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The Effect of Processing Variables on the Mechanical and Release Properties of Tramadol Matrix Tablets Incorporating *Cissus Populnea* Gum as Controlled Release Excipient

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of the article

Abstract

Background. Natural gums are polymers widely used as excipients in drug formulation. Polymer extraction and formulation processing methods could significantly affect formulation characteristics.
Objectives. To evaluate different methods of gum extraction and the effect of different compression methods on the mechanical and release properties of tramadol hydrochloride matrix tablets incorporating cissus gum as controlled release polymer.
Material and Methods. Water (CW) and acetone (CA) extracts of cissus gum were obtained from *Cissus populea* stem and two methods – wet granulation and direct compression – were used to compress the tablet and compare it with xanthan gum (X) formulations. Crushing strength and friability were used to assess mechanical properties while dissolution rate were used to assess release properties. Data were analysed using t-test and ANOVA at $p < 0.05$.
Results. The crushing strength of tramadol tablets has increased together with the increase in polymer concentration in all formulations, while friability has decreased for both methods. Tablets made by wet granulation had higher crushing strength than those made by direct compression method. The release mechanism for both direct compression and wet granulation methods was Fickian and non-Fickian respectively. The rank order for t25, t50 and t75 for all formulations was X > CA > CW. Generally, wet granulation method decreased the rate of tramadol release more than direct compression method, indicating a higher drug retarding ability.
Conclusions. Incorporation of cissus gum controlled the release of tramadol hydrochloride from the matrix tablets. Extraction method and formulation variables influenced mechanical and release properties of the tablets. Cissus gum acetone extract had comparable release properties with xanthan gum and could serve as a cheaper alternative in controlled release tablet formulations (**Polim. Med. 2014, 44, 4, 209–220**).

Key words: tramadol, controlled release, *Cissus populnea* gum, wet granulation, direct compression.

The goal of any drug delivery system is to provide a therapeutic amount of drug to a proper site in the body, so that the desired drug concentration can be achieved promptly and then maintained. How this is achieved is greatly influenced by the excipients used in the formulation [1].

Excipients play a wide variety of functional roles in pharmaceutical dosage forms ranging from modulating the solubility and bioavailability of active pharmaceutical ingredients, increasing the stability of active ingredients in dosage forms, helping active ingredients maintain preferred polymorphic forms or conformations,

assisting in product identification, maintaining the pH and/or osmolarity of liquid formulations. They also act as antioxidants, aerosol propellants, emulsifying agents, tablet binders, and tablet disintegrants and enhancing any other attributes of the overall safety and effectiveness of the drug during storage or use [2, 3].

Controlled-release, sustained-release, also known as, extended-release, time-release or continuous-release system, is formulated to dissolve slowly and release a drug over time. The primary objectives of a controlled release drug delivery are to ensure safety and enhancement of drug efficacy with improved patient compliance.

The use of controlled release drug delivery system over the years have gained acceptance in the treatment of acute and chronic diseases as they maintain drug concentration in the plasma above minimum effective concentration and below the minimum toxic level for an extended period of time. Among various sustained release dosage form, matrix tablets are widely accepted for oral controlled release as they are simple to formulate. Polymers and release retarding materials are used as matrix forming agent [4, 5].

Various formulation variables such as polymer type, polymer grade, drug-polymer ratio, drug stability and drug and polymer particle size affect drug release rate to various degrees.

Natural gums are a group of polymers now widely used in pharmaceutical dosage forms due to their non-toxic, non-irritant nature, ease of accessibility and relatively lower cost compared to synthetic polymers. The various natural gums used in sustained release drug delivery system include xanthan gum [6], guar gum [7], and okra gum [8].

Cissus gum is obtained from the stem of *Cissus populnea Guill. & Perr.* The plant is a tropical plant belonging to the family *Vitaceae*. It is a tall woody climber of up to 8 meters high. The plant has a natural tendency of retaining water, thus it remains fresh almost throughout the season. It is a gel forming plant. The gum is hydrocolloid and forms mucilage and it has been found to be effective as a binder in paracetamol tablet formulations [9, 10].

Tramadol is a synthetic opioid of the amino-cyclohexanol group. It is a centrally acting analgesic which causes no serious cardiovascular or respiratory side effects [11]. The usual oral dosage requirement of the drug is 50 to 100 mg every 4 to 6 hours with a maximum dosage of 400 mg per day [12]. A sustained-release formulation of tramadol is required to improve patient compliance and to reduce the administration frequency.

The present study was therefore aimed at determining the effect of extraction procedure and tablet compression methods on the controlled release properties of tramadol hydrochloride matrix tablets incorporating *Cissus populnea* gum.

Material and Methods

Material

The material used in the investigation was tramadol hydrochloride, a gift from Uripharm Specialties Ltd, Lagos, Lactose (DMV Veghel, Netherlands), xanthan gum (Jungbenzlauer Ges.M.B.H. Handelsgericht Wien, Germany), cissus gum extracted in Pharmaceutics Laboratory, University of Ibadan, Nigeria. All other solvents and chemicals were of analytical grade.

Methods

Preparation of Acetone-Extracted Cissus Gum

The gum was extracted from the incised sliced stem of *Cissus polpunea* by overnight soaking in distilled water, followed by filtration of the viscous solution and precipitation of the extracted gum with acetone. The precipitate was dried at 50ºC for 24 h and pulverized in an Osterizer blender (Model 857 Williamette Industries, Bowing Green Kentucky USA) to produce gum powder. The powder obtained was stored in an airtight bottle.

Preparation of Water-Extracted Cissus Gum

The gum was extracted from the incised sliced stem of *Cissus polpune*a by soaking in distilled water overnight, followed by filtration of the viscous solution. The filtered viscous solution was dried at 80ºC for 24 h and pulverized in an Osterizer blender, (Model 857 Williamette Industries, Bowing Green Kentucky USA) to produce gum powder. The powder obtained was stored in an airtight bottle.

Characterization of Cissus Gum

pH

The pH of aqueous dispersion of cissus gum at different concentrations were determined at room temperature using a microprocessor based pH meter (Model 1012, Esico, Mumbai, India).

Moisture Content

The moisture content was determined by weighing accurately 5 g each of the cissus gum in a tarred evaporated dish on a mettler AB54 Electronic balance (Mettler, A.G., Switzerland). This was then dried in a Gallenkamp size two oven BS at 105ºC for 5 h and the final weight noted. The percentage weight loss was calculated from equation 1.

$$\% \text{ moisture content} = \text{weight of moisture}/\text{Weight of sample} \times 100\% \quad (1)$$

Swelling Capacity

The swelling capacity was determined by the method adopted by [13] using equation 2.

$$\text{Swelling capacity} = V_s/V_o \quad (2)$$

V_s = tapped volume occupied by the powders,
V_o = sedimentation volume.

FTIR Determinations

Spectra were obtained for the physical mixtures of the samples using an IR spectrometer (Perkin-Elmer, 2000, USA). 2 mg each of the completely dried powdered samples was weighed and then dispersed in 200 mg KBr (pellet procedure). Signal averages were obtained at a resolution of 400 to 4,000 cm^{-1}.

