Synthesis and Characterization of poly (ε-caprolactone): A comparative study

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ABSTRACT
Poly (ε-caprolactone) (PCL) is an important bio-medical polymer and the same can be synthesized by ring opening polymerization method (ROP). ROP of ε-caprolactone (C.L) was carried out at 160 ^{0}C under nitrogen atmosphere for 2 hours with mild stirring condition by bulk polymerization method and by using stannous octoate (S.O) as a catalyst in the presence of a chemical initiator. Various chemical initiators are used for the synthesis of PCL. In the present investigation, different ring opening groups like -CO_2H, –NH_2, -OH, -SO_3H and –SH were used towards the ROP of C.L and their initiating efficiency were compared in terms of % yield and rate of polymerization (R_p). Thus synthesized PCL was characterized by Fourier Transform Infrared (FTIR) spectroscopy, differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), zeta potential measurement, particle size analysis and scanning electron microscopy like analytical tools. The thermal and surface properties of PCL are critically compared.

Keywords: *Caprolactone, Characterizations, Different initiators, Ring opening polymerization*

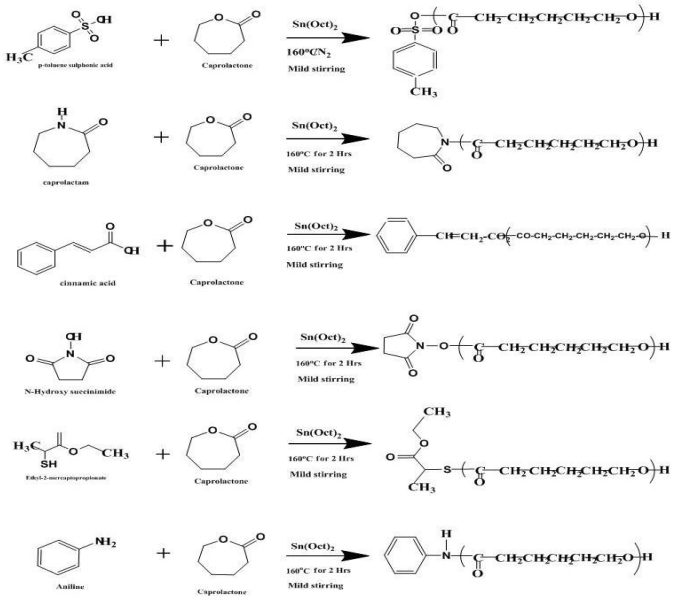
I. INTRODUCTION
Poly (caprolactone) (PCL) is an environmentally green bio-medical polymer and is being used as a drug carrier in the medicine field. Generally, it is prepared by ring opening polymerization (ROP) method via co-ordination-insertion mechanism by using stannous octoate as a catalyst. Owing to the bio-medical application of PCL, it is highly advisable to use an eco-friendly initiator. At the same time, the initiator must be effective one without any cytotoxic effect. Such a nice candidate is selectively used for the synthesis of PCL and their influence on the thermal and surface properties are critically compared here. The initiator used for the ROP of CL should be an effective one with maximum efficiency and without producing any unwanted side products. An initiator with two or more functional groups will produce a cross linked product or branched products. The cross inking or branching reaction leads to the dissolution problem. The main important issue associated with the initiator is after the drug delivery process, the initiator should not produce any toxicity inside the system. Moreover, if an initiator produces a polymer with nano size and with some micro voids on its surface that is well and good for further bio-medical applications. Above all, the initiator must be economically cheaper one. In order to tackle the above said problems, an initiator with different functional group was used for the ROP of C.L in an effective way by economically cheaper route. Before using the present initiator systems, various initiators available for the ROP of CL are reviewed here. For example, n-pentanol initiated ROP of C.L was reported in the literature [1]. For the ROP of C.L various initiators like aluminum thiolate [2], maleic acid [3], monomethoxy polyethylene glycol (mmPEG) [4], methanol [5], isopropanol [6], 2,6-ditertiary butyl phenol derivative [7], montmorillonite [8], starch [9], 4-hydroxy butyl vinyl ether [10], hydroxylated bipyridine [11], norflaxacin [12], carnitine [13], Fe_3O_4-glycolic acid hybrid system [14], lanthanum hydroxide [15], benzyl alcohol, quinolin-8-amine [16] and thiol functionalized silver [17] were used. Despite a thorough literature survey, we could not find any report based on the comparative study of the ROP of CL in the presence of different initiators under identical experimental conditions. The novelty of the present investigation is PCL prepared under identical experimental conditions with different initiators are compared based on molecular weight, T_m, T_d, zeta potential, particle size and surface morphology.

