SYNTHESIS AND CHARACTERIZATION OF BIODEGRADABLE POLYMERS USING ORGANOMODIFIED CLAY

A THESIS SUBMITTED TO
THE UNIVERSITY OF PUNE

FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY
IN CHEMISTRY

BY

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DEDICATED TO MY PARENTS

Acknowledgement

A research thesis is an enriching experience of knowledge enhancement, main importantly of realizing that individual effort is actually an outcome of support of many. That is probably why thesis writers feel the urge to write acknowledgement.

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CERTIFICATE

Certified that the work incorporated in the thesis “**Synthesis and Characterization of Biodegradable Polymers Using Organo Modified Clay**” submitted by Mr. Balaji S. Selukar for the Degree of *Doctor of Philosophy* in Chemistry was carried out by the candidate under my supervision at the Polymer Science and Engineering Division, National Chemical Laboratory, Pune. Such material as has been obtained from other sources has been duly acknowledged in the thesis.

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Candidate Declaration

I hereby declare that the research work incorporated in the thesis "**Synthesis and Characterization of Biodegradable Polymers using Organo Modified Clay**" submitted for the degree of **Doctor of Philosophy** in **Chemisty** has been carried out by me at Polymer Science and Engineering Division, National Chemical Laboratory Pune, under the supervision of Dr.(Mrs.) B. Garnaik. This work has not been submitted in part or full for a degree or diploma to this or any other University or Institution.

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ABSTRACT

A novel cloisite modified solid catalyst was prepared in a single step from commercially available starting materials for the first time. The ring opening polymerization of L-Lactide and D, D-lactide using this cloisite modified solid catalyst resulted in homopolymers of 75,000 and PDI=1.6 and the maximum molecular weight (M_w) i.e. 180,000 with PDI=1.9 were obtained. The catalytic activity of cloisite modified solid catalyst was compared with the conventional stannous octoate catalyst and found superior to stannous octoate in all respect such as conversion, molecular weight and molecular weight distribution etc. Moreover, the maximum molecular weight i.e. 180,000 was obtained at 220^0C, whereas transesterification reaction predominates in presence of stannous octoate. The linear structure was confirmed by quantitative ^{13}C-NMR. spectroscopy. Blend films were obtained by casting mixed solutions of poly (D-lactide) s and poly (L-lactide) s at various compositions and stereocomplex was formed at 50/50 composition with molecular weight of 75,000. SEM picture of stereocomplex showed uniform spherical shape except 50/50. Stereocomplex of 70/30 was treated with hydrogen plasma at various time periods. A nice honeycomb like structure was formed irrespective of plasma exposure time and the surface layer behaved hydrophilic in nature. The various types of clay such as cloisite-30B, cloisite-15A, cloisite-93A and cloisite-20A were incorporated during ROP of L-Lactide. Copolymer of β-butyrolactone with L-Lactide at various compositions (10:90, 20:80, 30:70, 40:60, 50:50, 80:20) were prepared.

The homopolymerization of ε-Caprolactone was carried out in presence of cloisite modified catalyst. Similarly, copolymerization with other lactones was also carried. The kinetic and thermodynamic parameter was studied. The end groups of the polymer were carried out MALDI-TOF.

Homopolymerization of Aleuritic acid and copolymerization of Aleuretic acid with L-Lactic acid were carried out using dehydropolycondensation method and the aggregation behavior of pendant hydroxyl groups was studied. Aleuritic acid (9, 10, 16-trihydroxy palmitic acid) contained 9, 10 vicinal diols which were protected by benzaldehyde dimethyl acetal and lactonized. The ring opening polymerization of macrocylic lactones

was carried out in presence of stannous stearate at 100 ^{0}C for 3hr.The molecular weight and DP were obtained as 3000 and 1.20 respectively. Similarly, 12-Hydroxy stearic acid was cyclized. The homo and copolymerization reaction were carried out with other lactones. Various kinetic and thermodynamic parameters were discussed. The resulting polymer was subsequently deprotected and pendant –OH groups were obtained at 9, 10 position. These groups aggregate due to hydrogen bonding.

Low molecular weight poly (lactic acid) s (PLA), having narrow molecular weight distribution was prepared using dehydropolycondensation method using tetraphenytin as a catalyst. Hydroxyl terminated linear polylactic acid was prepared reacting PLA with aliphatic diol compounds. The hydroxyl end groups were determined by ^{31}P NMR. The reaction of PLA oligomers and isocyanates (4, 4' methylenebis (phenylisocyanate), toluenediisocyanate, 4, 4' methylenebis (cyclohexylisocyanate), hexamethylene diisocyanate) was carried out. The effect of the reaction conditions, i.e., the reaction temperature, molar ratio, isocyanates and catalyst on the molecular weight were explored. The structure of the polymer samples was investigated with FT-IR, ^{1}H-NMR, ^{13}C-NMR and matrix-assisted laser-desorption ionization time-of-flight mass spectroscopy (MALDI– TOF MS) and TEM. The polymer of sebacic acid and terepthalic acid (ester-ester linkage) was prepared using dehydropolycondensation techniques in presence of tetraphenyltin.

Polylactides (Mw=75,000) were prepared using cloisite modified tin catalyst. The PLA nonwoven nanofibers with and without antibacterial drugs were fabricated using electrospinning technique. The PLA film was prepared using natural anti-inflammatory drug (Isobutrin). The mechanical and electrical properties were also studied. The degradation study of polylactides was carried out using compost.

GLOSSARY

LA	**Lactic acid**
L-LA	**L-Lactic acid**
PLA	**Poly (L-lactic acid)**
TPT	**Tetraphenyltin**
ROP	**Ring opening polymerization**
hr	**Hours**
AL	**Aleuritic acid**
TDI	**Toluene diisocyanate**
MPDI	**Methylenebis (phenyl diisocyanate)**
HDI	**Hexamethylene diisocyanate**
HMDI	**Methylenebis (cyclohexyl diisocyanate)**
PU	**Polyurethane**
PTSA	**p-Tolune sulphonic acid**
12-HSA	**12-Hydroxystearic acid**
ε-CL	**ε-Caprolactone**
PCL	**Poly (ε-caprolactone)**
M_n	**Number average molecular weight**
M_w	**Weight average molecular weight**
M_v	**Viscosity average molecular weight**
PDI	**Polydispersity index**
$[\eta]$	**Intrinsic viscosity**
T_g	**Glass transition temperature**
T_m	**Melting point**
ΔH_m	**Heat of enthalpy of melting**
m.p.	**Melting point (of an organic compound)**
b.p.	**Boiling point**

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CHAPTER - 1

CHAPTER-1: SYNTHESIS AND CHARACTERIZATION OF BIODEGRADABLE POLYMERS USING NANO CLAY

1.1 Introduction:

The conventional petrochemical-based polymers have a tremendous industrial impact since 1940s. These materials meet the worldwide demand in-terms of all properties, but two major drawbacks remain to be solved, namely, the use of non-renewable resources in their production and the ultimate fate of these large scale commodity polymers. Biodegradable polymers have long been considered as potential alternate friendly polymers. These material with specific physical, chemical, biological, biomedical and degradation properties to provide efficient therapy. Biodegradable polymeric biomaterials are preferred materials for developing therapeutic devices such as temporary prostheses, three dimensional porous structures as scaffolds of tissue engineering and controlled release drug delivery vehicles. There has been tremendous attention over the last 30 years in the synthesis, manufacture and processing of biodegradable polymers which have given rise to a broad range of practical applications from packaging to more sophisticated biomaterial devices. [1, 2, 3]

PLA is linear aliphatic thermoplastic polymer. High molecular weight PLA has good mechanical properties, thermal plasticity, and biocompatibility is readily fabricated and is thus a promising polymer for various end use applications.

Even when PLA is burnt, only one third of the combustible heat generated by polyolefin’s and it does not damage the incinerator and provide significant energy saving. Therefore, increasing realization of the various intrinsic properties can be improved to achieve the compatibility with thermoplastic processing, manufacturing and end-user requirements have fuelled technological and commercial interest of PLA.

The nanocomposite consisting of a polymer and organically modified layered silicate (OMLS) often exhibit remarkably improved mechanical, various other properties(thermal, clarity and barrier) as compared with those of virgin polymer. The concurrent property improvement in nanocomposite comes from interfacial interaction with the polymer matrix and OMLS as opposed to conventional composite. The organo modified clays are generally in nanometer dimensions and has to properly dispersed through the polymer matrix to create much more surface area for polymer/filler interaction then do conventional composites(both micro and macro composites).

Recently, another field research has attracted tremendous attention where solid clay modified transition metals are used as a catalyst for ROP in case of polymer synthesis as well as a filler to improve desired mechanical and other properties.

International organizations such as the American Society for Testing and Materials (ASTM), the Institute for Standards Research (ISR), the European Standardization Committee (CEN), the International Standardization Organization (ISO), the German Institute for Standardization (DIN), the Italian Standardization Agency (UNI), and the Organic Reclamation and Composting Association (ORCA), are all actively involved in developing definitions and tests of biodegradability in different environments and compostability.[4] Although a standard, global definition for biodegradable plastics has so far not evolved, each available definition (ASTM, CEN, ISO) correlates the degradability of a material with a specific disposal environment and to a specific standard test method.

Biodegradability must be looked at as a supplementary property for a thermoplastic product whose primary characteristic has to be a material, which is stable during its first use and then, after a certain induction time, becomes degradable until its complete assimilation in the biological cycle of nature.

Poly (lactic acid) (PLA, fig. 1.1 A) consists of aliphatic ester linkages, which are prone to both chemical and enzymatic hydrolysis. PLA is hydrolyzed by many enzymes such as protease, proteinase K, bromelain, esterase and trypsin.[5, 6, 7] But these ester linkages start hydrolyzing only when in contact with water and under certain specific conditions of pH and temperature. The primary degradation phase is purely hydrolytic, where no microorganisms are involved. Only after the weight average molecular weight goes down below approximately 10,000, microorganisms begin to digest the lower molecular weight lactic acid oligomers, producing carbon dioxide and water.

This two-stage mechanism of degradation is a distinct advantage of PLA over other biodegradable polymers, which typically degrade by a single-step process involving bacterial attack on the polymeric device itself. This is a useful attribute, particularly for product storage and in applications requiring food contact. PLA degrades rapidly in the composting atmosphere of high humidity and temperature (55-70 ^{0}C). But, at lower temperatures and/ or lower humidity, the storage stability of PLA products is considerably high.

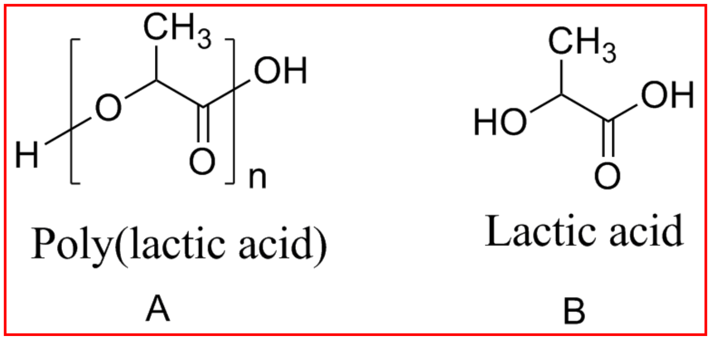


Fig. 1.1: A-PLA, B-Lactic acid.

The building block of poly (lactic acid) is lactic acid or 2-hydroxypropanoic acid (lactic acid fig. 1.1 B) in which the carbon in between the carboxylic acid and hydroxyl functional groups is chiral, which gives rise to the possibility of diastereoisomeric (isotactic, syndiotactic and hetero or atactic) polymer chains of PLA, depending on the direction of the methyl group with respect to the direction of propagation of the chain. PLA polymers range from amorphous glassy polymers with a glass transition temperature of about 50 – 60 ^{0}C to semicrystalline products with melting points ranging from 130 to 180 ^{0}C, depending on the sequence of enantiomeric repeating units (L and D) in the polymer backbone. A careful selection of stoichiometry of repeat units coupled with judicious plasticizer selection, therefore, allows flexible blown and cast film products to be successfully manufactured. Nucleated crystalline products of PLA are essentially opaque, whereas stress-induced crystalline materials are transparent. In summary, the basic properties of PLA lie between those of crystalline polystyrene and PET. In particular, certain properties worth noting include:

- Flexural modulus > polystyrene
- Fat barrier properties, comparable to PET
- Excellent gas barrier properties
- Good heat stability
- Clarity and gloss of amorphous and biaxial films exceeding those of PET and PP

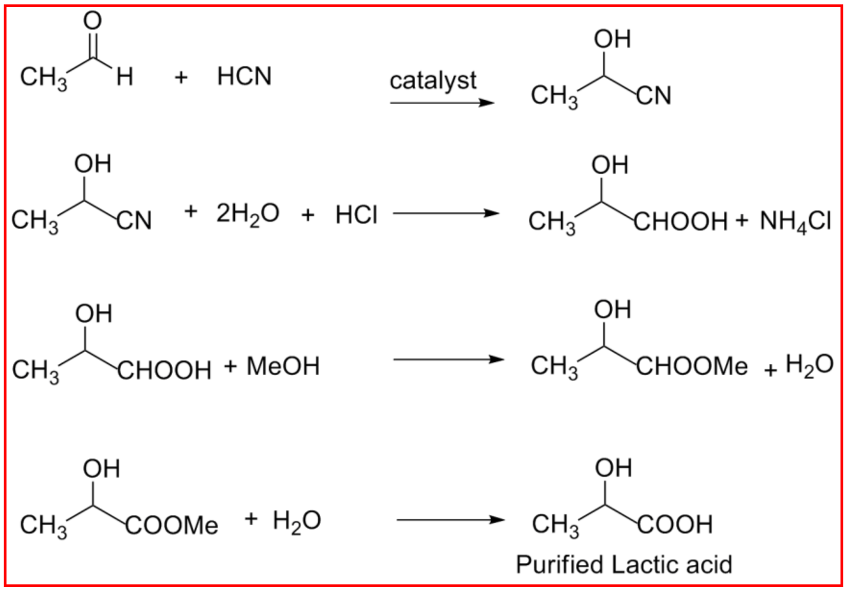
- High surface energy allowing easy printability.

United State demand for biodegradable plastic will grow 15.5 percent annually through 2012. Gains will be driven by escalating costs for petroleum-based resins and growing initiatives that favour renewable resources. Polyester-based and poly lactic acid resins will grow the fastest, while starch-based types remain the largest segment and PLA was clearly among the most promising ones. In an attempt to figure out its potential in near future, one may reasonably extrapolate a PLA only share of 720 million pounds in year 2012 and 2017, valued at $ 845 million.[8]

Poly (lactic acid) marked its beginning when Carothers made it in 1932, although with a low molecular weight and poor mechanical properties.[9] In the following years research and development activity about lactic acid production has come a long way, so that today a number of major players of the global chemical industry are into the production of lactic acid and PLA polymers. The major companies dealing in lactic acid are listed in the Table 1.1.

1.2 Source of monomer:

1.2.1 Source of L-lactic acid: Lactic acid or 2-hydroxypropanoic acid ($C_3H_6O_3$) and L, L-lactide, which is the monomer for poly (lactide), is present in almost every form of organized life. Almost all the lactic acid found in natural sources is dextrorotatory D (+), the L (-) form, on the contrary, being very uncommon. Lactic acid can be obtained in large, commercial scale from two different sources. One is the petrochemical source (Scheme 1) in which lactic acid is chemically synthesized by hydrolysis of lactonitrile and results in a 50/50 or racemic form.



Scheme 1: The synthetic route to lactic acid monomer through acetaldehyde.

Table 1.1: Lactic acid production: Global Scenario

Company	Plant location	Production capacity (in tons)
Purac	Holland, Spain, Brazil	80,000
Purac / Cargill	USA	34,000
Galactic	Belgium	15,000
ADM	USA	10,000
Mitsubishi	Japan	8000

On the contrary, lactic acid from the second source, that is fermentation broth of sugar and starch using different lactic acid bacteria (LAB), exists almost exclusively as the dextrorotatory D (+) form. Of the 100,000 tons of lactic acid that is produced worldwide every year about 90 % is made by lactic acid bacterial fermentation and the rest is produced synthetically. Presently, Musahino, Japan, is the sole producer of the synthetic variety.

Fermentative source has the advantage that by choosing a strain of lactic acid bacteria producing only one of the isomers, an optically pure product can be obtained. The ability to produce an enantiomerically pure lactic acid has important ramifications in the ultimate structure-property relationship of the PLA. Besides, Cellulose, hemicellulose and starch are abundantly available in nature, and when hydrolyzed to mainly glucose they are fermentable by a number of microorganisms of to produce Lactic acid.[10, 11, 12, 13, 14, 15]

LAB is unable to synthesize ATP (adenocine triphosphate), instead produce lactic acid as the major end product from anabolic (energy-conserving) fermentation of sugars. Most of them are facultative anaerobes and are highly acid-tolerant (down to pH. 5 and lower). Their optimal temperature for growth varies from 20 to 45 ^{0}C.[16, 17] Most of them are considered GRAS (generally regarded as safe), but some strains, e.g. *streptococci*, are pathogenic. Another common and very important characteristic of all the LAB is that they do not synthesize *vitamins-B* and amino acids[18], which renders them able to grow in a complex nutrient environment and metabolize many different carbohydrates.[19]

Lactic acid bacteria (LAB) and some filamentous fungi are the chief microbial sources of lactic acid. On the basis of the nature of fermentation, LAB is classified into (1) homofermentative and (2) heterofermentative. Homofermentative LAB produce virtually a single product, i.e., lactic acid, whereas the heterofermentative LAB produce other products such as ethanol, diacetyl formate, acetone or acetic acid, and carbon dioxide along with lactic acid.

Depending on the pH and temperature and also depending on the sugar which is fermented, LAB may produce either lactic acid only (homofermentation, for example, by *Lactobacillus delbrueckii*), or an equimolar mixture of lactic acid, carbon dioxide and ethanol or acetate (Heterofermentation), or a mixture of lactic acid, ethanol, acetate and formate (Mixed acid fermentation).[20] All other LAB except *lactrobacilli* of type**.**[21, 22] (e.g. *lactobacillus casei*) are facultative heterofermenters. Homofermenters start carrying out mixed acid fermentation when the sugar is other than glucose or when glucose is in short supply. Lactic acid-producing organisms, most of which are anaerobic, utilize pyruvic acid, which is the end product of Embden–Meyerhof pathway. The conversion of pyruvic acid to lactate can be effected by either of the two enzymes, L-lactate dehydrogenase or D-lactate dehydrogenase. The stereospecificity of the lactic acid depends on the type of organism, whose enzyme is involved in the process of lactic acid production. The major homofermentative LAB used in the lactic acid production from different carbon sources are *Lactococcus lactis* (Nolasco-Hipolito et al.).[23]

1.2.2 Isolation of lactic acid: Lactic acid the basic protocol is to extract the lactic acid from the fermentation broth by reactive extraction with a suitable extracting agent at a particular pH. Over 50 % yield of lactic acid was obtained from in a single extraction step, when using tertiary amine Hostarex A327 as the extractant, 1-decanol as the diluent and trimethylamine as the stripping solution. Mixtures of tripropylamine and triphenylamine dissolved in 1-octanol/n-heptane have been found to be successful in reactive extraction of L(+) lactic acid aqueous solution.[24 , 25] Alumina ceramic filters with mean pore diameter of 1.6 μm have also been successfully applied for continuous removal of lactic acid form the culture broth.[26]

1.2.3 Purity and impurities in lactic acid:

1.2.3a Chemical purity: Total impurities above a limit of about 100 ppm limit the maximum attainable molecular weight very drastically. Lactic acid contains, residual sugars and various biological impurities, certain alcohols like methanol and ethanol, mono and dicarboxylic acids like acetic, pyruvic, oxalic and succinic acids and esters of lactic acid such as methyl and ethyl lactate.[27]

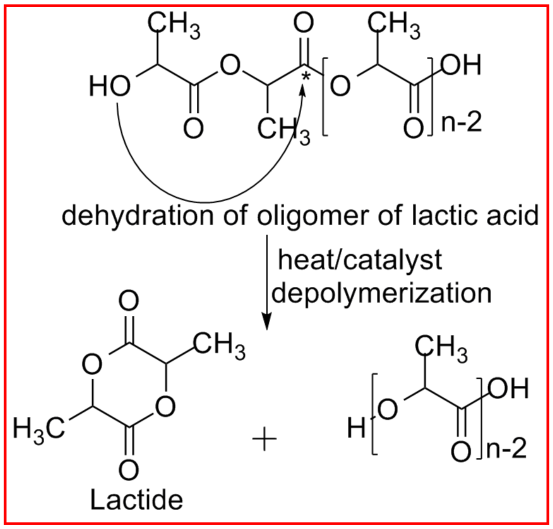
1.2.3b Purification of fermentation-produced lactic acid: Complete esterification is a viable means of purification. But that reduces the enantiomeric purity due to associated racemization of various extents. Besides, traces of the esterifying alcohol remain as impurity. Various other methods, largely physical, have been reported over a long period of time, including solvent extraction, steam distillation, electro-dialysis and fractional crystallization.[28, 29]

1.2.3c Analytical methods for purity determination: In a broad survey of different analytical methods including titration, photometry, fluorometry and enzymatic assays, an HPLC method, using a Sepharon SGX-C18 column, mobile phase of 2 % $(NH_4)_2HPO_4$ / H_3PO_4, pH 3.5 and differential refractometric detector, was proved more suitable and a practical one.[30]

1.2.3d Optical purity: Chiral resolution of D- and L-lactic acids has been performed by capillary electrophoresis using 2-hydroxypropyl-β-cyclodextrin as a chiral selector in a 90 mM phosphate buffer (pH 6.0). Another novel and recently developed method for enantiomeric purification of lactic acid is chiral recognition by macrocyclic receptors .A chiral HPLC technique has also been reported for identification of lactic acid isomers. In fact, this technique has been employed to investigate the chiral selectivity of an enzyme-catalyzed lactic acid polymerization.**[31, 32]**

1.3 Production and purification of lactide: A process for the continuous production of substantially purified lactide and lactide polymers from lactic acid or an ester of lactic acid comprises the steps of forming crude poly lactic acid, preferably in the presence of a catalyst means in the case of the ester of lactic acid, to form a condensation reaction byproduct and poly lactic acid, and depolymerizing the poly (lactic acid) in a lactide reactor to form crude lactide.**[33, 34]**

The basic technique is to depolymerize a lactic acid oligomer at high temperature in presence of certain catalysts (Scheme 2). The process is equilibrium one and necessitates constant or phase removal of the product. Favorable depolymerization temperatures are 190-260 °C and catalysts are various, for example zinc octoate, zinc oxalate, Sn-phthalocyanin, Sn-acetate, Zn (II) oxide, stannous octoate, dibutyltin oxide, Zinc (IV) oxide, Zn-powder and zinc lactate. The lactides are all volatile solids, which are to be condensed as sublimate between 20 and 35 ^{0}C fig. 1.2 shows the stereoisomer of lactide.



Scheme 2: Production of lactide from lactic acid oligomers by backbiting.

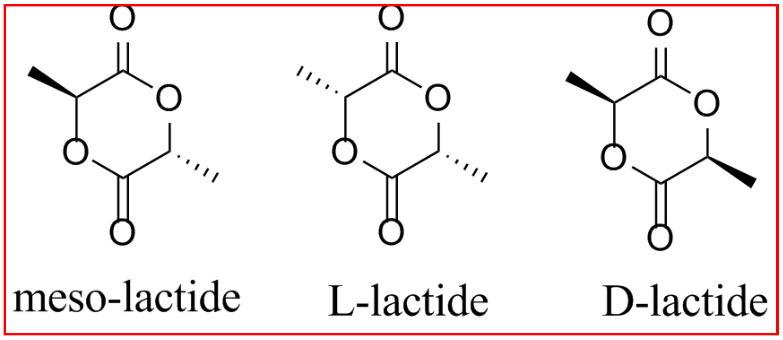
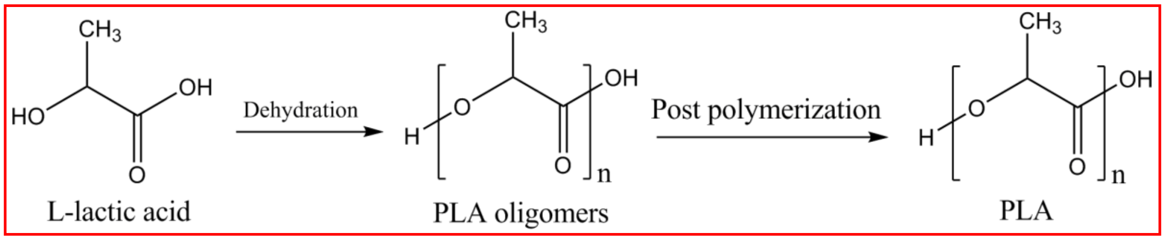


Fig. 1.2: Stereoisomers of lactide.

Lactide synthesized by depolymerization of poly (L-lactic acid) by using Al, Ti, Zn and Zr compounds i.e. their metal alkoxides, organic acid and enolate salts, resulting in L,L-lactide, meso-lactide and D,D-lactide. In presence of zinc alkoxide, lactic acid was heated at 190 ^{0}C under reduced pressure (100-25 Torr) to give lactic acid oligomers. Tri-Bu tin ethoxide was added, and the reaction mixture was heated at 190 ^{0}C (7.5 torr) to give 95% lactide and 89% yield.[35] Depolymerization of oligomer at 220-250 ^{0}C using ZnO as dehydrating agent and depolymerization agent for the lactide synthesis characterized by IR and ^{1}H-NMR.[36] L-lactic acid oligomer (M_w = 1700 and optical purity 98.5%) was heated at 200 ^{0}C under 3 Torr and depolymerized, using tin octylate at 160 ^{0}C for 1 hr to give 89.0% L, L-lactide.[37] Tin octanoate was used as catalyst at 200 ^{0}C gives 91.7% optically pure L,L-lactide.[38] Dibutyl tin chloride at 160 ^{0}C gives 57% L,L-lactide whereas Sn-powder, gave exclusively L,L-lactide with high enantiomeric purity (enantiomeric excess > 99 %) from L-lactic acid. Other tin compounds like $SnCl_2.2H_2O$ and $Sn(OH)_2$ have also been used as catalysts (enantio-purity not reported). Rare earth metals, for example $La(OAc)_3$, have also been employed as catalysts to improve enantiomeric purity.[39]

1.4 Synthesis and characterization of poly (lactic Acid):

PLA is synthesized mostly in two ways. One is direct dehydropolycondensation in melt or solution phase to from oligomers followed by various post polymerization processes (Scheme 3) for example melt or solution phase polycondensation, which basically means extension of the process of oligomer synthesis itself.



Scheme 3: Dehydropolycondensation followed by post polymerization.

The other means is to perform cationic, anionic or coordination, ROP of the lactide.

1.4.1 Dehydropolycondensation of lactic acid: One of the ways of producing poly (lactic acid) at least up to the level of oligomers is direct dehydropolycondensation of chemically pure lactic acid. The subject has seen extensive amount of research and development activity, but the literature is mostly scattered in numerous patents. Number of published literature is relatively few.

The process is basically an acid-catalyzed intermolecular esterification of the hydroxyl and carboxylic acid groups of lactic acid, in which numerous Lewis acids as well as protonic acids have been used for trials. Ajioka et al.[40] have accumulated results of lactic acid dehydropolycondensation with various catalysts and compared the results. Young Ha. et al. investigated a number of Lewis acids and different reaction conditions also,for the direct dehydropolycondensation of L-lactic acid to make PLA, and the polymers prepared thereof were characterized for molecular weight as well as conversion, cyclic dimer formation and racemization by proton NMR and for crystallinity by thermal analysis. 98 % H_2SO_4 was found to be the best polycondensation catalyst, which yielded a PLA of number average molecular weight 31,000, and minimum or no racemization. Sn $(Oct)_2$, which is a good Lewis acid and widely used in the coordination ring opening polymerization of the cyclic dimer of lactic acid, yielded a number average molecular weight of 30,000 in dehydropolycondensation, but racemization with this catalyst was high (about 48 mol%) and the product polymer consequently completely amorphous.

The lactic acid dehydropolycondensation, like any other esterification reaction, is an equilibrium-controlled process, in which both esterification of the alcohol and carboxylic group and hydrolysis of the ester linkages by water, which is a by-product of esterification, proceed simultaneously, thereby limiting the attainable molecular weight unless the by-product water is removed from the system very efficiently. A new type of tin-based Lewis acid catalyst, tetrabutyl distannoxane, which can retard the hydrolysis, has been exploited for lactic acid dehydropolycondensation reaction by Kobayashi et al. where a maximum weight i.e. average molecular weight of 126,000 has been attained.[41] Poly(lactic acid) is a pale polymer melting at about 160-184 °C with a glass transition temperature of 57 °C.

PLAs have a great potential for biodegradable biomedical materials. However limitation of their use still exists because of their crystallinity, lack of functionality. For further improvement of their properties and functionalities, Ohya Y et al. synthesized various lactic acid copolymers having reactivity and amphiphilicity and/or branched structures such as polydepsipeptide-block-PLA, comb-type PLA, branched PLA, PLA with terminal saccharide residues, and PLA-grafted polysaccharides. It was found that branched PLA can control the degradability and mechanical property of PLA.[42] Mechanical properties can be reached by suitable organo-polymeric and inorganic materials. Surface modification and characterization of the biosystem are having great interest. For the longer time a biodegradable material has to be considered that any material is degraded and hence should present continuously a renewable biocompatible surface. Currently available materials are PLA, PCL, polycarbonate and its and copolymers.[43] Many of the current polymers and processing techniques need to be improved in order to produce polymers with better performance in biological media. An important trend in related research and development is the synthesis of novel polymers, which would exhibit improved biocompatibility, and be bioresponsive.[44]

Biodegradable polymers have been the topic of many researches. They can be mainly classified as agro-polymers (starch, protein, etc.) and biodegradable polyesters PLA, PCL etc. For certain applications, biopolyesters cannot be fully replacement of conventional thermoplastics since some of their properties are too weak. Therefore the biopolymers have been formulated and associated with nano-sized fillers, which could bring a large range of improved properties such as stiffness, permeability, crystallinity, thermal stability.[45]

The crystallization and thermal behavior of biodegradable polyesters have been extensively studied in recent years, however Pan P. et al. mentioned polymorphic crystallization and phase transition of biodegradable polyesters, isomorphic crystallization of biodegradable random copolyesters, where the effects of comonomer composition and crystallization conditions are discussed.[46]

1.4.2 Ring Opening polymerization of lactide: Poly (lactic acid) can be obtained from an entirely different route, that is ring opening polymerization (ROP) of the cyclic dilactone of lactic acid, called dilactide or lactide, in presence of an initiator (also called catalyst). The lactide is prepared from lactic acid oligomers by a thermal depolymerization process using certain catalysts, as discussed elaborately in a previous section.

