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Novel *Lannea Woodier* gum matrices for controlled release of drugs

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ABSTRACT

The objective of the study is to establish the potential of Odina gum as a novel pharmaceutical aid for development of controlled release drug delivery systems. The influence of varying the proportion of the gum, the nature of diluents and their ratio in the preparation was also evaluated. Compatibility of the drugs with the gum was studied using FTIR and DSC. *In vitro* dissolution studies indicated that various proportions of Odina gum ranging from 10% to 70% are required depending on the nature of the drug. Furthermore, a blend of lactose and microcrystalline cellulose were also required to tailor the release profiles for attaining controlled release of both the moieties. Swelling studies were carried out to support the drug release mechanism. Peppas model was found to be the best fit model. Hence swelling and diffusion were concluded to be the basic mechanisms modulating drug release from the gum based matrices.

1. Introduction

Natural gums are hydrophilic in nature, cost-effective, safe, easily available, biodegradable, and non-toxic, hence are preferred for the development of matrices for drug delivery. Even the naturally occurring polysaccharides can be easily modified chemically and biochemically to impart desirable properties suitable for designing of drug delivery systems. In the past decade a number of studies have been performed employing the use of the natural gums as release modifiers both for controlled release and delayed release of drugs through a variety of routes (Fan, Wang, Liu, & He, 2008; Sinha & Kumria, 2001; Varshosaz, Tavakoli, & Kheirolahi, 2006). Owing to the safety and the commercial usefulness of this category of excipients, pharmaceutical technologists world over are extensively exploiting the use of natural gums as release modifiers. However the list of natural gums available for the said purpose are limited and it is pertinent to explore the other gums which are having suitable characteristics to be utilized as a pharmaceutical aid. In the recent years a lot of attention has been laid on the development of modified drug delivery systems due to innumerable reasons. Oral controlled release dosage forms offer many benefits over conventional dosage forms such as convenient usage, narrow fluctuation of drug concentrations in the plasma, lesser frequency of administration, lesser toxicity, and higher degree of patient compliance (Collett & Moreton, 2002).

Gum Odina was collected from the bark of *Lannea Woodier* or *Odina Woodier* Roxb., family *Anacardiageae*, locally known as Jingan, Kamlai tree, which is common in deciduous forests of India (Chauhan, 1999; Kirtikar & Basu, 1935). The structural composition of the gum *perse* and on degradation has been reported earlier (Bhattacharyya & Rao, 1964). Odina gum (OG) is indicated as a safe pharmaceutical excipient. Recently, Mukherjee, Samanta, and Dinda (2006) have evaluated the binding capability of the gum by comparing it with the standard starch paste as a tablet binder. In this study it was demonstrated that the gum provides desired hardness, binding and disintegration time to the formulation in quantities significantly lower than that of starch paste (Mukherjee et al., 2006). In view of the exponential increase in the use of natural gums as release modifiers in the last two decades, the current study was conducted to investigate the efficacy of the gum obtained from *Lannea Woodier* as a novel release retardant in matrix tablets.

Gum based matrices were designed and evaluated for both hydrophilic and hydrophobic drugs, since drug solubility considerably affects the release profile of the designed system. Different techniques are used to develop these systems amongst which the direct compression is the most extensively exploited as it is simpler, offers considerable ease of manufacture and scale-up is easier. Two drugs with different hydrophilicities, i.e. Pioglitazone hydrochloride (PIO) (hydrophobic), an antidiabetic and Tolterodine tartrate (TOL) (hydrophilic), used for the treatment of overactive bladder were chosen as the model drugs in the study. Both these drugs have a short elimination half-life and require frequent administration

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to maintain the therapeutic effect for a prolonged period (Peters & Huang, 2001; Waugh, Keating, Plosker, Easthope, & Robinson, 2006). Therefore, for the improvement in patient compliance, it is desirable to develop a controlled release oral dosage form of the aforementioned drugs. The tablets were prepared by direct compression which is preferred over wet granulation due to the prime benefits like ease of development and involvement of lesser money and time.

2. Materials and methods

2.1. Chemical and reagents

Pioglitazone hydrochloride (PIO) (99.78% pure) was obtained as a gift from Panacea Biotec Ltd., Lalroo (India). Tolterodine tartarate (TOL) (99.89% pure) was procured as a gift sample from Ranbaxy Laboratories Ltd., Gurgaon (India). Ethanol (Changshu Chemicals, China), Spray dried lactose (Lactopress®, Ind-Swift Labs Ltd.), Microcrystalline cellulose PH102 (Ranbaxy Laboratories Ltd.), Talc purified and Magnesium stearate (E. Merck Ltd., Mumbai, India) were used as supplied by their respective companies. All the other chemicals and solvents used for the study were of analytical grade and were used without further purification. RO water was used for preparation of dissolution medium throughout the study.