II. EXPERIMENTAL
1. Materials
Stannous (II)-2-ethyl hexanoate (S.O, catalyst, Across Chemicals, USA), ε-Caprolactone (CL, monomer, Across Chemicals) were freshly purchased and used as such. Chloroform ($CHCl_3$ Merck, India) solvent was purchased from Aldrich Chemicals, USA. Diethylether (non-solvent, Spectrum, India) and p-Toluene sulphonic acid (PTSA, Merck, India), Caprolactam (Himedia, India), Cinnamic acid (CA, Aldrich, USA), N-Hydroxy

succinimide (NHS, Lobachemie, India), Ethyl-2-mercaptoisopropinoate (E2MIP, Alfa Aeasar), Aniline (Spectrum, India) initiators were used.

2. Synthesis of PCL

A typical polymerization procedure was performed as follows. 0.10 mM of S.O (catalyst) was taken in a 25 mL capacity two necked round bottomed flask and 100 mM of C.L (monomer) and 0.02 g of PTSA initiator were charged and mixed well for 120 sec. After thorough mixing, the temperature was raised to 413 K for bulk polymerization under nitrogen purging [18, 19]. After 3600 sec of ROP, highly viscous liquid was obtained. The viscous liquid was cooled, dissolved in chloroform and re-precipitated by the addition of diethylether. Further, the sample was washed with de-ionized water to remove the un-reacted molecules and the water washing was repeated for three times. The polymer samples were subjected to freezing and dried under freeze drier. The dried samples were collected, weighed and stored in a vial. ROP was carried out under the following experimental conditions. The Monomer/Catalyst = 1000 and the Monomer/Initiator $[M_0/I_0]$ = 100. Reactions are mentioned in Scheme-1. The same procedure was followed for other initiators too.



Scheme.1. ROP of CL by different initiators

III. CHARACTERIZATIONS

FTIR spectra for the samples were recorded with the help of Perkin Elmer Spectrum 100 series instrument by KBr pelletization method from 400-4000 cm^{-1}. 3 mg of PCL sample was ground with 200 mg of spectral grade KBr and made into a disc under the pressure of 7 tons. DSC was measured by using STA $449F_3$ Jupiter (simultaneous DSC and TGA analyzer) under nitrogen atmosphere at the heating rate of 10 K/min from room temperature to 500^{o}C. The second heating scan of the sample was considered in order to delete the previous thermal history of the sample. The same instrument was used for TGA at the heating rate of 10 K/min under air atmosphere. A Zetasizer (Nano-ZS Malvern Instrument USA) was used to measure the zeta potential of dispersions. To determine the particle size distribution, the dispersion was analyzed by laser diffraction technique using a particle size analyser (Microtrac, Bluewave, Japan). The surface morphology of the samples was scanned by Scanning electron microscopy (SEM, JSM 6300, JEOL model) instrument.

IV. RESULTS AND DISCUSSION

1. FTIR study

2.

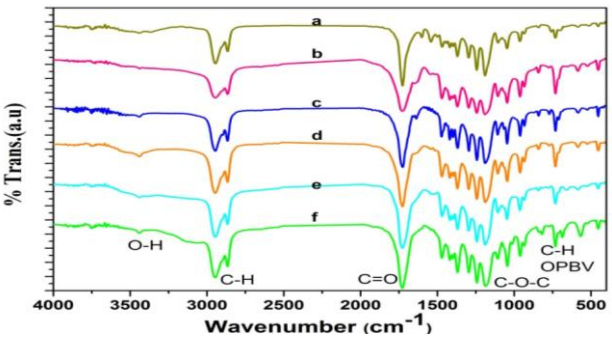


Fig. 1: FTIR spectrum of (a) PTSA-PCL, (b) Caprolactam-PCL, (c) CA-PCL, (d) NHS- PCL, (e) E-2-MIP-PCL, (f)Aniline-PCL systems.

