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Radiation-Grafting of Cotton-g-DMAEMA for Biomedical Applications

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ABSTRACT

This work covers the design of stimuli-responsive membranes and their ever-expanding range of use. Stimuli-responsive membranes that change their physicochemical properties in response to changes in their environment were synthesized for biomedical application. Responsive cotton-g-[2-(dimethylamino) ethyl methacrylate] membranes were obtained using γ-rays by mutual irradiation (direct method). The effect of absorbed dose, dose rate, and monomer concentration on the grafting yield was determined. The grafted samples were verified by the FTIR-ATR, ^{1}H and ^{13}C HRMAS NMR and ^{13}C CPMAS NMR spectroscopies; thermal properties were analyzed by TGA and DSC and the stimuli-responsive behavior was studied by DSC.

INTRODUCTION

Radiation grafting is a suitable technique for surface modification of polymeric materials since it allows introducing active functional groups on the polymer backbone [1-5]. This method is applicable for many substrates and monomers combinations and, unlike chemically induced grafting; it does not require initiators [6].
There are several methods of radiation grafting: i) the direct (or mutual) grafting method in which the polymeric material is irradiated in contact with a monomer; homopolymerization being a collateral effect; ii) the pre-irradiation method, which involves the irradiation of the polymer matrix in the absence of air and then the grafting is initiated by macroradicals trapped in the irradiated polymer backbone; radiation dose is usually larger than in the direct method and polymer degradation may occur; and iii) the pre-irradiation oxidative grafting method consists in the pre-irradiation of the polymer in the presence of air or oxygen, so that the macroradicals formed are converted to peroxides and/or hydroperoxides; then when the irradiated polymer is heated in the presence of monomer the peroxides decompose to give the macroradicals [6, 7].

Cotton is an abundant, natural, biodegradable and renewable biopolymer, which makes it a very promising raw material available for modification with various functional polymers. The surface properties of cotton are of crucial significance for its widespread applications [8, 9]; for example, the creation of super-hydrophobic and oleophobic cotton fabrics, which have great potentiality in industrial application [10]. Chemical modification of cotton has been extensively studied for the past years in order to improve its wrinkle resistance, shrinkage resistance and dimensional stability [11, 12].

Poly(N,N´dimethyldimethylaminoethyl methacrylate) (PDMAEMA) is a polymer that exhibits a low critical solution temperature (LCST) in the range of 38-40 °C [13] and pH sensitivity characterized by a critical point at pH around 7.0 [14], and is soluble over a wide range of temperature as a cationic polyelectrolyte because of the protonation of tertiary amine group. It is well known that the LCST should rise with increasing hydrophilicity of the polymer and decrease with increasing hydrophobicity of the polymer [15]. PDMAEMA is a cationic polymer widely used in biomedical applications such as in gene delivery and in pharmaceutical formulations [16, 17]. PDMAEMA is able to condense the structure of plasmid DNA by forming polymer–plasmid complex, which can enhance the transfection efficiency and decrease the cytotoxicity [18].

EXPERIMENTAL

2-(dimethylamino) ethyl methacrylate (DMAEMA) was obtained from Aldrich Chemical Co. USA and distilled under reduced pressure before use. Cotton fiber gauze (sterilized 100% cotton gauze (CG) from Dimacu S.A. Mexico). Ethanol, methanol, and toluene from Baker were also used as received.

Grafted gauzes were obtained by direct irradiation method (mutual irradiation), 6 cm x 9 cm samples were cut and washed with ethanol, dried at room temperature overnight and weighted. The samples were placed in glass ampoules with DMAEMA/MeOH 1:1 solution. The ampoules were bubbled with argon to remove air and sealed after 20 minutes. The ampoules then were exposed to ^{60}Co γ-source (Gammabeam 651 PT), at dose rates of 6.5 and 14.5 kGy h^{-1} at different irradiation exposure doses between 1 and 20 kGy, monomer concentration from 5 to 60 (v/v). The DMAEMA homopolymer and residual monomer were extracted by immersion in ethanol for 24 h and dried under vacuum at 40 °C for 24 h. The grafting yield (Yg) was calculated by the equation 1.

$$Y_g(\%) = 100 \times \left[\frac{W_g - W_o}{W_o} \right] \quad (1)$$

Where W_o and W_g being the weights of the pristine and grafted gauzes, respectively

Fourier transform infrared spectra (in the Total Attenuated Reflection, FTIR-ATR mode) of the films were recorded using a Perkin-Elmer Spectrum 100 spectrometer (USA). Thermogravimetric measurements were obtained using a TGA Q50 (TA Instruments), between 25 and 800 °C at heat rate of 10 °C min^{-1}. Differential scanning calorimetry results were obtained using a DSC 2010 calorimeter (TA Instruments, USA) from 25 to 250 °C at heating rate of 10 °C min^{-1}. An NMR spectrum was recorded with Bruker Avance 400 spectrometer.

