Shellac-Polyamidoamine: Design of a New Polymeric Carrier Material for Controlled Release Application

R. K. Dey,[1] G. S. Tiwary,[2] Tanushree Patnaik,[3] Usha Jha[2]

[1]*Post Graduate Department of Chemistry, Ravenshaw University, Cuttack, Orissa 753 003, India*
[2]*Department of Applied Chemistry, Birla Institute of Technology, Mesra, Ranchi, Jharkhand 835 215, India*
[3]*Department of Chemistry, Stewart Science College, Cuttack, Orissa 753 008, India*

Received 28 December 2009; accepted 16 February 2011
DOI 10.1002/app.36411
Published online 29 January 2012 in Wiley Online Library (wileyonlinelibrary.com).

ABSTRACT: The development of a pH sensitive, biodegradable polymer from the combination of Shellac (a natural polymer secreted by lac insect) and polyamidoamine (PAA) (a synthetic polymer) yielded a new biocompatible polymer Shellac-PAA in a photopolymerization process. Scanning electron micrograph of Shellac-PAA shows an interesting heterogeneous surface morphology supported with observation of two different melting temperatures obtained from differential scanning calorimetric measurement. The equilibrium swelling properties of the polymeric material was studied as a function of pH and time in buffer solutions similar to that of gastric and intestinal fluids. The controlled release kinetics of a model colon specific drug 5-aminosalicylic acid showed Fickian diffusion behavior. The new polymer is biocompatible, biodegradable and, hence, projected as a new kind of polymer with improved properties, which can be a potential candidate for controlled release of therapeutic agents in colon specific diseases. © 2012 Wiley Periodicals, Inc. J Appl Polym Sci 125: 2626–2635, 2012

Key words: polymer; poly(amido amine); shellac; 5-aminosalicylic acid

INTRODUCTION

Designing a new kind of drug delivery carrier system associated with biocompatibility, biodegradability, and cost effectiveness are some of the interesting challenges in recent year.[1] Many functionalized polymers, natural or synthetic origin, find immense usefulness for fabrication of new kind of materials for various biomedical uses.[2] Such polymers are mostly biocompatible in characteristics; examples of which include various natural polysaccharide based materials, functionalized polymers/copolymers of lactic acid, glycolic acid, and ethylene glycol, etc.[3–7] In this context, development of new biocompatible, biodegradable responsive polymeric materials is a challenge, which gains a lot of importance in fabrication of controlled release system that can simulates changes in its physical and chemical characteristics with changes in external physiological environment such as change in pH of the medium, ionic strength, and temperature.[8] Quite a number of responsive polymers have been designed, prepared and evaluated for their efficacy as oral controlled delivery systems.[9–13]

In many such cases use of natural biocompatible polymer is preferred as a starting material for synthetic purpose in order to minimize the formation of the toxic biodegradable products in body's physiological environment. The process of biodegradation is usually catalyzed by enzymes and it involves both hydrolysis and oxidation. Generally aliphatic compounds are preferred because aliphatic chains are more flexible than aromatic ones and can more easily fit into active sites of enzymes for degradation process.

In this context, search of natural materials and processes, which are biodegradable and biocompatible, is a subject of intense research in biomaterial field. Shellac is a natural material, secreted by lac insects, *Laccifer laca* (Kerr), which thrive on specific trees called lac hosts wax.[14,15] The purified, commercial form of lac is commonly called shellac; however, the term lac and shellac are often used synonymously. Shellac is widely used as adhesives, thermoplastics, sealants, insulating materials, and coating materials in food and pharmaceutical industries, because of its excellent film-forming and protective properties along with its nonpoisonous nature.[16] Shellac is a complex mixture of polyesters consisting of number of acidic and hydroxyl side chains.[17] Therefore, it is possible to modify the functional groups of shellac by adopting various chemical modification procedures.[17] Shellac molecule consists

Correspondence to: R. K. Dey (rkdey@rediffmail.com or rkdey@bitmesra.ac.in).

Contract grant sponsor: Department of Science and Technology, New Delhi; contract grant number: SR/S1/PC-24/2009.

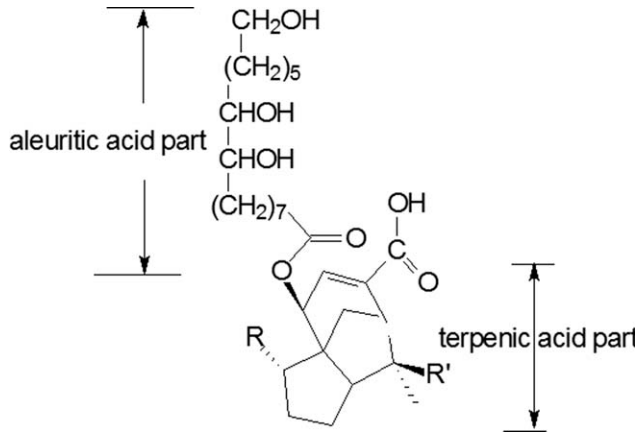


Figure 1 Structure of shellac showing a single polyester unit consisting of aleuritic acid part and terpenic acid part.

of hydroxyl and carboxyl groups and the polymerization can also occur by esterification among the functional groups present in shellac molecule (Fig. 1). Preparation of natural shellac based material in controlled drug release application is relatively new, although very few attempts were reported previously regarding modification of structure of shellac for improvement of its physical and chemical characteristics for various biomedical applications. For example, Wang et al.[17,18] in their recent publications reported the preparation of new environment friendly coating based material by chemical modification of functional groups of natural shellac.

