Annexure-X

UNIVERSITY GRANTS COMMISSION
BAHADURSHAH ZAFAR MARG
NEW DELHI-110002

Assessment Certificate

It is certified that the project entitled **"Studies on the controlled synthesis of linear and block copolymers by activators regenerated by electron transfer atom transfer radical polymerization (ARGET ATRP)"** by Prof. C. N. Murthy of **Applied Chemistry Department** has been assessed by the expert committee consisting the following members for submission to the University Grants Commission, New Delhi under the scheme of Major Research Projects:

Details of Expert Committee:

Sr. No.	Name of Expert	Remarks	Sign & Seal
1	Prof. Dr. N. V. Sastry Head, Dept-Chem. S. P. Univ. VV. Nagar, Gujarat	Work and progress is satisfactory	9/11 Professor & Head Department of Chemistry Sardar Patel University Vallabh Vidyanagar-388120 Gujarat
2	Dr. R. H. Patel Head, Dept. of Materials Science S. P. Univ. V V Nagar	Work done is satisfactory	Head G.H. Patel Institute of Materials Science Sardar Patel University Vallabh Vidyanagar-388120

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Summary of Findings

The summary of this research work is divided into four (4) major studies and their outcome as mentioned below

I. Investigation on reducing competency of β-cyclodextrin derivatives

II. Synthesis of linear homo polymers using non-conventional ATRP Initiators

III. Synthesis of Block copolymers via ARGET-ATRP

IV. Post-polymerization modification of acrylates block copolymers

I. Investigation on reducing competency of β-cyclodextrin derivative

The sugars are the prime constituents in diet of plants and animals. Sugars are generally termed as polyhydroxy aldehydes/ketones, the reducing sugars share their carbonyl group with one of the hydroxyl groups within the molecule to form 'hemiacetal' or 'hemiketal' typically in solutions. On the other hand, non-reducing sugars have cyclic-'acetal' and 'ketal' form, can not free its carbonyl groups for the reducing phenomena. Reducing sugar's free aldehyde group or an alpha-hydroxy ketone is capable of being oxidized in aldo- or keto-form at equilibrium. Analytically, there have been many techniques available for the determination of reducing sugars, among which, the chemical method uses an alkaline copper (II) reagent like Fehling's reagent or Benedict's reagent. In the mechanism, it is said to follow path from decyclization of sugar to give respective aldo- & keto- form under alkaline condition and enolization to get the brick red precipitates of Cu_2O from cupric complex of tartarate, citrate and carboxylate ions. The cyclodextrins (CDs) are made up of 5 or more glucose units with α-1,4-linkages in cyclic manner. Hence, they have the 'acetal' form to categories them as non reducing sugars. Although, knowing the fact that β-CD is non-reducing cyclic sugar, β-cyclodextrin (7 glucose units) have been studied for its reducing competency under the basic condition for the synthesis of Ag &/ Au nanoparticles. In the first report, Ritter et al used the N-isopropylacrylamide-co-β-CD polymer as independent reducing agent for silver nanoparticles. Recently, we have successfully described the role of β-CD not only as stabilizer for nanoparticles but also as reducing agent for Ag-Au bimetallic nanoparticles. The study revealed that β-CD also found to reduce the Ag/Au metals sequentially and hence not selective to metal ions. These two examples where β-CD was used in aqueous basic system, throw a light on the fact that the hydroxyl groups of β-CD could impart the little reducing character for the reduction of metal ions. This initiates us to check the reducing behavior of β-CD in non-aqueous solvents such as toluene and N,N-dimethyl formamide. The reason lies in the fact that the reduction of metal ion is of due to hydroxyl groups available.

In order to confirm the *in-situ* generation of Cu(I) from Cu(II) in the presence of CD, UV-VIS experiment was performed. As seen from the figure 1, the UV-VIS spectrum of Cu(II)/PMDETA complex with β-CD in toluene did not show characteristic d-d band transition in the region of 450-800nm which might be due to heterogeneous mixture. Whereas upon heating the same mixture at polymerization temperature for 30 minutes, the contents become homogeneous and a new absorption band appears at 282nm that can be attributed to Cu(I)/PMDETA complex only as β-CD does not absorb in this region.

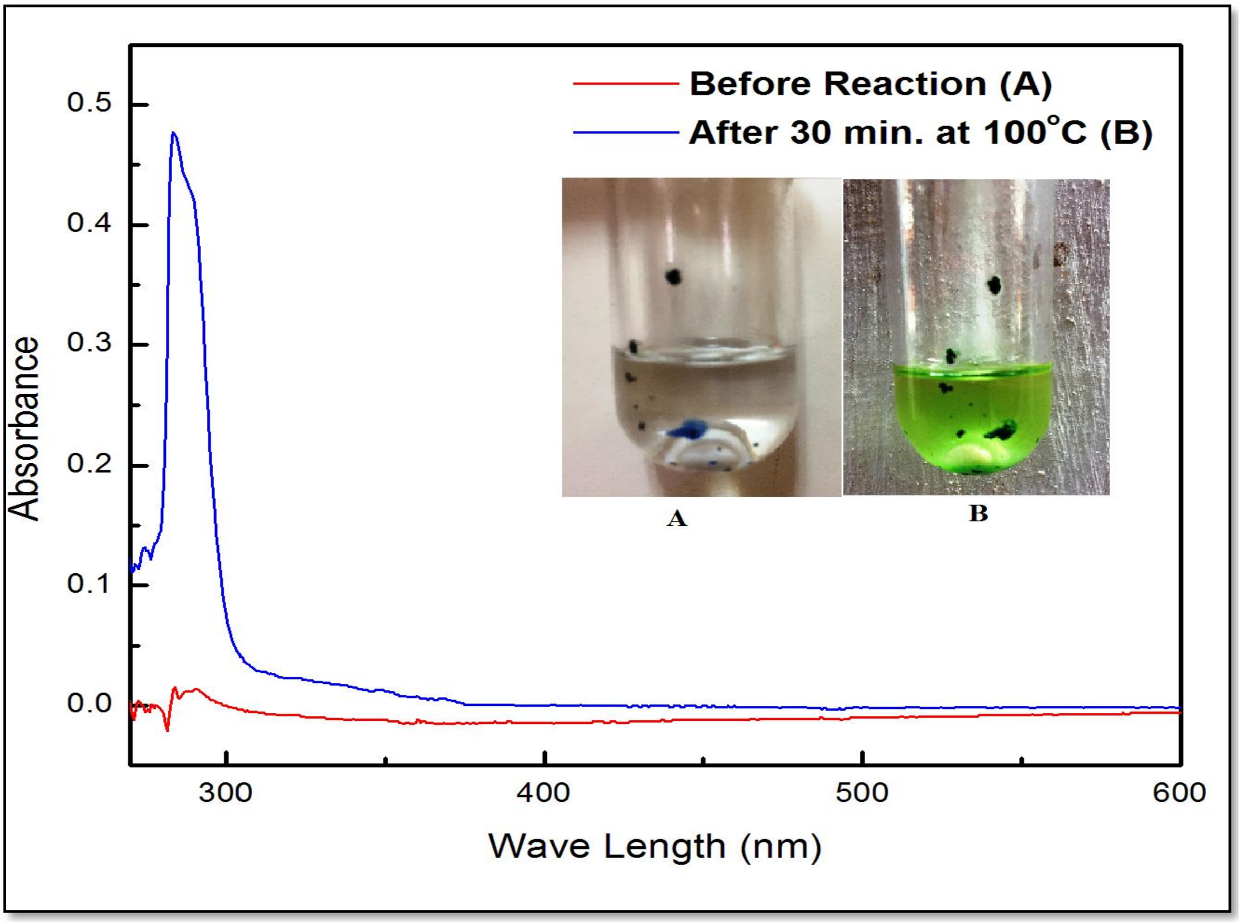


Figure 1 This study was performed with CuBr$_2$:PMDETA:β-CD = 0.17:1:0.17 milli molar ratio under argon atmosphere and 0.1 ml sample was withdrawn and diluted 100 times using toluene. The UV-VIS spectrum was taken immediately (A) and after keeping reaction mixture for 30 minutes at 100^{o}C (B). The spectra of toluene insoluble Cu(II)/PMDETA complex (A) shows no specific absorption where as Cu(I)/PMDETA complex (B) showed absorption maxima at 284nm. It explains that during the course of heating period Cu(II)/PMDETA complex is reduced to Cu(I)/PMDETA by hydroxyl groups of β-CD.

Thus the UV-VIS spectrum reveals that Cu(II)/PMDETA complex converts Cu(I)/PMDETA in the presence of β-CD due to the reducing character of β-CD. No other reactions can explain the conversion of Cu(II) to Cu(I) reversibly. The complete reduction of Cu(II) to Cu(0) or Cu(I) could not possible as position of Cu(II) in the electrochemical is lower than the easily reducible Ag(I) and Au(III) salts. It is worth to mention that due to the same halogen (-Br) attachments on catalyst hence the color change of the copper complex is not the ligand exchange reaction but the conversion of Cu(II) to Cu(I) can only happen under the influence of β-CD and hence β-CD possess mild reducing character due to their hydroxyl groups only. In another similar experiment, we used DMF as solvent and performed the UV-VIS analysis (t=0 min &

t=100^{o}C) to ensure the reduction of cupric ion using β-CD and it does the reduction and showed red shift with change of absorption maxima 16nm from 282nm to 298nm for Cu(II) and Cu(I) respectively (Figure 2).The controlled experiment was conducted using same mole ratio of catalyst, ligand and β-CD.