2.2. Purification and isolation of Odina gum

Crude gum was collected as dried exudates from the barks of *Odina Wodier*, Roxb., of family Anacardiaceae in the month of October from Himachal Pradesh, India. For purification, the gum exudates thus obtained were kept overnight in water. The gum was then allowed to swell and the viscous solution obtained was stirred vigorously by using a mechanical stirrer for 6 h at room temperature. The homogenized viscous solution was further filtered using a fine muslin cloth to obtain a clear solution. This solution was then slowly added to ethanol and the white amorphous precipitate obtained was collected. The precipitate was filtered and was purified further by treatment with absolute ethanol. The white precipitate finally obtained was dried in an oven at 40 °C and kept in an air tight container for optimum storage.

2.3. Evaluation of the gum

2.3.1. Particle size measurement

Particle size of the excipient also plays a critical role for optimum mixing of the tablet blends. Thus after purification the particle size of the gum was analyzed by the Malvern Mastersizer 2000 using the dry powder method. The instrument was operated at a pressure of 1 bar and the feed rate was set at 40% and the samples were analyzed using the airflow mode. Sufficient quantity of the sample was added in dry form to obtain the obscuration in the range of 0.5–6% and the particle size was measured in triplicate.

2.4. Rheological properties

The rheological behavior of OG in aqueous solutions was measured using the Brookfield digital viscometer (DV-II + Pro, Brookfield Engineering Laboratories Inc., USA). The aqueous dispersion of the gum was prepared at different concentrations (7.5–15%, w/v) by dispersing various quantities of the gum in water. These solutions were kept overnight on magnetic stirrer for complete dispersion of the gum. The flow properties were then measured at different shears rates at 37 °C using spindle S21 and the rotation speed was varied from 5 to 100 rpm. Prior to each measurement the solution was allowed to stand in the small sample adapter for a preset time of 5 min.

2.5. Thermal properties

Drug-excipient compatibility was evaluated using differential scanning calorimetry (DSC). All the components exhibit a specific DSC curve indicative of the purity and nature of the compound. A comparative study of the DSC curves of the formulation components both individually and in mixture form allows a rapid evaluation of any drug–excipient interactions based on the appearance, shift, or disappearance of endothermic or exothermic peaks and/or variations in the relevant enthalpy values. The DSC curves of OG, PIO and TOL individually and in a 1:1 blend were generated by a differential scanning calorimeter (Mettler TA4000 apparatus equipped with a DSC 25 cell, Japan) at heating rate of 10° min^{-1} in the 30–300 °C temperature range under static air.

2.6. Fourier transform infrared spectroscopy (FTIR)

Spectral analysis using FTIR is a useful technique to verify the formation of new complexes in the blends. FTIR studies were conducted on PerkinElmer FTIR using KBr pellets to investigate possible interactions between the respective drugs and OG. The weight ratio of a sample and potassium bromide was 1:100 mg. Background spectrum was collected before running each sample. The samples were compressed into pellets using a hydraulic press and the pellets thus obtained were analyzed between wave numbers 4000 and 400 cm^{-1}.

2.7. Preparation of the matrix system

Different percentages of OG were used as a polymer to prepare matrix tablets by direct compression technique. Composition of the prepared batches is enlisted in Table 1. Weighed quantities of the drugs were physically mixed with varying proportions of the purified form of the gum by geometric addition using a glass mortar and pestle. MCC PH102 in combination with Lactopress® was used as filler for increasing the compressibility and flow of the ingredients. Finally magnesium stearate and talc were added as the glidants/lubricant and thoroughly blended for 2 min. The homogeneous powder blend thus obtained was weighed individually for

Table 1
Composition of the various batches prepared.

Formulation code	Tolterodine tartarate (% w/w)	Pioglitazone HCl (% w/w)	Odina Gum (% w/w)	Lactopress (% w/w)	MCC 102 (% w/w)
P1	–	8.27	30	–	58.73
P2	–	8.27	30	29.37	29.37
P3	–	8.27	20	39.37	29.37
P4	–	8.27	10	39.37	39.37
T1	2.5	–	40	19.06	36.25
T2	2.5	–	50	19.06	26.25
T3	2.5	–	60	11.56	23.75
T4	2.5	–	70	6.56	18.75

a single matrix and manually fed into the die of a single punch tabletting machine (Modern Engineering Works, New Delhi, India) equipped with a biconvex die-punch set of 8.2 mm diameter, and compressed to a target weight (as per the nature of the drug). The obtained matrices were subjected to various pharmacopoeial and physical evaluations like appearance, weight variation, thickness, hardness, drug content, and *in vitro* drug release.

2.8. Evaluation of the prepared matrices

2.8.1. Content determination

The prepared matrix tablets were tested for their drug content. Twenty tablets of each batch were weighed and powdered using a mortar and pestle. A known weight of the powder was dissolved in known volume of methanol and water for PIO and TOL respectively, and the resultant dispersion was sonicated for 10 min. The samples were filtered through a 0.22 μm membrane filter after sufficient dilution. The drug concentration was assayed on a UV–vis spectrometer (UV-1601, Shimadzu) at 269 nm for PIO and 283 nm for TOL respectively. All the determinations were done in triplicate.

