

Preparation of Porous Cross-linked Microsphere through Electro spraying combined with Photopolymerization

SHUANGQI ZHAO¹, LIFEI HE², RUIXUE YIN^{3,4*} AND KEMIN WANG^{2,4*}

¹*School of Chemistry and Materials Science, Hubei Engineering University, Xiaogan, Hubei, 432000, China*

²*School of Materials Science and Engineering, Changzhou University, Changzhou, Jiangsu, 213164, China*

³*Complex and Intelligent Research Center, School of Mechanical and Power Engineering, East China University of Science and Technology, Shanghai, 200237, P. R. China.*

⁴*Division of Biomedical Engineering, University of Saskatchewan, Saskatoon, S7N 5A9, Canada.*

ABSTRACT

Porous cross-linked microspheres were manufactured from low-viscosity monomers through electro spraying combined with photopolymerization. Firstly, the liquid drops of monomer solution formed by electro spraying were crystallized by liquid nitrogen, and then the cross-linked polymer is formed by photopolymerization. Finally, the porous microspheres were obtained after the solvent was removed by freeze drying. The morphology, chemical structure, pore diameter and thermal stability of porous cross-linked microspheres were investigated by scanning electron microscope (SEM), fourier transform infrared spectroscopy (FTIR spectroscopy), mercury intrusion porosimetry and thermogravimetry analysis (TG). This approach provides a new stratage to prepare cross-linked porous microspheres from small molecules without using any template or other additives.

KEYWORDS: Porous Materials, Crosslinking, photopolymerization

1. INTRODUCTION

Polymer microspheres have potential and promising applications in nanotechnology

and bioengineering ^[1] because of their unique sizes and special structures. Due to the porous structure possesses a higher specific

surface area, a lower density as well as a better permeability; it is quite desirable if pores are introduced into the microspheres. The porous microspheres are required in many demanding applications, such as drug-controlled release^[2, 3], tissue engineering^[4–6], enzyme immobilization^[7–11], environmental sensing and catalysis^[12, 13].

Conventionally, porous polymer microspheres could be fabricated by template-assisted processing, porogen leaching methods, emulsion polymerization, self-assembly diffusion, reactive sintering methods and controlled solvent evaporation routes^[14–16]. Electrospaying, to prepare porous microspheres because of several advantages, such as relative ease of setup, open-atmosphere operation without a sophisticated chamber, high production efficiency and well dispersed microspheres^[17, 18]. However, to the best of our knowledge, the preparation of porous microspheres directly from monomers by electrospaying has not been reported yet.

Photoinitiated free radical polymerization is a widely used technique in coating, adhesion, printing, and photoresist fields^[19, 20]. It has several advantages over thermally initiated systems, including low energy consumption, solvent-free formulation and fast polymerization speeds^[21–25]. Nie's group showed the photopolymerization of acrylic acid at $-70\text{ }^{\circ}\text{C}$ had high double bond conversion of 96%^[26, 27]. Our previous work integrated low-temperature induced phase separation and photo-polymerization at low temperature to produce macroporous cross-linked polymers and microfibers directly from monomer solution^[28, 29].

In this study, we combined the advantages of photopolymerization and electrospaying techniques to fabricate cross-linked polymer porous microspheres. A simple model monomer, poly (ethylene glycol) diacrylate (PEGDA) with low viscosity, was chosen to fabricate porous cross-linked microspheres. Various electrospaying parameters, such as solution concentration, needle gauge and the collecting distance, were investigated in order to control the size of the obtained microspheres. We believe that this approach can be applied to a much wider range of monomers or cross-linkable biopolymers which could be polymerized by photo-induced free radical polymerization.

2. EXPERIMENTAL

Materials

Poly (ethylene glycol) diacrylate (PEGDA, molecular weight 700 g/mol) was purchased from Sigma-Aldrich (USA). The photo-initiator 2-hydroxy-4-(2-hydroxyethoxy)-2-methyl propiophenone (2959) was purchased from BASF Schweiz AG (Switzerland).

