Carbohydrate Polymers 86 (2011) 177–184

Contents lists available at ScienceDirect

Carbohydrate Polymers

journal homepage: www.elsevier.com/locate/carbpol

Gum kondagogu-g-poly (acrylamide): Microwave-assisted synthesis, characterisation and release behaviour

Swati Malik, Munish Ahuja*

Drug Delivery Research Laboratory, Department of Pharmaceutical Sciences, Guru Jambheshwar University, Hisar 125 001, India

ARTICLE INFO

Article history:
Received 8 December 2010
Received in revised form 30 March 2011
Accepted 13 April 2011
Available online 21 April 2011

Keywords:
Gum kondagogu
Acrylamide
Graft co-polymerization
Microwave
Diclofenac

ABSTRACT

Microwave-assisted grafting of gum kondagogu onto poly (acrylamide) was carried out employing two-level, four-factor full factorial experimental design. Gum kondagogu-g-poly(acrylamide) was characterized by Fourier transform infrared spectroscopy, differential scanning calorimetry, X-ray diffraction and scanning electron microscopy. Microwave power, microwave exposure time and the concentration of ammonium persulfate had significant synergistic effect on grafting efficiency, while the concentration of gum kondagogu had no significant effect. The optimal calculated parameters were microwave power-40%, microwave exposure time-120 s, concentration of ammonium persulfate-10 mmol and concentration of gum kondagogu 3% (w/v). Comparative evaluation of the *in vitro* release of diclofenac sodium from the matrix tablets of gum kondagogu and gum kondagogu-g-poly(acrylamide) revealed a faster release of drug from gum kondagogu-g-poly(acrylamide). Further, the matrix tablets of gum kondagogu and commercial tablets were found to release the drug by zero-order kinetics, while the gum kondagogu-g-poly(acrylamide) matrices released the drug by Higuchi square-root kinetics.

1. Introduction

Natural polysaccharides have been used extensively as food and pharmaceutical excipients because of their biodegradability, biocompatibility, easy availability and low cost. However, they also possess certain drawbacks such as uncontrolled hydration, pH-dependent solubility, and changes in viscosity during storage and lower shelf life, which limits their applications. These drawbacks can be overcome by **c**hemical modification of the natural polymers. Chemical modification of natural polymers can be achieved by variety of approaches such as etherification, cross-linking and graft copolymerization (Rana et al., 2011). Grafting of gums with synthetic polymers can be used to design new materials with desirable release characteristics. The properties of natural polymers have earlier been modified by grafting with a variety of vinyl monomers such as acrylic acid (Zhang, Zhang, Yuan, & Wang, 2007), methyl acrylate (Ei-Tahlawy, Ei-Rafie, & Aly, 2006), acrylonitrile (Mishra & Pal, 2007) and acrylamide (Toti & Aminabhavi, 2004).

Polyacrylamide grafted hydrogels have been reported to be biocompatible (Karadag, Saraydin, Çetinkaya, & Güven, 1996; Risbud & Bhonde, 2000). Polyacrylamide grafted xanthan gum tablets (Kumar, Singh, & Ahuja, 2009; Mundargi, Sangamesh, & Aminabhavi, 2007) and guar gum-g-polyacrylamide formulated as matrix tablets (Toti & Aminabhavi, 2004) and microspheres (Soppirnath & Aminabhavi, 2002) have been evaluated for controlled release applications.

Gum kondagogu, an anionic polysaccharide, is a tree exudate obtained from *Cochlospermum gossypium* (family: Bixaceae). It belongs to the class of substituted rhamnogalactouronans polymer, comprising of rhamnose, galacturonic acid, glucuronic acid, β-D-galactopyranose, α-D-glucose, β-D-glucose, galactose, arabinose, mannose and fructose with sugar linkage of (1 → 2)β-D-Gal p, (1 → 6)β-D-gal p, (1 → 4)β-D-Glc p, 4-O-Me-α-D-Glc p, (1 → 2)α-L-Rha. Gum kondagogu swells in water absorbing a large amount of water forming thixotropic gels (Vinod et al., 2008). Physicochemical characterization of gum kondagogu revealed its similarity to gum karaya with respect to its intrinsic viscosity, water binding capacity etc. (Janaki & Sashidar, 1998). The gum was found to be safe in a 90-day sub-chronic toxicity study conducted in rats (Janaki & Sashidar, 2000).

However, its potential as a pharmaceutical excipient is not yet fully explored. Only a few reports such as use of gum kondagogu as complex polyelectrolyte sustained release carrier (Naidu et al., 2009) and as a matrix for synthesis of silver nanoparticles have been published (Kora, Sashidhar, & Arunachalam, 2010). Polyelectrolyte complexes of gum kondagogu with chitosan were evaluated as sustained release matrix using diclofenac sodium as a model drug and were found to provide a 5-fold higher relative bioavailability of diclofenac from the polyelectrolyte complexes as compared to the free drug. Gum kondagogu was also used as template matrix

* Corresponding author at: Drug Delivery Research Laboratory, Department of Pharmaceutical Sciences, G.J. University of Science and Technology, Hisar 125 001, India. Tel.: +91 1662 263515; fax: +91 1662 276240.
E-mail address: munishahuja17@yahoo.co.in (M. Ahuja).

0144-8617/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carbpol.2011.04.027

Table 1
Full factorial design.

Run	MW Power (*A*) (%)	MW Time (*B*) (s)	Conc. of APS (*C*) (mmol)	Conc. of GK (*D*) (%, w/v)	GE (*Y*) (%)
1	20.00	30.00	10.00	2.00	3.18
2	40.00	120.00	10.00	3.00	92.35
3	20.00	120.00	40.00	3.00	36.33
4	20.00	30.00	40.00	2.00	14.48
5	40.00	30.00	40.00	3.00	18.06
6	20.00	30.00	10.00	3.00	7.69
7	40.00	120.00	40.00	3.00	87.05
8	20.00	120.00	40.00	2.00	40.68
9	40.00	120.00	10.00	2.00	46.03
10	20.00	120.00	10.00	2.00	27.46
11	20.00	30.00	40.00	3.00	12.81
12	40.00	30.00	10.00	3.00	4.85
13	40.00	120.00	40.00	2.00	87.02
14	40.00	30.00	40.00	2.00	57.55
15	20.00	120.00	10.00	3.00	30.52
16	40.00	30.00	10.00	2.00	1.4

gk, gum kondagogu; aps, ammonium persulfate, ge, grafting efficiency; mw, microwave.

for the synthesis of silver nanoparticles from silver nitrate. It was reported to provide the hydroxyl and carbonyl groups for complexation and subsequent reduction of silver ions to elemental silver. Further, the capping of protein molecules, which are present in the gum, on the silver nanoparticles, prevented their aggregation. The present study explores the modification of gum kondagogu by graft co-polymerization of acrylamide using microwave-assisted graft co-polymerization.