The FTIR spectrum of aniline initiated ROP of CL is given in (Fig. 1a). A broad peak around 3425 cm^{-1} is due to the OH stretching of PCL end group. The C-H symmetric and anti symmetric stretching are observed at 2868 and 2940 cm^{-1} respectively. The C=O stretching of PCL can be seen at 1723 cm^{-1}. The C-O-C stretching of PCL is observed at 1186 cm^{-1}. The C-H OPBV can be seen at 733 cm^{-1}. Apart from these peaks some other new peaks are also observed corresponding to the aniline moiety. The benzenoid as well as quinonoid structure of aniline can be seen at 15421cm^{-1} and 1605 cm^{-1} respectively. The quinonoid form of aniline is due to the thermal oxidation reaction. This is because of the ROP of CL was carried out at 160^{0}C. This ambient temperature leads to the formation of quinonoid structure. The C-N stretching is observed at 1307 cm^{-1}. Thus aniline initiated ROP of CL was confirmed. (Fig.

1b) represents the caprolactam initiated ROP of CL. Here also the peak corresponding to PCL units are observed. A new doublet peak at 1723 cm^{-1} (1723 & 1688 cm^{-1}) explains the C=O stretching of PCL [18, 19] and amide stretching of caprolactone. A peak at 1368cm^{-1} confirms the presence of C-N stretching.(Fig. 1c) indicates the FTIR spectrum of CA initiated ROP of CL. The important peak noted here is C=C stretching of CA observed at 1647cm^{-1}. (Fig. 1d) demonstrates the FTIR spectrum of E-2-MIP initiated ROP of CL. The C-S stretching is observed at 1287cm^{-1}. (Fig. 1e) represents FTIR spectrum of NHS initiated ROP of CL. Here also the doublet C=O peak and C-N stretching are observed at 1237cm^{-1}. Thus the FTIR spectrum confirmed the functional groups of both the polymer and the initiator. This suggested that one end of PCL chain was occupied by the initiator.The decrease order of $RI_{[C=O/C-H]}$ is given below: PTSA>NHS>E-2-MIP>CL>ANI>CA. On comparison, it is found that the SO_3H group of PTSA is involved more actively towards the ROP of CL in the presence of S.O as a catalyst through cationic mechanism. The other initiators also followed the cationic ROP mechanism and were accelerated by the cationic initiator. In the case of E-2-MIP which contains one thiol group, is a good hydrogen donor. The remaining initiators contain the strong electron withdrawing group and hence straight away produced to the cations.

2. DSC thermogram

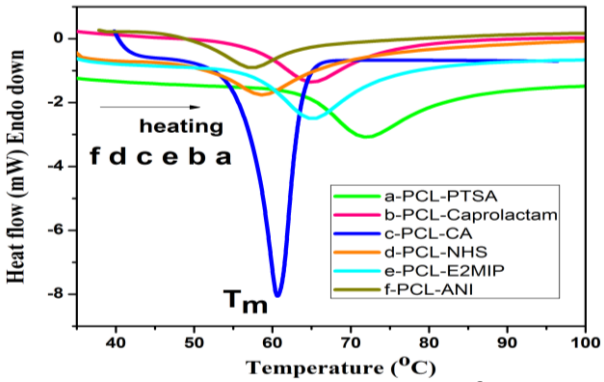


Fig. 2: DSC of: (a) PTSA-PCL-71.9^{O}C, (b) Caprolactam-PCL-65.3^{O}C, (c) CA-PCL-60.5^{O}C, (d) NHS-PCL-58.4^{O}C, (e) E-2-MIP-PCL-64.9^{O}C, (f) Aniline-PCL-57.4^{O}C.