RESULTS AND DISCUSSION

Poly [2-(dimethylamino) ethyl methacrylate] (PDMAEMA) is a weak polybase with a pKa at about 8.0. In a neutral or a basic solution, it exhibits temperature-dependent solubility and has a LCST in the range 32–53 °C depending on the molecular weight, pH, and salt concentration. DSC study was done from 16 ^{o}C to 70 ^{o}C at a 1 ^{o}C min^{-1} ramp, dry sample was

previously weighed and then swelling in distilled water by 24 h. LSCT was determined between 34.4 °C and –36.9 °C (Figure 1), this result match with human body temperature (36–38 °C).

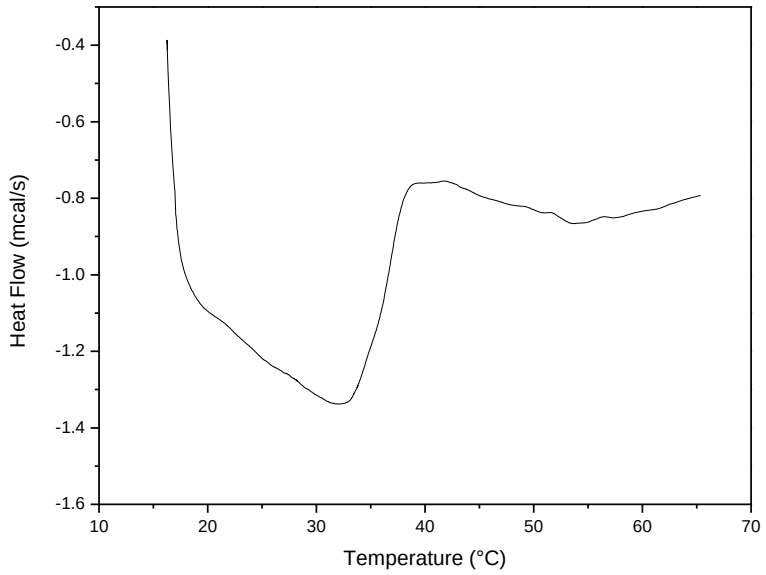

Figure 1. DSC analysis and LCST behavior of cotton-g-DMAEMA 75%. There are flow energy changes in 34.4 ^{o}C, 35.6 ^{o}C and 36.9 ^{o}C that show changes in graft copolymer structure.

A comparative thermogravimetric analysis (TGA) of three different materials, starter cotton gauze, PDMAEMA homopolymer, and grafted cotton gauze (58% graft) shows 10% of weight loss at 315 ^{o}C, 294^{o}C, and 268 ^{o}C respectively, it is showed in Figure 2.