Conventionally graft copolymerization reactions are carried out using redox-initiator induced reactions, which require a long time and give graft copolymer with lower grafting. The microwave irradiation is an efficient method, which results in rapid transfer of energy in the bulk of the reaction mixture. Earlier studies reported microwave-assisted synthesis of chitosan-g-styrene (Sharma & Mishra, 2010), guar gum-g-poly(ε-caprolactone) (Tiwari & Prabharan, 2010), xanthan-g-poly(acrylamide) (Kumar et al., 2009) and graft copolymer of *Mimosa* mucilage and acrylamide (Ahuja, Kumar, & Yadav, 2010) with higher grafting percentage in a short reaction time.

The purpose of the present investigation was to synthesize and characterize the graft copolymer of acrylamide and gum kondagogu, and to evaluate its drug release behaviour. The microwave-assisted graft-copolymerization of acrylamide on gum kondagogu was optimised using 2-level, 4-factor full factorial experimental design. Characterization of gum kondagogu-g-poly (acrylamide) was done by fourier-transform infrared spectroscopy (FT-IR), differential scanning calorimetry (DSC), X-ray diffraction and scanning electron microscopy (SEM). Further, the *in vitro* release behaviour of graft co-polymer was comparatively evaluated with ungrafted gum by formulating the matrix tablets using diclofenac sodium as the model drug.

2. Materials and methods

2.1. Materials

Gum kondagogu (grade I) was obtained as the gift sample from Girijan Co-operative Corporation, Hyderabad, India. Acrylamide extrapure (purity 99%) was procured from Sisco Research Laboratory (Mumbai, India) and was re-crystallized before use from methanol twice, followed by drying in oven at 40 °C. Ammonium persulfate GR (purity 99%) was obtained from Loba Chemie Pvt. Ltd. (Mumbai, India). Diclofenac sodium (purity 98.58%) was obtained as gift sample from Dabur Research Foundation (Ghaziabad, India). All other chemicals used were of reagent grade and were used as such.

2.2. Preparation of graft co-polymer of acrylamide and gum kondagogu

Microwave-assisted grafting of acrylamide on gum kondagogu was done using the method reported earlier (Kumar et al., 2009). Briefly, powdered gum kondagogu (2–3%, w/v) was added to the aqueous solution of acrylamide (10 mmol) and dispersed by stirring, followed by addition of ammonium persulfate (10–40 mmol), a redox initiator. The solution so obtained was irradiated by microwave oven (2300 ET-B, Bajaj Electricals Ltd., Mumbai, India) for different times and different power to prepare various batches of grafted gum (Table 1). The temperature of the reaction mixture was found to be <100 °C as measured by inserting the thermometer in the reaction vessel just after the exposure. The grafted gum was treated with acetone, and washed with mixture of methanol:water (80:20) to remove the unreacted monomer and reagent followed by drying in oven at 40 °C to a constant weight. The grafting efficiency (%) was calculated using the following equation-

$$\textit{Grafting efficiency}\,(\%) = \frac{W_1 - W_0}{W_2} \times 100 \quad (1)$$

where W_0 weight of gum, W_1 weight of grafted co-polymer and W_2 weight of acrylamide.

2.3. Experimental design

2.3.1. Full factorial design

Factorial designs (FDs) are very frequently used response surface experimental designs in which all levels of a given factor are combined with all levels of every other factor in the experiment. They are generally based on first-degree mathematical models. In the present study, two-level, four-factor, full factorial design (2^4 designs) was employed for optimisation of grafting of acrylamide on gum kondagogu. The concentrations of gum kondagogu and ammonium persulfate, and microwave power and exposure time were selected as the independent variables and grafting efficiency (%GE) was selected as the dependent variable. Each independent variable was investigated at two levels, high level (+1) and low level (−1). Eq. (2) is the general mathematical relationship for the FDs involving main effects and the interaction terms.

$$\begin{aligned} Y = {} & \beta_0 + \beta_1 A + \beta_2 B + \beta_3 C + \beta_4 D + \beta_{12} AB + \beta_{13} AC + \beta_{14} AD \\ & + \beta_{23} BC + \beta_{24} BD + \beta_{34} CD + \beta_{123} ABC + \beta_{124} ABD \\ & + \beta_{234} BCD + \beta_{134} CDA \end{aligned} \quad (2)$$

2.4. Characterization of gum kondagogu and grafted gum kondagogu

The graft co-polymer of acrylamide and gum kondagogu was characterized by FT-IR spectroscopy, differential scanning calorimetry, X-ray diffractometry, and scanning electron microscopy.

2.4.1. FT-IR spectroscopy

The samples were subjected to FT-IR spectroscopy in a Fourier-transform infrared spectrophotometer (IR Affinity-1, Shimadzu, Japan) in range of 4000–500 cm^{-1} as KBr pellet.

2.4.2. Differential scanning calorimetry

Differential scanning calorimetric thermogram of gum kondagogu, acrylamide, and gum kondagogu-g-poly (acrylamide) was recorded using differential scanning calorimeter (Q 10, TA Systems, USA) in the temperature range of 40–250 °C at a heating rate of 10 °C per minute in nitrogen atmosphere.

2.4.3. X-ray diffractometry

X-ray diffractogram of gum kondagogu, acrylamide, and graft co-polymer of gum kondagogu and acrylamide samples were recorded employing X-ray diffractometer (XpertPRO, Panalytical, Germany) using copper Kα-radiation generated at 40 kV and 35 mA in the differential angle range of 0–80° (2θ) using an X-ray diffractometer.

2.4.4. Scanning electron microscopy

Scanning electron micrographs of gum kondagogu, acrylamide, and graft co-polymer of gum kondagogu and acrylamide samples were taken using a SEM (JEOL, JSM-6100). These were coated with gold and mounted in a sample holder. The photomicrographs of sample were taken at an accelerating voltage at 10 kV at different magnifications.