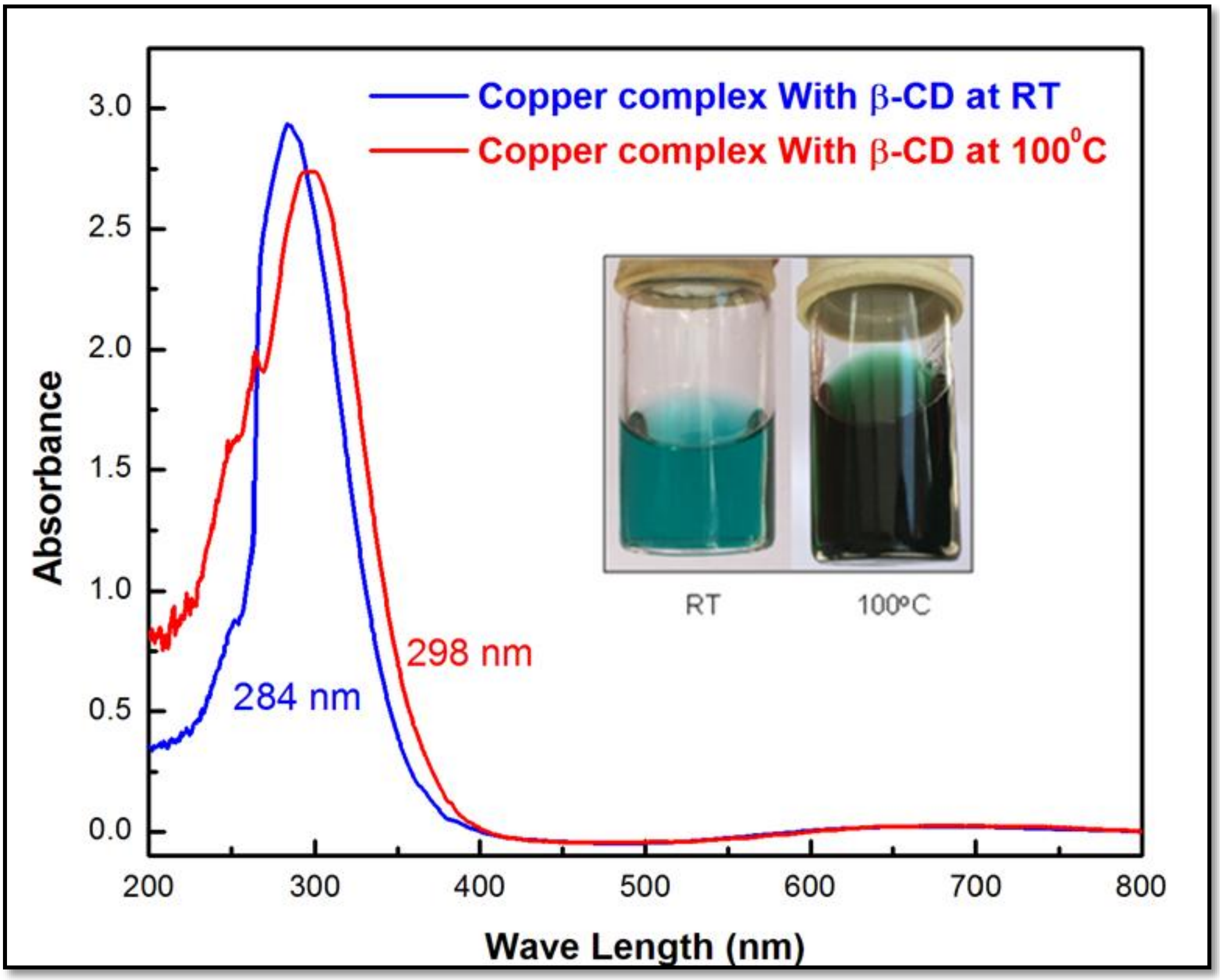


Figure 2 UV-VIS spectrum of β-CD with $CuBr_2$/PMDETA complex in DMF

In the above UV-VIS spectra, the shift of absorption maxima suggest the reduction but the peak height which covers the region of Cu(II)/PMDETA complex at RT which corresponds to reducing competency of β-CD which is mild and hence the Cu(II) complex is not completely converted to Cu(I) but it exists in both. To check the relative participation among the primary and secondary hydroxyl groups of β-CD in reduction of Cu(II)/PMDETA complex. We performed experiment replacing β-CD with heptakis(2,3,6-tri-O-methyl)-β-CD where all hydroxyl groups are methylated for the reducing phenomena at RT & at 100^{o}C. We found that there were no changes in UV-VIS spectrum before and after maintaining the reaction mixture at 100^{o}C. This indicates that due to protection on hydroxyl groups the reduction of Cu(II)/PMDETA could not occur. On the other hand with protection on 2, 6-position hydroxyls of β-CD, the physical colour change was observed and same was appeared in UV spectrum. The spectrum of both completely protected hydroxyl β-CD and partially protected is shown in Figure 3. The spectrum was recoded and found that with heptakis(2,6-di-O-methyl)- β-CD in which one secondary hydroxyl group is available for confirming reduction of Cu(II) by hydroxyl groups.

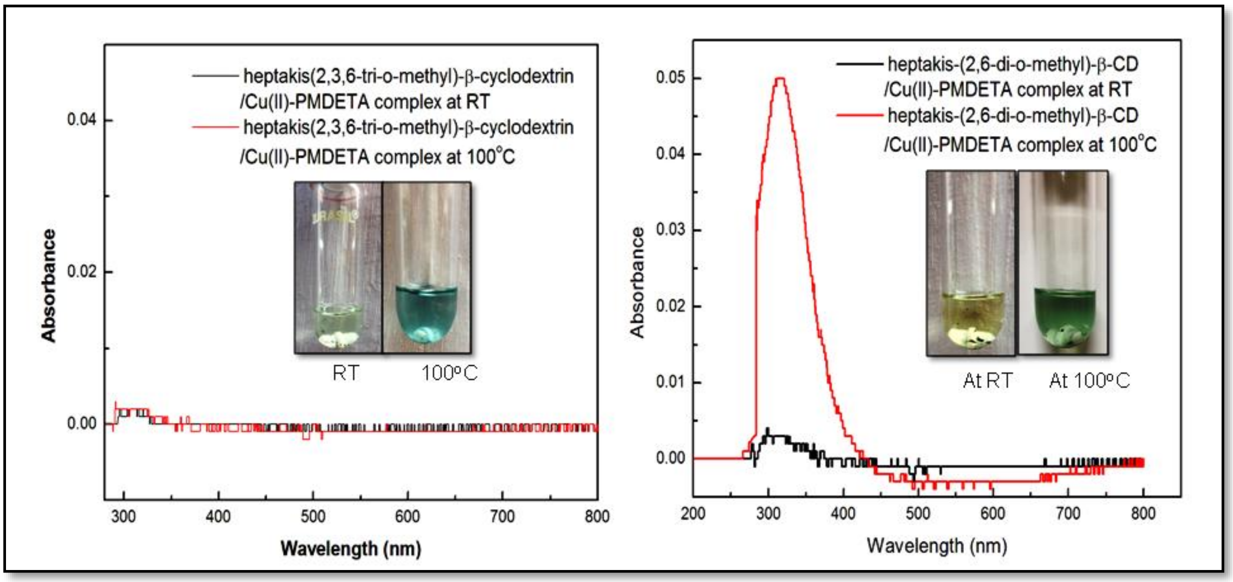


Figure 3 methyl substituted β-CD with Cu(II)/PMDETA complex for hydroxyl participation of β-CD in mild reduction of Cu(II)/PMDETA complex at 100^{o}C.

Conclusions

i. β-CD has active hydroxyl groups available for the mild reduction of the Cu(II)/PMDETA under non-aqueous solvent system.

ii. The reducing character of β-CD can be utilized under high temperature in the systems with low Cu(II) used as catalyst.

iii. The reduction phenomena and co-existence of both oxidized and reduced copper complex was confirmed using UV-VIS analysis.

II. Synthesis of linear homo polymers using non-conventional ATRP Initiators

The synthesis of macroinitiators require quantitative and formation of stable radical by redox reaction between transition metal halide and initiator both having common halogen end group. The initiators being used in ATRP based polymerization techniques are carbon containing halogen must attached to three (3) carbons so as upon hemolytic linkage of C-X will form 3^{o}-radical. The stability of reactive radical is important for the fast initiation and rapid deactivation of active species for the narrow molecular weight distribution of the resulting polymer. The most common initiators are halogenated alkanes, benzylic halides, α-haloester, α-halonitrile and sulphonyl halides. The most explored initiators are those who form tertiary radical on halogen exchange during initiation. The halo alkanes are cost efficient but very few have been utilized so far. In this study we used series of primary alkyl halides although having the knowledge of less efficiency of primary halides during initiation. We performed ATRP of styrene with different carbon chain starting from 1,3-dibromo propane (1,3-DBP), 1,4-dibromo butane (1,4-

DBB), 1,5-dibromo pentane (1,5-DBP), and 2,3-dibromo butane (2,3-DBB). The experimental details are as per below.

Table 1.Synthesis of polystyrene homo polymers using dibromo alkanes as initiator

Sr. No.	**Dihalo-Initiator**	**[M]:[I]**	**Time (hrs.)**	**Yield (%)**	**$M_{n\ theo.}$ $(1x10^{-3})$**	**$M_{n\ GPC}$ $(1x10^{-3})$**	**PDI**
1	1,3-DBP	50:1	3	12.43	6.67	19.29	1.29
2	1,3-DBP	50:1	4	12.65	6.79	21.18	1.30
3	1,3-DBP	50:1	5	12.41	6.66	18.33	1.25
4	1,3-DBP	50:1	6	12.09	6.49	19.62	1.22
5	1,3-DBP	50:1	24	35.44	18.65	37.14	1.38
6	**1,3-DBP**	**50:1**	**36**	**40.02**	**21.04**	**24.20**	**1.29**
7	**1,3-DBP**	**50:1**	**144**	**89.02**	**40.56**	**48.88**	**1.26**
7	2,3-DBB	50:1	24	0.70	0.58	2.73	1.33
8	2,3-DBB	50:1	24	1.25	0.87	1.54	1.37
9	1,4-DBB	50:1	24	6.48	3.59	5.34	1.28
10	1,5-DBPe	50:1	24	2.51	1.54	2.32	1.26

The ATRP was conducted in bulk using CuBr and PMDETA as catalyst/ligand complex during the course of study. The reaction temperature was kept at 100^{o}C with mole ratio of M:I:C:L=50:1:0.1:1 in which copper was kept 100 ppm. The synthesis of polystyrene homo polymers reveals that the ATRP could be happen with primary halides also. The initiation efficiency is found to be low as compared to other earlier reported ATRP initiators because of the fact that primary radicals are less stable than the 2^{o} & 3^{o} radicals, further more the low catalyst intake also affects in the formation of quantitative radicals. The rate of activation is hence found to be very slow which result in inefficient quantity of radicals during the initiation. Therefore, the rate of initiation directly decreases the rate of propagation, as seen from the Figure 4 that the rate of polymerization is slow and take longer period of time for the higher monomer conversion. It takes almost 5times more time to reach the 90% conversion from 12%.