Stereoselective and living ring opening of meso-dilactide with enantiomerically pure aluminum alkoxide initiator has yielded purely syndiotactic poly (lactic acid) with narrow polydispersity and controlled molecular weight.[47]

Preparation of heterotactic poly lactides from racemic lactide results from alternative incorporation of L and D lactide and thus requires chain-end control. Coates et al. demonstrated that *β*-diiminate dinuclear complex catalyzed the stereoselective ROP of *rac*-lactide yielding highly heterotactic microstructures, with stereoselectivities of 90 % at room temperature and 94% at 0 ^{0}C.[48] The isopropyl groups at the aryl substituents were found to play a key role on the chain-end control, as indicated by the decreased heterotacticities observed with ethyl (79% at room temperature) and *n*-propyl (76% at room temperature) groups. Comparatively, only modest stereocontrol has been reported for the analogous mononuclear tin initiator.This methodology has been successfully extrapolated to complexes featuring SALEN ligands, and the highest selectivity in heterotactic enchainment was obtained for the chlorinated ligands (88% and even 96% in toluene at 70 ^{0}C)[49]. Lastly, the yttrium complexes lead to stereoselectivities of 80% in tetrahydrofuran but only of 60% in toluene at room temperature. The chain-end control was of similar magnitude for alkyl and amido co-ligands (complexes but significantly lower for the lanthanum derivative **(**64% in tetrahydrofuran). Coates et al. recently demonstrated that regular alternation of L- and D-lactide units could also be achieved from *meso*-lactide and the racemic aluminum catalyst.[50]

Stannous Octoate gave a ring opening polymerization of L-lactide resulting high molecular weight and narrow polydispersity, but depolymerization started beyond a conversion of about 80 % that takes 72 hr at 130 ^{0}C in a bulk (solvent less) polymerization. Depolymerization starts sooner if the reaction temperature is higher.[51]

Poly (l-lactide) has been prepared using Zn (II) L-lactate in bulk at 120 ^{0}C or 150 ^{0}C. The highest number average molecular weight M_w=70,000 are formed at [M]/ [I] ratio was 4000 and 100 % optically pure PLA formed even at high reaction temperature.

The controlled polymerizations of L-lactide have been carried out using active zinc catalyst. The result showed good control of molecular weight and molecular weight distribution.[52]

Ring opening polymerization of D, L-lactide with Zn (II) lactate at 150 ^{0}C for 96 hr gave 96.7 % conversion of poly (lactide) having number average molecular weight ~ 100,000 and polydispersity 1.5.[53]

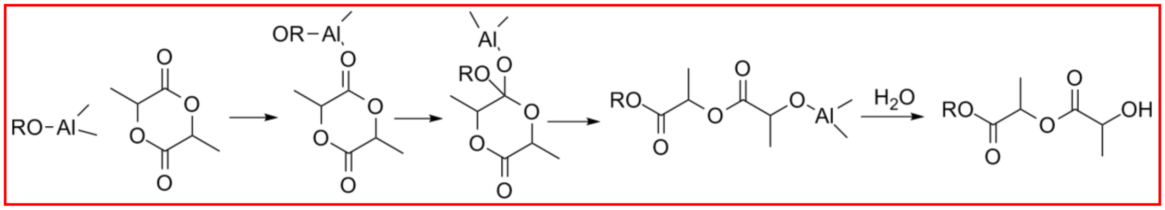
Copolymer of poly (lactide) and PEG have been synthesized by ROP of L-,D-lactide in the presence of mono or dihydroxy PEG using nontoxic Zn (II) lactate as catalyst. The result showed that the properties of polymeric micelle strongly depended on the chain structure and composition of copolymers.[54]

A "coordination insertion" mechanism of Sn $(Oct)_2$ initiated ROP of lactones has been proposed and demonstrated separately by both Penczek et al.[55], and Kricheldorf et al.[56] The mechanism is generally accepted for all lactones including the lactides and glyolides.

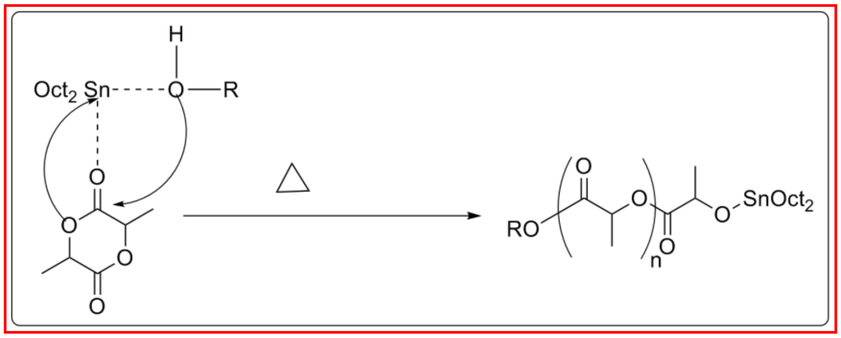
Six different acetylacetonato complexes (M (AcAc)n, M = Nd, Y, Zn, Zn, Fe, Co, Ni) as initiators have been found to give ring opening polymerization of D, L-dilactide with close to 99 % conversion in all cases, the conversion for the rare earth metal complexes being higher and decreasing remarkably with increase in reaction temperature, time.[57]

Aluminium alkoxides are also another class of ROP catalysts that proceeds through the coordination-insertion mechanism and give living polymerization, controllable molecular weights and low molecular weight distribution (1.1–1.4) of PLA[58], and also give rapid polymerization with high conversion, low transesterification and zero racemization, when ROP is carried out below 150 ^{0}C.[59] Dubois et al. have carried out thorough studies of the ROP of lactones (especially, lactides) catalyzed by aluminium isopropoxide, $Al(OiPr)_3$, and confirmed the coordination-insertion mechanism, involving three active sites per aluminum atom, no aggregation of catalyst and insertion of the lactide into the aluminium alkoxide bond with lactide acyl-oxygen cleavage, similar to the Sn. Octoate mechanism.[60]

1.4.3 Coordination-insertion polymerization: The most widely used complex for the industrial the three-step coordination-insertion mechanism for the ROP of cyclic esters was first formulated in 1971 by Dittrich and Schulz.[61] The first experimental proof for such a mechanism in the Al (*iso*-Pr)$_3$ (scheme 4) initiated polymerization of lactide was independently reported in the late 1980s by Kricheldorf.[59]

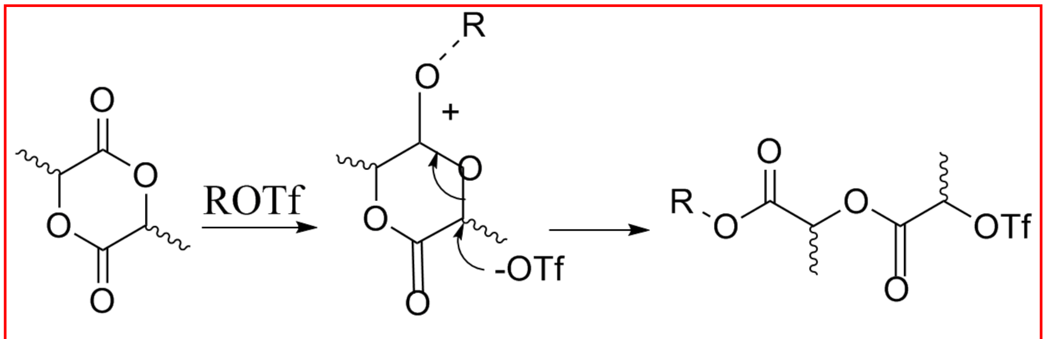


Scheme 4: ROP of lactide in presence of Al (*iso*-Pr)$_3$.



Scheme 5: ROP of lactide in presence of tin (II) bis (2-ethylhexanoate).

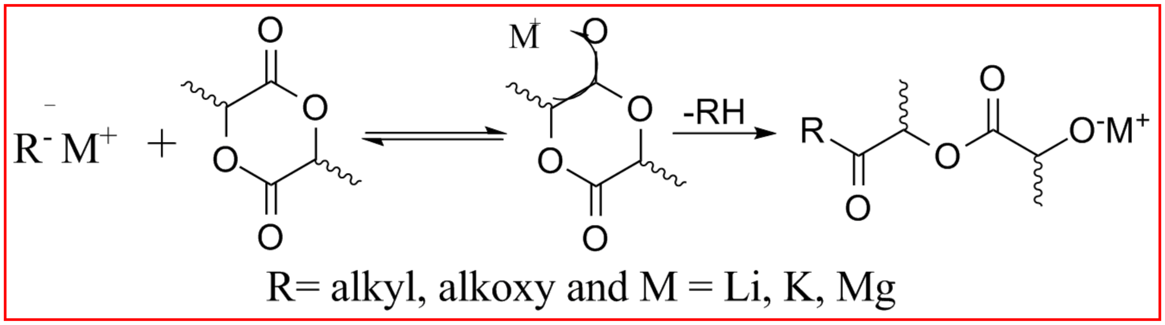
1.4.4 Cationic polymerization: After unsuccessful attempts reported in 1971 by Dittrich and Schulz,[61] the feasibility of such a cationic ROP of lactide was demonstrated by Kricheldorf et al. in the late 1980s.[62] Among the numerous acidic compounds investigated only trifluoromethanesulfonic acid (HOTf) and methyl trifluoromethanesulfonate (MeOTf) (scheme 6) proved to be efficient initiators. The polymerization rates were significantly higher in nitrobenzene than in chlorinated solvents, with 50 ^{0}C being found to be the optimum reaction temperature.



R = H, Me, or growing polymer chain , Tf = CF_3SO_2

Scheme 6: Cationic polymerization of lactide in presence of trifluoromethanesulfonic acid (HOTf) and methyl trifluoromethanesulfonate MeOTf.

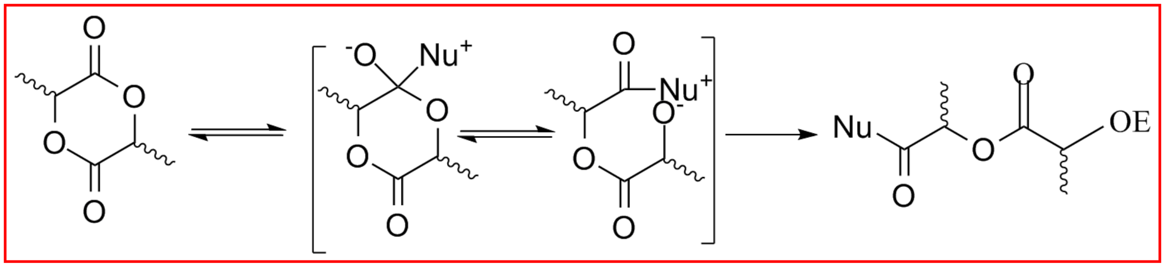
1.4.5 Anionic polymerization: Anionic polymerization (Scheme 7) of lactide has been much less investigated than the coordination insertion approach. Although higher activities might be anticipated for anionic promoters that typically display strong nucleophilic and/or basic character, the deleterious contribution of transesterification and racemization reactions might be expected to be significantly more important when naked or loosely bonded anionic species are involved.



R= alkyl, alkoxy and M = Li, K, Mg

Scheme 7: Anionic polymerization of lactide.

1.4.6 Nucleophilic polymerization: Metal-free catalysts are attracting growing interest as more economical and environment friendly alternatives for classical organic transformations. To this end, enzymes (such as lipases) as well as organocatalysts (such as amines, phosphines, and N-heterocyclic carbenes) have recently been investigated for transesterification reactions[63], including lactide ROP.[64] These metal-free nucleophilic catalysts (scheme 8) are particularly attractive for biomedical applications of the resulting polymers, since there is no concern of contamination, waste, and removal of metals.



Scheme 8: Lactide polymerization via nucleophlic ROP mechanism.

1.5 Structure and properties of poly (lactic acid)s:

1.5.1 General structure-property relationships: Pure poly (L-lactic acid) (PLA) and pure poly (D-lactic acid) (PDLA) are semicrystalline, with spherulites composed of crystalline lamellae and amorphous regions located between lamellae and between spherulites**[65, 66]** Within the lamellae the polymer adopts a 10/3 helical structure.**[67]** The degree of crystallinity and melting point of PLA are affected by the stereo irregularity in the polymer.**[68]** Incorporation of the other isomer in a primarily stereo pure PLA reduces both the degree of crystallinity and the spherulite size, with a concomitant decrease in the ΔH value of the crystalline melting endotherm related to one another by a best fitting straight-line equation**[68]** of the form.

$$Y = 1.63 + 1.27x,$$

Where y is % crystallinity and x is ΔH (in J/g) of the crystalline melting at T_m.

While de' Santis and Kovacs**[69]** propose a 10/3 helix, ten Brinke and coworkers**[67]** have shown that another helical structure, a 3/1 helical structure called the beta-structure (the 10/3 helix being called the alpha-structure henceforth) is also possible for PLA isotactic polymers. Only hot drawing of PLA fibers at high temperature and under high stress (high draw ratios) can make an alpha to beta-structure transformation possible. Besides, they have also calculated the relative atomic positions in a chemical unit of PLA.

Poly (lactide) s can exhibit different microstructures depending both on the monomer involved and on the course of the polymerization reaction.**[70]** Isotactic polylactides, either poly (L-lactide) or poly(D-lactide), contain sequential stereocenters of the same relative configuration, while syndiotactic polylactides, namely, poly (*meso*-lactide), contain sequential stereocenters of opposite relative configuration. Regular alternation of L- and D-lactide units leads to another ordered structure, namely, heterotactic polylactides, also described as disyndiotactic polylactides. Last, atactic polylactides are obtained when the polymerization occurs without any stereoregularity. The stereosequence distribution in poly lactide samples (fig. 1.3) is usually determined by NMR spectroscopy through inspection of the methine and/or carbonyl regions (^{13}C-NMR and homonuclear decoupled ^{1}H- NMR).**[71]**

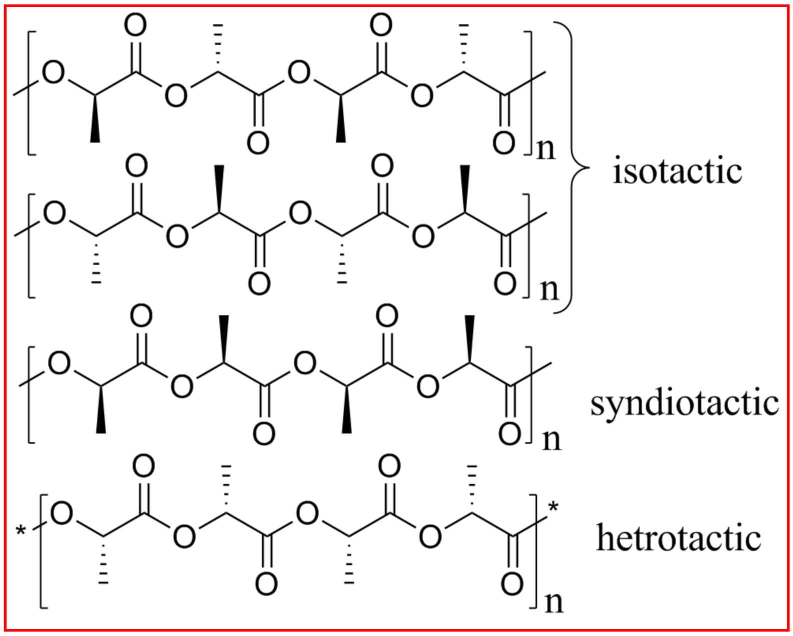


Fig. 1.3: Different stereotypes of poly lactides.

1.5.2 Stereocomplex: Stereo pure PLA polymers show another remarkable property called stereocomplex formation. Polymer-polymer complexation is known, when two different polymers with different chemical structures complex between themselves upon simple mixing because of favorable interactions existing between the different polymer chains.

The well-known inter-polymer complexes include (1) a poly-electrolyte complex between poly-anion and poly-cation[72] (2) a hydrogen-bonding complex between a poly(carboxylic acid) and a polyol or polyether[73] and (3) a charge-transfer complex polymeric donor and acceptor.[74]

Table 1.2: Effect of stoichiometry and crystallinity on mechanical properties

Properties	PLA		
	L-PLA	Annealed L-PLA	D,L-PLA
Yield strength (MPa)	70	70	53
Tensile strength (MPa)	59	66	44
Flexural strength (MPa)	106	119	88
Notched Izod impact ($J.m^{-1}$)	26	66	18
Vicat penetration (°C)	59	165	52

But stereocomplexes are complexes between two polymers of same chemical structures but different stereochemical configurations. This is comparable to two enantiomeric compounds forming a racemic crystal if their molecular affinity is sufficiently strong. For example, L,L-dilactide (cyclic monomer of PLA) and D, D-lactide (that of PDLA) possess a melting point of 97.5 ^{0}C each, while racemic mixture crystallizes differently to give a new crystalline melting point of 124 ^{0}C.

A stereo complex differs from a racemic mixture of the two, stereo pure polymers in the sense that the stereocomplex, unlike a racemic mixture, should have a new crystalline packing pattern. Recemate of optically active D- and L- polymers are well known, but among them only a few are stereocomplexes.[75, 76, 77]

Stereocomplex between separately prepared, pure poly (L-lactic acid) and poly (D-lactic acid) was first synthesized and reported by Ikada and coworkers.[78] They got the stereocomplex by mixing equal moles of the two polymers, both taken as dichloromethane solutions, together and precipitating into methanol and drying under vacuum. While the individual PLAs showed a single crystalline melting point of 180 ^{0}C each, the stereocomplex showed a single, new melting endotherm at 230 ^{0}C. Wide angle X-ray diffraction patterns also showed peaks at completely new positions for the 50-50 mixtures. All physical and material properties of the stereocomplex are different from the individual poly (lactic acid). An interesting property, for example, it forms gel in a concentrated solution.[79]

Stereocomplexes are generally made from a 50-50 mixtures of stereo pure PLAs in solution. But insitu stereocomplex has also been reported of late. There are mainly two different strategies. One is synthesizing a stereo pure poly (lactic acid) from an enantiopure lactide in presence of poly (lactic acid) of the opposite configuration.[80] The other strategy is insitu stereocomplex formation by polymerizing a racemic lactide in presence of a suitable chiral catalyst.[81] The stereocomplex has found use in the industry as a new poly (lactic acid) material because of its high crystallinity, good processability and good moldability.[82]

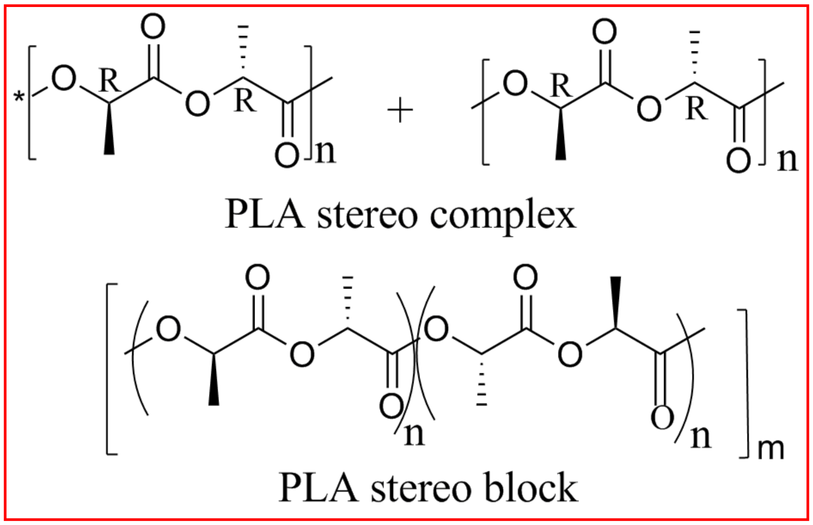


Fig. 1.4: PLA stereo complexes and stereo blocks.

Interestingly, high melting temperatures are not restricted to enantiomerically pure poly (L-lactide) or poly (D-lactide) (T_m 170-180 ^{0}C) and are even surpassed (T_m up to 230 ^{0}C) by PLA stereocomplexes[83] and PLA stereoblocks (fig. 1.4).

1.5.3 *Stereocontrol of Lactide ROP:*

So far, only a few preliminary results have been reported for the stereochemically controlled polymerization with nucleophilic catalysts: (i) no racemization occurred in the enzyme[84], and DMAP catalyzed[85], polymerization of the enantiomerically pure L-lactide and (ii) no stereosequence enrichment was detected when D,L-lactide was polymerized with lipase PS or chiral phosphines. The latter result has been attributed to the rather drastic conditions required with phosphines as ROP catalysts (bulk, 135 or 180 ^{0}C). However, higher stereocontrol might be anticipated for the much more active N-heterocyclic carbenes since these catalysts efficiently achieve lactide ROP in solution even at room temperature.

1.6 Properties of copolymers: The ability to make PLA polymers in two different ways, namely polycondensation and ring opening polymerization, leads to a wide variety of copolymers for improving or changing the final properties. The use of direct condensation leaves open the use of any hydroxy-acid, diol, or diacid, with which to form random or nearly random copolymers, mostly with increased flexibility and modified solubility. The use of ROP yields the ability the form random, block, or pseudo block copolymers to produce polymers with a wide range of mechanical properties.

However, beginning of a discussion of properties of poly (lactic acid) copolymers can as well be made with the aliphatic copolyesters of lactic acid, which in many cases have been found to be more processable due to lower glass transition temperatures and more thermally stable.

For example, copolyesters of L-lactic acid/ethylene glycol/adipic acid and L-lactic acid/1,4-butanediol/succinic acid were been prepared by direct dehydropolycondensation, yielding linear polyesters whose molecular weights were less than 30,000, while addition of a polyol such as pentaerythritol produced multibranched with a little higher molecular weights (>50,000).**[86]** The glass transition temperatures of linear and branched copolyesters were in the ranges from -17 to 43 ^{0}C and from 10 to 23 ^{0}C respectively, both of which are lower than that of linear poly (L-lactic acid), which is close to 60 ^{0}C. Initial thermal decomposition temperatures (TD) of the linear and branched copolyesters were in the ranges from 205 to 272 from 194 to 228 ^{0}C respectively, both of which are higher than that of linear PLA, which is about 170 ^{0}C.

High molecular weight copolyesters of L-lactic acid and ε-caprolactone were prepared using Sb_2O_3 as catalyst and dipentaerythritol as initiator. In this process short chain polycaprolactone (PCL) oligomers were produced by ROP, which simultaneously co-polycondensed with the lactic acid, thereby yielding copolyesters that was mostly amorphous. The T_g was in the range of 48 to 43 ^{0}C and decreased with increasing caprolactone content. The initial thermal decomposition temperature (TD) was in the range of 212 and 289 ^{0}C, while that of PLA homopolymer was 168 ^{0}C.

The most frequently synthesized and most largely exploited copolyesters of lactic acid, as far as material application is concerned, are the copolyesters of lactic and glycolic acid, prepared by both dehydropolycondensation of lactic and glycolic acids as well by ring opening polymerization of the lactides with dilactone of glycolic acid, called glycolide.**[87, 88, 89]** The higher (than PLA) melting point of 228 ^{0}C and a lower T_g of 37 ^{0}C for polyglycolic acid leads to a range of amorphous polymers, depending on the sequence of glycolic and lactic blocks in the backbone of the copolymer, with lower glass transition temperature yet more toughness than pure PLA. Increasing glycolic acid content also reduces the hydrophobicity of copolyesters with 30 mol% or more glycolic acid content are insoluble in non-polar aprotic solvents and more easily degradable than pure PLA.

Introduction of mandelic acid comonomer in a poly (lactic acid) synthesized by dehydropolycondensation improved thermal and mechanical properties, in spite of randomness of the incorporation and consequent destruction of crystallinity.[90] As amount of comonomer feed increased, the molecular weight of the copolymer decreased linearly. But the glass transition and decomposition temperature shifted higher, indicating improved thermal stability with increased mandelic acid content. Tensile strength of cast films also improved in copolymers with 5 - 10 wt% of mandelic acid.

Direct dehydropolycondensation of bis-carboxyl-terminated PLA with PEG yielded multiblock copolymers, in which PLA and PEG blocks were phase separated and the properties of one block were affected by the block length of the other.[91] The longer the PLA block the lower the crystallinity and melting temperature of the PEG block. These copolymers were having different crystallization behavior in melt and solution casting crystallization process, even though the chemical structures and molecular weights were the same in both cases. The crystallizability of the PLA block was more affected by the crystallization method than that of the PEG block. Such alternating multiblock copolymers formed interesting hydrogels, which are thermoplastic in nature.[92] They offer potential for application in drug delivery and various other biomedical projects.

Di and triblock copolymers of telechelic PEG with aliphatic polyesters like PLA showed thermo-reversible gelation because of the hydrophilicity-hydrophobicity balance between the two block components.[93] Such block copolymers formed micelle in water at lower concentrations while at higher concentrations the gel to sol transition was observed as temperature was increased up to a certain temperature beyond which the polymer precipitated. With increasing block length of the hydrophobic aliphatic ester block, the gel to sol transition is observed at lower concentrations and with a broad temperature range from 0 ^{0}C to 90 ^{0}C. Such properties are worth exploitation in the drug delivery industry.

Aqueous solutions of triblock copolymers, poly(ethylene glycol-b-(D, L-lactic acid-co-glycolic acid)-b-ethylene glycol) (PEG-PLGA-PEG), coupled with hexamethylene diisocyanate, have shown even more interesting thermo-reversing gelation, where there is a sol-to-gel transition at lower temperature and a gel-to-sol transition at a higher temperature. It is the lower transition, sol-to-gel, which is more important because the polymer will flow as a solution at room temperature while gel inside the body at body temperature. Such polymers are worth exploitation in the drug delivery industry as "injectable gel".

Investigation of surface topography of PLA-PEO diblock copolymer submerged in water by AFM visualized the apices of the PEO chains extending into the aqueous environment from the surface, corresponding to visualization of polymer brushes at molecular level and anticipated resistance to protein interactions.

Linear and star stereoblock copolymers of lactic acid are prepared by sequential polymerization of isomeric lactides in presence of diol or polyol. The most important message is that the block copolymers crystallize even at 35 mol % concentration of the D-isomer in a preponderance of the L-units, in contrast to the amorphous nature of random steerocopolymers similar and less incorporation of the stereoisomer.**[94]** The crystallinity of the stereoblock copolymer is a function of annealing temperature and time.

PLA has a very crucial hydrophile-lipophile balance that is severely affected, rather altered, by block-copolymerization with PEO. At the same time, fine-tuning the relative block lengths of PEO and poly lactide, its stability against rupture of microscopic liquid film and nanoemulsions can be controlled.**[95]**

The onset of weight loss during hydrolytic degradation of poly (lactic acid) is generally found to become more rapid when block-copolymerized with PEO, but with time the difference almost vanishes.**[96]** This is explained in terms of initial rapid diffusion of water in to the copolymer due to miscibility of the PLA and PEG blocks and greater water solubility of the PEG-PLA copolymer. But as water intake increases and chain scission of PLA blocks occurs, a gradual phase separation between the PLA and PEG blocks that makes the chain rates of the PLA blocks similar to that in a pure PLA homopolymer.

Copolymers of itaconic anhydride and methacrylate terminated PLA macromonomer was made with 15–85 mol % incorporation of the itaconic anhydride and retention of the cyclic anhydride structure in order to provide a new set of biodegradable polymers prepared from natural resources and with a wide range of properties.**[97]** The copolymers showed a range of glass transition temperatures from 31 to 73 ^{0}C, increasing with increase in the itaconic anhydride incorporation. No residue of crystallinity of the parent PLA is restored in these copolymers.

Comonomers that impart lower glass transition temperatures and flexibility have been increasingly researched in order to improve the low temperature properties and ductility of PLA. The work has been driven mainly by the need for biocompatible ingredients that would that would improve the properties of implantable medical devices and drug delivery systems. Extensive studies have been done on more common and commercial monomers to elucidate reactivity ratios and sequence formation during melt and/ or solution copolymerization.

The ring opening copolymerization of lactide and ε-caprolactone give polymers with wider spectrum of properties than the polymers synthesized by copolycondensation of the corresponding hydroxy acids, which have been discussed earlier. Such ring opened copolymers yield tough polymers with properties ranging from rigid thermoplastics to elastomeric rubbers[98], with tensile strengths ranging from 80 to 7000 psi (0.6 – 48 MPa), and elongations over 400 % . The larger reactivity of lactide over ε-caprolactone leads to copolymers that are blocky, where the block lengths depend on the starting comonomer composition, catalyst and polymerization temperature.[99] Poly (ε-caprolactone) (PCL) itself has a T_g of –60 ^{0}C with a melting point of 59 – 60 ^{0}C, which when the monomer is ring open polymerized with pure L-lactide yields a copolymer with flexibility because of the caprolactone segment and high crystalline melting points from the L-PLA blocks. These blocks must be sufficiently large to allow rapid crystallization. Grijpma has synthesized a copolymer with 1:1 monomer molar ratio, which crystallized at room temperature very quickly, in contrast to a similar copolymer with average block lengths of 8.5, which exhibited crystallinity only after weeks of annealing at room temperature and the former polymer with longer block lengths had a T_g of –39 ^{0}C, both PLA and PCL block melting points, a tensile strength of 18.2 MPa, and elongation at break of 480 %.[100]

Poly (lactic acid) is one of the highest glass transition temperature-possessing polymers among aliphatic polyesters and polyethers. Only a few monomers, including the mandelic as mentioned before, have been found to increase the glass transition temperature of PLA when copolymerized into the backbone. Lactones of salicylic acid are reported to have homopolymer glass transition temperatures of 73 – 110 ^{0}C and polymerize slowly with lactide to give copolyesters with higher T_g values than PLA homopolymers.[101, 102]

The size and chemistry of the rings and the variety of comonomers, which can be ring-open polymerized with lactides to form different block or random block copolymers, is thus largely dependent on their mode of propagation, reactivity and initiation.

Use of functional amino acids in the synthesis of the morpholinedione has thus become an effective way of incorporating functional pendant groups into the polymer. Comb-like graft copolymers of lactic acid, poly(L-lactic acid-co-L-lysine), with L-lysine side chains, of degree of polymerization ranging from 10 to 100, have been reported, with the overall L-lysine content in the copolymer varying from 7 to 72 %.[103] L-lysine residues of such poly (L-lactic acid-co-L-lysine) copolymers were further modified with an RGD (arginine-glysine-aspartic acid) cell adhesion promoting peptide, the modified copolymer being useful for tissue engineering. Its degradation rate was faster than poly (L-lactic acid) due to disruption of crystallinity by the lysine residues in the copolymers.

