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Albizia procera gum as an excipient for oral controlled release matrix tablet

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ABSTRACT

The purpose of this research was to develop and evaluate controlled release matrix tablets of paracetamol based on natural gum exudates of *Albizia procera*. Procera gum was characterized of its properties like compressibility index, angle of repose, viscosity and moisture content. The interaction between the gum and paracetamol was also studied through differential scanning calorimetry (DSC) and FTIR spectroscopy. Matrix tablets were then prepared by wet granulation method with different concentrations of procera gum and hydroxypropyl methylcellulose (HPMC) and evaluated for their physical properties like weight variation, hardness, friability and content uniformity. Dissolution study was conducted to characterize release mechanism from the matrix system and data were fitted to various kinetic models. The mechanism of drug release from both types of matrix tablets was found to be anomalous type. Results from various evaluations suggested that *A. procera* gum could be used as drug release retardant in controlled release matrix systems.

1. Introduction

Controlled release dosage forms are capable of achieving a variety of therapeutic benefits including a more constant or prolonged therapeutic effect, a reduction in dosing frequency and side effects and improved patient compliance (Lee & Li, 2010). Several technologies have been developed to control the release of drugs from a dosage form but oral matrix tablets are still the most frequently manufactured and used system. This popularity of matrix systems can be attributed to their technological simplicity, low cost, ease of fabrication and convenience (Genc & Jalvand, 2008). Matrix tablets usually consist of polymer, drug and other excipients which are homogenously distributed throughout the system and prepared through either direct compression or wet granulation methods. Several polymers including hydrophilic and hydrophobic types have been used in the preparation of matrix based controlled release drug delivery systems. These polymers are instrumental in giving the desired characteristics to the tablets and also influence the mechanism of drug release from the system. Upon contact with water, hydrophilic polymers hydrate to form a gel layer. This gel layer controls the entry of water into the matrix and influences the mechanism of drug release. Therefore, the mechanism of drug release from hydrophilic matrix systems is a combination of hydration and swelling of the tablet, drug dissolution, diffusion and outer matrix surface erosion.

Natural gums and mucilages have long been used in pharmacy for a variety of purposes. They are useful as tablet binders, disintegrants, emulsifiers, suspending agents, gelling agents, stabilizing agents and thickening agents (Gowthamarajan, Kumar, Gaikwad, & Suresh, 2011; Jani, Shah, Prajapati, & Jain, 2009; Odeku, 2005). In recent years, a number of natural gums and mucilages have been evaluated as matrix polymer for controlled drug delivery systems. This increased interest in natural polymers is due to their non-toxicity, cheap and easy availability, biodegradability and biocompatibility (Chivate, Poddar, Abdul, & Savant, 2008; Mukherjee, Dinda, & Barik, 2008). Apart from their safety, these natural polysaccharides are capable of providing the desired drug release characteristics and in some cases, have shown comparable drug release profiles with currently available sustained release products in market (Jani & Shah, 2008; Singh, Kumar, Langyan, & Ahuja, 2009).

Albizia trees are known to produce gums and have been reported as substitute for arabic gum as natural emulsifier for foods and pharmaceuticals (Avachat, Dash, & Shrotriya, 2011; De Paula, Santana, & Rodrigues, 2001). Structural studies on *Albizia* gums reveal the presence of β-(1-3)-D-galactopyranose units with some β-(1-6)-D-galactopyranose units and α-(1-3)-L-arabinofuranose units. Recent studies on *Albizia zygia* gum exudates have shown that it could be useful as binding agent in tablet formulations and also as a compression coating material for drug targeting to the colon (Odeku, 2005; Odeku & Fell, 2005). *Albizia procera* (Roxb.) Benth. is a fast growing, medium sized tree belonging to Mimosaceae family, native to Asia tropical, Asia temperate and Australasian region. It is known to exude gums in small transparent tears and

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vermiform pieces (Nussonovitch, 2010). To our knowledge, this exudate gum has not been studied or evaluated as an excipient for controlled release drug delivery systems. In the present study, procera gum based matrix tablets were prepared taking paracetamol as a model drug. Hydroxypropyl methylcellulose (HPMC) which has a long history of application in marketed products with wide global regulatory acceptance has been taken as standard for comparison purposes. HPMC has received the most attention among natural and semi-synthetic polymers due likely to its low toxicity and ease of manufacture (Mughal, Iqbal, & Neau, 2011). The compatibility of procera gum with the model drug was established through differential scanning calorimetry (DSC) and FTIR studies. Drug release mechanism, mechanical strength and other physical properties of procera gum based matrix tablets were compared with those of HPMC based formulations.

