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Comparative Study of the Influence of Mannitol and Sodium Chloride as Channeling Agents on the Release Profile of Diclofenac Tablets formulated using Acacia and *Grewia mollis* Gums

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ABSTRACT

The purpose of this study was to compare the influence of mannitol and sodium chloride as channeling agents on the release profiles of diclofenac matrix tablets formulated using *Grewia mollis* and acacia gums. Diclofenac matrix granules were prepared using wet granulation method. Acacia and grewia gums (10 %w/w) were used as binders. Varying amounts (50, 100, 150 and 200 mg) of mannitol or sodium chloride (channeling agent) were incorporated. Granules were evaluated for micromeritic properties while the formulated tablets were evaluated for hardness, friability and *in vitro* dissolution studies. Drug-excipient compatibility studies was done using Fourier Transform Infra-red (FTIR) spectroscopy. All granules were free flowing with angle of repose ≤33.2°. The hardness values were ≤8.5 KPa and the friability values were ≤0.88%. The higher the amount of the channeling agent, the higher the rate of drug release from the matrix tablets studied. The influence of mannitol on the release of diclofenac from the matrix system was significantly greater than that of sodium chloride ($P<0.05$) hence mannitol is a better channeling agent than sodium chloride which causes water retention therefore contraindicated in hypertensive patients.

Keywords: Channeling agent, mannitol, sodium chloride, diclofenac

INTRODUCTION

Drug delivery technology is highly dynamic and rapidly evolving. Sustained release dosage forms are formulated to modify and enhance the bioavailability of drugs by increasing the duration of action and reducing frequency of dosing of the drug. They are formulated to elevate the concentration of a drug in the blood to a therapeutic concentration as fast as possible and then maintain this concentration for a given period of time (Gonzalez-Rodriguez *et al.*, 2001). Channeling agents are the water-soluble constituents which play a vital role in sustained drug delivery systems. They increase and regulate the release of drugs from sustained release (SR) formulations. Some examples of channeling agents are polyethylene glycol, mannitol, sodium chloride and sorbitol (Airemwen *et al.*, 2020). Acacia gum is a natural polymer used in oral and topical pharmaceutical formulations as a suspending and emulsifying agent. Grewia gum is a natural polymer that consists of glucose and rhamnose as the main monosaccharide components and galacturonic acid as the main sugar acid (Okafor *et al*., 2001). Previous studies have been done to evaluate the floating (Airemwen and Uhumwangho, 2019), bioadhesive (Nep and Okafor, 2006) and binding (Emeje *et al*., 2008) properties of the gum. Several studies have been conducted on the influence of channeling agents on sustained release dosage forms however, a comparative study of the influence of mannitol and sodium chloride as channeling agents on the release profile of diclofenac tablets formulated using acacia and *grewia mollis* gums has not been investigated. Diclofenac possesses analgesic, antipyretic and anti-inflammatory effects and it belongs to the class of drugs called non-steroidal anti-inflammatory drugs (NSAIDs). It is a potent inhibitor of prostaglandin synthesis *in vitro*. Its mechanism of action involves inhibition of cyclooxygenase (COX-1 and COX-2) enzymes. It is used in the management of osteoarthritis, rheumatoid arthritis, mild to moderate pain and dysmenorrhea at a dose of 50 -100 mg 12 hourly for 3-5 days (Airemwen *et al.*, 2020).

MATERIALS AND METHODS

Materials: Mannitol and sodium chloride (Loba Cheme Pvt. Ltd., India) were used as the channeling agent in the matrix tablets. Diclofenac powder (Ranbaxy Ltd, India) was used as the model drug. Acacia gum was obtained from the laboratory and grewia gum was extracted by the method described previously by Nep and Conway (2010) with some modifications. Both gums were used as binders in the formulation.

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Preparation of Diclofenac Granules

Diclofenac potassium granules with mannitol and sodium chloride incorporated as channeling agents were formulated using wet granulation method. Four batches were formulated using either acacia or *Grewia mollis* gum at varying concentrations (50, 100, 150 and 200 mg). In each formulation, the lactose, and diclofenac were mixed in the dry state in a mortar using the geometric mixing method. Then the binder mixtures of the gum were used to wet mass the powder in the mortar. The damp mass formed was forced through a sieve mesh of 710 µm and dried at 60 ºC for 30 min. The granules were then passed through another sieve mesh of 850 µm and the micromeritic properties were evaluated. Talc was incorporated extragranularly. The formula of the diclofenac potassium matrix tablets is presented in Table 1.

