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Assessment of *Albizia zygia* gum as a binding agent in tablet formulations

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Albizia gum has been evaluated as a binding agent in tablet formulations in comparison with gelatin BP. Compressional properties were analyzed using density measurements and the compression equations of Heckel and Kawakita as assessment parameters, while the mechanical properties of the tablets were assessed using the crushing strength and friability of the tablets. Drug release properties of the tablets were assessed using disintegration time and dissolution time as assessment parameters. Formulations containing Albizia gum as a binding agent show a faster onset and higher amount of plastic deformation under compression pressure than those containing gelatin. The crushing strength, disintegration and dissolution times of the tablets increased with increased binder concentration while their friability decreased. Albizia gum produced tablets with better mechanical properties and longer disintegration and dissolution times than those containing gelatin BP. This suggests that Albizia gum could be useful as a binding agent especially when high mechanical strength and slower release rates are desired.

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Binding agents are used to impart the structural strength required during the processing, handling and packaging of tablets. A number of plant gums have been used as binding agents in tablet formulations (1–3). They have been found useful in producing tablets with different mechanical strength and drug release properties for different pharmaceutical purposes. The fact that these gums are non-toxic and widely available has made them of continuing interest.

Albizia gum is obtained from the incised trunk of the tree *Albizia zygia* (DC) J. F. Macbr (*Leguminosae*) and is shaped like round elongated tears of variable color ranging from yellow to dark brown (4). The trees are widespread in parts of Africa, India and

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Australia (5). The gum consists of β-1,3 linked D-galactose units with some β-1,6 linked D-galactose units (6). It has been investigated as a possible substitute for gum Arabic as a natural emulsifier for food and pharmaceuticals (7).

In the present work, Albizia gum has been evaluated as a binding agent in paracetamol tablet formulations in comparison with a standard binder, gelatin BP, using the compression equations of Heckel and Kawakita, and the mechanical and release properties of the tablets as assessment parameters (8–10). Paracetamol was used as the model drug for the present work because of its poor compression properties; hence it needs a binding agent among other excipients to form satisfactory tablets.

EXPERIMENTAL

Materials

The materials used were paracetamol obtained from Thornton and Ross (UK), lactose (Pharmatose® 200M) supplied by DMV (The Netherlands), corn starch and gelatin obtained from BDH Ltd. (UK), Albizia gum obtained from the incised trunk of *Albizia zygia* at the Forestry Research Institute of Nigeria (Ibadan, Nigeria) and purified using the established methods (2, 11). Briefly, Albizia gum was hydrated in 0.5 : 95.5 (*V/V*) $CHCl_3$/water mixture (12) for 5 days with intermittent stirring; extraneous materials were removed by straining through a muslin cloth. The gum was precipitated from solution using absolute ethanol. The precipitated gum was filtered, washed with diethyl ether, and then dried in hot air oven at 40 °C for 18 h. The gum was pulverized using a laboratory blender and the size fraction < 170 μm was used.

Characterization of Albizia gum

The pH and viscosity of 1% (*m/V*) Albizia gum were determined using a Microprocessor pH meter (pH 210, Hanna Instruments, UK) and an Ostwald U-tube viscometer made of borosilicate glass (Technico, UK), respectively. The swelling index of the polymer was determined by the *European Pharmacopoeia* method (13).

Preparation of granules

Batches (100 g) of a basic formulation of paracetamol (70%, *m/m*), lactose (20%, *m/m*) and corn starch (10%, *m/m*) were dry-mixed for 5 minutes in a planetary mixer (Model A120, Hobart Manufacturing Co., UK.) and then moistened with 18 mL of distilled water or appropriate amounts of binder solutions to produce granules containing different concentrations of Albizia gum or gelatin as binders. Massing was continued for 5 minutes and the wet masses were granulated by passing them manually through a mesh 12 sieve (1400 μm), dried in a hot air oven for 18 hours at 50 °C. Dried granules were sieved through a mesh 16 sieve (1000 μm) and then stored in airtight containers. The degree of granules mixing was determined by a chemical assay for paracetamol (12) and was found to be > 0.96. Particle densities were determined using the helium pycnometer (Micrometer AccuPyc 1330, Micromeritic Instruments, USA).