2. Materials and methods

2.1. Materials

The *A. procera* was identified and authenticated at the Department of Forestry, School of Earth Sciences, Mizoram University. Crude procera gum exudates were collected by hand picking in Mizoram (India) during the month of January–March and purified. Geographically, Mizoram is located between East Longitude 92°15′ to 93°29′ and North Latitude 21°58′ to 24°35′ with average altitude of 900 m. The purification procedure may be described briefly as follows. The crude gum powder was boiled with 80% ethanol to deactivate enzymes and dissolve out low molecular weight carbohydrates along with coloring matters. It was dispensed in deionized water and gently stirred overnight in magnetic stirrer. The gum solution was then allowed to stand for 12 h at room temperature to separate any undissolved matters. The gum solution was then filtered through triple folded muslin cloth and evaporated to 1/3rd of its original volume, cooled and precipitated with 3 vol. of propanol and air dried. They are passed through sieve no. 85, stored in desiccators until used. Microcrystalline cellulose (Avicel PH 101, Sigma–Aldrich), Paracetamol Extrapure (SD Fine Chem, Mumbai) and HPMC (hydroxypropyl methylcellulose, K10, SD Fine Chem, Mumbai) were procured from different sources. All other chemicals and reagents used were of analytical grade.

2.2. Characterization of procera gums

2.2.1. Moisture content

Moisture content was expressed as percentage weight loss on drying (% LOD). Two grams of ground gum sample was weighed and oven dried at 105 °C for 5 h to a constant weight. The experiment was done in three replications and an average of the three replicates was taken. The percent loss on drying was then calculated as follows (Rankell, Lieberman, & Schiffman, 1986):

$$\%\ \text{loss on drying} = \frac{\text{weight of water in sample}}{\text{total weight of wet sample}} \times 100 \quad (1)$$

2.2.2. Ash content

The ash content was determined by following the method of Yebeyen, Lemenih, and Feleke (2009). Two grams of the procera gum was first heated on a burner in air to remove its smoke. Then it was burned in a muffle furnace at 550 °C. The ash content was expressed as a percentage ratio of the weight of the ash to the oven dry weight of the powdered gum.

2.2.3. Angle of repose (θ)

Angle of repose (θ) was measured using a fixed height funnel fitted at the height of 10 cm from the base (the funnel is 60°, 10 cm in diameter, 0.7 cm internal stem diameter with 9.6 cm stem length). Twenty grams of the dried powder was allowed to flow through the funnel into the base and a pile was formed at the base. The angle of repose was then calculated as follows:

$$\text{angle of repose}\ \ (\theta) = \tan^{-1}\frac{h}{r} \quad (2)$$

where h and r are the height and radius of the pile respectively.

2.2.4. Compressibility index

The compressibility index of the procera gum was determined according to Carr's index after determining bulk and tapped densities. Twenty grams of the dried gum was taken into 50 ml graduated measuring cylinder and the initial volume (V_0) was recorded. The cylinder was then tapped 100 times using bulk density apparatus (ACM-157, Acmus Technocracy, New Delhi) to achieve a final volume (V_f). The bulk density was calculated from the initial volume and tapped density from the final volume after hundred tapping. Carr's index was then determined by the following equation (Nep & Conway, 2011):

$$\text{Carr's index} = \frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100 \quad (3)$$

2.2.5. Viscosity

5% procera gum solution prepared in distilled water and the viscosity was determined at 25 °C using Brookfield viscometer (Model DV-E, Spindle No. 62). Effect of shear rate (rpm) on viscosity was studied by varying the shear rate between 10 and 100 rpm. The change in viscosity with respect to rpm was recorded in triplicates. The viscosity–shear rate profile was then plotted on a graph.

2.3. Compatibility study

2.3.1. FTIR spectroscopy

FTIR spectroscopy was performed to assess the compatibility of paracetamol with procera gum. Samples are taken in 1:100 ratio with KBr and mixed uniformly in a porcelain dish. About 10 mg of the mixed sample was transferred into sample holder and pressed lightly to make a smooth surface. The transmittance was recorded between 400 and 4000 cm^{-1} on FTIR spectrophotometer (IR Prestige-21, Shimadzu). FTIR spectrum for the dried procera gum alone, paracetamol alone and gum–paracetamol mixture (1:1) were recorded for analysis.

2.3.2. DSC studies

DSC analysis was performed on differential scanning calorimeter (Jade DSC, Perkin Elmer) between 50 °C and 250 °C at a heating rate of 20 °C/min while nitrogen purging was maintained at 20 ml/min. For each analysis, about 6 mg of the sample was taken into the aluminum sample pan and sealed. Empty aluminum pan was used as a reference and the thermogram was then recorded for procera gum alone, paracetamol and gum–paracetamol mixture (1:1).

2.4. Preparation of paracetamol matrix tablet

Matrix tablets containing paracetamol were prepared by wet granulation method taking different proportions of procera gum and HPMC as per formulation given in Table 1. The calculated amount of the drug and polymers were dry blended and then granulated with 9:1 isopropyl alcohol and water mixture. The wet granules were passed through sieve no. 30 and dried overnight at 50 °C in tray drier and their flow property was evaluated. The final granules were blended with 2% magnesium stearate and 1% Talc and compressed at 19.6 kN using 11 mm round, concave punches

Table 1
Formulations of different batches of matrix tablets.