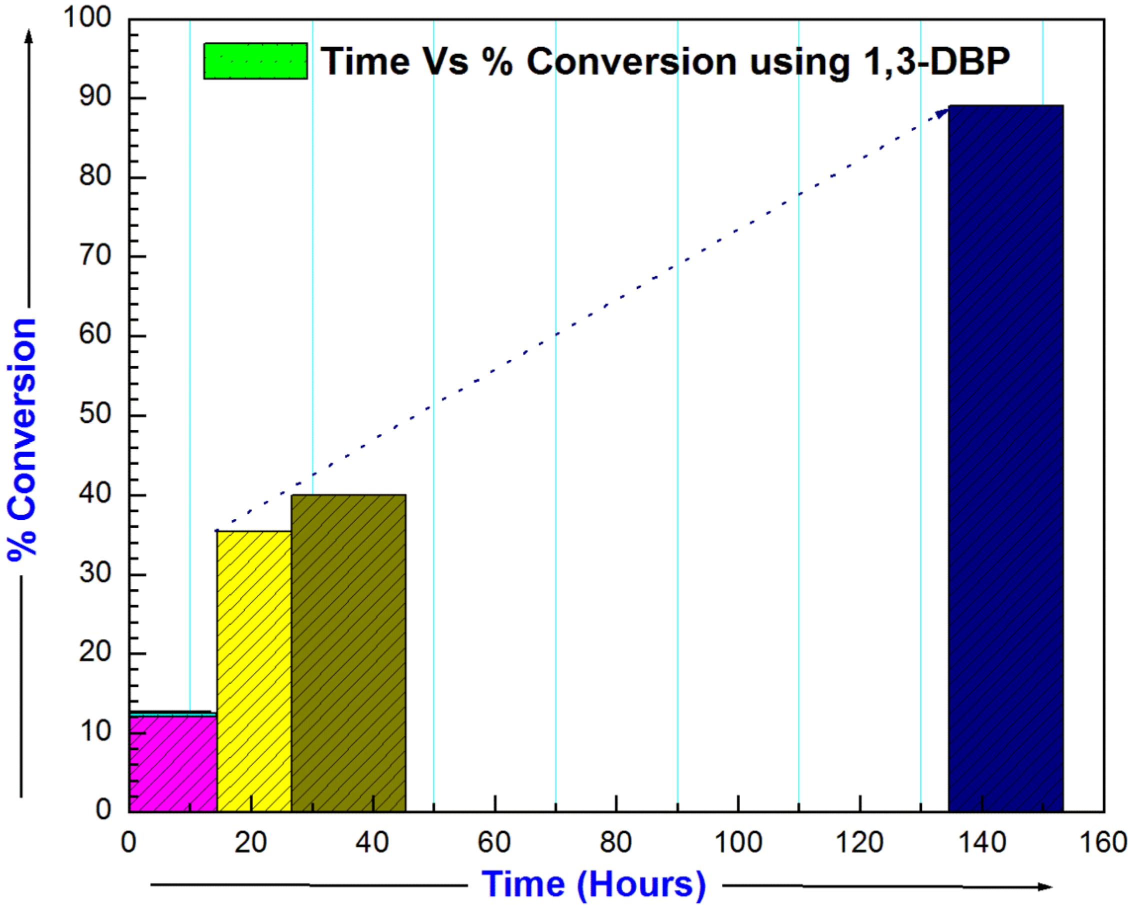
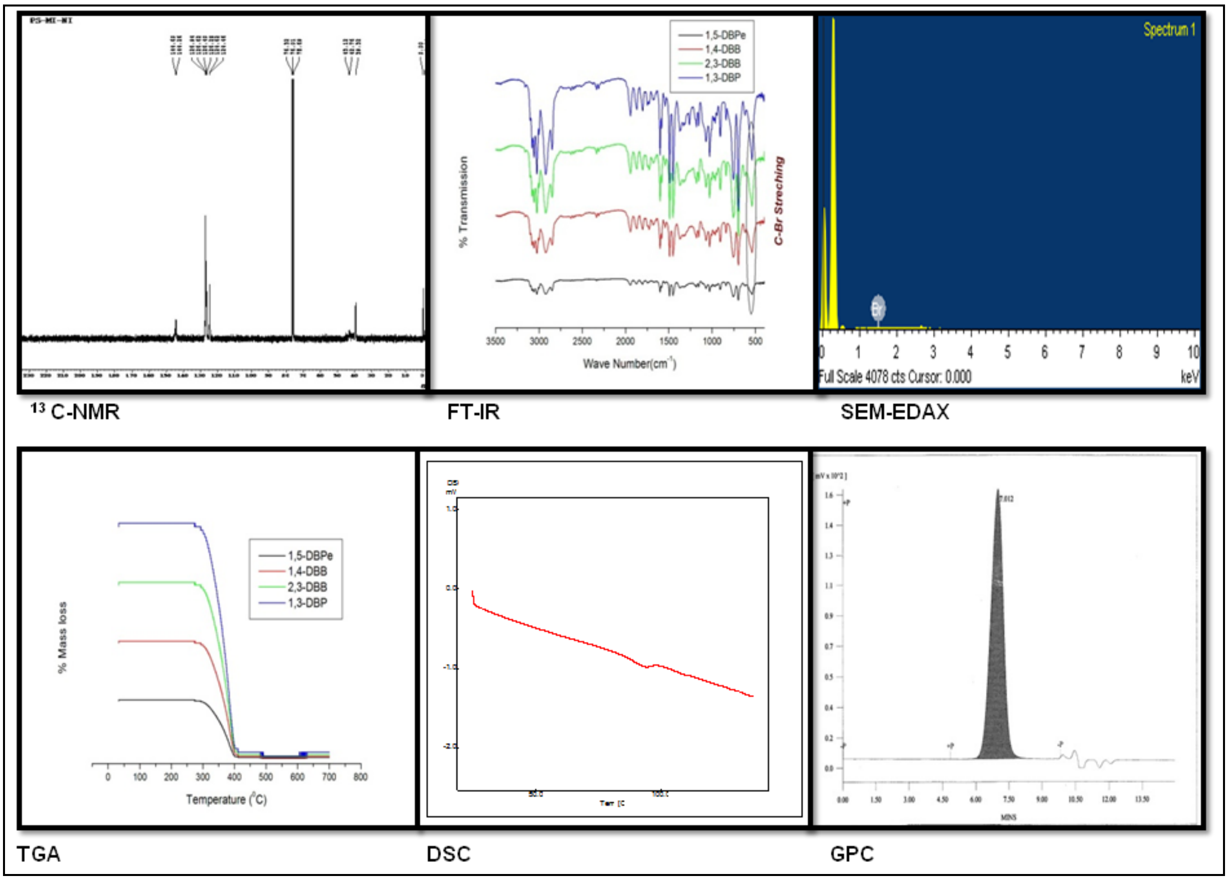


Figure 4 Time Vs %Conversion using 1, 3-DBP

The polymerization is found to impart the better control at the higher conversion which having close value of number average molecular weight (M_n) with the theoretical values (table 1, entry 6-7). This study revealed that the polystyrene homo polymers via the range of primary halides have dependency over the skeleton of the initiator. Here, it is found that even though having similar general structure but they have the reactivity differences which can be seen from the monomer conversion too. The Polystyrene synthesized using these 4 new initiators with 24 hours reaction time, the monomer conversion is highest with 1,3-DBP among all. This confirms that although primary haloalkanes are used but they have different reactivity towards polymerization.

The polymers characterization was done with spectroscopic techniques like ^{13}C-NMR, FTIR. In ^{13}C-NMR of polystyrene synthesized using 1,3-DBP show 39.7 ppm for the carbon attached to bromine and C-Br stretching vibration at 698.25 cm^{-1}for the bromine end functional polystyrenes. Not only these, but we confirmed the bromine attachment using SEM-EDAX also where %Br was 0.07% near the calculated. The thermal analysis indicates that the single and complete degradation is observed between 275^{o} to 485^{o}C using TGA, which is identical for polystyrene chain. The glass transition temperature of 94.2^{o}C was confirmed using DSC analysis. In the GPC chromatogram with single peak shows that single polymer has resulted at the end with sharp and narrow molecular weight distribution. Figure 6 includes all above characterization reports for the clearer view.



^{13} C-NMR FT-IR SEM-EDAX

TGA DSC GPC

Figure 5 characterization of polystyrene synthesized using 1, 3-DBP

Conclusion

(a) Synthesis of polystyrene linear homo polymers is successful using non-conventional primary halides as ATRP initiator.

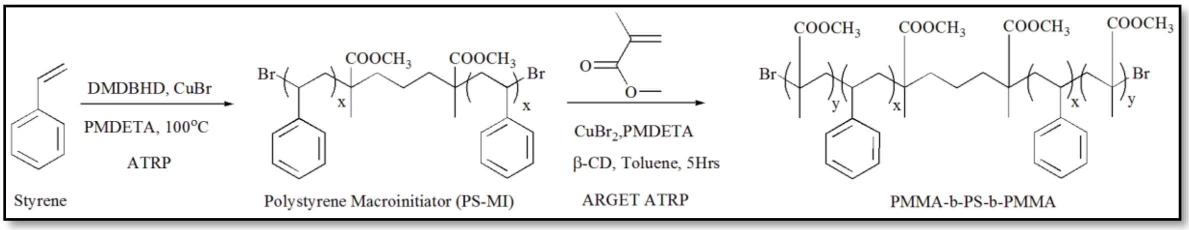
(b) The initiation is found to be slow due to formation of primary radical that impart slower rate of polymerization with narrow molecular weight distribution.

(c) The polymerization follows ATRP under high monomer conversion where the value matches the calculated molecular weights due to low efficiency of initiators (f < 0.5)

(d) Among these 4 new initiators 1, 3-dibromo propane has comparable reactivity for styrene.

III. Synthesis of block copolymers via ARGET-ATRP

In the first study, we identified the reducing potency of β-CD imparted by its hydroxyl functionalities present. In the search for mild reducing agent for ARGET-ATRP, hydroxyl groups have showed new hope in the role of reducing agent (RA). Recently, Wang et al reported how alcohols could work for the reduction of Cu(II) for activators generated by electron transfer atom transfer radical polymerization (AGET-ATRP) of acrylates and styrene. Liu et al used for the reduction of Cu(II) in ARGET ATRP of MMA. It was observed that the primary and secondary alcohols actively reduced Cu(II). Not only Cu(II), but Xie et al showed Fe(III) could also be reduced to Fe(II) where Fe mediated AGET-ATRP of methyl methacrylate in DMF was performed. To facilitate the redox reaction mild base sodium carbonate was used. Aiming to achieve improved reducing property by multiple hydroxyls as an active reducing site and biocompatible in nature, we choose cyclic sugars particularly β-cyclodextrin, which comprises 7 primary and 14 secondary hydroxyls groups active for reducing Cu(II) under solvent. We recently showed the reducing property of β-CD for the formation of the Ag & Au NPs. Not only that, the reducing property is active to carryout sequential reduction to give core-shell nano particles of Ag@Au and Au@Ag in the aqueous medium. With this background and to further prove its reducing character, we performed the use of β-CD as a reducing agent for Cu(II)/PMDETA complex in copper mediated ARGET ATRP of MMA on difunctional polystyrene macroinitiator for PMMA-*b*-PS-*b*-PMMA triblock copolymerization (Scheme 1). Here in situ generation of Cu(I)/PMDETA is achieved through redox reaction of β-CD and Cu(II)/PMDETA for the initiation of polymerization. Kinetics of the polymerization was carried out to understand the controlled nature during the course of polymerization. We have not just only explored the use of β-CD for its reducing character but also validated it for the synthesis of block copolymers in solution ARGET-ATRP. We found that reducing competency was comparable at high temperature and along with these the effect of concentration of β-CD and copper were also studied as shown below table 3-5.