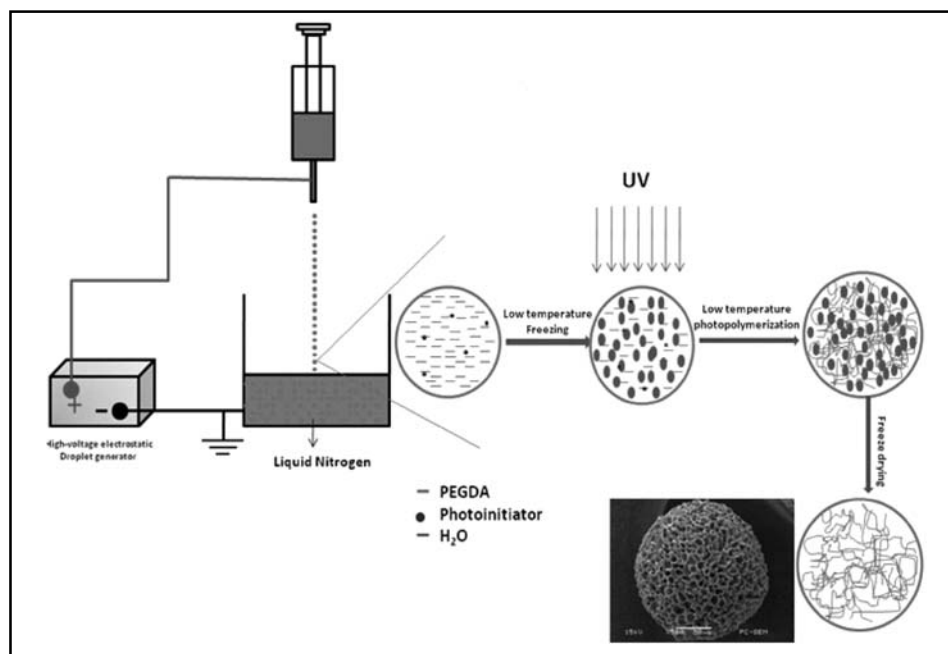
Preparation of PEGDA porous microspheres

The electrospay experimental equipment consisted of a syringe pump (WSZ-50FZ, Zhejiang University Medical Instrument Co., Ltd.), a stainless steel needle and a high voltage generator (BGG4-21, BMEI CO., Ltd.) (Scheme 1). The water solution of PEGDA monomer containing 1wt% photoinitiator 2959 was sprayed from a stainless steel needle (cathode) into a liquid nitrogen bath with an opposite charge (anode) in a foil-wrapped dish to induce crystallize and form frozen microspheres. The frozen microspheres were treated at low temperature ($-20\text{ }^{\circ}\text{C}$) for 5 hours and irradiated for 15 min at $-20\text{ }^{\circ}\text{C}$ by using a pointlite (Omni-Cure series 1000; wavelength range: 200–500 nm, light intensity= 100 mW/cm^2). The porous cross-linked PEGDA microspheres were obtained after removing of water by freeze-drying at $-69\text{ }^{\circ}\text{C}$ for 24 hours.

Characterization

The morphology of various microspheres was measured by SEM with the S-4700 (Hitachi) microscope. At least 50 microspheres from SEM picture were evaluated with the software Image J and an average diameter as well as a standard deviation was calculated.

FTIR spectra were obtained by using a Nicolet iS 5 Fourier transform infrared spectrometer (Thermo Fisher Scientific Inc.). Sample was prepared as KBr pellet and scanned against a blank KBr pellet background at wavenumber ranging from 4000 to 650 cm^{-1} with resolution of 4.0 cm^{-1} .



Scheme 1. General outline of porous cross-linked PEGDA microspheres prepared by electro spraying combined with low temperature photopolymerization

TGA was performed using a NETZSCH analyzer (TGA209F1D-0228-L) in nitrogen atmosphere.

Pore size distribution of the porous microspheres was recorded by mercury intrusion porosimetry using a PostMaster-33 porosimeter.

3. RESULTS AND DISCUSSION

A combination of electro spraying and low temperature photopolymerization was used to produce porous cross-linked PEGDA microspheres. The experimental set-up is

shown in scheme 1. When PEGDA solution is forced through a needle with an electric voltage, the surface tension of the solution becomes equal to the Coulomb repulsion. Under the electrostatic repulsion and the coulombic force caused by the electrical field, the solution at the tip of a needle forms a Taylor cone. The PEGDA solution is then sprayed spontaneously from the tip of the Taylor cone into a counter electrode. The obtained droplets

were frozen by liquid nitrogen and treated at low temperature (-20°C) for 5 hours to improve double bond conversion of PEGDA under UV irradiation [26]. After polymerization of the monomers at low temperature, a polymer network was generated while the solvent kept frozen. After water was removed by freeze-drying, a mass of pores were formed from the remained space occupied by frozen solvent. Controlled size of microspheres can be achieved by varying the parameters of manufacturing process, including solution concentration, needle gauge and the collecting distance.