Ingredients	Quantity (mg)						
	F1	F2	F3	F4	H1	H2	H3
Paracetamol	200	200	200	200	200	200	200
Procera gum	40	80	120	200	–	–	–
HPMC	–	–	–	–	40	120	200
Microcrystalline cellulose	160	120	80	–	160	80	–
Magnesium stearate	8	8	8	8	8	8	8
Talc	4	4	4	4	4	4	4
Total	412	412	412	412	412	412	412

and dies in a 12 Stations Mini Press II MT Tableting Machine (Karnavati Engineering, India).

2.5. Characterization of tablets

The matrix tablets prepared were evaluated through standard quality control parameters for tablets like weight variation, crushing strength, friability and content uniformity. For uniformity of weight, 20 tablets from each batch were selected and weighed individually and their mean weights were calculated, percent deviation from the mean weight was calculated for each tablet. The crushing strength of the tablets was determined using digital tablet hardness tester (EH-01, Electrolab, India) taking 5 tablets from each batch and the average was taken. Friability test was performed on dual drum unit friability tester (EF-2, Electrolab, India) taking 10 tablets for each test. The drums were rotated for 4 min at 25 rpm and the percent loss in weight was calculated from the original weight and determinations were done in triplicate. Content uniformity was performed according to Indian Pharmacopoeia (IP, 2007) and determinations were done in triplicate.

2.6. Water uptake studies

Each tablet was initially weighed (W_1) and then placed in a beaker containing 250 ml of distilled water maintained at $37 \pm 0.5\,^{\circ}C$ in a dissolution rate test apparatus. The paddles were rotated at 50 rpm and tablets were removed from the medium at different time intervals (1, 2, 3, 4, 5, 6, 7 and 8 h), dried between two filter papers to remove surface water and re-weighed (W_2). The percentage water uptake was determined by using the following equation and then plotted against time in a graph:

$$\%\ \text{water uptake} = \frac{W_2 - W_1}{W_1} \times 100 \tag{4}$$

2.7. In vitro release study

The in vitro drug release study was carried out using USP dissolution rate test apparatus, Type-I (ACM-501, Acmus, India) at $37 \pm 0.5\,^{\circ}C$. Dissolution medium taken was 900 ml of phosphate buffer pH 6.8 and the agitation speed was maintained at 50 rpm. Five milliliters of the sample was withdrawn at a predetermined time interval and replaced immediately with equal volumes of prewarmed dissolution media. The withdrawn samples were filtered through 0.45 μm membrane filter, diluted suitably and analyzed spectrophotometrically at 243 nm using UV-visible spectrophotometer (V-530, JASCO, Japan).

2.8. Release kinetics

The release data obtained from in vitro dissolution studies were fitted to various kinetic equations to find out the mechanism of drug release from the matrix tablets. The kinetic models used include zero-order equation, first-order equation, Higuchi equation and Hixson–Crowel cube root law (Costa & Lobo, 2001).

$$Q_t = Q_0 + k_0 t \quad \text{(zero order equation)} \tag{5}$$

$$\log Q_t = \log Q_0 + \frac{k_1 t}{2.303} \quad \text{(first order equation)} \tag{6}$$

$$Q_t = k_H t^{1/2} \quad \text{(Higuchi equation)} \tag{7}$$

$$Q_0^{1/3} - Q_t^{1/3} = k_s t \quad \text{(Hixson–Crowell equation)} \tag{8}$$

where Q_0 is the initial concentration of the drug in the solution, Q_t is the amount of drug release in time t, values k_0, k_1, k_H and k_s are the zero order release constant, first-order release constant, Higuchi release constant and constant incorporating the surface/volume ratio respectively.

To determine the release mechanism from the matrix tablets, in vitro drug release data were also fitted into Korsemeyer–Peppas equation, which is expressed as:

$$\frac{Q_t}{Q_\infty} = k_k t^n \tag{9}$$

where k_k is the kinetic constant, Q_∞ is the amount released at time $t = \infty$, thus Q_t/Q_∞ is the fraction of drug released at time t. The value n is the diffusion exponent which can be used to characterize mechanism for both solvent penetration and drug release. When the value of 'n' calculated from the above equation equals 0.5, it indicates that drug release from the system follows Fickian diffusion, when 'n' is between 0.5 and 1.0 it indicates non-Fickian (anomalous) diffusion. When 'n' equals 1.0, drug release from the system follows zero-order (case II transport) and 'n' larger than 1.0 indicates super case II transport. Correlation coefficients were determined from the plots which assessed fitness of the data into various kinetic models. The rate constants, for respective models were also calculated from slope.

