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Polyethylene glycol-based RAFT agent cum ATRP macroinitiator initiated block copolymerization of methyl methacrylate

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PMMA-*b*-PEG-*b*-PMMA block copolymer has been synthesized by the activators regenerated by electron transfer atom transfer radical polymerization (ARGET-ATRP) of methyl methacrylate (MMA) using modified polyethylene glycol (PEG) as initiator. PEG is chemically modified by CS_2 followed by an esterification to incorporate initiating sites for ATRP as well as for RAFT polymerization. The prepared macroinitiator has been characterized by FT-IR and NMR analyses for its structural validation. FT-IR and NMR analyses confirmed the successful synthesis of the macro initiator. This macro initiator has been used to prepare ABA type triblock copolymer with MMA via ARGET-ATRP. The polymerization reaction is carried out using cupric bromide ($CuBr_2$) as catalyst in combination with *N*,*N*,*N*′,*N*″,*N*″-pentamethyl diethylenetriamine (PMDETA) as ligand in *N*, *N* dimethyl formamide (DMF) at 70°C. Ascorbic acid is used as reducing agent. The conversion of the monomer was calculated gravimetrically. The successful preparation of the block copolymer is confirmed by FT-IR, ^{1}H NMR and ^{13}C NMR analyses. The MALDI-TOF mass analysis of the block copolymers also confirm the presence of monomer MMA, dithionate and PEG parts in the block copolymer. The purified block copolymer is analyzed by TGA, and SEM analyses. TGA analysis shows that the prepared block copolymer has better (T_{max} = 366°C) thermal stability than the PMMA (T_{max} = 349°C) homopolymer.

Keywords: ARGET-ATRP, Block copolymer, Methyl methacrylate, Polyethylene glycol

Block copolymers are very interesting materials with wide range of applications, for which they earn a unique place in polymer research field[1]. The targeted properties in these block copolymers are achieved by varying their blocks length and architecture in controlled way[2]. Polyethylene glycol (PEG) is another interesting polymer due to its unique properties like biocompatibility, lack of toxicity, solubility in almost every solvents etc[3,4]. PEG and its derivative are used in medical field for different activities such as in drug delivery, tissue engineering, etc[3,5-7]. This PEG has several advantages, however, it has no reactive groups in its ethylene oxide units and this is noted as a disadvantage for this material[3]. Therefore, the preparation of PEG with reactive groups has been of great interest to researchers. They have been trying to prepare block copolymers of PEG with other monomers to align its property with the monomers[8-12]. This PEG based block copolymer may find applications in nanotechnology[13], hydrogel nanoparticles[5], DNA delivery[10], thermo responsive hydrogel[14], etc.

There have been several reports on the synthesis of PEG based block copolymers by different methods ATRP[15], RAFT[16], ROP[17], etc. Baglan *et al*. reported the synthesis of tri-block copolymer PMMA-b-PEG-b-PMMA using Poly(ethylene glycol)(PEG) xanthate reversible addition fragmentation (RAFT) chain transfer agent by Raft Polymerization (RAFT)[16]. Nguyen *et al*. reported the synthesis of poly(ethylene glycol)-*block*-poly(styrene) (PEG-*b*-PS) block copolymer in 1-butyl-3-methylimidazolium hexafluorophosphate by atom transfer radical polymerization using PEG-Br as the macroinitiator[15]. Yang *et. al*. reported the preparation of poly (p-dioxanone)-*block*-poly(ethylene glycol)-*block*-poly (p-dioxanone) ABA triblock copolymer using PEG as the macroinitiator by ring-opening polymerization (ROP)[18]. Kawalec *et al*., also prepared the preparation of poly((R,S)-3-hydroxybutyrate)- *block*-poly (ethylene glycol)-*block*-poly((R,S)-3-hydroxybutyrate) (PHB-*b*-PEG-*b*-PHB) triblock copolymer using PEG macroinitiator by anionic ROP of ß-butyrolactone[19]. Garcia *et al*., reported the synthesis of triblock and

pentablock copolymers of methacryloyl uridine, methacryloyl adenosine and polyethylene glycol using PEG as macroinitiator via copper-mediated living radical polymerization[20].