Therefore, the basic objective of the present investigation is to prepare a new kind of environment friendly polymeric material by combination of shellac and functional polyamidoamine (PAA). PAA is an interesting biocompatible polymer characterized by the presence of amido and tertiary amino groups regularly arranged along the macromolecular chain. Linear PAAs are obtained by the polyaddition reaction of primary monoamines or bis(secondary amine)s to bis-(acrylamide)s.[19] The polymerization reaction can be carried out in water or alcohols, at room temperature and without any added catalyst. It takes place easily with almost every aliphatic and cycloaliphatic amine, also when side substituents such as hydroxyl, carboxylic, or additional tertiary amino groups are present. The main interest in PAAs lies in their potential use in the biomedical field. PAA-grafted biomaterials and PAA based cross-linked polymers are being considered as soluble carriers for anticancer drugs.[20,21] Preliminary *in vitro* studies have demonstrated that some PAAs are endowed with fairly good cell compatibility. Enzymatically degradable interpenetrating networks (IPNs) from proteins and polysaccharides have also been previously prepared.[22] These materials can erode with kinetics that is dependent on blend composition, enzyme concentration in the environment and preparation conditions. Apart from this, bioresponsive poly(amido amine)s are currently under development as endosomolytic polymers for intracellular delivery of proteins and genes.[23,24] The preferred amphoteric PAA structures are linear polymers and much less toxic than other polycations. PAAs are known to show pH-dependent behavior thus facilitating gene and toxin delivery *in vitro*. Furthermore, PAAs do not accumulate in the liver and intravenous injection and so it can be used to target tumors by the EPR (enhanced permeability and retention) effect.[24]

Thus, a new kind of polymer is expected to form by combination of PAA and shellac, which could crosslink in presence of one another. The reaction was initiated by irradiation process using 2,2-dimethoxy-2-phenyl acetophenone as photoinitiator. The advantage of photopolymerization in the preparation of biomaterials attributed to the fact that the polymers can be fabricated at temperature and pH values near physiological ranges and even in presence of biologically active materials.[8] The process also proceeds very rapidly in conditions suitable for most of the monomers and conventional initiators. The combination of properties of shellac and PAA is expected to produce a new kind of polymer that may be selectively enzymatically degradable, thus serves as an ideal carrier for drug delivery. Selective delivery of contents at desirable sites may also be possible where appropriate biological enzymes are present.

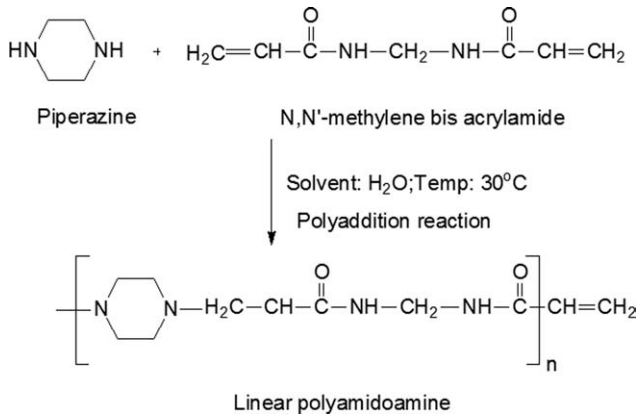
EXPERIMENTAL

Materials

Shellac was obtained as a gift sample from processing division of Indian Institute of Natural Resins and Gums (IINRG), Ranchi. Piperazine (Pip), *N*,*N*′-methylenebisacrylamide (MBA) (Fluka A.G.) were used without further purification. 2,2-dimethoxy-2-phenyl acetophenone was purchased from Acros Organics. 5-aminosalicylic acid (5-ASA) was a gift from Sun Pharmaceuticals, Mumbai, and used as a model drug in the sustained release processes. Phosphate buffers with different pH values (2.4, 6.8, 7.4, and 7.6) were prepared and used as physiological mediums. The buffer solutions were prepared from a mixture of phosphoric acid (54.0 mmol), boric acid (40.0 mmol), and acetic acid (42.0 mmol) then adjusting the pH to the required value by drop-wise addition of 0.2*N* NaOH solutions.

Preparation of poly(amido amine)

The preparation of poly(amido amine) from piperazine and methylene-bis-acrylamide was carried out using procedure similar to Tanzi and Levi[25] PAA



Scheme 1 Synthesis of polyamidoamine from piperazine and MBA.

was prepared by dissolving 7.7 g of MBA and 4.19 g of Pip (1 : 1.5 molar ratio) in 50 mL double distilled water. The reaction mixture was stirred under nitrogen atmosphere for 48 h at 30°C. The viscous solution was poured into 50 mL of acetone. The PAA (Pip-MBA) was separated out as a white crystalline product, which was filtered, washed with acetone, and recrystallized from diethyl ether. The product was stored in air-sealed bottle. The schematic reaction is shown in Scheme 1.

Preparation of polymer of Shellac-PAA

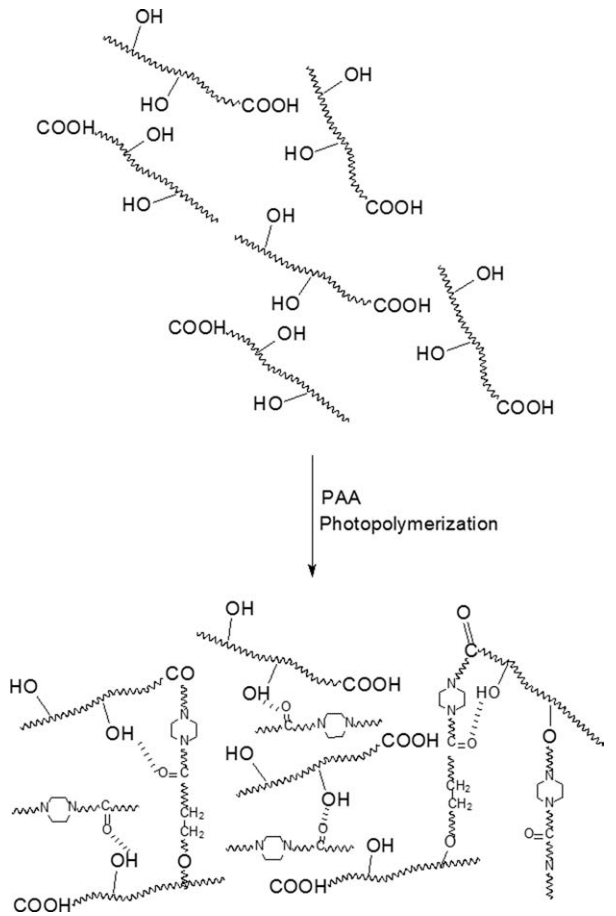
A series of new polymeric materials were prepared by variation of ratio of Shellac : PAA as 1 : 1, 1 : 2, and 1 : 3. However, for evaluation purpose in the present investigation sample material of Shellac-PAA polymer, prepared by taking Shellac and PAA in the ratio 1 : 1, was chosen. Other prepared polymers containing higher ratios of PAA were found to be either brittle in nature or yield was very less, giving a scope for detailed investigation in this regard at the later stage. The samples were prepared using the appropriate amount of PAA dissolved in 20 mL of methanol, added to a solution of Shellac in methanol. To this mixture a solution of 2,2-dimethoxy-2-phenyl acetophenone (2 wt % based on the PAA) was added in methanol (5 mL) with slow agitation. The reaction mixture was poured into a glass petridish and was maintained at room temperature. The polymerization was initiated by irradiation with an incandescent broad-spectrum lamp (Philips Comptalux, 150 W), positioned 25 cm above the petridish. Irradiation was continued for 7 h until gelation occurred. The schematic sketch of the reaction leading to the formation of polymeric material is shown in Scheme 2. The polymeric material was extensively washed with methanol to remove any residual monomer, then freeze-dried and stored until further use. The resultant product was cut in films, dry in air for three days, and place in a vacuum oven at 25°C until constant weight. The dry polymeric materials were polished up to the possible extent to achieve a smooth and uniform surface of 1.00 ± 0.05 mm thickness.