To compare the effects of polymers on the drug release, a model independent method of release profile comparison was also performed. The mean dissolution time (MDT) was calculated from the dissolution data using the following expression (Costa & Lobo, 2001; Nokhodchi et al., 2008).

$$\text{MDT} = \frac{\sum_{j=1}^{n} t \Delta M_j}{\sum_{j=1}^{n} \Delta M_j} \tag{10}$$

where j is the sample number, n is the number of dissolution sample times, t is the time at mid-point between t and $t-1$ (easily calculated with $(t + (t-1))/2$) and ΔM_j is the additional amount of drug dissolved between t and $t-1$.

2.9. Stability studies

To study the effect of temperature and humidity on the tablets, matrix tablets were stored at $40 \pm 2\,^{\circ}C$ and $75 \pm 5\%$ RH in humidity chamber (Standard Model, Thermolab, India). After three months, percent content of the drug was determined and FTIR spectrum

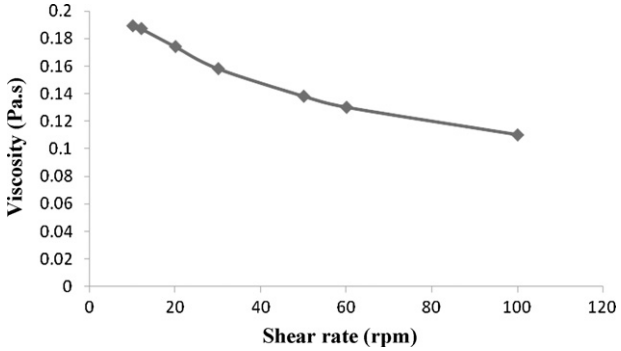

Fig. 1. Viscosity–shear rate profile of 5% procera gum solution.

along with DSC thermogram was also recorded to observe any effect caused on the tablets by the exposure to humidity and temperature.

2.10. Statistical analysis

Statistical analysis was performed using computer software SigmaStat 2.03 (SPSS, USA). One-way analysis of variance followed by Tukey Test was performed to compare the effects of different polymers on mechanical properties and drug release properties of the matrix tablets.

3. Results and discussion

3.1. Characterization of procera gum

The purified procera gum was pale white in color, odorless and slowly soluble in water yielding viscous solution. The percentage yield of the purified gum was found to be 93.78% (w/w). It was characterized for its moisture content and total ash to determine its purity. The moisture content was calculated as percentage loss on drying and it was found to be $8.8 \pm 0.53\%$. Since natural products like gums contain excess water it is therefore, important to assess the moisture content of natural gums which indicate to certain extent its stability. Pharmacopeial limit for moisture content of natural gums like acacia and tragacanth has been set at $\leq 15.0\%$ (Rowe, Sheskey, & Owen, 2006). The moisture content of the procera gum was within the limit set for natural gums like acacia and tragacanth. The total ash content is designed to measure the total amount of residual material remaining after ignition which may include extraneous matters such as sand and soil. The total ash value for the procera gum was found to be 4.1 ± 0.3. The Carr's Index and angle of repose were 21.01% and 34.63° respectively. This indicated that procera gum possesses a fairly good flow property and compressibility (Kumar, Kothari, & Banker, 2001; Marshall, 1986) but not good enough to be used as direct compression excipient. Therefore, wet granulation method was followed in the preparation of the matrix tablets and lubricated with magnesium stearate and talc.

Fig. 1 shows the viscosity–shear rate profile of 5% *A. procera* gum solution. The viscosity of the gum solution decreases with increase in shear rate showing non-Newtonian characteristics. Shear thinning region occurred between 10 and 50 rpm where there is a significant reduction in viscosity. After 50 rpm, the change in viscosity was not significant as in the lower shear rates. At high shear rates, the decrease in viscosity can be attributed to a decreasing number of chain entanglements (Nep & Conway, 2011).