Flow and Packing Properties of the Granules: These were determined by measuring the bulk density (BD) and tapped density (TB) using standard procedures (Onyekewli, 2000) and the values were obtained using equations 1 and 2 respectively. From the data, Carr's index (CI) values of the granules were calculated using equation 3 (Carr, 1965).

$$\text{Bulk density}\left(\text{g/cm}^3\right) = \frac{\text{mass of granules}}{\text{initial volume of granules}} \quad (1)$$

$$\text{Tap density (g/cm}^3\text{)} = \frac{\text{mass of granules}}{\text{tapped volume of granules}} \quad (2)$$

$$\text{Carr's Index} = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} x\ 100 \quad (3)$$

The flow property of the granules was determined by measuring the angle of repose formed when a sample of the granules (15 g) was allowed to fall freely from the stem of a funnel onto a plain paper placed on a horizontal surface (Airemwen *et al.,* 2020). The angle of repose was determined by measuring the height of the heap formed by the granules and the diameter of the base of the granules using equation 4.

$$\text{Angle of repose } (\theta) = \text{Tan}^{-1} h/r \quad ----(4)$$

Where, θ is the angle of repose, h is height and r is the radius of the heap formed in cm.

Formulation of Diclofenac Tablets

A Manesty Single Punch Tableting Machine (Type F3 Manesty Machines, UK) was used to formulate the tablets. Talc (1%) was added as a glidant. Diclofenac potassium granules equivalent to 100 mg of diclofenac were placed in the die and compressed at a pressure of 30 N/m^2. A constant pressure was maintained for all the batches of diclofenac tablets produced. The resulting tablets were collected, dusted and stored in an air tight jar containing activated silica gel as a desiccant.

Evaluation of the Formulated Diclofenac Tablets

Hardness: The hardness of five (5) tablets was determined using the Campbell Electronics Hardness tester machine (HT-30/50, India). The pressure required to break a tablet placed in the anvil of the hardness tester was recorded.

Friability: The friability test was done using ten (10) tablets that were randomly selected and placed in a Roche Friabilator (Erweka Germany). The initial weight of the tablets was obtained before they were placed in the friabilator. The friabilator was allowed to operate at 25 rpm for 4 min after which the final weight of the tablets was determined. These values were used to calculate the percentage friability using equation 4.

$$\text{Friability} = \frac{Initial\ weight - Final\ weight}{Initial\ weight} x\ 100$$

In vitro Dissolution Studies: The dissolution study was carried out using 900 ml of 6.8 buffer solution as the dissolution medium maintained at 37 ± 2 ^oC and the paddle method was used in the study. One (1) tablet was placed in the dissolution medium and the dissolution fluid was stirred at 100 rpm with the dissolution paddle. Samples (5 ml) of the leaching fluid were withdrawn using a pipette fitted with a cotton wool plug at predetermined time intervals (5, 10, 15 and 30 min; 1, 2, 4, 6, 8 and 10 h); Equal amount of fresh dissolution medium kept at the same temperature was used to replace the withdrawn sample. The withdrawn samples were filtered, adequately diluted and their absorbances determined with a UV/Visible spectrophotometer at a maximum wavelength ($\lambda \max$) of 297 nm. The determination was carried out in triplicate and the mean results reported. The corresponding amount of diclofenac potassium released at any time t, was then computed from the standard calibration curve. The dissolution data were further analyzed using zero order, first order, Higuchi and Korsmeyer and Peppas release models (Higuchi, 1963, Korsmeyer *et al.,* 1983 and Peppas, 1985). Fourier Transform Infra-Red Spectroscopy (FTIR) Studies

Compatibility studies between the active pharmaceutical ingredients and the excipients was done using FTIR. The potassium bromide (KBr) pellet method was used. 5 mg of the sample was

blended with KBr to 200 mg. The powder was compressed using a sigma KBr press into a tablet shape. The tablet was placed in the sample compartment and the scan was read. The pure samples, physical mixtures and the optimized tablet formulations were scanned at a range of 4000-500 cm^{-1}.