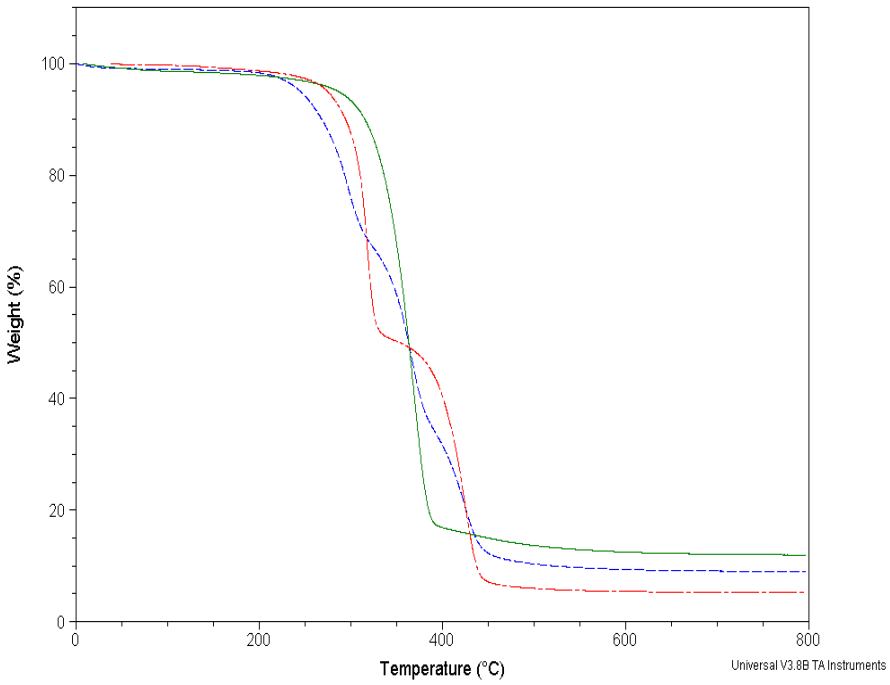

Figure 2. Thermogravimetric Analysis of cotton gauze (—), 58% cotton-g-PDMAEMA (-·-·-), PDMAEMA homopolymer (- - -).

Infrared comparative analysis (Figure 3) shows the grafting of PDMAEMA onto cotton gauze in relation with PDMAEMA homopolymer and starter cotton gauze infrared peak analyses, it showed C=O at 1722 cm^{-1} and 1724 cm^{-1} for poly(DMAEMA) and cotton-g-DMAEMA 58% graft respectively.

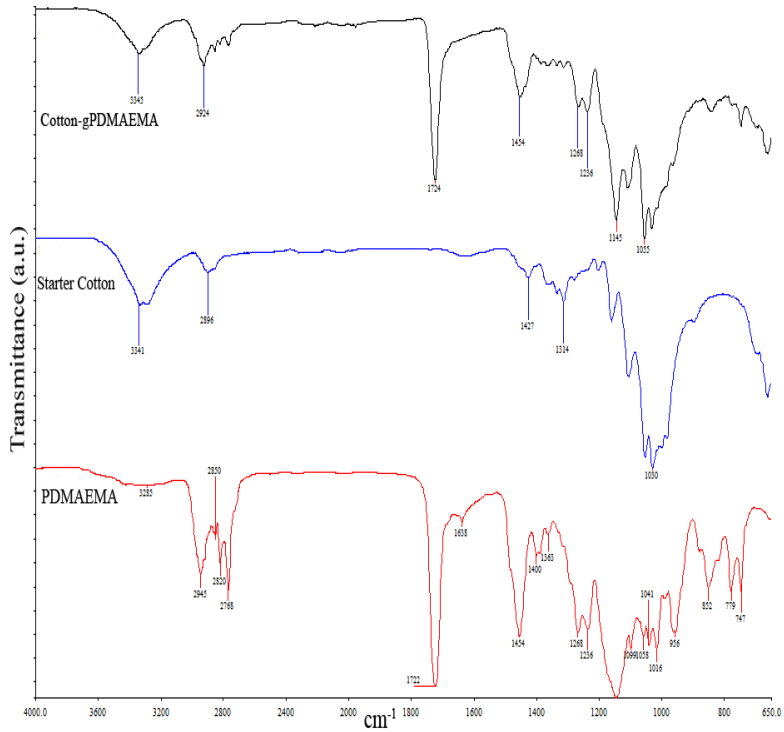

Figure 3. Infrared analysis of cotton-g-PDMAEMA 58% graft (dose 20 kGy), starter cotton gauze, and PDMAEMA homopolymer.

For this material it was important to find in which cellulose atoms the polymer was grafted and how much. If we number the cellulose molecule atoms as Figure 4, we find carbons 2, 3 and 6 as the most reactive sites, of which carbon 6 is more reactive than 2 and 3 [19].

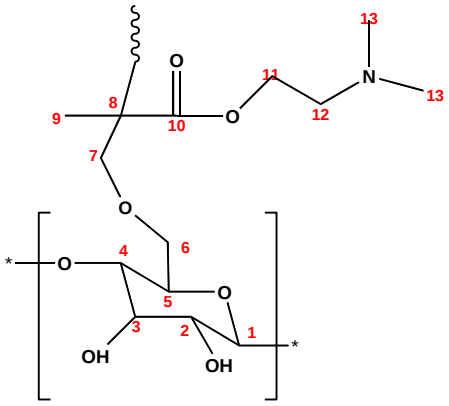

Figure 4. The molecular structure of cotton grafted with PDMAEMA and numbering for ^{1}H and ^{13}C NMR assignation.