2.5. Swelling studies

The swelling studies on gum kondagogu and gum kondagogu-g-poly(acrylamide) were performed in triplicate by placing the sample (100 mg) in baskets of dissolution apparatus. The baskets were immersed into solutions of different pH for 24 h at 25 °C. At various time intervals, baskets were taken out from swelling media and weighed immediately after blotting the surface of basket with blotting paper.

2.6. Preparation of matrix tablets of diclofenac sodium

The release properties of gum kondagogu-g-poly(acrylamide) were evaluated and compared with gum kondagogu by formulating the matrix tablets of diclofenac sodium. Various batches of matrix tablets of diclofenac sodium employing gum kondagogu or gum kondagogu-g-poly (acrylamide) as the matrix polymer with or without calcium phosphate as the diluent were prepared by direct compression method as per the formula given in Table 4. Drug, polymer, diluent and lubricant were blended in pestle mortar followed by direct compression in a single station hand-operated tableting machine (R&D model, Konark Instruments, Ambala, India) employing 8 mm biconvex punches and dies.

2.6.1. In vitro release study

The *in vitro* release studies (Singh, Kumar, Langyan, & Ahuja, 2009) of prepared batches of tablets were carried out in triplicate using USP type II apparatus (TDT-08 L, Electrolab, Mumbai, India). The dissolution media comprised of 0.1 N hydrochloric acid for the first 2 h followed by phosphate buffer (pH 6.8) until 24 h

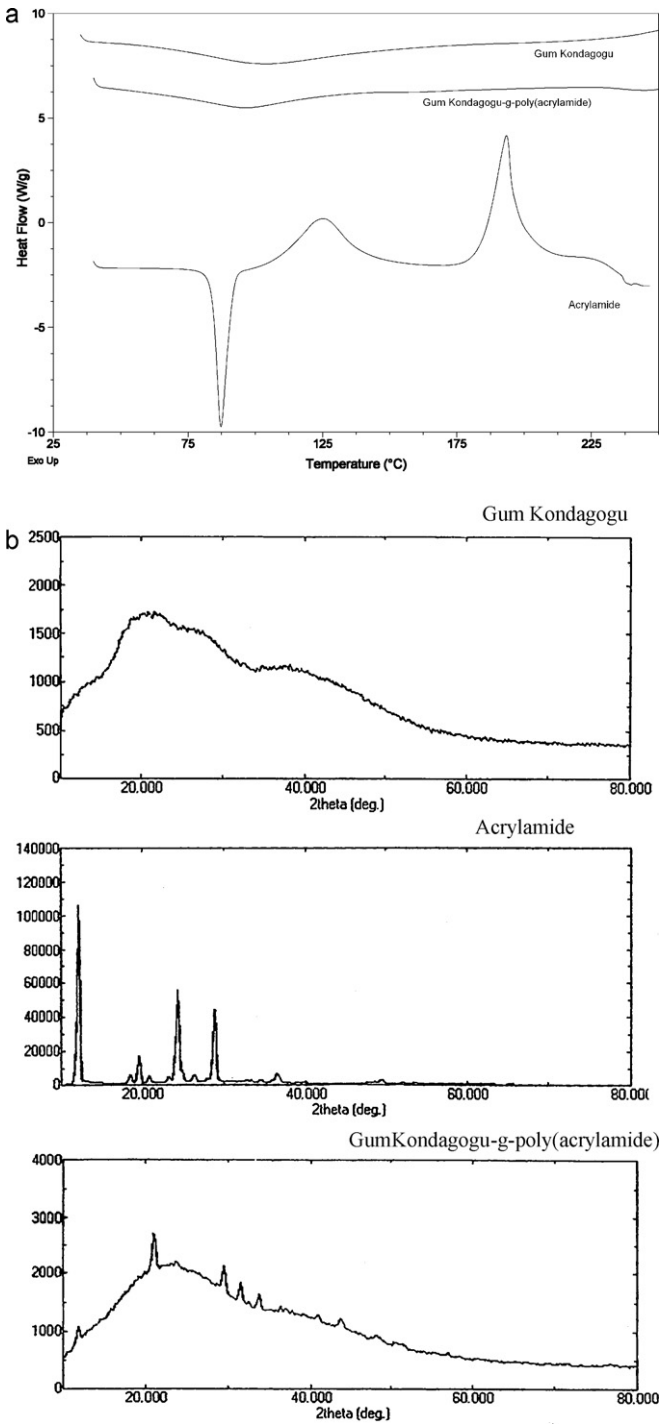

Fig. 1. (a) DSC curve of gum kondagogu, acrylamide, gum kondagogu-g-poly (acrylamide), (b) X-ray diffractogram spectra of gum kondagogu, acrylamide, gum kondagogu-g-poly (acrylamide).

(900 ml) kept at 37.0 ± 0.5 °C and 50 rpm. An aliquot of 5 ml sample was withdrawn and replaced with another 5 ml of fresh dissolution media at various time intervals. The contents of diclofenac sodium in sample were determined by measuring absorbance at 276 nm in a UV–Visible Spectrophotometer (Cary 5000, Varian Australia).

2.6.2. Modeling and release kinetics

The release rate data was fitted to zero-order, first-order and Higuchi square-root equation (Costa & Loba, 2001) to determine the order and mechanism of diclofenac sodium release from matrix