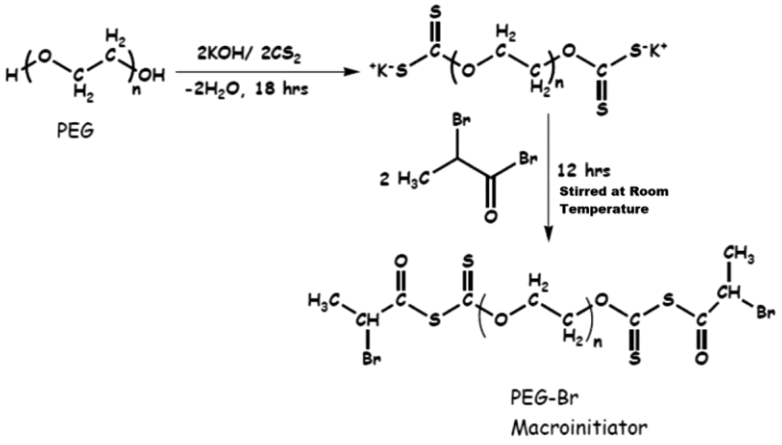
Methyl methacrylate (MMA) used in this work has several advantages like its ability to polymerize by different techniques, good mechanical and optical properties and most importantly its biocompatibility[21-23].

In this investigation, polyethylene glycol-based RAFT agent cum ATRP macroinitiator initiated block copolymerization of MMA via ARGET-ATRP to prepare an ABA type triblock copolymer has been reported. The synthesis of PEG macroinitiatorand PEG macroinitiator initiated ARGET-ATRP of MMA is shown in Scheme 1 and Scheme 2 respectively along with the use of their respective ingredients. ARGET-ATRP is a modified version of ATRP which uses catalyst in *ppm* level. This technique requires a reducing agent which continuously regenerates the activator and maintains the normal ATRP. It is also possible to prepare polymer with controlled molecular weight using this technique[24,25].

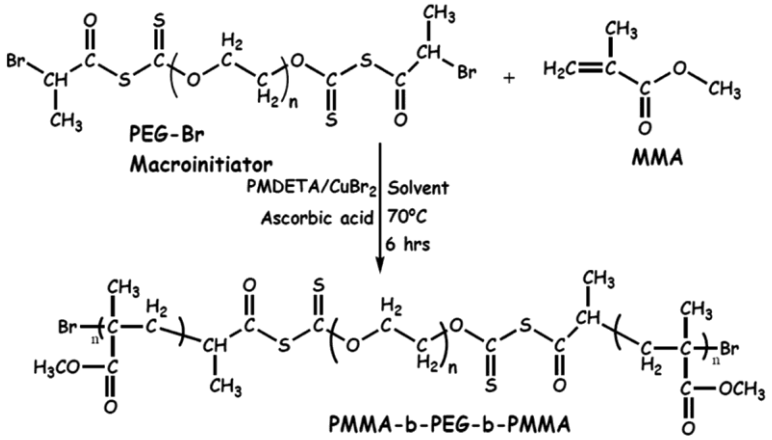
Experimental Section

Materials

MMA (Aldrich; 99%, USA) was purified by passing through basic alumina packed column and stored at 0°C. Polyethylene glycol (PEG-600) (Merck, India) (Mean M_w= 570-630) was used as received. The ligand N,N″,N″,N′,N′-pentamethyl diethylenetriamine (PMDETA) (99%, Aldrich, USA) and 2-Bromopropionyl bromide(97%, Aldrich, USA) were purchased from Sigma-Aldrich and were used as received. Catalyst cupric bromide ($CuBr_2$) (99%; SRL, India) were used as received. N, N-Dimethylformamide (DMF) (99%; Emplura, India) was used as received. Other chemicals acetone(99%, Merck, India), L-ascorbic acid (99.7%) (SRL Extrapure; AR, India), Dichloromethane (DCM) (99%, Merck, India), Ethyl acetate (99.5%, Merck,



Scheme 1 — Preparation of macroinitiator PEG-Br.