NMR is a versatile technique that can reveal at atomic level the structural aspects of grafted polymers. FTIR can tell if any molecule was grafted, but, in which place and how much, there are interesting questions mainly for future work in medical applications.

NMR analysis was made with a Bruker Avance 400 spectrometer; we used an 88% grafted sample, because the higher grafting yield, the clearest information in the spectrum. ^{1}H and ^{13}C-NMR HR-MAS is a good technique to find the real quantity of grafting monomer, micro structural aspects and different kinds of protons and carbons in the sample, due that it is insoluble but can be swollen in D_2O. Is important to say that ^{13}C spectrum for natural polymers is impossible due to relaxation times. The swollen polymer was put in a 4mm zirconium rotor capsule and spinning at 5 kHz.

Proton spectrum (Figure 5) shows that PDMAEMA C9 methyl protons 0.74 ppm and 1.18 ppm of the backbone polymer grafted, 1.5 ppm to 4 ppm zone shows a peak at 2.31ppm, may be cellulose hydrogen bonds that cover another grafted polymer signals and another in 3.4 ppm, may be cellulose signals. Signal at 4.78 ppm is H_2O residual solvent. ^{1}H water suppression spectrum (on the top) shows that proton cellulose signal are between 3 and 4.5 ppm, there are some polymer signal in 1.5 and 2.25ppm, but are not very clear. 0 ppm signal is due to 3-(trimethylsilyl)propionic-2,2,3,3-d_4 acid, sodium salt as reference.

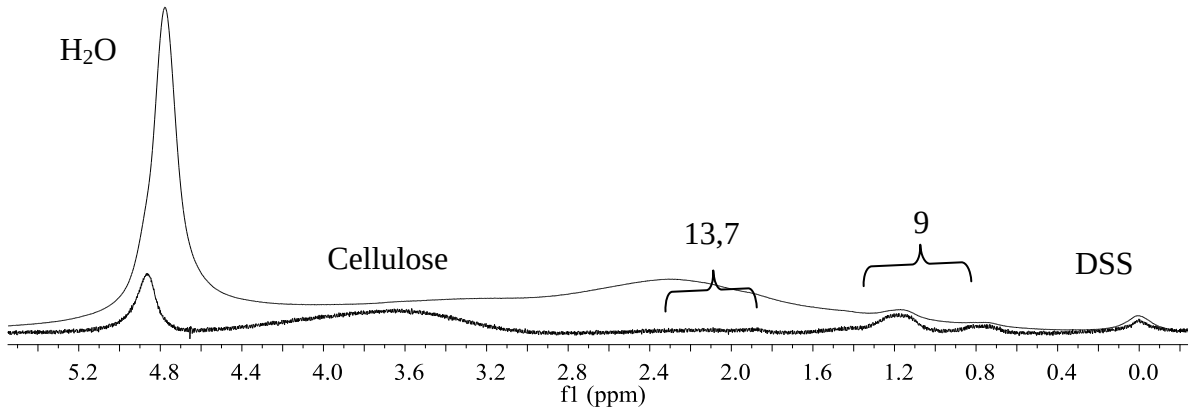

Figure 5. ^{1}H-NMR HR-MAS in D_2O to 5 kHz, proton spectrum (up), water suppression proton spectrum (down).

In the case of HR-MAS ^{13}C spectrum (Figure 6), natural polymer (cellulose) is difficult to get due to relaxation time. However only a part of grafted polymer (synthetic) is possible to see, C13 atom is the signal that appears at 44.81ppm. We think that C13 is present because that part is the more mobile part of the polymer and is the last part of the PDMAEMA polymer. Signal at 110 ppm is due to polytetrafluoroethylene (PTFE) that is used as insert in the zirconia rotor for balance and easy spin.