Entrapment of 5-ASA in the polymeric material (Shellac-PAA)

Polymer loaded with 5-ASA as a model drug were prepared in the same manner mentioned earlier. Known amounts of the drug (50 mg/100 L) were added to the reaction mixture, stirred vigorously, and then the polymerization reaction was carried out. The resulting polymer were washed with distilled water, freeze-dried, and stored until further use.

Measurements

Sample materials were characterized by FTIR (IR-Prestige 21, Shimadzu), and ^{1}H-NMR (JEOL-GX 300 FT NMR spectrometer, $D_2O/CDCl_3$ solvent) spectroscopy. Scanning electron microscope (SEM) of the sample materials were taken using JSM-6390 LV (Jeol, Japan). ^{13}C-NMR spectra were recorded at 300 MHz with a Bruker 300P spectrometer. The



Scheme 2 Synthesis of Shellac-PAA by photopolymerization technique.

differential scanning calorimetric (DSC) study was conducted on a TA Instrument, Model Q 10, in nitrogen environment. An UV–Vis spectrophotometer (Perkin Elmer, Lambda-25) was used for measurement of aliquot of drug sample.

Viscosity measurements of polymer solutions were carried out with an Ubbelohde viscometer using ethanol as a solvent at 28 (±0.5)°C. The flow time was measured for solutions at six different concentrations. The intrinsic viscosity was calculated by plotting specific viscosity,$[\eta]_{sp}$ at various concentrations versus concentrations (C) of solutions and then extra-plotting to zero concentration.

The swelling behavior of the polymeric materials were measured at 37°C temperature in three buffer solutions (pH 2.4, 6.8, and 7.4), similar to that of gastric and intestinal fluids. The buffer solutions were prepared from a mixture of phosphoric acid (54.0 mmol), boric acid (40.0 mmol), and acetic acid (42.0 mmol) then adjusting the pH to the required value by the drop-wise addition of 0.2*N* NaOH solutions. The pH values were precisely checked by a pH-meter (Systronic digital pH meter, model 335 equipped with calomel glass electrode (accuracy ±0.1). The swollen weights of the gels were determined at intervals, after removal of the surface liquid using tissue paper, until equilibrium swelling was attained. The percent swelling was calculated by the following equation.[1,5]:

$$\%\text{Swelling} = 100\ [W_t - W_0]/W_0$$

where W_0 is the initial weight and W_t the final weight of the gel at time t. Data points are means of three determinations. Less than 5% variation from the mean was observed in all cases.

In vitro cumulative release studies by ultraviolet spectroscopy

The release of entrapped 5-ASA *in vitro* was determined by placing the preweighed polymer loaded with drug in a buffer solution of 100 mL (pH 2.4, simulating gastric fluid; pH 6.8, 7.4, and 7.6 simulating intestinal fluid) at 37°C. At intervals, an aliquot was withdrawn and its absorbance at 214 nm maxima was measured. The withdrawn sample was replaced with an equal volume of fresh buffer, to keep the volume of release media constant. Data points were means of three determinations including standard deviation. The amount of drug at any selected time was calculated from the 5-ASA calibration curve.[26] This study was carried out for 24 h. The goodness of the kinetic results was verified by using the program Origin 6.0 for Windows XP Professional. Less than 5% variation from the mean was observed in all cases.

RESULTS AND DISCUSSION

Solubility and intrinsic viscosity

The freshly prepared polymer (5 mg) was suspended over 10 mL of the chosen solvent and the solubility was checked after 2 h. It was found that PAA was soluble in water where as the corresponding polymer of Shellac-PAA was insoluble in water. Ethanol served as an ideal solvent for dissolving both the PAA and Shellac-PAA. In acetone the Shellac-PAA was found to be partially soluble. These observations highlighted the fact that upon polymerization, the molecular arrangements and the degree of cross-linking within the domain of the polymer chain may vary to certain extent. The value of intrinsic viscosity in ethanol for Shellac-PAA was found to be 0.247 dL/g. The intrinsic viscosity for PAA in distilled water was found to be 0.232 dL/g.

CHN analysis and FTIR spectroscopy

C, H, N analysis report of Shellac shows the % of C and H as 28.3, 16.5. No nitrogen was detected as an element in the sample of shellac, where as the corresponding analysis of % of C, H, and N in Shellac-PAA shows the values as 30.2, 17.3, and 2.5. The increase in value of carbon content as well as the detection of nitrogen as an element in the Shellac-PAA could be related to the presence of PAA in the shellac moiety.

FTIR spectroscopy is one of the most important tools useful for elucidating the basic structural characteristics of materials. The FTIR spectrum of Shellac and Shellac-PAA is illustrated in Figure 2. The FTIR feature shows the characteristics bands related to the combined properties of shellac and PAA. The

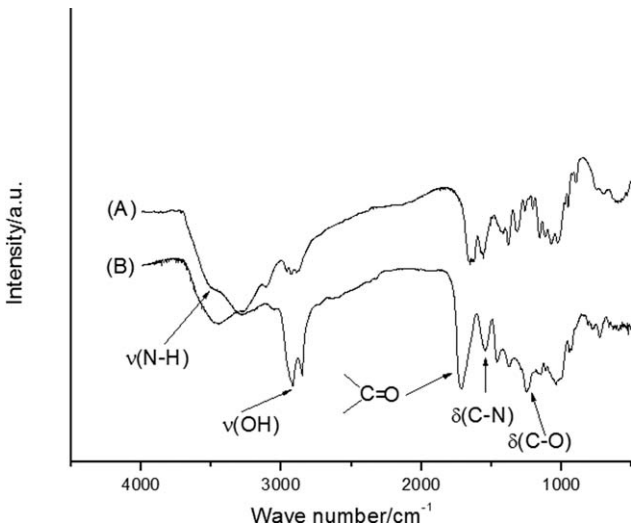


Figure 2 FTIR spectra of (A) Shellac-PAA and (B) Shellac.

