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Research Article

Terminalia Gum as a Directly Compressible Excipient for Controlled Drug Delivery

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ABSTRACT. The exudates from the incised trunk of *Terminalia randii* has been evaluated as controlled release excipient in comparison with xanthan gum and hydroxypropylmethylcellulose (HPMC) using carvedilol (water insoluble) and theophylline (water soluble) as model drugs. Matrix tablets were prepared by direct compression and the effects of polymer concentration and excipients—spray dried lactose, microcrystalline cellulose and dicalcium phosphate dihydrate on the mechanical (crushing strength (CS) friability (F) and crushing strength–friability ratio (CSFR)) and drug release properties of the matrix tablets were evaluated. The drug release data were fitted into different release kinetics equations to determine the drug release mechanism(s) from the matrix tablets. The results showed that the CS and CSFR increased with increase in polymer concentration while F decreased. The ranking of CS and CSFR was HPMC > terminalia > xanthan while the ranking was reverse for F. The ranking for t_{25} (i.e. time for 25% drug release) at a polymer concentration of 60% was xanthan > terminalia = HPMC. The dissolution time, t_{25}, of theophylline matrices was significantly lower ($p<0.001$) than those of carvedilol matrix tablets. Drug release from the matrices was by swelling, diffusion and erosion. The mechanical and drug release properties of the tablets were significantly ($p<0.05$) dependent on the type and concentration of polymer and excipients used with the release mechanisms varying from Fickian to anomalous. Terminalia gum compared favourably with standard polymers when used in controlled release matrices and could serve as a suitable alternative to the standard polymers in drug delivery.

KEY WORDS: excipients; hydroxypropylmethylcellulose; matrix tablets; terminalia gum; xanthan gum.

INTRODUCTION

Hydrophilic polymers have been used extensively in pharmaceutical formulations as matrix system for controlled drug release and drug targeting (1–5). There are a number of techniques applied in the formulation and manufacturing of controlled release dosage forms. However, the matrix tablets prepared by direct compression have attracted more attention due its technological simplicity in comparison with other controlled release systems (6). The matrix system usually consists of hydrophilic polymer, drug and other excipients distributed throughout the matrix. Drug release from these matrices has been found to be dependent on polymer wetting, polymer hydration and polymer dissolution. The mechanisms by which drug is released from the tablets are also dependent on many variables such as the rate of dissolution/diffusion of soluble excipients or drug out of the tablet and the rate at which the insoluble excipients or drug in the polymer/excipient/drug complex erodes or dissolves (7).

A number of natural and modified polymers such as xanthan gum, guar gum, alginates, carrageenan, karaya gum and khaya gum (1–5,8,9) have been found to be useful in the formulation of oral controlled release dosage forms due to their hydrophilic properties. Some of these polymers have been found to be useful in providing zero-order drug release kinetics and, in some cases, have shown superior properties to existing polymers. The fact that these natural hydrophilic polymers are readily available, biodegradable and non-toxic have fostered the interest in developing new natural polymer gums for pharmaceutical use to meet the needs of drug formulators.

Recent studies have shown the potential of terminalia gum, a natural polysaccharide obtained from the incised trunk of *Terminalia randii* (Family Combretaceae) tree as a binding agent in carvedilol tablet formulations (10). Terminalia gum has been shown to contain highly branched polysaccharides consisting of galacturonic, glucuronic and 4-*O*-methylglucuronic acids, as well as galactose, arabinose, rhamnose, mannose and xylose, although the neutral sugars and total uronic acid content have been shown to vary depending on the species of terminalia (11). The viscosity and pH of a 1% *w*/*v* solution of *T. randii* gum at room temperature have been shown to be 27.5 cp and 4.56, respectively. Terminalia gum is amorphous in nature and exhibits thixotropy which is the ability of some non-Newtonian

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pseudoplastic fluids to show a shear-dependent change in viscosity. When used as a binding agent, carvedilol tablet formulations containing terminalia gum showed slower disintegration and dissolution times when compared with those prepared with polyvinylpyrrolidone and corn starch, indicating its possible application in controlled release tablet formulations (10). The potential use of this inexpensive device for the release of drugs at controlled and perhaps time-independent rates is of particular interest.

Thus, in the present study, terminalia gum has been evaluated as a directly compressible controlled release excipient in carvedilol (water insoluble) and theophylline (water soluble) matrix tablets in comparison with xanthan gum (XG) and hydroxypropylmethylcellulose (HPMC). The properties of the tablets and drug release from the matrices were studied, and the effects of polymer type and polymer concentration on the release kinetics of the matrix formulations were investigated. Attempts were also made to determine the drug release mechanism(s) and to evaluate the effects of some tablet excipients on the mechanical and drug release properties of the matrix tablets.