Scheme 2 — ARGET ATRP of MMA using macroinitiator PEG-Br.

India), potassium hydroxide (KOH) (85%, Rankeem, India) and carbon disulphide (CS_2) (99%, Merck, India) were used as received.

Preparation of PEG macroinitiator

PEG (0.999 g, 0.00167 mol) and KOH (0.766 g, 0.01365 mol) were added to a 25 mL dry Schlenk tube and mechanically stirred at 0°C for about 30 min. With continuous stirring CS_2 (1.465g, 0.0192 mol) was added drop-wise into the tube and the reaction mixture was allowed to run till a transparent solution. The progress of the reaction was checked by TLC at different times. Finally, 2-bromopropionyl bromide (3.3g, 0.0153 mol) was added drop-wise to the reaction mixture at 0°C and was allowed to run at room temperature for 10 h. After completion of the reaction, the product mixture was extracted with water and ethyl acetate and was separated by using separating funnel. The filtrate was collected and the solvent was removed under vacuum to obtain the product, to this again DCM was added to form an azeotropic mixture with the remaining ethyl acetate and then it was removed under vacuum to obtain the pure macroinitiator. The yield of macro initiator was found to be 2.79 g and the percentage of yield was found to be 73%.

ARGET ATRP of MMA using the macroinitiator PEG-Br

In a typical solution polymerization, the catalyst $CuBr_2$ (0.0451 g, 0.20 mmol) and the ligand PMDETA (0.0519 g, 0.30 mmol) were added to a dry Schlenk tube equipped with a magnetic stirring bar and the tube was then sealed with a rubber septum. Acetone (2 g) was injected to the Schlenk tube to dissolve the catalyst and ligand. This mixture was stirred for 10 min to form the catalyst/ligand complex. PEG-Br (0.5g) was then injected to the Schlenk tube followed by the addition MMA (2 g, 0.02 mol). With continuous stirring, solvent DMF (2 g) and ascorbic acid (0.15 g, 0.85 mmol) were then injected to the Schlenk reaction tube and sealed. To carry out the polymerization the reaction tube was placed in preheated oil bath at 70°C.

Characterization

Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Advance Jeol 9.4 Tesla/400 MHz spectrometer with $CDCl_3$ as the solvent. Fourier Transform Infrared (FTIR) spectra were recorded with the samples on Perkin-Elmer, Spectrum RX I. MALDI-TOF-MS analysis was carried out using Applied Biosysytems 4800 Plus MALDI-TOF/ TOF mass spectrometry using 2,5-dihroxybenzoic acid (DHB) and salt (Sodium trifluoroacetate). Thermalstudies of the samples were done by STA 6000 model for Thermogravimetric analysis (TGA). Thermogravimetric analysis of the polymer approximately weight 2.048 mg was subjected to heat from 30 to 800°C at 10°C/min under nitrogen atmosphere. Scanning electron microscopy (SEM) image of polymer was analyzed using silicon vapour and then coating it with gold before analysis.