Boury and coworkers[104], have investigated the interfacial behaviour of PLA in comparison with influence of lactic acid and glycolic acid proportion in copolymers by studying on monolayer spreading at air/water interface, using Langmuir-Blodgett films. The size and chemistry of the rings and the variety of comonomers, which can be ring-open polymerized with lactides to form different block or random block copolymers, is thus largely dependent on their mode of propagation, reactivity and initiation. Fig. 1.5 shows some of the monomers (1.3 – 1.19) that have been studied extensively with regards to ring opening copolymerization with lactides. Thus, besides lactones and epoxides, morpholinediones are another important class of cyclic compounds that have been copolymerized with the lactides. The pure poly (L-lactide) gave a more rigid film and had higher surface pressure than the film of the copolymer. The extent of orientation decreases with increasing incorporation of the glycolide unit, while the parent pure poly (L-lactide) film is highly oriented, which is the cause of high surface pressure. The high surface area is attributed to strong lateral interaction between lactic groups, which form microdomains in small areas. Glycolic acid units disrupt this interaction and do not allow formation of the microdomains. In condensed state, the major contribution to the surface free energy was non-polar, although small polar component of the force, due to O atoms was measured. The lactic acid groups, particularly the methyl groups are oriented towards the air phase.

1.7 Stability of polymer: The stability of a polymer has a major impact on all of the different stages of a polymer life cycle. This is especially important for biodegradable polymers, where the biodegradation must proceed in a controlled way, although the appearance and the properties must be comparable to traditional polymers. The degradation of polymers has been defined as the number of chain scissions produced during a known period of time and can be expressed by equation (Reich and Stivala, 1971).[105] $1/DP = 1/DP_0 + K_Dt$

Where DP_0 and DP are respectively the initial and final numbers of the average degree of polymerization, K_D is the degradation rate constant, and t is the time. This equation is valid for condensation polymers when the amount of broken bonds are low; i.e. the term $K_D\ t$.

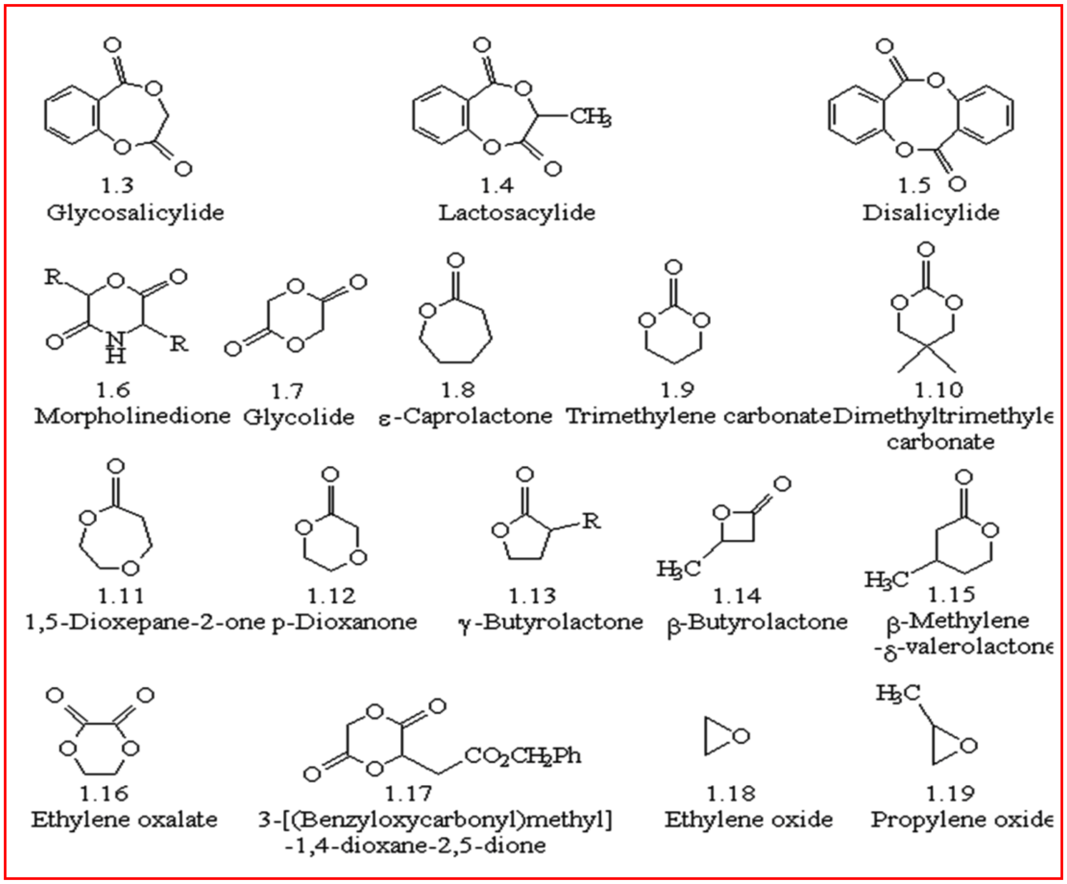
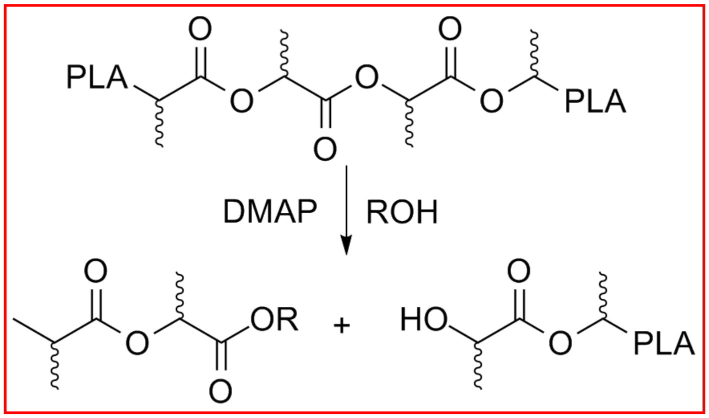


Fig. 1.5: Few comonomers that have been polymerized with lactide.

1.8 Depolymerization: Pyridine catalysts such as DMAP and PPY (scheme 9) have also been used for the chain scission of poly lactides.[106] Low as well as high molecular weight polymer samples were depolymerized with primary alcohols either in solution at 38 ^{0}C or in bulk at 185 ^{0}C. The resulting poly lactides have DPs consistent with the alcohol to polymer ratio and polydispersity index in the same range as the initial polymer. Thus, this transesterification approach allows for the preparation of controlled molecular weight and end group functionalized poly lactides. Promising results were also reported for more complexes macromolecular.



Scheme 9: DMAP-catalyzed PLA depolymerization.

Tian et al. focused on introduction to various types of synthetic biodegradable polymers with reactive groups and bioactive groups, and describes their structure, preparation procedures and properties. The focus is on advances in the past decade in functionalization and responsive strategies of biodegradable polymers and their biomedical applications.[107]

The crystallization kinetics and morphology of biodegradable diblock copolymers of PLA and PCL was studied in a wide composition range using DSC and polarized light optical microscopy. The two blocks were found to be partially miscible according to the variations of their thermal transitions with composition.Crystallization rates of the PLA block decrease with PCL content because PCL acts as a diluent for the PLA block in view of their miscibility.[108]

Polymer-layered silicate nanocomposites materials have attracted both academic and industrial attention because they exhibit dramatic improvement in properties at very low filler contents. The structure, preparation and properties of polymer-layered silicate nanocomposites are discussed in general.[109] PLA is the most extensively researched and utilized biodegradable and renewable thermoplastic polyester, with potential to replace conventional petrochemical-based polymers. In recent years, several PLA-based technologies have emerged with an emphasis on achieving chemical, mechanical, and biological properties equivalent or superior to conventional polymers. The frequent need for a chemical or physical modification of PLA to achieve suitable properties for its intended consumer and biomedical applications, however, has demanded significant attention in the last decade.[110]

The use of polymeric materials has increased dramatically for biomedical applications. Many amino acids derived biodegradable polymers have also been intensely developed with the main goal to obtain bio-mimicking functional biomaterials. Farah S. et al. have focused on biodegradable polymers derived from natural amino acids, their synthesis, biocompatibility and biomedical applications. It is observed that polymers derived from α-amino acids constitute a promising family of biodegradable materials. These provide innovative multifunctional polymers possessing amino acid side groups with biological activity and with innumerous potential applications.[111]

1.9 Source of clay:

A soft earth, which is plastic, or may be molded with the hands, consisting of hydrous silicate of aluminium. It is the result of the wearing down and decomposition, in part, of rocks containing aluminous minerals, as granite. Lime, magnesia, oxide of iron, and other ingredients, are often present as impurities.

A stiff, sticky fine-grained earth, typically yellow, red, or bluish-gray in color and often forming an impermeable layer in the soil. It can be molded when wet, and is dried and baked to make bricks, pottery, and ceramics.

The term "clay" refers to a naturally occurring material composed primarily of fine grained minerals, which is generally plastic at appropriate water contents and will harden with dried or fired. Although clay usually contains phyllosilicates, it contains other materials that impart plasticity and harden when dried or fired. Associated phases in clay may include materials that do not impart plasticity and organic matter.[112]

1.10 Organomodified clay:

Organo clay is an organically modified phyllosilicate, derived from a naturally occurring clay mineral. By exchanging the original interlayer cations for organocations (typically quaternary alkylammonium ions) an organophilic surface is generated, consisting of covalently linked organic moieties. Various modified clay shown in Table 1.3.

Table 1.3: Modifier, modifier concentration for organomodified clay

Cloisite	Organic modifier	Modifier concentration
Cloisite-Na^+	None	None
Cloisite-93A	M2HT	95 meq/100 g clay
Cloisite-30B	MT2EtOH	90 meq/100 g clay
Cloisite-25A	2MHTL8	95 meq/100 g clay
Cloisite-15A	2M2HT	125 meq/100 g clay

M2HT: methyl, dehydrogenated tallow ammonium.

MT2EtOH: methyl, tallow, bis-2-hydroxyethyl, quaternary ammonium.

2MHTL8: dimethyl, dehydrogenated tallow, 2-ethylhexyl quaternary ammonium.

2M2HT: dimethyl, dehydrogenated tallow, quaternary ammonium.

Where HT is Hydrogenated tallow (~65% C18; ~30% C16; ~5% C14).

Clay interactions with organic polymers as well as clay self assembly with organic involvement have been studied. Lin et al. emphasized on two aspects of these non-covalent interactions: first, plate-like clays had a considerable impact on polymer properties such as hydrogels and clay films, and also on the encapsulation of bio-molecules. Second, through ionic intercalation with polymeric amine-salts, the clay layered structure units got modified and enabled to self-assemble into ordered arrays such as rod, dendrite, and fiber-like microstructures.[113]

Extraordinary progress has been made in the development of practical processes and products from polymers such as starch, cellulose, and lactic acid. The need to create alternative biodegradable water-soluble polymers for down-the-drain products such as detergents and cosmetics has taken on increasing importance.[114]

Tailored compounds, based on alkyl-substituted derivatives of succinic anhydride, acid and dipotassium salt have been used to evaluate their role for intercalation of montmorillonite and the formation of nanocomposites based on polyethylene in the presence of maleic anhydride grafted polyethylene as compatibilizer. The samples have been prepared via a solution dispersion technique. It is found that these tailored compounds can be intercalated into the layers of montmorillonite. The higher affinity of the succinic groups for the organoclay has been explained as well as the decrease of the polar function influence on the gallery expansion when increasing the hydrophobicity of the organic compounds.[115]

Zhenyang Yu et al.[116] synthesized nano composites using organomodified clay and results is tabulate in Table 1.4.

Table 1.4: Thermal properties of PLA in PLA/PCL blend and its nanocomposites

Sample	T_C (^0C)	ΔH_m (J/g)	T_m (^0C)	χ_c
PLA/PCL	113.5	16.9	151.7	21.3
1% OMMT	113.2	19.9	151.9	23.9
3% OMMT	111.0	22.2	151.2	27.5
5% OMMT	109.1	24.8	151.4	31.1
10% OMMT	104.7	22.8	150.1	30.4

OMMT-Organomodified montmorillonite.

The technical feasibility of natural rubber nanocomposites with Cloisite-15A, commercial organoclay to substitute for conventionally used silica SiO_2 as filler. Three clay polymer nanocomposites have been prepared while varying the content of organoclay (2, 4 and 8 phr - parts per hundred of rubber). For comparative purposes, a sample with 50 phr of silica has been also prepared and analyzed. The compounds were characterized by their rheological, morphological, thermal and mechanical properties. The mechanical properties were also determined after the accelerated aging of the compounds. The results revealed the intercalation of the organoclay by the rubber chains in the polymer nanocomposites which reduced the enthalpy of the curing process and indicated a lower crosslink density.[117]

A novel biodegradable nanocomposite has been fabricated based on poly (3-hydroxybutyrate-co-3-hydroxyhexanoate) and silane-modified kaolinite/silica core-shell nanoparticles via solution-casting method using chloroform as solvent.[118]

Sodium montmorillonite was modified with several organic phosphonium salts. Organoclays with water soluble surfactants were prepared by the traditional cation exchange reaction. An alternative procedure hasbeen used to prepare organoclays with water insoluble salts. The effect of chemical composition and molecular weight of the salts on the thermal stability and basal spacing were evaluated. The phosphonium montmorillonites exhibited higher thermal stability than conventional ammonium organoclays.[119]

The barrier properties of PLA improvements, combinations of PLA with two nanofillers, laurate-intercalated Mg-Al layered double hydroxide and a cationic organomodified montmorillonite MMT clay Cloisite-30B, were investigated. The dispersion of these fillers in PLA by melt processing was explored using two methods, either by mixing the nanofillers with PLA granulate immediately before extrusion or by preparation and subsequent dilution of PLA-nanofiller masterbatches.[120]

Poly(ε-caprolactone)/organomodified montmorillonite nanocomposites have been prepared by in situ polymerization with dibutyltin dimethoxide as an initiator/catalyst. The montmorillonite was first modified with 1-decyl-l2-methyl-3-(11-hydroxyundecyl) imidazolium cation. The hydroxyl functionality was used not only for initiating polymer chains from the surface of the clay platelets but also for grafting polymer chains to the surface by acting as a reversible chain-transfer agent. The molecular weights of the polymer chains were controlled by the ratio of monomer to hydroxyl content.[121]

PCL masterbatches with the intercalated and the exfoliated morphology have been prepared by ROP of ε-caprolactone in the presence of organomodified montmorillonite (MMT) Cloisite-30B. PLA nanocomposites with Cloisite-30B or PCL masterbatches have been prepared by melt blending. The effects of the silicate type, MMT content and the nanocomposite morphology on thermal and mechanical properties of PLA nanocomposites were examined.[122]

Both intercalated and exfoliated PLA/organomodified montmorillonite nanocomposites were synthesized by insitu ROP of L-lactide, in bulk, directly in the presence of the nanofiller. Intercalation of polyester chains was found to appear even for natural unmodified montmorillonite-Na+, while exfoliation occurred when the aluminosilicate layers were modified by ammonium cations bearing primary hydroxyl groups. Clay delamination was effectively triggered by the grafting reaction of the growing PLA chains onto the hydroxyl groups. The influence of nanoclay content (from 1 to 10 wt%) on morphology and thermal, dispersion of modified nano clay into the polymer matrix has been studied.[123]

Clays, in situ polymerization of ε-caprolactone in the presence of organomodified clays, and initiation of ε-caprolactone polymerization from the silicate layer with appropriate organomodified montmorillonites and activator has been studied. The presence of clays did not modify the polymer crystallinity. It was shown that the in situ polymerization process from the clay surface improved the clay dispersion. The gas barrier properties of the different composite systems were discussed both as a function of the clay dispersion and of the matrix/clay interactions.[124]

Arshady R. described the manufacturing methods of microspheres and microcapsules based on biodegradable polyesters, including polylactides, polyglycolide, polyhydroxybutyrate, polycaprolactone, polycarbonates and related copolymers. Various procedures and modification of solvent evaporation and solvent extraction techniques employed for these preparations was described. The effects of process parameters i.e polymer concentration, stirring speed and mode of solvent removal on microsphere/microcapsule characteristics are also outlined.[125]

1.11 Isolation, purification, homopolymerization and copolymerization of Aleuritic acid with L-lactic acid: The lac (shellac) resin is not a single compound but consists of intimate mixture of several polar and non-polar components in a molecule. The manner in which these molecules are linked together to build up shellac complex has led to intensive chemical research during the last few decades. Shellac is always associated with an odoriferous compound, a wax and a mixture of dyes such as erythrolaccin and desoxyerythrolaccin, which are hydroxyanthraquinone derivatives. Due to the presence of the dyes, shellac gives a characteristic colour reaction with alkali. The shellac has been fractioned into three main components namely hard resin, soft resin and wax.

Resinous character of shellac is believed to be due to the association of the components through hydrogen bonding. When dewaxed shellac is slowly heated, it softens at 65-70 ^{0}C and melts between 75-80 ^{0}C. Both the resinous constituents of shellac, soft resin and hard resin, contain hydroxy acids[126. 127, 128]**,** and their polar groups are present at the interface of the molecule. It is presumed that the ability of shellac to adhere strongly to smooth surfaces is the result of orientation of these polar groups.

1.12 Chemical Structure of Shellac: Shellac in its refined form is a polyester type of resin consisting of inter and intra esters of polyhydroxy carboxylic acids[129], formed from certain hydroxy acids and sesquiterpene acids. It is believed to have five hydroxyl[130, 131]groups including vicinal hydroxyl group, one carboxyl group, in free state, three ester groups, one double bond and one partly masked aldehyde group[131] , and the probable linkages ester, acyal, acetal and ether in an average molecule. Shellac easily undergoes periodic acid oxidation, which is specific for vicinal hydroxyl groups and also to Tollen's reagent due to the presence of aldehyde group. The hydroxyl groups have been reported to react with various monohydric alcohols viz., ethyl alcohol, butyl alcohol, allyl alcohol and dihydric alcohols[132], to form ethers. This also seems to be the reason for the action of water on shellac molecules, although no chemical reaction takes place on its short contact.

Shellac structure, characteristics and modifications and epilaksholic acid, arise from a cannizaro reaction or jalaric acid-A. Sahu and Misra[133], have reported that there is no doubt that the most important components or shellac are aleuritic acid (fig. 1.6) (9, 10, 16 tri-hydroxy palmitic acid) and jalaric acid-A (a tricyclic sesquiterpene). These are connected with lactide through ester linkages.

1.12.1 Isolation of different constituent of Shellac: On hydrolysis[134], the constituent acids of shellac are liberated and consist mainly of hydroxy aliphatic and terpenic acids. The aliphatic acids are almost insoluble in water, while the terpenic acids are readily soluble and these are present almost in the proportion of 50:50. Among aliphatic acids, the main constituent acid is aleuritic (~35%) and amongst terpenic acids the main constituent acid is jalaric (25%). Other acids isolated are butolic acid (8%), shellolicjepishellolic and laccijalaric (8%) acids. Water-soluble jalaric acid and laccijalarie acids have aldehyde functions in the molecule.

1.12.2 Isolation of aleuritic acid: The structures of aleuritic acid and shellolic acid had been established by Sukh Dev. [135] He isolated laksholic acid , epilaksholic acid[136] , laccishellolic acid, epilaccishellolic and laccijalaric acid. Although it is generally accepted that shellac is a polyester (~35) formed from terpenes possessing the cadence skeleton and threo-aleuritic acid (9, 10, 16 trihydroxyhexadecanoic acid). The 9-and 10-hydroxy groups of aleuritic acid are involved in alkali-stable linkages, and a large part of the aleuritic acid remains in the combined form in the primary gum obtained after treatment with aqueous 20% sodium hydroxide.[137]

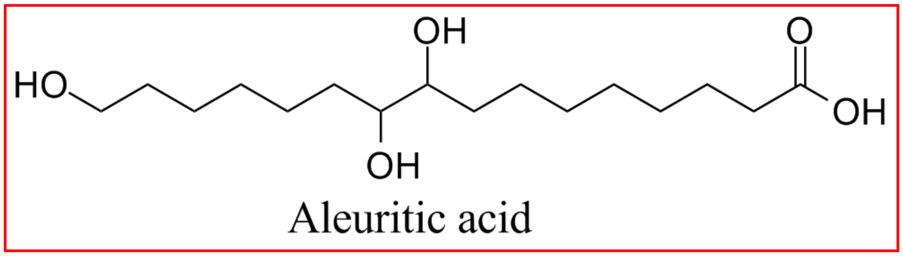


Fig. 1.6: Structure of aleuritic acid.

1.12.3 Physical Properties: Aleuritic acid is a white crystalline solid melting at 101 ^{0}C (Harries and Nagrl)[138], the acid crystallizes from boiling water or aqueous alcohol in the form of a mixture of rhombic plates and elongated parallelograms. Melted aleuritic acid, on cooling, looks like a wax and crystallizes from aqueous alcohol and chloroform in the form of rhombic plates. It is soluble in hot water and in alcohol, acetone and ammonia in the cold. Specific gravity of shellac varies between 1.14 to 1.21. It has an average molecular weight 1006, acid value 65-75 and saponification value 220-230. Shellac is insoluble in water, glycerol, hydrocarbon solvents and esters but dissolves readily in alcohol, aqueous solution of alkalies, organic acids and ketones. This finding has led to the conclusion that hydroxyl, carboxyl and carbonyl groups are present in shellac.[139]

1.12.4 Isomers of aleuritic acid: Aleuritic acid exists in two isomeric forms namely erythro and threo-aleuritic acid. Erythroform is in most abundant in nature.

1.12.5 Homopolymer and copolymer of aleuritic acid: Unstable macrolides (m + n = 10-15), useful for perfumes are prepared by lactonization of aleuritic acid.[140] An additional secondary hydroxyl group in the molecular structure further improves the 2D crosslinking as observed for aleuritic acid (9,10,16-trihydroxyhexadecanoic acid). These observations can be extended to the understanding of the short-range structure and the formation mechanism of some biopolymers such as cutin, a natural polyester supporting the lipidic extracellular membrane that have covered the aerial parts of leaves and fruits of plants.[141] The polyester resin compound is prepared by mixing aliphatic dicarboxylic acid and aliphatic glycol at a mole ratio of (1.2-1.8):1 for reaction to obtain polyester, adding 0.1-2.0 g tetra basic alcohol, adding 0.0001-0.002 g titanates organic metal catalyst (based on 1 mol aliphatic dicarboxylic acid), adding phosphates stabilizer 0.5-1 wt. parts of metal catalyst. Aliphatic dicarboxylic acid includes succinic acid 75-100, and other dicarboxylic acids with C_{2-3} or C_{5-10} alkylene group 0-25. Aliphatic glycol includes 1,4-butylene glycol and/or ethylene glycol 75-100, and other glycols with C_{2-3} or C_{5-10} alkylene group 0-25. Tetrabasic alcohol with aliphatic long main chain prepared from aleuritic acid and ethylene glycol is used as organic compound catalyst. The polyester resin compound has good processability, and adjustable mechanical strength, toughness and degradation rate, so as to be used for absorptive suture line, drug delivery carrier, and all kinds of medical materials.[142] Direct synthesis of functional polyesters from readily available monomers, ambrettolide epoxide, and isopropyl aleuriteate has been carried. These monomers allow for an easy and accessible synthesis of a variety of functional polyesters without the need for protection/deprotection strategies. Novozym-435, immobilized CALB on a polyacrylic resin and has been selected as the biocatalyst for the polymerization reactions.[143]

1.12.6 Uses of aleuritic acid: Synthesis of fragrances such as civetone, exaltone, ambrettolide and isoambrettolide and glucose manoaleuritate has been reported. The other suggested applications of aleuritic acid are the following:

1. Glucose manoaleuritate (a non-toxic, non-hemolytic water soluble compound) in medicine as an isocaloric substitute for dietary tripalmitin.
2. Preparation of plastics with good adhesive properties by the condensation of aleuritic acid with pthalic andydride and glycerin, rosin etc.
3. Aleuritic esters for compounding with cellulose esters for the preparation of lacquers, plastics and fibers.

1.13 Dehydropolycondensation of L-lactic acid with 12-hydroxy stearic acid and polymerization of macrocyclic lactones: 12-hydroxy stearic acid (12-HSA) or 12-hydroxyoctadecanoic acids, which is an aliphatic hydroxy-carboxylic acid, has been polymerized into aliphatic polyester by self-condensation. The dehydropolycondensation of 12-HSA has been performed in bulk polymerization at 160 ^{0}C under vacuum, using p-toluene sulphonic acid (PTSA) as a catalyst. A polymer with M_n up to 3500–4000 was obtained in 5 hr.[144] The low molecular weight homopolymers of 12-HSA (M_n 5000–50,000) have found application in diverse fields for example, as an adhesion tuner and carrier material in ink-compositions[145], as a softener in styrene-butadiene rubber[146], and as a surface active agent in finished cotton-polyester mixed fabric and leather treatment.[147]

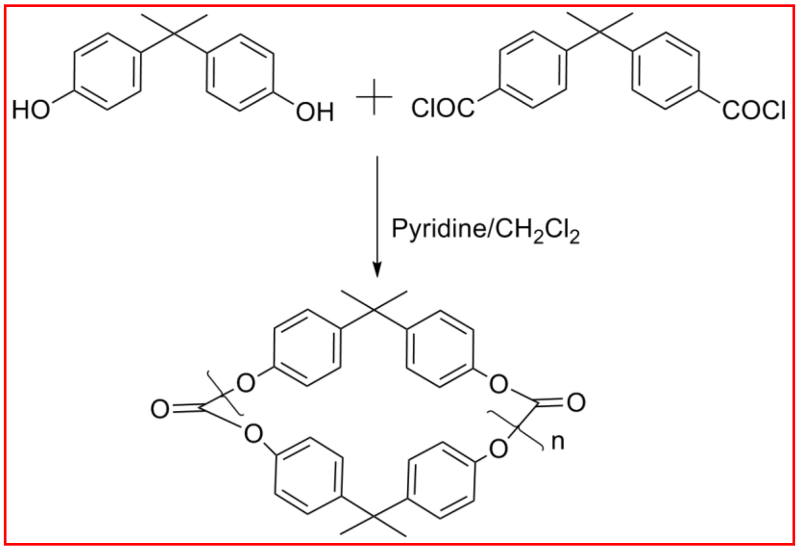
The PLA oligomers and isocyanates (4,4'- diphenylmethane diisocyanate and toluene diisocyanate) have been reported. The effects of the reaction conditions, that is, the reaction time, reaction temperature, molar ratios, isocyanates, and catalyst, M_n were demonstrated. The optimum reaction conditions are determined by the synthesis of relatively high M_n PLA-based linear polyurethanes.[148] A two-step process for lactic acid polymerization is studied: in the first step the lactic acid is condensation-polymerized to a low-molecular-weight hydroxyl-terminated prepolymer, and then the molecular weight is raised by joining prepolymer chains together using diisocyanate as the chain extender.[149] New potentially biodegradable, thermoplastic multiblock copolymers from PLA, PCL were synthesized using toluene diisocyanate (TDI) as chain extender and poly(ethylene glycol) as intrinsic plasticizer.[150]

Amphiphilic PLA, polyurethane containing carboxylic groups was synthesized via step polycondensation. Anionic polyurethane micelles were prepared by microphase separation process and the critical micelle concentration (CMC) was calculated by determining the solubilizing power to naphthalene in polyurethane aqueous solution through UV-visible spectrophotometer.[151] Biodegradable polyurethanes offer advantages in the design of injectable or preformed scaffolds for tissue engineering and other medical implant applications. Griffiths Ian et al. have developed injectable prepolymer systems consisting of lactic acid and glycolic acid based polyester star polyols, pentaerythritol and ethyl lysine diisocyanate. This study reports on the formulation and properties of a series of cross linked polyurethanes specifically developed for orthopaedic applications.[152] A series of novel poly(urethane-urea)s have synthesized from poly(lactide-co-p-dioxanone) macrodiol hexamethylene diisocyanate and butanediamine. The obtained poly(urethane-urea) may demonstrate enhanced phase separation and thus improved shape memory property.[153]

Polylactones are important biodegradable and biocompatible environmentally friendly polyesters widely used for many applications and more particularly for biomedical applications. The synthesis of novel adamantane thialactones are reported, and the results of the heavy and transition-metal cation extraction experiments are described. The results are compared with those obtained with similar thiamacrocyclic ligands that have flexible chains of methylene groups incorporated into the macrocyclic framework.

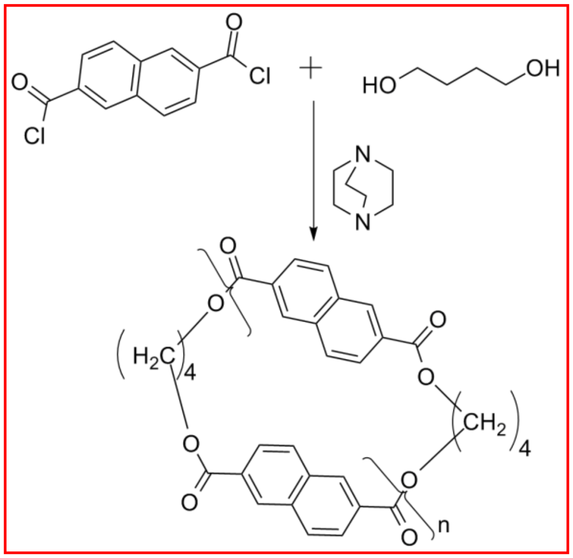
A selective, high-yielding procedure for the preparation of Bisphenol A cyclic oligomeric carbonates via a triethylamine-catalyzed hydrolysis/condensation reaction of bis(chloroformate) has been described. The reaction produces cyclic oligomers in 80-90% yield, along with about 15% high molecular weight polymer, but with almost total exclusion of linear oligomers.[154] The synthesis of PEK was made by Marks when the HF/BF_3 solvent system was found.[155]

In 1962 Schnell and Bottenbruch reported the preparation of the cyclic tetrameric carbonate of bisphenol-A. Their synthesis was carried out in methylene chloride by reacting bisphenol-A with its bischloroformate in the presence of excess pyridine under a high dilution condition of 0.05 M.(Scheme 1) The yield was only 21 %. Other similar macrocycles were also synthesized using different bisphenols. Polymerization of the macrocycle at the melting point was observed.[156]



Scheme 1: Polymerization of macrocyclic lactone.

Brittain’s group reported synthesis of cyclic poly(butylene naphthalene) oligomers from 2,6-naphthalene dicarbonyl chloride and 1,4-butanediol using diazabicyclo[2,3,2]octane catalyst as shown in scheme 2. The cyclic were obtained by extraction with methylene chloride to get a crude yield of 75 %. The cyclic were ring-opening polymerized with dibutyl tin oxide at 275 ^{0}C for 15 minutes to give the corresponding linear polymer. However, a polymer with a low inherent viscosity of 0.28 dL/g was obtained.**157**



Scheme 2**:** Polymerization of macrocyclic lactone.

Hodge’s group has developed a very novel approach to the synthesis of cyclic polyester oligomers. The monomers they used were Z-halogenocarboxylic acids. These monomers were attached to a commercial strong-base anion exchange resin as the carboxylate salts.