MATERIALS AND METHODS

Materials

The materials used were carvedilol (gift from Ranbaxy Pharmaceuticals New Delhi, India), theophylline (Sigma Chemical Co., St. Louis, USA), HPMC (Ranbaxy Laboratories Ltd, Gurgoan, India), microcrystalline cellulose (MCC; FMC Biopolymers, Newark, USA), dicalcium phosphate dihydrate (DCPD; Ranbaxy Research Laboratories, New Delhi, India), spray dried lactose (SDL; Vardhman Healthcare, Ambala, India), xanthan gum (Dabur India Ltd., Sahibabad, India), magnesium stearate (Loba Chemie Pvt Ltd, Mumbai, India), Talc (Loba Chemie Pvt Ltd, Mumbai, India) and terminalia gum obtained from *T. randii* (Family Combretaceae). The gum was collected from Olabisi Onabanjo University, Ago-Iwoye, Nigeria, and authenticated by Mr. O.S. Shasanya of the Forest Research Institute of Nigeria with a voucher number FHL no. 107917. All other materials are analytical grades. A description of the collection and purification of the gum has been given elsewhere (10).

Preparation of Tablets

The matrix tablets were prepared by direct compression, and the detailed compositions of the matrix tablet formulations are given in Table I. Briefly, the required amount of drug, polymer gum, excipients and lubricants (magnesium stearate and talc) were thoroughly mixed and the mixtures were compressed using a single punch machine (Modern Engineering, New Delhi, India). Carvedilol matrix tablets (200 mg) were prepared using an 8.2-mm-diameter die, while theophylline matrix tablets (350 mg) were compressed with a 9.2-mm-diameter die.

Tablet Properties

For uniformity of weight, 20 tablets from each batch were selected randomly and weighed individually using a

Table I. Composition of Matrix Tablet Formulations

Formulation code	Composition (% *w/w*)																	
	A1	A2	A3	B1	B2	B3	C1	C2	C3	D1	D2	D3	E1	E2	E3	F1	F2	F3
Carvedilol	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5			
Theophylline																33.3	33.3	33.3
Terminalia gum	40	50	60	–	–	–	–	–	–	60	–	–	60	–	–	60		
Xanthan	–	–	–	40	50	60	–	–	–	–	60	–	–	60	–		60	
Hydroxypropylmethylcellulose	–	–	–	–	–	–	40	50	60	–	–	60	–	–	60			60
Spray dried lactose	–	–	–	–	–	–	–	–	–	–	–	–	32	32	32			
Microcrystalline cellulose	–	–	–	–	–	–	–	–	–	32	32	32	–	–	–			
Dicalcium phosphate dihydrate	52	42	32	52	42	32	52	42	32	–	–	–	–	–	–	3.7	3.7	3.7
Magnesium stearate	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Total (%)	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100

Table II. Mechanical and Drug Release Properties of Carvedilol Matrix Tablets

Polymer	Polymer concentration (%)	Average weight	Crushing strength (N)	Friability (%)	CSFR	Drug content (%)	t_{25} (hours)
Terminalia	40	201.73±0.72	39.98±2.73	0.75±0.02	53.31	100.12±2.05	0.05±0.00
	50	202.04±0.74	41.65±2.00	0.62±0.02	67.18	95.63±4.06	4.50±0.02
	60	202.49±0.24	45.77±2.06	0.52±0.03	88.02	95.21±3.83	10.00±0.92
Xanthan	40	199.10±0.68	22.83±1.00	0.94±0.03	24.29	90.30±1.53	0.40±0.02
	50	198.45±0.59	23.72±2.68	0.95±0.02	24.97	93.58±2.02	11.00±0.97
	60	197.63±0.78	26.17±1.07	0.94±0.03	27.84	98.30±7.97	11.70±1.01
HPMC	40	201.18±0.54	96.33±5.00	0.18±0.06	535.17	97.70±1.55	7.80±0.65
	50	200.50±0.60	72.72±2.00	0.27±0.05	269.33	99.61±0.69	8.60±0.87
	60	200.39±0.42	82.52±3.85	0.19±0.07	434.32	100.73±0.63	10.00±1.24

Mettler Toledo electronic balance (Zurich, Switzerland) and their mean weights were calculated.

The crushing strength (CS) of the tablets was determined using Monsanto hardness tester (MAC, Macro Scientific Works, New Delhi, India) while the friability (F) of the tablets was determined using a friabilator (MAC, Macro Scientific Works, New Delhi India) at 25 rpm for 4 min (100 revolutions). All determinations were done in triplicate.