Statistical Analysis

The results obtained were expressed as mean ± standard deviation (SD). All the data obtained were subjected to graphpad instat test ($p < 0.05$) to test for significance of difference.

RESULTS

Micromeritic Properties of the Channeling Agents Matrix Granules of Diclofenac Potassium Prepared using Acacia and *Grewia Mollis* Gums. The results of the packing and flow properties of the diclofenac potassium matrix granules prepared using acacia and G*rewia mollis* gums as matrix former are presented in Table 2. The angle of repose which was used to characterize the flow properties of the granules showed that the granules produced with *Acacia gum* and *Grewia mollis* gums were free flowing because the values ranged from 26.5 – 33.2° and 27.2 – 31.2° respectively. The Carr's index is the ability of the granules to be compressed due to application of a given stress and consequently a reduction in volume. Carr's index values for all the granules formulated with *Acacia* gum ranged from 9.5 – 15.9%, while those formulated with *Grewia mollis* gum ranged from 9.8 – 13.8%. The Hausner's ratio values for all the granules formulated with both *Acacia gum* and *Grewia mollis* gums ranged from 1.06 – 1.20.

Hardness and Friability

The results of the physicotechnical properties of the formulated diclofenac potassium tablets are shown in Table 3. Hardness is defined as the "force required to break a tablet in a diametric compression test" (Nasa *et al.*, 2010). The hardness of the channeling agent matrix of diclofenac potassium tablets produced with *Acacia* gum ranged from 4.6 – 8.5 KPa while the tablets produced with *Grewia mollis* gum showed hardness values ranging from 4.3 – 8.0 KPa.

The friability test values for the channeling agent matrix of diclofenac potassium tablets produced with Acacia gum ranged from 0.58 – 0.92% and those with *Grewia mollis* gum ranged from 0.64 – 0.89% as shown in Table 3.

Dissolution Parameters of Diclofenac Matrix Tablets Formulated using Acacia And Grewia With Varying Concentrations of Channeling Agents

The drug release profiles and dissolution parameter from diclofenac matrix tablets without and with channeling agents (i.e. sodium chloride or mannitol) are shown in Figures 1 and 2 and Table 4 respectively. It was observed generally that as the amount of the channeling agents in the diclofenac matrix tablet formulation increased, there was an increase in the dissolution profile of the matrix tablets. For instance, the dissolution rates ($m_\infty/_{t\infty}$) for tablets formulated with acacia gum without the incorporation of either mannitol or sodium chloride as channeling agent (AM0 and AS0) were 4.02 and 2.87%h^{-1} respectively and for tablets formulated with acacia gum; with the incorporation of varying concentrations of mannitol as channeling agent (AM1, AM2, AM3 and AM4) were 7.86, 8.89, 9.24. 9.58 %h^{-1} respectively. Also for tablets formulated with acacia gum; with the incorporation of varying concentrations of sodium chloride as channeling agent (AS1, AS2, AS3 and AS4), the dissolution rates were 5.63, 6.44, 6.87 and 7.48 %h^{-1} respectively (Table 4). Also, the dissolution rates ($m_\infty/_{t\infty}$) for tablets formulated with grewia gum without the incorporation of either mannitol or sodium chloride as channeling agent (GM0 and GS0) were 4.13 and 2.48%h^{-1} respectively and for tablets formulated with grewia gum; with the incorporation of varying concentrations of mannitol as channeling agent (GM1, GM2, GM3 and GM4) were 7.28, 8.17, 9.08, 9.87%h^{-1} respectively. Similarly, for tablets formulated with grewia gum; with the incorporation of varying concentrations of sodium chloride as channeling agent (GS1, GS2, GS3 and GS4), the dissolution rates were 4.32, 5.84, 6.37 and 7.07 %h^{-1} respectively (Table 4).