Results and Discussion

Synthesis of macroinitiator PEG-Br

The PEG macroinitiator was prepared in one step at room temperature by reacting PEG with 2-bromopropionyl bromide, KOH and CS_2as shown in Scheme 1. FT-IR [Fig. 1(a)], ^{1}H NMR [Fig. 2(a)] and ^{13}C NMR [Fig. 2(b)] spectra were employed to determine the successful synthesis of the macroinitiator. The absorption peak at 1739 cm^{-1} is assigned to the stretch of C=O from the initiator. The

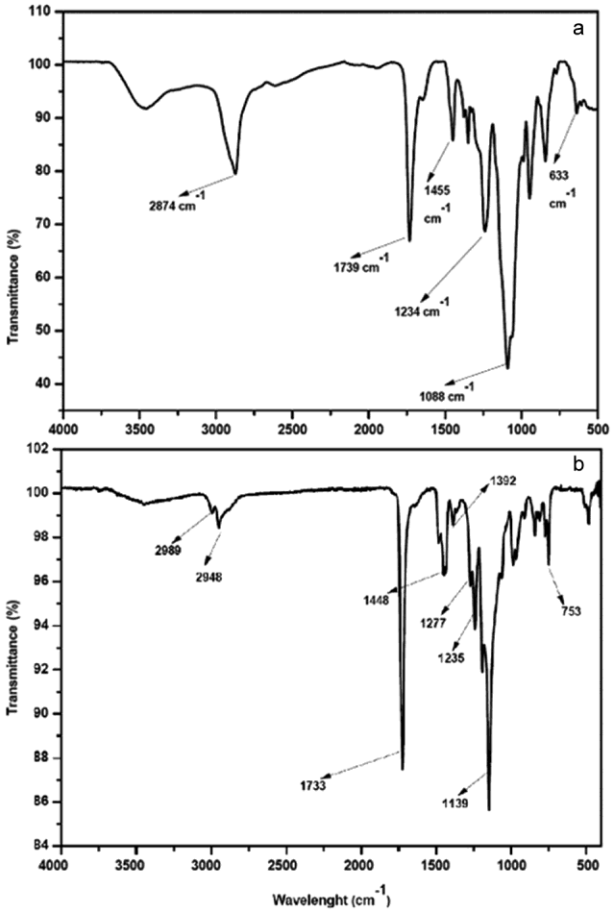


Fig. 1 — (a) FTIR spectrum of PEG-Br and (b) FTIR spectrum of PMMA-*b*-PEG-*b*-PMMA.