Determination of Drug Content

Ten tablets each were finely powdered, and an amount equivalent to the weight of 6.25 mg of carvedilol and 100 mg of theophylline was weighed respectively into a 100-mL volumetric flask and 0.1 N HCL was added. The solution was sonicated for 15 min to allow the drug to go completely into solution. The solution was made up to volume and then filtered. Dilutions were made and the absorbance was taken at 242 and 271 nm for carvedilol and theophylline, respectively, and the drug content was calculated. Determinations were done in triplicate.

Water Uptake

Each tablet was initially weighed (W_1) and then placed in 900 ml of 0.1 M HCL at 37±0.5°C in a shaking water bath. The tablets were removed from the medium at different time intervals (0.5, 1, 2, 3, 4, 5 and 6 h), dried between two filter papers to remove surface water and re-weighed (W_2). The percentage water uptake was determined by using the following equation (12):

$$\% \text{ water uptake} = [(W_2 - W_1)/W_1] \times 100 \quad (1)$$

In Vitro Dissolution Studies

The *in vitro* dissolution test was carried out in 900 ml 0.1 M HCL maintained at a constant temperature of 37±0.5°C for 24 h using a USP type 2 dissolution apparatus (Labindia Dissolution Test Apparatus DISSO 2000, Labindia Instruments PVT Ltd, Thane, India) rotated at 50 rpm. The pre-weighed tablet was placed into the dissolution medium, and 5 ml sample was withdrawn at different time intervals and replaced with same volume of fresh medium. The samples were analysed using a UV spectrophotometer (Genesys 6, Thermospectronic, Houston, USA) at a wavelength of 242 and 271 nm for carvedilol and theophylline, respectively. Determinations were done in triplicates or more.

Release Kinetics

Data obtained from the release studies were fitted to various kinetic equations to find out the kinetics and mechanism of drug release from the matrix tablets. The drug

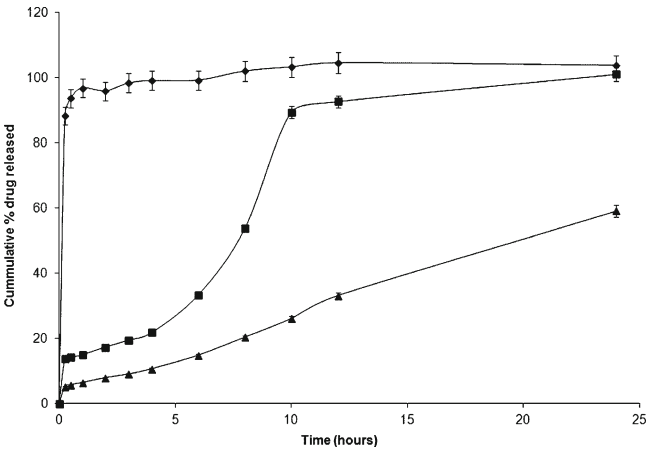

Fig. 1. Effect of terminalia gum concentration on the release profile of carvedilol tablets. *Diamond* 40% *w/w* (A1), *square* 50% *w/w* (A2), *triangle* 60% *w/w* (A3)

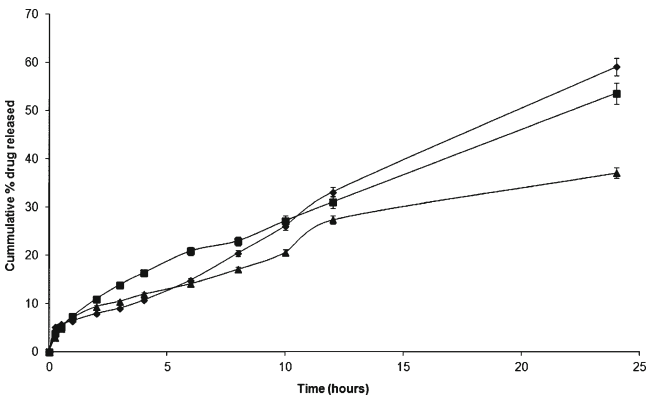

Fig. 2. Drug release profiles of carvedilol matrices containing the different polymers at a concentration of 60% *w/w*; *diamond* terminalia (A3), *triangle* xanthan (B3), *square* HPMC (C3)

Table III. Drug Release Parameters Obtained by Fitting Release Data for Carvedilol Matrix Tablets into the Different Release Kinetics Models