Scheme 1. Synthesis of PMMA-b-PS-b-PMMA triblock copolymer

Table 2 Synthesis of PMMA-*b*-PS-*b*-PMMA triblock copolymers

Sr. No.	**Experiment**	**$[M]_o:[I]_o$**	**% Yield**	**$^bM_{n\ theo.}$**	**$M_{n\ GPC}$**	**PDI**
1	PS-MI[a]	20:1	55	1495	1140	1.05
2	BAB1	200:1	52	11575	13892	1.28
3	BAB2	300:1	53	15804	19128	1.37
4	BAB3	400:1	50	21250	21920	1.20
5	BAB4	500:1	52	26989	28736	1.23
6	BAB5	750:1	54	41550	42232	1.30

[a] Styrene:DMDBHD:CuBr:PMDETA=20:1:0.2:0.2 in bulk. [b] $M_{n\ theo.}=[MI/I] + [M]_o/[MI/I]_o*[M_w]_{monomer}*$yield. BAB1 to BAB5 – 100 vol% toluene vs. [M] at 100°C for 5 hours.

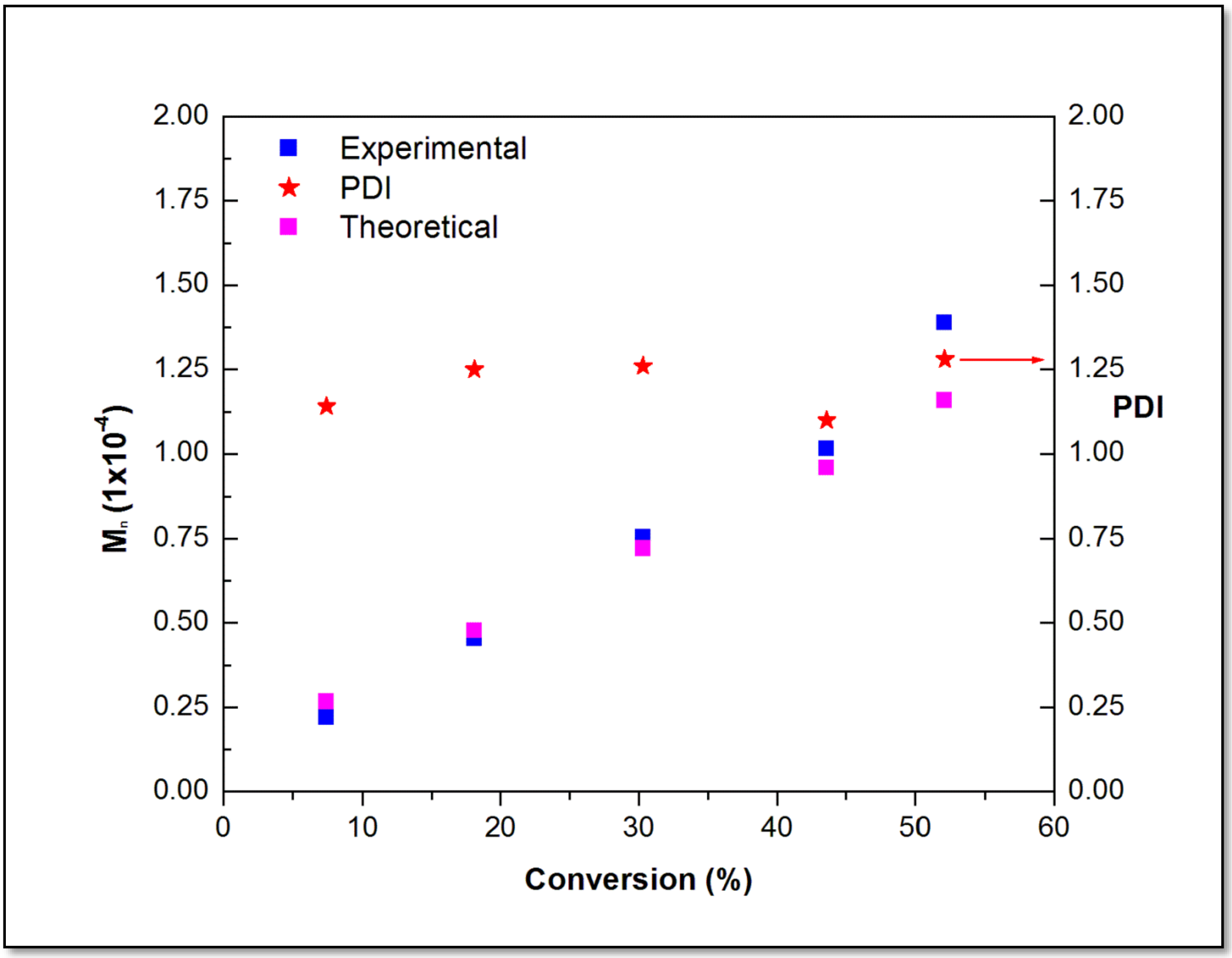


Figure 6 Kinetics of BAB1 using β-CD as reducing agent at 500ppm Cu.

Table 3 Synthesis of PMMA-*b*-PS-*b*-PMMA triblock copolymers at different temperature

Sr. No.	**SET**	**Temperature °C**	**%Yield**	**$^bM_{n\ theo.}$**	**$M_{n\ GPC}$**	**PDI**
1	T1	80	10.0	3163	2511	1.20
2	T2	60	10.0	3103	2518	1.16
3	T3	RT (28)	8.0	2663	2412	1.16

The polymerization was done using M:I:C:L:RA = 200:1:0.17:1:0.17 in 100vol% toluene vs [M] at above given time for 5 hours.

Table 4 Effect of concentration of copper and reducing agent

Sr. No.	**Cu ppm**	**[Cu]:[RA]**	**%Yield**	**$M_{n\ theo.}$**	**$M_{n\ GPC}$**	**PDI**
1	500	1:1	52	26989	28736	1.23
2	250	1:1	50	26328	26301	1.32
3	100	1:1	46	23974	21610	1.20
4	500	1:3	53	27580	29739	1.24

5	500	1:5	54	27930	30920	1.27
6	500	1:0.5	51	26778	29072	1.27

The polymerization was using M:I:C:L:RA = 500:1:0.17:1:0.17 in 100vol% toluene vs [M] at 100^{o}C for 5 hours.

Conclusion

(a) Synthesis of PMMA-PS-PMMA triblock copolymer using reducing hydroxyls of β-CD is achieved

(b) The block copolymerization follows 1st order kinetics and values of $M_{n\ GPC}$ matches with the calculated M_n.

(c) ARGET-ATRP of acrylates block copolymers was achieved till 100ppm of copper concentration.

(d) The reducing behavior of β-CD is a state function and under high temperature of the reaction it could facilitate mild reduction of Cu(II).

IV. Post-polymerization modification of block copolymers

The synthesis of block copolymers is often used to impart the dual functionality within the same molecule. In which the selective solubility of one block interact to fulfill the application. These happen due to self assembly behavior of the polymer chain into the selective solvent. We performed the hydrolysis of the PMMA blocks using two techniques (i) acid catalyzed hydrolysis and (ii) base catalyzed hydrolysis for the formation of PMAA-PS-PMAA in which completely different segments can be obtained i.e. hydrophilic PMAA chains and lyophilic PS chains. The modification details are as per below.

Acid catalyzed hydrolysis:

In this method, triblock copolymer is dissolved in acidic methanol with ratio of 20:80 and reaction mixture is then allowed to reflux for desired time (18-24hours). This period of reflux can be change upon the requirement of completion of hydrolysis, the hydrolyzed polymer is converted to water soluble polymer and hence the indication of clear viscous reaction mixture is resulted. Meanwhile, the methanol is then evaporated and excess acid is neutralized using mild basic solution of sodium carbonate. The polymer solution is the added to ethyl acetate for removal of salt and the resultant ethyl acetate is removed to get purified hydrolyzed polymer. The average degree of hydrolysis is >50% based on the ^{1}H-NMR and 61%yield by weight.

Base catalyzed hydrolysis:

The triblock copolymer (M_n~10k) is taken into THF and to it KOH dissolved in water is added under stirring. Now, methanol is added to this two phase system to make the homogeneous mixture. The reaction mixture is then refluxed for 24 hours for the hydrolysis. At the end of the reflux the some part of polymer is fallen out as precipitates, the reaction mixture is dried by complete evaporation of methanol and THF. The polymer resulted is then re-dissolved in water and again put for18 hours reflux. The reaction mixture is then cool to RT and mixture of water in glacial acetic acid is added to it, toluene is added in order to separate out un-hydrolyzed PMMA blocks from the PMMA block copolymers. The aqueous layer is separated out and evaporated under reduced pressure that results in dried purified PMAA-PS-PMAA triblock copolymer. The characterization of this block copolymer is done using ^{1}H-NMR where the earlier ester proton of 3.6 δppm is absent completely it means that all the ester of the PMMA blocks are converted into PMAA. It was further checked using FT-IR spectrum in which broad –OH of acid is found within the region of 3000-3500 cm^{-1}.