Determination of pre-compression density

The bulk density of each formulation at zero pressure (loose density) was determined by pouring the granules at an angle of 45° through a funnel into a glass measuring cylinder with a 24 mm diameter and a volume of 50 mL (14). Determinations were done in triplicate. The relative density D_o, of each formulation was obtained from the ratio of its loose density to its particle density.

Preparation of tablets

Tablets (500 mg) were prepared from the 250–710 mm size fraction of granules by compressing them for 30 s with predetermined loads on a hydraulic press (Beckman, Model 16, UK). The 12.5 mm die and flat-faced punches were lubricated with a 1% (*m/V*) dispersion of magnesium stearate in dichloromethane. After ejection, the tablets were stored over silica gel for 24 h. Their masses (*m*) and dimensions were then determined to within ± 1 mg and 0.01 mm, respectively, and their relative densities (*R*) were calculated using the equation:

$$R = m / V_t \rho_s \qquad (1)$$

where V_t is the volume (cm^3) of the tablet and ρ_s is the particle density ($g\ cm^{-3}$) of the solid material.

Crushing strength and friability tests

Crushing strengths of the tablets were determined at room temperature by diametral compression (2) using a hardness tester (Type C50, Engineering Systems, UK).

The percent friability of the tablets was determined using a Roche friabilator (Type TAR 100, Copley Scientific, UK) operated at 25 rpm for 4 minutes.

Disintegration and dissolution tests

Disintegration times of the tablets were determined in distilled water at 37 ± 0.5 °C using a disintegration tester (Type ZT 31, Copley Scientific).

The dissolution test was carried out on the tablets using the USP XXIII basket method (Erweka dissolution tester, Type DT 700, Copley Scientific) rotated at 50 rpm in 900 mL of 0.1 mol L^{-1} HCl, maintained at 37 ± 0.5 °C (15). Samples (5 mL) were withdrawn at different time intervals and replaced with equal amounts of fresh medium. The sample was diluted and the amount of paracetamol released was determined using a UV spectrophotometer (Cecil CE 1020, Cecil Instrument, UK) at 243 nm.

Statistical analysis

Statistical analysis was done to compare the effects of Albizia gum and gelatin on the tablet properties using the *t*-test. At 95% confidence interval, the *p* value lower than or equal to 0.05 was considered the limit of significance.

RESULTS AND DISCUSSION

Gums are generally macromolecular acids and good buffers and hence the liquid penetrating the tablet on forming a gel will attain a fairly constant pH in the gel, regardless of its original pH (16). The pH of 1% (*m/V*) suspension of Albizia gum at 21 °C is 3.79 and its viscosity is 1.23 mPa s. The swelling index indicates that Albizia gum swelled rapidly to about 450% of its initial volume in distilled water. This indicates that Albizia gum is hydrophilic. It hydrates and swells in cold water, forming a viscous colloidal dispersion or gel.

The Heckel equation is widely used for relating the relative density, D, of a powder bed during compression to the applied pressure, P (8, 9). It is written as:

$$\ln[1/(1 - D)] = KP + A \tag{2}$$

The slope of the straight line portion, K, is the reciprocal of the mean yield pressure, P_y , of the material. From the intercept A, the relative density, D_A, can be calculated using the following equation (17):

$$D_A = 1 - e^{-A} \tag{3}$$

Relative density of the powder at the point when the applied pressure equals zero, D_o , is used to describe the initial rearrangement phase of densification as a result of die filling. Relative density, D_B, describes the phase of rearrangement at low pressures and is the difference between D_A and D_o:

$$D_B = D_A - D_o \tag{4}$$

The Kawakita equation is used to study powder compression using the degree of volume reduction (C) (10) and is written as:

$$C = (V_o - V_p)/V_o = abP/(1 + bP) \tag{5}$$

The equation, in practice, can be rearranged to give:

$$P/C = P/a + 1/ab \tag{6}$$

where V_o is the initial bulk volume of the powder and V_p is the bulk volume after compression. Constant a is equal to the minimum porosity of the material before compression while constant b is related to the plasticity of the material. The reciprocal of b gives the pressure term P_k, which is the pressure required to reduce the powder bed by 50% (18).