		Zero order		Higuchi		Hixson Crowell		First order		Korsmeyer		
Polymer	Polymer concentration (% *w/w*)	k_0 (h^{-1})	r^2	k_h	r^2	k	r^2	k	r^2	n	k	r^2
Terminalia	40	–	–	–	–	–	–	–	–	–	–	–
	50	5.37	0.911	10.94	0.790	0.18	0.961	0.04	0.868	0.57	5.10	0.939
	60	3.57	0.990	13.99	0.732	0.12	0.957	0.08	0.824	0.87	2.35	0.825
Xanthan	40	–	–	–	–	–	–	–	–	–	–	–
	50	1.39	0.994	0.36	0.967	0.06	0.953	0.08	0.768	0.45	1.60	0.971
	60	1.34	0.994	3.04	0.961	0.06	0.919	0.08	0.773	0.53	1.49	0.960
HPMC	40	2.75	0.999	7.57	0.979	0.09	0.942	0.08	0.804	0.74	2.83	0.990
	50	2.20	0.998	10.05	0.972	0.08	0.930	0.08	0.794	0.68	2.28	0.992
	60	1.94	0.994	6.40	0.972	0.07	0.925	0.08	0.785	0.60	2.10	0.992

released data were fitted to zero-order, Higuchi, first-order, Hixson–Crowell and Korsemeyer–Peppas models.

Zero-order equation (13):

$$Q = Q_0 + k_0 t \tag{2}$$

where Q is the amount of drug release at time t, k_0 is the apparent dissolution rate constant or zero-order release constant and Q_0 is the initial concentration of the drug in the solution resulting from a burst effect.

First-order equation (13,14):

$$\ln Q = \ln Q_0 + k_1 t \tag{3}$$

where k_1 is the first-order release constant, and in this case, the drug released at each time is proportional to the residual drug inside the dosage form.

Higuchi equation (15):

$$Q = k_H t^{1/2} \tag{4}$$

where Q is the amount of drug release at time t and k_H is the Higuchi release constant. This is the most widely model to describe the drug release from pharmaceutical matrices.

Hixson–Crowell equation (16):

$$Q_0^{1/3} - Q_t^{1/3} = k_s t \tag{5}$$

where Q_0 is the initial amount of drug in the matrix tablet, Q_t is the amount of drug remaining in the pharmaceutical dosage form at time t, and k_s is a constant incorporating the surface/volume ratio.

Korsmeyer–Peppas equation (7):

$$Q_t/Q_a = k_k t^n \tag{6}$$

where k_k is the release rate constant which considers the structural and geometric characteristics of the tablet, and n is the diffusional exponent or release exponent, indicative of the drug release mechanism. The value of $n=0.5$ indicates Fickian Diffusion (Higuchi Matrix), $0.5<n<1.0$ indicates anomalous (non-Fickian) diffusion, $n=1.0$ indicates case II transport (zero-order release) and $n>1.0$ indicates super case II transport (7,17).

Statistical Analysis

Statistical analysis was carried out using analysis of variance with computer software GraphPad Prism® 4 (GraphPad Software Inc. San Diego, USA). Tukey–Kramers multiple comparison tests were used to compare the effects of the excipients on the mechanical and drug release properties of the tablets. At 95% confidence interval, P values less than or equal to 0.05 were considered significant.

RESULTS AND DISCUSSIONS

Effect of Polymer Type and Concentration

The results of the mechanical and drug release properties of the carvedilol matrix tablets are presented in Table II. The results show that all the tablets were within acceptable limits of weight variation (18). The crushing strength (CS) of the tablets generally increased with increase in the polymer concentration while friability (F) decreased. This could be due to the fact that polymers are plasto-elastic, and as the concentration of the polymer increased in the matrix tablets, there would be an increase in plastic deformation subsequently leading to the formation of more solid bonds in the

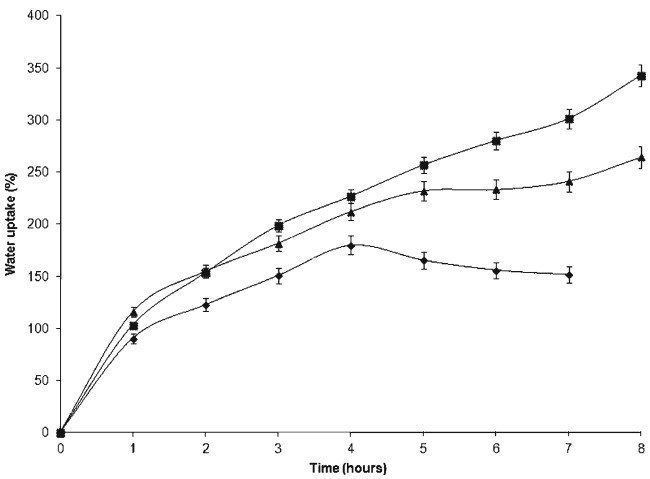

Fig. 3. Water uptake of matrix tablets containing different polymers at 60% concentration; *diamond* terminalia (A3), *triangle* xanthan (B3), *square* HPMC (C3)