The influence of the collecting distance on the morphology and size of obtained microspheres was shown in Fig. 1. The size of the porous cross-linked PEGDA microspheres decreased with increasing collecting distance of

electrospraying from 10 cm to 16 cm. However, when the collecting distance was larger than 10 cm, the microspheres did not show a perfect spherical shape. Some of the microspheres collapsed to form several large voids (Fig. 1 b-d). This phenomenon was related to the coulomb breakup during the electrospraying process. When the collecting distance was short, the solvent evaporation was not rapid enough to form a hard and dense shell on the surface of the charged droplets. Then, the coulomb breakup increased with increasing collecting distance; this led to porous microspheres collapsed. As porous microspheres at the collecting distance of 10 cm had lower polydispersity and better sphericity, the collecting distance of 10 cm was used for all future experiments.

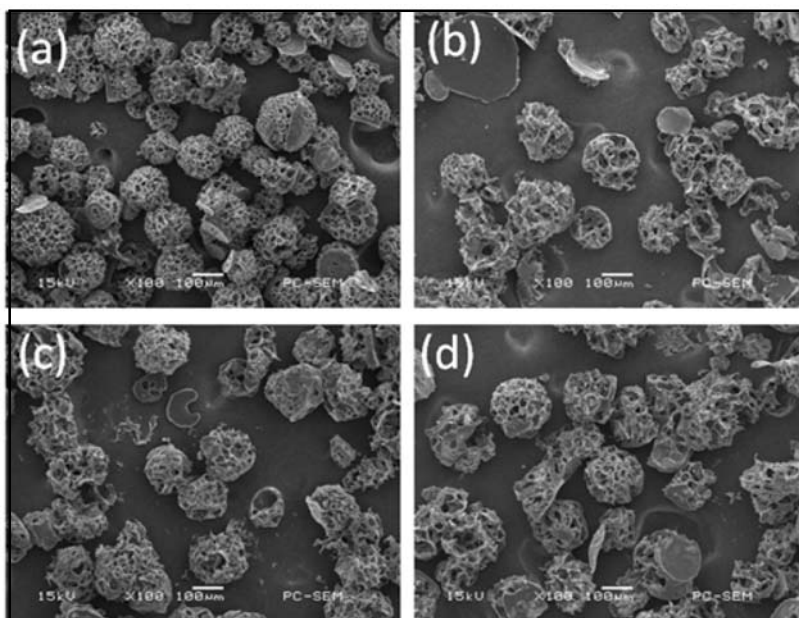


Fig. 1. The morphology of porous PEGDA microspheres formed with different collecting distances: (a) 10 cm, (b) 12 cm, (c) 14 cm, (d) 16 cm, with concentration of 9 wt%, needle gauge of 20 G, and voltage of 20 kV.

The concentration of monomer solution plays a key role in the formation of the electrospayed porous cross-linked microspheres. The change in the solution concentration led to a change in the surface tension and viscosity and, as a result, further influenced the size of spheres. As shown in Fig. 2a and b, increasing the concentration of PEGDA solution from 9 to 11 wt%, the obtained microspheres maintained a good roundness and the number of the holes on their surface increased. Moreover, the size of obtained microspheres increased from 143 μm to 216 μm . Such a size increase is mainly

caused by the viscosity increase of PEGDA solution. The higher the liquid viscosity is, the larger the droplets form through the jet break-up process, and more easily the chain entanglement could occur, leading to the formation of microspheres with a larger size.

The inner diameter of a needle is commonly expressed in gauge (G). Needles of various gauges were used and their influence on the size and morphology of resulted microspheres was shown in Fig. 2. The needle gauges used were 20 G and 23 G, with internal diameter (I.D.) of 0.6 mm and 0.3 mm, respectively.

