



## PREPARATION AND IN VITRO CHARACTERISTICS OF TABLET CORES COATED WITH ALBIZIA, ALBIZIA/KHAYA AND ALBIZIA/HPMC FILMS

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### ABSTRACT

This study was carried out to assess the in vitro behaviour of tablet cores coated with novel films of albizia, albizia/khaya and albizia/HPMC. Diclofenac sodium tablet cores, ~ 225 mg, were formulated and coated with aqueous film formulations consisting of albizia gum only, albizia/khaya (25:75), and albizia/HPMC (90:10). The thickness, breaking strength, disintegration time, swelling index and drug release properties of the uncoated and film coated tablets were evaluated. Tablet thickness increased with increase in coating time. The breaking strength of the film coated tablets was higher than that of the tablet cores and increased with increase in coating time. The disintegration time of the uncoated and film coated tablets in the media used was pH-dependent and followed the rank order: 0.1 M HCl > pH 6.8 phosphate buffer > distilled water. The extent of swelling (water absorption) of the film coated tablets in 0.1 M HCl was dependent on film composition and followed the order: albizia/HPMC > albizia > albizia/khaya. Drug release in pH 6.8 phosphate buffer was faster than in 0.1 M HCl solution. Albizia and albizia/HPMC film coated tablets exhibited the slowest drug release in the acidic and basic media, respectively. The study shows the potential of albizia, albizia/khaya and albizia/HPMC films as coating materials for tablets.

**KEYWORDS:** Albizia gum, khaya gum, aqueous film coating, disintegration of film coated tablets, drug release properties

### INTRODUCTION

Film coating of tablets and other pharmaceutical solid dosage forms is carried out for a variety of reasons. These includes protecting the active pharmaceutical ingredients against environmental conditions such as moisture, air and light; to mask the unpleasant taste and odours; to improve the appearance of dosage forms; for ease of swallowing; to achieve colonic drug delivery and controlled drug delivery, among others. Several natural polysaccharides have been studied as potential film coating materials for pharmaceutical products<sup>1-5</sup>. The naturally occurring polysaccharides tend to have good film forming properties, high safety profiles as well as being biodegradable.

Khaya and albizia are naturally occurring gums obtained from the incised trunk of *Khaya grandifolia* C.D.C (Meliaceae) and the incised trunk of *Albizia zygia* (DC) J.F. Macbr (Leguminosae), respectively. While khaya gum is composed of arabinose, galactose, 4-*O*-methylglucuronic acid and 1, 4- or 1, 2, 4-linked L-rhamnose, albizia gum comprises of mannose, galactose, glucuronic acid and 4-*O*-methylglucuronic acid<sup>6</sup>. Khaya and albizia gum have been successfully employed as binders in tablet formulations<sup>7-8</sup>, and as vehicles for the delivery of drugs to the colon<sup>9</sup>.

The mechanical properties of free films prepared from khaya and albizia gums as possible tablet film coating materials has been described in the literature<sup>10-11</sup>. The study which involved the use of

khaya and albizia gum blends, with or without HPMC, showed that the film formulations possessed the requisite mechanical properties of hardness, flexibility and toughness required for pharmaceutical coating. The addition of HPMC improved the film forming properties of the gums <sup>10</sup>.

The aim of the current study is to assess the behaviour of diclofenac sodium tablet cores, coated with albizia, albizia/khaya and albizia/HPMC films. The coated tablets were evaluated for tablet thickness, breaking strength, disintegration time, swelling index and drug release properties.

## MATERIALS AND METHODS

### Materials

Diclofenac sodium (2-[(2, 6-dichlorophenyl) amino]benzeneacetic acid monosodium salt) was supplied by Kinapharma Ltd. (Kumasi, Ghana). Lactose, maize starch, talc, magnesium stearate, and polyvinylpyrrolidone (PVP) were obtained from the chemical store, Department of Pharmaceutics, Kwame Nkrumah University of Science and Technology (KNUST), Ghana. Glycerol, chloroform and hydrochloric acid were received from UK Chemicals Ltd. (Kumasi, Ghana). Hydroxypropylmethylcellulose 2 % (HPMC) 1500 cps @ 25 °C was obtained from Pacegrove Chemicals, UK. Petroleum ether was received from May and Baker Ltd. (Dagenham, UK). Disodium hydrogen orthophosphate and potassium dihydrogen orthophosphate were obtained from BDH Ltd. (UK). Khaya gum was obtained from the incised trunk of *Khaya grandifolia* at the nursery of the Forest Research Institute of Ghana (FORIG), Fumesua. Albizia gum was obtained from the incised trunk of *Albizia zygia* at the botanical gardens, KNUST, Kumasi, Ghana. The gums which were collected,

authenticated and supplied by an official of FORIG were purified as previously reported <sup>10</sup>.