spectrum shows O—H stretching vibration band around 2850–3000 cm^{-1} for the presence of hydroxyl groups in shellac molecule. Similarly, the strong carbonyl stretching vibration band observed at 1716 cm^{-1} along with bending mode of vibration at 1255 cm^{-1} supported the presence of amide linkage of PAA as well as carboxylic acid moiety of shellac molecule. The N—H stretching vibration band is observed at 3350 cm^{-1}. Presence of bands within the range 1650–1550 cm^{-1} is attributed to the amide I and II linkage.[27]

Nuclear magnetic resonance spectroscopy

Nuclear magnetic resonance (NMR) spectroscopy is also used as an important auxiliary tool to elucidate the structure of the organic moiety present in the polymeric material. The ^{13}C-NMR spectrum of the PAA, presented in Figure 3, displayed signals in consistent with previously reported data on similar kind of materials synthesized earlier, indicating the successful preparation of PAA by the adopted methodology.[28] The signals at δ28.2 and 30.2 ppm are assigned to the ethylenic carbon atoms C_1 and C_2. The carbonyl carbon is observed at 170 ppm as a sharp signal. Other peaks appeared at δ45.2, 52.4, 55.6, 128.2, and 129.6 ppm were assigned to different carbon atoms of PAA as shown in the inserted figure.

The corresponding proton NMR spectroscopy of PAA, in Figure 4, was also analyzed in which the presence of peaks at δ5.8 and 6.2 ppm were attributed to the presence of vinylic carbon atom (—$CH{=}CH_2$) in the moiety. Other aliphatic carbon atoms of PAA moiety were also observed in the range δ 1.2–3.3 ppm. Presence of peaks observed at δ4.5 and 4.6 ppm were attributed to the protons of piperazine moity (—NCH_2CH_2N—) in the structure.[29,30]

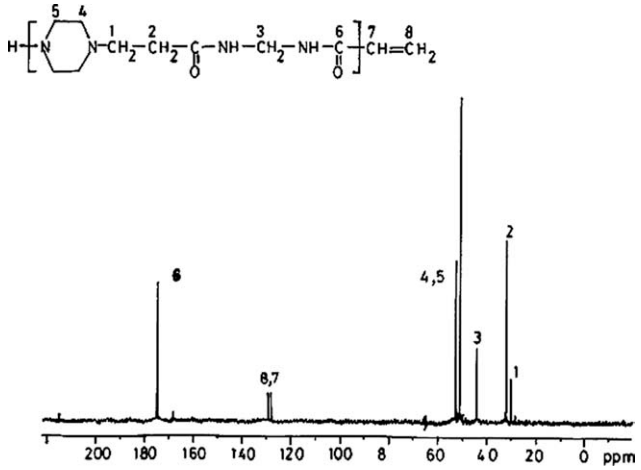


Figure 3 ^{13}C-NMR spectra of PAA.

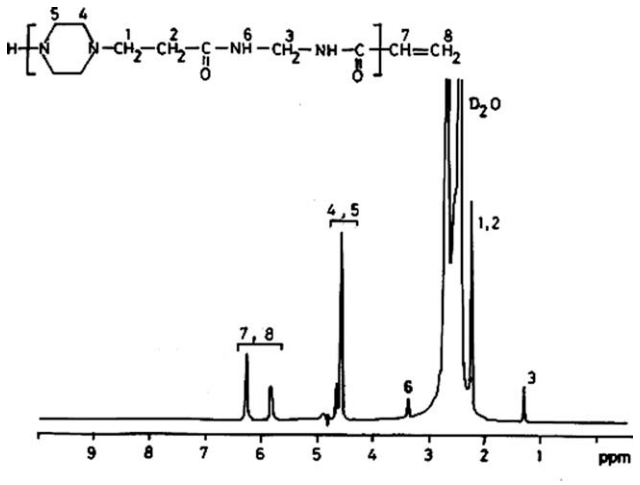


Figure 4 ^{1}H-NMR spectra of PAA.

Similarly, the proton NMR of polymer of Shellac-PAA was recorded and comparatively evaluated. The ^{1}H-NMR spectrum of Shellac-PAA, as shown in Figure 5 with the embedded structure of shellac molecule, recorded the presence of resonance peaks for the presence of hydrogen of methylene group (—CH_2—OH) at δ3.5 ppm and hydrogen of methine group (—CH—OH) at δ3.3 ppm. The group of signals generated from the hydrogen of methylene group of PAA in the moiety appeared in the range δ1.8–2.8 ppm in combination with the proton signals generated from the shellac molecule. Resonance peaks attributed to the various other protons connected to aliphatic chain of PAA in the polymeric structure was found in the range δ4.2–6.4 ppm. Thus, the characterization gave sufficient information regarding the incorporation of PAA in the shellac moiety.

Thus on the basis of photochemical reaction process, a free-radical mechanism was formulated to explain the formation of Shellac-PAA polymer. The mechanism, as outlined in Scheme 3, shows the formation of unstable oxygen free-radical species (—$O^{\bullet}$) generated from the hemolytic cleavage of

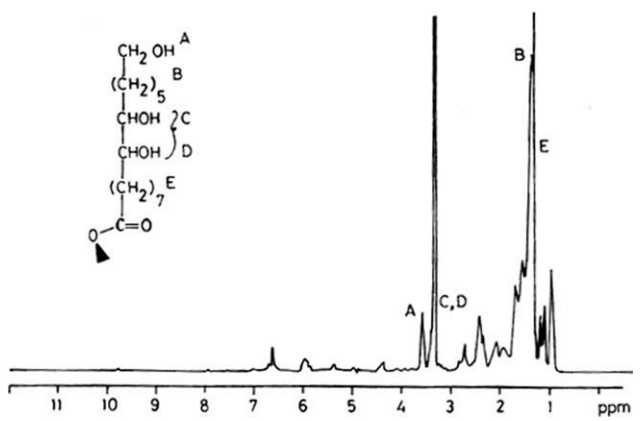
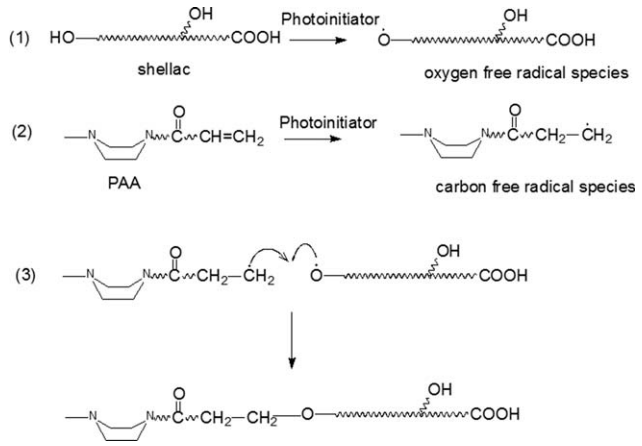


Figure 5 ^{1}H-NMR spectra of Shellac-PAA.