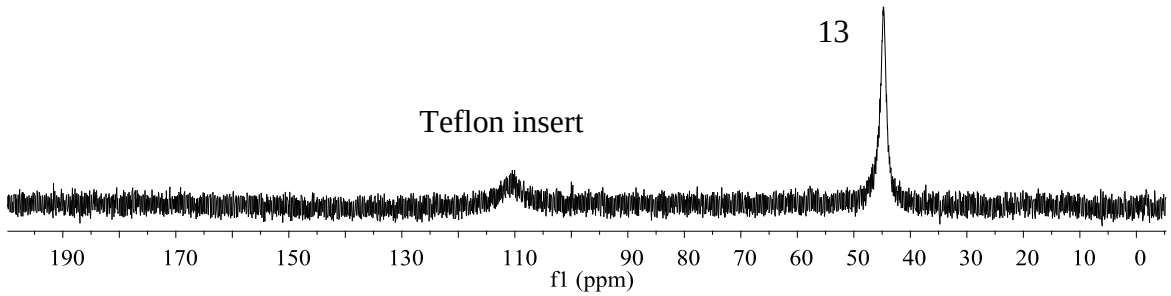

Figure 6. ^{13}C-NMR HR-MAS in D_2O to 5000Hz, 44.81 ppm signal (C13) is due DMAEMA $_3HC\text{-}N\text{-}CH_3$.

^{13}C-NMR CP-MAS is another technique to use with solid samples, this technique too uses 4 mm ZrO_2 rotors and sample does not need any special preparation. With solid state experiments we can see all kind of carbons and study structural characteristics like polymer soft and hard part by manipulating contact time pulse (CT). Fine differences are meaningful, for example the size and proportion of the peaks.

According to Figure 7, ^{13}C chemical shifts are C10:172.75, C1:100.57 and 99.31, C4:83.81, C5:69.76 and 66.36, C2:60.09 and 57.80, C3:52.65, C6:40.07, C9:10.66, SSB: spinning side bands. Spectra were taken at different CT (pulse p15 in CP-MAS sequence, the part where there are polarization transfer from protons to carbons), we choose 1ms for all the material, 5ms for the soft part and 0.2 ms for material hard part. So we found changes in C6 (CH_2), C2 (CH_2) and C10 (C=O), C6 is the most variable part, followed by C10 and C2. C6 is the substituted part in cellulose followed by C2, C3 does not have any perceptible change.

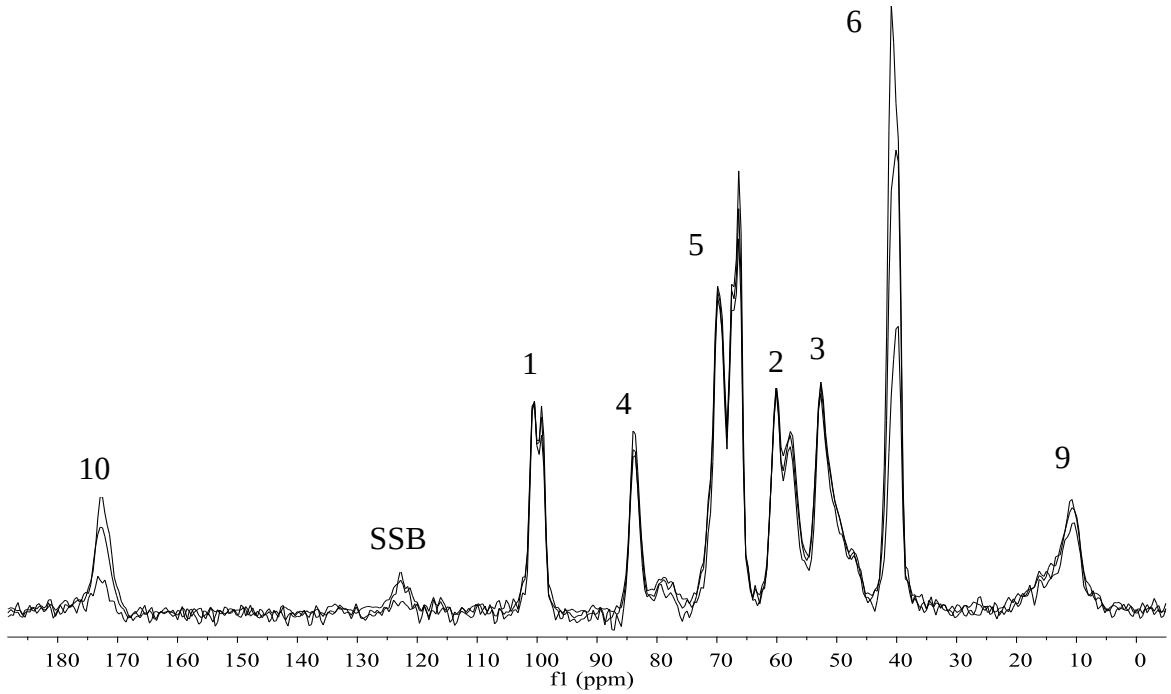

Figure 7. Overlaping of ^{13}C-CPMAS-NMR at 5000Hz cotton-g-PDMAEMA spectra, 1ms CT – all the material (center), 5ms CT– soft part (up), 0.2ms CT – hard part (down).