### Preparation of tablet cores

Diclofenac sodium tablets (225.5 ± 0.01 mg, *n* = 20) were prepared from granules comprising of diclofenac sodium (25.3 % w/w), lactose (62.2% w/w), maize starch (10.2 % w/w), talc (2.0 % w/w) and magnesium stearate (0.3 % w/w). The powders (except magnesium stearate and talc) were massed with 10 % w/v PVP. The damp mass was passed through 1.18 mm sieve and dried in hot air oven at 50 °C for 90 min. The dried granules were sieved through an 850 µm sieve and blended with magnesium stearate and talc. Tablet cores containing ~ 57 mg diclofenac sodium were compressed with a lubricated single punch tableting machine (DP30 tablet press, Pharmao Industries Co. Ltd., China) fitted with a concave punch and die set. The compressed tablets, having a breaking strength of 10.22 ± 1.02 kp, *n* = 20 (tested with a Schleuniger tablet tester, Model 6D, USA) and friability of 0.92 % (Erweka friabilator, Type TA20, Heusenstamm, Germany) were stored in a plastic container until use.

### Preparation of film coating formulations

Three film coating formulations of composition albizia gum only, albizia/khaya (25:75); and albizia/HPMC (90:10) were prepared and used for tablet coating. Table 1 shows the detailed composition of the three film coating formulations. Aqueous gels of khaya gum (4 % w/w), albizia gum (4 % w/w) and HPMC (2 % w/w) were prepared individually by dispersing the required amount of the gum or polymer in distilled water. The samples were left overnight to dissolve and then stirred with a mechanical stirrer (Silverson

L4R, Silverson Machines Ltd., England) for 5 h to obtain uniform gels. For the albizia/khaya formulation, the required amount of albizia gum gel was added to that of khaya gum gel whilst in the case of albizia/HPMC formulation, the required quantity of HPMC was added

to that of albizia gum gel. In both cases the mixture was stirred with a mechanical stirrer for 30 min. The film coating formulations were plasticised with glycerol (20 % w/w – related to total solids content) and stirred for a further 15 min.

**TABLE 1: Detailed composition of film formulations used to coat the diclofenac sodium tablets**

Materials	Formulations		
	F1	F2	F3
Weight of 4 % w/w khaya gum (g)	150	-	-
Equivalent weight of khaya gum (g)	6	-	-
Weight of 4 % w/w albizia gum (g)	50	200	180
Equivalent weight of albizia gum (g)	2	8	7.2
Weight of 2 % w/w HPMC (g)	-	-	40
Equivalent weight of HPMC (g)	-	-	0.8
Weight of glycerol (g)	1.6	1.6	1.6
Concentration of glycerol (% w/w) (related to total polymer content)	20	20	20
Albizia: khaya: HPMC ratio	25:75:0	100:0:0	90:0:10

F1 = albizia/khaya (25:75); F2 = albizia only; F3 = albizia/HPMC (90:10)

#### **Aqueous film coating of tablets**

A Manesty tablet coater fitted with a spray gun (Manesty Ltd., Liverpool, England) was used to coat the film formulations onto the tablet cores. The exhaust for dry air was turned on and the temperature of the set up was allowed to reach the maximum of 60 °C. Diclofenac sodium tablets (~ 100 g) were introduced into the coating pan of the Manesty tablet coater rotating at a rate of 25 revolutions per min. The nozzle of the spray gun was directed at the centre of the rotating pan and one coating formulation was pumped continuously onto the tablet cores at a spray rate of 15 ± 2 ml/min for 2 min. The tablets were allowed to dry for 5 min in the coating pan and collected. The tablets were stirred while drying to prevent aggregation. Another batch of tablets were coated for 4 min, dried for a further 5 min and collected. The coating procedure was repeated using the other film coating formulations to produce in each case two batches of

tablets with coating times of 2 and 4 min. The film coated tablets were stored in plastic containers until use.