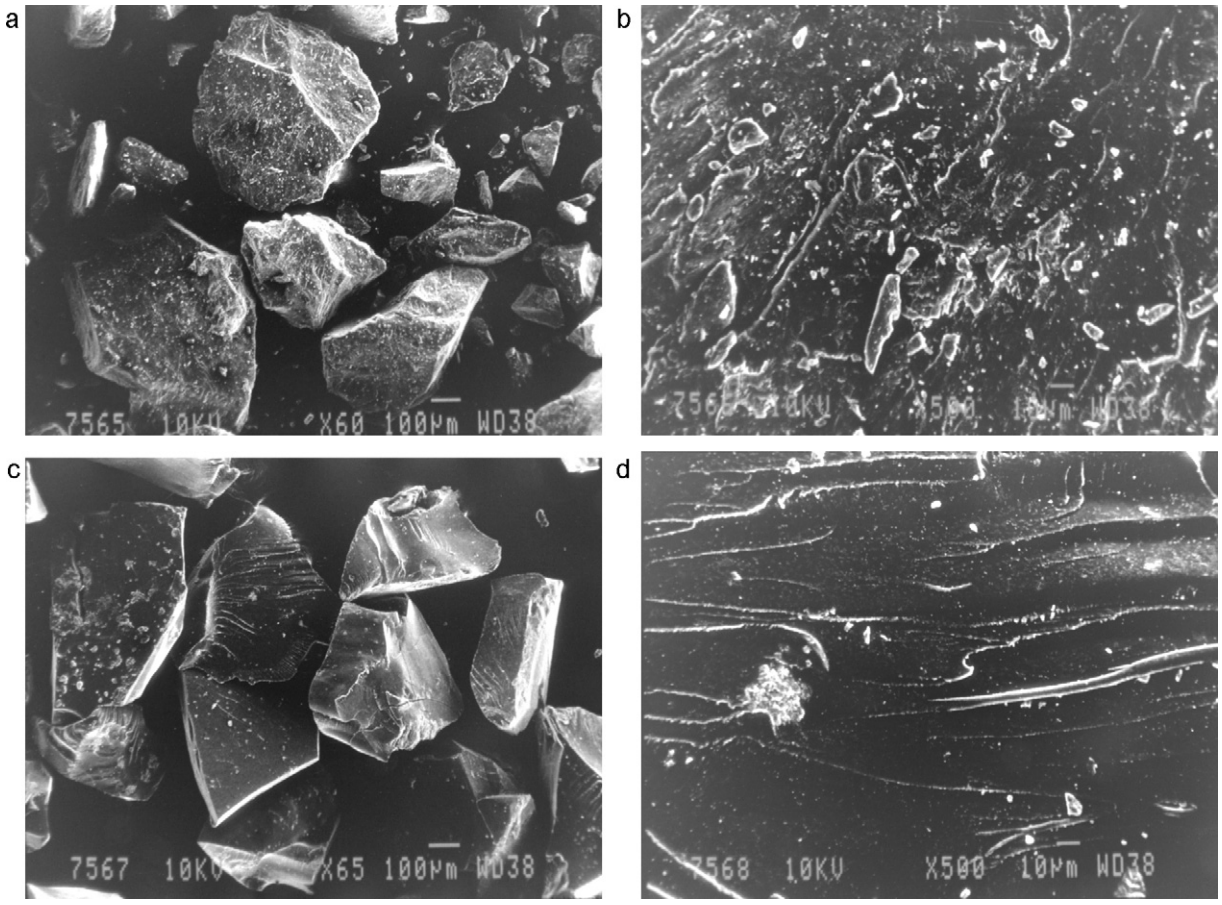

Fig. 2. Scanning electron micrograph showing (a) shape and (b) surface morphology of gum kondagogu, (c) shape and (d) surface morphology of gum kondagogu-g-poly (acrylamide).

tablets. However, these equations fail to explain the drug release mechanism from matrices that undergo swelling and/or erosion during dissolution. Therefore, the dissolution data was fitted to the Korsmeyer-Peppas equation, which is often used to describe the drug release mechanism from polymeric system.

$$\log\left(\frac{M_t}{M_f}\right) = \log k + n \log t \tag{3}$$

where M_t is the fraction of drug released at time t, M_f is the amount of drug released after infinite time, and k is the release rate constant incorporating structural and geometric characteristic of the tablets and 'n' is the diffusion exponent indicative of the release mechanism. To determine the release exponent, 'n' for different batches of the matrix tablets, the log value of percentage drug dissolved was plotted against log time for each batch, according to Eq. (3). For determination of exponent n, only the initial portion of release curve ($M_t/M_f < 0.6$) was used. A value of $n = 0.45$ indicates Fickian (case I) release; the rate of drug release is much less than that of polymer relaxation (erosion). Thus, the release of drug is primarily by diffusion through the matrix. A value of n ($0.45 < n < 0.89$) indicates non-Fickian (anomalous) release, the release of the drug occurs by combined effect of drug diffusion and polymer relaxation. The value of $n > 0.89$ indicates super case II type of release. Case II generally refers to the erosion of the polymeric matrix (Costa & Loba, 2001)

3. Results and discussion

3.1. Synthesis and characterization of grafted gum kondagogu

Modifications of properties of gum kondagogu were carried out by the graft polymerization of acrylamide onto gum kondagogu. Conventionally, graft co-polymerization of acrylate monomers onto natural polymers has been carried out using free-radical initiator-induced polymerization reactions. Recently, microwave-assisted grafting reactions are becoming more popular as they require a very short reaction time and proceed even in the absence of any redox initiator (Singh, Sethi, Tiwari, Srivastava, & Sanghi, 2003). Microwave-assisted grafting of acrylate monomer on guar gum (Singh, Tiwari, Tripathi, & Sanghi, 2004), chitosan (Singh, Tiwari, Tripathi, & Sanghi, 2006), starch (Huang & Chen, 1999) and artemisia gum (Zhang et al., 2007) have been reported. In the

Table 2
Model summary statistics.

Response factor	Model						
	F-value	Prob. > *F*	R^2	Adj. R^2	Pred. R^2	Adeq. prec	C.V. (%)
Y	1395.23	0. 0007	0.9999	0.9992	0.9929	108.981	2.52

adj R^2, adjusted R^2; pred R^2, predicted R^2; adeq prec, adequate precision; c.v., coefficient of variance.