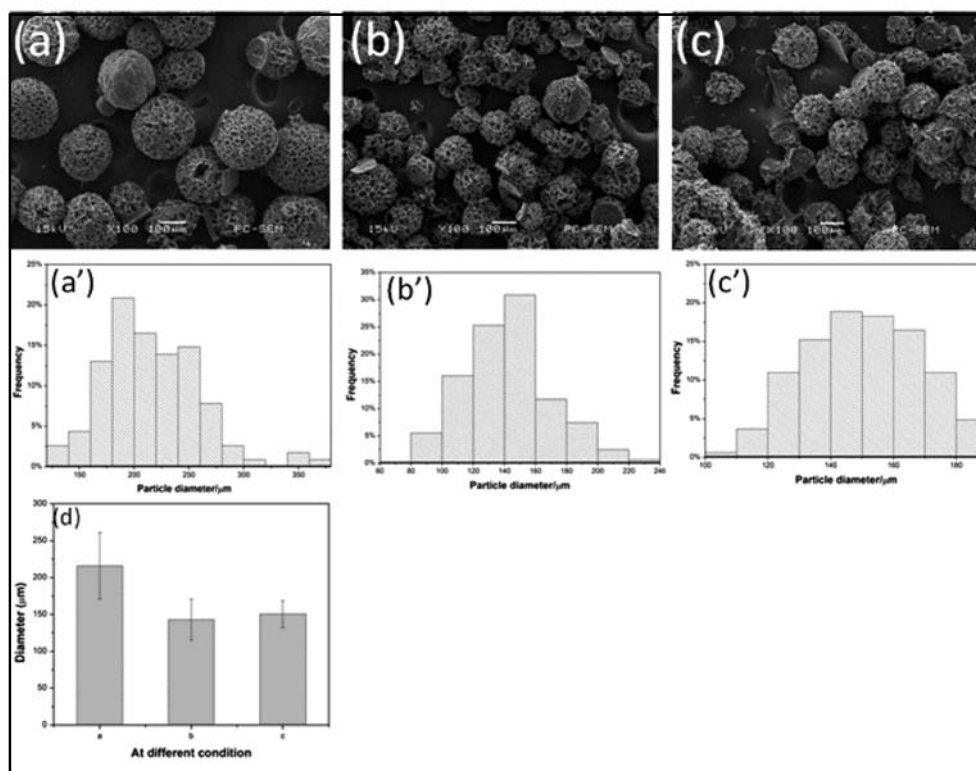


Fig. 2. The morphology of porous cross-linked PEGDA microspheres under different conditions (a) PEGDA concentration 11 wt%, needle gauge 20 G, (b) PEGDA concentration 9 wt%, needle gauge 20G (c) PEGDA concentration 9 wt%, needle gauge 23 G with height of 10 cm, voltage of 20 kV, (d) mean particle diameter of porous cross-linked microspheres in different conditions.

When the needle diameter changed from 0.3 mm to 0.6 mm, no significant change occurred in microsphere size. The average diameters of the microspheres only slightly decreased from 151 μm to 143 μm (Fig. 2d), and the diameter range changed from 100-190 μm to 80-240 μm (Fig. 2 b' and c'). The needle with the smaller inner diameter of 0.3 mm can generate a narrow size distribution. These results suggest that the needle size mainly affect the dispersity of microspheres rather than the size.

The chemical structures of the monomer before electrospaying and the obtained porous cross-linked microspheres were characterized by

FTIR spectroscopy. As shown in Fig. 3, compared to the PEGDA monomer, the typical stretching vibration and bending vibration peaks at 3100 cm^{-1} and 810 cm^{-1} (C=CH) of PEGDA microsphere were dramatically decreased, which indicated that the cross-linked reaction of monomer really happened during low temperature photopolymerization.

The volume fraction determined from mercury intrusion measurements carried out at high pressure (Fig. 4) revealed that the majority of the pore volume in the microspheres formed under different conditions was located in the macropore diameter range of 10-45 μm . It is