Preparation of Matrix Tablets

Batches of all formulations comprising of tramadol hydrochloride and different polymer ratios were prepared by either wet granulation or direct compression methods. Each batch was compressed into tablet (400 mg) at various compression pressures between 28.31 and 198.15 MNm^{-2} using a hydraulic hand press (Model C, Carver Inc., Menomonee Falls, Wisconsin, USA) fitted with a pressure gauge reading up to 2.5 metric tons.

Direct Compression Method

The powder blends were prepared by mixing tramadol hydrochloride and the polymer uniformly. Lactose (when required) was added to the drug and the polymer mixture and blended thoroughly for 5 min. The powder blends were compressed for 30 s into tablets at compression pressures between 28.31 and 198.15 MNm^{-2} using a hydraulic hand press (Model C, Carver Inc., Menomonee Falls, Wisconsin, USA) with a 10.5 mm die and flat-faced punches lubricated with a 2% dispersion of magnesium stearate in acetone before each compression. The pressure was maintained at the pre-selected compression pressure for 30 s and the tablet was carefully ejected and removed. The tablets prepared were stored in airtight containers over silica gel for 24 h to allow for elastic recovery and hardening.

Wet Granulation Method

The granules were prepared by mixing tramadol hydrochloride and the polymer uniformly. Lactose (when required) was added to the drug and the polymer mixture and blended thoroughly for 5 min. Aqueous dispersion of the polymer was then added to the mixture to form coherent mass. Massing was continued for 5 min and the wet mass was granulated and passed through a number 12 mesh sieve (1400 μm). The granules were collected and dried in a hot air oven for 24 h at 40°C.

The granules were compressed for 30 s into tablets at compressional pressures between 28.31 and 198.15 MNm^{-2} using a hydraulic hand press (Model C, Carver Inc., Menomonee Falls, Wisconsin, USA) with a 10.5 mm die and flat-faced punches lubricated with a 2% dispersion of magnesium stearate in acetone before each compression. The pressure was maintained at the pre-selected compression pressure for 30 s and the tablet was carefully ejected and removed. The tablets prepared were stored in airtight containers over silica gel for 24 h to allow for elastic recovery and hardening.

The compositions of the tablets are given in Table 1.

Table 1. Matrix tablet formulations containing tramadol hydrochloride

Component/Ratio	1:1	1:2	1:3
Tramadol hydrochloride	25	25	25
Polymer	25	50	75
Lactose	50	25	–

Tablet Evaluation

Tablet Crushing Strength

The load required to break each tablet diametrically into 2 halves was determined following the procedure of [14] using a Tablet Hardness Tester (DKB instrument, Mumbai. Model EH 01). Tablets were placed in between the spindle and the anvil, and the pressure was applied until the tablet fractured diametrically. Mean of three determinations were taken.

Tablet Friability

The weight of 10 tablets were taken and placed in the Veego Tablet Friablity Apparatus (Veego Scientific Devices, Mumbai, India) which was then operated for 4 min at 25 revolutions per min. After the revolutions, the tablets were dusted and weighed again. Mean of three determinations was taken.

Dissolution Test

The rate of dissolution of tramadol from the tablets was studied on a 6 station rotating basket USP Dissolution Apparatus operated at 50 rpm. The dissolution medium was 900 mL of 0.1 N hydrochloric acid at 37 ± 0.5°C. Five mL samples were withdrawn at specified time intervals and immediately replaced with 5 mL samples of fresh 0.1 N hydrochloric acid maintained at the same temperature. The amount of tramadol in each sample was analysed spectrophotometrically at 271 nm using Jenway UV-780 print UV-Spec. The percentage drug release was plotted against time to determine the release profile.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism 5 software. Data was analysed using *t*-test and one-way ANOVA. Differences were considered to be statistically significant at $p < 0.05$.

Results

For the preformulation studies, the pH of cissus gum of both extracts was acidic: CW – 5.92 and CA – 5.29. The moisture content of CW was 10.73%, CA 9.72% and X 1.25% while the swelling index is shown in Fig. 1. FTIR shows that tramadol is compatible with both extract of cissus gum used in the formulation as shown in Fig. 2–6.

For the formulation studies, a general increase in crushing strength was observed with increase in compression pressure (Fig. 7–8). One-way Anova analysis of the crushing strength shows that there is a significant difference between the crushing strength of the tablets containing different polymers ($p < 0.0001$). This shows that xanthan gum produced the strongest tablets. One-way Anova analysis also shows that there is a significant difference in the crushing strength of the tablets with an increase in polymer concentration in all the formulations ($p < 0.0001$). The student *t*-test analysis of the crushing strength shows that there is a significant difference between the crushing strength of formulations prepared by wet granulation method and direct compression method ($p < 0.0001$). Also, there is a significant difference between the crushing strength of formulations containing CW and CA ($p < 0.0001$). Wet granulation method and water extract of cissus gum produced tablets with higher crushing strength.

The friability values were observed to significantly decrease as polymer concentration increases in all formulation ($p < 0.0001$) (Fig. 9–10). However, student *t*-test analysis shows there is a significant difference in the friability of formulations prepared by wet granulation and direct compression methods. The friability of all the polymers was below 1%.

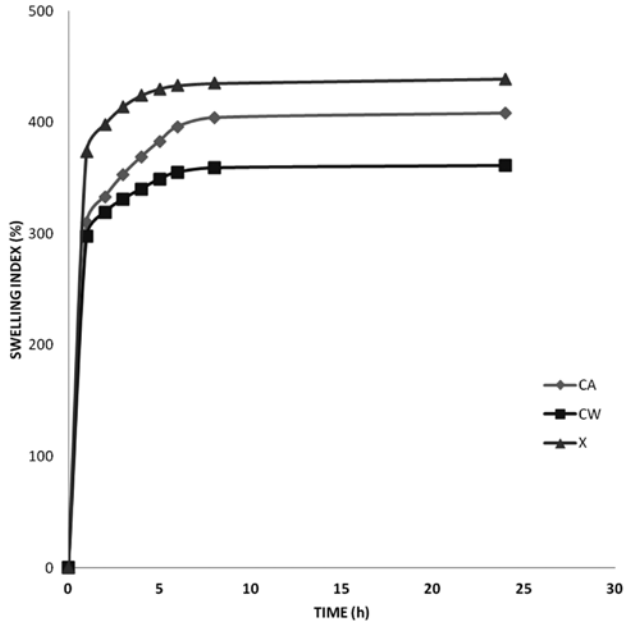

Fig. 1. Swelling index profile of polymers against time

The t_{25}, t_{50}, t_{75} and mean dissolution time (MDT) of tramadol tablets formulations with different polymer