Release Kinetics of Diclofenac Matrix Tablets

Drug release kinetics provide vital information on the drug release mechanism. The release data for all the formulations (i.e. without channeling agents, with sodium chloride or mannitol as channeling agents) were analyzed based on zero-order kinetics, first-order kinetics, Higuchi mechanism and Korsmeyer and Peppas model to ascertain which release model best fit the system studied (Uhumwangho *et al.*, 2014). The values of the correlation coefficients (r^2) and the release rate constants are presented in Table 5. The r^2 - values for the tablets formulated with acacia gum without the incorporation of either mannitol or sodium chloride as channeling agent (AM0 and AS0) were 0.844 and 0.848 for zero order, 0.994 and 0.986 for first order and 0.977 and 0.975 for Higuchi. For tablets formulated with acacia gum; with the incorporation of varying concentrations of mannitol as channeling agent (AM1, AM2, AM3 and AM4), the correlation coefficients (r^2) were between

0.926-0.945 for zero order, 0.954-0.984 for first order and 0.947-0.972 for Higuchi release models . Also for tablets formulated with acacia gum; with the incorporation of varying concentrations of sodium chloride as channeling agent (AS1, AS2, AS3 and AS4), the correlation coefficients (r) were between 0.901-0.938 for zero order, 0.968-0.988 for first order and 0.954-0.979 for Higuchi release models (Table 5). Also, the r^2 - values for the tablets formulated with grewia gum without the incorporation of either mannitol or sodium chloride as channeling agent (GM0 and GS0) were 0.827 and 0.837 for zero order, 0.992 and 0.983 for first order and 0.976 and 0.979 for Higuchi release models. For tablets formulated with grewia gum; with the incorporation of varying concentrations of mannitol as channeling agent (GM1, GM2, GM3 and GM4), the correlation coefficients (r) were between 0.929-0.958 for zero order, 0.957-0.988 for first order and 0.945-0.977 for Higuchi release models . Also for tablets formulated with grewia gum; with the incorporation of varying concentrations of sodium chloride as channeling agent (GS1, GS2, GS3 and GS4), the correlation coefficients (r) were between 0.932-0.976 for zero order, 0.968-0.987 for first order and 0.967-0.982 for Higuchi release models (Table 5).

Fourier Transform Infra-Red (FTIR) Results:
It was observed that there were no obvious changes in peaks and troughs due to the presence of other excipients and also due to compression to final tablets (Figures 3 and 4). This indicates that the API (diclofenac) and the other excipients were compatible.

Table 1: The formula of the diclofenac potassium tablet

BATCH	INGREDIENTS (mg)							
	Diclofenac (mg)	Acacia (%)	Grewia (%)	Sodium Chloride (mg)	Mannitol (mg)	Lactose (mg)	Magnesium Stearate (mg)	Talc (mg)
AS0	100	1.0	1.0	-	-	50	5	5
AS1	100	1.0	-	50	-	50	5	5
AS2	100	1.0	-	100	-	50	5	5
AS3	100	1.0	-	150	-	50	5	5
AS4	100	1.0	-	200	-	50	5	5
AM1	100	1.0	-	-	50	50	5	5
AM2	100	1.0	-	-	100	50	5	5
AM3	100	1.0	-	-	150	50	5	5
AM4	100	1.0	-	-	200	50	5	5
GS0	100		1.0	-	-	50	5	5
GS1	100	-	1.0	50	-	50	5	5
GS2	100	-	1.0	100	-	50	5	5
GS3	100	-	1.0	150	-	50	5	5
GS4	100	-	1.0	200	-	50	5	5
GM1	100	-	1.0	-	50	50	5	5
GM2	100	-	1.0	-	100	50	5	5
GM3	100	-	1.0	-	150	50	5	5
GM4	100	-	1.0	-	200	50	5	5

Table 2: Micromeritic properties of the diclofenac potassium matrix granules prepared using *Acacia and grewia* gums as binders with sodium chloride and mannitol as channeling agents