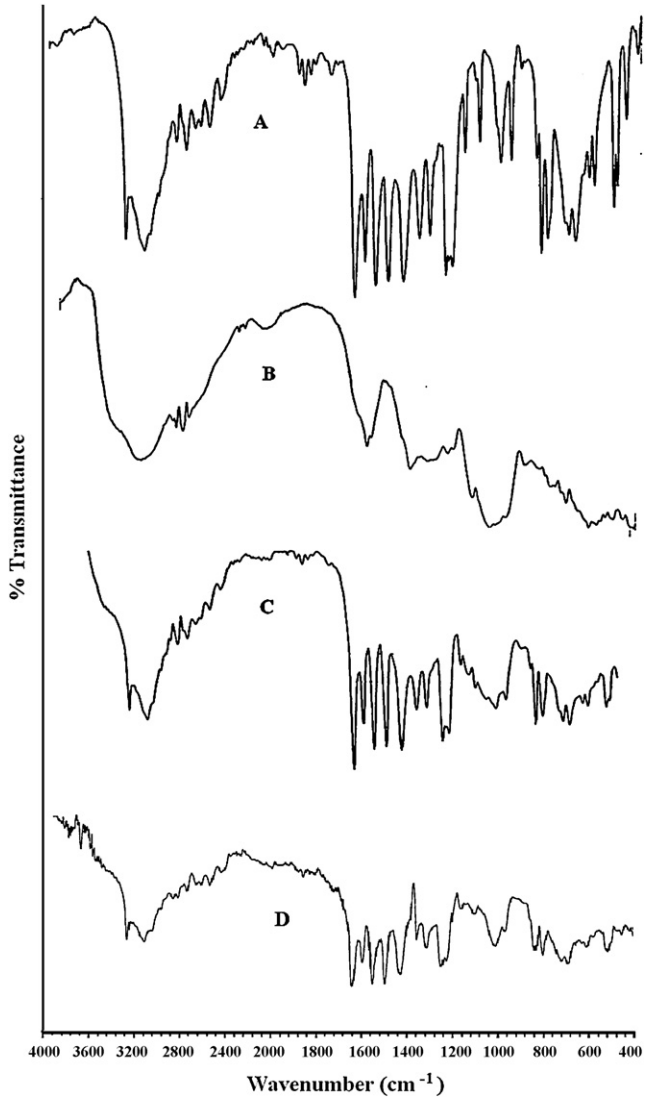

Fig. 2. FTIR spectrum of (A) paracetamol, (B) *Albizia procera* gum, (C) solid admixtures of paracetamol with procera gum and (D) matrix tablet after 3 months storage.

3.2. FTIR spectroscopy

FTIR spectroscopy was performed to assess the compatibility of paracetamol with procera gum. Analysis of paracetamol structure reveals that its typical IR spectrum should contain characteristic C=O stretching vibration at around 1700 cm^{-1} and a weak secondary amine stretch at around 3400 cm^{-1}. The FTIR spectra of paracetamol, procera gum and paracetamol–procera gum admixture were depicted in Fig. 2. The spectrum for paracetamol confirms the presence of characteristic –NH, –OH and C=O stretching bands at 3325.28 cm^{-1}, 3163.26 cm^{-1} and 1654.92 cm^{-1} respectively. Peaks at 1564.27 cm^{-1}, 1257.59 cm^{-1} and 837.11 cm^{-1} were attributed to –NH in plane bending, C–O stretching and p-disubstituted aromatic ring respectively (Burgina, Baltakhinov, Boldyreva, & Shakhtschneider, 2004; Ivanova, 2005; Wang, Lin, & Wei, 2002). The FTIR spectrum of paracetamol–procera gum mixture showed all the characteristic peaks of paracetamol which signifies that there are no significant chemical interaction and changes taking place when these compounds are taken together confirming the compatibility of paracetamol with procera gum. Further, all the characteristic peaks of paracetamol are also

Table 2
Physicochemical characteristics of the matrix tablets.

Formulation	Average weight (mg)	Crushing strength (N)	Content uniformity (%)	Friability (% w/w)	$t_{25\%}$ (min)	$t_{80\%}$ (min)	MDT (min)
F1	408.78 ± 3.71	80.73 ± 5.96	98.92 ± 0.88	0.020 ± 0.004	60 ± 2.25	345 ± 4.06	166 ± 3.66
F2	409.29 ± 2.40	62.27 ± 4.22	96.25 ± 0.75	0.056 ± 0.007	105 ± 5.12	465 ± 3.12	204 ± 4.12
F3	398.67 ± 3.65	48.53 ± 2.56	98.02 ± 0.22	0.239 ± 0.063	120 ± 4.42	525 ± 5.24	210 ± 4.41
F4	401.07 ± 2.81	42.50 ± 1.92	95.82 ± 0.78	0.852 ± 0.075	150 ± 4.22	720 ± 3.82	220 ± 3.06
H1	402.02 ± 3.22	108.83 ± 1.77	97.08 ± 0.64	0.014 ± 0.005	60 ± 1.64	480 ± 3.22	164 ± 3.45
H2	404.08 ± 2.12	88.70 ± 5.20	97.26 ± 0.86	0.113 ± 0.008	110 ± 3.78	720 ± 8.12	226 ± 6.33
H3	404.66 ± 1.34	56.73 ± 3.84	96.22 ± 0.96	0.267 ± 0.039	240 ± 8.14	960 ± 5.88	292 ± 4.08

observed when the FTIR spectrum was recorded for matrix tablets after three months storage under accelerated conditions.