CONCLUSIONS

Poly(DMAEMA) was successfully grafted onto cotton gauze around 58 % at 20 kGy, grafted cotton was confirmed by FTIR-ATR and TGA showed 10 % weight loss 315, 294, and 268 °C for cotton, poly(DMAEMA), and cotton-g-PDMAEMA 58 % graft.

^{1}H, ^{13}C HRMAS spectra shows that a part of PDMAEMA carbonyl C10 form hydrogen bonds with cellulose OH´s, that is the reason why is impossible to see carbons C7 to C12 in ^{13}C spectrum, once they are grafted his relaxation time is very similar to cellulose carbons. ^{13}C CPMAS NMR spectra showed structural information and reveals that OH joined to C6 is the most reactive site. OH`s joined to C2 and C3 have are similar reactivity, but C2 is slightly higher.

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REFERENCES

1. Z. S. Nurkeeva, A. S. A. Aal, A. I. Kupchishin, V. V. Khutoryanskiy, G. A. Mun and A. G.Beksyrgaeva, Radiat. Phys. Chem. **6**, 793 (2003).
2. H. I. Meléndez-Ortiz, E. Bucio and G. Burillo, Radiat. Phys. Chem. **78**, 1, 2009.
3. A. Contreras-Garcia, G. Burillo, R. Aliev and E. Bucio, Radiat. Phys. Chem. **77**, 936 (2008).
4. Y. S. Ramírez-Fuentes, E. Bucio and G. Burillo, Nucl. Instrum. Meth. B **265**, 183, (2007).
5. C. Alvarez-Lorenzo, E. Bucio, G. Burillo and A. Concheiro, Expert Opin. Drug Del. **7**, 173 (2010).
6. E. Bucio, A. Contreras-García, H. I. Meléndez-Ortiz, F. D. Muñoz-Muñoz, C. Alvarez-Lorenzo and A. Concheiro, in *Smart Polymeric Materials for Biomedical Applications*, (NOVA Science Publishers Inc., New York, 2010).
7. G. Burillo and E. Bucio, in *Research Signpost* (Kerala India 2009) p. 45.
8. Y. Q. Zheng, S. Deng, L. Niu, F. J. Xu, M. Y. Chai and G. Yu., J. Hazard Mater. **192**, 1401 (2011).
9. H. H. Sokker, S. M. Badawy, E. M. Zayed, F. A. N. Eldien and A. M. Farag, J. Hazard Mater **168**, 137 (2009).
10. H. Miao, F. Bao, L. Cheng and W. Shi, Radiat. Phys. Chem. **79**, 786 (2010).
11. L. Yeqiu, H. Jinlian, Z. Yong and Y. Zhuohong, Carbohyd. Polym. **61**, 276 (2005).
12. G. Desme, Takács E., L. Wojnárovits and J. Borsa, Radiat. Phys. Chem. **80**, 1358 (2011).
13. G. Burillo, E. Bucio, E. Arenas and G. P. Lopez, Macromol. Mater. Eng. **292**, 214 (2007).
14. G. A. Titaux, A. Contreras-García and E. Bucio, Radiat. Phys. Chem. **78**,485 (2009).
15. W. Xue, S. Champ, M. B. Huglin and T. G. J. Jones, Euro. Polym. J, **40**, 703 (2004).
16. F. Dai, P. Sun, Y. Liu and W. Liu, Biomaterials, **31**, 559, (2010).
17. M. Soares da Silva, R. Viveiros, P. I. Morgado, A. Aguiar-Ricardo, I. J. Correia and T. Casimiro, Int. J. Pharm., **416**, 61 (2011).
18. L. Sheng, H. Ding, Z. Wang and G. Song, J. Mol. Struct., **979**, 152 (2010).
19. D. Roy, M. Semsarilar, J. T. Guthrie and S. Perrier, Chem. Soc. Rev. , **38**, 2046 (2009)