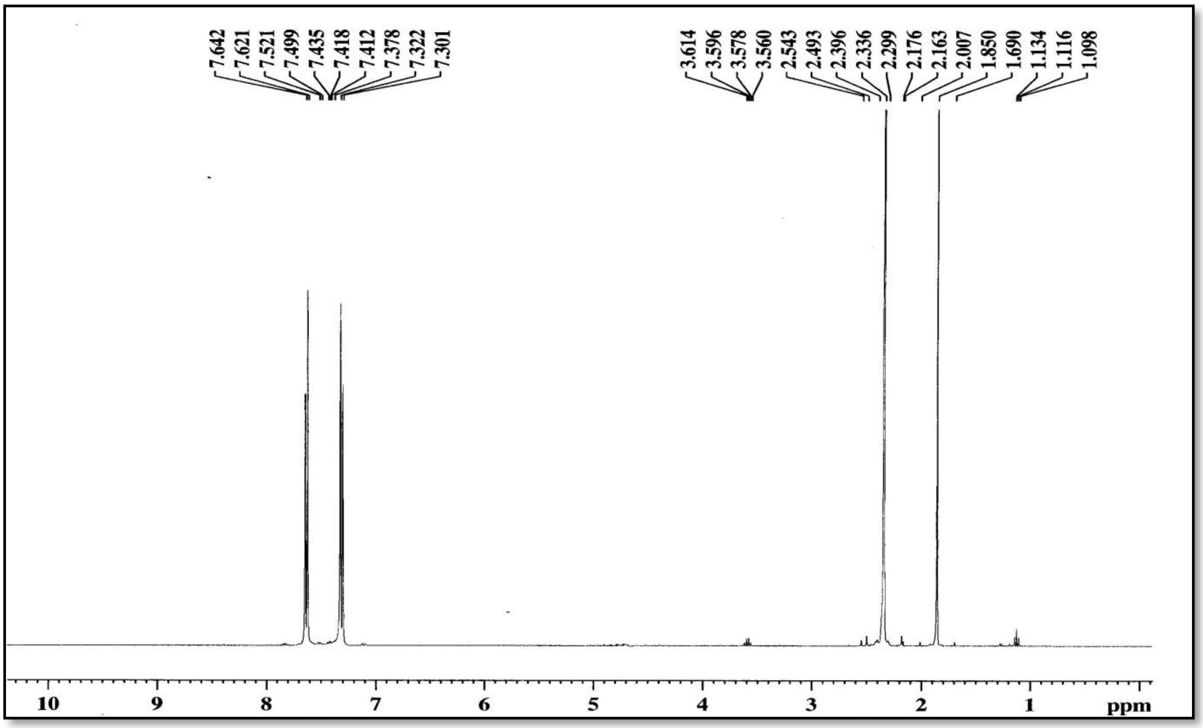


Figure 7 ^{1}H-NMR of PMAA-PS-PMAA triblock copolymer

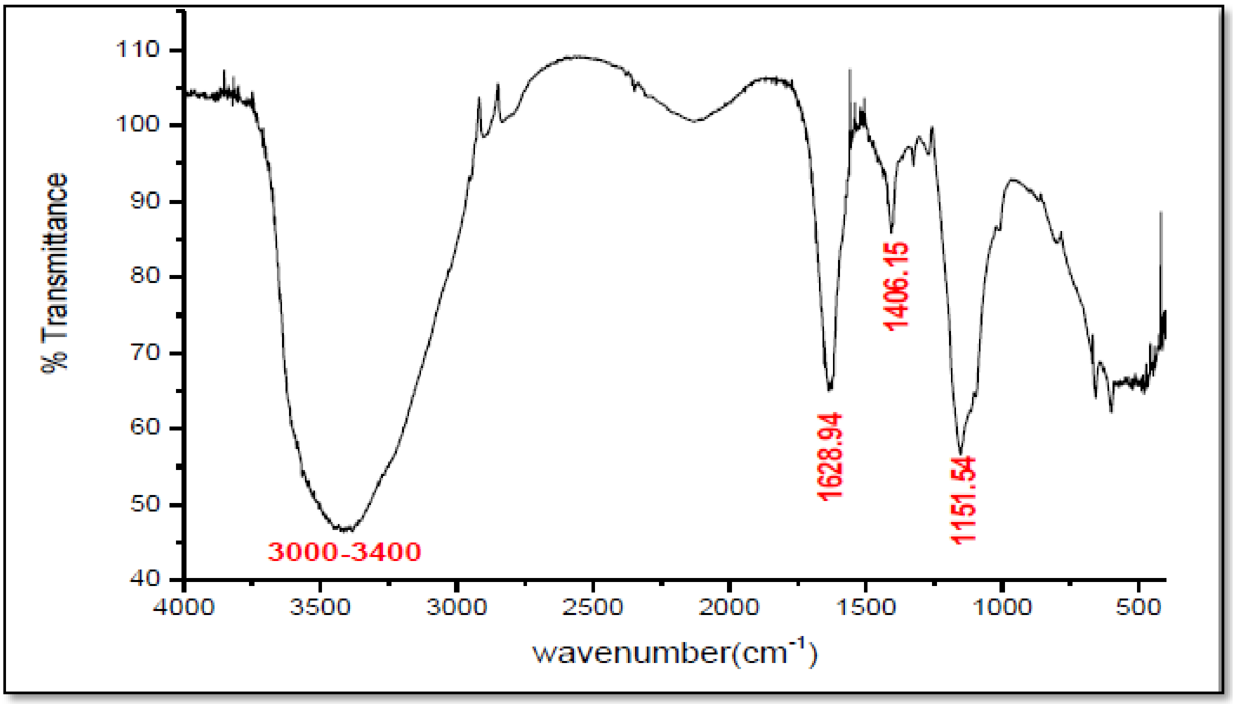


Figure 8 FT-IR of PMAA-PS-PMAA triblock copolymer

The most important observation of the block copolymers is to study the self assembly of the selective block in solvent. We took 1mg of polymer in toluene and in water to understand the self-assembly of the selective blocks under the influence of the solvent. The hydrolyzed triblock copolymer which has hydrophilic –OH groups of PMAA blocks arrange in two ways with the solvent. In water these methacrylic acid blocks goes towards inside core and polystyrene chains is to be arranged towards outer side. The graphical representation is shown below.

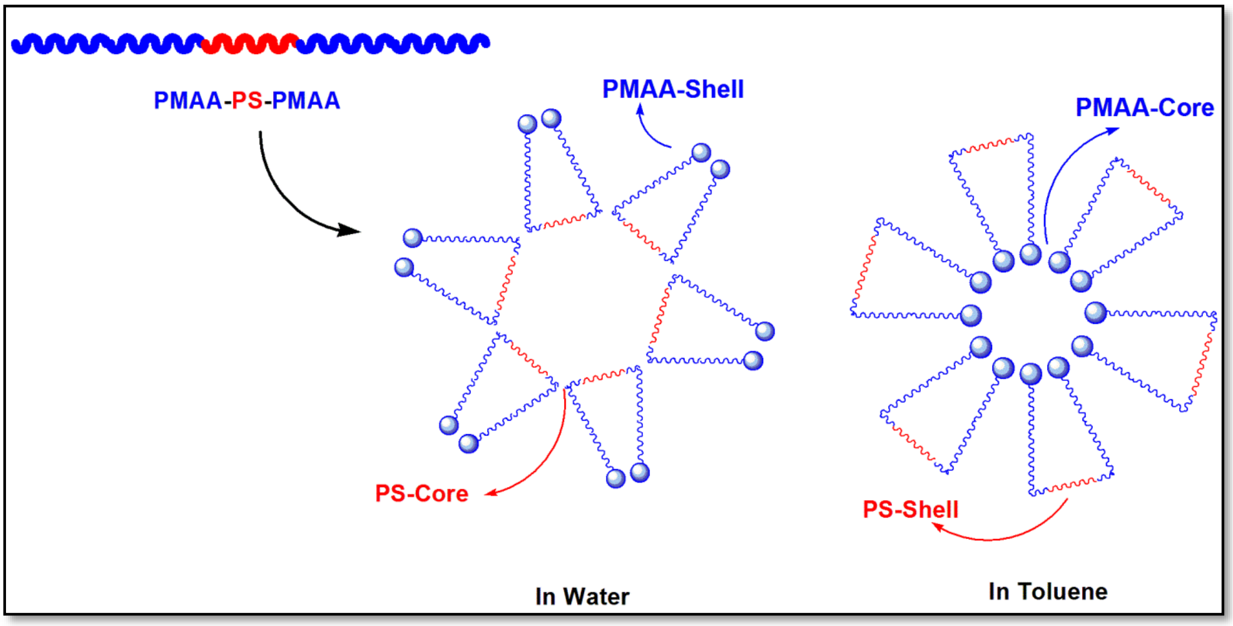


Figure 9 Self-assembly of PMAA-PS-PMAA in solvents

The self assembly was characterized using dynamic light scattering (DLS), the hydrodynamic diameter of the self assembled polymers were analyzed in water and found to be ~360 nm and in toluene ~100 nm. It has been reported that the self assembly <30 nm result in spherical where as 80-300 nm range result in core-shell type self assembly. In the figure 8, DLS of triblock copolymer confirms that the polymers are distributed uniform in size with only 1(one) peak. This explains the triblock polymer is of single compound with two distinct behaviors with water and toluene.

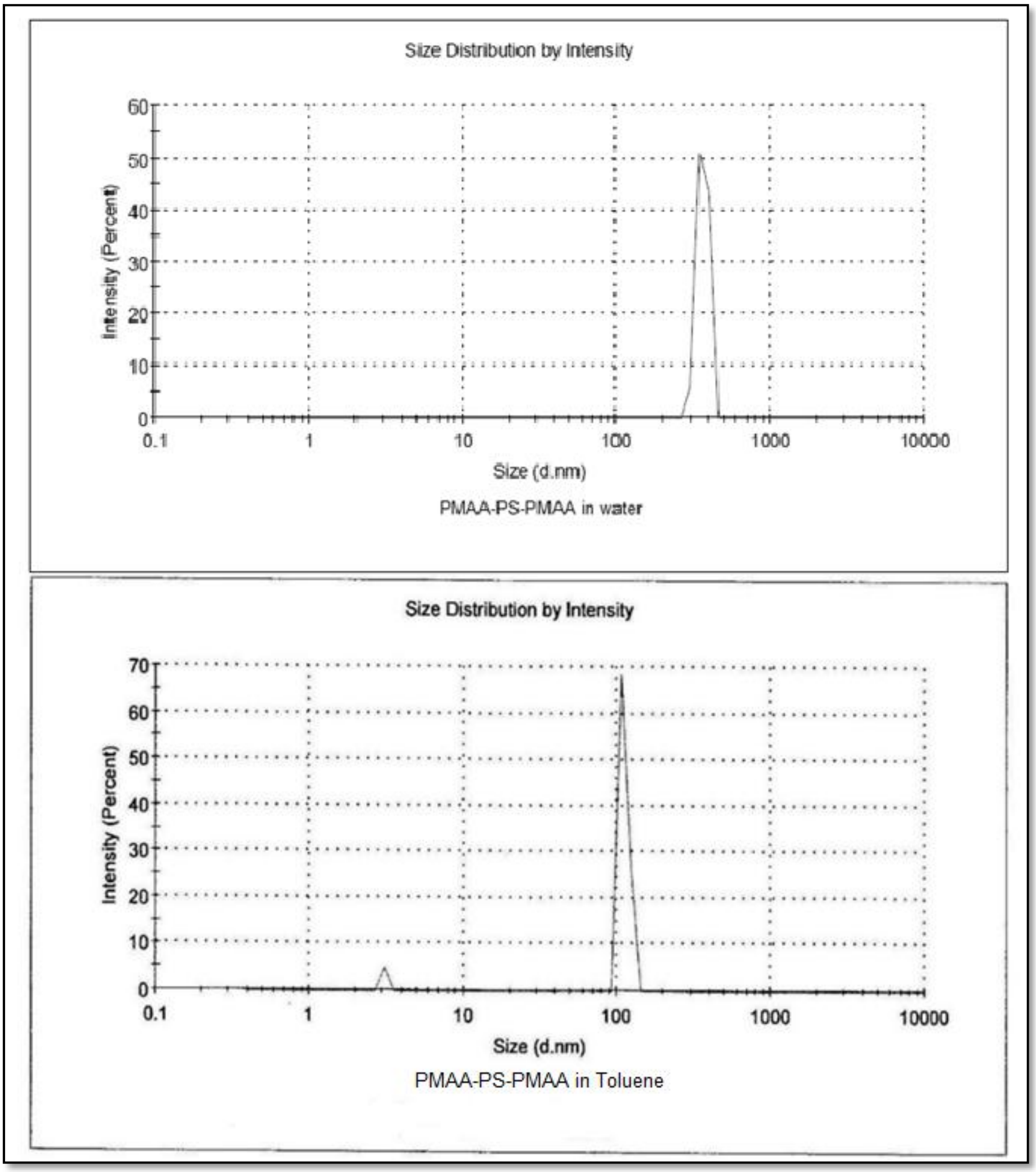


Figure 10 DLS of triblock copolymer in water and toluene

Conclusion

(a) PMMA-PS-PMMA triblock copolymer was hydrolyzed successfully using acid and base and supported by ^{1}H-NMR, FT-IR analysis.