3.3. DSC analysis

DSC thermograms were given in Fig. 3. DSC trace for paracetamol showed a sharp endothermic peak at 173.46 °C corresponding to its melting point. Physical mixture of paracetamol with procera gum showed an endothermic event at 172.86 °C and the same peak was observed at 175.95 °C for matrix tablets stored at 40 ± 2 °C/75 ± 5 RH for three months. It was observed that there was no considerable change in the endothermic values of paracetamol when it was mixed with procera gum and other excipients. Further, after three months storage under accelerated condition, there was no significant change in the endothermic characteristics of the drug and this support the absence of interaction between the drug and polymer as shown by IR spectra results.

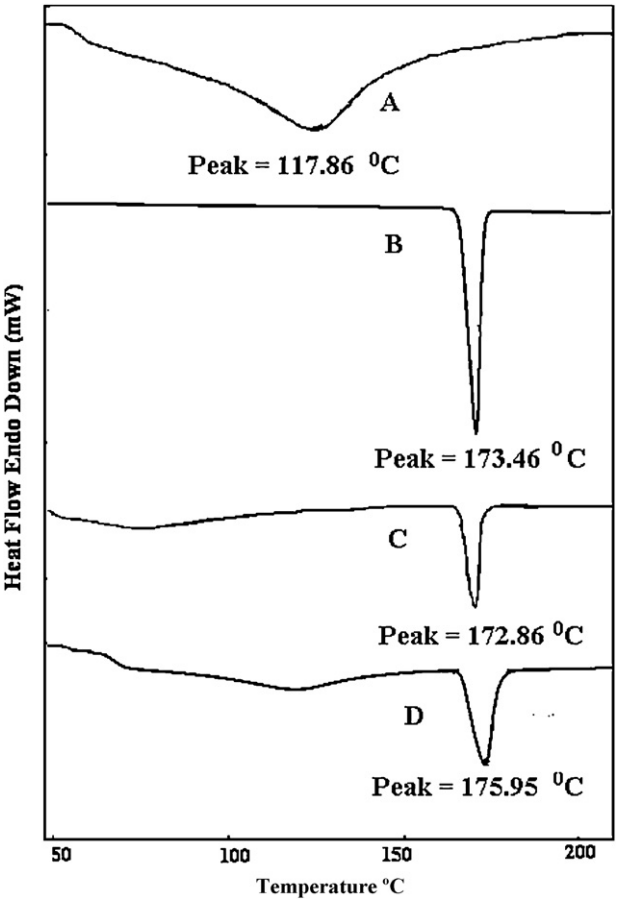

Fig. 3. DSC traces of (A) procera gum, (B) paracetamol, (C) gum–paracetamol physical mixture and (D) matrix tablet after 3 months storage.

3.4. Effect of polymers on physical properties of matrix tablets

Wet granulation method followed in the preparation of granules significantly improve the flow of properties as all the batches of formulations showed Carr's index of less than 15 which indicate good powder flow. Table 2 presents the results of analysis on weight, drug content uniformity, friability and crushing strength of the matrix tablets prepared with *A. procera* gum and HPMC. Results show that all the formulations are within the limit of weight variation and content uniformity (IP, 2007). There is no statistical difference ($P = 0.170$, procera gum; $P = 0.172$, HPMC) in weight variation and content uniformity between different batches. All these results showed that procera gum and HPMC produced good quality matrix tablets as per standard specified in pharmacopeia.

Mechanical properties of pharmaceutical tablets are quantifiable by crushing strength and friability of the tablets. Crushing strength provides a measure of tablet strength while friability is a measure of tablet weakness (Odeku, 2005). Friability study shows that in all the formulations including procera gum and HPMC matrix tablets, increase in the concentration of polymers results in increase in friability; however, all the batches were within the limit of 1% friability suggested in the Indian Pharmacopeia (IP, 2007). The crushing strength varies from 42.50 N in F4 (50% Procera gum) to 80.73 N (10% Procera gum) in F1 batches which shows that procera gum matrix tablets have a good strength. There is significant decrease ($P \leq 0.001$) in the crushing strength while friability is increased when the concentration of procera gum is increased. Similar trend was also observed with HPMC based matrix tablet formulations where the crushing strength varies from 56.73 N in H3 (50% HPMC) to 108.83 N in H1 (10% HPMC). The mechanical strength of tablets depends on the extent of plastic deformation particles underwent during compression. The trend for mechanical properties observed in this study may be due to the lower amount of total plastic deformation exhibited by the procera gum during compression. Between the formulations at similar concentration, HPMC undergoes higher plastic deformation than procera gum and this resulted in higher crushing strength in HPMC matrix tablets than that of procera gum matrix tablets.

3.5. Water uptake

Water uptake study was performed to observe the swelling behavior and erosion characteristics of the matrix tablets. Fig. 4 is the plot of water uptake against time for both procera gum and HPMC based matrix tablet formulations. Procera gum based formulations exhibit higher water uptake than HPMC based tablets which results in rapid increase in the weight. Procera gum based formulations showed sign of erosion after 2–5 h depending on the amount of the procera gum. HPMC based formulations showed slow water uptake and steady hydration for 3–7 h depending on the polymer concentration. The hydration and erosion also correlated well with drug release characteristic of the formulations. Faster water uptake leads to increased osmotic force and polymer chain relaxation and this result in erosion of the tablets.