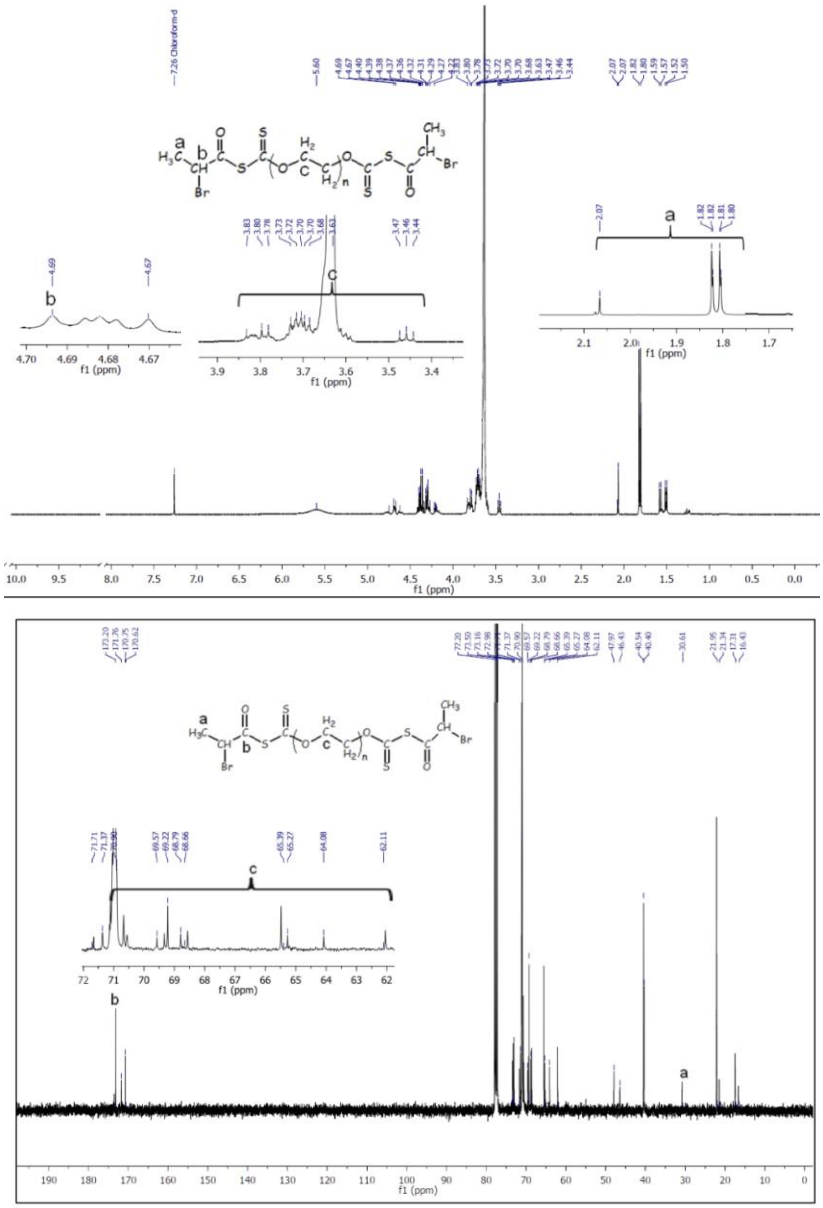


Fig. 2 — (a) ^{1}H NMRspectrum of PEG-Brand and (b) ^{13}C NMR spectrum of PEG-Br.

peak at 633 and 1234 cm^{-1}, and 1088 cm^{-1} are assigned to the stretching of C-S and C=S and the absorption band at 2874 cm^{-1} and 1455 cm^{-1} are assigned to PEG. FT-IR analysis confirms the presence of dithioate group in the macroinitiator which can be used for RAFT polymerization. In the ^{1}H NMR spectrum, the chemical shift at 4.69 ppm is assigned to methine protons of 2-bromopropionyl bromide unit and the range of 3.4-3.8 ppm, 1.8-2.07 ppm are assigned to the protons of methylene of PEG and the methyl protons of 2-bromopropionyl bromide unit, respectively. In the ^{13}C NMR spectrum, the chemical shift at 30.6 and 173.2 ppm are assigned to the carbon of methyl and carbonyl group of 2-bromopropionyl bromide unit and the range 60.11-70.9 ppm are assigned to the carbon of methylene group of PEG unit.

Preparation of Block copolymer

PEG macroinitiator was used to prepare PMMA-*b*-PEG-*b*-PMMA triblock copolymer via ARGET-ATRP of MMA as shown in Scheme 2. Fig. 1(b) shows the FT-IR spectrum of the tri block copolymer. The absorption peaks at 1733, 2989, 2948 and 1235 cm^{-1} are assigned to stretching frequency of carbonyl, methyl and carboxyl group of

PMMA part respectively while the absorbance band at 1448 cm^{-1} is assigned to the methylene group of PEG part. Figure 3 shows the NMR spectra of the block copolymer. In the ^{1}H NMR spectrum [Fig. 3(a)], the range of 3.36-3.72 ppm and 1.8-2.16 ppm are assigned to the protons of methylene of PEG and the methyl protons of 2-bromopropionyl bromide unit, respectively. The region from 0.87 to 1.0 ppm and 3.59 ppm are assigned to α-methyl proton and methoxy proton resonances of PMMA unit[23]. In the ^{13}C NMR spectrum [Fig. 3(b)], the chemical shift at 30.55 ppm is assigned to carbon of methyl group of 2-bromopropionyl bromide unit and the range 65.35-70.66 ppm is assigned to the carbon of methylene group of PEG unit. The peak in the large chemical shift region from 44.6-45.0 ppm is assigned to the quaternary carbon resonances, while the single peak at 51.97 ppm is assigned to methoxy (–OCH_3) group of PMMA[26]. Thus these FT-IR and NMR analyses of the prepared block copolymer confirms the successful preparation of the block copolymer.