Table IV. Mechanical and Drug Release Properties of Carvedilol Matrix Tablets Containing Different Excipients

Excipient type	Polymer type	Crushing strength (N)	Friability (%)	CSFR	t_{25} (hours)
SDL	Terminalia	16.37±1.02	4.77±0.02	3.43	7.90±0.24
	Xanthan	22.05±1.82	1.48±0.02	14.90	11.32±0.89
	HPMC	30.18±1.82	1.29±0.03	23.40	5.80±0.56
MCC	Terminalia	22.83±2.53	1.07±0.02	21.34	15.00±1.32
	Xanthan	39.20±2.20	0.45±0.01	87.11	17.00±1.68
	HPMC	61.25±2.10	0.41±0.02	149.39	8.00±0.12
DCPD	Terminalia	45.77±2.06	0.52±0.03	88.02	10.00±0.92
	Xanthan	26.17±1.07	0.94±0.03	27.84	11.70±1.01
	HPMC	82.52±3.85	0.19±0.07	434.32	10.00±1.24

tablet resulting in tablets with higher crushing strength and more resistance to fracture and abrasion (19). The crushing strength–friability ratio (CSFR) which has been used to measure the mechanical strength of tablets (19) also increased with increase in the concentration of the polymers. The ranking of CS and CSFR for the tablets was HPMC > terminalia gum > xanthan gum while the ranking was reverse for F. Statistical analysis shows that there were significant ($p<0.001$) difference in the mechanical strength of the matrix tablets.

The release profiles of carvedilol matrix tablets containing different concentrations of terminalia gum are presented in Fig. 1 while the values of t_{25} (i.e. time for 25% drug release) for all the matrix tablets are presented in Table II. Terminalia gum at a concentration of 40% provided an immediate release of carvedilol while 50% and 60% provided a controlled release to varying degrees. The amount of drug released after 10 h was 89% and 26% for matrices containing 50% *w/w* and 60% *w/w* of terminalia gum, respectively. When polymer concentration is low, the hydrated matrix would be highly porous with a low degree of tortuosity leading to low gel strength and rapid diffusion of the drug from the matrix (20). The results of the t_{25} for the matrix tablets (Table II) showed that the time taken for 25% of the drug to be released increased significantly ($p<0.005$) with increase in the concentration of terminalia polymer in the matrix tablets. Xanthan gum matrices also provided immediate release of carvedilol at a concentration of 40% but gave a similar pattern of controlled drug release at concentration of 50% and 60%. On the other hand, there was no significant difference ($p>0.05$) in the values of t_{25} from HPMC matrices containing the different concentration of the polymers employed in the formulations. This result is in agreement with previous reports (21). HPMC has been shown to form strong viscous gel when the polymer hydrates on contact with the dissolution fluid with few interstitial spaces between the macrogels and drug release in controlled by diffusion through the interstitial spaces (22).

The release profiles of carvedilol matrix tablets containing the different polymers at concentration of 60% *w/w* are shown in Fig. 2. There was a sustained release of carvedilol from the matrix tablets over 24 h indicating a gradual release which is desirable in controlled release formulations. The amount of carvedilol released after 10 h for terminalia, xanthan and HPMC matrices was 26% *w/w*, 20% *w/w* and 27% *w/w*, respectively. There was no statistically significant ($p<0.05$) difference in the amount of drug released after 10 h for the tablets prepared using all the polymers at a concentration of 60% *w/w*. It would be expected that HPMC matrix formulation with the highest crushing strength would have the highest t_{25}, but this was not so. Some workers have shown that drug release from HPMC matrix tablets was not affected by the hardness of the tablets (23).

The kinetic of drug release from dosage forms are important as they influence the dosing interval, bioavailability, overall patient compliance and in many instances the occurrence of toxic or untoward effects (24). The mechanism of release of carvedilol from the matrix tablets were elucidated by fitting the dissolution data into different release kinetic models. The kinetic parameters and fitting ability (correlation coefficient, r^2) derived from the equations are presented in Table III. It has been established that tablet formulations with up to 60% drug release within the first 15 min of the dissolution test should not be used for the determination of release mechanisms since they do not provide a controlled release of the drug from the matrix tablets (7). Hence, the release mechanism for formulations containing 40% terminalia and xanthan gum could not be evaluated.