Fig. 1 shows representative Heckel plots for paracetamol formulations containing 3% (*m/m*) binder. The Heckel plots showed an initial curve followed by a linear region with the correlation coefficient of ≥ 0.990 for all formulations. The initial curve suggests that fragmentation as well as particle rearrangement occurred at the initial stages of the

compression process. The mean yield pressure values for the paracetamol formulations were calculated from the slope of the linear portion of the Heckel plots, and the intercept, *A*, was determined from the extrapolation of the region. The values of D_A and D_B were calculated from *Eqs. (3)* and *(4)*, respectively. The values of P_y, D_o, D_A, and D_B for the formulations are presented in Table I. The value of D_o, which represents the degree of initial packing in the die as a result of die filling, increased with increased concentrations of the binders. Formulations containing gelatin showed higher values than formu-

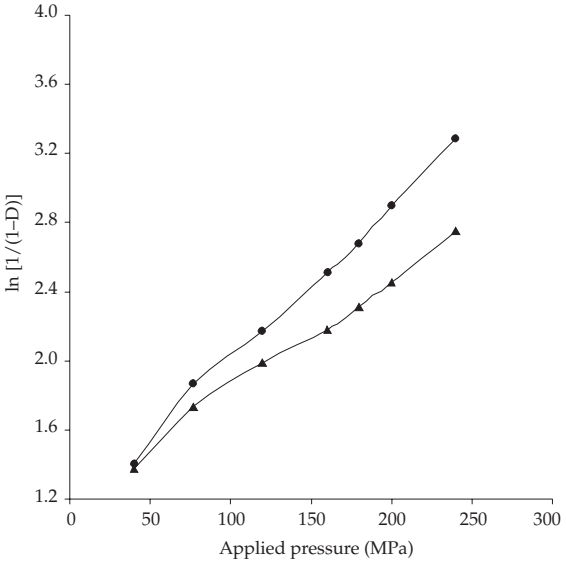

Fig. 1. Heckel plots for paracetamol tablet formulations containing 3.0% (*m/m*) binder: ▲ Albizia gum, ● gelatin.

Table I. Parameters derived from the Heckel and Kawakita plots for paracetamol tablets

Binder	Binder conc. (%, *m/m*)	Heckel plots				Kawakita plots	
		D_o	P_y (MN m^{-2})	D_A	D_B	D_I	P_k (MN m^{-2})
	0.0	0.265	208.33	0.679	0.414	0.348	8.793
Albizia	1.0	0.269	172.41	0.704	0.435	0.404	6.187
	2.0	0.272	161.29	0.700	0.428	0.380	5.294
	3.0	0.280	156.25	0.695	0.415	0.373	4.825
	5.0	0.287	121.95	0.639	0.352	0.294	3.761
Gelatin	1.0	0.271	185.19	0.731	0.460	0.402	6.762
	2.0	0.281	172.41	0.727	0.446	0.385	6.460
	3.0	0.289	158.73	0.689	0.400	0.365	5.356
	5.0	0.297	131.58	0.678	0.381	0.305	4.766

lations containing Albizia gum. This indicates that formulations containing gelatin exhibited a higher degree of packing in the die as a result of die filling than formulations containing Albizia gum.

The value of D_B represents the phase of particles rearrangement in the early stages of compression. D_B values tend to indicate the extent of fragmentation of particles or granules, although fragmentation can occur concurrently with plastic and elastic deformation of constituent particles. The values of D_B also decreased with an increase in the binder concentration. Formulations containing gelatin showed higher values than those containing Albizia gum, indicating that fragmentation of the granules decreased with an increased concentration of the binders (2).

