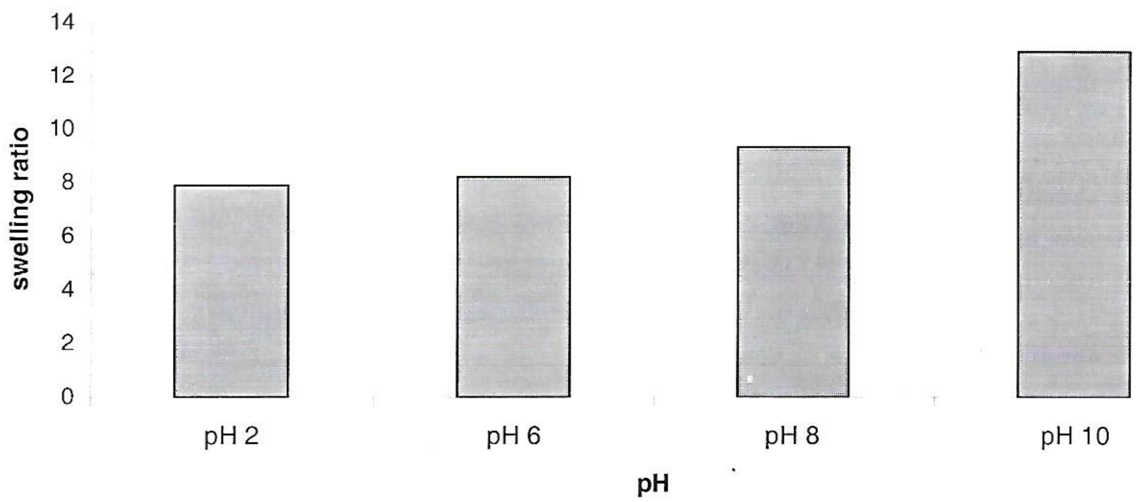
A considerable initial swelling is desirable for any hydrophilic or gel forming polymer for use in the controlled release or site specific delivery of bioactive agents so as to prevent premature dose dumping that is characterized by uncontrolled burst release of bioactive agents (17). The rapid water uptake by ADM compacts within the first hour gradually decreased with time in all the fluid types probably because of the introduction of a retardation factor as equilibrium is approached. The water uptake by the ADM compacts in PBS and DW (≈ pH 7) was very rapid. The ADM compact in DW and PBS rapidly lost its physico-structural and gel consistency, so that after 7 h of exposure of the ADM compact to DW and PBS further measurement of its water uptake was not possible as the compact started to disintegrate. This behavior could be due to the neutral pH of the fluids, which probably did not affect the arrangement of the discrete polymer particles in the network thus leading to rapid penetration of excess fluid leading to a rapid relaxation of the unordered polymer network (17). The swelling in PBS was higher than that in DW even though both have an approximate pH of 7. This may be due to the effect of solutes and solute type on certain physicochemical properties of polymers. Though the pH of their solutions may be identical, the ionic strength of such solutions may differ (10). This factor could be responsible for the difference in swelling exhibited by ADM in PBS and DW. Solutes are known to have unpredictable effect on the swelling of hydrogels because of their interactions with polymers. The solute in solution can enhance or disrupt specific interactions between the swelling solvent and the polymer thereby causing increased or decreased swelling of the polymer (18, 19). The rapid and extensive water uptake of the ADM compact in all the fluids assessed is indicative of a probable dominant amorphous polymorphism (17). The physico-structural and gel consistency of the ADM compact was maintained in SIF and SGF. However, it began to diminish after 28 h of standing in SIF but in SGF the physico-structural and gel consistency of the compact remained intact even after 48 h although there was no appreciable increase in swelling. These observations could be either due to the differences in pH of fluids or the solute content of the two physiological solutions.

When swellable polymers are in a fluid environment the fluid penetrate the polymer causing it to swell with a resultant lowering of the glass transition temperature below the environment temperature. Below the glass transition temperature the polymer will start to lose consistency and become rubbery (20). The results indicate that the glass transition temperature of ADM in PBS and DW tend to be lowered faster than in SIF and SGF.

Equilibrium Swelling

Equilibrium swelling condition is the state of the polymer in excess fluid where there is no more appreciable increase in swelling or water uptake. Equilibrium swelling of ADM could not be directly assessed in DW and PBS using the polymer compaction method because of the rapid loss of physico-structural and gel consistency. In both SIF and SGF equilibrium swelling was attained within 24 h. The equilibrium swelling capacity of ADM compact is shown on Table 1. ADM compact reached maximum swelling in SIF within 22 h and 24 h in SGF. The equilibrium swelling of ADM compact in SIF is about twice that in SGF (Table 1). The bar chat representation Fig-. 2 shows the effect of pH on the equilibrium swelling of ADM. The differences in the equilibrium swelling capacity of ADM in the different pH system are indicative of the sensitivity of ADM to pH change. The result indicates that swelling of ADM is enhanced at high pH and diminished by low pH. This indicates that when ADM is used as matrix for the controlled delivery of bioactive agents it would be expected that the polymer, due to its expected poor swelling in the low pH environment of the stomach will keep the drug almost intact until it reaches the small intestine where it will absorb enough fluid to effect the diffusion of the drug. This property can be exploited to achieve site-specific delivery of bioactive agents. Linear re-presentation of swelling data of ADM.