#### **Evaluation of tablet properties**

The thickness of the uncoated and coated tablets was determined with a micrometer (Moore and Wright, UK) at different parts of the tablets (n = 5). The hardness of the coated tablets (mean ± SD, n = 20) was examined with the use of a Schleuniger tablet tester (Type 6D, USA). The friability (mean ± SD, n = 10) of randomly selected uncoated tablets was determined with an Erweka friabilator (Type TA20, Heusenstamm, Germany). The disintegration time of the uncoated and the film coated tablets was determined at 37 ± 0.5 °C with an Erweka disintegration tester (Type ZT3/1, Heusenstamm, Germany). Three different media were used, namely: distilled water, 0.1 M HCl (pH 1.5) solution, and phosphate buffer (pH 6.8) solution. The time taken for six randomly selected tablets to disintegrate in each case was recorded.

### Swelling index of tablets

The film coated tablets were weighed individually and separately placed in 50 ml of 0.1 distilled water, 0.1M HCl or phosphate buffer pH 6.8 in a water bath thermostatically set at  $37 \pm 0.5$  °C. The tablets were removed at specified time intervals, blotted dry with filter paper and weighed. Ten tablets from each batch of tablets were used. The swelling index (SI) was determined using the relationship:  $(T_a - T_b/T_b) \times 100$ , where  $T_a$  and  $T_b$  are tablet weights after and before incubation at time  $t$ , respectively.

### In vitro drug release

In vitro drug release studies were carried out on the albizia only, albizia/khaya, and albizia/HPMC film coated diclofenac sodium tablets using the British Pharmacopoeia dissolution apparatus II (paddle method)<sup>12</sup>. An Erweka Dissolution machine (Type DT6, Heusenstamm, Germany) was used. Phosphate buffer (pH 6.8) solution and 0.1M HCl (pH 1.5) solution were used as the dissolution media. Drug release tests were carried out with 900 ml dissolution media at  $37 \pm 0.5$  °C, and a paddle speed of 50 rpm. At specified time intervals (0.25, 0.50, 0.75, 1, 2, 4, 6 and 8 hours), 5 ml samples of the dissolution media were taken and replaced with fresh media pre-warmed at 37 °C. The samples obtained were filtered through 0.45 µm HA membrane filters and the amount of diclofenac sodium in the dissolution media determined by measuring the absorbance at 275 nm using an ultraviolet spectrophotometer (Cecil CE 8020 Series UV machine). Drug release ( $\pm$  SD,  $n = 3$ ) was determined using regression data obtained from calibration plots of diclofenac sodium (0.1 - 0.4 mg/100ml) in pH 6.8 phosphate buffer solution ( $R^2 = 0.9967$ ) and 0.1 M HCl solution ( $R^2 = 0.9886$ ). From the data obtained, plots of drug

released (%) from the tablets against time were made.

### RESULTS AND DISCUSSION

Tablet cores of diclofenac sodium of nominal weight 225 mg, friability  $\sim 0.9$  % and breaking strength  $10.22 \pm 1.02$  kp ( $n = 20$ ), were produced for film coating. A small amount of the hydrophobic lubricant, magnesium stearate (0.3 % w/w) was combined with talc (insoluble but not hydrophobic) and used as lubricant in the formulation of the tablet cores. This was to minimize any possible negative effects that the hydrophobic lubricant could have on the mechanical strength of the tablets and on the adhesion of the film coating to the tablet cores<sup>13</sup>. The tablets produced possessed the requisite mechanical strength for film coating and complied with all the pharmaceutical standards for compressed tablets. Glycerol was added to the film formulations as plasticizer to improve the smoothness, ductility and flexibility of the film coatings<sup>14</sup>. Even though friability of  $> 0.3$  % for uncoated tablets is considered to be high for film coating<sup>13</sup>, the diclofenac sodium tablets were film coated without any break-up of the tablets and did not suffer any other physical imperfections.

The film coating process produced tablets that had uniform appearance and uniform coating thickness. The film coatings also exhibited good adhesion properties to the surface of the tablet cores. Table 2 shows the physicochemical properties of the uncoated and the albizia, albizia/khaya and albizia/HPMC film coated tablet formulations. Tablet thickness increased with increase in coating time. At a particular coating time, the tablet thickness changed with the application of different coating formulations onto the tablet cores. This is probably due to differences in viscosity of the three

aqueous film formulations. The breaking strength of the film coated tablets was higher than that of the uncoated tablets. The film coated tablets became harder when the total coating weight was increased, giving an indication that the film coating increased the mechanical strength of the tablets.