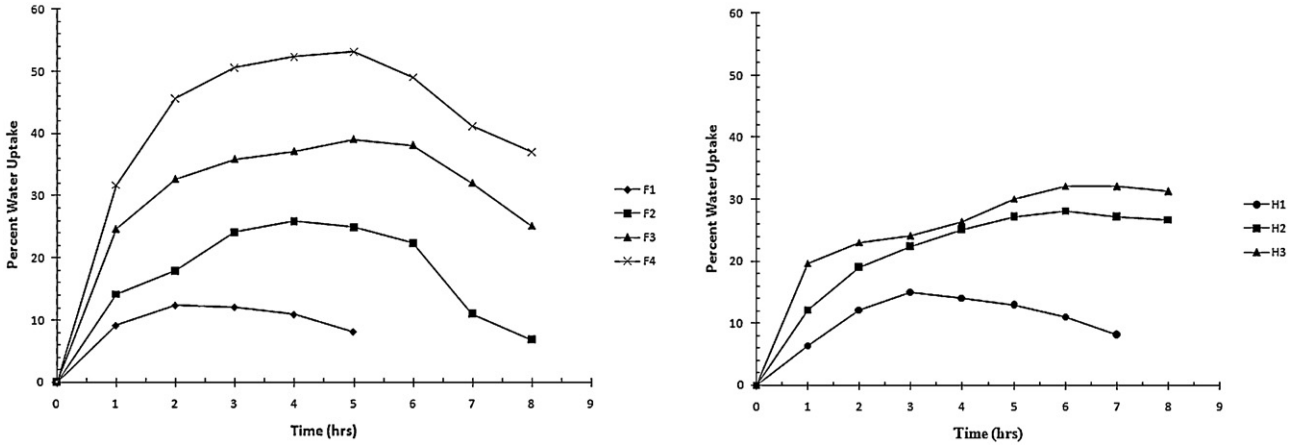

Fig. 4. Swelling behavior of different batches of formulations.

3.6. Effect of polymers on in vitro drug release

The in vitro drug release profiles of controlled release matrix tablets containing procera gum and HPMC are depicted in Fig. 5. Hydration and swelling of the polymers take place which was correlated with the level of the polymers in the formulations. In the procera gum based formulations, release of paracetamol in the first hour varies between 25.03% in F1 (10%) and 12.09% in F4 (50%) while it was between 24.35% in H1 (10%) and 16.21% in H3 (50%) HPMC based formulations. The release of drug extended from 8 h in F1 to more than 12 h in F4 in case of procera gum matrix tablets. HPMC based matrix tablets extend drug release from 12 h in H1 (10% HPMC) to more than 24 h in H3 (50% HPMC). The time to release 25% ($t_{25\%}$) of the drug and 80% ($t_{80\%}$) for all the formulation batches are given in Table 2 along with mean dissolution time (MDT). Statistical analysis shows that $t_{25\%}$ of the drug increase significantly ($P \leq 0.001$) with increase in the concentration of procera gum. Gum or HPMC containing tablets take up water on contact with the release medium allowing dissolution of certain percent of the drug found at and near the tablet surface prior to gel or viscous medium formation. The increase in the level of the polymers results in more sustained release of the drug which was probably due to the formation of thicker gel or more viscous region. At the end of the dissolution study, formulations containing procera gum were found to be more eroded than HPMC based formulations.

Four criteria were established for the desired drug release profile for sustained release formulations (Jani & Shah, 2008). These are: (a) a release of 20–25% drug within the first hour, (b) drug release after 5 h was between 40% and 60%, followed by (c) prolonged drug release of the remaining drug over 12 h, preferably at a relatively constant rate, and (d) time to release 80% drug was $490 < t_{80\%} < 590$ min. It was observed from the dissolution study that procera gum was able to sustain the release of the drug and the rate and amount of drug release can be controlled by varying the amount of the polymer added to the formulations. The mean dissolution time (MDT), which is a model independent method of comparing dissolution profiles, also increases with increase in the concentration of procera gum indicating lower release rate at higher polymer concentrations.

3.7. Release kinetics

The release kinetics from matrices composed of varying amounts of procera gum or HPMC were analyzed through various equations and the release kinetic table (Table 3) was prepared. The correlation (r^2) was used as an indicator of the best fitting for each of the models considered. Evaluation of release kinetics and application of best fit by correlation coefficient shows that procera gum release the drug following Higuchi square root kinetics and approaches zero-order with increase in concentration. HPMC was reported to sustain release of drugs by first-order kinetics (Mughal et al., 2011) which may be true for the present study as well. Determination of correlation coefficients from various formulations, containing different proportions of HPMC indicates that first-order and Higuchi equations seemed to be a better fit than other equations.