(b) The modified base catalyzed method of hydrolysis which uses solvent to separate out un-hydrolyzed triblock copolymer gave high degree of hydrolysis.

(c) Self-assembly of selective blocks is studied using DLS technique.

(d) The uniform size distribution blocks are obtained in both aqueous/organic solvent.

(e) The hydrolyzed triblock copolymer show core-shell type flower like structure depending on selective solvent.

Outcome

1. ARGET-ATRP using β-CD as reducing agent for the synthesis of PMMA-*b*-PS-*b*-PMMA Triblock copolymers, Pavan Karkare, Santosh Thakur, C. N. Murthy* *J. App. Polym. Sci.* 2019, **136**, DOI:10.1002/app.47117
2. Post-polymerization modification of acrylate triblock copolymers synthesized via homogeneous ARGET-ATRP, Pavan Karkare, C. N. Murthy* (Paper under preparation)
3. Investigation onto efficiency of primary halides for as initiator for atom transfer radical polymerization, Pavan Karkare, C. N. Murthy* (Paper under preparation).

Conferences / Seminar / Workshop / Symposium

1. Karkare, P., Murthy, C. N., (2015) Synthesis and characterization of polystyrene macroinitiators via Atom Transfer Radical Polymerization, Advancements in Polymer Science & Technology (APA-2015), Department of Chemistry, Saurashtra University, Rajkot, Gujarat, 29th – 31st October.
2. Karkare, P., Murthy, C. N., (2015) A New Approach for the synthesis of high molecular weight end functional polystyrenes by Atom Transfer Radical Polymerization, National Conference on Recent Trends in Science of Materials (NCSM-2K15), Faculty of Science, The M. S. University of Baroda, Vadodara, Gujarat, 28th – 30th December.
3. Karkare, P., Murthy, C. N., (2016) Investigation into the efficiency of dihalo alkyl halides as initiators for atom transfer radical polymerization, National Seminar on Recent Scenario in Science and Technology, Faculty of Tech. & Engg., The M. S. University of Baroda, Vadodara, Gujarat, 27th February.
4. Karkare, P., Murthy, C. N., (2017) Synthesis & Characterization of Acrylate Block Copolymers via ARGET-ATRP using Cyclic Sugar as Reducing Agent, International Conference on Polymer Science and Technology Advances In Polymer Science and New Generation Technologies SPSI-ACS Jubilee Symposium, Thiruvanathapuram, Kerala, India, 8th – 11th January.
5. Karkare, P., Murthy, C. N., (2017) Biphasic Systems for Aqueous ARGET-ATRP Of Acrylates: Exploring The Limits Of Control, 10th Plastvision Exhibition in India, Bombay Exhibition Centre, Nesco Complex Ground, Off Western Express Highway, Goregaon, Mumbai, Maharashtra, 19th – 23rd January.
6. Karkare, P., Murthy, C. N., (2018) Investigation onto reducing character of b-cyclodextrin for the synthesis of PMMA block copolymers using ARGET-ATRP, All Gujarat Research Scholars Meet, Chemistry Dept., Faculty of Science, The M. S. University of Baroda, Vadodara, Gujarat, 25th Feb, 2018.
7. Karkare, P., Ahire, M., Murthy, C. N., (2018) Self assembly of PMAA-Triblock copolymers in solutions, International Conference on Polymer Science & Technology SPSI-MACRO-2018, IISER Pune, Pune, Maharashtra, 19th – 22nd December.

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ARGET-ATRP using β-CD as reducing agent for the synthesis of PMMA-*b*-PS-*b*-PMMA triblock copolymers

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ABSTRACT: We studied the role of β-cyclodextrin (CD), a polyhydroxy cyclic sugar as reducing agent (RA) for the copper mediated activators regenerated by electron transfer atom transfer radical polymerization (ATRP) with the successful chain extension of methyl methacrylate blocks on the bifunctional polystyrene macroinitiator (PS-MI) using nonaqueous solvent system for the first time. The PS-MI was prepared by ATRP, had a polydispersity of 1.05 and gave triblock copolymers in the presence of β-CD. We found that alcoholic groups of β-CD show provisional reducing character and *in situ* convert Cu(II) to Cu(I) during polymerization. A well-defined triblock copolymer with narrow molecular weight distribution (polydispersity index < 1.5) was obtained at 100 °C. The molecular weight of the block copolymers increased linearly with monomer conversion and the reaction showed good control over the molecular weights when compared to the theoretical values. We show that the mild reducing power of β-CD is retained in a nonaqueous solvent also and is efficient with catalyst/RA ratio of 1:0.5. The effect of temperature on the reducing competency of β-CD was evaluated and found to be active at around 80 °C even though its melting temperature is 290 °C. © 2018 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2018**, *135*, 47117.

KEYWORDS: Copolymers; Kinetics; Radical Polymerization; Structure-Property Relationships

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INTRODUCTION

Reversible deactivation radical polymerization is being extensively used for getting homopolymers and block copolymers.[1,2] It facilitated the polymers with tailor-made chemical composition, well-defined polymeric architecture, and high chain-end functionality with low polydispersity, which was impossible with conventional radical polymerization.[3–5] Catalysis played an important role in the development of techniques like atom transfer radical polymerization (ATRP).[6–8] However, classical ATRP required high metal concentration which results in added expense associated in purifying the generated polymer, thus effective reduction of metal catalyst is required to parts per million (ppm) level. In order to achieve this, ATRP techniques have been explored such as initiators for continuous activator regeneration, supplemental activator and reducing agent (RA), electrochemically mediated ATRP, metal free and photo-induced ATRP.[9–12] The use of environmentally benign RA in activators regenerated by electron transfer (ARGET) ATRP had been the most viable extension to ATRP that lowered the metal concentration to few ppm levels with its applicability for the industrial scale up. However, ARGET-ATRP surprisingly got restricted due to many reasons like continuous formation of oxidized product of RA, solubility, and its effect on the reducing efficacy. Not only these but the selected chemical RAs must be known for its effect on the other components of the polymerization.[13,14] Typical RAs used for successful ARGET-ATRP have been ascorbic acid,[15] tin(II) ethyl hexanoate,[16] glucose,[16] hydrazine,[17] amines[18] and zero valent metal,[19] and many more. Even though these RAs have been successfully employed irrespective of organic[20,21] and/or aqueous[22,23] nature of the system but the choice remained involving the tin (II) ethyl hexanoate or ascorbic acid. It has been found that among these two RAs, ascorbic acid is strong RA that rapidly reduces Cu(II) to Cu(I) and hence increases the radical concentration impairing the control during polymerization. On the other hand, RAs should be mild in nature for lowering the side reactions caused by generation of oxidized form of RA.[24] The major concern has been on searching for new mild RAs which minimize the adverse effect on the polymerization components and provide environmentally benign solution for future developments. Polymer supported RAs have also shown some good results for the organic synthesis.[25] In the quest for mild RA, hydroxyl groups have showed new hope in the role of RA. Recently, Wang *et al.*[26]

Additional Supporting Information may be found in the online version of this article.

reported how alcohols could work for the reduction of Cu(II) for ARGET-ATRP of acrylates and styrene. Liu *et al.*[27] used the same for the reduction of Cu(II) in ARGET-ATRP of methyl methacrylate (MMA). It was observed that the primary and secondary alcohols actively reduced Cu(II). In an another example, Xie and coworkers[28] showed Fe-mediated AGET-ATRP of MMA in dimethylformamide, where alcohols have reduced Fe(III) to Fe(II). However, in all these experiments, additional sodium carbonate was used to decrease the redox potential.

Aiming to achieve improved RA having multiple hydroxyls as an active reducing site and biocompatible in nature, we choose cyclic sugars particularly β-cyclodextrin (CD), which comprises 7 primary and 14 secondary hydroxyls groups active for reducing Cu(II) under solvent.[29] The unique class of cyclic oligosaccharides CDs that show different physical and chemical properties have been reviewed thoroughly,[30,31] and among them β-CD forms inclusion complexes with diverse applications in pharmaceuticals as stabilizing agent, capping agent, and as catalyst promoters in organic synthesis.[32–35] Similar to reducing monosaccharides like glucose, β-CD copolymer has also been reported for the synthesis of Ag nanoparticles (NPs).[36] We recently showed the reducing property of β-CD for the formation of not only Ag and Au NPs but also for inverted core–shell bimetallic NPs (Ag@Au and Au@Ag) in the aqueous medium.[29] With this background and to further prove its reducing character, we report the use of β-CD as an RA for Cu(II)/*N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDETA) complex in copper-mediated ARGET-ATRP of MMA on difunctional polystyrene macroinitiator (PS-MI) for poly(MMA) (PMMA)-*b*-PS-*b*-PMMA triblock copolymerization (Scheme 1). Here, *in situ* generation of Cu(I)/PMDETA is achieved through redox reaction of β-CD and Cu(II)/PMDETA for the initiation of polymerization. Kinetics of the polymerization was carried out to understand the controlled nature during the course of polymerization. We have not only just explored the use of β-CD for its reducing character but also validated it for the synthesis of block copolymers in solution ARGET-ATRP. We found that reducing competency was comparable at high temperature and along with these the effect of concentration of β-CD and copper were also studied.

EXPERIMENTAL

Materials

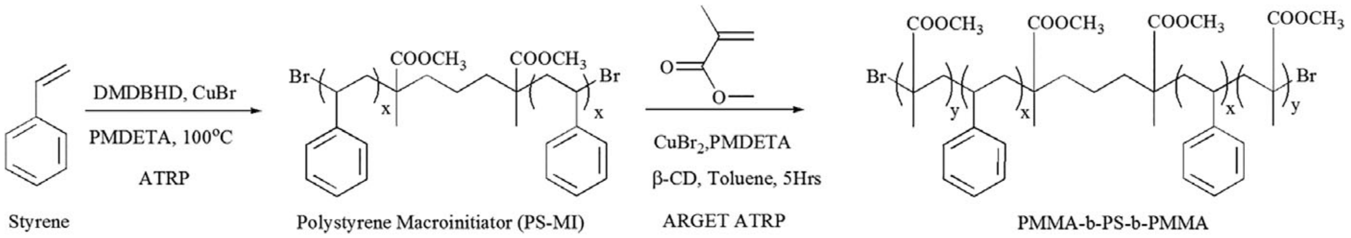
The monomers styrene (Aldrich, 99%) and MMA (Aldrich, 99%) were passed through activated basic and neutral alumina to remove inhibitors, subsequently dried over molecular sieve for 24 h. CuBr (Aldrich, 98%) was purified by washing with glacial acetic acid, absolute ethanol, diethyl ether followed by vacuum drying. $CuBr_2$ (Aldrich, 99%) also vacuum dried before use, toluene (Aldrich, 99.5%) was distilled under reduced pressure and stored over molecular sieve for 24 h. Dowex Marathon MSC macroporous ion-exchange resin (Aldrich, 20–50 mesh), β-CD (Chem Dyes Corporation, 99%), PMDETA (Aldrich, 99%), dimethyl-2,6-dibromoheptanedioate (DMDBHD, 97%), methanol (Sisco Research Laboratories, 99.5%), tetrahydrofuran (THF; Sisco Research Laboratories, 99.5%), and other chemicals were used as received.