Scheme 3 Free-radical mechanism for the formation of polymeric material Shellac-PAA.

O—H bond of shellac molecule, which further combines with available free-radical species of carbon generated over PAA facilitating a chain reaction process in the reaction medium. Thus formation of a number of short chain/long chain molecule could also be possible, combination of which could lead to the formation of a semi-network kind of structure.

Thermogravimetric analysis

Thermogravimetric analysis (TGA) of material is immensely helpful in evaluating the relative thermal stability of the material with respect to change in temperature of the environment. The thermal degradation pattern of Shellac and PAA incorporated Shellac, studied in the temperature range of 32–600°C, are presented in Figures 6 and 7, respectively. The rise in temperature was monitored at 10°C/min in a nitrogen atmosphere. The thermogravimetric analysis curve of shellac sample material, in Figure 6, shows a negligible weight loss that occurred within a temperature range of 250°C and a relatively good thermal stability was observed within 250°C temperature range. Further increasing temperature beyond 250°C resulted in a gradual weight loss showing a uniform degradation pattern in the analysis result. For Shellac-PAA polymer, the TGA curve, in Figure 7, showed weight loss within 100°C attributed to the loss of water/solvent molecule present in the matrix. Within a temperature range of 200–300°C, a deflection in the TGA curve was observed indicating a weight loss attributed to the presence of PAA in the moiety. Increasing temperature beyond 300°C resulted in a gradual weight loss in the material. From the overall analysis of TGA curve of Shellac-PAA, it may be inferred that with the incorporation of PAA in the moiety of Shellac, a structural attachment of shellac to PAA occurred, possible evidence of which can further be corroborated from DSC studies.

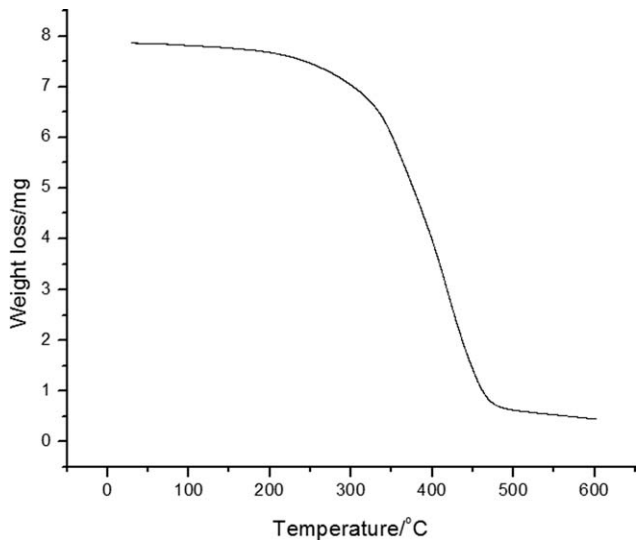


Figure 6 Thermogravimetric analysis curve of Shellac showing the gradual degradation pattern.

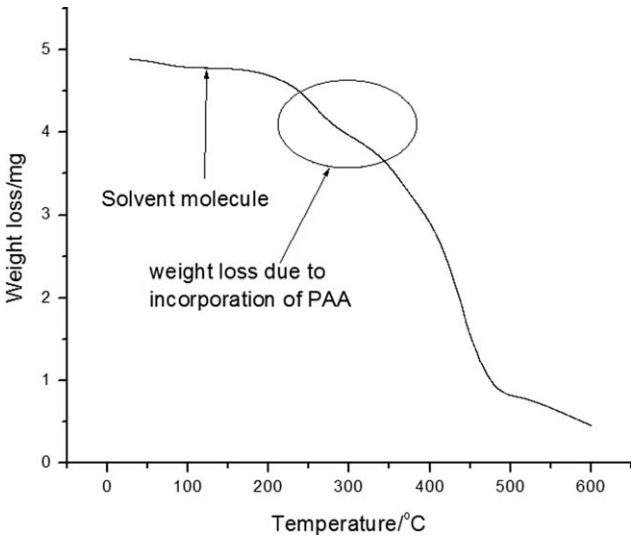


Figure 7 Thermogravimetric curve of Shellac-PAA showing the deflection in curve due to incorporation of PAA in the moiety.

Differential scanning calorimetric analysis

DSC is often used in combination with TGA to draw the useful structural information regarding the material properties. The DSC of both shellac (A) and Shellac-PAA (B) are illustrated in Figure 8, which was recorded up to a temperature range of 250°C. The observation was monitored in a nitrogen atmosphere with a slow heating rate (at 5°C/min) to draw some conclusive information regarding the structural characteristics of the materials. Shellac, in Figure 8(A), shows a broad endothermic peak at 57°C attributed to its melting point for which the amount of energy involved was calculated to be 72.2 J g^{-1}.

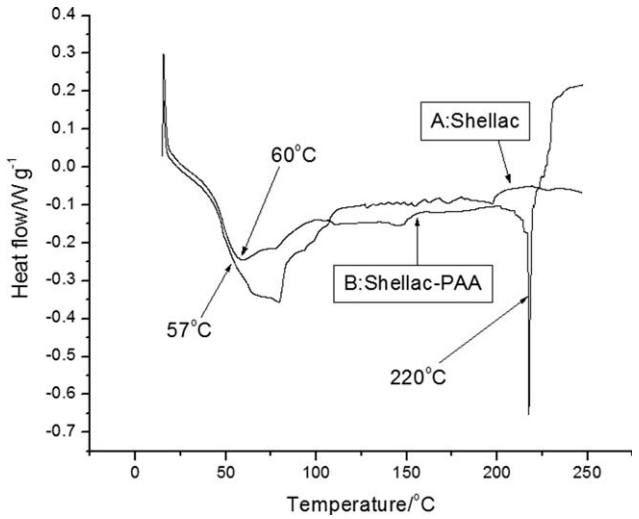


Figure 8 Differential scanning calorimetric studies of Shellac and PAA-incorporated Shellac.