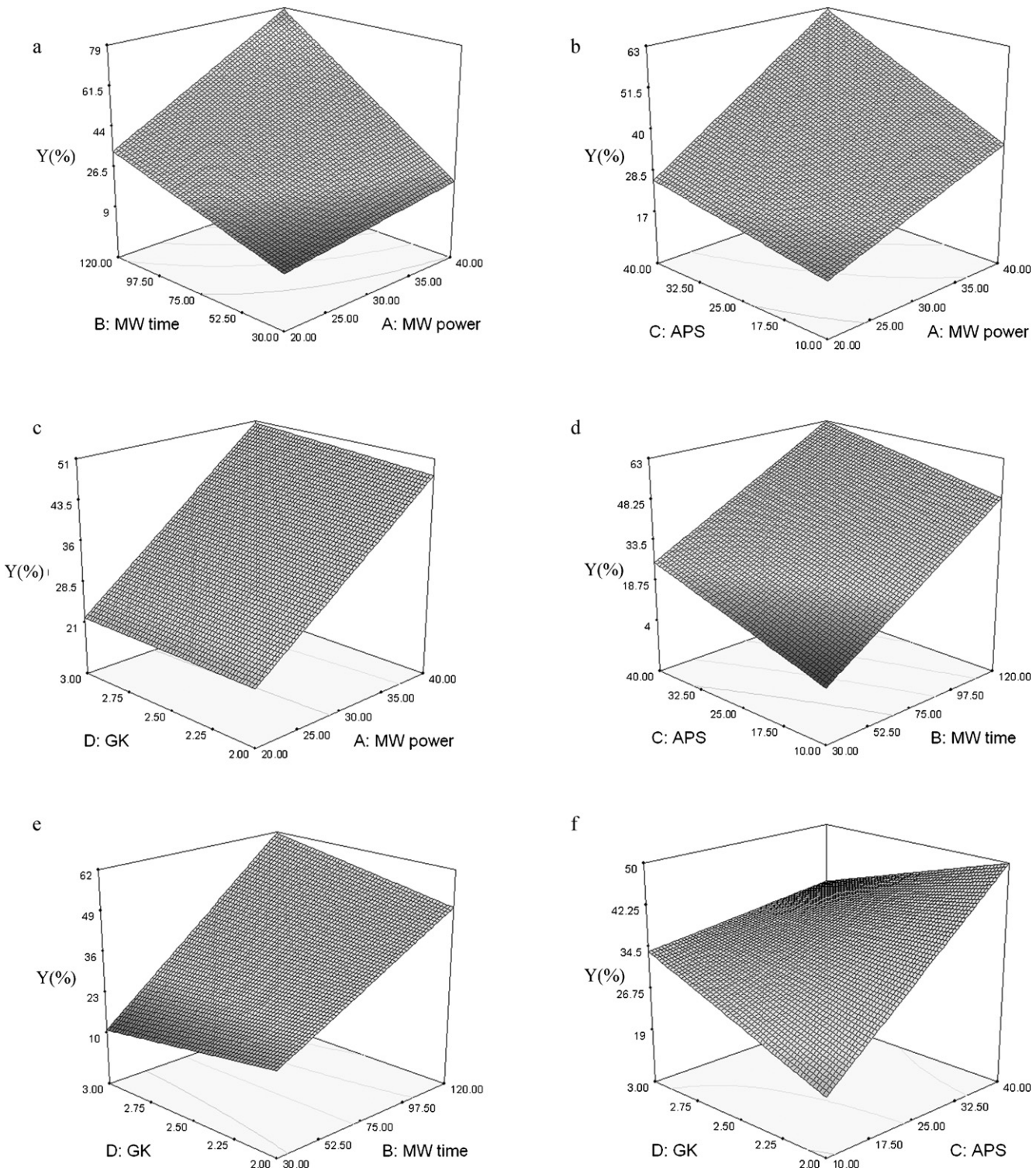

Fig. 3. Three dimensional response surface plots showing the combined effect of (a) A–B (b) A–C (c) A–D (d) B–C (e) B–D (f) C–D.

present study, the microwave assisted graft co-polymerization of acrylamide on gum kondagogu has been explored.

Gum kondagogu is a large molecule with pendant –OH groups. Irradiation with MW may result in dielectric heating of the gum kondagogu molecules resulting in cleavage of O–H bonds of gum kondagogu molecule to form gum kondagogu macroradicals. These macroradicals may also be formed by the abstraction of hydrogen ions by the persulfate free radicals (Liu et al., 2009). These free radicals further react with acrylamide monomer to form acrylamide free radicals resulting in a series of free radical initiated chain reactions which ultimately terminate in formation of graft copolymer and homopolymer as shown below.

Chain initiation

$$S_2O_8^{2-} \rightarrow 2SO_4^{\bullet -}$$

$$GKOH + R^{\bullet} \xrightarrow{MW} GKO^{\bullet} + RH$$

where R• is $SO_4^{\bullet -}$ and GKOH is gum kondagogu

$$GKO^{\bullet} + M \rightarrow GKOM^{\bullet}$$

$$R^{\bullet} + M \rightarrow RM^{\bullet}$$

Chain propagation

$$GKOM^{\bullet} + M \rightarrow GKOM_1^{\bullet}$$

$$GKOM^{\bullet} + M_1 \rightarrow GKOM_2^{\bullet}$$

$$GKOM_{n-1}^{\bullet} + M \rightarrow GKOM_n^{\bullet}$$

$$RM^{\bullet} + M \rightarrow RM_1^{\bullet}$$

$$RM_1^{\bullet} + M \rightarrow RM_2^{\bullet}$$

$$RM_{n-1}^{\bullet} + M \rightarrow RM_n^{\bullet}$$

Chain termination

$$GKOM_n^{\bullet} + GKOM_n^{\bullet} \rightarrow \text{Graft co-polymer}$$

$$GKOM_n^{\bullet} + RM_n^{\bullet} \rightarrow \text{Graft co-polymer}$$

$$RM_n^{\bullet} + RM_n^{\bullet} \rightarrow \text{Homopolymer}$$

Acrylamide grafted gum kondagogu was characterized by FT-IR, DSC, XRD and SEM study. The FT-IR spectra of gum kondagogu showed the characteristic peaks at 3480 cm^{-1} (–OH), 1729 cm^{-1} (CH_3CO–), 1605 cm^{-1} (–COO–), 1406 cm^{-1} (–COO–) and 1250 cm^{-1} (–CH_3CO). Peaks at 1605 cm^{-1} and 1406 cm^{-1} are due to carboxylate groups of the uronic acid residues. The spectra of acrylamide presented absorption bands at 3343 cm^{-1} and 3191 cm^{-1} due to asymmetric and symmetric NH stretching of NH group. The amide I band (CO stretching) appeared at 1622 cm^{-1} and amide II (NH bending) appeared at 1611 cm^{-1}. The spectra of acrylamide presented a band at 1433 cm^{-1} which can be attributed to CN stretching, while the CH stretching appeared at 2809 cm^{-1} and CH out of plane bending at 974 cm^{-1}. The NH out of plane wagging appeared at 818 cm^{-1}. The IR spectra of acrylamide grafted gum kondagogu showed a broad absorption band at 3526 cm^{-1} due to overlap of OH stretching band of gum kondagogu and NH stretching band of acrylamide.