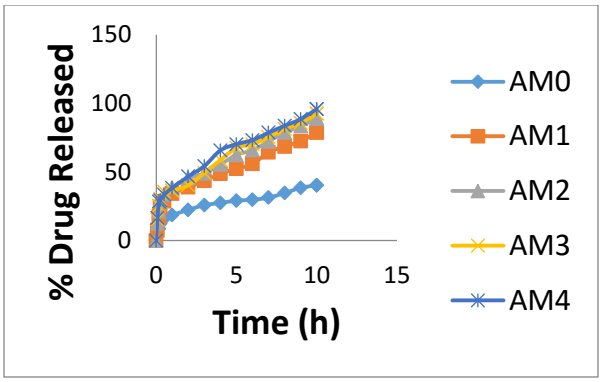
Batch	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Angle of Repose (^{o})	Carr's Index (%)	Hausner's Ratio
AS0	0.58±0.01	0.65±0.01	31.2±1.0	10.8±1.0	1.12±0.01
AS1	0.57±0.02	0.63±0.02	33.2±1.0	09.5±1.1	1.18±0.02
AS2	0.59±0.01	0.68±0.01	26.5±1.2	13.2±1.3	1.12±0.02
AS3	0.54±0.01	0.62±0.01	28.2±1.1	12.9±1.2	1.10±0.01
AS4	0.55±0.02	0.64±0.02	32.7±1.0	14.1±1.1	1.13±0.02
AM1	0.53±0.01	0.63±0.02	26.8±1.3	15.9±1.2	1.20±0.01
AM2	0.54±0.02	0.64±0.02	27.3±1.1	14.3±1.0	1.15±0.02
AM3	0.56±0.01	0.67±0.01	30.4±1.2	15.1±1.1	1.12±0.01
AM4	0.53±0.01	0.61±0.01	26.8±1.1	13.1±1.2	1.14±0.02
GS0	0.53±0.02	0.60±0.01	27.2±1.0	11.7±1.2	1.06±0.02
GS1	0.58±0.01	0.66±0.02	31.1±1.2	12.1±1.0	1.13±0.01
GS2	0.55±0.01	0.66±0.02	28.9±1.1	13.6±1.1	1.12±0.02
GS3	0.58±0.02	0.66±0.01	31.2±1.0	12.1±1.2	1.14±0.01
GS4	0.56±0.02	0.65±0.02	25.1 ±1.3	13.4±1.3	1.15±0.02
GM5	0.54±0.01	0.62±0.01	28.5±1.2	12.9±1.2	1.16±0.01
GM6	0.55±0.03	0.63±0.01	29.3±1.1	12.7±1.1	1.17±0.02
GM7	0.55±0.02	0.61±0.01	26.4±1.3	09.8±1.1	1.11±0.01
GM8	0.56±0.02	0.65±0.02	27.2±1.2	13.8±1.2	1.16±0.03

Table 3: Hardness and friability results of diclofenac matrix tablets formulated using *Grewia mollis* gum as binder with mannitol and sodium chloride as channeling agent.

Batch	Hardness (KPa)	Friability (%)
AM0	4.6 ± 0.1	0.74 ± 0.01
AM1	7.6 ± 0.1	0.75 ± 0.01
AM2	7.9 ± 0.2	0.82 ± 0.02
AM3	8.5 ± 0.1	0.90 ± 0.02
AM4	8.5 ± 0.1	0.92 ± 0.02
AS1	6.2 ± 0.1	0.84 ± 0.01
AS2	6.6 ± 0.2	0.75 ± 0.01
AS3	7.0 ± 0.1	0.65 ± 0.02
AS4	7.3 ± 0.2	0.58 ± 0.03
GM0	4.3 ± 0.1	0.79 ± 0.02
GM1	6.8 ± 0.2	0.64 ± 0.02
GM2	6.9 ± 0.1	0.74 ± 0.02
GM3	7.2 ± 0.2	0.78 ± 0.01
GM4	7.6 ± 0.1	0.84 ± 0.02
GS1	5.5 ± 0.1	0.83 ± 0.01
GS2	6.8 ± 0.1	0.72 ± 0.02
GS3	7.0 ± 0.1	0.65 ± 0.02
GS4	8.0 ± 0.1	0.89 ± 0.01

Table 4: Dissolution parameters of diclofenac tablets prepared using acacia gum with mannitol or sodium chloride as channeling agents.