2.9. Determination of swelling index

The dissolution mediums recommended by FDA were chosen for the study for both the drugs. The swelling studies were carried out in 100 ml of 0.3 M KCl–HCl buffer (pH: 2.0) for PIO and pH 6.8 phosphate buffer for TOL respectively. The beakers containing the tablets were placed in a constant temperature water bath for the period of 24 h at 37 °C. The diameters of the tablets were noted at various time intervals and the swelling indices were determined by using following formula:

$$\text{swelling index}\,(\%) = \frac{\text{diameter of the matrix tablet at time}\,(t) - \text{initial diameter}}{\text{initial diameter}} \times 100 \quad (1)$$

The diameter of the tablets was determined at defined time intervals using the divisions printed on the graph paper (Talukdar & Kinget, 1995).

2.10. In vitro release studies

In vitro studies were performed by using US Pharmacopeia type II dissolution apparatus (paddles method) at 50 rpm. Dissolution studies for PIO were carried out using 900 ml 0.3 M KCl–HCl buffer (pH: 2) and 500 ml of phosphate buffer (pH 6.8) for TOL maintained at a temperature of 37 °C ± 0.5 °C. An aliquot (5 ml) was withdrawn at specific time intervals and release was determined by UV–vis spectrophotometer (UV-1601, Shimadzu) at 269 nm and 283 nm for PIO and TOL respectively. All the studies were conducted in triplicate. The release behavior of the matrices containing OG was compared with the immediate release marketed formulations PIOGLIT® (Sun Pharma, 15 mg) and ROLITEN® (Ranbaxy, 2 mg).

2.11. Drug release kinetics

In order to study the mechanism of drug release from the prepared matrix tablets, the release data obtained was evaluated using zero-order release kinetics (Eq. (2)), Higuchi's square root of time equation (Eq. (3)) (Higuchi, 1961), Korsemeyer and Peppas Equation (Eq. (4)) (Korsmeyer, Gurny, Doelker, Buri, & Peppas, 1983) and Hixon–Crowells cube root of time equation (Eq. (5)) (Hixson & Crowell, 1931). The goodness of fit was evaluated by comparing the correlation coefficient values for batches P1-4 and T1-4.

$$M_t = M_0 + k_0 t \quad (2)$$

where M_t is the amount of drug dissolved in time t, M_0 is the initial amount of drug in the solution, K_0 is the zero order release rate constant and t is the release time.

$$M_t = k_h \sqrt{t} \quad (3)$$

where M_t is the amount of drug dissolved in time t, k_h is the Higuchi dissolution constant and t is release time.

$$\frac{M_t}{M_\infty} = kt^n \quad (4)$$

Here, M_t and M_∞ are the absolute cumulative amount of drug released at time t and infinite time, respectively; k is a constant which incorporates structural and geometric characteristics of the device, and n is the drug release exponent (DRE), indicative of the mechanism of drug release. The values of DRE assigned to a cylinder are 0.45 for Fickian diffusion and $0.45 < n < 0.89$ for non-Fickian diffusion, respectively.

$$M_0^{1/3} - M_t^{1/3} = k_s t \quad (5)$$

where M_0 is the initial amount of drug in the formulation, M_t is the amount remaining at any time t and k_s is the constant incorporating the surface–volume relation.

3. Results and discussion

3.1. Evaluation of the gum

3.1.1. Particle size measurement

The mean particle size of the OG particles was found to be 200.822 μm and that of both the drugs was 65.157 and 3.086 μm for PIO and TOL respectively. During direct compression for effective compaction the blend should be uniform without any significant segregation. Thus, the mean particle sizes of all the components of the blend are comparable enough to avoid non-uniform mixing and improper drug content on the prepared batches.

3.2. Viscosity and rheological properties

The pH of Odina gum aqueous dispersions (5%, w/v at 25 °C) was around 5.21. It produced slightly viscous dispersions at concentrations 7.5–15% (w/v) indicating that below this concentration very weak molecular interactions exist and beyond this further entanglement of the molecules of the gum would take place. The rheograms for various concentrations (7.5–15%, w/v) of the gum are presented in Fig. 1. The rheograms indicated that the aqueous dispersion of the gum exhibited pseudoplastic flow. This property is exhibited by non-Newtonian systems such as polymeric solutions as well as mucilages of gums (Gómez-Díaz, Navaza, &

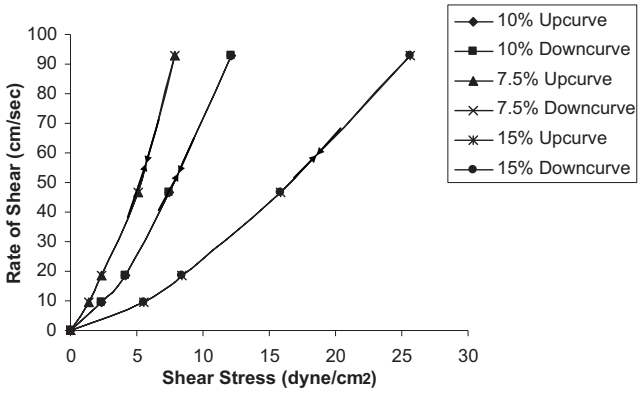

Fig. 1. Rheograms of Odina gum solutions in concentrations ranging from 7.5 to 15% (w/v).