Fig. 1(a) displays the DSC curve of gum kondagogu, acrylamide, and acrylamide grafted gum kondagogu. The thermogram of gum kondagogu showed broad endotherm at 104.69 °C with the heat of fusion of 440.1 J/g indicating the amorphous nature of gum kondagogu. The thermogram of acrylamide showed the sharp endothermic peak at 87.5 °C with the heat of fusion of 199.7 J/g with two exotherms at 131.4 °C with heat flow of 291.8 J/g and at 204.1 °C with heat flow of 50.28 J/g. The DSC curve of acrylamide grafted gum kondagogu showed the endothermic peaks at 95.41, 160.33, 243.95, and 262.29 °C with heat of fusion of 250.7, 3.449, 9.483, and 18.78 J/g, respectively.

Fig. 1(b) displays the X-ray diffractogram of gum kondagogu, acrylamide and acrylamide grafted gum kondagogu. The XRD spectra showed the amorphous nature of gum kondagogu, as no characteristic peaks in the spectrum were observed while the diffractogram of acrylamide showed the crystalline nature of acrylamide with the prominent characteristic peaks of acrylamide appearing at 12.2°, 19.6°, 24.3°, and 28.8° (2θ). The diffraction spectra of acrylamide grafted gum kondagogu showed the characteristic peaks of acrylamide but with the decreased intensity, which confirms the formation of graft co-polymer.

Fig. 2(a)–(d) shows the scanning electron micrographs of gum kondagogu and gum kondagogu-g-poly (acrylamide). The SEM images of grafted copolymer shows that the grafting of acrylamide onto gum kondagogu brings about the change in the shape and size of gum kondagogu particles. Further, it can be observed that the particles of acrylamide grafted gum kondagogu show numerous striations while the surface of gum kondagogu was rough.

3.2. Effect of grafting conditions on grafting parameters

Microwave power, exposure time, and the concentrations of ammonium persulfate and gum kondagogu were selected as independent variables for the optimisation study, while % grafting efficiency (%GE) was chosen as the dependent variable for this study. The optimisation study was conducted using four-factor, two level, full factorial experimental designs. The results (Table 1) of response generated using the experimental designs were analyzed by factorial models using Design Expert software (Version 7.1.6, Stat-Ease, Inc., Minneapolis). For choosing an appropriate model, the significant factors affecting the response were selected using half-normal probability plots.

The factorial model describing the correlation between the independent variables and % grafting efficiency of graft co-polymerization can be represented as:

$$\begin{aligned} Y_{(\%)} = {} & 35.47 + 13.82^{*}A + 20.46^{*}B + 8.78^{*}C + 0.74^{*}D \\ & + 8.36^{*}A^{*}B + 4.35^{*}A^{*}C + 0.55^{*}A^{*}D - 1.94^{*}B^{*}C \\ & + 4.89^{*}B^{*}D - 6.43^{*}C^{*}D - 2.27^{*}A^{*}B^{*}C \\ & + 5.41^{*}A^{*}B^{*}D - 4.73^{*}A^{*}C^{*}D \end{aligned}$$

The results revealed that the microwave power (A), microwave exposure time (B) and concentration of ammonium persulfate (C) had a significant synergistic effect on the grafting efficiency, while concentration of gum kondagogu (D) had no significant effect. The grafting efficiency was significantly affected by the synergistic interaction effects of AB, BD, AC and ABD while the interaction effects of CD, BC, ABC and ACD affected the grafting efficiency antagonistically. The ANOVA test was applied to the model to estimate its significance (Table 2). The ANOVA analysis of the factorial model showed the model to be significant ($P < 0.05$). Further, the higher

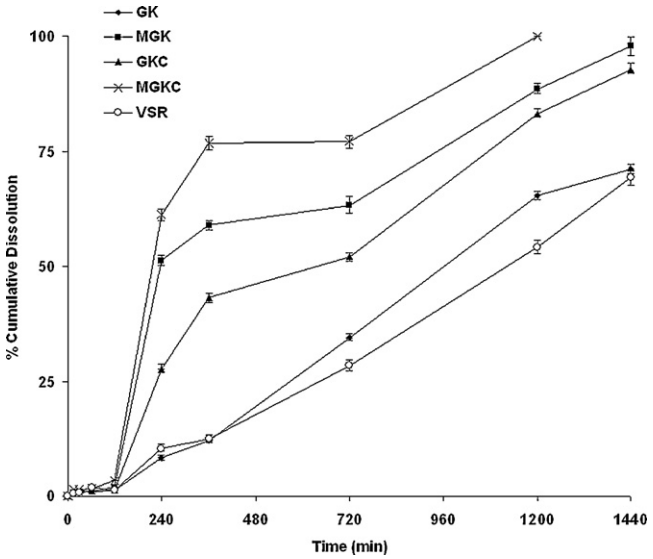

Fig. 4. *In vitro* release profile of diclofenac sodium from various batches of matrix tablets and Voveran-SR.

Table 3
Swelling of gum kondagogu and gum kondagogu-g-poly (acryalmide) at different pH.

Time (h)	% Swelling					
	Gum kondagogu			Gum kondagogu-g-poly(acryalmide)		
	pH 3.4	pH 5.4	pH 6.8	pH 3.4	pH 5.4	pH 6.8
1	536.36 ± 0.88	1583.79 ± 0.85	1064.18 ± 0.74	846.95 ± 0.64	1609.09 ± 0.63	1638.01 ± 0.65
2	965.75 ± 0.57	2071.14 ± 0.60	2287.16 ± 0.78	3389.63 ± 0.65	1790.90 ± 0.80	1827.27 ± 0.55
3	1509.39 ± 0.53	2222.92 ± 0.63	2188.17 ± 0.86	1276.21 ± 0.45	2272.72 ± 0.78	2007.43 ± 0.62
24	500.60 ± 0.93	2607.50 ± 0.56	2060.47 ± 0.73	1120.73 ± 0.51	2218.18 ± 0.41	742.97 ± 0.87

value of R^2 (>0.9) indicated a good correlation between the experimental and predicted response. In addition, the predicted R^2 value is in reasonably good agreement with adjusted R^2 value, resulting in reliable model. Moreover, the higher value (>4) of adequate precision indicates an adequate signal. The relatively lower value of coefficient of variance indicates better precision and reliability of the experiments carried out.