The values of $D_{A,}$ which represent the total degree of packing achieved at zero and low pressures, also decreased with an increase in the binders concentration. Formulations containing Albizia gum generally showed lower D_A values than those containing gelatin.

The mean yield pressure P_y is inversely related to the ability of the formulations to deform plastically under pressure. The values of P_y decreased with an increase in the binders concentration, with formulations containing Albizia gum showing lower values than formulations containing gelatin. The results indicate that formulations containing Albizia gum as binder exhibited a faster onset of plastic deformation during compression than formulations containing gelatin. This implies that Albizia gum deforms plastically during compression faster than the standard binder.

Fig. 2 shows representative Kawakita plots for paracetamol formulations containing 3% (*m/m*) of the binding agent. A linear relationship was obtained at all compression pressures employed with the correlation coefficient of 0.999 for all formulations. Values of *a* and *ab* were obtained from the slope and intercept of the plots, respectively. Values

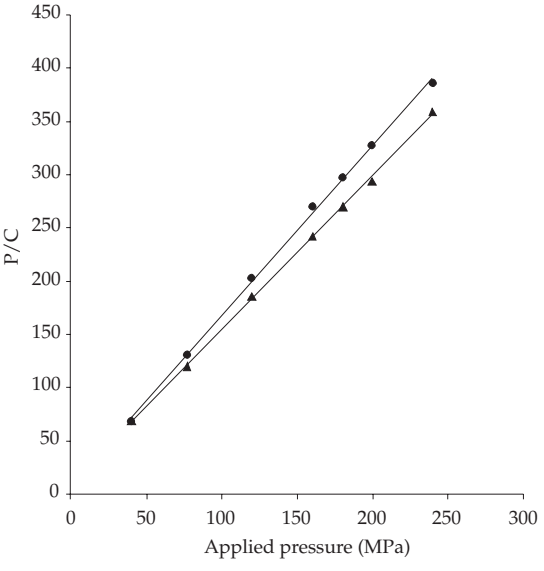

Fig. 2. Kawakita plots for paracetamol tablet formulations containing 3.0% (*m/m*) binder: ▲ Albizia gum, ● gelatin.

of 1- a give the initial relative density of the formulations, D_I, while P_K values were obtained from the reciprocal of the values of b. The values of D_I and P_k are included in Table I.

The values of D_I, which is a measure of the packed initial relative density of the formulation with the application of small pressure or tapping (2), are seen to decrease with an increase in the binders concentration. These values are also seen to be higher than the corresponding values of the loose initial relative density, D_o. This is in agreement with previous findings of Odeku and Itiola (2).

The value of P_k, which is an inverse measure of the amount of plastic deformation occurring during the compression process, was also found to decrease with increased concentration of the binding agents. Formulations containing Albizia gum had lower values than those containing gelatin. This implies that formulations containing gelatin exhibited a lower amount of total plastic deformation during the compression process than formulations containing Albizia gum. It has been shown that the lower the P_k value, the higher is the total plastic deformation during compression (2). Thus, formulations containing Albizia gum, which showed a faster onset of plastic deformation during compression as indicated by the low P_y values, also exhibited the highest amount of plastic deformation during the compression process.

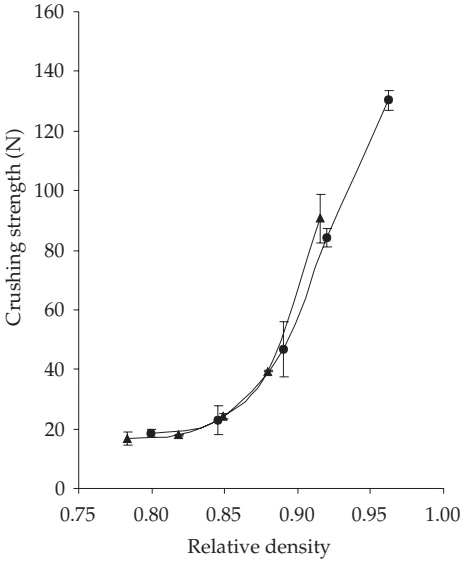

Fig. 3. Crushing strength *vs.* relative density for paracetamol tablets containing 3.0% (*m/m*) binder: ▲ Albizia gum, ● gelatin (mean ± SD, n = 3).