On heating a suspension of the bonded carboxylate salts polymerization occurred by displacing halide with carboxylate anion. The linear chain that was formed remained attached to the insoluble resin via the carboxylate end group. However, the cyclic formed by the same reaction was not bonded to the insoluble support. Thus the linear oligomers and the cyclic can easily be separated.[158]

Cis-syn-cis-Triquinane diol, with its folded topology, hydrophobic posterior and inwardly directed endo, endo-hydroxy groups, readily enters into cyclooligomerization reaction with terephthaloyldichloride. As many as nine cyclic oligomers, with macrocyclic ring size varying from 28- to 98-membered, have been isolated and characterized. The cyclic oligomers exhibit interesting spatial relationships through the relative orientation of methylene groups on the central five membered ring of the triquinane moiety.[159]

Five macrocyclic paclitaxel bis-lactones and their corresponding open chain taxoids were synthesized as models of the tubulin-binding conformation of paclitaxel. Macrocyclic lactones with a 19-21-membered ring underwent isomerization to form smaller rings. The lactones were evaluated for cytotoxicity and tubulin-polymerization ability.[160] Ring-closing metathesis of the terminal diene esters with the Ru catalyst resulted in the formation of the 20-21 membered macrolactones in high yields. Ring-closing metathesis of the diene oleate esters 19, 20 membered macrolactones.[161]

The ring-opening polymerization (ROP) of trimethylene carbonate (TMC) initiated by water or n-pentanol and catalyzed by methanesulfonic acid has been investigated.[162] Aluminium and tin salen complexes have been shown to effectively catalyze the ring-opening polymerization (ROP) of TMC to polycarbonate.[163] OH-terminated poly(trimethylene carbonate)s were synthesized by ring-opening polymerization (ROP) of TMC in the melt at 120 ^{0}C using an alcohol such as benzyl alcohol, 1,4-butanediol, ethanol, isopropanol, or tertiary butanol as a respective initiator in the presence or in the absence of acid catalyst.[164]

1.14 Degradation Mechanisms and Degradability:

1.14.1. Hydrolytic / Enzymatic: A sort of quantitative correlation can be drawn among the degree of crystallinity, orientation and enzymatic degradability of poly(lactic acid), the rate of enzymatic degradation decreased with increase in crystallinity.[165] A threshold was observed when the heat of fusion was less than 20 J/g. Effects of temperature, pH, molecular weight and copolymerization on the hydrolysis rate of poly(lactic acid) have been studied.[166]

Impurities and residual monomer increase the hydrolysis rate.[167] Peroxide modification increases the hydrolysis rate. In larger size devices of PLA, the rate of hydrolytic degradation is higher inside than at the surface of the material because of the autocatalyzing effects of the carboxylic acid groups trapped inside the device.[168]

Whether there are microorganisms in nature that are able to biodegrade PLA polymers of any molecular weight is still under discussion and investigation. There have been only a few studies where PLA or its oligomers have been subjected to selected microorganisms. In general, these studies tell us that the molecular weight is initially decreased by abiotic hydrolysis, but after the initial abiotic degradation, the molecular weight of samples aged in a biotic medium goes down faster than samples aged in an abiotic medium.[169] Presence of certain enzymes such as pronase, proteinase K and bromelain decreases the degradation rate of PLA, but effect of certain other important and likely enzymes such as esterase and lactate dehydrogenase is yet to be ascertained.

The relationship between the biodegradability of PLA, polyurethane compounds and their polymer composition has been investigated. The biodegradability (weight loss) by fungi of these polyurethanes increased when the polymethylene polyphenyl polyisocyanate content of the polyurethane was reduced, the molecular weight of the polyethylene glycol.[170]

A novel polyester urethane based on lactic acid and polyethylene glycol has been synthesized and checked the biodegradation of the polyester urethane under soil burial condition and by cultured bacteria (*pseudomonas aeruginosa*) at different temperatures. The biodegradation was assessed from the weight loss.[171] This study investigated the microbial action in soil on PLA and polyvinyl chloride (PVC) films and a PLA/PVC blend. The films were obtained from the evaporation of dichloromethane solutions and buried in soil columns, in controlled conditions, for 120 days. The results showed that the surface of the PLA films and blend became 18 and 31% more hydrophilic, respectively.[172] The degradation of bio-based food utensils during composting. PLA based forks lost 34% of their initial mass and were reduced to small friable fragments after 7 weeks of composting.[173]

1.14.2 Thermo-oxidative: When examined by heating under nitrogen within a temperature range of 180 and 240 ^{0}C, PLA showed thermal instability and loss of mass even at temperatures as low as 190 ^{0}C. There may be several reasons for its poor thermal stability: (1) hydrolysis by trace amounts of water catalyzed by hydrolyzed monomer (lactic acid), (2) depolymerization in unzipping fashion resulting lactide molecules, catalyzed by residual polymerization catalyst, (3) oxidative, random main chain-scission and (4) intermolecular transesterification with monomer and oligomeric esters.[174] The dominant reaction pathway is an intramolecular transesterification-giving rise to formation of cyclic oligomers. In addition, acrylic acid from cis-elimination as well as oxides of carbon and acetaldehyde from fragmentation reactions were detected.[175]

Thermal degradation of PLA in air involves an initial rapid decrease in molecular weight and high rate of loss of mass, accompanied by an initial decrease of the melting point and then increase with time die to chain stiffening.[176] Thermal decomposition of PLA forms cyclic oligomers, which are detected by pyrolysis mass spectroscopy accompanied with positive and negative chemical ionization, but unstable under electron impact ionization method.[177]

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CHAPTER - 2

CHAPTER – 2: SCOPE AND OBJECTIVE OF THE PRESENT WORK

2.1. Objectives of the present thesis:

The increasing waste plastic is more and more recognized as an ecological threat. Therefore, considerable amount of research and development efforts have been devoted towards making single use, biodegradable substitutes of conventional thermoplastics. Poly (lactic acid) (PLA) polymers have been known for quite sometimes, but the interest in these materials is only accelerating. A lot of research effort is currently concentrated on the development of different polylactide modifications to make the material suitable for a wider range of products. In many cases the modification of PLA by copolymerization,[1, 2, 3] surface treatment[4], stereocomplex [5, 6, 7] or blending[8, 9] changes the properties and degradation pattern of the inherent polymer drastically and consequently affects its suitability for different end-use applications. The present industrial production of lactic acid is based on microbial carbohydrate fermentation because it is chemically and economically more feasible compared with the chemical route and enables the production of optically pure lactic acid.[10]

One of the ways preparing PLA from lactic acid is the intermolecular dehydropolycondensation of lactic acid, catalyzed by various lewis acid as well as protonic acids.[11,12] Dehydropolycondensation is an equilibrium reaction in which both esterification and hydrolysis of the ester linkages proceed simultaneously. Otera et al.[13] have exploited a new family of tin-based Lewis acid catalyst, namely tetrabutyl distannoxanes, which can retard the hydrolysis, for lactic acid dehydropolycondensation. Solid state and melt polymerization have been carried out to build high molecular PLA and sequence determination of PLA has also been examined.

Polycaprolactone (PCL) occupies a unique position in the family of polyesters because of its biodegradability, miscibility and crystallizability, permeability and lack of toxicity. ε-Caprolactone is also a suitable comonomer for the preparation of a diversified family of copolymers with mechanical properties ranging from elastomeric to rigid. The way chosen to produce these polymers is almost exclusively ring-opening polymerization. The synthesis of ε-caprolactone /LA copolymers and other lactones polymers has been widely studied and focused on the polymerization parameters and different catalysts. Most studies have focused on the polymerization parameters and different catalysts.

Polyurethanes are an industrially useful and unique class of polymers with broad range of applications. Their properties can be tailored by varying the type and amount of their components: the chain extender, polyol, polyisocyanates and catalyst. By copolymerization, there are many possible combinations of biodegradable monomers that can lead to prepolymers with required properties.

Poly ester-ester linkages also attribute in the end application depending of the aliphatic or aromatic ester moiety.

The homopolymer of aleuritic acid has been attempted by several groups**[14, 15]** and found crossslinked polymers of aleuritic acid. Poly (aleuritic acid) (Mn=5.6, PDI=3.2) has been prepared from isopropyl aleuriteate. Homopolymerization of protected aleuritic acid has not been attempted and copolymerization with L-lactic acid has also not explored. The cyclization of aleuritic acid to form macrocyclic lactones has been reported.**[16]** The homo and copolymerization macrocyclic lactones with other lactones have not been found in the literature.

Similarly, the cyclization of 12-hydroxy stearic acid (12-HSA) to form macrocyclic lactones has been reported. The homo and copolymerization macrocyclic lactones with other lactones have not been found in the literature.

The films of biocompatible and biodegradable polymer with and without natural anti-inflammatory drug (Isobutrin) and their characterization have not been reported. The electospun nonwoven mat of low molecular weight PLA has not been fabricated. The bacterial and biodegradability test have been studied in details.

2.2. Approaches:

2.2.1 Synthesis and characterization of novel cloisite modified solid catalyst and application in ring opening polymerization of lactides: A novel cloisite modified solid catalyst would be prepared in a single step from commercially available starting materials for the first time. The ring opening polymerization of L-Lactide and D, D-lactide using this cloisite modified solid catalyst resulted would be explored. The catalytic activity of cloisite modified solid catalyst will be compared with the conventional stannous octoate catalyst in order to understand the effect in terms conversion, molecular weight and molecular weight distribution etc. The linear structure would be examined by quantitative ^{13}C-NMR. spectroscopy. Blend films would be obtained by casting mixed solutions of poly (D-lactide) s and poly (L-lactide) s at various compositions and stereocomplex. The morphology of stereocomplex would be characterized by SEM. Hydrophilic groups would be incorporated on the surface of stereocomplex using plasma technique.

2.2.2 Synthesis and characterization of homo and copolymers of ε-Caprolactone using cloisite modified catalyst: The homopolymerization of ε-Caprolactone would be carried out in presence of cloisite modified tin catalyst. Similarly, copolymerization with other lactones would also be carried. The kinetic and thermodynamic parameter would be studied. The end groups of the polymer would be determined using MALDI-TOF.

2.2.3 Synthesis and Characterization of the linear biodegradable polyesters via dehydropolycondensation route and ROP of macrocyclic lactones from renewable resources:

Homopolymerization of Aleuritic acid and copolymerization of Aleuretic acid with L-Lactic acid would be carried out using dehydropolycondensation method and the aggregation behavior of pendant hydroxyl groups would be studied. Aleuritic acid (9, 10, 16-trihydroxy palmitic acid) contained 9, 10 vicinal diols which would be protected by benzaldehyde dimethyl acetal and lactonized. The ring opening polymerization of macrocylic lactones would be carried out in presence of stannous stearate at 100 ^{0}C for 3hr and characterized. Similarly, 12-Hydroxy stearic acid would be cyclized. The homo and copolymerization reaction would be carried out with other lactones. Various kinetic and thermodynamic parameters would be studied in details. The resulting polymer would be subsequently deprotected to obtain pendant -OH groups at 9, 10 positions. The aggregation behavior due to hydrogen bonding will also be studied.

2.2.4. Synthesis and Characterization of PLA based ester-urethane, ester-ester and ester-carbonate linkages: Low molecular weight poly (lactic acid) s (PLA), having narrow molecular weight distribution would be prepared in presence of tetraphenyltin catalyst using dehydropolycondensation method. Hydroxyl terminated linear polylactic acid would be prepared reacting PLA with aliphatic diol compounds. The hydroxyl end groups would be determined by ^{31}P-NMR. The reaction of PLA oligomers and isocyanates (4, 4’ methylenebis (phenylisocyanate), toluenediisocyanate, 4, 4’ methylenebis (cyclohexylisocyanate), hexamethylene diisocyanate) would be carried out. The effect of the reaction conditions, i.e., the reaction temperature, molar ratio, isocyanates and catalyst on the molecular weight would be explored. The structure of the polymer samples would be investigated with FT-IR, ^{1}H-NMR, ^{13}C-NMR and matrix-assisted laser-desorption ionization time of flight mass spectroscopy (MALDI– TOF MS) and TEM.

The polymer of sebacic acid and terepthalic acid (ester-ester linkage) would be prepared using dehydropolycondensation techniques in presence of tetraphenyltin.

2.2.5 Application of biocompatible and Biodegradable polymer: Polylactides (Mw~75,000) would be prepared using cloisite modified tin catalyst. The PLA nonwoven nanofiber with and without antibacterial drugs would be fabricated using electrospinning technique. The PLA film would be prepared using natural anti-inflammatory drug (Isobutrin). The mechanical and electrical properties would also be studied. The degradation study of polylactides would be carried out using compost.

2.2.6. Summary and Conclusion: This chapter would summarize the results of the present work and salient conclusions. Future directions of research in the field of PLA, PAA, Poly (12-HSA) and copolymers of L-lactic acid with other monomers through dehydropolycondensation, ring opening polymerization of lactides, ε-caprolactone-lactides, ε-caprolactone-β-butyrolactone etc, would be studied. Fabrication of nonwoven nanofibers with and without drugs would be examined. The natural product (Isobutrin) would be used to enhance the mechanical and electrical properties of polymeric matrices. Biodegradability study would be explored.

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CHAPTER - 3

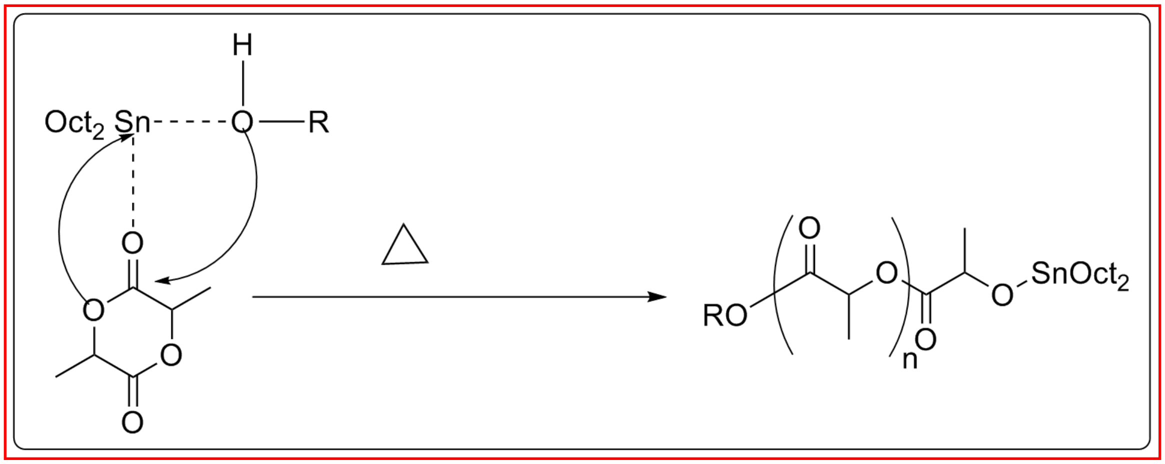
CHAPTER-3: SYNTHESIS AND CHARACTERIZATION OF NOVEL CLOISITE MODIFIED SOLID CATALYST AND APPLICATION IN RING OPENING POLYMERIZATION OF LACTIDES

3.1 Introduction:

3.1.1 Coordination insertion Polymerization:

It is the most widely studied method for the synthesis of high molecular weight PLA. In this method, catalysts like metal alkoxide are used. These metal alkoxide which possess a covalent bond between metal atom and oxygen atom and behave like weak Lewis acids.[1] The first step of the coordination insertion mechanisms occurs when one of the exocyclic oxygens of the lactide become temporarily coordinated with the metal atom of the initiator. This coordination increases the nucleophilicity of the alkoxide part of the initiator as well as the electrophilicity of the lactide carbonyl group. In the second step, the acyl–oxygen bond (between the carbonyl group and the endocyclic oxygen) of the lactide is broken and the lactide chain produced is inserted into the metal–oxygen bond of the initiator.[1, 2] The polymerization continues as additional lactide molecules are opened and inserted into the bond between the metal atom and its adjacent oxygen atom, while the other end, i.e. the alkoxide end of the initiator, becomes a dead chain end. By varying, the polymerization variables allow for the control of molecular weights over a broad range. A high molecular weight is obtained by this method. A large number of catalysts have been studied for the ring opening polymerization of lactide. The effects on the properties like molecular weight, molecular weight distribution and racemisation of the PLA have been mainly studied. The different catalyst and studied for the synthesis of PLA consist of different metals and their salts.

Now a day's Stannous Octoate $Sn(Oct)_2$ is used worldwide for coordination insertion mechanism. Hans R and et al have used $Sn(Oct)_2$ as a catalyst and various alcohols (benzyl alcohol 1-decanol, triethylene glycol monomethyl ether, and neopentane diol) coinitiator at 180 ^{0}C. These reactions was carried out by Sn(II) and not by proton of free octonic acid.[3]



Scheme 3: Coordination insertion ROP for PLA.

The kinetics and mechanism of ROP of L, L-dilactide (LA), initiated with tin(II) butoxide $Sn(OBu)_2$ and has been carried out in THF solvent (from 20 to 80 °C) or in bulk (at 120 °C). Polarimetric and size exclusion chromatography (SEC) measurements showed that initiation is fast and quantitative; termination and intermolecular transesterification (backbiting) has not been observed. According to the ^{1}H-NMR and MALDI-TOF spectra analysis, both alkoxide groups in $Sn(OBu)_2$ are converted into poly(L-lactide) (PLA) growing chains, and monomer addition proceed with the acyloxygen bond scission.[4]

The mechanism of the ring opening polymerization of *rac*-butyrolactone using yttrium complexes has been supported by dianionic aminoalkoxybis(phenolate) ligands as initiators the coordination insertion pathway has been investigated by NMR. Some thermal properties of these PHBs have been studied and thermo analytical techniques and by the syndiotacticity degree has been observed.[5]

The mechanism of lactide polymerization initiated with zinc (II) acetylacetonate monohydrate has been reported. Rare earth metal bis (amide) complexes have served as highly active initiators for L-lactide polymerization in toluene at 50 ^{0}C. In addition, they also showed high activity towards rac-lactide polymerization in tetrahydrofuran at room temperature, affording a moderate level of heterotactic polymers employing Li-Y as an initiator, a controllable polymerization fashion has been observed both in L-lactide polymerization and rac-lactide polymerization under certain conditions. The polymerization proceeds via a coordination insertion mechanism verified experimentally by end group anaysis of the oligomers.[6]

The ring-opening polymerization (ROP) of D,L-lactide catalyzed by the titanium(IV) complex has been carried out at 130 ^{0}C and the maximum number-average molecular weight (M_n) of poly(D,L-lactic acid) (PDLLA) is 88,000 g/mol. Kinetics experiments indicate that the polymerization shows second-order kinetics in D,L-lactide monomer concentration and first-order kinetics in catalyst concentration. ^{1}H-NMR spectroscopy of polymer terminated by benzyl group suggests that the polymerization proceeds via a conventional coordination insertion mechanism and Ti-O active centers initiate the cleavage of acyl-oxygen bond of D, L-lactide monomer.[7]

A series of novel magnesium and zinc aminophenoxide complexes have been successfully synthesized and zinc complex has been characterized by X-ray crystallography. They are also investigated as initiators for the ring opening polymerization of L-lactide. The complexes are effective in forming polylactides with good conversions. The nature and steric bulk of the ligands coordinate to the central metal ions enormously influence the polymer properties. Among all the complexes, the zinc aminophenoxide complexes as initiators produce polymers with good molecular weight control and relatively narrow PDIs.[8]

Single (SWNTs) and multiwalled (MWNTs) carbon nanotubes were functionalized with a titanium alkoxide catalyst through a Diels-Alder cycloaddition reaction. The catalyst-functionalized carbon nanotubes (CNTs) were used for the surface initiated titanium-mediated coordination polymerizations of L-lactide (L-LA), ε-caprolactone.[9] Racemic and mes*o* D,L-lactide were polymerized at 90 or 120 °C in xylene or at 120, 150 and 180°C in bulk using Dibutyl tin complexes, copolymerizations of racemic D,L-lactide and L,L-lactide have been conducted at 180°C in bulk with tributyltin methoxide (Bu_3SnOMe), dibutyltin dimethoxide ($Bu_2Sn(OMe)_2$) and Sn(II) octoate.[10]

Aluminium alkoxide is also another class of ROP catalyst. The ROP proceeds through the coordination insertion mechanism and gives living polymerization, controlled molecular weights and low molecular weights distribution(1.1- 1.4) of PLA and also give PLA when ROP is carried out below 150 ^{0}C.[11, 12, 13, 14] Dubois et al have polymerized lactides using aluminium isopropoxide, ($Al(OiPr)_3$) as catalyst. They have also confirmed the coordination mechanism which involves three active sites per aluminium atom, no aggregation of the catalyst and insertion of the lactides so the aluminium alkoxide bond with lactide acyl-oxygen cleavage, similar to Sn-Octoate mechanism.[15, 16, 17]

Lanthanum and Ytttrium based ROP catalysts, have been studied in detail separately by McLain et al[18, 19, 20, 21, 22, 23] and Feijan and coworkers[24, 25, 26] also showed similar coordination mechanism, but the reason is fast reaction. At room temperature and the turnover frequencies of these catalysts for the ROP of lactides at 25 ^{0}C are more than 30 times as much as the turnover frequencies of $Al(OiPr)_3$ for the same reaction at 70 ^{0}C. ROP of L-Lactide efficiently triggered by amido indole reagents and studied hydrogen bonding.[27]

Clay minerals provide distinct nanometer-scaled layers and interlayers for engineering and as active catalysts. As such, strategic design and preparation has led to a variety of catalysts, including ion exchanged catalysts, acidic activated clay catalysts, intercalated catalysts, pillared clay catalysts, clay-supported catalysts, inorganic, inorganic organic composites, hybrids, and hierarchically structured solid catalysts. In many cases, the combination of several protocols has been implemented so that the resultant materials function with synergetic effects. Electric, optical, photonic, and magnetic functionalities can also be endowed on the resulting clay-based catalysts. Synthetic clay minerals and their derivatives, including layered double hydroxides, have peculiar features in purity and composition to be designed and transformed to catalysts, showing a complementary relationship with their naturally-occurring counterparts.

The clay-based heterogeneous catalysts have many practical and potential applications in green catalysis. The catalysts used mainly consist of metal powders, Lewis acids, Lewis bases, organometallic compounds and different salts of metals. However, organometallic compounds are very effective in the synthesis of high molecular weight PLA particularly alkyl metals and metal halides, oxides, carboxylates and alkoxides. Metal halides, oxides and carboxylates act as Lewis acid catalysts in ROP and are actually initiated with a hydroxyl containing compound such as water or x-hydroxy acid. A large number of catalysts have been studied for the polymerization of lactide for various applications, including biomedical applications, such as iron [28] $Sn(Oct)_2$, $SnCl_4$, $Sn(C_6H_6)_4$, Zinc lactate $[(n\text{-}C4H_9O_2)AlO]_2Zn$.[29] Organic compounds like crown ethers are found very effective to the synthesis of PLA with high optical purity and molecular weight, and the effect of crown ether has been studied on the synthesis of PLA using dibutylmagnesium. [30, 31] The reaction between pentaerythritol ethoxylate compounds and dibutyltin oxide has been developed as a route to synthesize two new spirocyclic tin initiators.[32] The initiators has been successfully synthesized and they were characterized by ^{1}H-NMR and differential scanning calorimetry (DSC). Furthermore, the usefulness of the new initiators has been examined in ring-opening polymerizations of L-lactide in chloroform at 60 ^{0}C. L-Lactide has been polymerized at monomer to initiator ([M]/[I]) ratios between 20 and 500. The results indicate that the initiation is instantaneous and that the molecular weight distribution was very narrow, <1.13. The number average molecular weight could be controlled by the [M]/[I] ratio, and the yield was very high.

Michel Guillaume et al reported that selective monotosylation of a 1,2-diol is possible using only 0.1 mol % of Bu_2SnO.[33] More interestingly, they found that the corresponding tin acetal gave faster conversions and more reproducible reaction times. Moreover, the loading of this catalyst could be as low as 0.05-0.005 mol %.

Two biodegradable polymer intermediates, triacrylate and tetraacrylate , were prepared by polycondensation reaction of ethyl β-hydroxybutyrate using glycerol and pentaerythritol as initiators and dibutyltin oxide as a catalyst followed by functionalization of the hydroxyl end groups with acryloyl chloride in the presence of triethyl amine.[34]

W, J, Considine et al. reported reaction between dibutyltinoxide and vic-diols and used as a catalyst.[35] They also prepared derivative of dibutyltin oxide as i.e. dibutyltin diphenoxide .

The product of the reaction $R\text{-}CO\text{-}O\text{-}(C_4H_9)_2Sn\text{-}O\text{-}(C_4H_9)_2Sn\text{-}OR')_2$ of both ethylene-vinyl acetate copolymers (EVA) and ethylene-methyl acrylate copolymers (EMA) with dibutyltin oxide at 200 ^{0}C, and characterized by ^{119}Sn-NMR spectroscopy. [36]

The ring opening polymerization of L-lactide was studied in bulk using stannous octoate $Sn(Oct)_2$ as initiator and, triphenylphosphine, a Lewis base was used as co-initiator.[37] The polymerization was carried out at 130 ^{0}C up to 29 hr. The best results have been obtained with coinitiator2-(tritylsulfanyl) ethan-1-ol.[38] D-glucose and D-galactose used end-functionalized polylactide oligomers were synthesized by controlled ring-opening polymerization of lactide using aluminium, triisopropoxide, triethyl-aluminium or stannous octoate initiator monosaccharides were studied as coinitiators.[39] The effect of the average length of the copolymer block on the properties of the networks has been evaluated with three different coinitiator contents.[40] Various triblock copolymers were prepared by ring-opening polymerization of L-lactide in the presence of poly (ethylene glycol), using Calcium Hydride or zinc metal as co-initiator.[41]

Linear 1-arm and 2-arm PLA polymers having relatively low number-average molecular weights M_n=50,000 were synthesized by ring-opening polymerization of L-lactide initiated with tin(II) 2-ethylhexanoate and coinitiators as L-lactic acid, 1-dodecanol, and ethylene glycol.[42] PLA/PCL diblock, triblock and four-armed copolymers with the same monomer feed ratio (50/50) have been synthesised by two step ring opening polymerization of successively added ε-caprolactone and L-lactide, using isopropanol, ethylene glycol, or pentaerythritol as initiator and zinc lactate as coinitiator.[43]

The use of clay nanofillers gives a potential pathway to improve barrier properties in polylactide films. Magnesium aluminium layered double hydroxides have been used for synthesis of PLA- layered double hydroxides nanocomposites by ring-opening polymerization. This method is attractive because of its good dispersion of layered double hydroxides in the polymer.[44] Melt-state and solid state mechanical properties and thermal stability of polylactide layered silicate nanocomposites was studied by melt intercalation as a function of clay content.[45] Distribution of cloisite-30B in the polylactide matrix has been confirmed by different technique. The dispersion of clay into the PLA matrix has also been approved by Food and Drug Administration for medical use.[46] The biodegradability of PLA, PLA/PCL blend enhanced due to dispersion of organomodified clay.[47]

An experimental study was carried out to design polylactide (PLA)-clay nanocomposites for developing fibers. PLA and 1 wt % of a selected organomodified bentonite were melt mixed to examine the effect of processing conditions (temperature, shear, residence time) on the morphology of performed polymer nanocomposites.[48] Because of a good compatibility with PLA matrix, the dispersion of bentonite clay has been occurred under different conditions without difficulty, and showed similar morphology. Nanocomposites of PLA and ethylene glycol oligomer containing organo-modified montmorillonites protonated ammonium cations of octaclecylamine and poly (ethylene glycol) stearylamine were prepared by melt intercalation method.[49] In the X-ray diffraction analysis composites showed a clear enlargement of the difference of interlayer spacing between the composite and clay itself, indicating the formation of intercalated nanocomposite.