Measurements

The number- and weight-average molecular weights, polydispersity index (M_n, M_w, and PDI) were determined by gel permeation chromatography (GPC). GPC was conducted using Agilent 1200 Infinity series with PLgel Mixed-B column having a pore size of 10 μm with a refractive index detector at a flow rate of 1 mL min^{-1} THF as elution solvent at 40 °C and the instrument was calibrated with polystyrene standards. Nuclear magnetic resonance (^1H NMR) spectra were run on Bruker, 400 MH_z Fourier transform NMR, AVANCE-III in $CDCl_3$, 10 mg/0.5 mL $CDCl_3$ in 5 mm glass tube and spectra were analyzed using software TOPSPIN 2.1. The internal standard was tetramethylsilane as reference for chemical shift at 0 ppm. Ultraviolet–visible (UV–vis) spectra of copper complexes were recorded on a Shimadzu-2450 spectrophotometer.

Synthesis of PS-MI Via Bulk ATRP

Macroinitiator synthesis was performed as per our previous report,[37] In a dry 50 mL two-necked round-bottom flask (RBF) equipped with magnetic stirrer bar was charged with CuBr (0.417 g, 2.852 mmol) under the flowing stream of argon and sealed with rubber septum. To this, deoxygenated PMDETA (0.499 g, 2.852 mmol) in 25 mL of styrene (215.34 mmol) were added using argon flushed syringes with high argon atmosphere. To above homogeneous solution, the addition of deoxygenated DMDBHD (5.083 g, 14.26 mmol) in 8 mL styrene (69.82 mmol) via a gas tight syringe. The RBF was kept in preheated oil bath maintained at 100 °C for 2 h, the reaction was stopped by air exposure and the reaction content was dilute by adding 150 mL of THF. This reaction mixture was then left for 1 h with Dowex Marathon MSC macroporous ion-exchange resin followed by passing it through activated neutral alumina column to remove catalyst-ligand complex. The resulting solution was concentrated by rota evaporation, and polymer was precipitated in large excess of methanol. The polymer was dried, again dissolved in minimum amount of THF and precipitated in methanol in same manner; this procedure is repeated thrice for the purified



Scheme 1. Synthesis of PS-MI via ATRP and PMMA-*b*-PS-*b*-PMMA via ARGET-ATRP using β-CD.

polymer. It was then dried under vacuum at 40 °C for 24 h. GPC is shown as Figure S1, Supporting Information with M_n = 1140 and a PDI = 1.05. Yield = 55.25% by weight determined gravimetrically. ^{1}H NMR is shown as Figure S2, Supporting Information: δH(400 MHz; $CDCl_3$; Me_4Si) 6.3–7.2 (m, -Ph), 4.45 (br t, -CHBr), 3.7 (br s, $-OCH_3$).

Chain Extension of PS-MI with MMA, Triblock Copolymerization Via ARGET-ATRP Using β-CD as RA

ARGET-ATRP of MMA was performed in a dry 20 mL round-bottom glass vial equipped with magnetic bar. Typical batch of polymerization was carried out at 100 °C with the mole ratio of [MMA]:[PS-MI]:[$CuBr_2$]:[PMDETA]:[β-CD] = 200:1:0.17:1:0.17. First, $CuBr_2$ (0.0088 g, 0.039 mmol), PS-MI (0.268 g, 0.235 mmol), and β-CD (0.045 g, 0.0394 mmol) was charged under flowing stream of argon, sealed with rubber septum and degassed thrice, and left under argon atmosphere. In another glass vial MMA (4.7 g, 46.94 mmol) and PMDETA (0.0041 g, 0.235 mmol) in 5 mL toluene was charged, sealed with rubber septum, degassed thrice and left under high argon atmosphere. Aforementioned monomer-ligand solution was transferred into the reaction flask using gas tight syringe and kept in preheated oil bath for 5 h. Samples were collected at regular interval of time for the GPC analysis. The polymerization was terminated by adding small amount of methanol and the contents were diluted in excess of THF followed by passing the solution through basic alumina. The resulting transparent solution was concentrated by rota evaporation, after which the polymer was precipitated in 10-fold excess of methanol. Similar procedure was employed thrice for the purification of the polymer using solvent/nonsolvent system (THF/methanol) followed by vacuum drying at 40 °C for 24 h and yield was calculated gravimetrically.

RESULTS AND DISCUSSION

β-CD in a Role of RA

Since decades, the CDs and their derivatives have been very important sugars although not being RAs as they do not possess straight chain form with free aldehyde or ketone. Reducing sugar's free aldehyde group or an alpha-hydroxy ketone is capable of being oxidized in aldo- or keto-form at equilibrium. Analytically, there have been many techniques available for the determination of reducing sugars by Fehling's reagent[38] or Benedict's reagent.[39] In fact, studies have also shown that the solution behavior of monosaccharide and thermodynamic parameters for glucose have found the isomeric existence in cyclic form as predominant rather than the linear.[40,41] CDs are class of nonreducing sugars which comprising α (1-4) linkage between the glucose units but they are rich in hydroxyl groups, both primary and secondary. The structure of β-CD is similar to other CDs made up of seven glucose units arranged in cyclic manner imparting 7 primary and 14 secondary hydroxyls as can be seen from Figure 1.[41] The hydroxyl functionalities of β-CD, in the presence of base, provide efficient oxidizing sites that could result in mild reduction of Cu(II)/PMDETA under high temperature. In order to confirm the *in situ* generation of Cu(I) from Cu(II) in the presence of CD, UV–vis experiments were performed. As can be seen from Figure 2, the UV–vis spectrum of Cu(II)/PMDETA complex with β-CD in toluene did not show characteristic d-d band transition in the region of 450–800 nm which might be due to insolubility of Cu(II) complex.

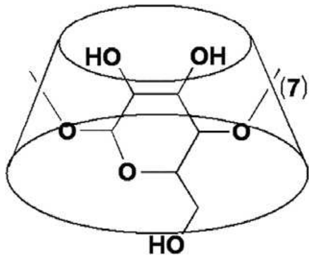


Figure 1. Structure of β-CD.

Whereas upon heating the same mixture at polymerization temperature for 30 min, the green-colored content was found to be soluble in toluene and a new absorption band appears at 282 nm that can be attributed to Cu(I)/PMDETA complex only[42] as β-CD does not absorb in this region. Thus, the UV–vis spectrum reveals that Cu(II)/PMDETA complex converts into Cu(I)/PMDETA in the presence of β-CD due to the reducing character of β-CD. No other reactions can explain the conversion of Cu(II) to Cu(I). The complete reduction of Cu(II) to Cu(0) could also take place similar to that of Ag(I) to Ag(0) and Au(III) to Ag(0) as reported earlier; however, Ag is higher in the electrochemical series with respect to Cu, therefore the conversion of Cu(II) to Cu(I) can only happen under the influence of β-CD[43] and hence it is worth mentioning that β-CD possess mild reducing character due to their hydroxyl groups. The ARGET-ATRP using β-CD at 100 °C was done for the synthesis of PMMA-*b*-PS-*b*-PMMA with 500 ppm copper concentration. The initial result was very indicative as BAB1 (Table I,

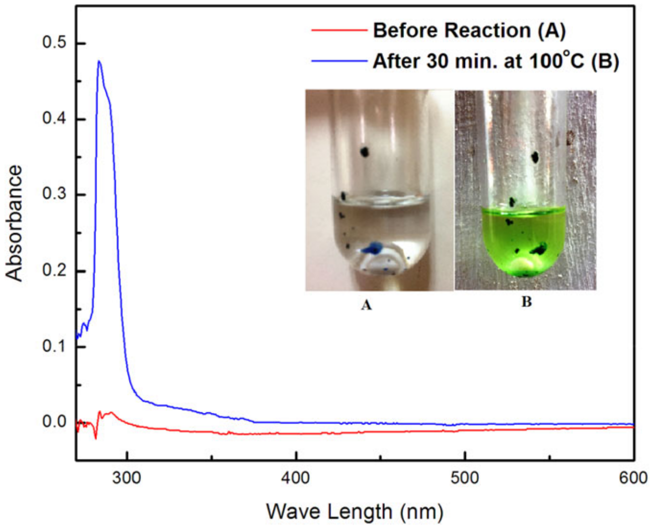


Figure 2. UV–vis spectra of Cu complexes in toluene. This study was performed with $CuBr_2$:PMDETA:β-CD = 0.17:1:0.17 m*M* ratio under argon atmosphere and 0.1 mL sample was withdrawn which was further diluted to 100 times using toluene. The UV–vis spectrum was taken immediately (a) and after keeping mixture for 30 min at 100 °C (b). The spectra of toluene insoluble Cu(II)/PMDETA complex (a) shows no specific absorption where Cu(I)/PMDETA complex (b) has showed absorption maxima at 284 nm. It explains that during the course of heating period Cu(II) complex is reduced by β-CD to Cu(I). [Color figure can be viewed at wileyonlinelibrary.com]

Table I. Synthesis of PMMA-*b*-PS-*b*-PMMA Triblock Copolymers

Sr. No.	Experiment	$[M]_o$:$[I]_o$	%Yield	$^bM_{n\ theo.}$	$M_{n\ GPC}$	PDI
1	PS-MI^a	20:1	55	1495	1140	1.05
2	BAB1	200:1	52	11 575	13 892	1.28
3	BAB2	300:1	53	15 804	19 128	1.37
4	BAB3	400:1	50	21 250	21 920	1.20
5	BAB4	500:1	52	26 989	28 736	1.23
6	BAB5	750:1	54	41 550	42 232	1.30

DMDBHD, dimethyl-2,6-dibromoheptanedioate; GPC, gel permeation chromatography; PDI, polydispersity index; PMDETA, *N,N,N′,N″,N″*-pentamethyldiethylenetriamine; PMMA, poly(methyl methacrylate); PS-MI, polystyrene macroinitiator.
BAB1 to BAB5–100 vol % toluene versus [M] at 100 °C for 5 h.
[a] Styrene:DMDBHD:CuBr:PMDETA = 20:1:0.2:0.2 in bulk.
[b] $M_{n\ theo.}$ = $[MI/I] + [M]_o/[MI/I]_o \times [M_w]_{monomer} \times$ yield.