The mechanical properties of pharmaceutical tablets are quantifiable by the crushing strength and the friability of the tablets. Crushing strength provides a measure of tablet strength while friability is a measure of tablet weakness (3). There are now official requirements for crushing strength and friability in the *British Pharmacopoeia* (12) but there are no clear limits for acceptance or rejection of tablet batches probably because in the case of crushing strength, the desired crushing strength is largely dependent on the

intended use of the tablet (3, 19). For friability, conventional compressed tablets that lose less than 1% of their mass during the friability test are generally considered acceptable (19). Representative plots of the crushing strength and friability of the tablets *vs.* the relative density for tablets containing 3% (*m/m*) of the binding agents are presented in Figs. 3 and 4, respectively. Values of the crushing strength and friability of all samples at a relative density of 0.90, which is representative of commercial tablets, are given in Table II.

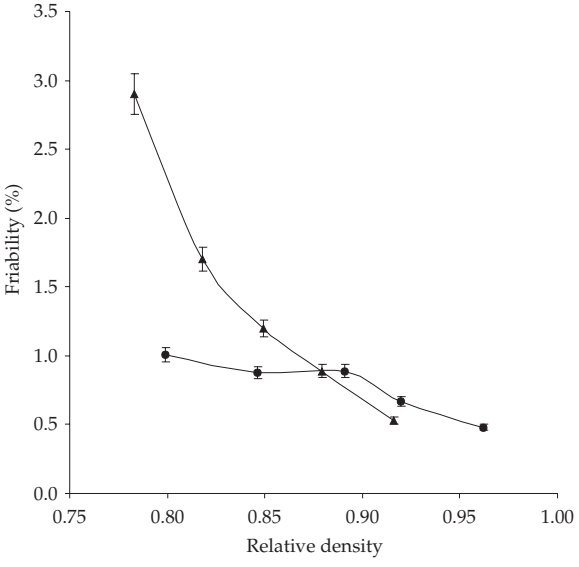

Fig. 4. Friability *vs.* relative density for paracetamol tablets containing 3.0% (*m/m*) binder: ▲ Albizia gum, ● gelatin (mean ± SD, $n = 3$).

Table II. Crushing strength, friability and crushing strength-friability ratio (CSFR) for paracetamol tablets[a]

Binder	Binder conc. (%, *m/m*)	Crushing strength (N)[b]	Friability (%)[b]	CSFR
	0.0	12.00 ± 1.24	1.65 ± 0.06	7.27
Albizia	1.0	25.55 ± 2.64	1.22 ± 0.04	20.94
	2.0	68.52 ± 1.18	0.98 ± 0.02	69.92
	3.0	69.20 ± 2.32	0.70 ± 0.03	98.86
	5.0	170.67 ± 1.64	0.65 ± 0.04	262.57
Gelatin	1.0	19.62 ± 1.34	1.10 ± 0.08	17.84
	2.0	56.75 ± 2.86	1.00 ± 0.06	56.75
	3.0	59.40 ± 1.15	0.83 ± 0.05	71.57
	5.0	129.89 ± 1.78	0.78 ± 0.06	166.53

[a] Relative density = 0.90, [b] Mean ± SD, $n = 3$.

The crushing strength values increased while those of friability decreased with an increase in relative density and concentration of the binding agent. It is well known that a high concentration of a plasto-elastic binding agent leads to an increase in plastic deformation of the formulation and subsequently to the formation of more solid bonds, resulting in tablets with more resistance to fracture and abrasion (3). All the paracetamol tablets generally had a friability value of < 1% (*m/m*) at concentrations greater than 2% (*m/m*) of the binder. Furthermore, tablets containing Albizia gum generally showed significantly higher crushing strength *($p < 0.001$)* and lower friability *($p < 0.05$)* values than tablets containing gelatin as binding agent. This suggests that at certain concentrations Albizia gum should provide adequate protection for tablets against abrasive motions during handling and subsequent use.