Chitosan and PLA at different ratios were blended with different wt% of montmorillonite (cloisite-30B) solution by the solvent evaporation method montmorillonite was incorporated in the formulation as a matrix material Paclitaxel was loaded and vitro drug delivery has been studied.[50] The degradation of PLA/cloisite-30B nanocomposites has been studied as a function of clay loading (1, 3 and 5%).[51]

Novel biodegradable polymers have been synthesized by ROP of L-lactide on chitin in an N, N-dimethyl acetamide/lithium chloride (LiCl) solvent system, and chitin was used as macroinitiator to afford new materials. Lithium chloride (LiCl) is used as catalyst. The synthesized copolymers chitin-graft-poly (L-lactide) (PLA) were developed and characterized.[52] A series of lithium and sodium iminophenoxide complexes have been successfully synthesized and used as catalysts for the ring opening polymerization of L-lactide.[53, 54] Recent developments in the preparation and application of lithium catalysts/initiators such as, alkyl lithium, alkoxy lithium and bimetallic lithium compounds for ROP of cyclic esters, cyclic carbonates, cyclo-silazanes, cyclo-silanes, cyclo-siloxanes, cyclo-carboxylate, cyclic phosphirene and quinodimethanes have been reported.[55] Alkali-metal (Na, K) compounds were synthesized, characterized and checked their catalytic activity for L-lactide polymerization.[56] Heterobimetallic complexes can initiate the ring-opening polymerization of L-lactide.[57] And the experiment results Mg containing complex can initiate the ring-opening polymerization of L-lactide under an air atmosphere with high conversion.[58] A series of magnesium, zinc, and calcium metal complexes are highly active for the ring-opening polymerization of rac-lactide and give preference for heterotactic polylactide.[59]

New lithium salts can act as efficient single-component initiators for the ring-opening polymerization of lactide and ε- caprolactone and give low molecular weights polymers with of polydispersities 1.05 and T_m of resulting polymer is 165 ^{0}C.[60, 61] Lithium complexes show excellent catalytic activities toward the ring-opening polymerization of L-lactide in the presence of benzyl alcohol.[62] LiCl is found to be an effective and biocompatible catalyst for the ring-opening polymerization of lactide in the presence of hydroxyl-containing compounds. The polymerization was carried out as 128 ^{0}C in bulk with 1% (w/w) of LiCl. PLA of different molecular weights are obtained with varied molar ratios of monomer/initiator.[63] Lithium alkoxide initiated polymerizations of L-lactide and were conducted in toluene at 50 ^{0}C.[64, 65]

The application scope of PLA is limited because of its hydrophobic nature. In addition, the hydrolytic degradation rate of PLA for application in delivery purpose is slow due to its high crystallinity, which results in poorer soft tissue compatibility. To overcome the drawback of the PLA homopolymer, many kinds of co-monomer i.e. glycolide unit have inserted into PLA chain.[66] It was prepared by ring-opening polymerization of lactide and glycolide in order to obtain a well-defined material.[67] Polylactide-co-glycolide (PLGA) is a rapidly degradable copolymer and widely used in pharmaceutics and nanomedecine.[68, 69, 70] Freichels et al. prepared Polylactide-co-glycolide (PLGA) which is essential material used for *in vitro and in vivo* studies.[71] Direct cellular localization of drug delivery systems based on these materials allows better understanding of the internalization mechanism and determination of the pharmacokinetics DL-lactide-co-glycolide (PLGA) nanoparticles prepared for antitumor drug delivery.[72, 73, 74] PLGA nanofibers (900 nm) was fabricated by electrospinning for tissue-engineering scaffolds.[75, 76]

PLGA was synthesized by several catalysts instead of conventional catalyst i.e. stannous octoate. Among all catalysts most promising result was obtained with Zn(Oct)$_2$ and alcohols as initiators. The polymerization was examined in order to improve reaction rate and study their effect on molecular weight distribution, polymer microstructure, and side reactions, such as transesterification reaction.[77] Ehrenfried et al. investigated the effect of alpha-tri-calcium phosphate on L-Lactide copolymerization. They have also studied the degradation properties, mechanical properties of PLGA.[78]

Biodegradable polymers have attracted attention as a replacement for conventional synthetic materials.[79] Among the new biodegradable polymers aliphatic polyester that have been developed during the last decade, polyhydroxyalkanoates (PHA)s are of particular interest. These materials show the film-barrier properties and mechanical performance properties like petroleum-based polyethylene and polypropylene. One of the most convenient and promising synthetic routes is (PHA)s is carried out using metal initiators using effect the ring-opening polymerization (ROP) of β-butyrolactone(β-BL). Novel gold (I) complexes containing N-heterocyclic carbene ligands have been resulting mononuclear gold complexes act as active initiators in the polymerization of rac-β-butyrolactone under solvent-free conditions to provide the corresponding biodegradable poly (3-hydroxybutyrate).[80] ROP of β-butyrolactone with dinuclear salen compounds of zirconium and hafnium are efficient initiators gives poly (3-hydroxybutyrate) with a good M_n and molecular weight distribution.[81] The polymerization of β-BL with the Magnesium and zinc complexes demonstrated in a living fashion with a narrow polydispersity index, PDI = 1.01-1.10. A greater ratio of monomer to alcohol catalyzed by Zn complex served to form poly (hydroxybutyrate) (PHB) with a large molecular weight M_n= 60,000.[82, 83, 84]

Copolymers of racemic β-butyrolactone and ε-caprolactone were synthesized by ring-opening polymerization initiated by sodium hydride and copolymers are stable up to 200 ^{0}C.[85] Ring opening polymerization of (R,S)-β-butyrolactone using dibutylmagnesium as initiator was investigated both in bulk and in solution.[86] Two random copolyesters of of (RS)-β-butyrolactone with L-lactic acid and (R, S)-3-hydroxybutyric acid with L-lactide, respectively, and were characterized by electrospray ionization ion trap mass spectrometry (ESI-ITMS). The influence of an intermolecular transesterification reaction on the microstructure of the copolyester synthesized by equimolar reaction of (R,S)-3-hydroxybutyric acid with L-lactide has been observed.[87] Copolymers were synthesized by ROP of γ-butyrolactone with cyclicesters. Comonomers used were L-lactide, glycolide β-propiolactone, δ-valerolactone and ε-caprolactone and tetraphenyl tin was used as an initiator.[88, 89]

3.2 Materials and Methods:

3.2.1 Materials: cloisite-30B, cloisite-15A, cloisite-20A and cloisite-93A from southern clay products (Rockwood Additives Limited) were dried at 60 ^{0}C for 2 hr using high vacuum before use. Toluene was obtained from SRL chemicals and was made sulphure free and dried over sodium using standard technique before use. Dibutyl tin oxide (98%) was procured from Aldrich, $Sn(Oct)_2$ from Aldrich, LiCl (Aldrich), Isopropyl alcohol (SRL Synthesis grade), Solvent n-hexane (SRL AR grade). L-Lactide (LA) was prepared as per procedure (5.2.2 a chapter 5), Glycolide from PURAC, β-Butyrolactone (98%) and Titanium (IV) butoxide 98% was procured from Aldrich.

3.2.2 Synthesis of clay modified catalyst:

Catalyst was prepared by condensing 1.443 gm (0.0040mole) cloisite-30B, where T is Tallow (65% C_{18}; 30% C_{16}; 5% C_{14}) and 1 gm (0.0040 mole) di-n-butyltin oxide in toluene at 110 ^{0}C for 7hr. The reaction mixture was cooled at room temperature and filtered. Crude product was washed with n-hexane several times and dried using vacuum to obtain constant weight. The yield was ~95%. The catalyst was schematically represented below (Scheme-4). Polymerizations were carried out using lactides. The specific optical rotation [α] of the polymers was measured in chloroform at a concentration of 1 g/dl at 25 ^{0}C using a Perkin Elmer Polarimeter at a wavelength of 589 nm. $[\alpha]^{25}$ values of PDLA and PLA were approximately +150 and -150^0, respectively in good agreements with literature value**.**

3.2.3 Procedure for ROP of L, D lactides:

L-lactide (recrystallized and dried) along with cloisite modified tin catalyst is crushed in mortar and pestle and transferred into glass ampoule. High vacuum has been applied for half an hour in order to remove moisture and thereafter glass ampoule containing reaction mixture is sealed under high vacuum and polymerization was carried out in sand bath at different temperature and time.

3.2.3a Procedure for ROP of L-Lactides using LiCl

L-lactide (recrystallized and dried) along with LiCl catalyst, cloisite-30B is crushed in mortar and pestle and rest of the procedure according to 3.2.3

3.3.3b Procedure for ROP of L-Lactides using isopropyl alcohol as a coinitiator:

L-lactide (recrystallized and dried) along with Sn(Oct)$_2$ catalyst and isopropyl alcohol as an coinitiator transferred into glass ampoule and rest of the procedure according to 3.2.3

3.2.4 Procedure for dispersion of clay and ROP of L-Lactide:

cloisite-30B, cloisite-15A, cloisite-20A, cloisite-93A are dispersed into the lactide with stirring using dry dichloromethane (DCM) at room temperature for 48 hr and DCM is evaropated using rotavapour and resulting material is used for ROP using Sn(Oct)$_2$ as catalyst into the sand bath.

3.2.5 Synthesis of copolymers:

A) Lactide/Glycolide Copolymers: Lactide and Glycolide were recrystallized and dried along with cloisite modified tin catalyst was crushed in mortar and pestle and transferred into glass ampoule along with lactide and glycolide monomers. High vacuum was applied in order to remove moisture. The glass ampoule was sealed under high vacuum and polymerization was carried out using sand bath at different temperature and time.

B) Butyrolactone/L-Lactide Copolymers:

β-Butyrolactone was purged into the activated ampoule through syringe then lactide and catalyst Ti (IV) butoxide were added into it and mixure was subjected for drying using high vacuum and ampoule was sealed to perform polymerization reaction.

3.3 Analysis:

3.3.1 Molecular weights:

Molecular weights and polydispersity (M_n/M_w) were determined with respect to polystyrene standards by size exclusion chromatography on a Thermo Finnigan Spectra Series AS300 machine at 25 ^{0}C by eluting PLA, PLA copolymers solutions of 10 mg/ mL concentration in $CHCl_3$, with toluene as internal standard, through a series of five μ-Styragel columns of pore sizes 10^5, 10^4, 10^3, 500, and 100 A^0 respectively, and length 30 cm each. $CHCl_3$ was used as the mobile phase (flow rate 1 mL/ min) and a refractive index detector (Spectra Series RI-150) was used for detection of different molecular weight fractions. Molecular weights were calculated with respect to polystyrene calibration.

3.3.2 NMR spectroscopic analysis:

3.3.2a Quantitative ^{13}C-NMR and ^{119}Sn NMR:

For NMR measurements, the samples were dissolved in chloroform-d in 5 mm dia. NMR tubes at room temperature. The chemical shifts in parts per million (ppm) were reported up field with reference to internal standard chloroform-d at 7.25 ppm. The sample concentration for ^{13}C-NMR measurements was 10 % by weight. Proton decoupled ^{13}C-NMR spectra with NOE were recorded on a Bruker DRX 500 MHz NMR spectrometer working at 125.577 MHz for carbon-13. $CDCl_3$ served as solvent and TMS as internal standard for all ^{13}C-NMR measurements. ^{119}Sn-NMR also studied for cloisite modified catalyst.

3.3.2b ^{1}H-NMR:

NMR tubes are cleaned using chloroform, DCM; acetone dried using vacuum in order to remove volatile impurities then samples to be determined taken into the NMR tubes along with $CDCl_3$ for analysis.

3.3.3 Thermal analysis:

Differential scanning calorimetric (DSC) measurements were made on a Perkin-Elmer thermal analyzer model DSC-Q10 in a nitrogen atmosphere. The measurements were run from –40 to 250 ^{0}C at a heating rate of 10 ^{0}C/ min and a cooling rate of 100 ^{0}C/ min. The glass transition temperature (T_g) recorded from the second and curve. Melting temperature (T_m) is recorded from first cycles.

Thermal stability was analyzed using Perkin-Elmer TGA-7, by heating the samples from 50–700 ^{0}C with a heating rate of 10 ^{0}C/min under nitrogen atmosphere with a flow rate 50 mL/min.

3.3.4 X-ray analysis:

Wide-angle X-ray scattering (WAXS) pattern of the samples was obtained in reflection mode using a Rigaku Dmax 2500 diffractometer and Ni filtered copper radiation. The sample was scanned in the range $2\theta = 10 - 30^{0}$, 50^{0} and the generator was operated at 40 kV and 150 mA. The FWHM of the 110 peak was determined by peak fitting software available with the Rigaku diffractometer.

3.3.5 MALDI-TOF MS Analysis:

MALDI-TOF MS analysis was performed on a Kratos Kompact MALDI IV spectrometer equipped with 0.7-m linear and 1.4-m reflection flight tubes as well as a 337-nm nitrogen laser with a pulse width of 3 ns. All experiments were carried out at an accelerating potential of 20 kV. In general, mass spectra from 200 shots were accumulated to produce a final spectrum. The obtained data were smoothened to reduce the spikiness by the average method; the smoothening filter moved along the collected data channels, adding together a number of channels and dividing by that number to give an average signal. This smoothening, however, did not eliminate or hide minor signals distinct from the baseline noise. The samples were dissolved in tetrahydrofuran (1 mg/mL) and mixed with the matrix (15 mg/mL of tetrahydrofuran) before being dried on the sample plate. 2, 4, 6-Trihydroxyacetophenone was used as the matrix. The sample plate was inserted into the apparatus under a high vacuum ($\sim 10^{-5}$ Pa).

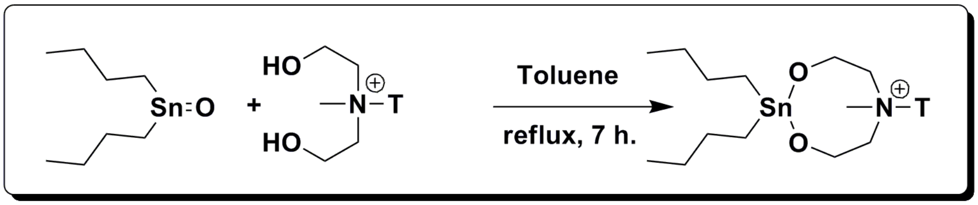
3.3.6 Transmission Electron Microscopy Analysis (TEM):

Sample Preparation: Polylactides was crushed in mortar pestle and crushed sample was dispersed in isopropyl alcohol solvent to understand the dispersion behavior. The solutions were collected on 300 mesh carbon coated copper grids. The copper grids were kept overnight on filter paper for drying. TEM imaging was performed using a FEI Tecnai 20 TEM operating at an accelerating voltage of 200 kV with 1.7A^{o} point resolution. Images were captured using charged couple detector camera and viewed using Gatan Digital Micrograph software.

3.4 Result and discussion:

3.4.1 Synthesis of clay modified catalyst:

The clay modified catalyst was characterized and confirmed the structure by ^{13}C and ^{119}Sn-NMR. ^{13}C CP/MAS (Cross-Polarization/Magic Angle Spinning) NMR of the clay modified catalyst was recorded. The peaks at 23.65, 25.28, 27.28 ppm are attributed due to the presence of dibutyl groups attached to the tin atom. The disappearance of the peak at ~70 ppm due to the absence of hydroxyl group and appearance of methylene and methyl groups at 23.65 and 16.04 ppm confirm the structure of the catalyst as shown in Scheme 1.



Scheme- 4: Synthesis of cloisite modified catalyst.

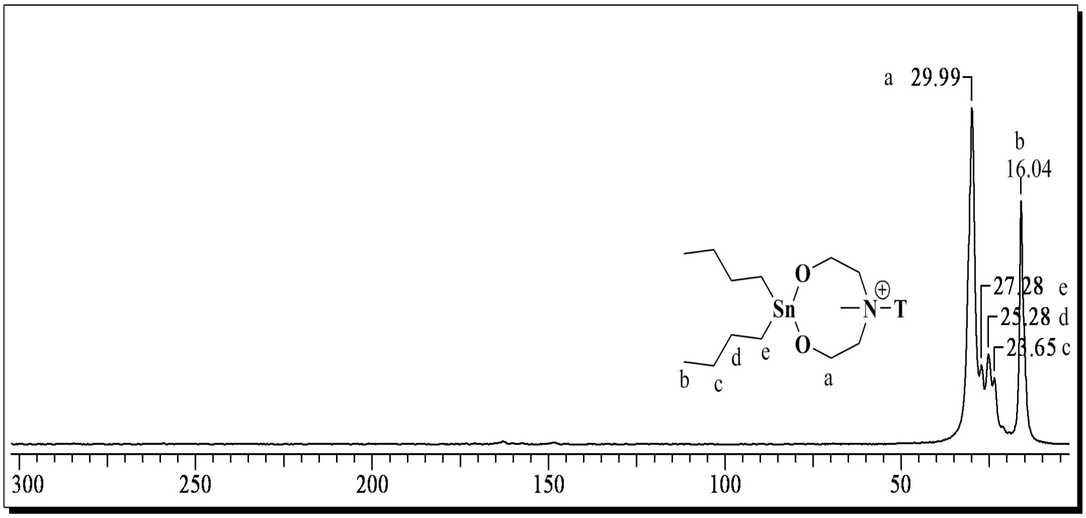


Fig. 3.1: ^{13}C CP/MAS-NMR spectra of clay modified catalyst.

The ^{119}Sn-NMR spectra of modified clay catalyst were recorded and the results with probable assignment were given in Scheme 1. The high field signals at -176.15 ppm is attributed to Sn (I) which is coordinated by two oxygen atoms and two butyl groups. The catalyst gave rise to an unusually low field signal (- 86.82) which may be attributed due to presence of anionic species coordinated with tin atom.

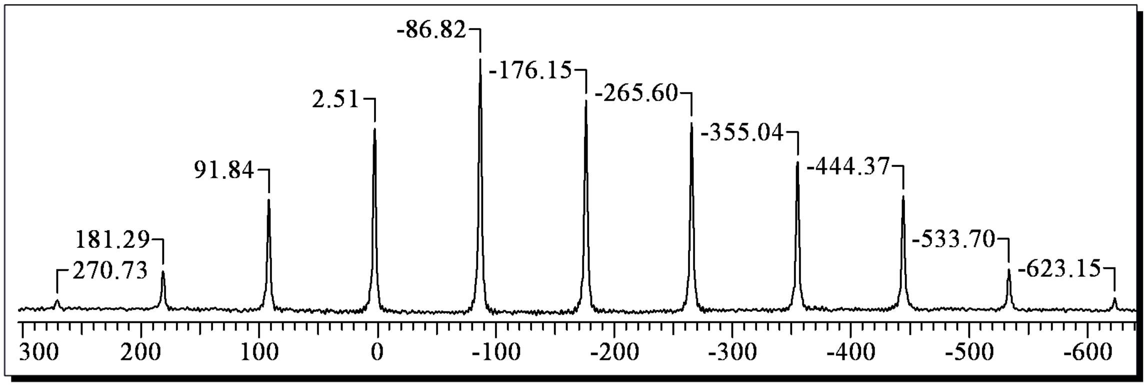


Fig. 3.2: ^{119} Sn-NMR spectra of clay modified catalyst.

TGA curve of the cloisite-30B (fig. 3.3) shows two decomposition temperatures 298.9 and 405.8 ^{0}C respectively. The weight losses are 5 and 30.30 % and became steady.TGA curve of the catalyst showed that the clay modified catalyst starts decomposition at 293.96 ^{0}C. The weight loss was calculated as 51.52 % and became steady. The remaining 48.48 % is due to the presence of tin as well as clay.

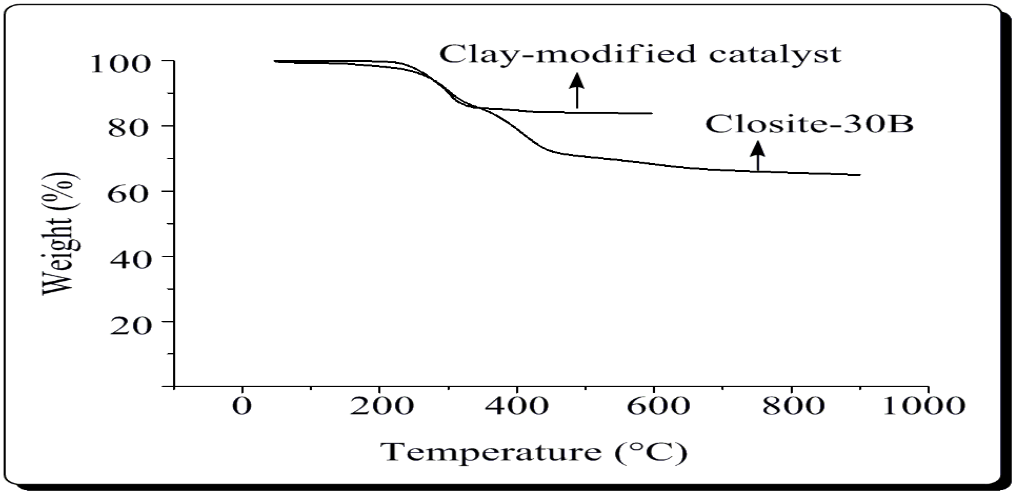


Fig. 3.3: TGA thermograms of cloisite-30B and **c**lay-modified catalyst.

3.4.2 ROP of Lactides:

The lowest temperature was applied to a ring opening polymerization 96-97 ^{0}C because of the melting point of L-lactide in the same range. For modified clay tin as catalyst, a rather low reactivity was expected and thus a first “test experiment” with a concentration of catalyst (catalyst=0.75%) was conducted at 96-98 ^{0}C. After 20 hr an almost complete polymerization was found. Therefore, a series of five experiments was performed 150-240 ^{0}C using a constant (monomer/catalyst, M/C) ratio. As indicated by data summarized in Table 3.1 (experiments 1-5, PLA-1-5), the conversion steadily increased up to 99 %. The molecular weight derived with polystyrene standards and hence indicates apparent values. PLA-(1-4) polymers were prepared by ring opening polymerization with catalyst 1 as a catalyst and with various temperatures (150, 180 and 200 ^{0}C) respectively. The M_n, M_w values were observed to increase with increase in temperature profile from 150 to 200 ^{0}C. The M_n and M_w value further increased in case of PLA-4. However, the M_w/M_n value is also increased. GPC curves shown in fig. 3.4. This was presumably due to the presence of macrocycles. A similar observation has been made by Kricheldorf et al.[90] for

PLA macrocyclics containing tin atoms in their chains. PLA-3a, PDLA-a and PLA-4a were prepared using conventional stannous octoate catalyst.

It is apparent from Table 3.1 that the catalytic activity of cloisite modified tin catalyst is superior to stannous octoate. Moreover, the highest molecular weight of PLA was obtained at 220 ^{0}C, whereas transesterification reaction is predominated in case of stannous octoate. The better catalytic activity was also observed in case of ring opening polymerization of D,D-lactides using cloisite modified tin catalyst in comparison with stannous octoate (Table 3.1, PDLA, PDLA-a).

Thermal stability of these polymers (PLA-1 to PLA-4, Table 3.1a and PDLA ,PDLA-a) shown in fig. 3.5 and fig. 3.6 respectively.

The melting behaviors of PLA (1-4) are depicted in fig. 3.7 and T_m of PLA 1 is 178 ^{0}C. The T_m value of PLA 2-3 showed reasonable enhancement and decreased in case of PLA-4. This may be attributed due to the intermolecular transesterification reaction at higher temperature (220 ^{0}C). T_g values (fig. 3.8) remained unaltered. The ΔCp values ranged from 0.36 to 0.46 (J/ g ^{0}C) respectively.

Table 3.1: PLA Polymers by ring opening polymerization using Clay modified catalyst for 1 hr

Polymer	Temp. (^{0}C)	Conversion (%)	M_n (SEC)	M_w (SEC)	T_m (^{0}C)	ΔH_m (J/g)	T_g (^{0}C)	ΔC_p (J/g^{0}C)
PLA-1	150	57	34400	57600	178	46	55	0.42
PLA-2	180	74	38100	63800	165	44	54	0.44
PLA-3	200	99	45600	75000	171	43	55	0.46
PLA-4	220	99	53000	100000	162	28	55	0.36
PLA-4a	220	99	21600	36000	143	26	47	0.30
PLA-5	240	-	brown	-	-	-	-	-
PDLA	200	99	46000	71000	167	66	41	0.53
PDLA-a	200	99	38000	63000	162	29	50	0.42

a: Poly(lactide)s synthesized using Stannous Octoate $Sn(Oct)_2$

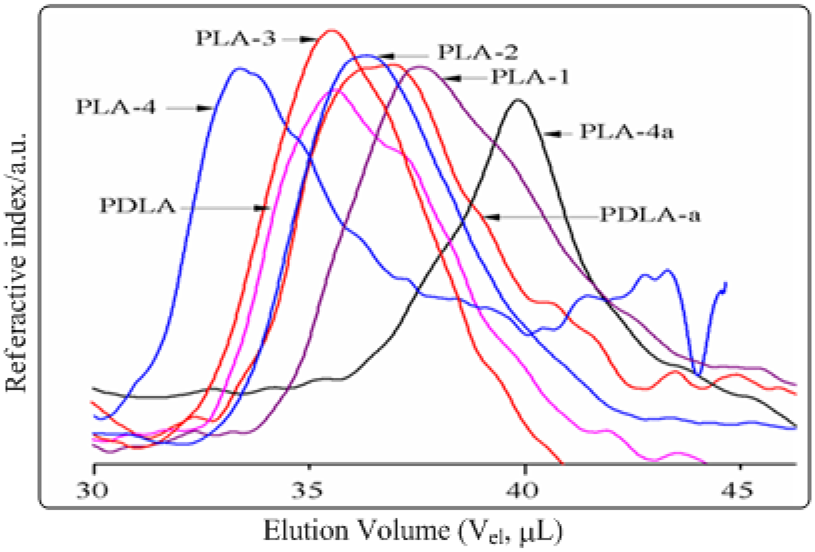


Fig. 3.4: Size Exclusion Chromatography (SEC) of Poly(lactide)s.

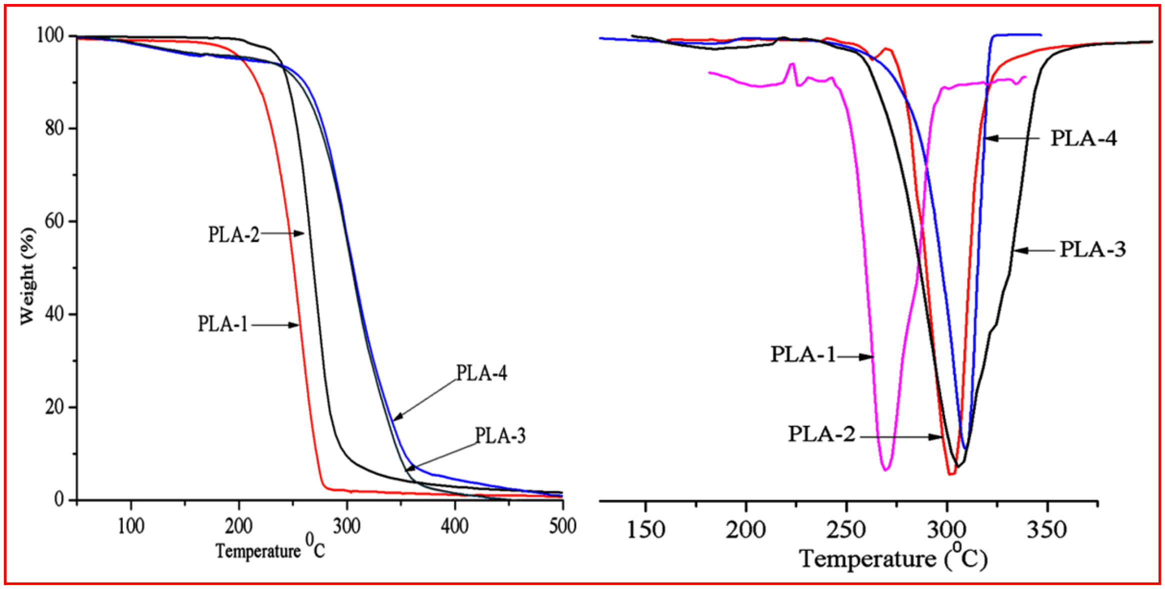
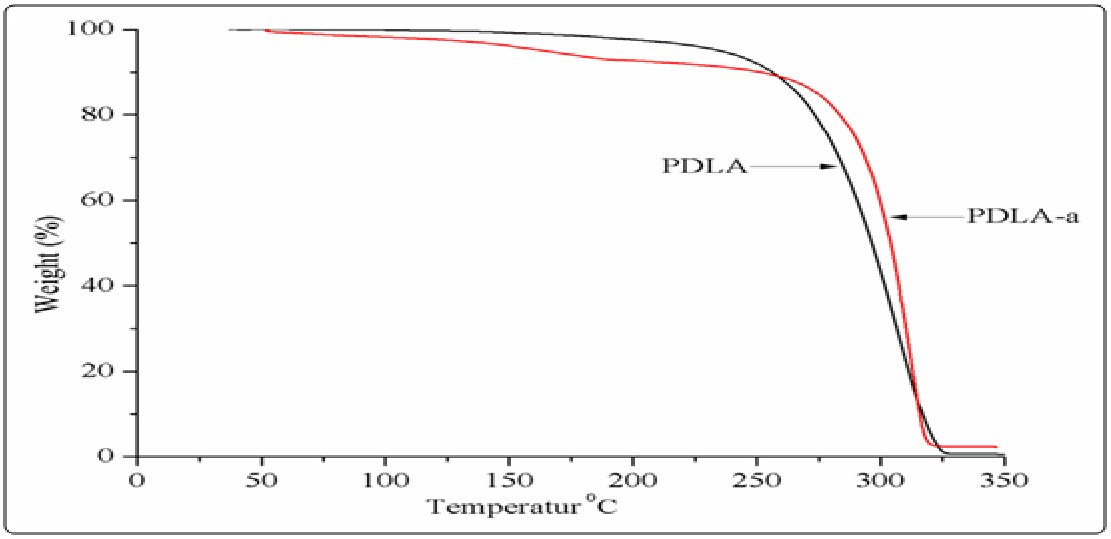


Fig. 3.5: Thermogravimetric analysis (TGA) of poly(lactide)s synthesized using cloisite modified catalyst showing decomposition temperatures.

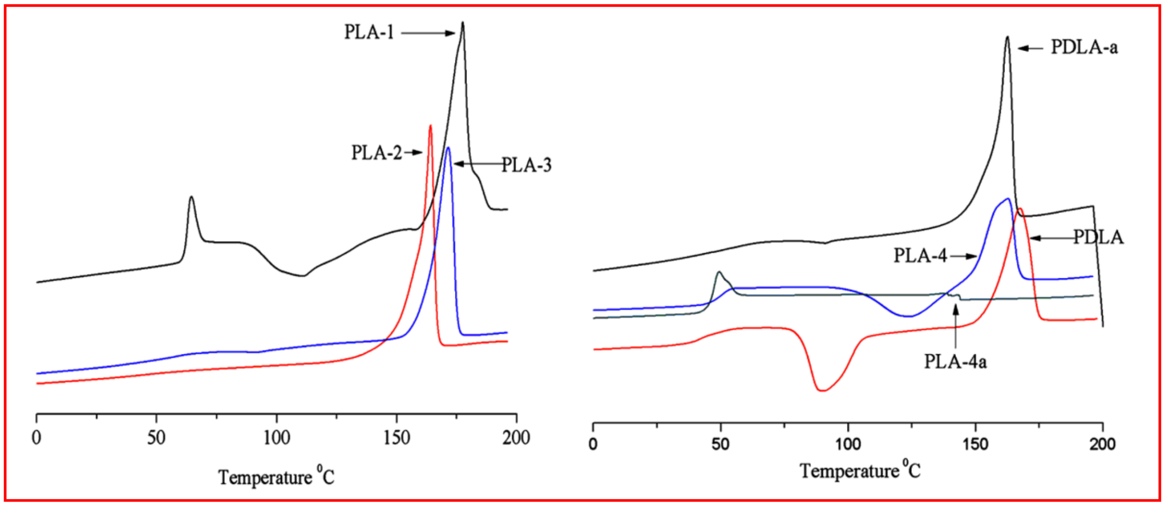
Table 3.1a: Thermal Stability of polylactides

Polym.→	PLA-1	PLA-2	PLA-3	PLA-4
Deg. Temp (°C)	271	309	300	304



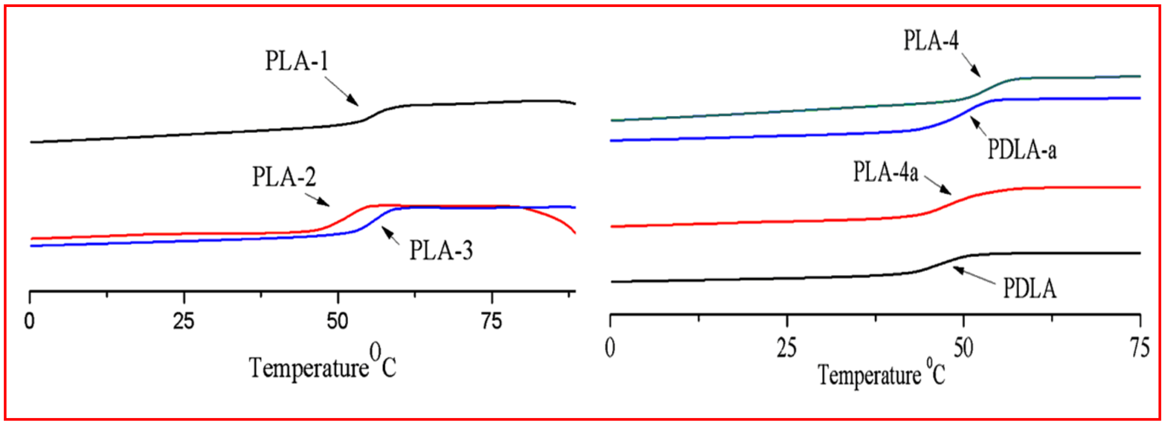
a: Poly(lactide)s synthesized using Stannous Octoate $Sn(Oct)_2$

Fig. 3.6: Thermogravimetric analysis (TGA) of poly(lactide)s synthesized using cloisite modified catalyst showing decomposition temperatures.



a: Poly(lactide)s synthesized using Stannous Octoate $Sn(Oct)_2$

Fig. 3.7: Differential Scanning Calorimetry (DSC) of poly(lactide)s synthesized using cloisite modified catalyst showing melting points.



a: Poly(lactide)s synthesized using Stannous Octoate Sn(Oct)$_2$

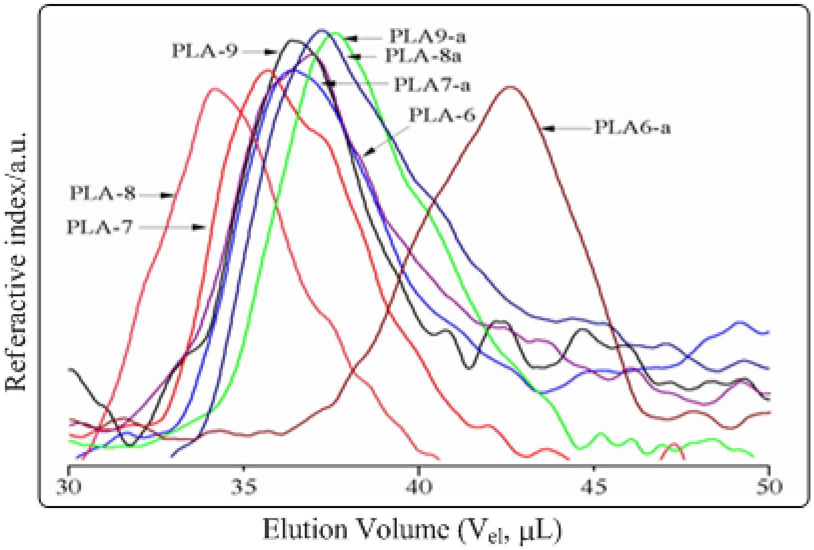
Fig. 3.8: Differential Scanning Calorimetry (DSC) of poly(lactide)s synthesized using cloisite modified catalyst showing glass transition temperatures.