Formulations	m_∞ (%)	t_∞ (h)	m_∞/t_∞ ($\%h^{-1}$)
AM0	40.2	10	4.02
AM1	78.6	10	7.86
AM2	88.9	10	8.89
AM3	92.4	10	9.24
AM4	95.8	10	9.58
AS0	28.7	10	2.87
AS1	56.3	10	5.63
AS2	64.4	10	6.44
AS3	68.7	10	6.87
AS4	74.8	10	7.48
GM0	41.3	10	4.13
GM1	72.8	10	7.28
GM2	81.7	10	8.17
GM3	90.8	10	9.08
GM4	98.7	10	9.87
GS0	24.8	10	2.48
GS1	43.2	10	4.32
GS2	58.4	10	5.84
GS3	63.7	10	6.37
GS4	70.7	10	7.07



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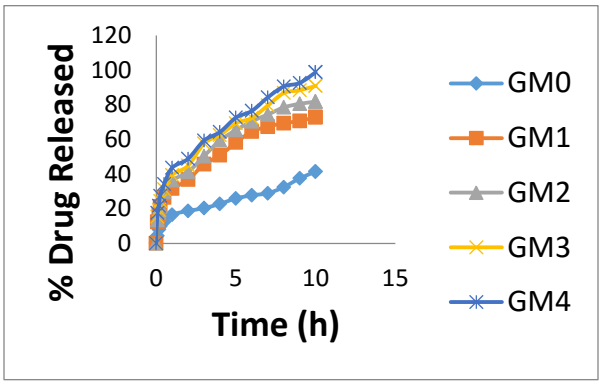

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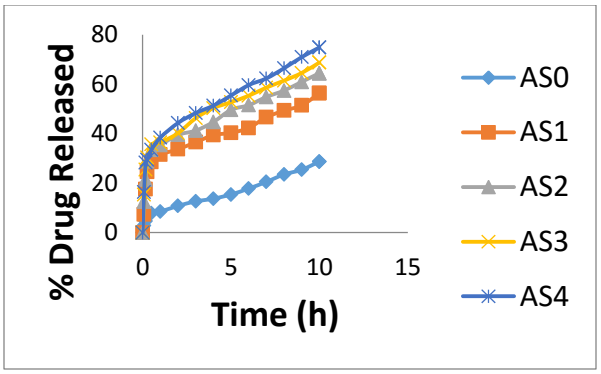
Figure 1: Drug release profile from diclofenac matrix tablets prepared using (a) acacia gum as a binder; (b) using grewia gum as binder and mannitol as channeling agent.



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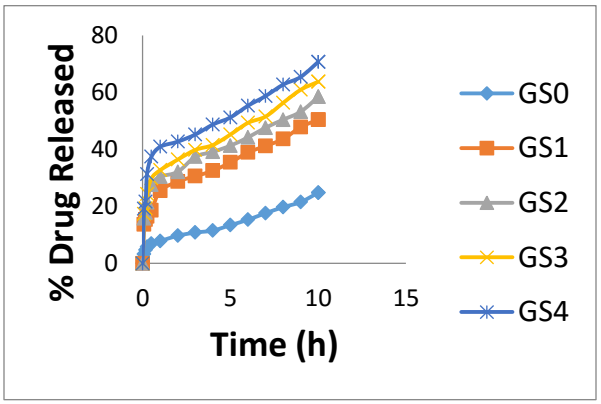

b

Figure 2: Drug release profile from diclofenac matrix tablets prepared using (a) acacia gum as a binder; (b) using grewia gum as binder and sodium chloride as channeling agent.

Table 5: Correlation coefficient and release kinetics of diclofenac tablets formulated using grewia gum with mannitol or sodium chloride as channeling agents.