The mechanical strength of tablets can also be measured by the crushing strength--friability ratio (*CSFR*) (3). Generally, the higher the *CSFR* values, the stronger the tablet. The values of *CSFR* for the tablets at a relative density of 0.90 are included in Table II. The *CSFR* increased with an increase in the binding agent concentration, with tablets containing Albizia gum showing higher values than tablets containing gelatin. This implies that Albizia gum produced tablets that are generally stronger than gelatin. Furthermore, there was a marked increase in the *CSFR* values when the concentration of the binder was increased to 5% (*m/m*). Hence, the concentration of the binding agent used in tablet formulation needs to be carefully chosen.

It is notable that formulations containing Albizia gum, which had a faster onset and higher amount of plastic deformation during compression, as indicated by lower P_y and P_k values, respectively, also showed significantly ($p < 0.05$) higher mechanical strength as indicated by the higher *CSFR* values, especially at the high concentration of 5% (*m/m*) This result is in agreement with previous findings (2).

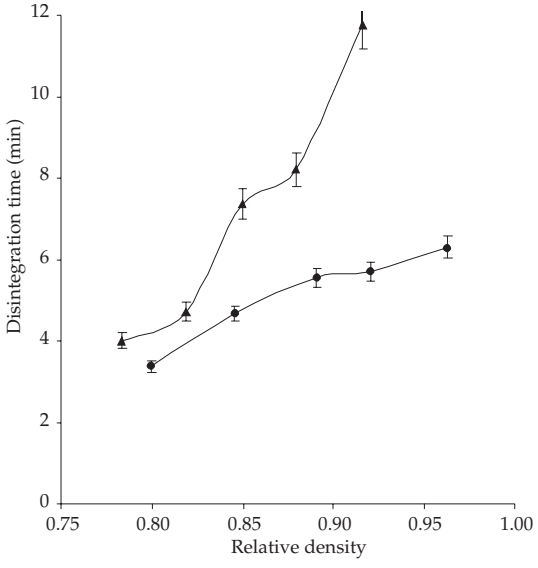

Fig. 5. Disintegration time *vs.* relative density for paracetamol tablets containing 3.0% (*m/m*) binder: ▲ Albizia gum, ● gelatin (mean ± SD, $n = 3$).

Disintegration time was plotted against the relative density of the tablet. Representative plots for tablets containing 3% (*m/m*) of the binding agent are presented in Fig. 5. The disintegration time of the tablet at a relative density of 0.90 is presented in Table III. The disintegration time generally increased with increased relative density of the tablets and with an increase in binder concentration. Tablets containing Albizia gum generally showed a significantly higher *($p < 0.001$)* disintegration time than tablets containing gelatin as binder. Furthermore, all the tablets conformed to the *British Pharmacopoeia* requirements (12) for uncoated tablets on disintegration, *i.e.*, disintegration within 15 min, except formulations containing 5% (*m/m*) Albizia gum with a disintegration time of 17 min. Thus, Albizia gum facilitated extensive plastic deformation, which would lead to an increase in the area of contact between particles, reducing the rate of fluid penetration into the interstitial void spaces. This results in the swelling of the disintegrant and disruption of the tablet is reduced at the higher relative density, thereby prolonging the disintegration time of the tablets.