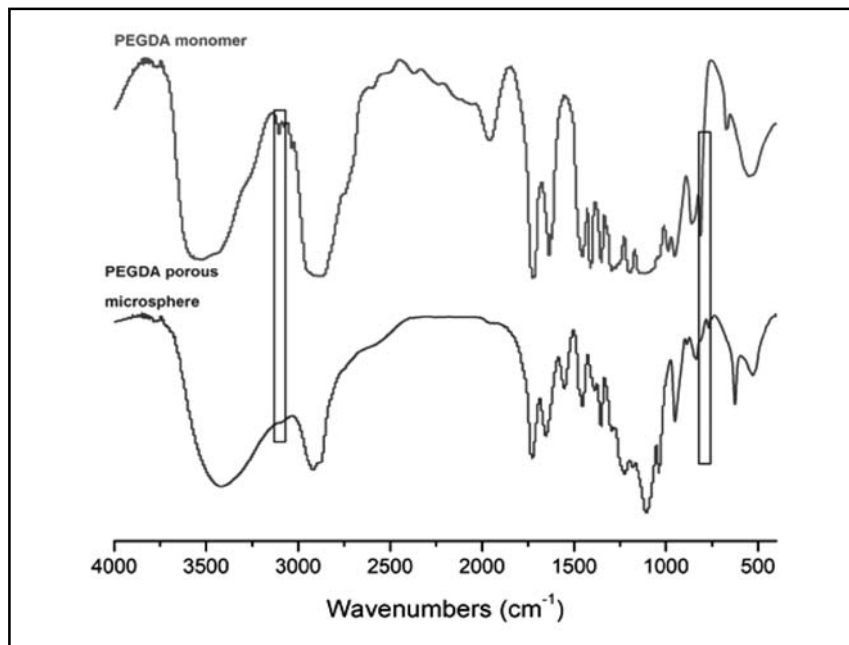


Fig. 3. FT-IR spectra of PEGDA and porous cross-linked PEGDA microspheres.

evident that with the increase of the concentration of PEGDA solution from 9 wt% to 11 wt%, the pore number fraction of smaller

pores increased and that of bigger pores decreased. The reason might be that with higher concentration of PEGDA solution, less

crystallized ices dispersed around the photopolymerized cross-linked polymer, leading to the decrease of the pore diameter. When then needle gauge increased from 20 G to 23 G, the resulting pores with higher diameter increased. This is because the Taylor cone became more stable when large needle gauge were used. The time required to freeze the PEGDA solution droplets is dependent on the droplet stability with more stable droplets taking shorter time. Hence, the solvent-rich

regions have shorter time to form and air dissolved in the PEGDA solution may be expelled to form big bubbles in the stable droplets due to the slightly faster rate of heat transfer.

The thermal stability of obtained PEGDA microspheres was characterized by TG. Figure 5 showed that the initial thermal decomposition temperatures with 10% weight loss of the PEGDA microspheres at concentration 11 wt%,

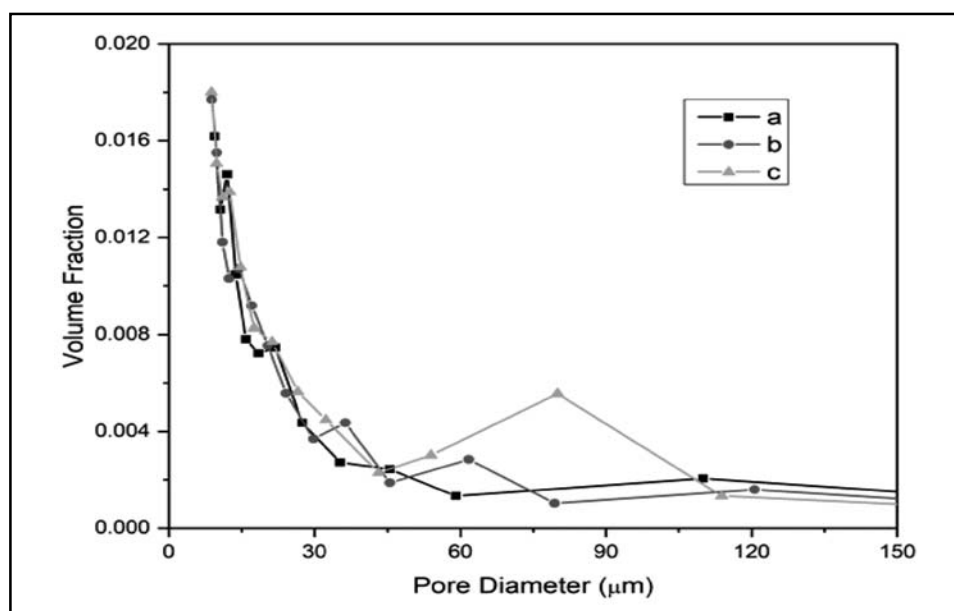


Fig. 4 Pore diameter distribution of obtained porous cross-linked PEGDA microspheres prepared under different conditions (a) PEGDA concentration 11 wt%, needle gauge 20 G, (b) PEGDA concentration 9 wt%, needle gauge 20 G (c) PEGDA concentration 9 wt%, needle gauge 23 G, with height of 10 cm and voltage of 20 kV