Models	Zero		First		Higuchi		Korsemeyer and Peppas	
Formulation	r^2	K_0	r^2	K_1	r^2	K_H	r^2	n
AM0	0.844	8.487	0.994	-0.13	0.977	30.59	0.448	0.513
AM1	0.926	7.797	0.958	-0.08	0.947	26.48	0.535	0.557
AM2	0.945	7.356	0.984	-0.07	0.968	25.76	0.467	0.479
AM3	0.938	7.475	0.966	-0.28	0.955	34.65	0.489	0.487
AM4	0.926	8.198	0.978	-0.45	0.972	28.48	0.458	0.458
AS0	0.848	7.196	0.986	-0.61	0.975	41.25	0.487	0.595
AS1	0.901	8.348	0.988	-0.18	0.979	25.37	0.432	0.479
AS2	0.924	8.653	0.979	-0.09	0.966	28.39	0.478	0.575
AS3	0.938	8.745	0.985	-0.17	0.978	31.27	0.457	0.586
AS4	0.914	8.836	0.968	-0.36	0.954	35.47	0.487	0.547
GM0	0.827	8.545	0.995	-0.16	0.976	30.54	0.436	0.558
GM1	0.929	7.257	0.957	-0.07	0.945	26.49	0.554	0.545
GM2	0.947	7.179	0.988	-0.09	0.965	25.71	0.447	0.487
GM3	0.958	7.384	0.968	-0.26	0.956	34.67	0.476	0.554
GM4	0.934	8.197	0.978	-0.47	0.977	28.42	0.486	0.496
GS0	0.837	7.568	0.983	-0.53	0.979	41.21	0.454	0.576
GS1	0.932	8.875	0.986	-0.19	0.975	25.34	0.479	0.487
GS2	0.976	8.456	0.974	-0.08	0.967	28.31	0.479	0.545
GS3	0.969	8.479	0.987	-0.20	0.973	31.23	0.487	0.547
GS4	0.976	8.648	0.968	-0.35	0.982	35.42	0.454	0.596

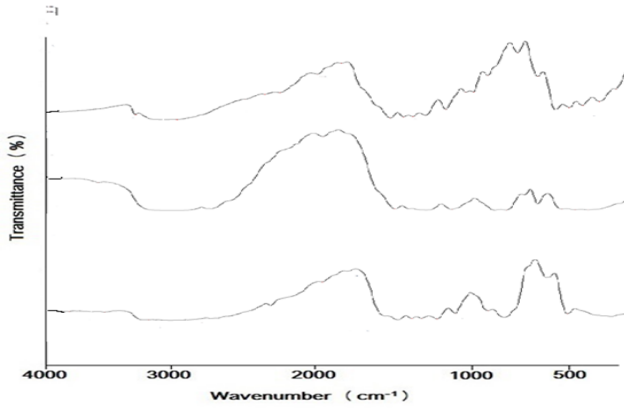

Figure 3: FTIR Spectra of diclofenac matrix tablets formulated using acacia gum (a) Diclofenac pure sample (b) Physical mixture of diclofenac powder, acacia gum and mannitol and (c)Tablets containing diclofenac, acacia and mannitol.

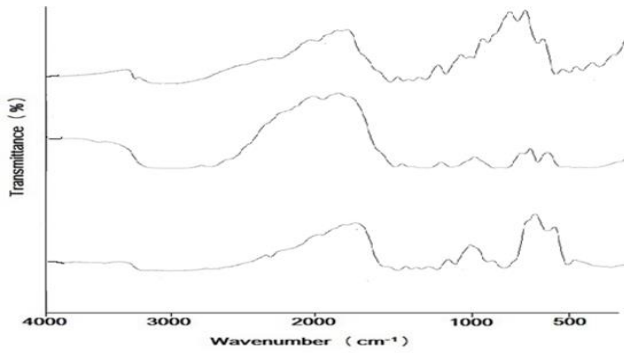

Figure 4: FTIR Spectra of diclofenac matrix tablets formulated using grewia gum (a) Diclofenac pure sample (b) Physical mixture of diclofenac powder, grewia gum and mannitol and (c) Tablets containing diclofenac, acacia and mannitol.

DISCUSSION

The values of the angle of repose indicate good flow characteristics of the granules. Since the observed values of angle of repose were ≤ 35°, all the granules exhibited good flow properties which is very essential in ensuring weight and content uniformity during tableting as well as capsule filling. The flow property of solid particle is affected predominantly by surface forces such as frictional forces or van der Waal's forces (Orakwe *et al.,* 2015).