Table 3.2 showed the summarized data from PLA-6 to PLA-9. The conversion steadily increased up to 1 hr so that quantitative conversion was reached after 1 hr at 200 ^{0}C. However, PLA-8 showed the highest value of M_w 185,000 and broad distribution (~1.9) in comparison with PLA-6, PLA-7. The broad distribution may be attributed due to the presence of macrocyclic. PLA-9 showed degradation behavior at 90 min at 200 ^{0}C. The results of the thermal characterization are shown in Table 3.2. PLA-7a showed maximum molecular weights, molecular weight distribution such as M_n, M_w and distribution are 33,000, 57,000 and 1.72 respectively. Thereafter there is a decline trend of molecular weight and weight distribution till 90 min. The transesterification reaction is predominated with increase in time.[91] GPC curves shown in fig 3.9. In fig. 3.11 T_g values (PLA-6-8) varied from 51 to 52 ^{0}C for the polymer prepared 30, 75 and 90 min. Similarly, T_g values (PLA-6a-8a) varied from 40 to 48 ^{0}C for the polymer prepared 30, 75 and 90 min which are relatively lower than the polymer PLA (6-8). The fig. 3.10 shows the melting temperatures (T_m) of the polymers (PLA-6-8) prepared at 30, 75 and 90 min are for from 167 to 172 ^{0}C. It is important to note that the T_m value of PLA-8 are comparatively lower than PLA-7, in spite of higher molecular weight. This result may be attributed due the occurrence of some racemization reaction.[91] The melting temperatures (T_m) monotonously decreases from 164 ^{0}C (PLA-7a) to 157 ^{0}C (PLA-9a) with decrease in molecular weights.

Table 3.2: Clay modified Catalyzed Polymerizations of L-lactide at 200 ^{0}C in Bulk

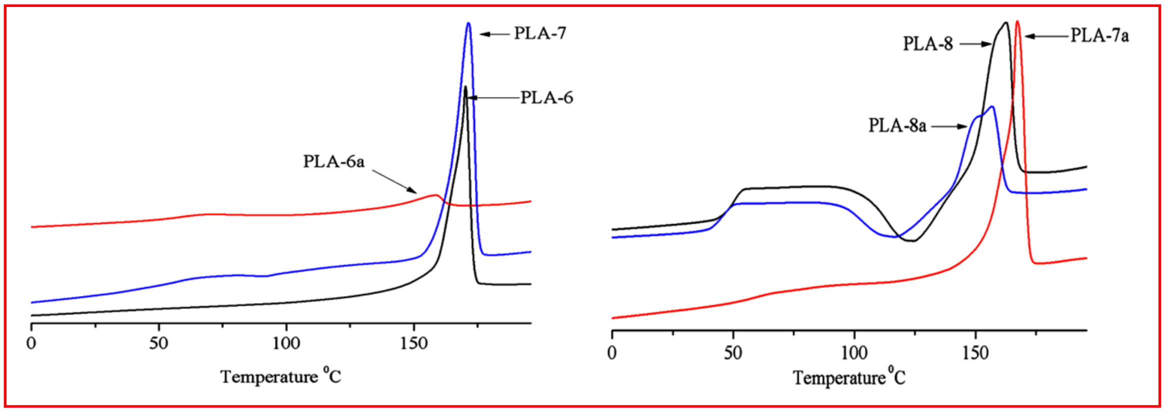
Polymer	Time (min)	Conversion (%)	M_n (SEC)	M_w (SEC)	T_m (^{0}C)	ΔH_m (J/g)	T_g (^{0}C)	ΔC_p (J/g)
PLA-6	30	70	33300	52200	170	28	52	0.26
PLA-6a	30	61	21000	36000	157	20	46	0.37
PLA-7	60	99	45600	75000	171	43	55	0.46
PLA-7a	60	99	33000	57000	164	40	49	0.41
PLA-8	75	99	97300	185000	167	34	51	0.35
PLA-8a	75	99	27000	44000	163	31	45	0.39
PLA-9	90	99	28200	66200	172	54	52	0.54
PLA-9a	90	99	20000	37000	157	20	48	0.37

a: Poly(lactide)s synthesized using Stannous Octoate Sn(Oct))



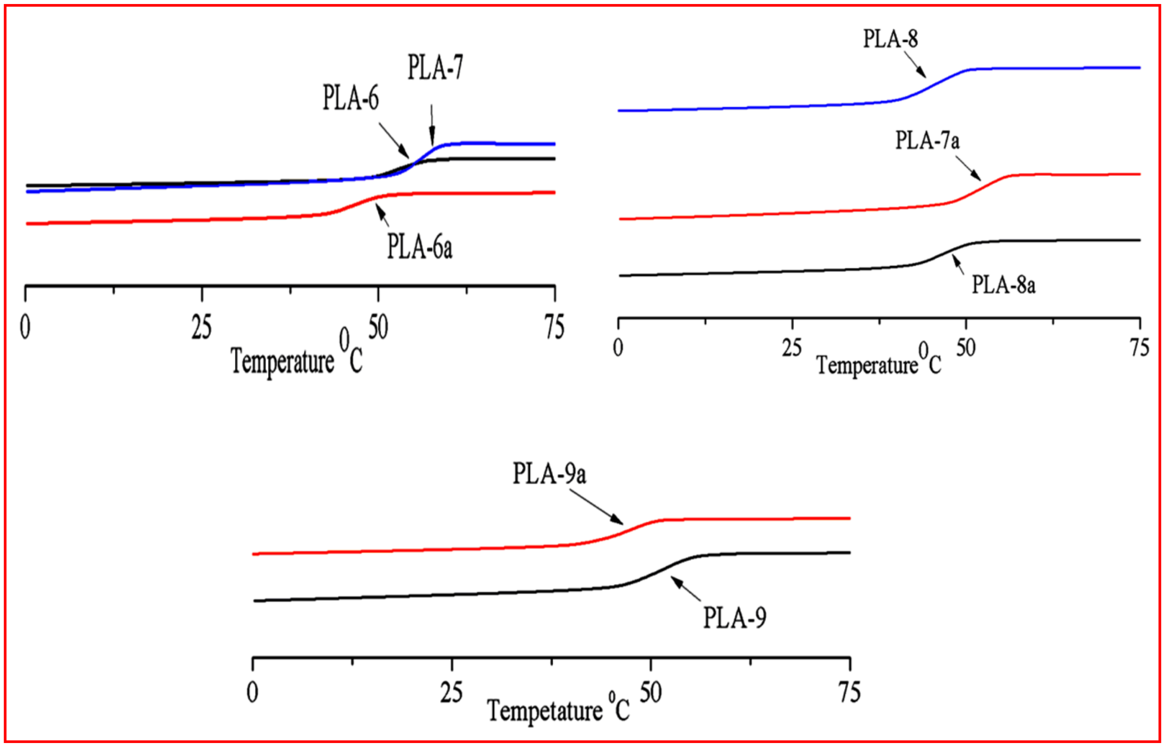
a: Poly(lactide)s synthesized using Stannous Octoate $Sn(Oct)_2$

Fig. 3.9: Size Exclusion Chromatography(SEC) of Poly(lactide)s.



a: Poly(lactide)s synthesized using Stannous Octoate Sn(Oct)$_2$

Fig. 3.10: Differential Scanning Calorimetry (DSC) of poly(lactide)s synthesized using cloisite modified catalyst showing melting points.



a: Poly(lactide)s synthesized using Stannous Octoate Sn(Oct)$_2$

Fig. 3.11: Differential Scanning Calorimetry (DSC) of poly(lactide)s synthesized using cloisite modified catalyst showing glass transition temperatures.

XRD:

Wide angle X-ray diffraction also shows a different pattern as shown in fig. 3.12. The diffraction profile of PLA and PDLA polymers showed the diffraction peaks at 2θ around 15^0,16^0, 18.5^0 and 22.5^0.

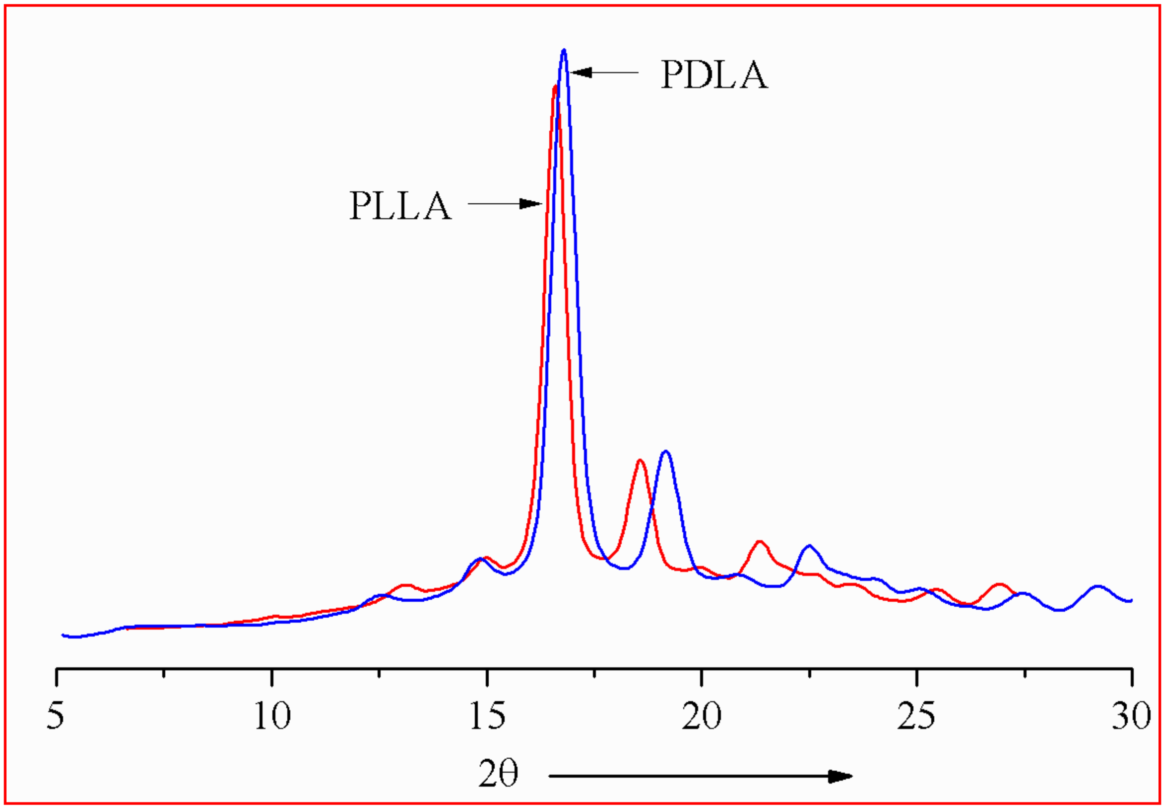


Fig. 3.12: Powder X-Ray Diffraction (XRD) patterns of PLA and PDLA synthesided using cloisite modified catalyst.

MALDI TOF: Fig. 3.13 shows the MALDI spectrum of polymer PLA-3. The spectrum is dominated by two series of intense peaks of masses ranging from 959 to 1536 (n>13) and from 960 to 1680 Da (n>13). In this region, the spectrum also shows two mass series a mass series of higher intensity that can be assigned to cyclic oligomers of PLA, which appear as oligomers doped with sodium ions with masses of 72n +23. Fig. 3.13 also indicates equal quantities of even and odd no cycles at least more than C12. Similar finding have been observed.[92]

There are two distinct series of intense peaks ranging from 977 to 1697 Da and from 1050 to 1698 Da, corresponding to linear PLA oligomers doped with sodium ions (mass=72n+18+23, where n ranges from 13 to 23) in both the cases. These two series expected to be formed by oligomers bearing -COOH and -OH as terminal groups, corresponding to the general formula H [-O-CH (CH3-CO)]-OH-Na^+.

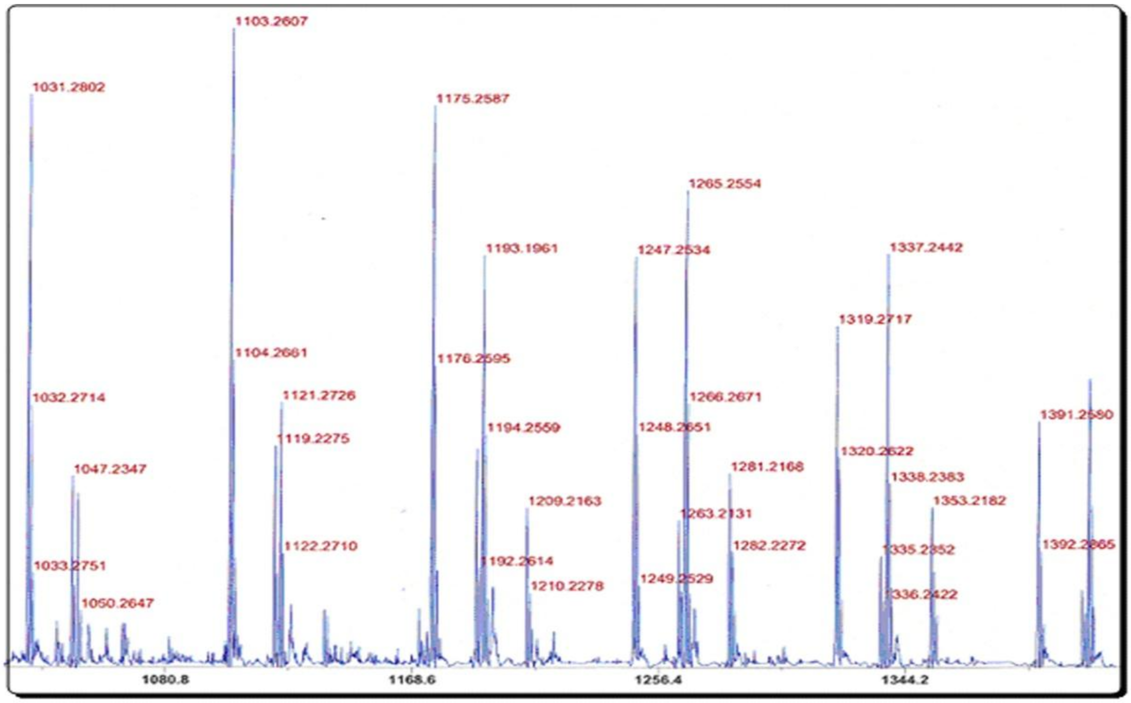


Fig. 3.13: MALDI-TOF mass spectrum of polylactide using clay modified catalyst.

NMR:

In the spectrum of PLA (fig. 14), the peaks appearing from 168.5 to 169.7 ppm are due to ester carbonyl groups. The peak at 167.6 ppm assigned to lactonic carbonyl groups of L-Lactide. The absence of peak at 167.6 ppm indicated the complete conversion of lactide to polylactide at 1 hr reaction time. The peaks appear at 69.01 and 16.63 ppm are due to methine group and methyl group respectively. The structure of the polylactide was confirmed. No lactide was detected in the sample.

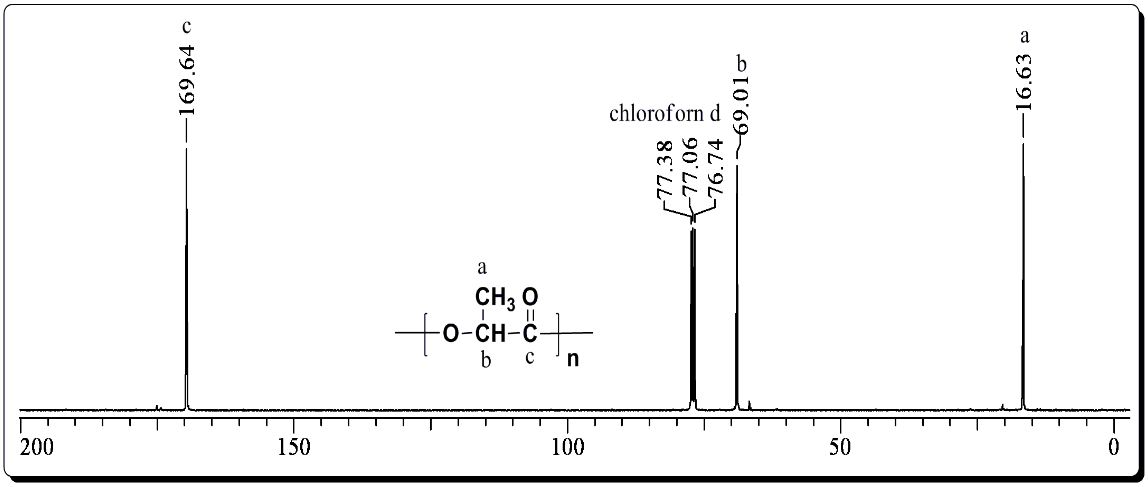


Fig. 3.14: 100 MHz ^{13}C-NMR of Polylactide using clay modified catalyst.

3.4.3 Effect of Coinitiator on ROP of L-Lactide:

The effect of coinitiator was studied using isopropyl alcohol in ROP of L-L lactide. The solid cloisite modified Tin catalyst is not thought to be actual initiator since the molecular weight does not depend on the monomer to catalyst molar ratio. The most promising mechanism is a coordination insertion mechanism where hydroxy functional group in thought to coordinate to modified cloisite catalyst forming the initiating Tin alkoxide complex.

Polymerization with solid cloisite modified Tin catalyst is assumed to proceed through a coordination insertion mechanism which consists of monomer complexation to the active species and insertion by rearrangement of the covalent bonds. The mechanism leads to cleavage of acyl-oxygen bond of the monomer and of the metal-oxygen bond of the propagating species. The complete conversion of monomer to polymer was shown is Table 3.3. The number average molecular weight increased with increased in the ratio of [M]/[CoI]. The molecular weight distribution is narrow ~ 1.2 up to 2.66 and broaden thereafter. This result indicates that the amount of transfer reactions was almost negligible up to [M]/[CoI]~2.66.

Actually the literature report reveals two slightly different pathways in case of coordination insertion mechanism. Kricheldorf and coworkers have proposed a mechanism where the coinitiating alcohol functionality and the monomer are both coordinated to the Sn(Oct)$_2$ complex during propagation. Penczek and co-workers have presented a mechanism where the Sn(Oct)$_2$ complex is converted into a tin alkoxide before complexing and ring opening of the monomer. In the present case, it follows the former strictly than the later.

Fig. 3.15 shows the SEC curves of polylactieds (PLA-10 to PLA-13). The gradual increment of M_n was observed as the ratio of [M]/[CoI] increased up to 5.3.The TGA curves were presented in fig. 3.16. The DSC curves were presented in fig. 3.17. The T_g values increased monotonically from 24-48 ^{0}C as the ratio of [M]/[CoI] increased. Similarly T_m values increased from 118 to 165 ^{0}C. The reaction proceeds with acyl-oxygen bond scission with retention of the configuration and could be achieved in bulk (solvent free) polymerization. No transesterification, back-biting reactions were observed.

Table 3.3: Effect of coinitiator (Isopropyl alcohol) concentration on ROP of Lactide at 180 ^{0}C

Polymer	Time (min)	[M/[CoI]	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	T_g (^{0}C)	ΔC_p (J/g^{0}C)	Deg. T
PLA-10	60	1.33	20150	33800	1.6	165	43	48	39	307
PLA-11	60	1.77	3115	3880	1.1	146	20	39	33	282
PLA-12	60	2.66	2866	3580	1.2	119	07	24	06	278
PLA-13	60	5.30	1459	1624	1.2	118	09	24	22	176

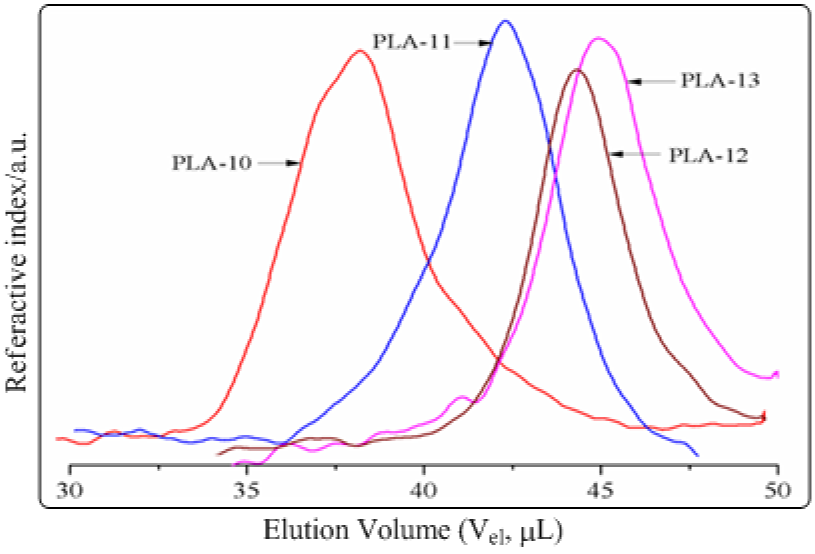


Fig. 3.15: Size Exclusion Chromatography(SEC) of Poly(lactide)s.

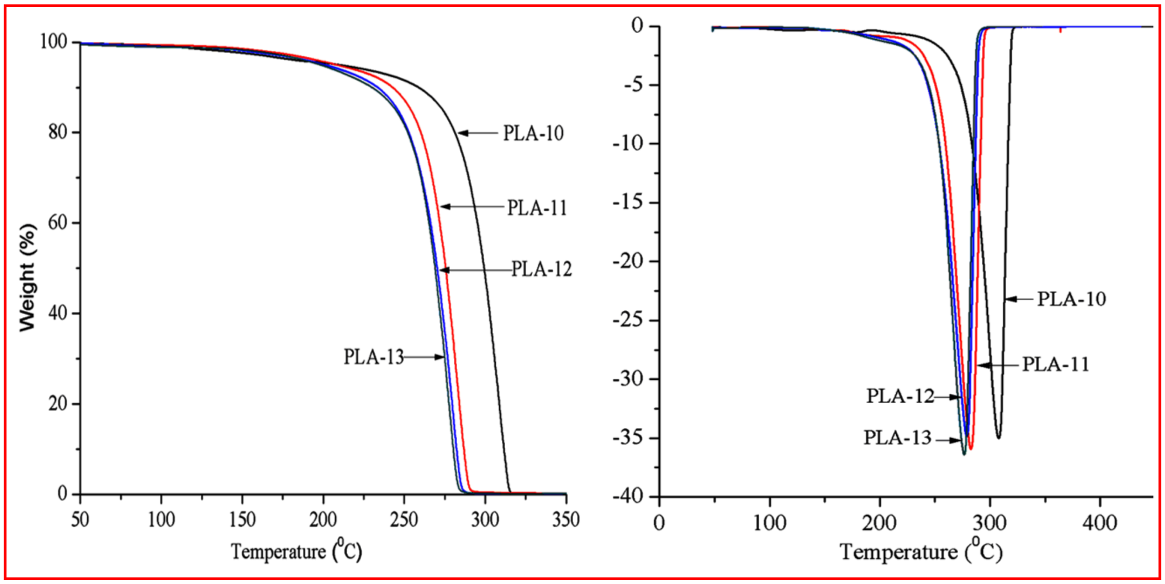


Fig. 3.16: Thermogravimetric analysis A: TGA, B: DTG curves of poly(lactide)s synthesized using cloisite modified catalyst showing decomposition temperatures.

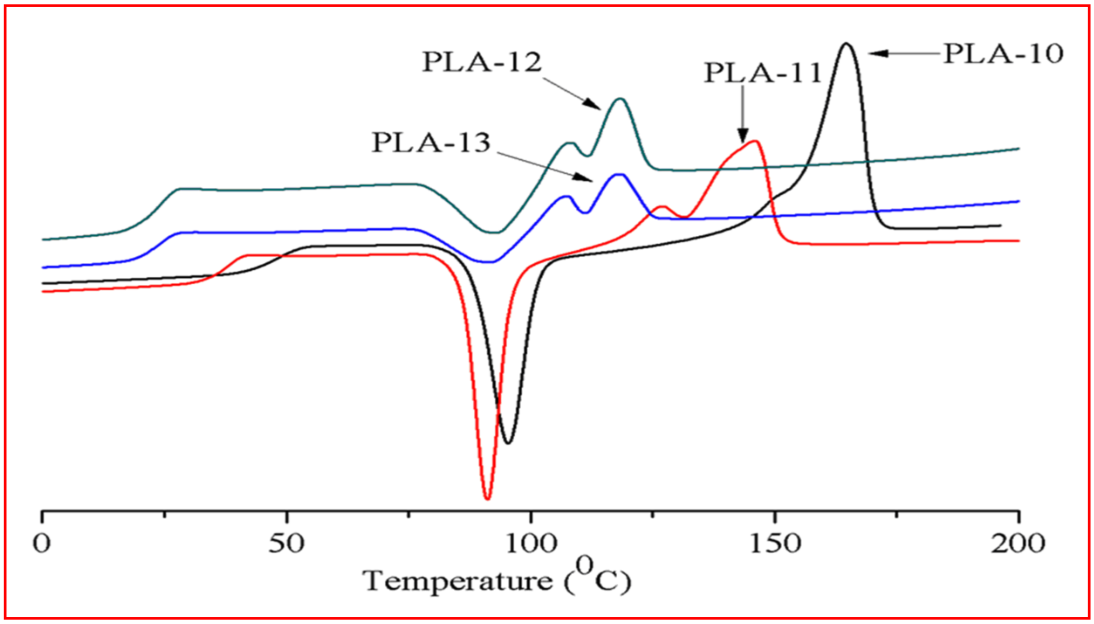


Fig. 3.17: Differential Scanning Calorimetry (DSC) of poly(lactide)s synthesized using cloisite modified catalyst and Isopropyl alcohol (coinitiator) showing melting points as well as glass transition temperatures respectively.

3.4.4 Dispersion of clay and ROP of lactide:

Table 3.4 shows the various types of clay incorporation using ring opening polymerization of L-lactide using organo modified clay catalyst. The structure of various clay used in this study was depicted in fig. 3.17 a.

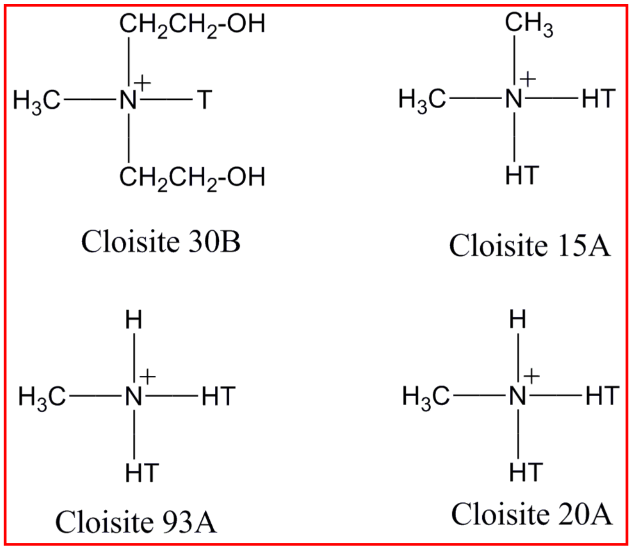


Fig. 3.17a: Structures of organomodified clays.

The role of the type of organo-modified in presence of $Sn(Oct)_2$ was studied in case of ROP of L-Lactide. Four commercial clays i.e. cloisite-30B, cloisite-15A, cloisite-93A and cloisite-20A were selected for the *in-situ* polymerization of L-Lactides. Clay wt % (0.75) was kept constant for all polymerization reactions and clay was dispersed in sodium dry dichloromethane (DCM) with magnetic stirrer. The clay dispersion time is 48 hr at room temperature. Cloisite-30B resulted highest M_n and M_w as 13700 and 32700 Da. PLA-15 showed M_n and M_w as 19000 and 31000 Da where cloisite-15A was incorporated.PLA-16 shown M_n and M_w as 14100 and 27,000Da.

PLA-17 showed M_n and M_w as 9240 and 16200Da. Cloisite-30B contains two hydroxyl groups wich act as a co-initator in the presence of solid cloisite modified tin catalysts. The other two clays i.e. cloisite-15A and 20A are structurally almost similar but modifier concentration and weight loss on ignition are entirely different. The cloisite-93A has different structure as well as modifier concentration, weight.