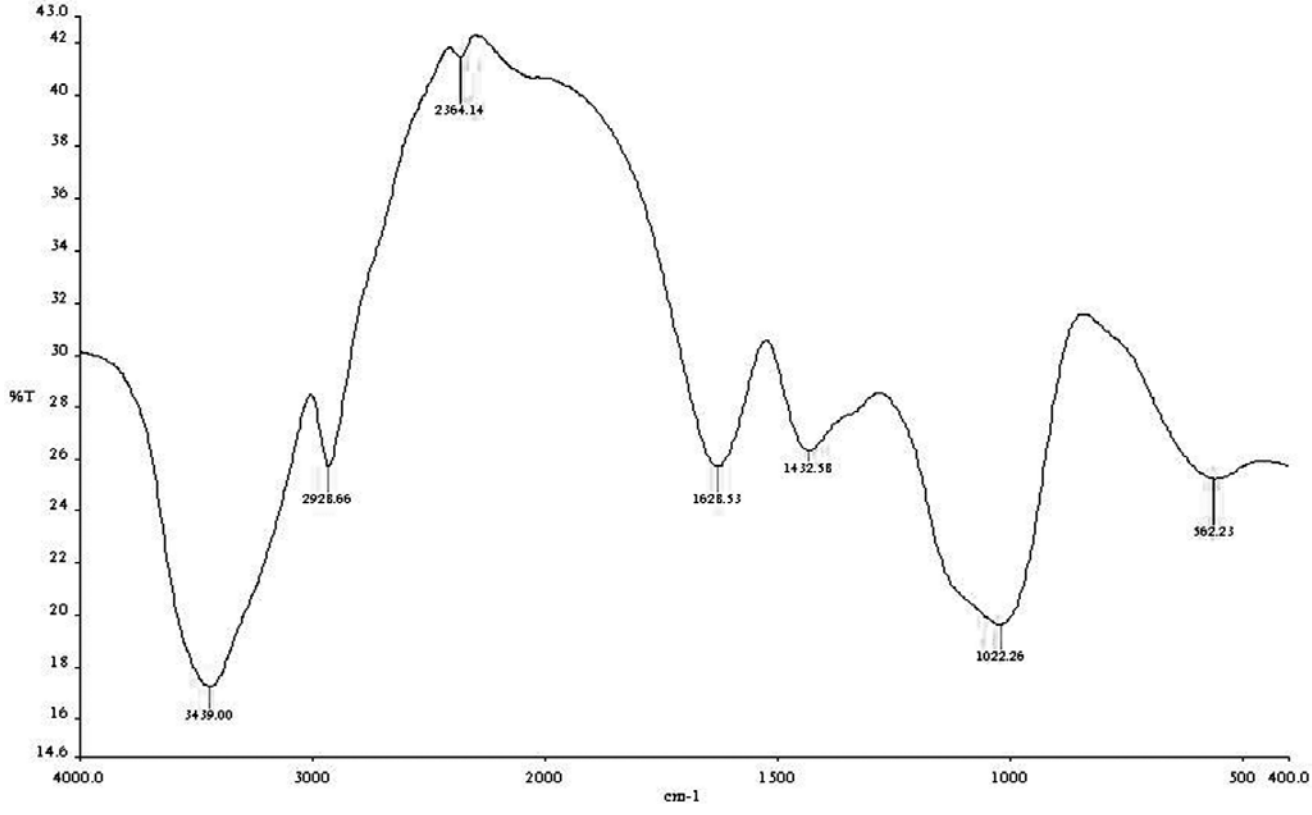

Fig. 2. FTIR spectrum of water extract of cissus gum

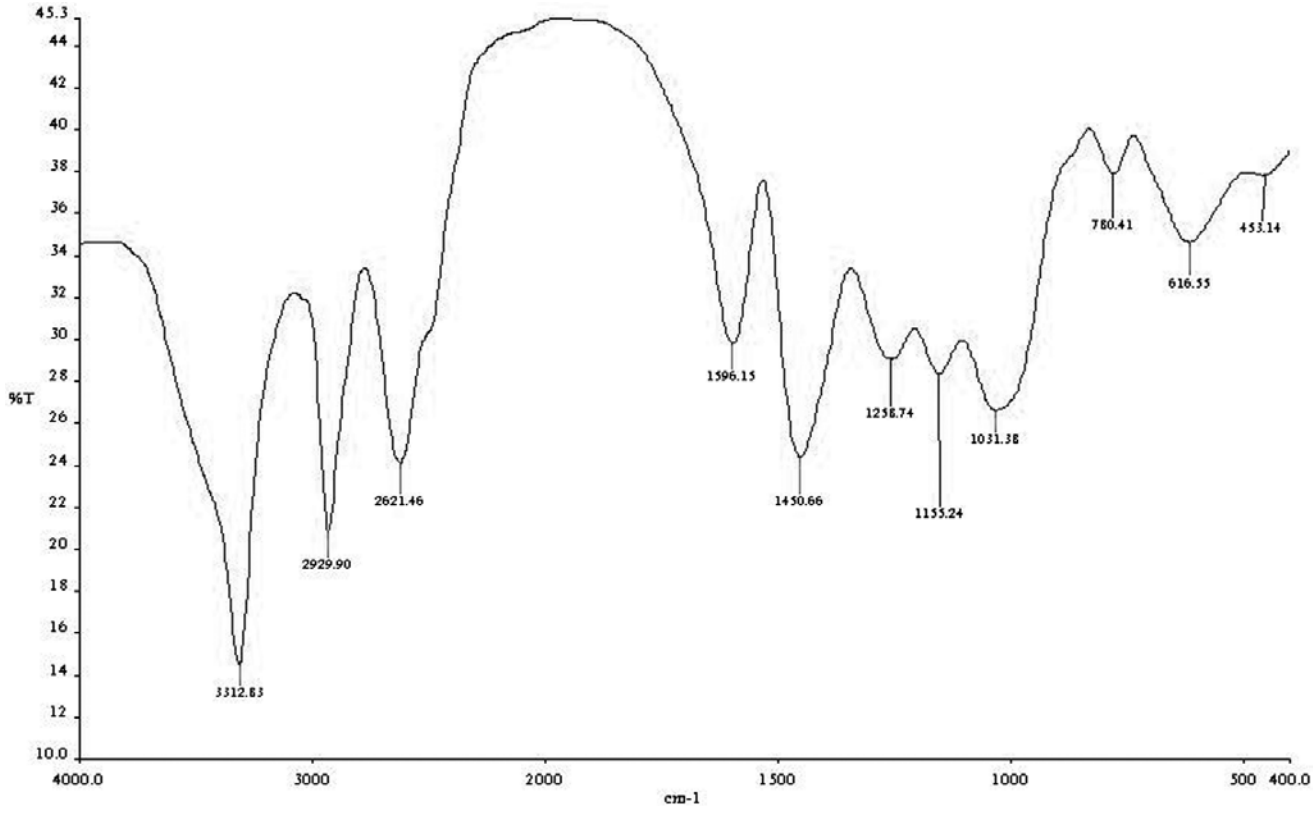

Fig. 3. FTIR spectrum of water extract of cissus gum + tramadol

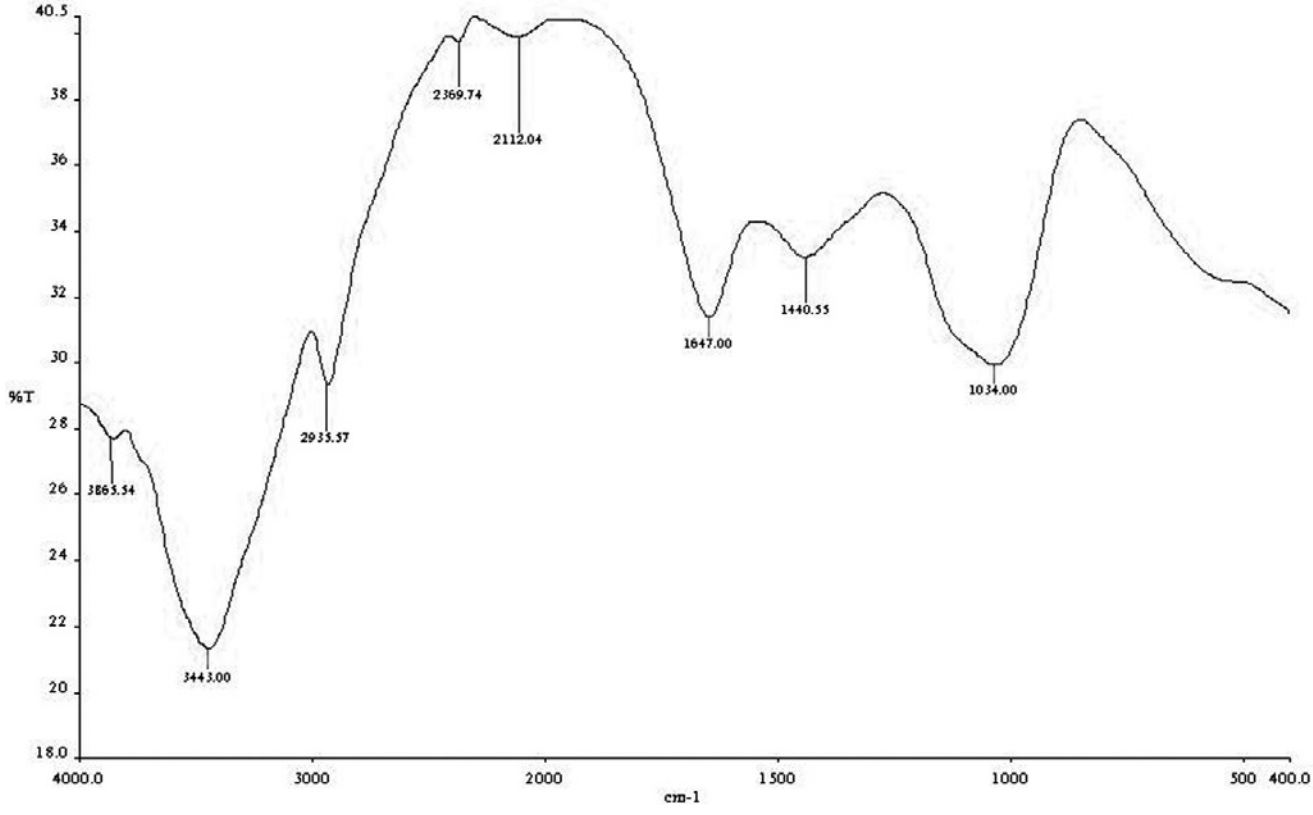

Fig. 4. FTIR spectrum of acetone extract of cissus gum

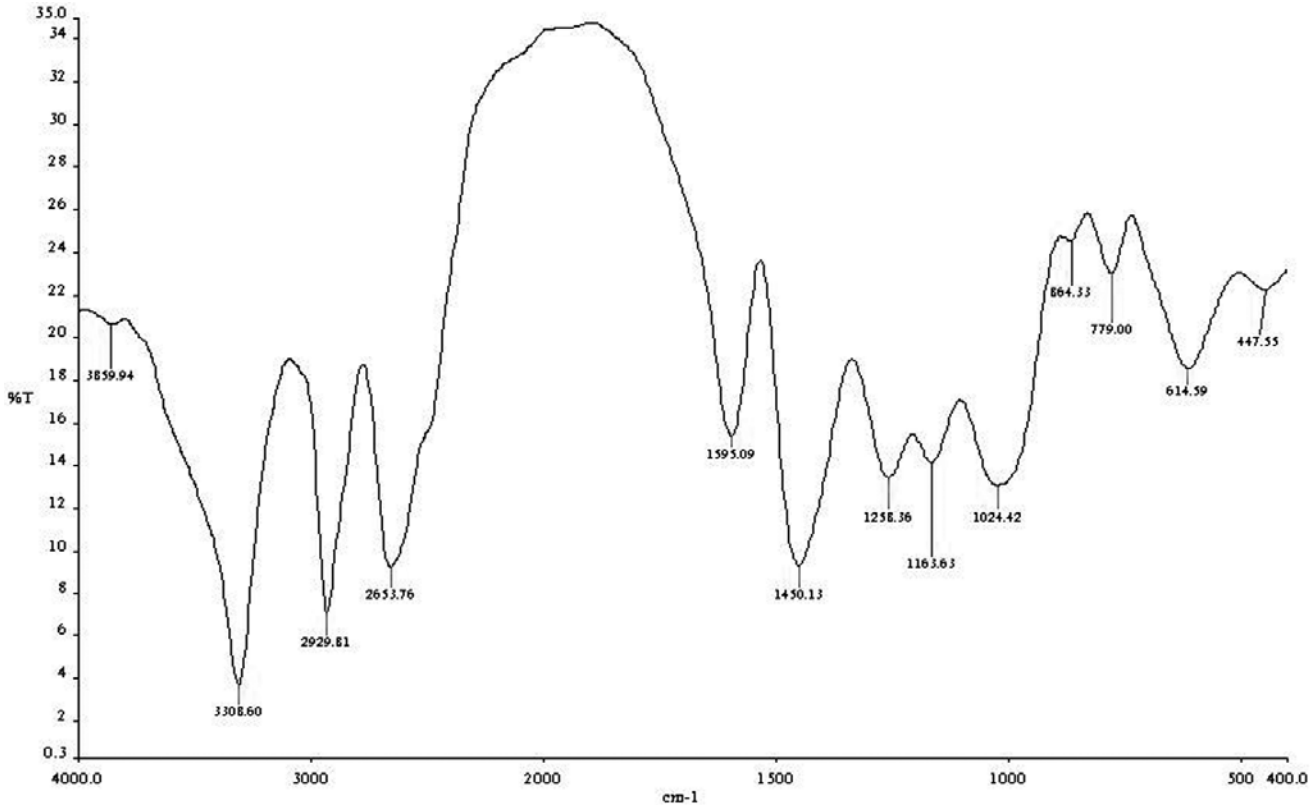

Fig. 5. FTIR spectrum of acetone extract of cissus gum + tramadol

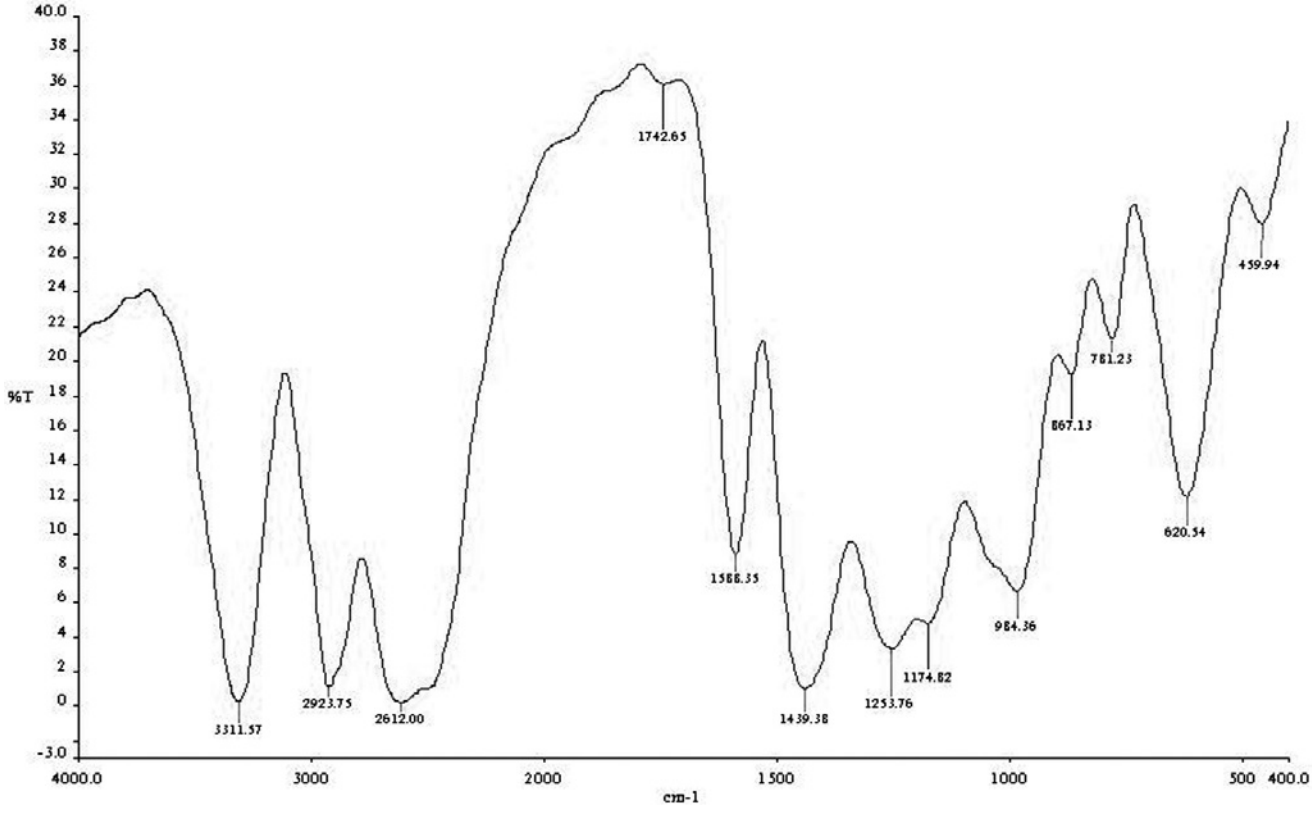

Fig. 6. FTIR spectrum of tramadol