The DSC thermogram explains the melting temperature of PCL (Fig. 3). Among the initiators used the PTSA system produced the highest T_m of 71.2^{o}C whereas the aniline system exhibited the T_m value of 57.4^{o}C. This confirmed that PTSA is acting as a strong initiator towards the ROP of CL, based on T_m results. Moreover, the PTSA is a strong acid and hence the ROP follows the cationic mechanism. Aniline produced the lowest melting temperature corresponding to the M_w of 2873 g/mol. In this case the ROP followed the radical mechanism. At higher temperature aniline can be oxidized to yield anilinium radical cation. Based on the DSC analysis the PTSA initiator is an excellent initiator towards the ROP of CL. The following is the queue based on T_m of PCL. PTSA > Caprolactam > E-2-MIP > CA > NHS > Aniline. The earlier literature indicates that the amine functionalized MWCNT initiated ROP of CL exhibited the T_m value of 60.43^{0}C [18]. On comparison with literature, the substituted aniline yielded a higher T_m value due to the increase in the molecular weight of the initiator with possible secondary forces of attraction.

3. TGA thermogram

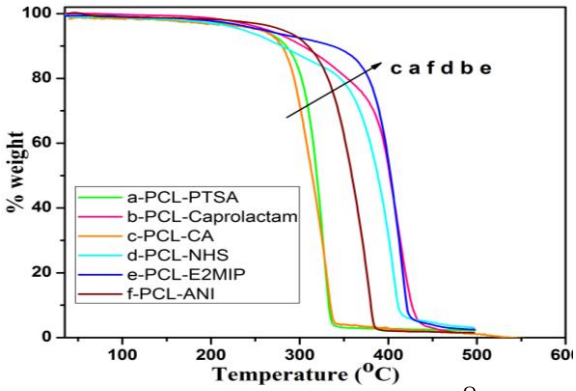


Fig. 3: TGA of (a) PTSA-PCL-318.5^{O}C, (b) Caprolactam-PCL-400.9^{O}C, (c) CA-PCL-313.5^{O}C, (d) NHS-PCL387.4^{O}C, (e) E-2-MIP-PCL-404.3^{O}C, (f)Aniline-PCL-357.2^{O}C systems.

The thermal stability of the polymer not only depends on the molecular weight of the polymer but also on the nature of initiator ended polymer chain. In the present investigation, all the systems show a single step degradation process (Fig. 4). Generally, the hydrophilic polymer system undergoes the rapid degradation process rather than the hydrophobic polymer due to the easy oxidative degradation reaction. Based on this concept the following is the queue: E-2-MIP > Caprolactam > NHS > Aniline > PTSA > CA. In the case of E-2-MIP having one free thiol group, is available and the same can be involved in the ROP of CL via radical mechanism. After the ROP of CL the total polymer chain became hydrophobic. The nature of ester group is water hating group and hence the total PCL chain length became a

hydrophobic polymer. Due to this reason the E-2-MIP consumed higher amount of energy for its 50% degradation and the CA exhibited the poorest thermal stability. The CA has one hydrophobic phenyl ring which is acting as an electron rich centre and is having one hydrophilic carboxyl group which acts as a poor proton donor. The queue indicates that an initiator with hydrophobic nature played a vital role during the prediction of thermal stability of the polymer. The hydrophilic initiators [18] even though having high molecular weight polymer, due to the water seeking ability they exhibited lower thermal stability.