Table III. Disintegration and dissolution characteristics of paracetamol tablets[a] (mean ± SD, n = *3).*

Binder	Binder conc. (%, *m/m*)	*D* (min)	t_{50} (min)	t_{90} (min)	k_1	k_2	t_1
	0.0	0.75 ± 0.12	9.56 ± 0.88	23.00 ± 1.84	0.036 ± 0.001	0.185 ± 0.011	37.0 ± 0.50
Albizia	1.0	1.66 ± 0.64	23.20 ± 1.46	73.20 ± 2.64	0.039 ± 0.004	0.108 ± 0.008	30.0 ± 3.00
	2.0	4.64 ± 0.28	25.80 ± 1.23	79.80 ± 2.24	0.031 ± 0.002	0.094 ± 0.009	30.0 ± 4.00
	3.0	10.32 ± 1.01	27.80 ± 1.04	93.20 ± 3.46	0.028 ± 0.005	0.080 ± 0.023	60.0 ± 2.00
	5.0	17.58 ± 1.46	112.50 ± 0.24	290.50 ± 2.96	0.009 ± 0.003	0.038 ± 0.014	205.0 ± 5.00
Gelatin	1.0	2.01 ± 0.24	9.00 ± 1.06	22.20 ± 3.14	0.251 ± 0.086	–	–
	2.0	3.80 ± 0.86	11.10 ± 1.28	22.50 ± 2.14	0.088 ± 0.046	0.127 ± 0.018	10.0 ± 1.00
	3.0	6.15 ± 0.76	12.05 ± 1.46	23.00 ± 1.31	0.070 ± 0.009	0.104 ± 0.012	10.0 ± 2.00
	5.0	13.20 ± 0.84	31.00 ± 0.89	62.80 ± 2.42	0.021 ± 0.004	0.064 ± 0.005	30.0 ± 4.00

[a] Relative density = 0.90, [b] Mean ± SD, $n = 3$.

The amount of paracetamol released was plotted against time and representative plots for tablets containing 3% (*m/m*) are represented in Fig. 6. The values of t_{50} and t_{90} (time required for 50% and 90% of paracetamol to be released) were calculated. Values of t_{50} and t_{90} for all samples at a relative density of 0.90 are presented in Table III. The t_{50} and t_{90} generally increased with an increase in relative density of tablets containing Albizia gum, showing higher values than that for tablets containing gelatin.

The integrated form of the equation of Noyes and Whitney (20) is:

$$\ln[C_s / (C_s - C)] = kt \qquad (7)$$

where C_s is the concentration of the solute at saturation, C is the concentration at time t, and k is a dissolution rate constant. Values of $\ln [C_s / (C_s - C)]$ were plotted versus t (21)

as shown typically for tablets containing 3% (*m/m*) of binders in Fig. 7. In all cases, except for tablets containing 1% (*m/m*) of gelatin at certain relative densities, two straight regression lines of slopes k_1 and k_2 were obtained. The time at which the lines intersect is denoted by t_1.

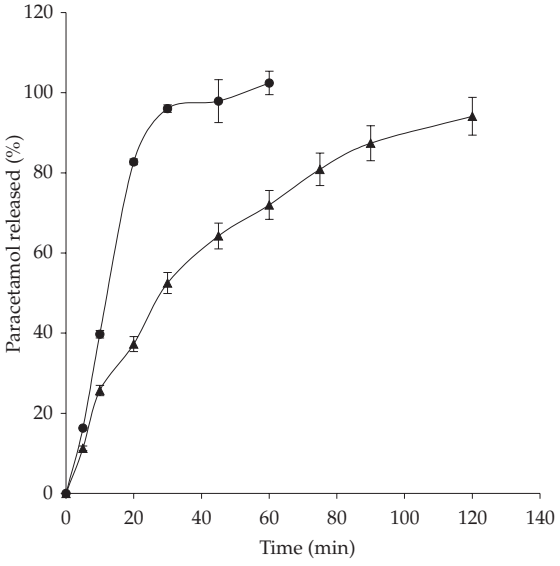

Fig. 6. Paracetamol released *vs.* time for paracetamol tablets containing 3.0% (*m/m*) binder: ▲ Albizia gum, ● gelatin (mean ± SD, $n = 3$).