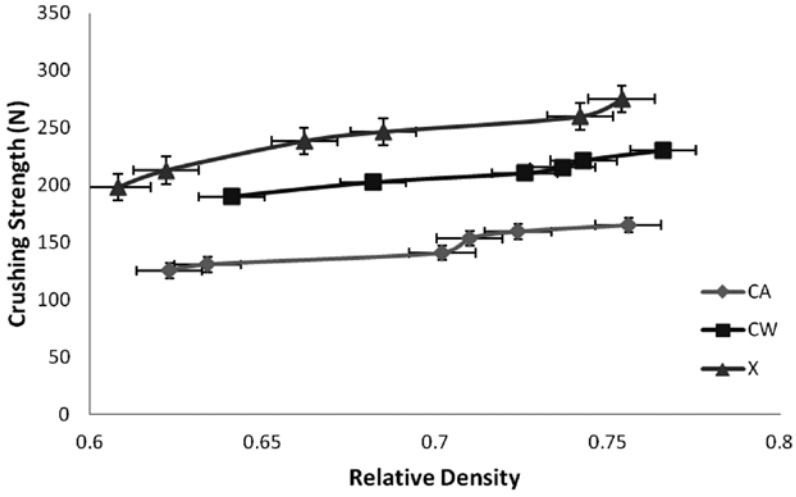

Fig. 7. Crushing strength of direct compression formulation of tramadol/polymer (1:3)

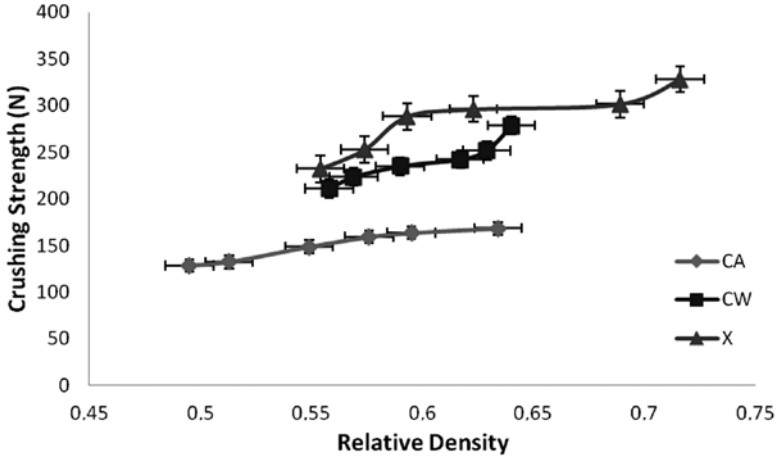

Fig. 8. Crushing strength of wet granulation formulation of tramadol/polymer (1:3)

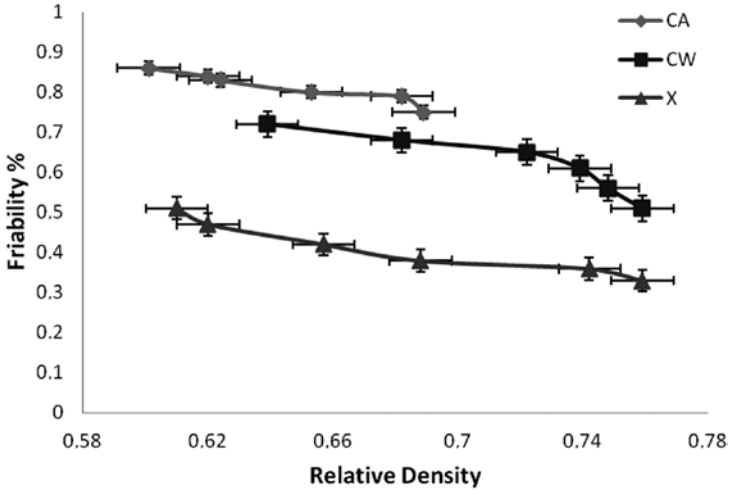

Fig. 9. Friability of direct compression formulation of tramadol/polymer (1:3)

ratios, prepared using different methods are shown in Tables 2 and 3.

For the determination of release mechanism and kinetics of tramadol matrix, data obtained from the dissolution profiles was fitted into different release models – Zero order, First order, Higuchi, Hixson Crowell and Korsemeyer. Regression equations were obtained and the correlation coefficient (r^2), diffusional release exponential (n) and kinetic constant (k) were obtained (Tables 4 and 5). The model with the highest correlation coefficient (r^2) was chosen as the best fit.