The release exponent '*n*' calculated from the Korsemeyer–Peppas equation, shows that in all the batches,

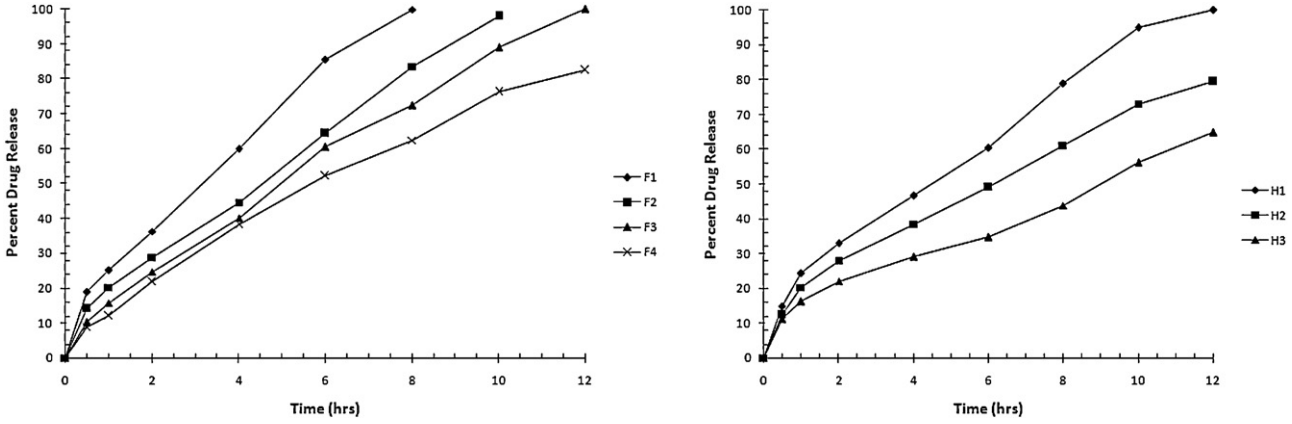

Fig. 5. Comparative drug release profiles of procera gum and HPMC based matrix tablet formulations.

Table 3
Release kinetics.

Formulations	Zero-order		First-order		Higuchi		Hixson–Crowell		Korsemeyer–Peppas		
	r^2	k_0	r^2	k_1	r^2	k_H	r^2	k_s	n	r^2	k_k
F1	0.978	13.68	0.763	5.212	0.987	32.61	0.975	2.601	0.554	0.984	0.262
F2	0.989	10.38	0.844	4.862	0.965	27.41	0.971	2.515	0.596	0.990	0.205
F3	0.991	8.930	0.942	5.315	0.963	24.50	0.956	2.314	0.701	0.994	0.159
F4	0.982	7.603	0.988	4.638	0.976	21.98	0.924	2.280	0.740	0.993	0.134
H1	0.972	9.378	0.884	4.719	0.981	27.93	0.956	2.641	0.546	0.992	0.226
H2	0.968	7.406	0.985	4.569	0.988	21.73	0.937	2.572	0.545	0.993	0.189
H3	0.969	4.895	0.973	4.516	0.967	14.57	0.934	2.429	0.516	0.990	0.156

the '*n*' values were between 0.45 and 1. The '*n*' values for procera gum based formulations ranges from 0.554 to 0.740. It can be suggested that the release mechanism was non-Fickian, anomalous transport where release is dependent on both drug diffusion as well as polymer relaxation. The '*n*' value was found to increase with increase in the concentration of procera gum indicating that the influence of polymer relaxation on mechanism of drug release increased with increase in the concentration of procera gum. The exponent '*n*' in Korsemeyer–Peppas model was 0.546, 0.545 and 0.516 for H1 (10%), H2 (30%) and H3 (50%) for HPMC indicating anomalous release mechanism.

3.8. Stability studies

The results of accelerated stability studies indicated that there was no significant change in the matrix tablets. The drug content was found to be within $100 \pm 5\%$ for all the formulations at the end of the 90 days. FTIR and DSC analysis as shown in Fig. 2 and Fig. 3 respectively also suggested that there was no significant degradation or changes taking place in the matrix tablets during the study period.

4. Conclusion

Controlled release matrix tablets formulations based on gum exudates of *A. procera* were prepared by wet granulation method and its properties were evaluated and compared with HPMC based formulations. Drug release from the procera gum was found to be dependent on the polymer concentration and determination of release mechanism by Korsemeyer–Peppas model indicated that drug release was anomalous, where drug release is dependent on both drug diffusion as well as polymer relaxation. It was observed that by varying the amount of procera gum, controlled or sustained release of paracetamol for more than 12 h can be achieved indicating its suitability as release retardant in controlled release formulation.

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