Drug release from hydrophilic matrices has been shown to be a complex interaction between swelling, diffusion and erosion mechanisms (25,26). The results showed that the zero-order and Korsmeyer equations gave the best fit with highest correlation coefficient (r^2) for all the polymers. This

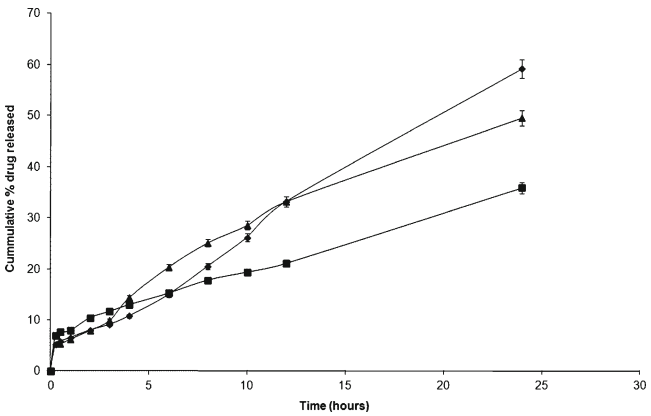

Fig. 4. Drug release profiles of terminalia matrix tablets containing the different excipients at a concentration of 32% *w/w*; *diamond* DCPD (A3), *triangle* MCC (D1), *square* SDL (E1)

Table V. Drug Release Parameters Obtained by Fitting Release Data for Carvedilol Matrix Tablets Containing the Various Excipients into the Different Release Kinetics Models

		Zero order		Higuchi		Hixson Crowell		First order		Korsmeyer		
Polymer	Polymer concentration (% *w/w*)	k_0 (h^{-1})	r^2	k_h	r^2	k	r^2	k	r^2	n	k	r^2
SDL	Terminalia	1.94	0.961	8.18	0.991	0.08	0.859	0.08	0.840	0.71	2.05	0.982
	Xanthan	1.45	0.993	1.05	0.961	0.06	0.954	0.08	0.769	0.46	1.59	0.968
	HPMC	2.35	0.958	8.25	0.998	0.08	0.846	0.08	0.820	0.68	2.54	0.998
MCC	Terminalia	1.17	0.995	0.47	0.961	0.05	0.959	0.08	0.792	0.45	1.27	0.969
	Xanthan	1.09	0.996	1.90	0.970	0.06	0.952	0.08	0.760	0.50	1.19	0.965
	HPMC	2.01	0.985	8.08	0.990	0.08	0.890	0.08	0.794	0.68	2.19	0.999
DCPD	Terminalia	3.57	0.990	13.99	0.936	0.12	0.957	0.08	0.824	0.87	2.35	0.939
	Xanthan	1.34	0.966	3.04	0.961	0.06	0.919	0.08	0.773	0.53	1.49	0.960
	HPMC	1.94	0.994	6.40	0.972	0.07	0.925	0.08	0.785	0.60	2.10	0.992

indicates that drug release from the polymer matrices was independent of time and concentration of the drug present in the matrix tablets. The release parameters, n, derived from Korsmeyer kinetics model increased with increase in polymer concentration. The release mechanism was generally non-Fickian which approached case II transport for 60% terminalia matrix tablets. The non-Fickian release mechanism implies that the release is controlled by diffusion or a combination of diffusion and macromolecular chain relaxation mechanisms. On the other hand, the release from the xanthan gum matrices was Fickian at 50% but approaches case I release mechanism as the concentration of the polymer increases. For HPMC matrices, the release mechanism was anomalous non-Fickian diffusion. The release rate constant, k, derived from the Korsmeyer equation decreased with increase in polymer concentration. This could probably be due to the hydration of the polymers and formation of a gel layer with a longer diffusion path length as the polymer content was increased (27).

Representative plots of the water uptake of the matrix tablets made with the different polymers at concentration of 60% *w/w* are presented in Fig. 3. The result showed that there was an initial rapid water uptake for all the polymer matrices leading to the formation of a viscous gel layer around the matrix, which subsequently slows diffusion of the drug from the tablets. The rate and degree of hydration of polymers have been shown to depend on the chain length and the degree of substitution (27). The three polymer matrices used in the present study exhibited different rate and extent of water uptake. However, for terminalia matrix tablets, erosion of the matrix started after 4 h. It has been shown that when water penetrates into polymer matrix, polymer chain mobility is enhanced and the chain eventually disentangles at the advancing front separating the gel layer from the erosion/dissolution front. Polymer swelling usually occurs as a result of osmotic stress exerted at the advancing glassy core (28).