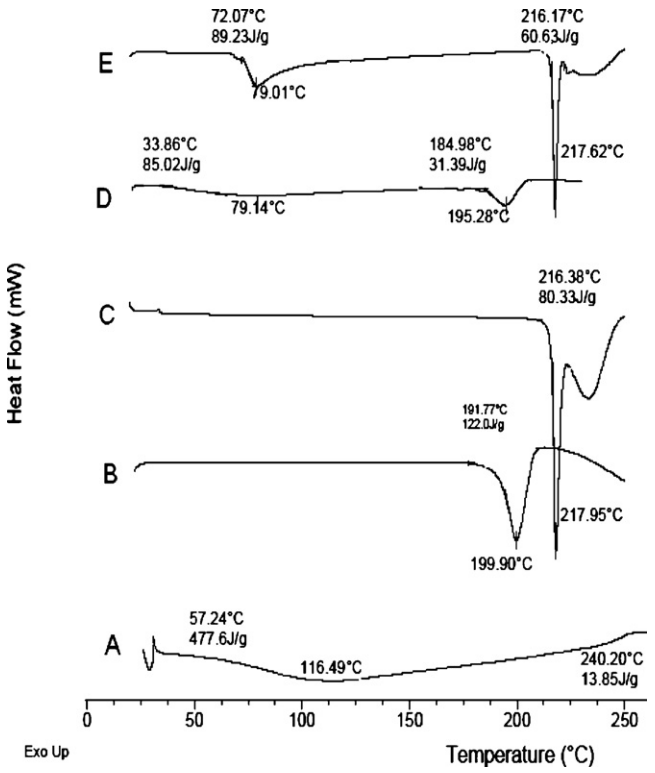

Fig. 2. DSC thermogram of (A) pure OG, (B) pure PIO, (C) pure TOL, (D) blend of PIO and OG (1:1), and (E) blend of TOL and OG (1:1).

Quintáns-Riveiro, 2008; Zhang, Zhang, Yang, Zhu, & Hu, 2008). The curves indicated that the viscosity of the solutions at different rates of shear is different and no single value can be used to express its viscosity. However, in general, the viscosity of a pseudoplastic system decreases with increase in rate of shear. Thus, the data obtained supports the fact that OG dispersion exhibited pseudoplastic behavior.

3.3. Thermal properties

Fig. 2(A–C) shows the DSC thermograms of pure OG, PIO and TOL respectively. OG thermogram exhibits a very broad endothermic peak at 116.49 °C which is associated with the loss of water from the polymer. Further an exothermic transition is recorded above 240.20 °C, which is indicative of degradation of the gum. The characteristic endothermic peak of PIO and TOL were observed at 199.90 °C and 216.38 °C respectively. Both the drug peaks were individually retained in their respective physical blends with the gum as shown in Fig. 2(D and E) along with an initial endothermic peak at around 79 °C. Any initial endothermic peak in the range of 63–134 °C corresponds to the transitions associated with loss of water (2–10 wt%) owing to the hydrophilic nature of functional groups of the natural polymer (Zohuriaan & Shokrolahi, 2004). This indicates absence of any physical or chemical interaction between the components.

3.4. Fourier transform infrared spectroscopy (FTIR)

FTIR spectra of the pure OG, PIO, TOL and their respective blends are presented in Fig. 3. In the FTIR spectra, curve A refers to pure OG while curves B and C represent pure PIO and TOL respectively. In case of pure OG, a broad band appearing around 3349.2 cm^{-1} corresponds to OH stretching, wave number 1615.3 cm^{-1} depicts the stretching zone of C=O and 1081.3 cm^{-1} depicts the stretching vibration of C–O group which is characteristic of polysaccharides (Schnitzer & Khan, 1972). FT-IR curves B and C represent characteristic peaks of PIO (3416.8 cm^{-1} (N–H stretching); 1742.8 cm^{-1}(C=O stretching) and 1150.8 cm^{-1} (C–O stretching)) and TOL (3572.7 (OH stretching), 1266.1 cm^{-1} (C–N stretch) and 1069.5 (C–O stretching)) respectively (Pavia, Lampman, & Kriz, 2001; Rai & Rai, 2003). However, in the spectra of the respective blends (curves D and E), major characteristic peaks of both the drugs individually and OG were retained respectively. This confirms no physical or chemical interactions amongst the components of the formulation and compatibility of the drug with the natural polymer.

3.5. Physical evaluation and content determination of the prepared matrices

The results indicated that all the tablets prepared in this study meet the USP-27 requirements for weight variation tolerance. Drug content of all tablet formulations were found in the range of 97.90–101.05%. The thickness, diameter, and hardness variation of all the prepared batches are indicated in Table 2.

3.6. Determination of swelling index

Drug release from a matrix system is basically regulated by the swelling behavior of the polymer (Talukdar & Kinget, 1995). The swelling behavior of the prepared matrix tablets in 0.1 N HCl and in PBS (pH 6.8) for PIO and TOL respectively, was studied as a function of time and the results obtained are presented in Fig. 4. It was observed that the hydrophilic matrix tablets underwent swelling at a rate which is proportional to the fraction of the gum, irrespective of the nature of the drug. Polysaccharidic matrices usually show initial rapid swelling at the periphery which results in the formation of a gelatinous zone around the core of the matrix system through which drug diffusion takes place. The thickness and the strength of this zone is mainly responsible for controlling drug release (Alvarez-Manceñido, Landin, & Martínez-Pacheco, 2008). The tablets containing various proportion of OG achieved rapid initial swelling in the first 30 min followed by maximum swelling at the end of 24 h. The axial swelling was less steep after the initial 4 h which is attributable to the increase in the diffusional path length to be traveled by the dissolution medium to reach the inner dry core of the matrix, as it increases with time. As a result the drug release profiles fitted well into the Peppas model. However, with

Table 2
Physical evaluation parameters for all the batches (P1–4; T1–4).