4. Particle size analysis

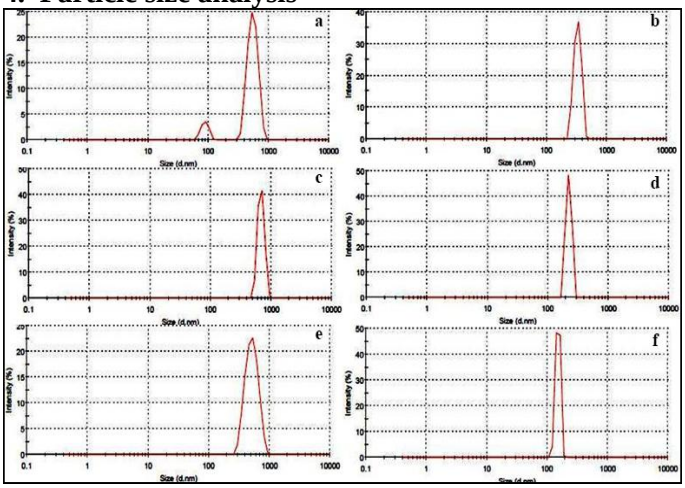


Fig. 4: Particle size of (a) PTSA-PCL-88.8nm, (b) Caprolactam-PCL-330.8nm, (c) CA-PCL-638.8nm, (d) NHS-PCL-222.2nm, (e) E-2-MIP-PCL-520.4nm, (f) Aniline-PCL-151.8nm.

Recently, the synthesis of polymer with nano size is a fascinating field of research. In order to achieve the same, the present investigation was made with different initiators. Figs. 5(a-f) represents the PSA of PCL synthesized by using different initiators. The PTSA-PCL system produced a size of 88.8 nm (approximately 3% of total content) and 553 nm (approximately 25% of total content) whereas the aniline-PCL system yielded the size of 151.8 nm (approximately 50% of total content). For the sake of comparison, the following queue was made: PTSA > Aniline > NHS > Caprolactam > E-2-MIP > CA. From the above queue, one can come to a conclusion that the $-SO_3H$ group is a better initiator with smaller polymer size rather than the carboxyl initiator. Polymer nano particle with smaller size is a key material for the effective drug delivery application [19].

5. Zeta potential measurement

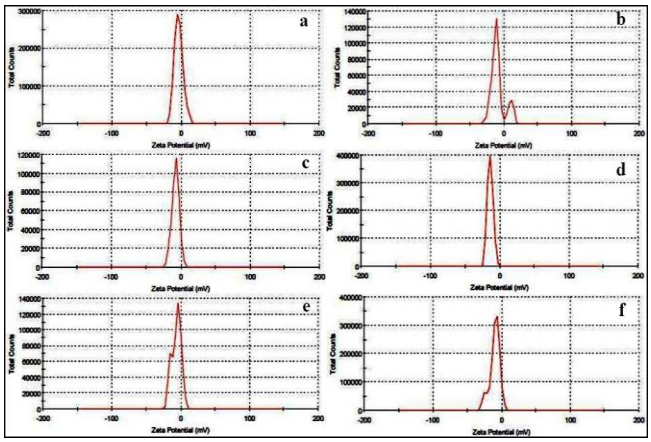


Fig. 5: Zeta Potential of PCL initiated by (a) PTSA (-3.43mV), (b) Caprolactam(-8.77mV), (c) CA(-7.50mV), (d) NHS(-13.7mV), (e) E-2-MIP(-6.17mV), (f) Aniline(-9.79mV).

Generally, the polymer with zeta potential value ranges from +30 to -30 is working well in the biomedical field for drug delivery application. During the drug carrying application, the interaction between drug and the backbone polymer is very important. The surface charge on the PCL initiated by different initiator is given in Table 1 and the figure is shown in Fig. 6. Among the initiator used for the ROP of CL, the NHS exhibited the lowest one (i.e) -13.7 mV whereas the PTSA system exhibited the highest zeta potential value of -3.43 mV. On critical comparison, the $-SO_3H$ group of PTSA exhibited the highest negative charge. Moreover, these negative charges are compatible with the amino acid and proteins. It means that a ligand with the positive charge can easily interact with the PCL-PTSA system. The important point noted here is a drug with +ve charge can easily be attracted by PCL. This proved the drug carrying property of PCL. Here is the queue: NHS > ANI > Caprolactam > CA > E-2-MIP > PTSA.

6. Surface morphology study

The surface morphology of aniline initiated ROP of CL is given in (Fig. 7a). The image exhibited some micro voids. This void is very much useful in the bio-medical field particularly as a drug carrier. This is in accordance with our earlier publication [18, 19]. (Fig. 7b) indicates the surface morphology of CA initiated ROP of CL. The surface morphology of CA initiated ROP of CL is shown in (Fig. 7b). (Fig. 7b) reveals the agglomerated structure of PCL with some micro voids. This type of material is very much useful in the bio-medical application as a drug carrier. (Fig. 7c) represents the surface morphology

of the PCL-Caprolactam system with a broken stone like morphology.