Effect of Excipients

The addition of directly compressible excipients into matrix formulations has been used not only to alter the tablet size but also to improve the compaction and mechanical properties of the tablet and to aid optimum release of drug from the matrix (3,4,29). The excipients used were spray dried lactose (SDL) which is water soluble, and microcrystalline cellulose (MCC) and dicalcium phosphate dihydrate (DCPD) which are water insoluble. The results of the mechanical and drug release properties of carvedilol matrix tablets prepared with the different concentrations of the excipients are shown in Table IV. The ranking of the crushing strength and CSFR for matrix tablets containing the different excipients was generally DCPD > MCC > SDL while for friability the ranking was reverse. This result shows that the type of excipients used significantly ($p<0.001$) altered the mechanical properties of the matrix tablets with matrices containing DCPD producing tablets with the highest mechanical properties. Thus, the excipients included in the formulation of the matrix tablets need to be carefully selected to obtain tablets with optimum mechanical strength.

The release profiles of terminalia matrix tablets containing the different excipients at a concentration of 32% *w/w* are shown in Fig. 4 while the results of the dissolution time (t_{25}) are presented in Table IV. The ranking of t_{25} was generally MCC > DCPD > SDL. It was observed that matrix formulations containing SDL has the lowest t_{25} values for all formulations containing the different polymers. Spray dried lactose is freely soluble and will dissolve in the dissolution medium, thereby providing a pathway for diffusion of drug and erosion of matrix,

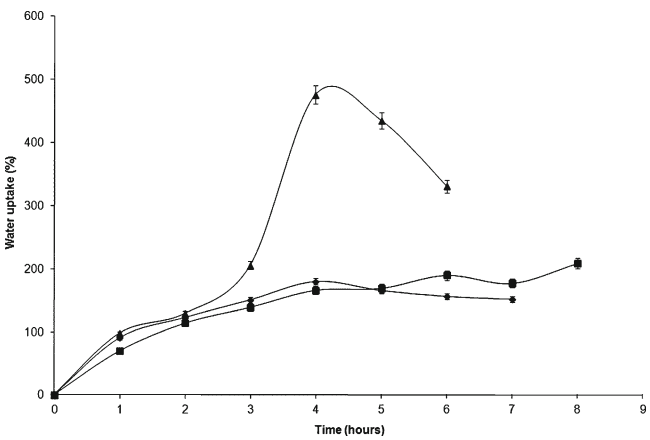

Fig. 5. Water uptake of terminalia matrix tablets containing different excipients at a concentration of 32% *w/w*; *diamond* DCPD (A3), *triangle* SDL (E1), *square* MCC (D1)

Table VI. Mechanical and Drug Release Properties of Carvedilol and Theophylline Matrix Tablets

Polymer	Drug	Crushing strength (N)	Friability (%)	CSFR	t_{25} (hours)
Terminalia	Theophylline	55.53±0.01	0.54±0.02	102.83±1.45	1.50±0.14
	Carvedilol	45.77±2.06	0.52±0.03	88.02±2.42	10.00±0.92
Xanthan	Theophylline	84.93±2.83	0.28±0.01	303.32±1.24	2.60±0.56
	Carvedilol	26.17±1.07	0.94±0.03	27.84±0.95	11.70±1.01
HPMC	Theophylline	111.07±3.26	0.05±0.00	2,221.40±1.45	2.80±0.37
	Carvedilol	82.52±3.85	0.19±0.07	434.32±1.25	10.00±1.24

leading to faster dissolution of the drug from the tablet (4,30). In the early stage of the dissolution test, matrix thickness increases due to polymer swelling and successive polymeric chain disentanglement (true polymer dissolution) leading to the formation of a gelatinous layer with high viscosity. However, the dissolution of the drug and/or fillers in the tablet counteracts this increase in thickness, producing a reduction of the volume of the matrix as a result of the erosion of the swollen polymer until the polymer matrix completely disintegrates (31). There appears to be an interaction between the polymer and excipients which affected the rate of drug release from the matrix tablets.

The data obtained by fitting the dissolution data into the different release kinetics models are presented in Table V. Terminalia matrix formulations containing SDL and DCPD gave anomalous non-Fickian release mechanism while those containing MCC gave Fickian release mechanism. Xanthan gum matrix tablets generally exhibited Fickian diffusion while HPMC matrices exhibited non-Fickian release mechanism. Non-Fickian/anomalous release mechanism indicates that a combination of diffusion and polymer erosion is occurring within the formulation. The nature and type of excipients appeared to have no effect on the release mechanism of formulations containing HPMC. This is similar to the results obtained by other workers (32).