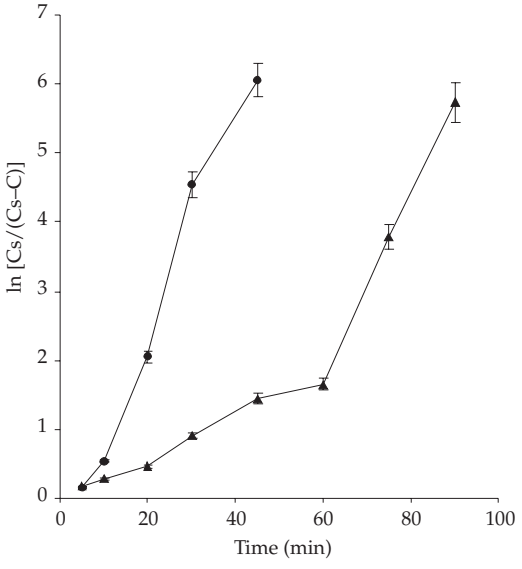

Fig. 7. In $[C_s/(C_s - C)]$ *vs.* time plots for paracetamol tablets containing 3.0% (*m/m*) binder: ▲ Albizia gum ($R = 0.916$), ● gelatin ($R = 0.920$) (mean ± SD, $n = 3$).

Values of t_{50}, t_{90}, t_1, k_1 and k_2 for all samples at the relative density of 0.90 are presented in Table III. It is seen that the values of t_{50}, t_{90} and t_1 increased with an increase in binder concentration while the values of k_1 and k_2 decreased. There was a marked increase in the disintegration and dissolution times of the tablet when the concentration of Albizia gum was increased to 5% *(m/m)*. Tablets containing Albizia gum generally had significantly ($p < 0.001$) higher disintegration and dissolution times than tablets containing gelatin as a binding agent. Furthermore, the values of k_1 for the tablets were lower than the values of k_2 with the implication that the dissolution rate of the drug was faster after t_1. The change from k_1 to k_2 at time t_1 is attributable to a change in the surface area due to the break up of the tablets into fragments (3, 21). However, it can be seen from Table III that t_1 values were generally higher than the disintegration time values. This can probably be ascribed to the greater agitation employed in the disintegration test than in the dissolution test (3, 19).

Tablets prepared from Albizia gum showed higher dissolution times compared to formulations containing gelatin, as indicated by their t_{50} and t_{90} values.

This suggests that Albizia gum could be useful when slower dissolution rates are desired and also in the formulation of controlled release dosage forms at certain concentrations. A similar application has been found for khaya gum, which was found to form a hydrophilic matrix that facilitated the release of paracetamol from the tablet formulation in a controlled manner (16).

CONCLUSIONS

The results of the present study show that formulations containing Albizia gum as a binding agent show a faster onset and higher amount of plastic deformation under compression pressure. Albizia gum produced tablets with stronger mechanical properties and longer disintegration and dissolution times than gelatin BP. This suggests that Albizia gum could be useful as a binding agent, especially when higher mechanical strength and slower dissolution rates are desired.

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S A Ž E T A K

Evaluacija *Albizia zygia* gume kao veziva u tabletama

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Albizia guma je evaluirana kao vezivo u tabletama i uspoređena sa želatinom BP. Svojstva stlačivosti analizirana su mjerenjem gustoće i uporabom Heckelove i Kawakitine jednadžbe, dok su mehanička svojstva tableta evaluirana mjerenjem lomljivosti. Sposobnost oslobađanja lijeka iz tableta procijenjena je mjereći vrijeme dezintegracije i otapanja. Pripravci s Albizia gumom kao vezivom manje se plastično deformiraju uslijed tlaka kompresije nego pripravci sa želatinom. Jačina loma, vrijeme dezintegracije i

otapanja povećalo se s povećanjem udjela veziva, dok se lomljivost smanjila. Tablete s Albizia gumom imaju bolja mehanička svojstva i dulje vrijeme dezintegracije i otapanja od tableta sa želatinom. Zbog toga se Albizia guma može uporabiti kao vezivo, posebice kada su poželjna bolja mehanička svojstva i sporije oslobađanje lijeka.

Ključne riječi: Albizia guma, želatina, Heckelova jednadžba, Kawakita jednadžba, mehanička svojstva, oslobađanje lijeka

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