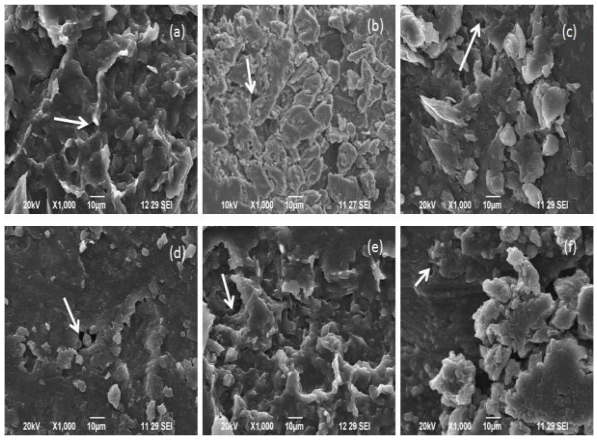


Fig. 6: Surface morphology of PCL conjugated with (a) Aniline-PCL, (b) CA-PCL, (c) Caprolactam - PCL, (d) E-2-MIP – PCL, (e) NHS - PCL, (f) PTSA - PCL.

The size of the stones was varied from 10 to 30 µm. Here also one can observe the presence of micro voids. (Fig. 7d) represents the surface morphology image of PCL-E-2-MIP system, here also the above said morphology is observed. (Fig. 7e) also indicates the same phenomenon for PCL-NHS system. (Fig. 7f) indicates the surface morphology of PCL-PTSA system, here one can observe the agglomerated stone like morphology. On critical comparison, all the systems exhibited the stone like morphology with some micro voids. Among the initiators used in the present investigation, we are particularly interested in PCL-CA system due to the extended conjugation system. The structure of PCL-CA system was further supported with NMR spectrum as mentioned below.

V. CONCLUSIONS

The ROP of CL was carried out under the N_2 atmosphere in the presence of S.O as a catalyst in the presence of different initiators with the different functionalities. The FTIR spectrum confirmed the C=O stretching at 1730 cm^{-1} and the ether C-O-C linkage of PCL at 1070 cm^{-1}. The PTSA end capped PCL exhibited the higher melting temperature of $71.9^{O}C$. The CA end capped PCL reported the highest thermal stability for the PCL due to the rigidity enforced by phenyl ring of CA. The PTSA end capped PCL showed the particle size of 88.8 nm whereas the CA end capped PCL exhibited the particle size of 638.8 nm. The zeta potential of PTSA end capped PCL was determined at -3.43 mV. The PCL end capped with the all the six initiators exhibited the micro voids on the surface of the PCL which confirmed the bio-medical application of PCL. Among the initiators used in the present investigation, NHS is a more suitable candidate for the ROP of CL in the presence of S.O as a catalyst and it is also useful for further structural modification of PCL. This proved that –OH group is more effective towards the ROP of CL

REFERENCES

[1] S.G. Bureau, D. Delcroix, B.L. Vaca, D. Bourissou, C. Navarro, S. Magnet, Organo–catalyzed ROP of ε–Caprolactone: Methane Sulfonic Acid Competes with Trifluoromethane Sulfonic Acid, *Macromolecules*, 41, 2008, 3782-3784.

[2] C.H. Huang, F.C. Wang, B.T. Ko, T.L. Yu, C.C. Lin, Ring-Opening Polymerization of ε-Caprolactone and l-Lactide Using Aluminum Thiolates as Initiator,*Macromolecules*, 34, 2001, 356-361.

[3] Y. Song, L.J. Liu, R.X. Zhuo, Microwave assisted polymerization of ε-CL with maleic acid as a initiator and drug release behaviour of Ibuprofen– PCL system, *Chin. Chem. Let*, 14, 2003, 32-34.

[4] Z.X. Du, J.T. Xu, Y. Yang, Z.Q. Fan, Synthesis and characterization of poly(ϵ-caprolactone)-***b***-poly(ethylene glycol) block copolymers prepared by a salicylaldimine-aluminum complex, *J. Appl. Polym. Sci.*, 105, 2007,771-776.