Table II. Synthesis of PMMA-*b*-PS-*b*-PMMA Triblock Copolymers at Different Temperatures

Sr. No.	SET	Temperature (°C)	%Yield	$^bM_{n\ theo.}$	$M_{n\ GPC}$	PDI
1	T1	80	10.0	3163	2511	1.20
2	T2	60	10.0	3103	2518	1.16
3	T3	RT (28)	8.0	2663	2412	1.16

GPC, gel permeation chromatography; PDI, polydispersity index; PMMA, poly(methyl methacrylate); RA, reducing agent; SET, single electron transfer.
The polymerization was done using M:I:C:L:RA = 200:1:0.17:1:0.17 in 100 vol % toluene versus [M] at above given time for 5 h.

entry 2) showed good agreement in the theoretical and the experimental molecular weights with narrow PDI value. Similarly, we linearly increased monomer concentration with respect to macroinitiator from 200:1 to 750:1 (Table II, entries 2–6) gave the comparable PDI values. This further confirms that there is no inclusion complex formation between the monomer and the low-molecular-weight macroinitiator with β-CD. The first-order kinetics of BAB1 block copolymerization resulted in narrow molecular weight distribution as shown in Figure 3. This linear growth in the polymerization at high temperature shows that in the polymerization process constant concentration of propagating radicals and ratio of [Cu(I)/PMDETA]/[Cu(II)/PMDETA] were maintained by this new hydroxyl RA. Experimentally determined molecular weight ($M_{n,\ GPC}$) increased in a linear fashion with respect to time and conversion which closely matched with theoretical molecular weight ($M_{n\ theo.}$) having narrow PDI values of 1.16–1.30.

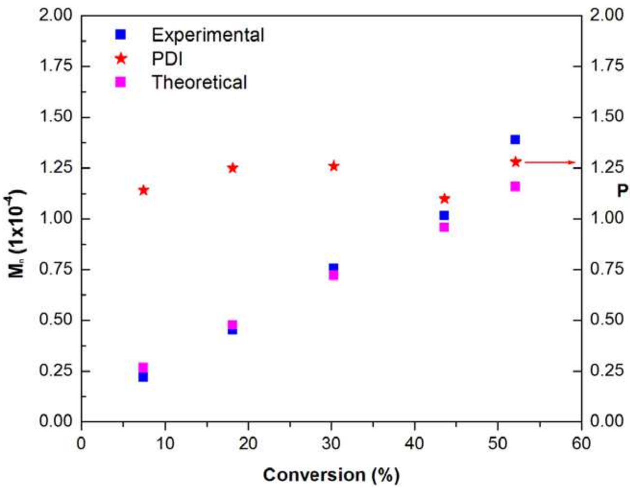


Figure 3. Kinetics of BAB1 using β-CD as RA at 500 ppm Cu. [Color figure can be viewed at wileyonlinelibrary.com]

Effect of Temperature

It has been a known observation so far that the rate of polymerization often correlates to higher conversion upon increasing the reaction temperature due to rise in rate constants of atom transfer equilibrium and propagating radicals.[2] In our findings, the results were quite surprising and critical as the effect of temperature adversely affected on the rate of polymerization, as shown in Table II. We observed that on decreasing the reaction temperature the hydroxyl groups of β-CD could not regenerate active Cu(I) species from Cu(II) dormant species which results in low-molecular-weight block copolymers even after 5 h. This confirms that below 100 °C, the induction period required for generation of Cu(I) active species from the Cu(II) changes drastically to very longer period of time. This was observed by physical color change during the polymerization at 80 °C. It took more than 2 h to start reduction of Cu(II)/PMDETA at 80 °C which further increases to 3 and 4.5 h in case of 60 °C and at room temperature (28 °C), respectively. However, the block copolymers were found to have narrow molecular weight distribution. Moreover, the monomer conversion in the copolymers was very low as compared to polymerization at 100 °C. Therefore, it is apparent from the results that the ARGET-ATRP using β-CD depends upon temperature for the efficient use of the β-CD as hydroxyl RA.

Effect of Concentration of Copper and RA

The concentration of the active catalyst and the RA play important role in ARGET–ATRP technique. The combination of them imparts higher concentration of Cu(I)/PMDETA from Cu(II)/PMDETA and it accelerates the rate of polymerization thus

Table III. Effect of Concentration of Copper and RA

Sr. No.	Cu (ppm)	[Cu]:[RA]	%Yield	$M_{n\ \mathrm{theo.}}$	$M_{n\ \mathrm{GPC}}$	PDI
1	500	1:1	52	26 989	28 736	1.23
2	250	1:1	50	26 328	26 301	1.32
3	100	1:1	46	23 974	21 610	1.20
4	500	1:3	53	27 580	29 739	1.24
5	500	1:5	54	27 930	30 920	1.27
6	500	1:0.5	51	26 778	29 072	1.27

GPC, gel permeation chromatography; PDI, polydispersity index; RA, reducing agent; SET, single electron transfer.
The polymerization was using M:I:C:L:RA = 500:1:0.17:1:0.17 in 100 vol % toluene versus [M] at 100 °C for 5 h.

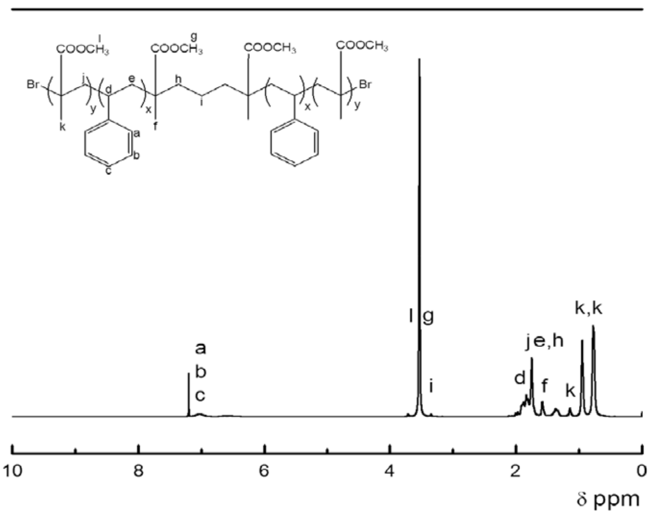


Figure 4. ^{1}H-NMR of BAB1 triblock copolymer.

giving higher conversion. We investigated the effect of catalyst concentration and observed that the rate of polymerization decreases by decreasing the copper concentration from 500 to 100 ppm, as shown in Table III, entries1–3. The monomer conversion was found low at 100 ppm catalyst in the stipulated 5 h of reaction time, confirms the rate of polymerization is faster with high copper concentration. The low catalyst concentration increases the induction period that ended up with low polymer conversion. We also studied the effect of RA concentration on the block copolymerization, as in entries 4 and 5 where the RA was in excess to that of copper which gently increases the rate of polymerization. It shows that in given period of time, β-CD converts Cu(II) to Cu(I) efficiently even at equimolar portion of copper too. However, entry 6 in Table I where we used RA half of the copper concentration was also found to give controlled polymerization with almost same monomer conversion. These results show that β-CD even in low molar portion reduces Cu(II)/PMDETA easily, this could be due to more than one hydroxyl group participating in the reducing action. The advantage of toluene as solvent is significant as it is being used commercially for the production of purified β-CD. Toluene could easily solubilize the growing polymer and active Cu(I) complex in the presence of low or high concentration of RA. These studies demonstrate that ARGET-ATRP using β-CD could be efficiently utilized to give controlled PMMA-*b*-PS-*b*-PMMA triblock copolymers at 100 °C.

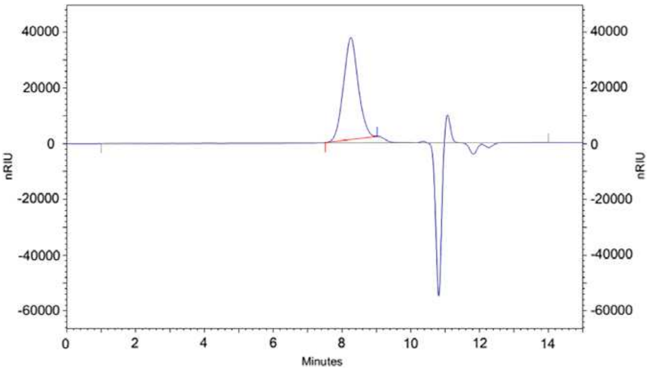


Figure 5. GPC of PMMA-*b*-PS-*b*-PMMA triblock copolymer. [Color figure can be viewed at wileyonlinelibrary.com]

Characterization of PMMA-*b*-PS-*b*-PMMA (BAB1) Triblock Copolymer

The PS-MI obtained via bulk ATRP was used for the triblock copolymerization reaction. The mole ratio of [M]:[I]:[C]:[L]:[RA] was kept 200:1:0.17:1:0.17 at 100 °C in 100% toluene by volume. The resultant block copolymer was analyzed using ^{1}H-NMR for the uniform structural arrangement of protons. Figure 4 shows the clear proton distribution for the MMA blocks attachment on PS-MI with halogen exchange mechanism that the signal at 3.5 δ ppm attributes to the methyl proton of -OCH_3 of MMA. The aromatic protons were found in the range of 6.3–7.2 δ ppm; here, signal shows relatively low intensity as compared to MMA backbone protons due to high number of monomer attachment on both sides of PS-MI. The backbone protons showed signal within 0.767–1.96 for the -CH_2-, -CH of PS-MI and -CH_2- of MMA. Here, the PMMA blocks show their unique tacticity arrangement in the final polymers as can be seen from ^{1}H-NMR, δ ppm of 0.767–776 for syndiotactic (rr), 0.951 for atactic (mr), and 1.145 for isotactic (mm) of methyl group of PMMA blocks in the ratio of 58.41:36.70:4.89 (rr:mr:mm), a similar high syndiotactic ratio was observed by sawamoto in Fe(II) catalyzed PMMA homopolymers.[44] Whereas Figure 5 shows the GPC of triblock copolymer with a single sharp peak it nullifies the possibilities of forming oligomers or blends.

CONCLUSIONS

In summary, the reducing character of β-CD is evaluated and utilized in copper mediated ARGET-ATRP for the synthesis of

PMMA-*b*-PS-*b*-PMMA triblock copolymer. The polymerization followed first-order kinetics, M_n GPC values increased linearly with monomer conversion with $CuBr_2$/PMDETA system. This further elaborates the dependency of reducing character of β-CD on temperature and multiple hydroxyl functionalities used during the reduction of Cu(II)/PMDETA.

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