Representative plots of water uptake against time for terminalia gum matrix tablets containing the different excipients at a concentration of 32% *w/w* are shown in Fig. 5. It can be observed that terminalia matrix containing SDL exhibited higher water uptake than those containing the other excipients but after 4 h, erosion of the matrix starts. SDL being a water-soluble excipient facilitated faster water penetration into the polymer, thus creating excessive osmotic force and polymer chain relaxation (33), leading to a decrease in tortuosity and/or increase in the matrix porosity. These results in an increase in the dissolution rate of the tablets and the weakening of the matrix lattice due to the presence of the water-soluble excipient which provided a diffusion pathway for erosion/disintegration of the matrix (4). Terminalia matrix containing DCPD showed the least water uptake, and it was observed that after 4 h, erosion of the matrix tablet commenced. Xanthan and HPMC matrix formulations had steady hydration for 8 h due to water uptake. Xanthan gum has been shown to demonstrate high degree of swelling due to water uptake and low degree of erosion due to polymer relaxation (34).

Effect of Drug Solubility

The results of mechanical and drug release properties of matrix tablets prepared using carvedilol and theophylline are presented in Table VI while the drug release profiles for terminalia matrices containing the two model drugs are shown in Fig. 6. Matrix formulations containing theophylline gave higher mechanical strength but lower dissolution times than those containing carvedilol. The release of theophylline from the matrix formulations was significantly ($p<0.001$) faster than the release of carvedilol from all the polymer matrices. This could be due to the solubility of theoplylline which is more freely soluble than carvedilol. The release parameters shown in Table VII indicated that the mechanism for the release for the theophylline and carvedilol were similar as indicated by the release exponent, n, which was non-Fickian or anomalous, implying that the drugs were released by diffusion and/or erosion. However, the release exponent approaches zero-order (case II transport), with n values of 0.83 and 0.87 for terminalia matrices containing theophylline and carvedilol, respectively.

CONCLUSION

The results of the present work showed that terminalia gum compared favourably with HPMC and XG as matrix system for the controlled release of carvedilol and theophylline. Terminalia gum at a concentration of 60% provided a near zero-order time-independent release of carvedilol for over 24 h. The mechanical and drug release properties of the matrix were affected by the type and concentration of excipients used in the formulations, and the drug release was controlled by diffusion, swelling and erosion. Terminalia gum compared favourably with standard polymers when used in controlled release matrices and could serve as a suitable alternative to the standard polymers in drug delivery.

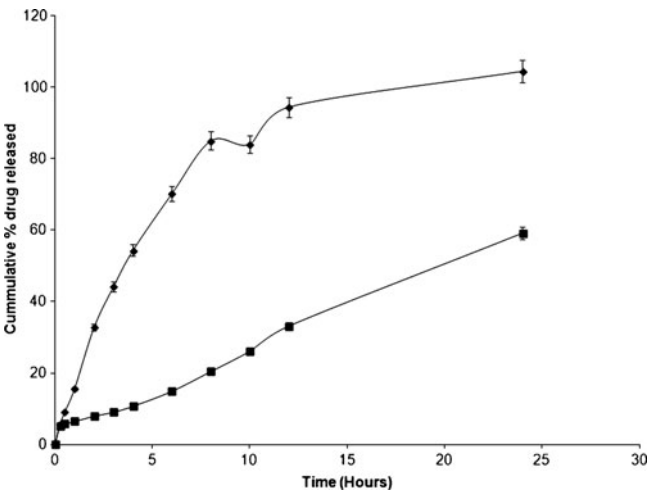

Fig. 6. Release profiles of carvedilol and theophylline from tablets containing 60% *w/w* terminalia gum; *square* carvedilol (A3), *triangle* theophylline (F1)

Table VII. Drug Release Parameters Obtained by Fitting Release Data for Carvedilol and Theophylline Matrix Tablets into the Different Release Kinetics Models

		Zero order		Higuchi		Hixson Crowell		First order		Korsmeyer		
Polymer	Drug	k_0 (h^{-1})	r^2	k_h	r^2	k	r^2	k	r^2	n	k	r^2
Terminalia	Theophylline	11.57	0.979	14.95	0.992	0.40	0.897	0.09	0.999	0.83	4.66	0.996
	Carvedilol	3.57	0.990	13.99	0.732	0.12	0.957	0.08	0.824	0.87	2.35	0.825
Xanthan	Theophylline	7.20	0.984	10.25	0.978	0.27	0.922	0.05	0.992	0.73	4.80	0.992
	Carvedilol	1.34	0.994	3.04	0.961	0.06	0.919	0.08	0.773	0.53	1.49	0.960
HPMC	Theophylline	4.65	0.973	5.87	0.988	0.19	0.884	0.03	0.884	0.66	3.57	0.994
	Carvedilol	1.94	0.994	6.40	0.972	0.07	0.925	0.08	0.785	0.60	2.10	0.992

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