[5] R.J. Pounder, A.P. Dove, Towards poly(ester) nanoparticles: recent advances in the synthesis of functional poly(ester)s by ring-opening polymerization, *Polym. Chem.*, 1, 2010, 260-271.

[6] V. Darcos, S.E. Habnouni, B. Nottelet, A.E. Ghaoui, J. Coudane, Well-defined PCL-***graft***-PDMAEMA prepared by ring-opening polymerisation and click chemistry, *Polym. Chem.*, 1, 2010, 280-282.

[7] S.D. Mun, Y. Hong, Y. Kim, Bull, Synthesis, X-ray Structure, and *l*-Lactide/ε-Caprolactone Polymerization Behavior of Monomeric Aryloxytitanatrane, *Korean Chem. Soc.*, 28, 2007, 698-700.

[8] L. Liao, C. Zhang, S. Gong, Preparation of Poly(***ε***-caprolactone)/Clay Nanocomposites by Microwave Assisted In Situ Ring-Opening Polymerization, *Macromol. Rapid Commun.*, 28, 2007, 1148-1154.

[9] A.K. Sugih, F. Picchioni, H.J. Heeres, Synthesis of poly-(ε)-caprolactone grafted starch co-polymers by ring-opening polymerisation using silylated starch precursors, *Carbohyd. Polym.*, 77, 2009, 267-275.

[10] S.S. Liow, L.K. Widjaja, V.T. Lipik, and M.J.M. Abadie, Synthesis, characterization and photopolymerization of vinyl functionalized poly (ε-caprolactone), *Express Polym. Lett.*, 3, 2009, 159-167.

[11] E. Holder, V. Marin, A. Alexeev, U.S. Shubert, Greenish-Yellow-, Yellow-, and Orange-Light-Emitting Iridium(III) Polypyridyl Complexes with Poly(ε -caprolactone)–Bipyridine Macroligands, *J. Polym. Sci. Part A Polym. Chem.,* 43, 2005, 2765-2776.

[12] M. Sobczak, E. Witkowska, E. Oledzka, W. Kolodziejski, Synthesis and Structural Analysis of Polyester Prodrugs of Norfloxacin, *Molecules*, 13, 2008, 96-106.

[13] M. Sobczak, W. Kolodziejski, Polymerization of Cyclic Esters Initiated by Carnitine and Tin (II) Octoate, *Molecules*, 14, 2009, 621-632.

[14] A. Nan, R. Turcu, I. Craciunescu, C. Leostean, I. Bratu, J. Liebscher, Surface initiated ring-opening polymerization of lactones on iron oxide nano particles, *J. Phys. Conf. Ser.*, 182, 2009, 1-4.

[15] M. Zhou, J.Y. Yuan, W.Z. Yuan, X.H. Hong, Y.W. Yin, Cylindrical PCL brushes on the surface of lanthanum hydroxide nanowires by ring-opening polymerization, *Chin. Sci. Bull*., 55, 2010, 1376-1381.

[16] M. Shen, W. Zhang, K. Nomura, W.H. Sun, Synthesis and characterization of organoaluminum compounds containing quinolin-8-amine derivatives and their catalytic behaviour for ring-opening polymerization of ε-caprolactone, *Dalton Trans.*, 2009, 9000-9009.

[17] B.C. Wilson, C.W. Jones, A Recoverable, Metal-free Catalyst for the Green Polymerization of ε-caprolactone, *Macromolecules*, 37, 2004, 9709-9714.

[18] B. Meenarathi, H.H. Chen, P.H. Chen, R. Anbarasan, Near infrared dye functionalized MWCNT as an effective initiator for the ring opening polymerization of ε-caprolactone, *J. Polym. Res.*, 20, 2013, 118-130.

[19] H.H. Chen, R. Anbarasan, L.S. Kuo, P.H. Chen, Application of Eosin Y functionalized MWCNT as an initiator for the ring opening polymerization of ε – caprolactone, *Mater. Chem. Phys.*, 126, 2011, 584-590.