One-way Anova analysis shows that there is a significant difference in the dissolution rate of the ma-

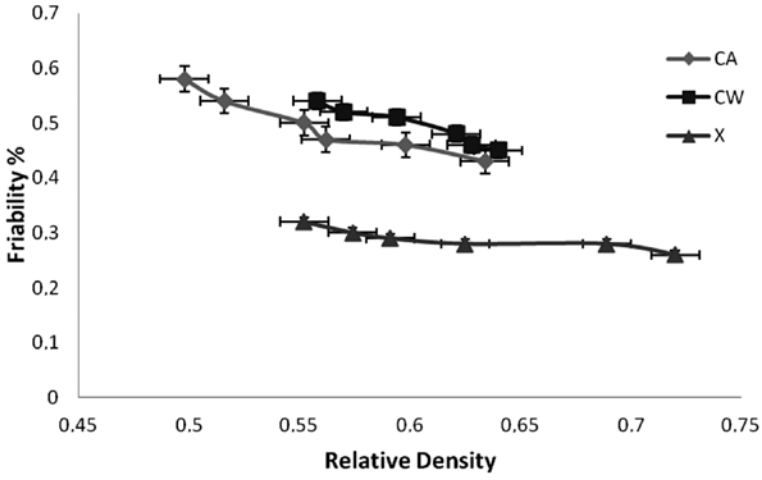

Fig. 10. Friability of wet granulation formulation of tramadol/polymer (1:3)

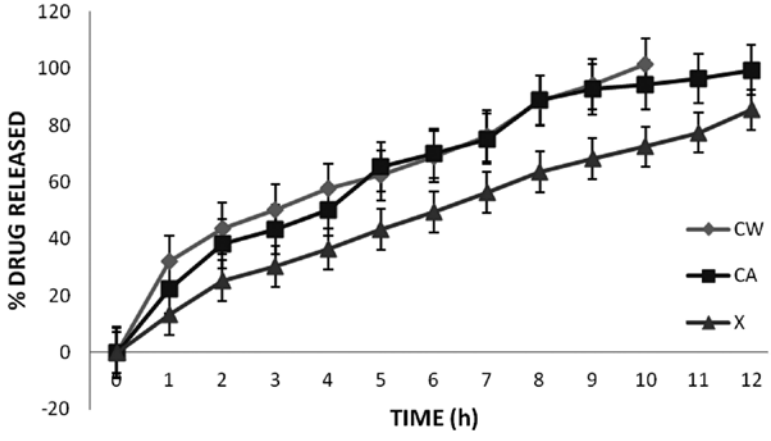

Fig. 11. Dissolution profile of tramadol formulation at ratio 1:3 using direct compression method at compression pressure of 113.16 MNm^{-2}

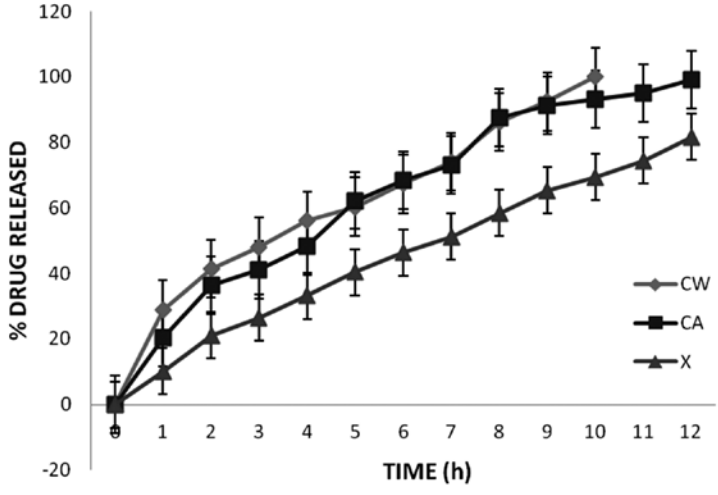

Fig. 12. Dissolution profile of tramadol formulation at ratio 1:3 using wet granulation method at compression pressure of 113.16 MNm^{-2}

trix tablets with changes in concentration of polymer ($p < 0.001$). Student t-test analysis of the rate of tramadol release in wet granulation and direct compression methods of formulations is significantly different ($p < 0.0001$). There is also a significant difference between the rate of tramadol release in formulations containing CW and CA ($p < 0.0001$).

The one way ANOVA statistical analysis shows that the t_{25} and t_{50} of all the polymers used in formulating the tablets processed by direct compression and wet granulation are not significantly different ($p > 0.05$), but t_{75} showed a significant difference.

Discussion

The use of excipients in the formulation of pharmaceutical dosage forms greatly affects drug delivery and maintenance of the desired drug concentration at the site of action. They provide enhanced functionality to

Table 2. Effect of polymer type and concentration on dissolution times at compression pressure 113.16 (MNm^{-2}) for direct compression method

Sample		t_{25}% (h)	t_{50}% (h)	t_{75}% (h)	MDT (h)
CA	1:1	0.170	0.970	2.686	1.655
	1:2	0.554	2.283	5.230	3.133
	1:3	1.050	3.424	6.835	4.090
CW	1:1	0.361	0.814	1.459	1.039
	1:2	0.530	1.196	2.146	1.599
	1:3	1.438	3.245	5.821	3.842
X	1:1	0.071	0.864	3.731	2.445
	1:2	1.272	3.979	7.754	4.699
	1:3	2.307	5.936	10.319	5.232

Table 3. Effect of polymer type and concentration on dissolution times at compression pressure 113.16 MNm^{-2} for wet granulation method

Sample		t_{25}% (h)	t_{50}% (h)	t_{75}% (h)	MDT (h)
CA	1:1	0.690	1.556	2.791	1.955
	1:2	1.280	2.888	5.180	3.372
	1:3	1.620	3.654	6.554	4.272
CW	1:1	0.188	0.752	1.693	1.103
	1:2	0.320	1.279	2.877	1.648
	1:3	0.723	2.892	6.507	3.956
X	1:1	0.116	1.132	4.284	2.659
	1:2	1.604	4.549	8.369	5.033
	1:3	2.768	6.590	10.944	5.417

Table 4. Release parameters of tramadol HCl from matrix tablets at compression pressure 113.16 (MNm^{-2}) prepared by direct compression from different release models

Formulation code		Zero-order	First-order	Higuchi			
		r^2	k	r^2	k	r^2	k
CA	1:1	0.661	20.51	0.999	0.598	0.971	44.00
	1:2	0.743	12.11	0.989	0.300	0.997	32.72
	1:3	0.845	9.92	0.974	0.222	0.979	28.98
CW	1:1	0.875	38.106	0.992	0.971	0.996	59.235
	1:2	0.614	20.877	0.995	0.650	0.955	44.909
	1:3	0.826	11.254	0.948	0.239	0.984	30.195
X	1:1	0.203	12.545	0.927	0.434	0.876	34.641
	1:2	0.865	9.239	0.938	0.186	0.965	26.917
	1:3	0.955	7.582	0.986	0.126	0.950	21.876

the pharmaceuticals and aid the innovations in the drug development [15]. Polymers generally have been used in drug formulation to modulate drug release [8] and as binders [9, 10, 16], disintegrants [17], emulsifying agent and as suspending agents [18].