The broadness of peak also suggested the presence of solvent molecule/hydroxyl groups in the structure. On the other hand, the DSC profile of Shellac-PAA, in Figure 8(B), shows two sharp endothermic peaks, 1st endotherm at 60°C and 2nd endotherm at 220°C, clearly attributed to the melting temperature of shellac and PAA, respectively. Similar kind of observations was also reported by other researches in PAA incorporated polymeric materials.[27] The peak integration calculation showed the associated energy values in the melting process as 28.3 and 15.7 J g^{-1}, respectively, for 1st and 2nd endotherms. Calculation of various kinetic and thermodynamic parameters from the data obtained from TGA and DSC may be helpful in elucidating the details of kinetics of polymerization process, details of which forms a part of our future investigations.

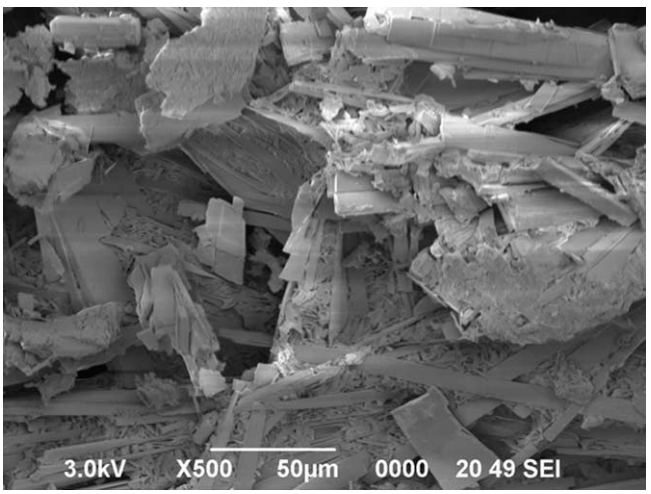


Figure 10 Scanning electron microscopic images of PAA.

Morphological features

The morphological features of Shellac and PAA incorporated Shellac were studied using scanning electron microscopic (SEM) technique. The image of Shellac, as shown in Figure 9, exhibits a more uniform surface. On the other hand, the image of PAA (Fig. 10) shows needle-like structure with uniformity over the surface. Interestingly, the PAA incorporated Shellac surface, in Figure 11, shows appearance of small globule shaped structures embedded in the matrix, which resulted in formation of a heterogeneous kind of surface. Further, this can also be correlated to the DSC studies where two different melting peaks were observed for shellac-PAA material supporting the formation of heterogeneous kind of surface morphology. The literature survey reveals few research articles highlighting the surface morphologies of various kinds of PAA incorporated materials.[30,31] Almost similar kind of optical texture was

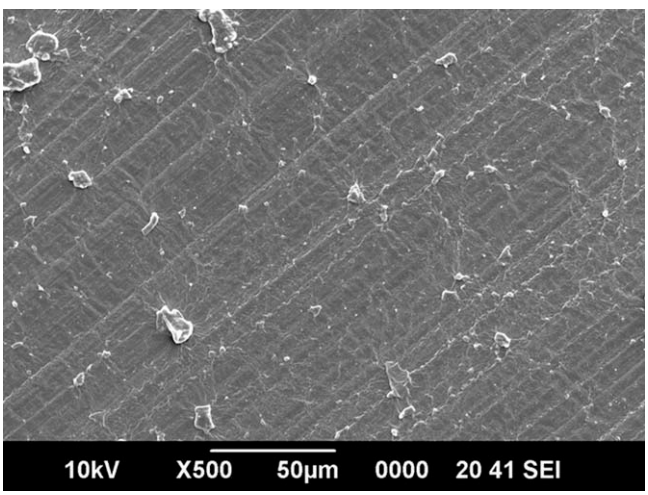


Figure 9 Scanning electron microscopic images of Shellac.

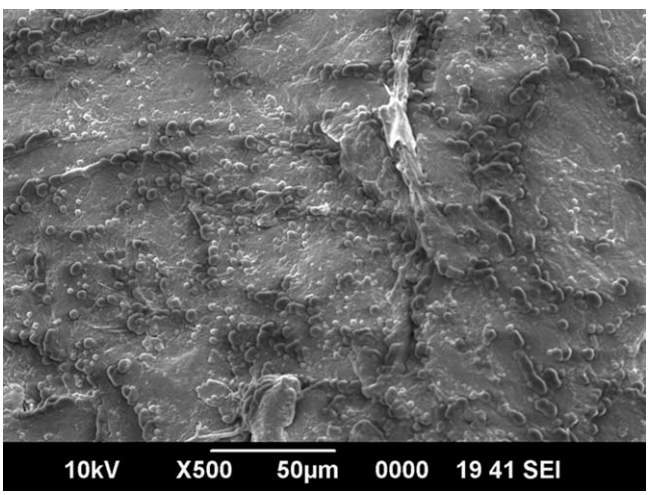


Figure 11 Scanning electron micrograph of PAA incorporated Shellac.

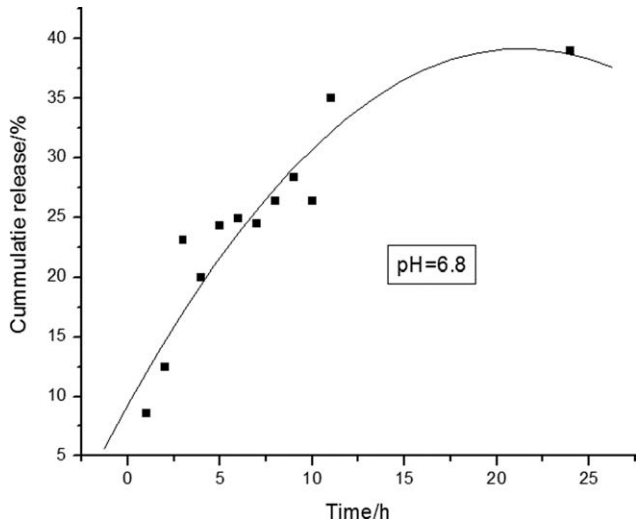


Figure 12 Cumulative release of 5-ASA at pH 6.8; (RSD = 0.34 – 0.55%).