Formulation code	Weight (mg) (mean ± SD)	Thickness (mm)	Hardness (kg cm^2) (mean ± SD)	Friability (% weight loss)
P1	199.40 ± 1.14	4.2	3.33 ± 0.29	0.30
P2	199.61 ± 1.18	4.2	4.00 ± 0.05	0.71
P3	200.48 ± 0.29	4.2	3.53 ± 0.06	0.80
P4	199.28 ± 0.34	4.2	4.53 ± 0.06	0.60
T1	159.99 ± 0.75	3.2	3.65 ± 0.24	0.85
T2	161.2 ± 0.88	3.3	3.7 ± 0.19	0.80
T3	159.76 ± 0.84	3.3	3.73 ± 0.26	0.72
T4	159.53 ± 0.75	3.8	3.95 ± 0.28	0.70

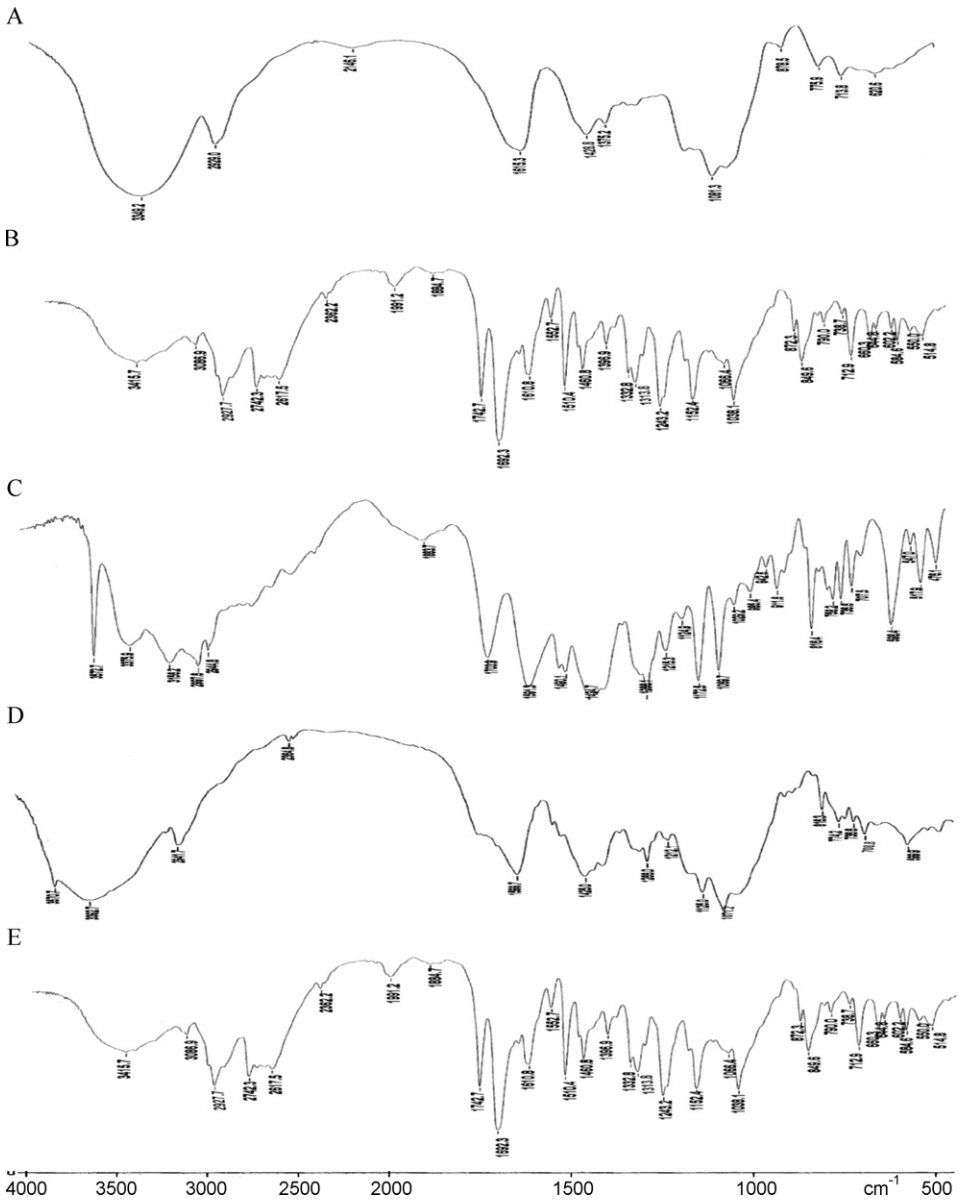

Fig. 3. FTIR spectra of (A) pure OG, (B) pure PIO, (C) pure TT, (D) blend of PIO and OG (1:1), and (E) blend of TOL and OG (1:1).

an increase in gum concentration beyond 50% the swelling was almost constant after 6 h which is indicative of the role of erosion of the matrix in drug release along with diffusion. As a result the drug release followed first order release kinetics. Thus, the amount of OG present in the system sufficiently controlled the rate of drug release from the designed matrices.