TGA curves showed that the thermal stability is different with different types of clays. Fig. 3.19 and Table 3.4 also showed that the maximum thermal stability occurred at 300 ^{0}C in the presence of cloisite-30B and least at 280 ^{0}C in the presence of cloisite-20A. PLA -15 and PLA-16 showed moderate stability i.e. at 294 ^{0}C and 283 ^{0}C.

Table 3.4 and fig.3.18 shows that T_g and T_m values of PLA -14 to PLA-16.The T_g and T_m values increased chronologically from cloisite-20A, cloisite-93A, cloisite-15A and cloisite-30B. The highest T_g and T_m values were observed in case of cloisite-30B incorporation because of high molecular weight.

Table 3.4: Effect of dispersed organo-modified clay (0.75 wt %) on ROP of L-Lactide using catalyst $Sn(Oct)_2$ (0.75 wt %) at 180 ^{0}C

Polymer	Clay	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	T_g (^{0}C)	ΔC_p (J/g^{0}C)	Deg.T (^{0}C)
PLA-14	C-30B	13700	32700	2.3	163	24	53	22	300
PLA-15	C-15A	19000	31000	1.6	162	23	51	20	294
PLA-16	C-93A	14100	27000	1.9	160	18	51	26	283
PLA-17	C-20A	9240	16200	1.7	152	19	34	29	280

C- Cloisite

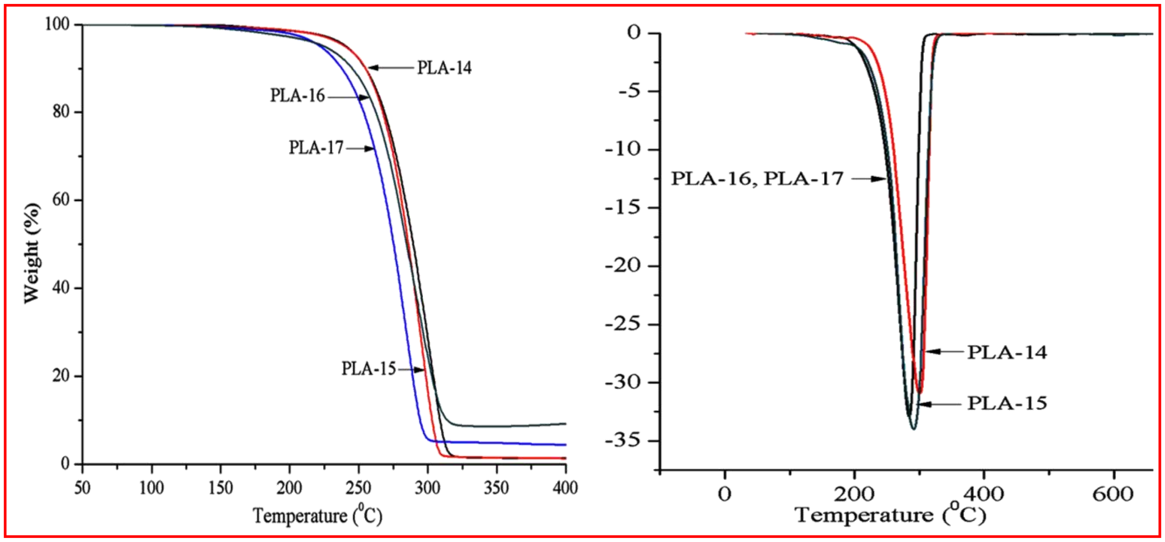


Fig. 3.18: Thermogravimetric analysis (TGA) of poly(lactide)s synthesized using different cloisite showing decomposition temperatures.

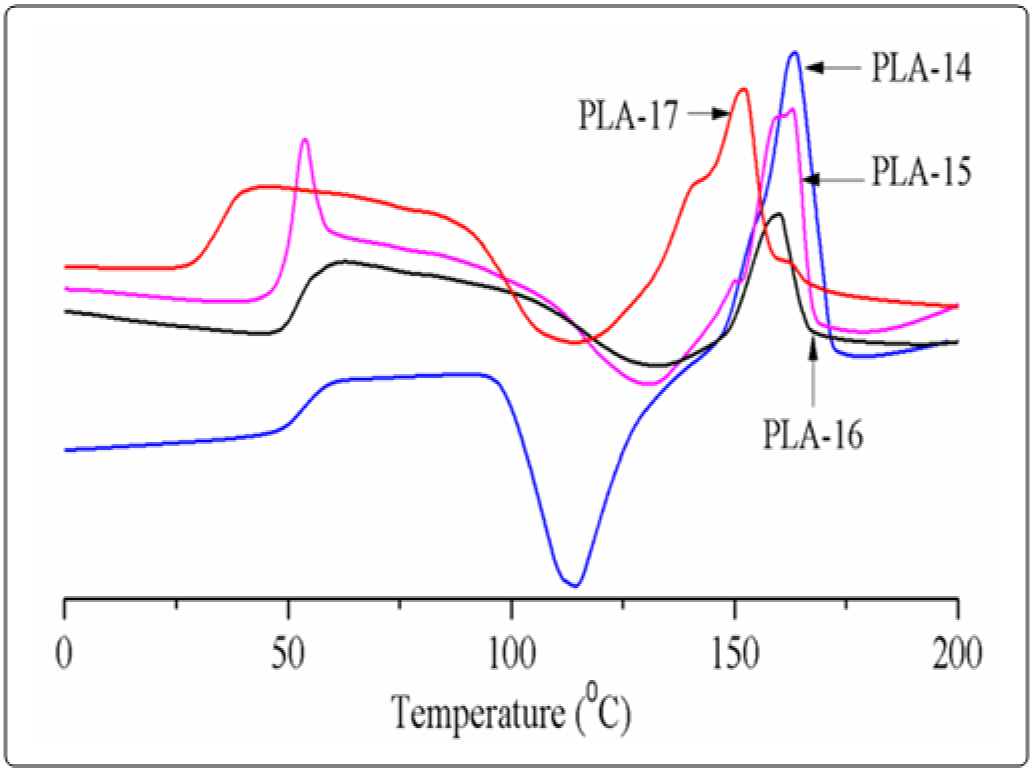
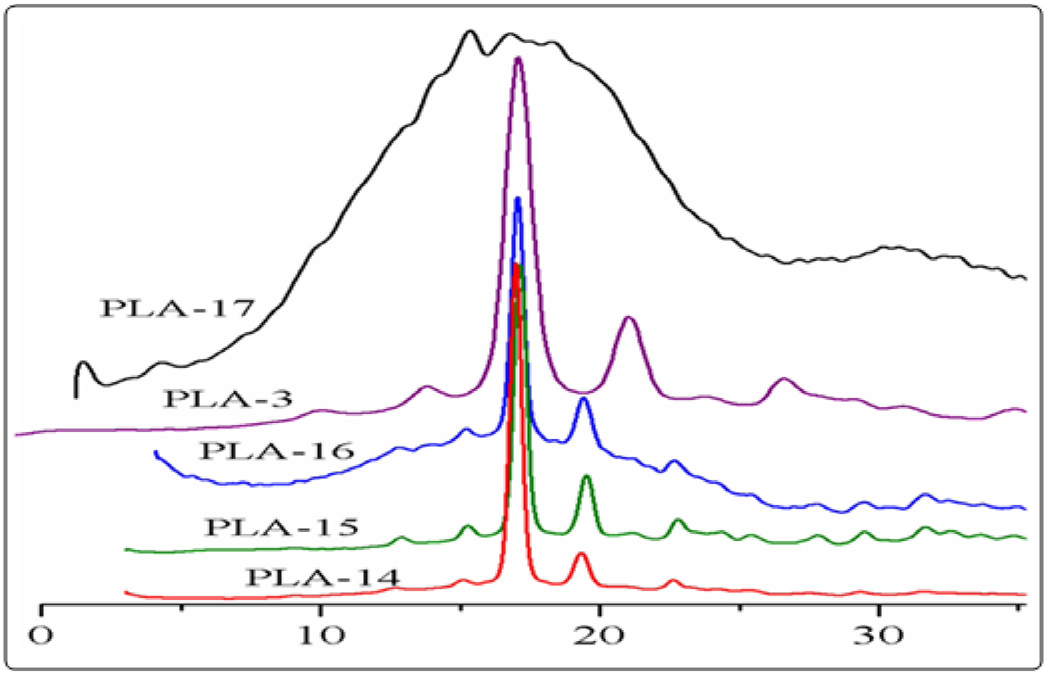


Fig. 3.19: Differential Scanning Calorimetry (DSC) of poly(lactide)s synthesized using different cloisite showing melting points as well as glass transition temperatures respectively.

Fig. 3.20 showed X-ray powder pattern diffraction (XRD) of poly (L-lactides) prepared using various clays.The prominent peaks at θ values 18^0 and 22^0 appeared to be narrower in case of PLA-14, PLA-15 and PLA-16 in comparision with PLA-3.The results are attributed to polymer in clay gallery. The contrast result was obtained in case PLA-17. There was a gussian type of distribution curve which may be attributed to explotion of polymer chains in the clay gallery. DSC results also supported this result where T_g and T_m values are comparatively lower.



2θ (deg) →

Fig. 3.20: Powder X-Ray Diffraction (XRD) patterns of poly(lactide)s synthesided using different cloisite.

Transmission Electron Microscopy (TEM):

Fig. 3.20 depict the morphological characterization of pure PLA,PLA-14,PLA-16 and pla-17 nanoparticles are measured using transmission electron microscopy (TEM).The nanoparticles exhibited a spherical shape, fairly uniform size and relatively smooth surface;they are also well dispersed. The pure PLA nanoparticle varies from 3.08 to 3.96 nm ranges. PLA -14 showed nanoparticles where size varies from 2.64 to 3.52 nm.PLA -16 exhibited uniform distribution of nanoparticles where size of most of the nanoparticles are 2.69 nm. PLA-17 showed a wide range of nanoparticles ranging from 2.11 nm to 3.26 nm. These results confirmed that cloisite-93A shows better dispersion property in comparison with other clays in corporation polymer such as PLA-14, PLA-15 and PLA-17.

The dispersion of all four clays such as cloisite-30B, cloisite-15A, cloisite-93A and cloisite-20A in the polymer matrix are uniform and appeared in the nano range. This is probably the first instance where clay nano particles were formed during the *in situ* ring opening polymerization.

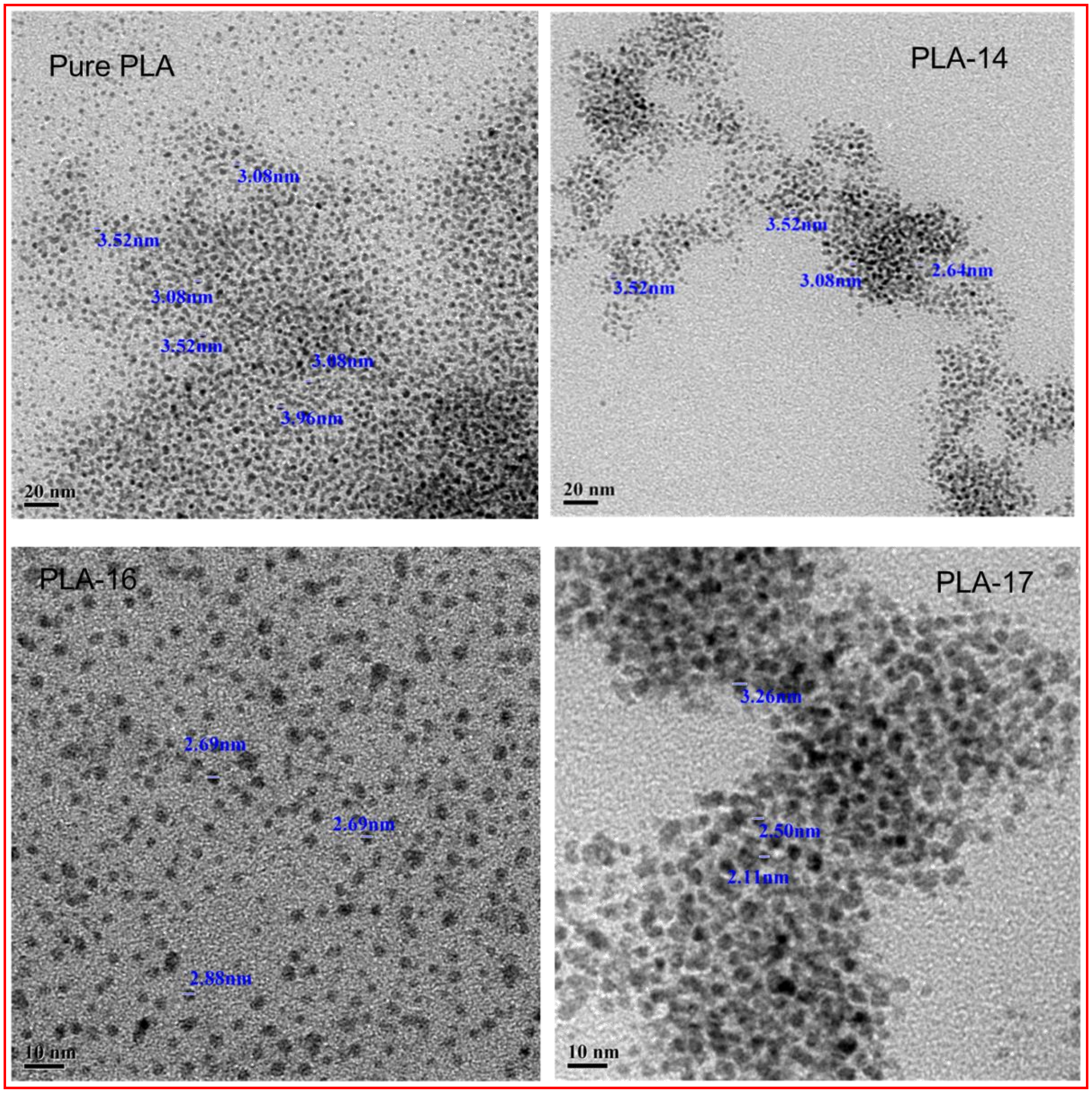


Fig. 3.20a: TEM Images of polylactides using dispersion method.

3.4.5 ROP of L-Lactides Using LiCl: The effect of Lithium Chloride as an catalyst with cloisite-30B as a (coinitiator) for the ring opening polymerization of L-Lactide was studied for first time. The polymerization was performed at 200 ^{0}C using break seal technique. The melting temperatures (T_m) of these polymers were studied using Differential Scanning Calorimetry (DSC). The observed T_g and T_m were shown in fig. 3.21. The T_m of PLA-18 is 93 ^{0}C. As the monomer to initiator ratio (M/I) increases molecular weight (M_n and M_w), T_g increase as shown in Table 3.5. Polydispersity index

(PDI) is observed 1.1 and it is constant throughout all M/I ratio. GPC curves shown in fig. 3.20b and molecular weights tabulated in Table 3.5.

Table 3.5: Effect of cloisite-30B (coinitiator) on ROP of L-Lactide using LiCl catalyst (0.75 wt %) at 200 ^{0}C

Polymer	M\Co-I	Time (min)	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	T_g (^{0}C)
PLA-18	Blank	60	29703	33349	1.1	93	15	05
PLA-19	200	60	9751	10903	1.1	87	13	14
PLA-20	400	60	21700	24287	1.1	88	12	15
PLA-21	600	60	25986	30282	1.1	91	13	12

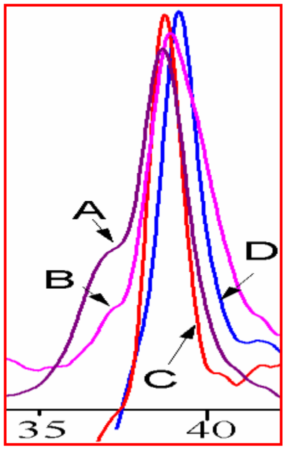


Fig. 3.20b: GPC curves showing PDI A: PLA-18, B: PLA-19, C: PLA-20, D: PLA-21.

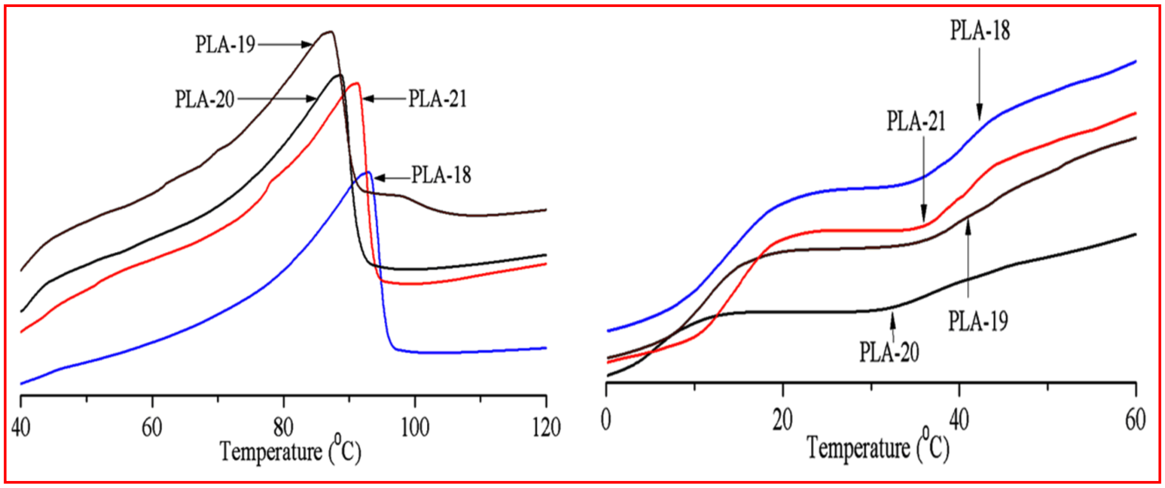


Fig. 3.21: Differential Scanning Calorimetry (DSC) of poly(lactide)s synthesized using different LiCl catalyst and cloisite-30B (coinitiator) showing melting points as well as glass transition temperatures.

COPOLYMERS:

3.4.6 PLGA copolymers:

The result of L-lactide/glycolide copolymerization initiated by cloisite modified Sn catalyst was discussed here. Copolymerization of lactide/glycolide was performed by sealing ampoules. The copolymerization of L-lactide and glycolide was carried out up to 150 ^{0}C. The conversion was very low. At 180 ^{0}C, some amount of unreacted reacted L-lactide and glocolide were found. Therefore copolymerization was carried out at 200 ^{0}C. In all case satisfactory molecular weights was achieved using this new catalyst. High temperature (200 ^{0}C) was maintained for all polymerization reactions.The obtained copolymer showed molecular weight distribution ranging from 1.6 to 2.9. ^{1}H-MNR spectra of prepared copolymers was recorded and shown in fig. 3.22 which contain both lactide and glycolide unit. The results of TGA, DSC studies were presented in fig. 3.24, 3.25 and Table 3.6. The main features are the melting endotherm at 223 ^{0}C and this thermogram indicated that polyglycolide is highly crystalline material and is full agreement with the result of D. Cohn and G. Marom.[93] The data were mainly obtained from the fig. 3.25 and tabulated in Table 3.6. The obtained DSC traces clearly indicate glass transitation temperature and sharp melting temperatures for all copolymer series.

The highly crystallinie nature of the glycolide decreased with the incorporation lactide comomoner unit in copolymers as shown in fig. 3.26 (XRD Studies). The glass transitation temperature decreased from 33 to 31 as the percentage of lactide changes during copolymerization. SEC results were shown in fig. 3.23 and Table 3.6. All these lactide/glycolide copolymer and are thermally stable up to 300 ^{0}C shown in fig. 3.24

Table 3.6: PLGA Copolymers using clay modified catalyst (0.75wt %)

Polym.	Ratio (Mol.) LA:GA	Time (hr)	Temp. (^{0}C)	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	T_g (^{0}C)	ΔC_p (J/g ^{0}C)
Polygly.	0:100	0.5	200	nd	nd	nd	223	171	-	-
COP-1	80:20	0.5	200	6710	12100	1.8	203	28	33	16
COP-2	75:25	0.5	200	9520	15710	1.6	204	27	31	13
COP-3	60:40	0.5	200	6090	17800	2.9	205	36	31	14
COP-4	50:50	0.5	200	7750	14040	1.8	nd	nd	nd	nd

LA-L-Lactide, GA- Glycolide

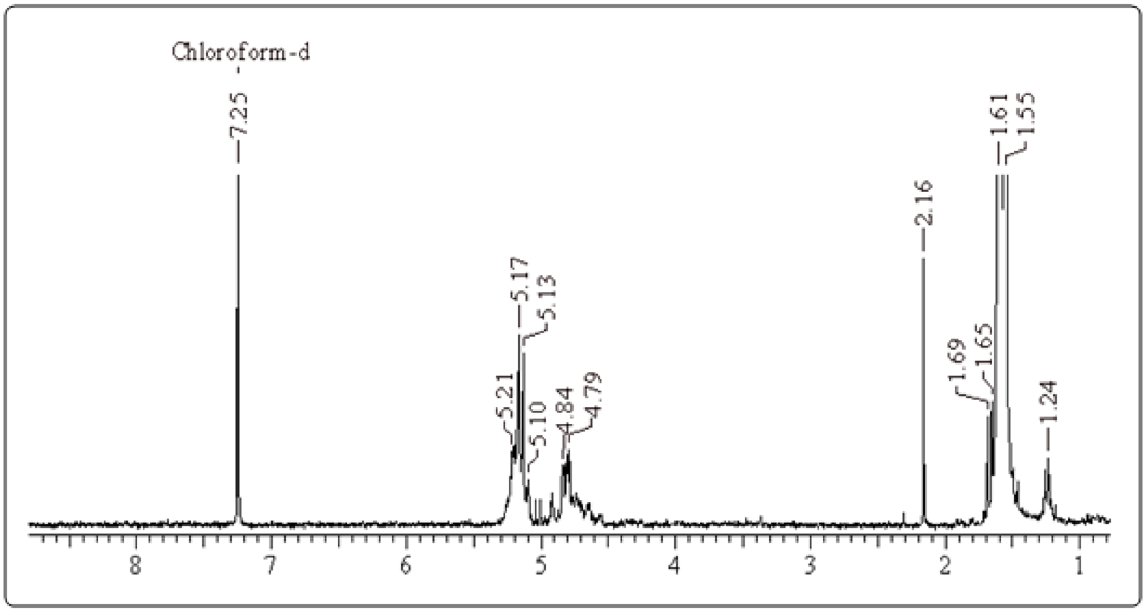


Fig. 3.22: ^{1}H-NMR spectra of poly(L-lactide-co-glycolide).

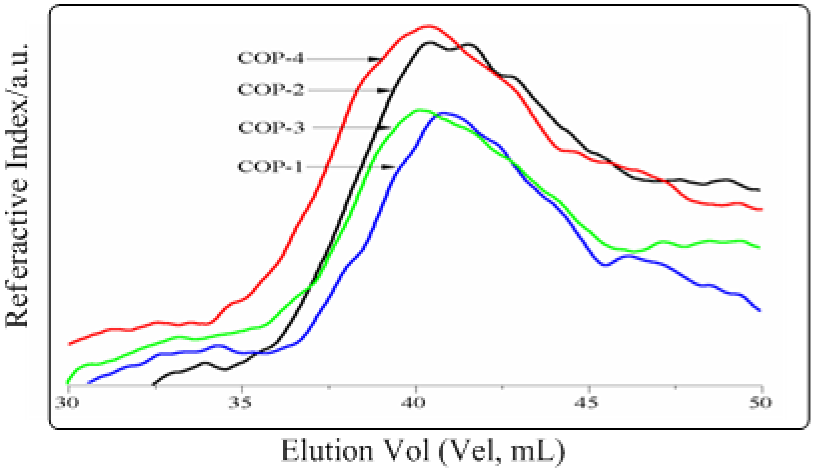


Fig. 3.23: Size Exclusion Chromatography (SEC) of poly(L-lactide-co-glycolide).

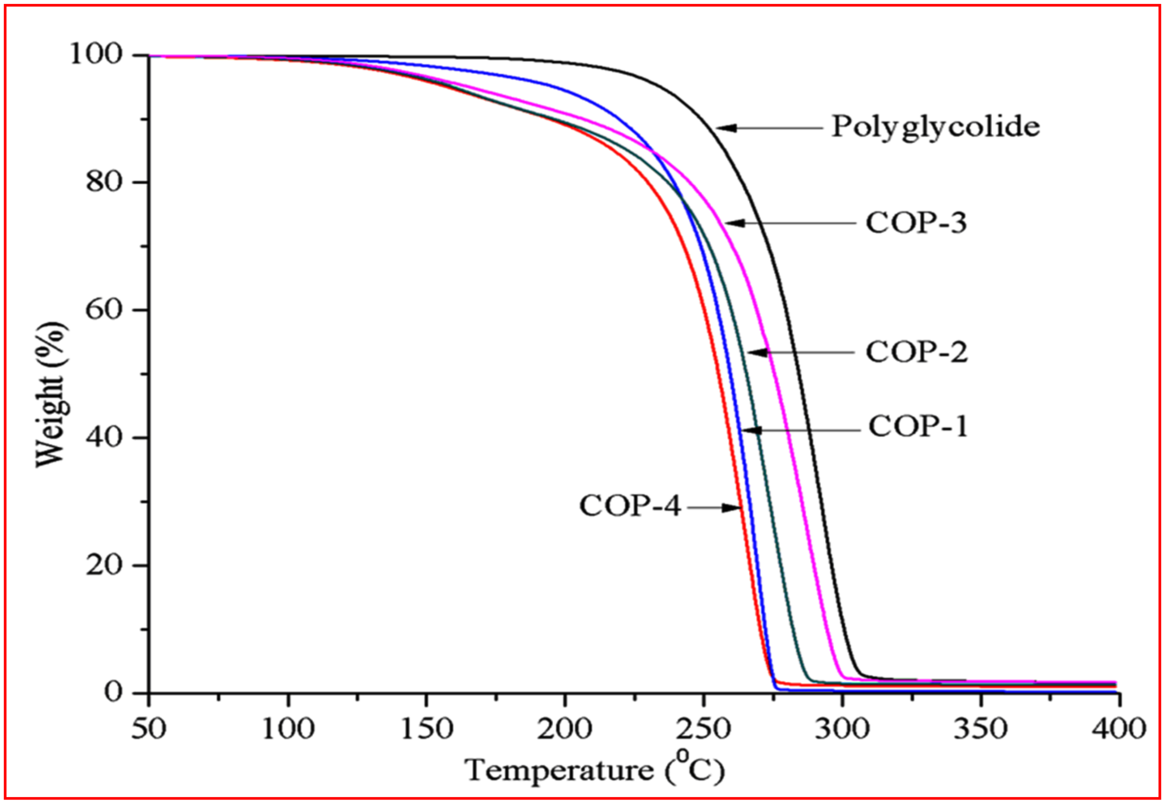


Fig. 3.24: Thermogravimetric analysis (TGA) of L-Lactide-co-Glycolide synthesized using cloisite modified catalyst showing decomposition temperature.

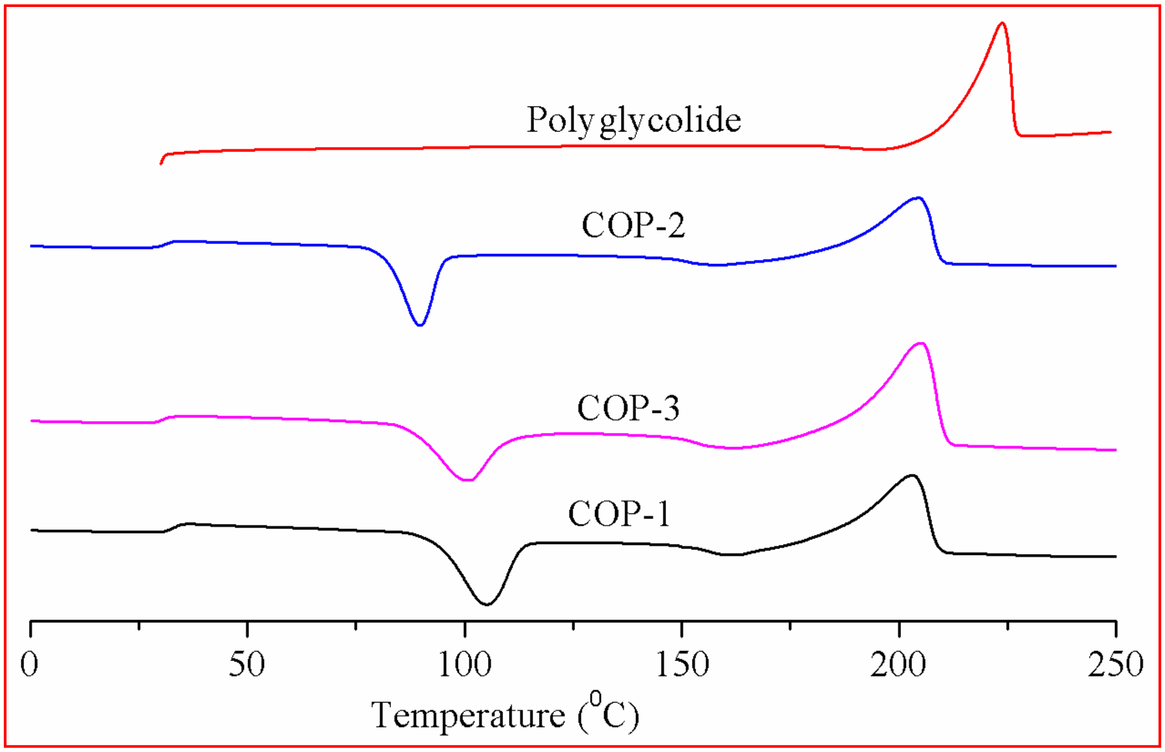


Fig. 3.25: Differential Scanning Calorimetry (DSC) of L-Lactide-co-Glycolide synthesized using cloisite modified catalyst melting points as well as glass transition temperatures respectively.