Carr's indexes of ≤ 10% indicate excellent flow, values between 11 – 15% indicate good flow, values between 16 – 20% show fair flow while values ≥ 30% indicate a powder or granular material with poor flow property (USP, 2004). From these results, Carr's index was generally below 15% which indicates good compressibility of the granules. The Hausner ratio is a number that is correlated with the flowability of a powder or granular material. Hausner ratio values for all the granules was below 1.20, indicating that they all exhibited good flow properties. Therefore, it can be concluded that all the granules of diclofenac potassium prepared exhibited good micromeritic properties irrespective of the concentration of *Acacia gum* or *Grewia mollis* gums used. The results of the hardness tests indicate that as the concentration of the gum increased, the hardness of the tablets also increased. Thus, an increase in tablet hardness is due to the ability of the gum to increase the inter-particulate bond between the granules of the tablet (Orakwe *et al.,* 2015). The friability of the diclofenac potassium tablets was a measure of the tendency of the tablets to crumble by allowing them to roll and fall within the rotating apparatus after 100 revolutions. Friability also shows the ability of the tablet to withstand abrasion during packaging, processing, transportation and handling. Conventional compressed tablets that lose between 0.5 to 1.0% of their weight are generally acceptable (Nasa *et al.,* 2010). It was observed that the friability values decreased with increase in gum concentration irrespective of the type of gum used. This was as a result of increased in inter-particulate bonding in the tablets similar to their effects on hardness. The friability values for all the tablets produced were below 1% which is an indication of good mechanical resistance of the tablets. It can therefore be said that the concentration of the gum in the tablets is a major determinant of the tablet friability. The friability result was also indicative of the ability of the tablets to withstand mechanical stress during shipping, transportation, packaging and handling (Airemwen *et al.,* 2020). There was no significant difference in the values of the hardness and friability of the tablets formulated with the incorporation of mannitol or sodium chloride as the channeling agents ($P>0.05$). The results of the dissolution parameters and release profile indicate that the presence of channeling agents facilitated the drug release from the matrix system (Razzak *et al.,* 2008). Previous studies conducted by Uhumwangho *et al.,* (2014) also reveals that higher amount of channeling agents increased the rate and extent of ibuprofen release from matrix tablets of ibuprofen formulated using *Khaya ivorensis* as a natural polymer. There was a statistically significant difference between the release profiles of tablets formulated with and without the incorporation of channeling agent ($P<0.05$). The release profile of the drug from the tablets was concentration dependent. The higher the concentration of the channeling agent, the faster the release of the drug from the matrix system. The possible reason for the increased rate and

extent of the drug release for formulations containing channeling agents compared with those without channeling agent could be due to increased porosity in the tablet matrices created by the different channeling agents in the tablets which increased the dissolution rate (Uhumwangho *et al.,* 2014). It was also observed that the maximum amount of drug released (m_∞) increased with increase in concentration of the channeling agents and the time to attain maximum release (t_∞) was the same irrespective of the concentration of the channeling agents. Drug release from the matrix tablets resulted from slow diffusion of dissolved drug molecules through aqueous filled channels in the polymeric matrix network (Razzak *et al.,* 2008). The dissolution rates of drugs from the tablets formulated with the addition of mannitol as significantly greater than those formulated with the incorporation of sodium chloride as channeling agent ($P<0.05$). There was no significant difference in the release kinetics of tablets formulated with the incorporation of mannitol or sodium chloride as the channeling agents as all the formulations simulated first order release model since they had the highest r^2 values of 0.994 ($P>0.05$). In order to characterize the release mechanism, the diffusional release exponent was determined. The values of release exponent (n) for all the formulations were $\geq$ 0.45. The indication is that release of diclofenac from these formulations followed non-Fickian diffusion release (Airemwen *et al.,* 2020).

CONCLUSION

The presence of channeling agents influenced the release of drugs from the matrix system studied. The higher the amount of the channeling agent, the higher the rate of drug release from the matrix tablet. The influence of mannitol on the release of diclofenac from the matrix system was significantly greater than that of sodium chloride ($P<0.05$) hence mannitol is a better channeling agent than sodium chloride which causes water retention therefore contraindicated in hypertensive patients. Therefore; controlled amount as well as appropriate channeling agents can be used to enhance and modulate the release of drugs from diclofenac matrix systems.

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