Fig. 3(a)–(f) portrays the combined effect of different variables on the grafting efficiency. It can be inferred from Fig. 3(a) that microwave exposure time had a more significant effect on grafting efficiency than the microwave power. Moreover increasing both of these factors resulted in an increase in grafting efficiency due to the formation of more amounts of free radicals and better transfer of energy. The effect (Fig. 3(b)) of the concentration of ammonium persulfate on grafting efficiency was more pronounced at higher microwave power. Similarly, the effect of microwave power was more prominent at higher concentration of ammonium persulfate. Fig. 3(c) shows that there were no significant interaction effects between microwave power and the concentration of gum kondagogu. Increasing the microwave exposure time and concentration of ammonium persulfate (Fig. 3(d)) resulted in better grafting with the effect of microwave exposure time more pronounced. Fig. 3(e) displays the antagonist interaction between gum kondagogu and microwave exposure time, with one factor modifying the effect of another. At lower values of microwave exposure time, increasing the concentration of gum kondagogu resulted in decrease in grafting efficiency, presumably due to inadequate formation of free radicals. Fig. 3(f) exhibits the combined effect of concentration of ammonium persulfate and concentration of gum kondagogu. It can be inferred from the plot that a curvilinear relationship exists between the concentration of gum kondagogu and the concentration of ammonium persulfate with one factor modifying the effect of another. Increasing the concentration of gum kondagogu and the concentration of ammonium persulfate results, first in an increase, followed by, the decrease in grafting efficiency. The highest grafting was obtained at low concentration of gum kondagogu and at high concentration of ammonium persulfate.

A numerical optimisation tool of Design Expert software, using the desirability approach was employed to obtain grafted gum with desired response. In this study, optimisation of independent variables was performed with a goal of maximizing grafting efficiency. The numerical optimisation tool provided us with different sets of optimal solutions. From among these solutions, an optimal batch of grafted gum was prepared and analyzed for % grafting efficiency. The optimal calculated parameters were microwave power (A) 40%, microwave exposure time (B) 120 secs, concentration of ammonium persulfate (C) 10 mmol and concentration of gum kondagogu (D) 3% (w/v).

3.3. *In vitro release behaviour*

To ascertain whether the grafting of acrylamide on gum kondagogu results in modification of the release properties of the gum, the graft co-polymer and the gum kondagogu samples were subjected to swelling studies at various pH values (Table 3). It can be observed from the results that the graft co-polymer has higher initial % swelling followed by faster erosion while the gum kondagogu samples swelled slowly over a prolonged period of time.

Gum kondagogu-g-poly (acrylamide) was used for formulating the sustained release matrix tablets of diclofenac sodium and compared with the tablets of gum kondagogu (Table 4). The *in vitro* release study of diclofenac sodium from various batches of formulated tablets was carried out in 0.1 N HCl for first 2 h, followed by phosphate buffer (pH 6.8) for the next 24 h. It can be observed from the results (Fig. 4) that tablets prepared using gum kondagogu-g-poly(acrylamide) (MGK) provided higher and faster release of drug as compared to tablets prepared using gum kondagogu (GK). Further, the use of calcium phosphate (water insoluble diluent) in tablets (GKC/MGKC) provided much faster release of drug as compared to tablets formulated without calcium phosphate (GK/MGK). The commercial tablets (Voveran-SR) showed the slowest release with only 70% of the drug being released in 24 h. To further investigate the mechanism of drug release, the data was subjected to modeling and release kinetics (Table 4). The results of modeling study revealed that the release of drug from matrix tablets of gum kondagogu and commercial tablets fitted best into zero-order kinetics, while the release from MGK, MGKC and GKC fitted best into Higuchi square-root kinetics. Further, the value of '*n*' (>0.9)

Table 4
Composition and release kinetics of gum kondagogu matrix tablets.

Composition		Quantity/tablet (mg)				
		MGK	GK	MGKC	GKC	Voveran-SR
Diclofenac sodium		100	100	100	100	–
Gum kondagogu		–	100	–	20	–
Gum kondagogu-g-poly(acrylamide)		100	–	20	–	–
Calcium phosphate		–	–	80	80	–
Magnesium stearate		2	2	2	2	–
Release kinetics						
Zero-order	R^2	0.8551	0.9894	0.773	0.9541	0.9917
First-order	R^2	0.6049	0.8522	0.602	0.6815	0.8157
Higuchi square-root	R^2	0.9229	0.9222	0.8675	0.9689	0.9200
Korsmeyer-Peppas	R^2	0.8912	0.9106	0.8584	0.8718	0.9460
	n	1.6161	0.9655	1.2076	1.2672	1.0700

indicated that all batches of tablets released the drug by matrix erosion.

The kinetics and mechanism of drug release depends upon the interplay of various factors such as the solubility of drug and the excipients, swelling and erosion characteristics of polymeric matrix and the relative ratio of drug and polymer used in the formulation of tablets. Natural polysaccharides usually have uncontrolled hydration. Grafting of gums with acrylamide alters their swelling characteristics. Natural gums on hydration with water swell rapidly forming the viscous gel layer on the surface, which increases the diffusion path length and slows down the diffusion of dissolution media controlling the release of drug. During earlier studies, grafting of xanthan gum with acrylamide was found to decrease the swelling ratio of xanthan gum (Kumar et al., 2009; Mundargi et al., 2007) which was found to correlate with the grafting %. Matrix tablets formulated using graft copolymers provided a slower release of atenolol and carvedilol, while a faster release of diclofenac was observed. The difference in release rates of drugs from the matrix tablets of graft copolymers can be attributed to the different grafting ratios, drug solubility and different excipients used in the study. The initial faster rate of swelling of gum kondagogu-g-polyacrylamide matrix compared to gum kondagogu can be attributed to the formation of porous matrix, which allowed faster diffusion of dissolution media into the core. However, the faster diffusion of dissolution media also led to the faster erosion of the gum kondagogu-g-poly(acrylamide) matrix resulting in faster release of diclofenac. Similar results were earlier obtained with xanthan-g-poly(acrylamide) matrix tablets containing diclofenac (Kumar et al., 2009)

4. Conclusion

Microwave-assisted graft co-polymerization of acrylamide on gum kondagogu was optimised using 2-level, 4-factor full factorial experimental design. The results revealed that the microwave power, microwave exposure time and concentration of ammonium persulfate had a significant synergistic effect on the grafting efficiency, while concentration of gum kondagogu had no significant effect. Further, the graft co-polymer was characterized by FT-IR, DSC, XRD, and SEM analysis that confirmed the formation of graft co-polymer of acrylamide and gum kondagogu. In addition, the graft co-polymer was evaluated for modification of release rate employing the matrix tablets of diclofenac sodium. The study revealed the faster release of drug from graft copolymer matrix tablets as compared with the ungrafted gum kondagogu. Thus, microwave-assisted graft co-polymerization can be used as an efficient tool to modify the release properties of gum kondagogu by grafting of acrylamide on gum kondagogu.