Figure 4 shows a selected part of MALDI-TOF mass spectrum of PMMA-*b*-PEG-*b*-PMMA block copolymer prepared via solution ARGET-ATRP. The spectrum shows a constant difference of 44 mass units in two consecutive major peaks according to their occurrence in the spectrum. The peak at 613 [613=100.121*2 + 44*6 + ($C_4H_4O_2S_2$) 148.13] can be assigned to "block copolymer″ which has two MMA units attached to one end of PEG

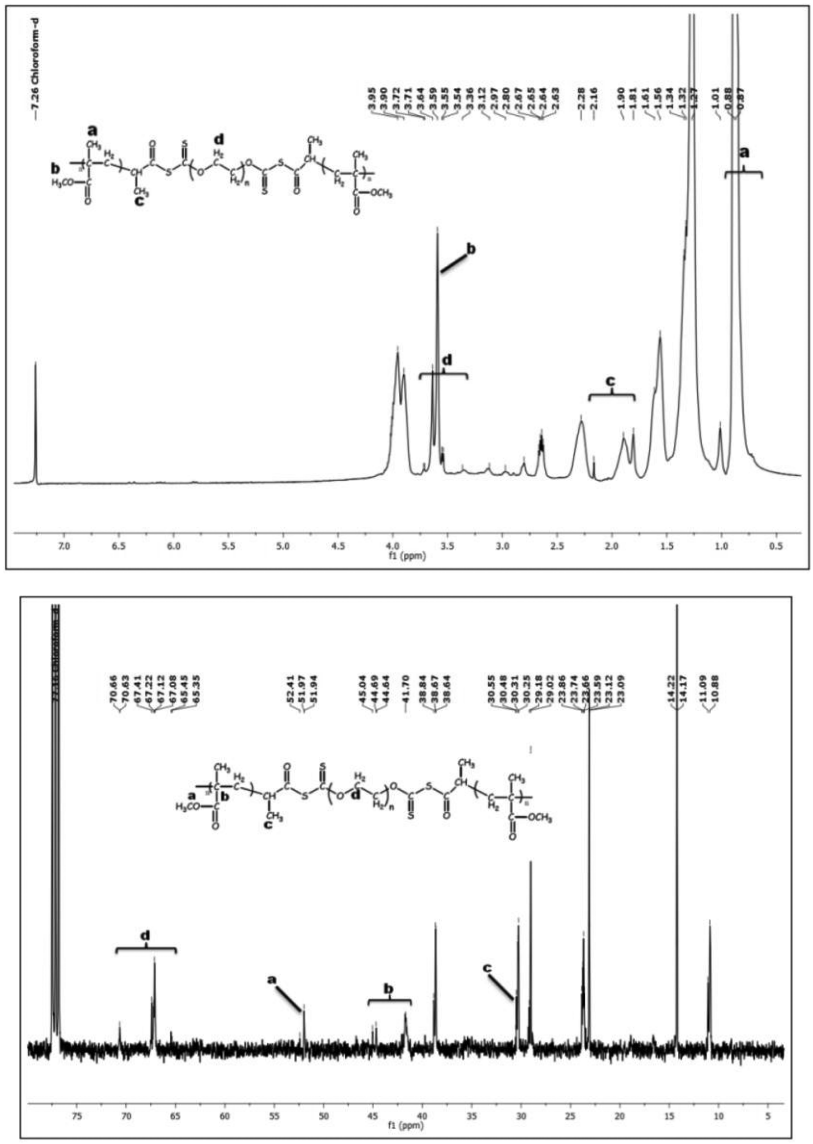


Fig. 3 — (a) ^{1}H NMR spectrum of PMMA-*b*-PEG-*b*-PMMA and (b) ^{13}C NMR spectrum of PMMA-*b*-PEG-*b*-PMMA.