The characteristic peaks associated with cissus gum were present in all the FTIR spectra involving tramadol and cissus gum and there are no significant changes in the position of the characteristic bands associated with tramadol and cissus gum indicating no interaction between the drug and polymer.

The amount of moisture present in a powder may affect the frictional properties of the compact formed. The formation of moisture film may reduce friction at

Table 5. Release parameters of tramadol HCl from matrix tablets at compression pressure 113.16 (MNm^{-2}) prepared by wet granulation from different release models

Formulation code		Zero-order	First-order	Higuchi			
		r^2	k	r^2	k	r^2	k
CA	1:1	0.684	17.771	0.991	0.501	0.963	40.823
	1:2	0.823	11.783	0.987	0.269	0.995	31.666
	1:3	0.873	9.743	0.973	0.210	0.973	28.397
CW	1:1	0.903	37.212	0.990	0.890	0.998	57.640
	1:2	0.634	20.580	0.996	0.616	0.960	44.217
	1:3	0.855	10.983	0.955	0.224	0.982	29.401
X	1:1	0.302	12.224	0.928	0.379	0.906	33.656
	1:2	0.907	8.828	0.943	0.167	0.954	25.603
	1:3	0.977	7.153	0.985	0.113	0.928	20.531

the die wall by acting as a lubricant, thus decreasing tablet adhesion to the die wall [19]. It was also reported that any water expressed during compaction also functions as a low-viscosity lubricant [20].

Cissus gum extracts had higher moisture content xanthan gum. This means that tablets produced with cissus gum extracts will easily be ejected during tableting from the die than xanthan gum.

Swelling is a measure of hydrophilicity and water retention capacity of a material. The swelling rate generally increased with time for all the polymers. The rate of swelling for all the polymers was rapid within the first hour after which it became reduced. This occurs because at first, hydration of polymer at the surface takes place fast so the swelling is more pronounced, but when the diffusional path length is increased, water penetration slows down, which slows swelling of the polymer. The thickness of the gel layer depends on water penetration, polymer chain disentanglement and mass transfer in water [8].

Swelling index of Acetone extract of cissus gum and aqueous extract of cissus gum were significantly different ($p < 0.05$). Acetone extract of cissus gum was shown to have higher water retention capacity than the aqueous extract; the ranking was X > CA > CW with significant difference ($p < 0.05$). Previous studies have shown that capacity of materials to capture water molecules influence parameters such as mechanical properties and surface mobility [13, 21]. The high swelling index of cissus gum suggests that it may be used as a sustained release excipient in a matrix tablet system.

According to Gomez et al., [22], the knowledge of the pH of an excipient is an important parameter in determining its suitability in formulations since the stability of physiological activity of most preparations depends on it. Both extracts were acidic and this was expected as plant gums are commonly macromolecular acids [23].

The values of the crushing strength of the tablets increased with increase in polymer concentration in all the formulations. The increase in crushing strength with increase in polymer concentration is an indication that the polymers were acting as a binding agent in the matrix system. However, formulations containing xanthan gum had the highest crushing strength values, with the ranking; X > CW > CA with significant difference ($p < 0.05$). As the concentration of the polymer increases in the formulation the number of particle – particle contact of the polymer increases, thereby increasing particle-particle interaction of the polymer leading to the formation of a strong bond which increases the mechanical strength of the tablet at high polymer concentrations.

The crushing strength values of formulations prepared by wet granulation method were higher than those prepared by direct compression method and also aqueous extract of cissus gum produces tablets with higher crushing strength than acetone extract. This shows that wet granulation and aqueous extract of cissus gum produced stronger tablets than direct compression method and acetone extract respectively. This is probably due to the higher moisture content of aqueous extract of the gum than the acetone extract. For the formulation methods, it could probably be due to the fact that the moisture content of the dried granules could be more than that of the powder mixture for direct compression formulation. Moisture increases the compact strength by increasing the tensile strength of the powder bed, decreasing the density variation within the tablet, and by recrystallization.

Pande and Shangraw [24] studied the role of moisture in the compression of α-cyclodextrin and found that samples lost their compactibility upon the removal of water. This demonstrates the essential role of moisture in tablet compression. Rees and Hersey [20] in a previous report showed that moisture improved consolidation, especially at low applied pressure. It has been reported that some effects of moisture on the flow and granule compaction properties of phenacetin, paracetamol, and dextrose monohydrate without the

addition of excipients [25]. Their results showed that there was increase in compact strength on drying. Bangudu and Pilpel [26] stated that paracetamol–cellulose mixtures containing 2 or 4% w/w water formed stronger tablets than those without moisture. As moisture content of pharmaceutical substances increases, the tensile strength of tablets increases (specifically at low moisture contents), reaches a maximum and then decreases (specifically at higher moisture content).

Friability was found to decrease with increase in relative density and concentration of polymer in all the formulations. The friability values were below 1% in all formulations. Convectional tablets which lose less than 1% of their weight during the friability test are generally considered acceptable. This suggests an optimum concentration of use for the polymers. However, formulations prepared by wet granulation method had lower values than formulations prepared by direct compression probably due to their higher crushing strength. Aqueous extract of cissus gum produces tablets with lower friability values than acetone extract of cissus gum.

According to Kalu et al., [8], drug release from the tablet matrix occurs when it is placed in contact with dissolution medium, the matrix gets hydrated and a number of porous channels are formed within the polymeric structure.

As the concentration of the polymer in the matrix increased, the dissolution rate of tramadol tablets decreased. There was a significant difference in the dissolution rate of the matrix tablets with changes in concentration of polymer ($p < 0.001$). This could be due to increase in the viscosity of the gel formed and the diffusional path length of the gel layer. This may decrease drug diffusion and erosion leading to reduction in drug release rate [16, 27]. It was observed that wet granulation method decreased rate of tramadol release more than direct compression method. Also, CA decreased rate of tramadol release more than CW. This is also in agreement with the result of swelling index.

Assessing the release of tramadol using t_{25}, t_{50} and t_{75}, it was observed that, these times increased with increase polymer concentration for both formulations. The rank order generally for t_{25}, t_{50} and t_{75} for all formulations was X > CA > CW at compression pressure of 113.16 and ratio 1:3 tramadol/polymer. Statistical analysis shows that the t_{25} and t_{50} of all the polymers used in formulating the tablets processed by direct compression and wet granulation are not significantly different ($p > 0.05$), but t_{75} showed a significant difference ($p < 0.05$).

Generally, wet granulation method decreased the rate of tramadol release more than direct compression method. This may be due to an increase in moisture content of the granules which causes solid bridge to be formed, thus reducing the tablet porosity and thereby reducing water penetration into the tablet matrix.

The release mechanism for both direct compression and wet granulation methods was Fickian and non-Fickian respectively. Also, for both formulation methods, the model of best fit for the matrix tablets depending on the tramadol/polymer ratio was First order, indicating that drug release is dependent on drug concentration [28], Higuchi, indicating that drug release is mainly by diffusion [29], Korsemeyer, indicating that drug release from the matrix is by diffusion and polymer relaxation and Hixson Crowell indicating that drug release is dependent on the change in surface area and diameter of tablets with progressive dissolution of the matrix as a function of time [30].