References

Ahuja, M., Kumar, S., & Yadav, M. (2010). Microwave-assisted synthesis and characterization of polyacrylamide grafted co-polymers of Mimosa mucilage. *Polymer Bulletin*, doi:10.1007/s00289-010-0341-7

Costa, P., & Loba, J. M. S. (2001). Modelling and comparison of dissolution profiles. *European Journal of Pharmaceutical Sciences*, *13*, 123–133.

Ei-Tahlawy, K. F., Ei-Rafie, S. M., & Aly, A. S. (2006). Preparation and application of the chitosan/poly(methacrylic acid) graft copolymer. *Carbohydrate Polymers*, *66*, 176–183.

Huang, M., & Chen, M. (1999). Studies on graft co-polymerization of acrylamide and starch under microwave heating. *Huaxue Shijie*, *40*, 426–429.

Janaki, B., & Sashidar, R. B. (1998). Physico-chemical analysis of gum kondagogu (*Cochlospermum gossypium*): A potential food additive. *Food Chemistry*, *61*, 231–236.

Janaki, B., & Sashidar, R. B. (2000). Subchronic (90-day) toxicity study in rats fed gum kondagogu (*Cochlospermum gossypium*). *Food and Chemical Toxicology*, *38*, 523–534.

Karadag, E., Saraydin, D., Çetinkaya, S., & Güven, O. (1996). In vitro swelling studies and preliminary biocompatibility evaluation of acrylamide-based hydrogels. *Biomaterials*, *17*, 67–70.

Kora, A. J., Sashidhar, R. B., & Arunachalam, J. (2010). Gum kondagogu (*Cochlospermum gossypium*): A template for the green synthesis and stabilization of silver nanoparticles with antibacterial application. *Carbohydrate Polymers*, *82*, 670–679.

Kumar, A., Singh, K., & Ahuja, M. (2009). Xanthan-g-polyacrylamide: Synthesis, characterization and in vitro release behaviour. *Carbohydrate Polymers*, *76*, 261–267.

Liu, C., Dai, X., Chen, J., Chen, Y., Guo, X., & Huang, Y. (2009). Graft copolymerization of 4-vinyl pyridine onto konjac glucomannan initiated by ammonium persulfate. *Journal of Applied Polymer Science*, *113*, 2339–2345.

Mishra, A., & Pal, S. (2007). Polyacrylonitrile-grafted okra mucilage: A renewable reservoir to polymeric materials. *Carbohydrate Polymers*, *68*, 95–100.

Mundargi, R. C., Sangamesh, A. P., & Aminabhavi, T. M. (2007). Evaluation of acrylamide-grafted-xanthan gum copolymer matrix tablets for oral controlled delivery of antihypertensive drugs. *Carbohydrate Polymers*, *69*, 130–141.

Naidu, V. G. M., Madhusudhana, K., Sashidhar, R. B., Ramakrishna, S., Khar, R. K., Ahmed, F. J., et al. (2009). Polyelectrolyte complexes of gum kondagogu and chitosan, as diclofenac carriers. *Carbohydrate Polymers*, *76*, 464–471.

Rana, V., Rai, P., Tiwary, A. K., Singh, R. S., Kennedy, J. F., & Knill, C. J. (2011). Modified gums: Approaches and applications in drug delivery. *Carbohydrate Polymers*, *83*, 1031–1047.

Risbud, M. V., & Bhonde, R. R. (2000). Polyacrylamide–chitosan hydrogels: In vitro biocompatibility and sustained antibiotic release studies. *Drug Delivery*, *7*, 69–75.

Sharma, A. K., & Mishra, A. K. (2010). Microwave-assisted synthesis of chitosan-graft-styrene for effective Cr(IV) removal. *Advanced Materials Letters*, *1*, 170–177.

Singh, K., Kumar, A., Langyan, N., & Ahuja M. (2009). Evaluation of Mimosa pudica seed mucilage as sustained release excipient. *AAPS PharmSciTech*, *10*, 1121–1127.

Singh, V., Sethi, R., Tiwari, A., Srivastava, V., & Sanghi, R. (2003). Hydrolysis of plant seed gums by microwave irradiation. *Carbohydrate Polymers*, *54*, 523–525.

Singh, V., Tiwari, A., Tripathi, D. N., & Sanghi, R. (2004). Microwave assisted synthesis of guar-g-polyacrylamide. *Carbohydrate Polymers*, *58*, 1–6.

Singh, V., Tiwari, A., Tripathi, D. N., & Sanghi, R. (2006). Microwave enhanced synthesis of chitosan-graft-polyacrylamide. *Carbohydrate Polymers*, *47*, 254–260.

Soppirnath, K. S., & Aminabhavi, T. M. (2002). Water transport and drug release study from cross-linked polyacrylamide grafted guar gum hydrogel microspheres for the controlled release application. *European Journal of Pharmaceutics and Biopharmaceutics*, *53*, 87–98.

Tiwari, A., & Prabharan, M. (2010). An amphiphilic nanocarrier based on guar gum-graft-poly(ε-caprolactone) for potential drug delivery applications. *Journal of Biomaterials Science, Polymer Edition*, *21*, 937–949.

Toti, U. S., & Aminabhavi, T. M. (2004). Modified guar gum matrix tablet for controlled release of dilitiazem hydrochloride. *Journal of Controlled Release*, *95*, 567–577.

Vinod, V. T. P., Sashidhar, R. B., Suresh, K. I., Rama Rao, B., Vijaya Saradhi, U. V. R., & Prabhakar Rao, T. (2008). Morphological, physico-chemical and structural characterization of gum kondagogu (*Cochlospermum gossypium*): A tree gum from India. *Food Hydrocolloids*, *22*, 899–915.

Zhang, J., Zhang, S., Yuan, K., & Wang, Y. (2007). Graft co-polymerization of Artemisia seed gum with acrylic acid under microwave and its water absorbency. *Journal of Macromolecular Science A: Pure and Applied Chemistry*, *44*, 881–885.