needle gauge 20G (a), concentration 9 wt%, needle gauge 20 G (b), concentration 9 wt%, needle gauge 23 G (c) were 352°C, 352°C and 354°C, respectively. The maximum weight loss rate (Tmax) for the PEGDA porous microspheres at concentration 11 wt%, needle

gauge 20G (a), concentration 9 wt%, needle gauge 20G (b), concentration 9 wt%, needle gauge 23G (c) happened at 400 °C, 398 °C and 405 °C. When the PEGDA concentration increased from 9 wt% to 11 wt% or needle gauge increased from 20 G to 23 G, the

crosslink density would increase, which resulted in the better thermal stability of the obtained microspheres.

4. CONCLUSION

In this study, porous cross-linked PEGDA microspheres were prepared directly from low-

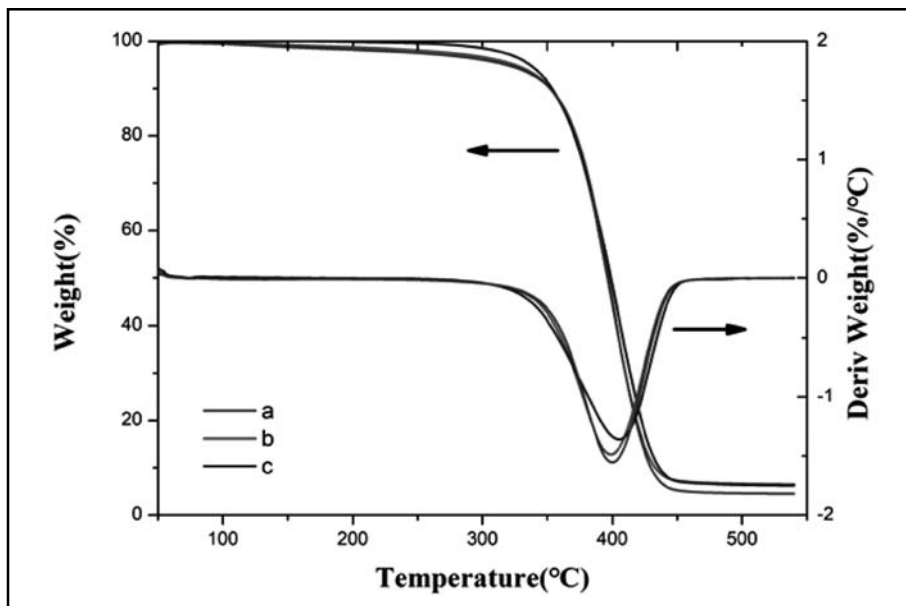


Fig. 5. TGA of obtained porous cross-linked PEGDA microspheres prepared under different conditions, PEGDA concentration 11wt%, needle gauge 20 G, (b) PEGDA concentration 9 wt%, needle gauge 20 G () PEGDA concentration 9wt%, needle gauge 23 G with height of 10 cm, voltage of 20 kV

viscosity monomers by electrospraying combined with low temperature photopolymerization. The microspheres had lower polydispersity and better sphericity prepared with the collecting distance of 10 cm. The size of microspheres increased with the increase of the concentration of PEGDA solution. The needle size mainly affected the dispersity of microspheres rather than the size. When the needle gauge increased, the fraction of larger pores and the thermal stability of the microspheres increased. This study provides a simple and eco-friendly method to prepare porous cross-

linked microspheres from model monomer PEGDA with low viscosity, and further efforts will be applied to a wider range of monomers or crosslinkable polymers with various functionalities.

REFERENCES

1. Y Wu, R. L. Clark, *J. Colloid Interf Sci* 2007, 310, 529-535.
2. L. S. Liu, S. Q. Liu, S. Y. Ng, M. Froix, T. Ohno, J. Heller, *J Control Release* 1997, 43, 65-74.
3. H. Kim, H. Park, J. Lee, T. H. Kim, E. S. Lee, K. T. Oh, K. C. Lee, Y. S. Youn, *Biomaterials* 2011, 32, 1685-1693.