3.7. *In vitro release studies*

To understand the drug release profile from the tablets dissolution studies were carried out for PIO and TOL in 0.3 M KCl–HCl (pH 2) and PBS (pH 6.8) respectively. In Fig. 5(A and B) the release profiles of PIO and TOL from tablets prepared with the various concentrations of OG are reported. All the *in vitro* profiles follow the expected pattern as on increasing the concentration of the gum a relative decrease in the release of both the hydrophilic and hydrophobic drugs was noted. Incorporation of the gum in the matrix lowered the release of both PIO and TOL as their respective immediate release formulations PIOGLIT® and ROLITEN® gave complete release within an hour approximately. The fillers in the composition also play a key role in the optimum delivery of the drug moiety. Addition of soluble fillers like lactose to the matrix enhances the release of the drug irrespective of the nature of the drug (Ford, Rubinstein, McCaul, Hogan, & Edgar, 1987). This is attributed to the decrease in the tortuosity of the diffusion path and greater imbibition of water in the peripheral layer of the matrix (Nandita and Sudip, 2004) and further the addition of MCC modifies the swelling behavior of the tablets (Nellore, Singh Rekhi, Hussain, Tillman, & Augsburger, 1998). As shown in Fig. 5A incorporation of lactose in the matrix exhibited substantial enhancement in the drug release rate from the tablets due to increase in swelling of the polymer. Hence higher the concentration of lactose in the tablets higher drug release rate is obtained due to increase in the number of channels formed in the hydrated gelitonous layer formed around the hard core of the tablet. The *in vitro* results indicated that a proper blend of lactose, a water soluble filler and MCC PH102, water swellable filler (i.e. Batch P4 and T4) was required in all the cases to achieve the desired constraints in the release profile. The standard deviation at all the time points was below 5%, which is suggestive of the reproducibility of the batch. It was also

Table 3
An overview of the comparative characteristics of different drug release models, best fit model for batches.

Batch no	Release model										
	Zero order		First order		Higuchi		Korsmeyer–Peppas		Hixson–Crowell		Best fit model
	K_0	R_0	K_1	R_1	K_h	R_h	n	R_k	K_s	R_s	
P1	1.631	0.967	−0.080	0.784	7.431	0.924	0.750	0.996	−0.077	0.855	PEPPAS
P2	2.049	0.925	−0.079	0.811	11.806	0.987	0.597	0.979	−0.070	0.792	PEPPAS
P3	1.956	0.914	−0.079	0.785	8.504	0.894	0.697	0.989	−0.080	0.918	PEPPAS
P4	3.079	0.961	−0.079	0.873	17.244	0.987	0.543	0.992	−0.079	0.872	PEPPAS
T1	3.052	0.631	−0.095	0.713	27.55	0.704	0.423	0.922	−0.060	0.588	PEPPAS
T2	3.17	0.645	−0.096	0.715	26.96	0.758	0.456	0.928	−0.064	0.595	PEPPAS
T3	3.284	0. 658	−0.088	0.939	25.82	0.811	0.522	0.922	−0.070	0.587	FIRST
T4	3.218	0.755	−0.080	0.976	23.13	0.897	0.546	0.941	−0.073	0.646	FIRST

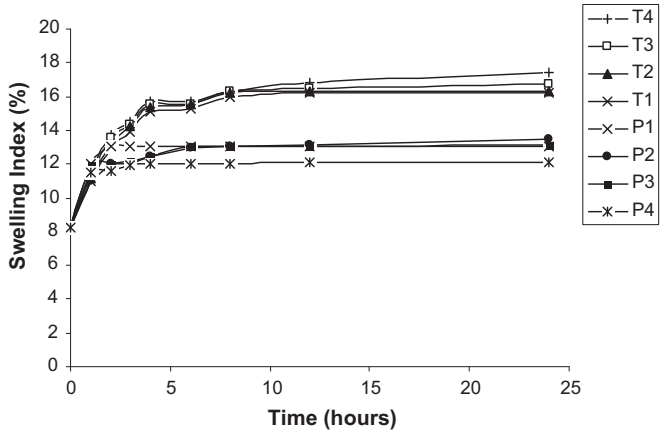

Fig. 4. Swelling behavior showing the swelling indices of both PIO and TOL, in 0.3 M KCl–HCl buffer (pH 1.2) and phosphate buffer (pH 6.8) respectively.