Mean dissolution time (MDT) was used to characterize the drug release rate and to determine the retarding efficacy of the polymers. The MDT of all the formulations increased with the increase in polymer concentration. CA for both methods of compression had higher MDT values than CW and compares favorably well with formulations containing X. Formulations of wet granulation method had higher MDT values than those of direct compression method, indicating that wet granulation method has higher drug retarding ability than direct compression method.

This study has shown that polymer type, concentration, and method of compression affected the release properties of tramadol from the matrix delivery system. Thus, cissus gum has the potential to be used as a sustained release excipient in matrix tablets since it compares favorably well with xanthan, a standard polymer used in controlling drug delivery and so it may be used as an alternative to the standard gum.

References

[1] **Fuentes-González K.I., Villafuerte-Robles L.:** Powder flowability as a functionality parameter of the excipient Galeniq 720. Int. J. Pharm. Sci. 2014, 6, 9, 66–74.

[2] **Robertson M.I.:** Regulatory issues with excipients. Int. J. Pharm. 1999, 187, 273–76.

[3] **Ayorinde J.O., Itiola O.A., Odeniyi M.A.:** Effects of excipients and formulation types on compressional properties of diclofenac. Acta Pol. – Drug Res. 2013, 70, 557–566.

[4] **Chowdary K.P., Mohapatra P., Murali Krishna M.N.:** Evaluation of *olibanum* and its resin as rate controlling matrix for controlled release of diclofenac. Indian J. Pharm. Sci. 2006, 68, 4, 497–500.

[5] **Odeniyi M.A., Khan H.N., Peh K.K**.: Release and mucoadhesion properties of diclofenac matrix tablets from natural and synthetic polymer blends. Acta Pol. – Drug Res. 2014 (in press).

[6] **Varshosaz J., Tavakoli N., Kheirolahi F**.: Use of hydrophilic natural gums in formulation of sustained release matrix tablets of tramadol hydrochloride. AAPS Pharm. Sci. Tech. 2006, 7, 1, 21–30.

[7] **Al-Saidan S.M., Krishnaiah Y.S., Satyanarayana V.R., Rao G.S.:** *In-vivo* evaluation of guar gum based matrix tablets of rofecoxib for colonic drug delivery. J. Current Drug Del. 2005, 2, 2, 155–163.
[8] **Kalu V.D., Odeniyi M.A., Jaiyeoba K.T.**: Sustained release of water-soluble drug from directly compressed okra gum matrix tablets. East and Central African J. Pharm. Sci. 2006, 9, 2, 46–51.
[9] **Adeleye A.O., Odeniyi M.A., Jaiyeoba, K.T.:** The influence of cissus gum on the mechanical and release properties of paracetamol tablets – a factorial analysis. J. Basic and Appl. Pharm. Sci. 2010, 31, 2, 131–136.
[10] **Adeleye A.O., Odeniyi M.A., Jaiyeoba, K.T.:** Evaluation of cissus gum as binder in a paracetamol tablet formulation. Farmacia 2011, 59, 1, 85–96.
[11] **Lehmann K.A.:** Tramadol in acute pain. Drug 1997, 53 (suppl 2), 25–33.
[12] **Scott L.J, Perry C.M.:** Tramadol: a review of its use in perioperative pain. Drug 2002, 60, 1, 139–176.
[13] **Odeniyi M.A., Ayorinde J.O.**: Material and rheological properties of yam starch/polymer blend hydrogels. Int. J. Pharmacol. Pharm. Tech. 2012, 1, 2, 23–28.
[14] **Fell J.T., Newton, J.M.:** Determination of tablet strength by diametrical compressiontest J. Pharm. Sci. 1970, 59, 8, 688–691.
[15] **Nachaegari S.K., Bansal A.K.:** Co-processed excipients for solid dosage forms. Pharm. Tech. 2004, 4, 2, 52–64.
[16] **Femi-Oyewo M.N., Aremu O.I., Kehinde O.J.:** Evaluation of *Beilschmiedia* seed gum as a tablet binder. East and Central Afr. J. Pharm. Sci. 2009, 12, 2, 15–18.
[17] **Alebiowu G., Itiola O.A.:** The influence of pre-gelatinized starch on interacting variables that act on disintegrants properties. Pharm. Technol. 2003, 27, 8, 28–33.
[18] **Femi-Oyewo M.N, Adedokun M.O., Olusoga T.O.:** Evaluation of the suspending properties of *Albizia zygia* gum on sulphadimidine suspension. Trop. J. Pharm. Res. 2004, 3, 1, 279–284.
[19] **Bakre L.G. and Jaiyeoba K.T.:** Evaluation of a new tablet disintegrant from dried pods of *Abelmuscusesculentus L* (Okra). Asian J. Pharma. Clin. Res. 2009, 2, 3, 81–91.
[20] **Rees J.E., Hersey J.A.:** Simulation device for preliminary tablet compression studies. J. Pharm. Sci. 1972, 61, 8, 1313–1315.
[21] **Akhila R.T., Emila A.**: Enzymatic modification of cassava starch by bacterial lipase. Bioprocess Biosyst. Eng. 2006, 29, 65–69.
[22] **Gomez G., Pikal M.J., Rodriguez-Hornedo N.:** Effect of initial buffer composition on pH changes during far-from equilibrium freezing of sodium phosphate buffer solutions. Pharm. Res. 2001, 18, 1, 90–97.
[23] **Al-Assaf S., Phillips G.O., Williams P.A.:** Studies on acacia exudate gums. Part I: the molecular weight of acacia senegal gum exudate. Food Hydrocolloids 2005, 19, 4, 647–660.
[24] **Pande G.S., Shangraw R.F.:** Characterization of a-cyclodextrin for directcompression tabletting: II. The role of moisture in the compactibility of a-cyclodextrin. Int. J. Pharm. 1995, 124, 2, 231–239.
[25] **Armstrong N.A., Haines-Nutt R.F.:** The compaction of magnesium carbonate. J. Pharm. Pharmacol. 1970, 22, 2, 8S–10S.
[26] **Bangudu A.B., Pilpel N.:** Effect of composition, moisture and stearic acid on the plasto-elasticity and tableting of paracetamol-microcrystalline cellulose mixtures. J. Pharm. Pharmacol. 1985, 37, 5, 289–293.
[27] **Ford J.L., Rubinstein M.H., Hogan J.E.:** Formulation of sustained released promethazine hydrochloride tablets using hydroxypropyl methyl cellulose matrixes. Int. J. Pharm. 1985, 24, 2, 327–338.
[28] **Najib N., Suleiman J.:** Dissolution kinetics of commercially available controlled release theophylline preparations. Int. J. Pharm. 1989, 52, 1, 63–70.
[29] **Boza A., Caraballo I., Alvarez-Fuentes J., Rabasco A.M.:** Evaluation of eudrajit RS-PO and ethocel 100 matrices for controlled release of lobenzarit disodium. Drug Dev. Ind. Pharm. 1999, 25, 2, 229–233.
[30] **Hixson A.W., Crowell J.H.:** Dependence of reaction velocity upon surface and agitation I: Theoretical consideration. Ind. Eng. Chem. 1931, 23, 923–931.

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