4. S. E. Kim, J. H. Park, Y. W. Cho, H. Chung, S. Y. Jeong, E. B. Lee, I. C. Kwon, *J Control Release* 2003, 91, 365-374.
5. D. Green, D. Walsh, X. Yang, S. Mann, R. O. C. Oreffo, *J Mater Chem* 2004, 14, 2206-2212.
6. H. J. Chung, T. G. Park, *Tissue Eng Part A* 2009, 15, 1391-1400.
7. M. Matsumura, T. Yamamoto, P. Wang, K. Shinabe, K. Yasuda, *Water Res* 1997, 31, 1027-1034.
8. J. Huang, N. Jin, T. Katsuda, H. Fukuda, H. Yamaji, *Biochem Eng J* 2009, 46, 65-68.
9. S. Omi, K. Kaneko, A. Nakayama, K. Katami, T. Taguchi, M. Iso, M. Nagai, G. H. Ma, *J Appl Polym Sci* 1997, 65, 2655-2664.
10. M. Omer-Mizrahi, S. Margel, *Polymer* 2010, 51, 1222-1230.
11. Y. Li, F. Gao, W. Wei, J. Qu, G. Ma, W. Zhou, *J. Mol Catal B: Enzym* 2010, 66, 182-189.
12. A. Thomas, P. Kuhn, J. Weber, M. M. Titirici, M. Antonietti, *Macromol Rapid Commun* 2009, 30, 221-236.
13. J. Wang, J. Zhao, Y. B. Li, M. Yang, Y. Q. Chang, J. P. Zhang, Z. W. Sun, Y. P. Wang, *ACS Macro Lett* 4, 2015, 392-397.
14. J. Reignier, M. A. Huneault, *Polymer* 2006, 47, 4703-4717.
15. Y. S. Lee, K. S. Lim, J. E. Oh, A. R. Yoon, W. S. Joo, H. S. Kim, C. O. Yun, S. Kim, *J Control Release* 2015, 205, 128-133.
16. C. Takai, T. Hotta, S. Shiozaki, Y. Boonsongrit, H. Abe, *Chem Commun* 2009, 37, 5533-5535.
17. Q. Zhang, Y. Zhang, Q. Wei, X. Wang, J. Liu, J. Yang, C. Zhao, *J Appl Polym Sci* 2011, 120, 2648-2653.
18. Q. Zhang, J. Liu, X. Wang, M. Li, J. Yang, *Colloid Polym Sci* 2010, 288, 1385-1319.
19. Y. Yagci, W. Schnabel, *Prog Polym Sci* 1990, 15, 551-601.
20. Y. Yagci, S. Jockusch, N. J. Turro, *Macromolecules* 2010, 43, 6245-6260.
21. F. Xu, J. Yang, Y. Gong, G. Ma, J. Nie, *Macromolecules* 2012, 45, 1158-1164.
22. R. Shenoy, C. N. Bowman, *Macromolecules* 2010, 43, 7964-7970.
23. S. H. S. Dickens, J. W. Choi, K. M. C. J. E. Floyd, *Macromolecules* 2003, 36, 6043-6053.
24. C. Dietlin, S. Schweizer, P. Xiao, J. Zhang, F. Morlet-Savary, B. Graff, J. P. Fouassier, Lalevee, *J. Polymer Chem* 2015, 6, 3895-3912.
25. P. Xiao, J. Zhang, F. Dumur, M. A. Tehfe, F. Morlet-Savary, B. Graff, D. Gigmes, J. Fouassier, P.; Lalevee, *J. Prog Polym Sci* 2015, 41, 32-66.
26. B. Lu, P. Xiao, M. Sun, J. Nie, *J Appl Polym Sci* 2007, 104, 1126-1130.
27. M. Dai, M. Xiao, P. Xiao, J. Nie, *Polym Adv Technol* 2011, 22, 738-742.
28. R. Yin, K. Wang, Y. Lu, J. Nie, *Macromol Mater Eng* 2015, 300, 291-298.
29. K. Wang, J. Guan, F. Mi, J. Chen, H. Yin, J. Wang, Q. Yu, *Mater Lett* 2015, 161, 317-320.

Received: 07-04-2018

Accepted: 25-06-2018