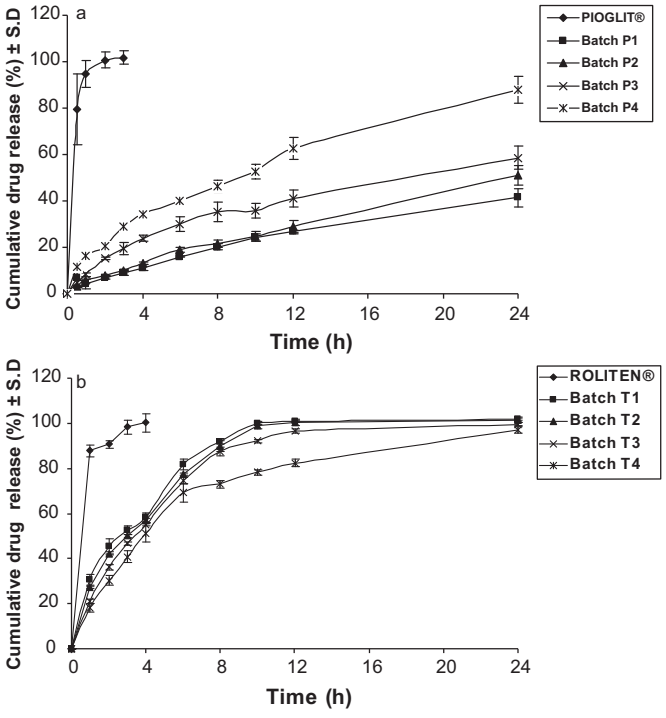

Fig. 5. (A) *In vitro* mean cumulative % release of PIO from matrices containing various proportions of OG. Each point is the mean value of three samples ($n = 3$). (B) *In vitro* mean cumulative % release of TOL from matrices containing various proportions of OG. Each point is the mean value of three samples ($n = 3$).

observed that lower concentrations of OG were required to sustain the release of PIO, as it is a hydrophobic moiety. However, the release of the drug decreased on increasing the proportion of the gum in the matrix. Batch P4 containing the lowest concentration (10%, w/w) of OG gave an optimum controlled release profile over a period of 24 h. It resulted in 20.52 ± 0.38% of drug release in the initial 2 h, followed by 46.34 ± 2.40% in 8 h, 62.79 ± 4.64% in 12 h and 87.79 ± 5.65% in 24 h. On the other hand owing to the hydrophilic nature of the drug the controlled release matrix tablets of TOL were formulated with a higher percentage of the gum (40–70%). A good initial release of approximately 15–30% was reported in the first hour with an extension in release up to 16–24 h depending on the percentage of OG in all the TOL batches (T1–4). Thus, irrespective of the nature of the dissolution medium the *in vitro* release rate decreased with increase in proportion of the gum and a relatively higher fraction of the gum is required for sustaining the release of a hydrophilic moiety as compared to a hydrophobic moiety. Similar findings have also been reported by other researchers where established polysaccharides like guar gum (Al-Saidan, Krishnaiah, Patro, & Satyanaryana, 2005), locust bean gum (Sujja-areevath, Munday, Cox, & Khan, 1996), xanthan gum (Dhopeshwarkar & Zatz, 1993) have been used individually or in combination as release retardants resulting in a proportional effect on the release rates of the incorporated drugs.

3.8. Drug release kinetics

Values of drug release exponents and coefficient of correlation for all the release models obtained are as indicated in Table 3. The release data is in good agreement with the Peppas model, with coefficient of regression values between 0.922 and 0.996. A value of n in the range of 0.42–0.54 was obtained for time-dependent release of TOL and for PIO the values of n were in the range of 0.54 and 0.75. Therefore, it was concluded that swelling is the main mechanism influencing the drug release from the matrices composed of OG. However, as the concentration of gum increases in the system the release profile changes from non-Fickian release to first order release kinetics due to contribution of both erosion and diffusion in drug release.

4. Conclusion

Gum Odina is a potential candidate for the design of sustained release delivery systems. It is a natural, biodegradable, non-toxic material and requires lower production cost. The overall findings of the study indicated that OG demonstrated an inherent property to provide retardation in drug release depending on the proportion of the gum in the tablets. According to the swelling studies the matrix was characterized by initial rapid swelling followed by the formation of loose gelatinous network which assisted in drug release. Furthermore, the matrix integrity was disrupted by incorporation

of a water soluble filler in the matrix which aided in slight erosion of the gelatinous layer formed due to the swelling of the gum, controlling the release rate of the drug. The analysis of the drug release kinetics indicated that the nature of drug release from the OG matrices was dependent on the diffusion of the drug from the matrix and polymer relaxation and therefore followed non-Fickian or anomalous release in both acid buffer (pH 2) and phosphate buffer (pH 6.8). The composition ratio containing beyond 60% of the gum affected the release and it followed first order release kinetics. All these results demonstrate that OG is a useful pharmaceutical aid and can be used for effectively controlling the release of drugs from the designed matrix systems.

References

Alvarez-Manceñido, F., Landin, M., & Martínez-Pacheco, R. (2008). Konjac glucomannan/xanthan gum enzyme sensitive binary mixtures for colonic drug delivery. *European Journal of Pharmaceutics and Biopharmaceutics*, *69*(2), 573–581.