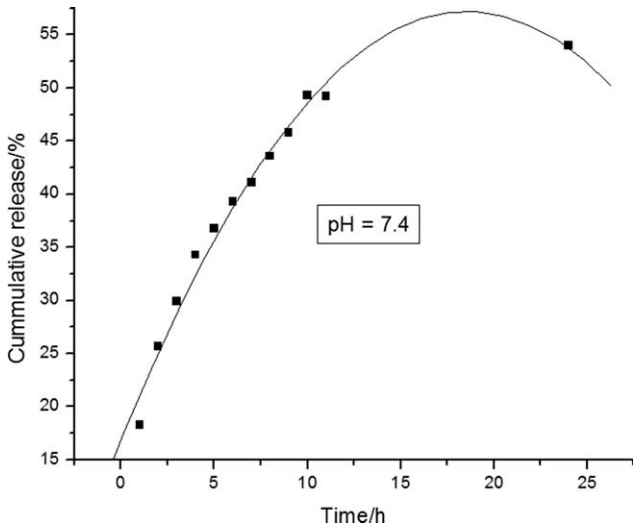


Figure 13 Cumulative release of 5-ASA at pH 7.4; (RSD = 0.24 – 0.43%).

observed by Suzuki et al.[30] during the study of PAA based liquid crystalline dendrimers. Tomalia and coworkers[31] in his publication reasoned the electrostatic repulsion might be one of the factors for such kind of observation. In our case, the reasons could be attributed to the intermolecular or intramolecular hydrogen bonding that possibly occurred between the amide units present in the PAA core resulted in formation of a coagulated structure as observed in the SEM. However, some detail investigations using advance instrumentation techniques may also be more useful in highlighting the mechanism of formation of such kind of textural features, study of that is quite interesting for this kind of new materials.

Equilibrium swelling studies

The % equilibrium swelling values of the prepared polymer shllac-PAA was determined at 37°C for pH 2.1, 6.8, and 7.6 only. The % equilibrium swelling of polymer in a 24 h time period was found out to be 0%, 185%, and 233% at pH 2.1, 6.8, and 7.6, respectively, thus indicating more swelling at higher pH of the medium. No swelling was observed in the acidic pH of the medium. The swelling mechanism can suitably be explained on the basis of ionization of functional groups present in the polymeric matrix. Ionization process is known to affect significantly the penetrant transport mechanism of the polymer networks. In case of anionic polymeric material, an increase in the degree of ionization contributes to electrostatic repulsion between charged groups and, therefore, swells the polymer to a high degree. In this investigation, the ionization of charged group is attributed to the presence of carboxyl acid group in the structure, which effectively ionizes in a basic medium and contributed to the physical swelling process. A swollen polymer also contains large amounts of unbound water that allows greater solute release.

Study of controlled release of 5-aminiosalicylic acid

The polymeric material shellac-PAA was utilized for the study of controlled release of a model drug 5-ASA. For such study, in this investigation only the basic buffer medium, i.e., pH 6.8, 7.4, and 7.6 was preferred because Shellac-PAA shows almost no swelling in an acidic pH. The initial drug loading concentrations of 5-ASA in polymeric material was evaluated to be 100 mg L^{-1}. It was observed that with increase in pH of the medium, the cumulative release percentage of the drug molecule also increases, which is illustrated in corresponding release profile curves Figures 12–14. The reason of increasing trend in the release

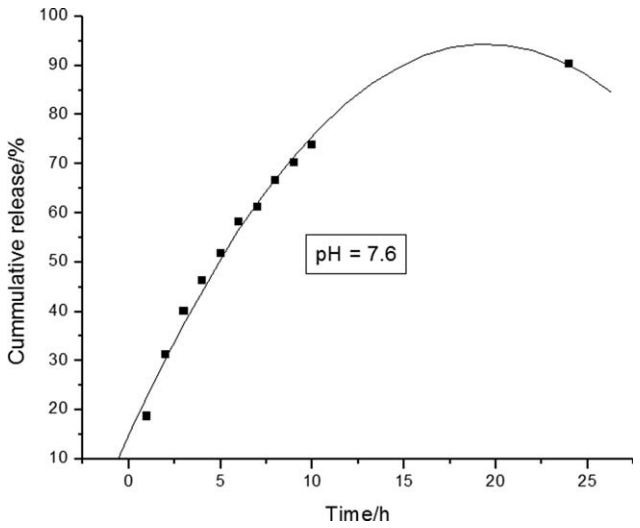
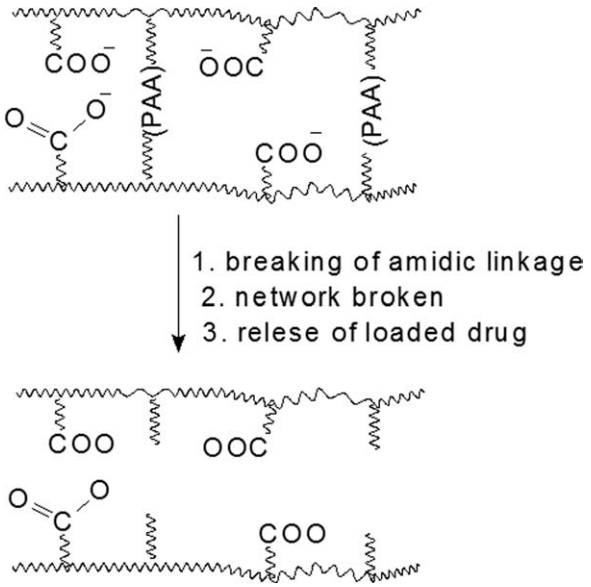


Figure 14 Cumulative release of 5-ASA at pH 7.6; (RSD = 0.43 – 0.57%).



Scheme 4 Pictorial presentation of release of drug molecule from the polymeric matrix by breaking of amidic linkage.

profile could be attributed to the interaction between 5-ASA and the polymeric material, where at higher pH of the medium, the polymer remains in swelling state and associated with larger equilibrium water content. Thus, 5-ASA molecule, which is embedded within the polymeric material and associated with water molecule, can diffuse more easily from the polymeric network structure because of the availability of more water as a diffusion medium. This resulted in greater amount of drug release at higher pH of the medium. The observed drug release rate was also found in the order of pH 7.6 > pH; 7.4 > pH 6.8, which is in agreement with the explanation given for the purpose.