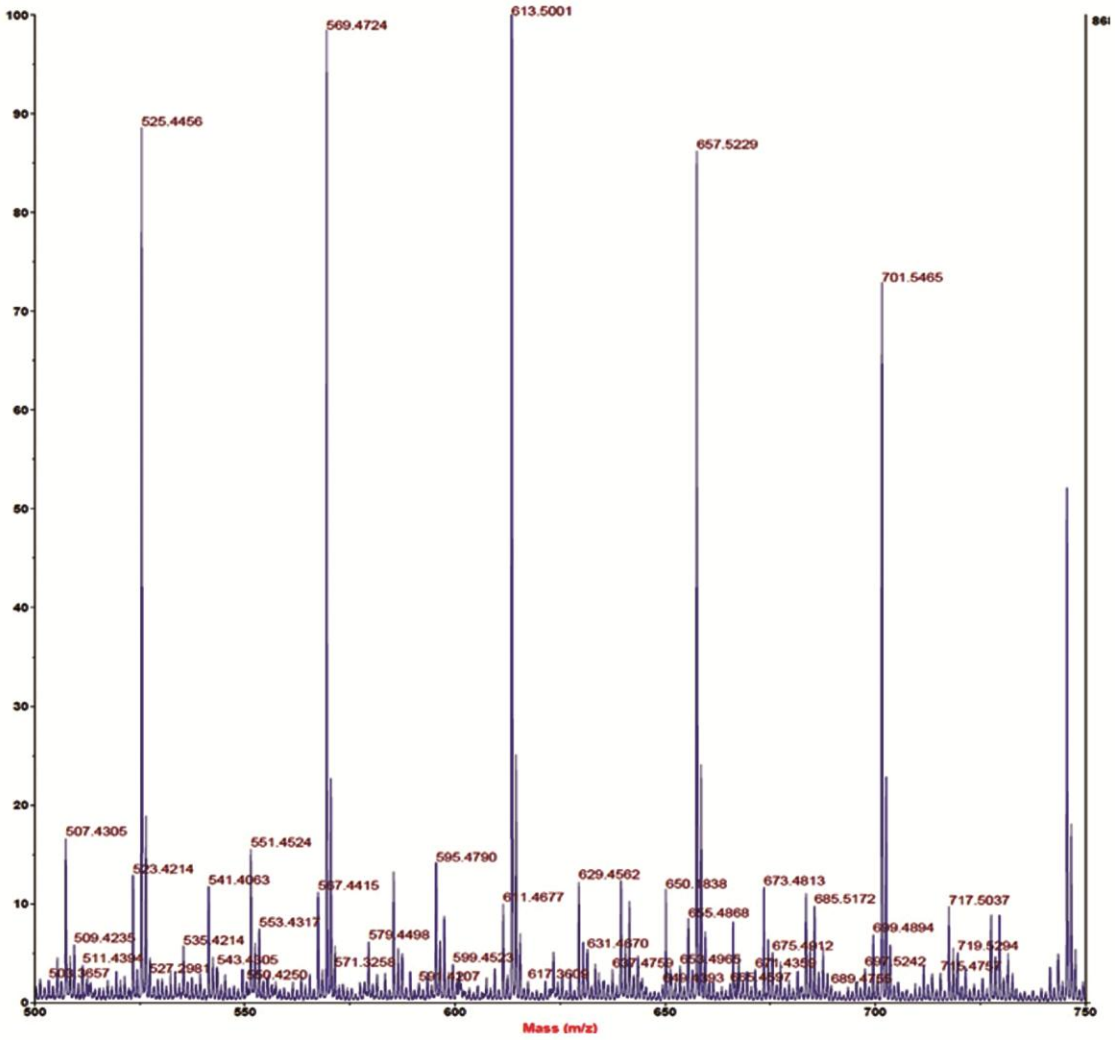


Fig. 4 — MALDI-TOF of PEG-*b*-PMMA-*b*-PEG.

macroinitiator (PEG-Br). Thus, the MALDI-TOF mass analysis of PMMA-*b*-PEG-*b*-PMMA confirms the presence of monomer MMA, dithionate and PEG parts in the block copolymer which eventually establishes the successful preparation of the block triblock copolymer.