The disintegration time of the uncoated and film coated tablets in the three media used followed the order: 0.1 M HCl > phosphate buffer (pH 6.8) > distilled water. For instance, for tablets coated for 4 minutes with albizia-only film formulation, the disintegration times in distilled water, 0.1 M HCl and phosphate buffer (pH 6.8) solutions were ~ 14 min, 330 min and 17 min, respectively. In all the media used, the disintegration times for the coated tablets were higher than that of the uncoated tablets. Also, the disintegration times increased with increase in coating time of the tablets. There was a direct correlation between breaking strength and disintegration time of the tablets. Thus, hard tablets have high breaking strength values and long disintegration times. For all the

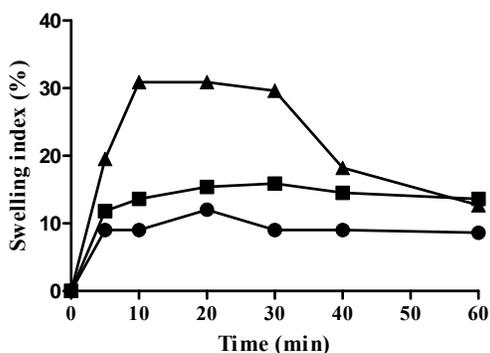
media used, the disintegration times were highest for albizia/HPMC film coated tablets and lowest for albizia/khaya film coated tablets.

Figure 1 shows the swelling behavior of the film coated tablets in acidic medium (0.1M HCl solution). In neutral (distilled water) and basic (pH 6.8 phosphate buffer) solutions, the tablets disintegrated within 5 min after absorbing some water. The extent of water uptake by the film coated tablets in 0.1 M HCl was: albizia/HPMC > albizia > albizia/khaya. Inclusion of HPMC (10 % w/w) to albizia film coatings resulted in a marked increase in water uptake by the coated tablets whilst the addition of khaya gum reduced the swelling properties of albizia film coatings. Swelling of the film coated tablets increased to a maximum value and started to decrease, reaching their minimum values (range: 9 – 14 %) in 60 min. The apparent difference in the swelling and disintegration properties of the coated tablets in aqueous media of varying pH is indicative of the effect of pH and ionic strength on the behavior of the film coatings.

**TABLE 2: The thickness, breaking strength and disintegration time of uncoated and film-coated diclofenac sodium tablets**

Tablet properties	Tablet thickness (mm)	Breaking strength (kp)	Disintegration time (min)		
			A <sup>1</sup>	B <sup>2</sup>	C <sup>3</sup>
Uncoated	3.517 ± 0.12	10.0 ± 1.0	10	186	12
Albizia/khaya (25:75); 2 min	3.519 ± 0.01	12.4 ± 1.2	12	249	14
Albizia/khaya (25:75); 4 min	3.525 ± 0.04	12.8 ± 0.5	13	253	15
Albizia; 2 min	3.520 ± 0.01	13.2 ± 1.0	13	259	15
Albizia; 4 min	3.527 ± 0.02	13.2 ± 0.6	14	330	17
Albizia/HPMC (90:10); 2 min	3.526 ± 0.05	13.3 ± 0.4	14	354	17
Albizia/HPMC (90:10); 4 min	3.537 ± 0.07	13.0 ± 0.6	15	379	20

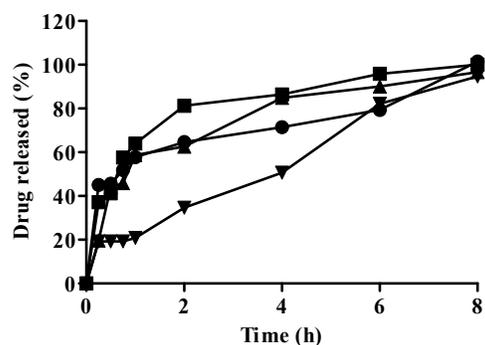
A<sup>1</sup> = distilled water; B<sup>2</sup> = 0.1 M HCl (pH 1.5) solution; C<sup>3</sup> = pH 6.8 phosphate buffer solution