In this context, Scheme 4 shows the schematic process of release of drug molecule from the prepared polymeric material. The release of drug molecule could occur because of the degradation of the polymeric chain (semi-IPN structure) where the breaking of amidic linkage in simulated body fluid resulted in release of drug molecule in physiological medium. To know the type of diffusion process in different buffered solutions, model eq. (1) valid for films with a constant thickness, was also applied.[32] During the investigation, the polymeric material was used at the early stages of the swelling process (until the first 30 min of the experiment) where the thickness of the sample remains almost constant. The Fick's equation can be written as:

$$M_t/M_e = kt^n \quad (1)$$

where M_t and M_e are the amount of buffer solution (drug) absorbed by the polymeric material at time t and in the equilibrium, respectively. k is a characteristic constant of the system, and n an exponent related to the kind of transport of the buffer solutions. The value of $n = 0.5$ indicates a Fickian diffusion process, but $0.5 < n < 1$ indicates non-Fickian or anomalous diffusion. In the special case in which $n = 1$, the transport mechanism is named Type II diffusion. In the representation of ln (M_t/M_e) vs. lnt, a linearity was observed until values of the swelling fraction M_t/M_e = 0.60 (first 60% of the dynamics water uptake data), and n and k are computed from the slope and the intercept, respectively. In all the cases, value of n close to 0.50 was obtained, so it can be considered a Fickian behavior.[32]

CONCLUSIONS

In summary a new polymeric material, Shellac-PAA, was prepared from the combination of natural shellac and PAA derived from piperazine and methylene-bis-acrylamide. The swelling characteristic of the polymer was studied in buffer medium. The *in vitro* release profiles of a model colon specific drug 5-ASA from the polymer matrix was estimated in basic buffers which shows a Fickian diffusion behavior. Since, both shellac and PAA are used primarily for different material-in-medicine application purposes because of its biocompatible structural features, the new polymer resulted from combination of shellac-PAA is expected to find newer applications in biomedical science. The preliminary investigation result of new shellac-PAA based polymer for sustained release application of a model drug is quite encouraging and may be exploited to expand the utilization of these systems in drug delivery applications.

The authors are thankful to Central Instrumentation Facility (CIF)-TEQIP, BIT, Mesra, CDRI, Lucknow, for providing necessary instrumentation facilities.

References

1. Gillies, E. R.; Fréchet, J. M. J. Bioconjug Chem 2005, 16, 361.
2. Joseph, J.-G. React Funct Polym 1999, 39, 99.
3. Rossi, N. A. A.; Mustafa, I.; Jackson, J. K.; Burt, H. M.; Horte, S. A.; Scott, M. D.; Kizhakkedathu, J. N. Biomaterials 2009, 30, 638.
4. Patil, Y. B.; Toti, U. S.; Khdair, A.; Ma, L.; Panyam, J. Biomaterials 2009, 30, 859.
5. Xu, D.-Y.; Li, G.-J.; Liao, Z.-F.; He, X.-H. Polym Bull 2009, 62, 183.
6. Zhang, J.; Chen, X. G.; Liu, C. S.; Park, H. J. J Mater Sci Mater Med 2009, 20, 991.
7. Sokolsky-Papkov, M.; Agashi, K.; Olaye, A.; Shakesheff, K.; Domb, A. J. Adv Drug Delivery Rev 2007, 59, 187.
8. El-Sherbiny, I. M.; Lins, R. J.; Abdel-Bary, E. M.; Harding, D. R. K. Eur Polym J 2005, 41, 2584.
9. Ganta, S.; Devalapally, H.; Shahiwala, A.; Amiji, M. J Controlled Release 2008, 126, 187.
10. Ahn, S.-K.; Kasi, R. M.; Kim, S.-C.; Sharma, N.; Zhou, Y. Soft Matter 2008, 4, 1151.
11. Ferreira, L.; Vidal, M. M.; Gil, M. H. Int J Pharma 2000, 194, 169.

12. Oral, E.; Peppas, N. A. J Biomed Mater Res 2004, 68A, 439.
13. Weaver, J. V. M.; Williams, R. T.; Royles, B. J. L.; Findlay, P. H.; Coopera, A. I.; Rannard, S. P. Soft Matter 2008, 4, 985.
14. Kamel, M. M.; El-Shishtawy, R. M.; Yussef, B. M.; Mashaly, H. Dyes Pigments 2005, 65, 103.
15. Bose, P. K.; Sankaranarayanan, Y.; Sengupta, S. C. Chemistry of Lac; Indian Lac Research Institute: Ranchi, India, 1963.
16. Pearnchob, N.; Dashevsky, A.; Bodmeier, R. J Controlled Release 2004, 94, 313.
17. Wang, L.; Ishida, Y.; Ohtani, H.; Tsuge, S. Anal Chem 1999, 71, 1316.
18. Wang, J.; Chen, L.; He, Y. Prog Org Coat 2008, 62, 307.
19. Ferruti, P.; Marchisio, M. A.; Duncan, R. Macromol Rapid Commun 2002, 23, 332.
20. Bignotti, F.; Sozzani, P.; Ranucci, E.; Ferruti, P. Macromolecules 1994, 27, 7171.
21. Ferruti, P.; Manzoni, S.; Richardson, S. C. W.; Duncan, R.; Pattrick, N. G.; Mendichi, R.; Casolaro, M. Macromolecules 2000, 33, 7793.
22. Kosmala, J. D.; Henthorn, D. B.; Brannon-Peppas, L. Biomaterials 2000, 21, 2019.
23. Richardson, S. C. W.; Pattrick, N. G.; Man, Y. K. S.; Ferruti, P.; Duncan, R. Biomacromol 2001, 2, 1023.
24. Pattrick, N. G.; Richardson, S. C. W.; Casolaro, M.; Ferruti, P.; Duncan, R. J Controlled Release 2001, 77, 225.
25. Tanzi, M. C.; Levi, M. J Biomed Mater Res 1989, 23, 863.
26. Wiwattanapatapee, R.; Lomlim, L.; Saramunee, K. J Controlled Release 2003, 88, 1.
27. Ghosh, S.; Banthia, A. K. Eur Polym J 2003, 39, 2141.
28. Wang, D.; Liu, Y.; Hong, C.-Y.; Pan, C.-Y. Polymer 2006, 47, 3799.
29. Hobson, L. J.; Feast, W. J. Polymer 1999, 40, 1279.
30. Suzuki, K.; Haba, O.; Nagahata, R.; Yonetake, K.; Ueda, M. High Perform Polym 1998, 10, 231.
31. Balogh, L.; Leuze-Jallouli, A.; Dvornic, P.; Kunugi, Y.; Blumstein, A.; Tomalia, D. A. Macromolecules 1999, 32, 1036.
32. Bajpai, A. K.; Choubey, J. J Macromol Sci A: Pure Appl Chem 2005, 42, 253.