Al-Saidan, S. M., Krishnaiah, Y. S. R., Patro, S. S., & Satyanaryana, V. (2005). In vitro and in vivo evaluation of guar gum matrix tablets for oral controlled release of water-soluble diltiazem hydrochloride. *AAPS PharmSciTech*, *6*(1), E14–E21.

Bhattacharyya, A. K., & Rao, C. V. N. (1964). Gum Jeol: The structure of the degraded gum derived from it. *Canadian Journal of Chemistry*, *42*(1), 107–112.

Chauhan, N. S. (1999). *Medicinal and aromatic plants of Himachal Pradesh*. Indus Publishing.

Collett, J., & Moreton, C. (2002). *Pharmaceutics: The science of dosage form design*. Churchill Livingstone.

Dhopeshwarkar, V., & Zatz, J. L. (1993). Evaluation of xanthan gum in the preparation of sustained release matrix tablets. *Drug Development and Industrial Pharmacy*, *19*, 999–1017.

Fan, J., Wang, K., Liu, M., & He, Z. (2008). In vitro evaluations of konjac glucomannan and xanthan gum mixture as the sustained release material of matrix tablet. *Carbohydrate Polymers*, *73*(2), 241–247.

Ford, J. L., Rubinstein, M. H., McCaul, F., Hogan, J. E., & Edgar, P. J. (1987). Importance of drug type, tablet shape and added diluents on drug release kinetics from hydroxypropylmethylcellulose matrix tablets. *International Journal of Pharmaceutics*, *40*(3), 223–234.

Gómez-Díaz, D., Navaza, J. M., & Quintáns-Riveiro, L. C. (2008). Intrinsic viscosity and flow behaviour of Arabic gum aqueous solutions. *International Journal of Food Properties*, *11*(4), 773–780.

Higuchi, T. (1961). Rate of release of medicaments from ointment bases containing drugs in suspension. *Journal of Pharmaceutical Sciences*, *50*, 874–875.

Hixson, A. W., & Crowell, J. H. (1931). Dependence of reaction velocity upon surface and agitation. *Industrial & Engineering Chemistry*, *23*(8), 923–931.

Kirtikar, K. R., & Basu, B. D. (1935). *Indian medical plants*. Dehradun, India: International Book Distributors and Sellers.

Korsmeyer, R. W., Gurny, R., Doelker, E., Buri, P., & Peppas, N. A. (1983). Mechanisms of potassium chloride release from compressed, hydrophilic, polymeric matrices: Effect of entrapped air. *Journal of Pharmaceutical Sciences*, *72*(10), 1189–1191.

Mukherjee, B., Samanta, A., & Dinda, S. C. (2006). Gum Odina—a new tablet binder. *Trends in Applied Sciences Research*, *1*(4), 309–316.

Nandita, G. D., & Sudip, K. D. (2004). Development of mucoadhesive dosage forms of buprenorphine for sublingual drug delivery. *Drug Delivery*, *11*, 89–95.

Nellore, R. V., Singh Rekhi, G., Hussain, A. S., Tillman, L. G., & Augsburger, L. L. (1998). Development of metoprolol tartrate extended-release matrix tablet formulations for regulatory policy consideration. *Journal of Controlled Release*, *50*(1–3), 247–256.

Pavia, D. L., Lampman, G. M., & Kriz, G. S. (2001). *Introduction to spectrometry: Guide for students of organic chemistry*. Thomson Books.

Peters, K. M., & Huang, R. R. (2001). Tolterodine once-daily in treatment of the overactive bladder. *Urology*, *58*(5), 829.

Rai, A. K., & Rai, D. K. (2003). Spectroscopic studies of some antidiabetic drugs. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *59*(8), 1673–1680.

Schnitzer, M., & Khan, S. U. (1972). *Humic substances in the environment*. New York: Dekker.

Sinha, V. R., & Kumria, R. (2001). Polysaccharides in colon-specific drug delivery. *International Journal of Pharmaceutics*, *224*(1–2), 19–38.

Sujja-areevath, J., Munday, D. L., Cox, K. A., & Khan, K. A. (1996). Release characteristics of diclofenac sodium from encapsulated natural gum mini-matrix formulations. *International Journal of Pharmaceutics*, *139*(1–2), 53–62.

Talukdar, M. M., & Kinget, R. (1995). Swelling and drug release behaviour of xanthan gum matrix tablets. *International Journal of Pharmaceutics*, *120*(1), 63–72.

Varshosaz, J., Tavakoli, N., & Kheirolahi, F. (2006). Use of hydrophilic natural gums in formulation of sustained-release matrix tablets of tramadol hydrochloride. *AAPS PharmSciTech*, *17*(7), E1–E7.

Waugh, J., Keating, G. M., Plosker, G. L., Easthope, S., & Robinson, D. M. (2006). Pioglitazone: A review of its use in Type 2 diabetes mellitus. *Drugs*, *66*(1), 85.

Zhang, G., Zhang, M., Yang, W., Zhu, X., & Hu, Q. (2008). Effects of non-Newtonian fluid on centrifugal blood pump performance. *International Communications in Heat and Mass Transfer*, *35*(5), 613–617.

Zohuriaan, M. J., & Shokrolahi, F. (2004). Thermal studies on natural and modified gums. *Polymer Testing*, *23*(5), 575–579.