Fig 2: Effect of pH on the swelling equilibrium of ADM



The data presented is a mean of three determinations

Linear representation swelling data of ADM

The Offner and Schott second order equation as well as Peppas and Korsenmayer power equation have been used to analyze the swelling kinetics of hydrogels (10, 11). The swelling profile of hydrophilic polymers may fit into either of the linear equations, however both have their peculiar merits. The linear curve of the Offner and Schott second order equation (Eq. 2) can be used to estimate the initial swelling rate and the equilibrium swelling of the hydrogel without empirically reaching equilibrium swelling (11) whereas the mechanism of solvent transport in the polymer can be determined directly from the linear swelling curve of the Peppas and Korsenmayer power equation (Eq. 1) (10).

When the swelling data of ADM in the various fluids (SIF, SGF, DW and PBS) were fitted into Eq. 1 and 2, a curve linear correlation was only obtained with Ofner and Scoot second order equation and is shown on Fig. 3. The linear curve was obtained for the entire swelling period until equilibrium was obtained in SIF (22 h), SGF (24 h) and until physico-structural inconsistency set in for PBS and DW (7 h). The equilibrium swelling ($1/B = W_\alpha$) and the initial swelling rate ($1/A$) as determined by the regression equation ($W = A + Bt$) and the correlation coefficient (r) at the various degrees of freedom (n) are shown in Table 1. The observed equilibrium swelling capacities of ADM compact in the various fluids are lower than those obtained by estimation with the regression of the Ofner and Scoot second order equation. The difference in the equilibrium swelling capacity of ADM determined directly from the experiment and from the graph in SGF is less than 0.4 % while in SIF it is about 21 %. This difference could be due to the relatively low correlation coefficient (r), between the experimental and the calculated values for SIF. The mean values of the percentage swelling within first one hour and equilibrium swelling capacity by actual swelling experiment were estimated at 95% confidence limit.

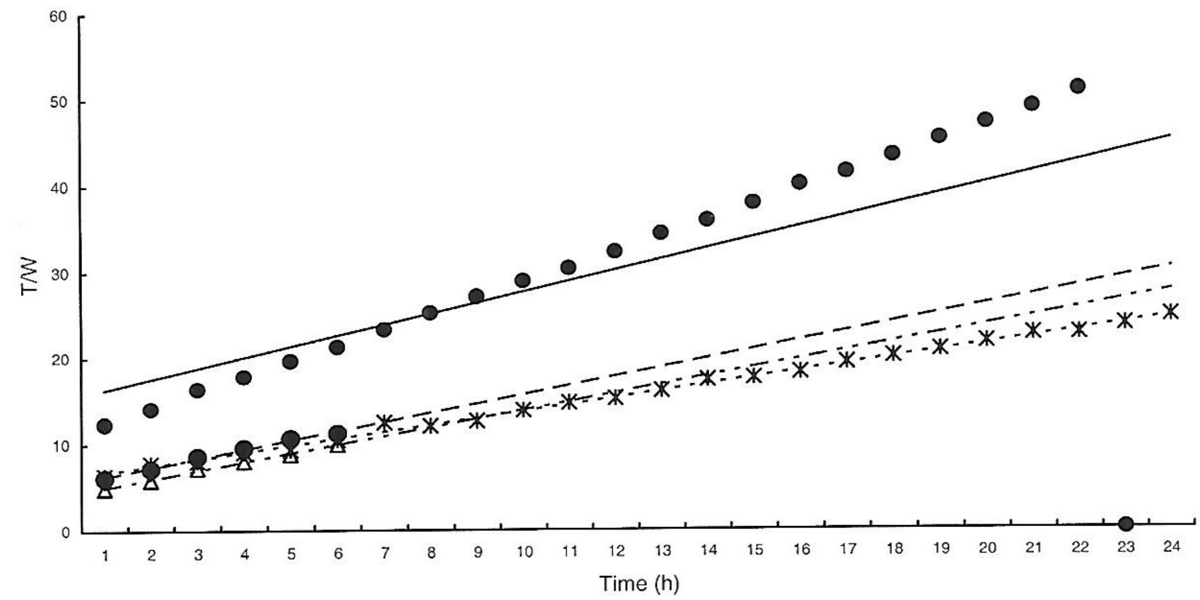


Fig. 3 Linear regression curve of ADM swelling isotherm in SIF, SGF, PI ; and DW

CONCLUSION

The swelling of the ADM in the various fluids was rapid and extensive, swelling to 12 times and 5 times its initial weight in SIF and SGF respectively. ADM exhibited a pH sensitive swelling profile. The swelling of ADM in buffer solutions of various pHs ranging from acidity through neutral to basic revealed that its water uptake capacity was higher in the basic pH than at the acidic pHs. The presence and nature of the solute in the fluids was found to be another important factor that may affect the swelling of ADM.

The rapid but minimal swelling of ADM in SGF and the extensive swelling in SIF makes it a polymer for the controlled and targeted delivery of bioactive agents to the intestine.

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