Thermal and morphological study

Thermal study of a material is very important because it gives information about the thermal stability of the material. The thermal stability of a material is studied by TGA analysis. Figure 5 shows the TG and DTG curves of the block copolymer (PMMA-*b*-PEG-*b*-PMMA) and PMMA prepared by ARGET-ATRP. The thermal stability of the block copolymer was found to be better (T_{max} = 366°C) than the PMMA (T_{max} = 349°C). This is also reflected in the TG curves. The SEM image of PMMA-b-PEG-b-PMMA is shown in Fig. 6. In the SEM image, spherical ball type of morphology is seen.

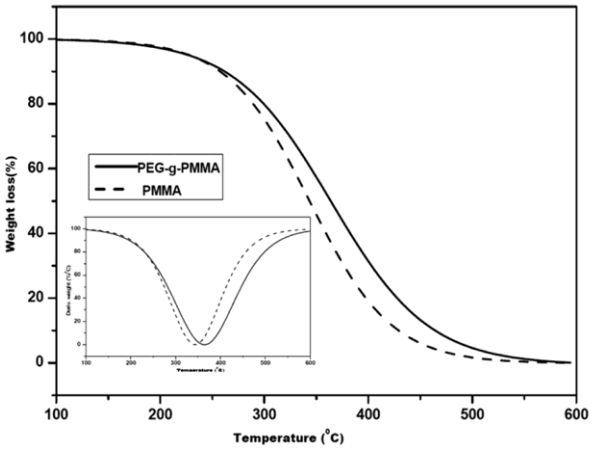


Fig. 5 — TGA and DTG curves for PMMA and PMMA-*b*-PEG-*b*-PMMA.

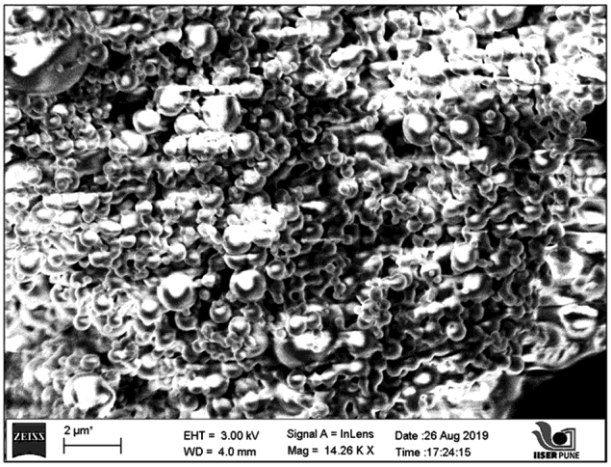


Fig. 6 — SEM image of PMMA-*b*-PEG-*b*-PMMA.

Conclusion

PEG based macroinitiator is synthesized successfully with RAFT and ATRP initiating sites. Presence of RAFT and ATRP initiating sites in the same PEG macroinitiator is confirmed by FT-IR, NMR and MALDI TOF analyses. This specially designed PEG macroinitiator is used to prepare tri block copolymer, PMMA-*b*-PEG-*b*-PMMA via ARGET-ATRP. The successful preparation of the block copolymer is confirmed by the FT-IR, NMR and MALDI-TOF analyses. Thermal stability of the prepared triblock copolymer is checked and found to be better than the neat PMMA prepared via ARGET-ATRP.

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