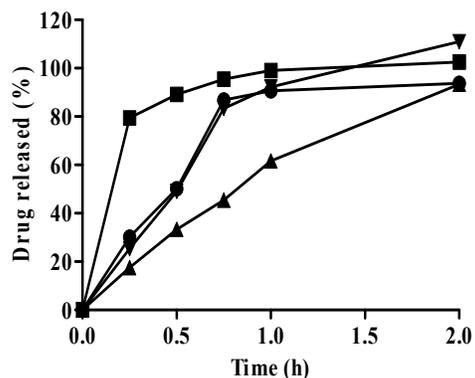
**FIG. 1: Effect of film composition and time on the swelling index of film coated diclofenac sodium tablets (coating time = 2 min) in 0.1 m hcl (ph 1.5) solution. Composition of film coatings: ■ = albizia; ● = albizia/khaya (25:75); ▲ = albizia/hpmc (90:10)**

Figures 2 and 3 shows the release profiles of uncoated and film coated diclofenac sodium tablets in 0.1 M HCl and pH 6.8 phosphate buffer solutions, respectively. Drug release from the uncoated tablets was pH dependent, as release was higher in the basic medium than in the acidic medium. Almost 99 % of drug release occurred in the pH 6.8 phosphate buffer solution in 60 min, whilst ~ 64 % drug was released in 0.1 M HCl solution, in the same period. In the phosphate buffer solution, there was an initial burst of drug release (~ 79 %) within 25 min, followed by a relative decrease in the release rate with time. Drug release from the film coated tablets was low and relatively controlled than that of the uncoated tablets, in both the acidic and basic media used. Complete drug release (~ 100 %) from the film coated tablets occurred in the phosphate buffer solution in about 2 h, whilst complete release in the acidic medium occurred in about 8 h. This observation can be attributed to the much slower

disintegration of the tablets in the acidic medium (249 – 379 min) compared to the basic medium (14 – 20 min) (Table 2). The low release rate of diclofenac sodium (pKa = 4), in 0.1 M HCl (pH 1.5) has also been attributed to its low solubility in acidic medium<sup>15-17</sup> while the drug is known to be soluble in water and basic media<sup>18-19</sup>. The albizia/HPMC film coated tablets showed the slowest drug release in the basic medium, while albizia film coated tablets showed the slowest and more controlled drug release in the acidic medium. Thus, film coatings fabricated with albizia gum alone or albizia gum containing 10 % HPMC (albizia/HPMC) offered greater protection to the tablet cores against drug release than with the use of albizia/khaya film coatings. This observation is in agreement with a previous study which showed albizia gum to be a better film coating material than khaya gum<sup>10</sup>.



**FIG. 2: Release profiles of uncoated and film coated diclofenac sodium tablets (coating time = 4 min) in 0.1 m hcl (ph 1.5) solution. tablet properties: ■ = uncoated; ▼ = albizia film coated; ● = albizia/khaya (25:75) film coated; ▲ = albizia/hpmc (90:10) film coated**



**FIG. 3: Release profiles of uncoated and film coated diclofenac sodium tablets (coating time = 4 min) in ph 6.8 phosphate buffer solution. Tablet properties: ■ = uncoated; ▼ = albizia film coated; ● = albizia/khaya (25:75) film coated; ▲ = albizia/hpmc (90:10) film coated**

Albizia, albizia/khaya and albizia/HPMC film coatings, being hydrophilic, will swell to varying extents in dissolution media to form hydrated viscous gels around the tablet cores. These viscous gels constitute a diffusion barrier and will act to retard the release of drug from the tablets <sup>10, 20</sup>. Drug release from the film coated tablets may occur either by diffusion of drug molecules through the viscous gel layer or by erosion of the gel layer. Any erosion of the gel layer

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will reduce the diffusion path length of the drug molecules and may also expose the surface of the tablets cores to the dissolution medium. The higher the viscosity, and the thicker the gels formed around the tablet cores, the lower the rate of drug release.

#### CONCLUSIONS

Albizia, albizia/khaya and albizia/HPMC film coated tablets with the requisite physical properties were produced using aqueous film coating technique. The swelling, disintegration and drug release properties of the film coated tablets were dependent on the pH of the media, the composition of the film coatings, as well as the physicochemical properties of the tablet cores. A manipulation of these factors would produce albizia and khaya film coatings suitable for various pharmaceutical applications.

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