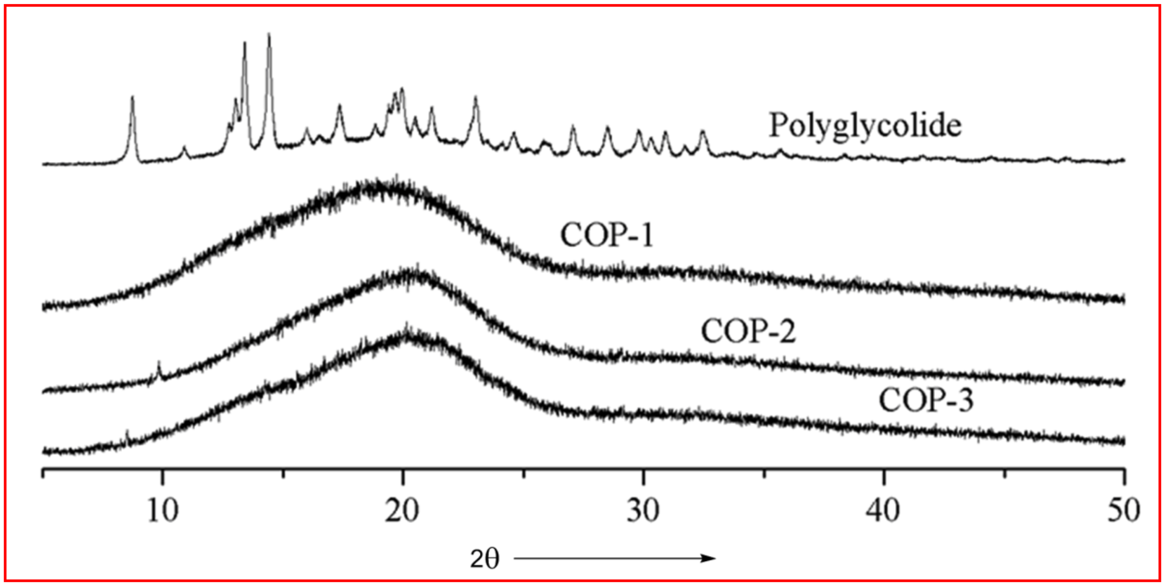


Fig. 3.26: Powder X-Ray Diffraction (XRD) patterns of poly(L-lactide-co-glycolide).

3.4.7 β-Butyrolactone/L-Lactide Copolymers:

β-Butyrolactone, L-Lactide, Ti(IV)butoxide (10 mo%) was added into the activated dried ampoule. These mixtures were dried and sealed under high vacuum. The ampoule was buried in sand bath at 180 ^{0}C for polymerization for 2 hr. A series of copolymers with different compositions were prepared. GPC result showed that polymer molecular weight increased up to 15600 and molecular weight distribution is unimodel (1.4). As the percentage of β-buterolactone increases, there is successive decreament in molecular weight successively as shown in Table 3.7. An increase the concentration of β-Bytolactone in the copolymer resulted in lower glass transitation temperature and melting temperatures as shown in Table 3.7. Thermogravimetric analysis (TGA) was used to study weight loss property as a function of temperature for all the copolymers and these copolymers are thermally stable up to 350 ^{0}C shown in fig. 3.27. Melting temperature and glass transitation temperature show in fig. 3.28.

The COP-5 was selected to study effect of organomodified clay i.e. cloisite-15A on the thermal properties. Cloisite-15A were used for a series of copolymers (COP-11 to COP-15) prepared using ROP technique. DSC (fig. 3.30 and fig. 3.31) result showed that melting temperature (T_m) and glass transitation (T_g) temperatures increased up to 4 wt % addition of cloisite-15A and then decrease. T_g increased from 37 ^{0}C to 46 ^{0}C and melting temperatures decreased by 4 ^{0}C shown in Table 3.7. This decrease in thermal properties is due to more quaternary ammonium salt present in cloisite-15A in ROP of β-butyrolactone.

Table 3.7: β-Butyrolactone/L-Lactide Copolymers using Ti(IV)butoxide catalyst (10 mol %)

Polym.	Ratio (Mol.) (BL:LA)	Time (hr)	Temp. (^{0}C)	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	T_g (^{0}C)	ΔCp (J/g ^{0}C)
COP-5	10:90	2	180	10800	15600	1.4	150	41	37	58
COP-6	20:80	2	180	10700	15300	1.4	142	52	35	44
COP-7	30:70	2	180	5390	7500	1.4	126	44	28	43
COP-8	40:60	2	180	4140	6350	1.5	121	14	10	-
COP-9	50:50	2	180	3430	5170	1.5	104	08	07	-
COP-10	80:20	2	180	3330	4130	1.2	nd	nd	nd	nd

BL: β-Butyrolactone, LA: L-Lactide

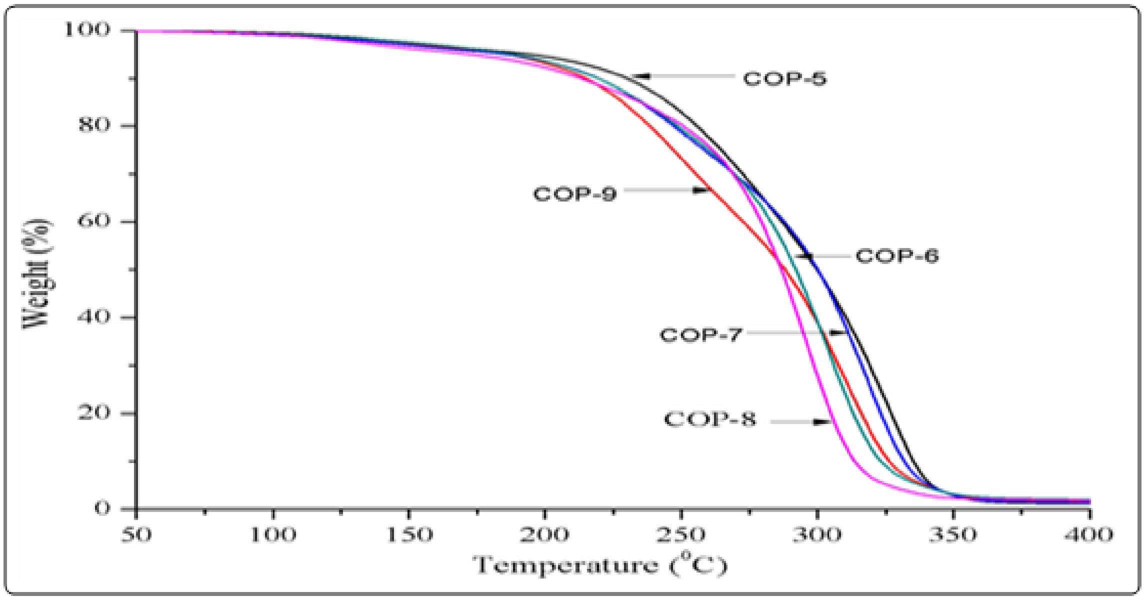


Fig. 3.27: Thermogravimetric analysis (TGA) L-Lactide-co-β-Butyrolactone synthesized Ti(IV)butoxide showing decomposition temperatures.

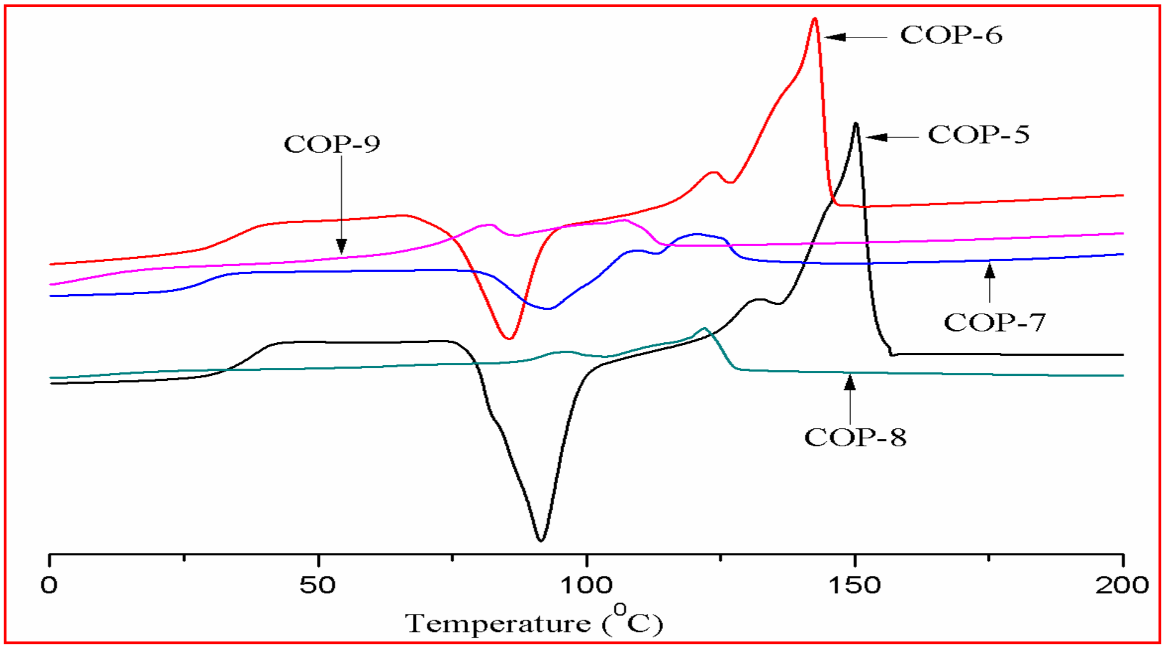


Fig. 3.28: Differential Scanning Calorimetry (DSC) of L-Lactide-co-β-Butyrolactone synthesized suing Ti(IV)butoxide showing melting points as well as glass transition temperatures respectively.

Table 3.8: Effect of Organo-modified clay (cloisite-15A) on COP-5

Polymer	Clay (Wt. %)	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	T_g (^{0}C)	ΔCp (J/g ^{0}C)
COP-11	1	18180	38070	2.0	154	18	46	21
COP-12	2	14550	31590	2.1	151	24	44	16
COP-13	3	9308	13590	1.4	144	24	41	19
COP-14	4	6688	13530	2.0	142	24	36	25
COP-15	5	6290	8711	1.3	117	12	35	08

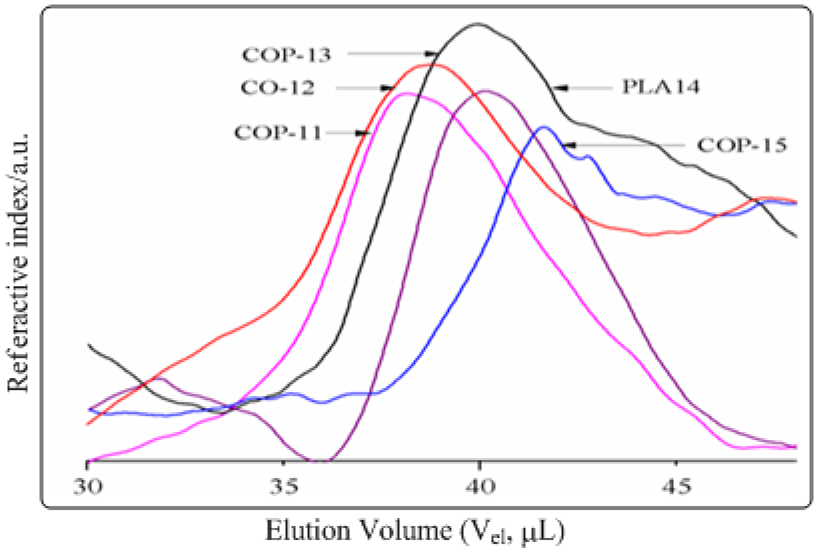


Fig. 3.29: Size Exclusion Chromatography(SEC) of L-Lactide-co-β-Butyrolactone with clay

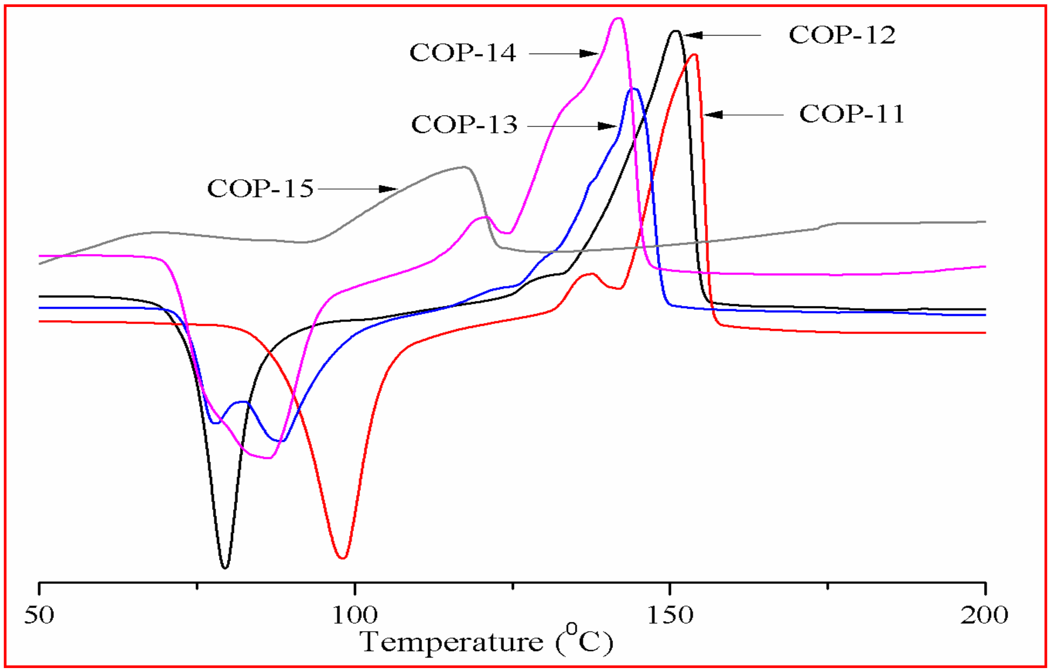


Fig. 3.30: Differential Scanning Calorimetry (DSC) of L-Lactide-co-β-Butyrolactone synthesized using Ti(IV)butoxide with clay showing melting points.

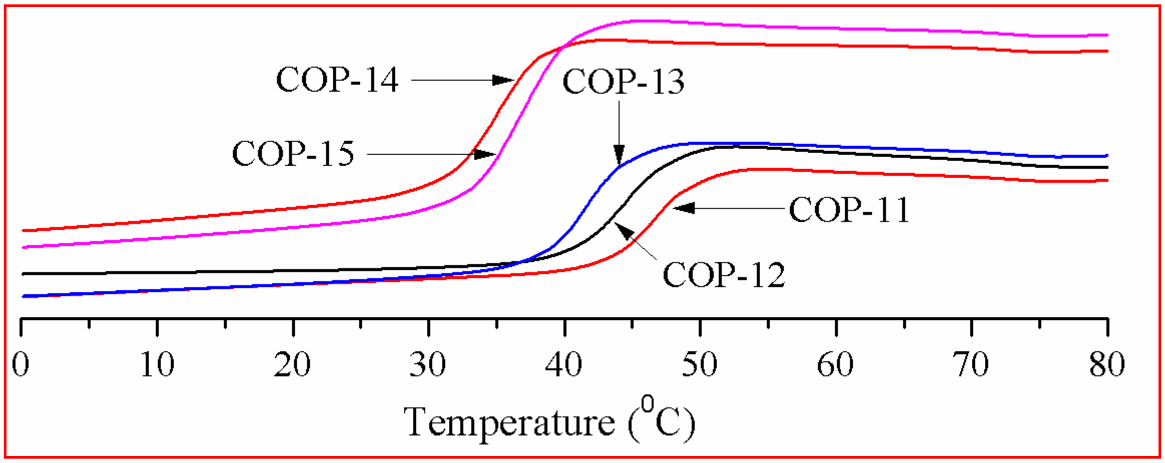


Fig. 3.31: Differential Scanning Calorimetry (DSC) of L-Lactide-co-β-Butyrolactone synthesized using Ti(IV)butoxide with clay showing glass transitation temperatures.

3.5 Conclusion:

In conclusion, novel solid cloisite modified tin catalyst was prepared and fully characterized using various spectral techniques. The structure and properties PLA and PDLA polymers produced by ring opening polymerization using cloisite modified tin as well as conventional stannous octoate catalyst were determined. Results showed that the activity of modified catalyst is superior to stannous octoate catalyst in several aspects. Both PLA and PDLA polymers using modified catalyst showed molecular weight and molecular distribution (M_w/M_n) as M_w~7.0 x10^4 and ~1.6 respectively. The maximum molecular weight, M_w~185000 Da of PLA was obtained. NMR spectra confirmed the presence of linear polymer containing both hydroxyl and carboxyl as their end functional groups. The molecular weight, M_w~7x10^4 of both PLA and PDLA was selected for formation of racemic crystallites. Both PLA and PDLA were dissolved in methylene chloride and allowed to evaporate from mixture for stipulated time at room temperature.

The various types of clay such as cloisite-30B, cloisite-15A, cloisite-93A and cloisite-20A were incorporated during ROP of L-Lactide. The maximum molecular weight was obtained as 32700 Da in case of cloisite-30B and least for cloisite-20A i.e. M_w= 16200 Da. The T_g and T_m values can also be turned in presence of clay, cloisite-30B acts as a coinitiator as well as filler. The other clays behaved as filler during ROP. Cloisite-30B was also used as an initiator along with LiCl catalyst in ROP of L-Lactides. The M_n increased from 9750 to 25986 Da as the [M]/[I] value increased from 200 to 600.

PLGA copolymer was prepared using clay modified catalyst and maximum molecular weight was obtained as 14000 Da, soluble in chlorinated solvent. Copolymer of β-butyrolactone with L-Lactide at various compositions (10:90, 20:80, 30:70, 40:60, 50:50, 80:20) were prepared. The maximum M_w was obtained as 15000 Da. The molecular weight distribution was around 1.4 in all case. The T_g and T_m values can be altered with copolymer compositions.

Stereocomplex

3.1 A Introduction:

Semicrystalline polylactides (PLA)s have attracted much attention for their potential applications in medical devices due to its biodegradability, biocompatibility, excellent optical and good mechanical properties. Stereocomplexation between poly(L-lactide)s (PLA) and Poly(D-lactide)s PDLA can occur between some polymers, which is based on CH_3--C=O interactions of stereoselective Van der Waals forces On the other hand, equimolar mixtures of PLA and PDLA are able to form a stereocomplexed PLA which is different from homopolymer PLA or PDLA, in different aspects. Stereocomplexed PLA shows a melting temperature (T_m) of 50 ^{0}C higher than that of PLA or PDLA, it crystallizes in a triclinic unit cell with helical conformation, it is more compact and has higher mechanical properties than PLA or PDLA. The potential factors on stereocomplexation of PDLA and PLA have been reported, including M_w of the constituents, mixing ratio, optical purities, and crystallization temperature and time, etc. PLA and PDLA has been formed at low as well as high molecular weight the crystalline morphologies of PDLA/PLA blends with equal molecular weight have been extensively studied.[94]

Molecular modeling has been used to explain how the blending of PLA and PDLA affects the resistance PLA to hydrolysis. Amorphous PLA/PDLA blends have been created using molecular modeling and the minimum potential energy of the blends before and after hydrolysis were obtained. The 50/50 blend has the greatest resistance to hydrolysis due to its having stronger hydrogen-bonding and dipole-dipole interactions than pure PLA or PDLA.[95]

PLA/PDLLA was blended with four different commercial adipates to obtain films with enhanced mechanical and thermal properties. Efficiency of plasticizers has been evaluated by studying their compatibility with the polymer and their effect on its glass transition temperature. Polyadipates with low molar mass showed a promising behaviour to overcome the brittleness in PLA/PDLA films.[96]

Ren JD et al. investigated the thermal and dielectric behavior of blends consisting of semicrystalline PLA/amorphous.[97] Blends consisting of linear shape polylactic acid and star shape polylactic acid have been prepared by melt and solution blending. The effect of blending method on the thermal properties and crystallization behavior of linear shape polylactic acid and star shape polylactic acid blends has been investigated.[98] Direct prepration of the polylactic acid stereocomplex from racemic lactide has been reported by Radano et al.[99]

Block-copolymer containing a PLA segment was blended with PDLA chain in chloroform solution and casted into the dried film. This method could form the stereocomplex crystal of PLA/PDLA within the nanometer-sized phase separation self-assembled by block-copolymer.[100] Shin Boo et al. PLA have blended with chemically modified thermoplastic starch in a twin-screw extruder. The characteristic properties of PLA/chemically modified thermoplastic starch blends has been investigated by observing the morphology, thermal, and mechanical properties, and biodegradability.[101] Effects of poly(3-hydroxybutyrate) (PHB) on crystalline morphology of stereocomplexing capacity of PLA and PDLA in blends of high PHB contents i.e 50 wt.% or higher, PHB acts as an amorphous species.[102] PLA and PDLA were synthesized in bulk at 140 ^{0}C by ROP of L-lactide and D-lactide as a monomer using $Sn(Oct)_2$ and lauryl alcohol as a catalyst and an initiator with changing the amounts of catalyst (0.25 similar to 1.0 wt%) and initiator (0.1 similar to 0.5 wt%). The stereocomplex of PLA have been prepared by PLA and PDLA by solution casting having different mixing ratio. The melting temperature, thermal degradation temperature and thermal stability of stereocomplex-PLA were higher than those of homo-polymers of PLA and PDLA.[103]

Stereocomplex fibers has been fabricated by spinning process for various periods of time after prepration.[104, 105, 106] Significant improvements of thermal and mechanical properties have been reported for the high molecular weeight stereocomplex obtained by supercritical method compared with either the solution casting method or their homopolymers.[107] Opaprakasit Pakorn et al. reported thermal properties and crystallization behaviors of polylactide and its enantiomeric blends, stereocomplex, can be achieved by mixing the two PLAs in a 1:1 ratio.[108, 109] The thermal degradation of PLA stereocomplex was investigated to clarify the pyrolysis mechanism.[110] Stereocomplexes of PLA and PCL were formed between pairs of enantiomeric block copolymers and their thermal properties examined the melting temperatures of the crystalline PCL and PLA phases are depending on the composition of block copolymers.[111]

Nitrogen plasma treatment at atmospheric pressure has been used to modify the surface of especially its low surface energy and wet ability, which do not favor the interface adhesion with another material when blended. Treatment time was varied, and induced chemical and topographical surface modifications were assessed. Attention was first focused on the effect of the treatment duration on the hydrophilicity, and results showed that plasma treatment enhanced the PLA surface hydrophilicity.[112]

Nonporous and porous membranes from PLA/PDLA 80/20 have been treated with low-temperature oxygen, ammonia, or sulphur dioxide- hydrogen plasmas and the late effects of plasma treatment on physicochemical characteristics of the membranes' surface were analyzed.[113] Non-woven fibres of stereocomples PLA/PDLA (70/30) are modified with an ultrathin plasma-polymerized allylamine coating.[114] Biodegradation of PLA films and filaments recovered with hydrophilic layer from allylarnme plasma polymerization was investigated under aerobic conditions in sludge. [115]

3.2 A Analysis:

3.2.1 A Thermogravimatric Analysis (TGA): were described in 3.3.3

3.2.2 A Differential Scanning Calorimetry (DSC): were described in 3.3.3

3.2.3 A X-ray analysis: were described in 3.3.4

3.2.4 A Preparation of Stereocomplex: PLA and PDLA were synthesized by ring opening polymerization of L-Lactide and D-Lactide, at 200 ^{o}C using clay modified metal catalyst.

The M_n, M_w and polydispersity values were determined by GPC. The thermal characteristics of PLA and PDLA were studied using DSC-7. Percentage of crystallinity was determined using XRD.

The stereocomplex of PLA and PDLA were separately prepared and blended at various compositions (L: D=15:85, 35:65, 50:50, 70:30, 80:20) dissolving aliquot amount of PLA and PDLA in dry methylene dichloride and stirred for 3 hr at room temperature. The resulting solution in a Petri dish was kept over a night in order to get uniform film and further vacuum dried up to constant weight.

3.2.5 A Scanning Electron Microscopy (SEM):

SEM was taken on a gold-coated surface of polymer sample after careful washing and drying by using a Leica Cambridge Stereo scan Model 440.

3.2.6 A Plasma treatment **:**Polymer samples were exposed to hydrogen plasma for various time (10 min, 20 min and 30 min) using an open air Plasma Technology system. (single rotating FLUME Jet RD 1004, Plasmatreat, Steinhagen, Germany). The Plasma Jet was generated by ioinizing the feed hydrogen gas at $6x10^{-2}$ mbar and at a flow rate of 35 L/min during the plasma ignition. The plasma was operated with a power of 2.1 kW (V=2963 V, I=7±0.2 A), and the distance between the polymer samples and the plasma jet was kept at 20 cm. One specimen was used for each combination of polymer type, plasma hydrogen gas type and treatment time.

The morphology of stereocomplex samples and plasma treated samples was examined by using a Philips XL30 ESEM under reduced pressure below 1 torr.

3.3 A Result and Discussion:

Table 3.9 shows the thermal characterization results of stereocomplexes. Fig. 3.32 shows DSC thermograms of films casted from mixed solutions of PLA and PDLA having similar molecular weights. The mixing ratio X_D, was varied. As the previous work has established that the peak at 180 ^oC was due to fusion of the homopolymer crystallites and the peak 220 ^oC was due to fusion of the racemic crystallites (stereocomplex).**[116]** The peak temperatures were assumed to be equal to the melting temperatures T_{f1} and T_{f2} of the homopolymer and the racemic crystallites respectively. It had also been observed that only T_{f2} appears when the molecular weight of the polymer is below $8x10^4$, whereas both T_{f1} and T_{f2} appear for the polymers have been molecular weight greater than $8x10^4$. This implies that the average size of racemic crystallites decreased with increasing molecular weights of polymers. The crystallization took place exclusively for blends of polymers lower than $8x10^{4.}$ Therefore, the molecular weight of PLA and PDLA in the range of $7.4x10^4$ was chosen for blending.

Fig. 3.32 presents the thermal behaviors of the PLA/PDLA blend. In the first run, T_m along with ΔH_m values were calculated and tabulated. The enthalpy of fusion at T_{f1} (ΔH_{f1}) approaches ~ 57 j/ (g-polymer). Similar finding has been observed and emphasized that soly racemization was observed in blend of PLA and PDLA at the low molecular weight. Tsuji and Ikada**[116]** previously reported that the melting of stereo complex crystallites occurs at 220-225 ^{0}C with ΔH_m of 68-86 J/g. The authors estimated the equilibrium melting temperature (T_m) of PLA stereocomplex crystallites to be 279 ^{0}C by extrapolation of (T_m) values for different optical purities. A ΔH_f value of ca. 146 J/g has also been reported for the stereocomplex crystals having an infinite thickness. Therefore, T_m value of the PLA/PDLA blend (228 ^{0}C) confirmed that stereocomplex exclusively formed from the blend without homocrystallization of either PLA or PDLA, indicating that 50/50 blending benefits stereocmplexation. The higher T_m (224 to 228 ^{0}C) and ΔH_f (29 to 57 J/g) values could thus be attributed to highly formed stereocomplex crystallization.

Fig. 3.32 shows that T_{f1} and T_{f2} appear in case of PLA/PDLA blend ratio 80:20 and 70:30 implying that recemic crystallites are preferentially formed with virtually low homopolymer crystallites. T_{f2} predominantly appears in case PLA/PDLA blend ratio 35:65 and 50:50. T_{f1} and T_{f2} reappears again in case of PLA/PDLA blend ratio 15:85 implying the presence both homopolymer crystallites as well as recemic crystallites. This similar finding has also been observed.**[117]**

XRD studies:

Wide angle X-ray diffraction also shows a different pattern as shown in fig. 3.34. The diffraction profile of homopolymer of D-Lactide showed the diffraction peaks at 2θ around 15^0,16^0, 18.5^0 and 22.5^0 where as the composition (50:50) blend polymer has the diffraction peaks appearing at 2θ equal to $12^{0,}$ 21^0 and 24^0.

In fact, the corresponding WAXD spectrum (fig. 3.34) exhibits three main diffraction peaks at θ values of 12, 21 and 24°, which are characteristic of stereocomplex. The diffraction peaks of the 80/20 (poly (L-Lactide)/ (poly (D-Lactide) blend polymer involve all the peaks corresponding to the homopolymers and 50/50 blend polymer. The diffraction peaks of the 15/85 (poly (L-Lactide)/ (poly (D-Lactide) blend polymer also involve all the peaks corresponding to the homopolymers and 50/50 blend polymer This X-ray diffraction study supports the formation of a polymer complex with crystalline structure entirely different from that of homopolymers. Since the crystalline structure poly (L-Lactide) and (poly (D-Lactide) consists of left-handed and right-handed helical chains, it is likely that the stereocomplex is formed through Van der Waals forces such as dipole-dipole interactions between the two different helical chains in solution where molecular motion is sufficiently adequate. Cartier et al.[118] have reported that triangular morphology due to differences in molecular weights and imbalance composition.

Table 3.9: Thermal Characterization Results of PLA/PDLA Stereocomplex

Polymer	Stereocomplex (L/D) (wt/wt)	T_m (^0C)	ΔH_m (J/g)	T_g (^0C)
PLA-22	80/20	224	36	49
PLA-23	70/30	227	34	43
PLA-24	50/50	228	64	55
PLA-25	35/65	213	55	50
PLA-26	15/85	213	30	50

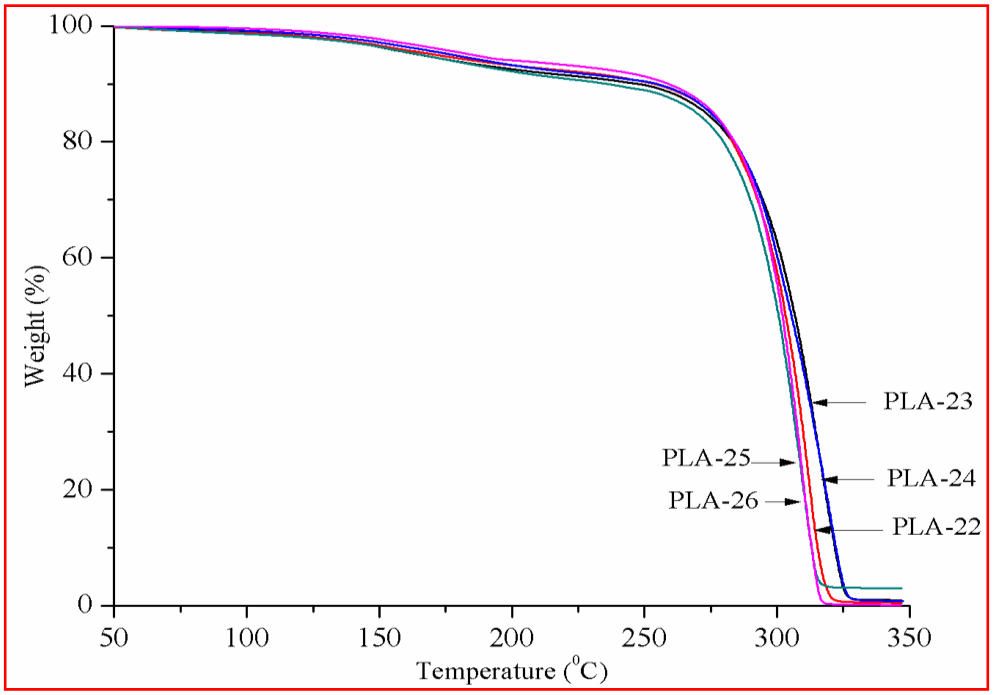


Fig. 3.32: Thermogravimetric analysis (TGA) of poly(lactide)s stereocomplex synthesized using cloisite modified catalyst showing decomposition temperatures.

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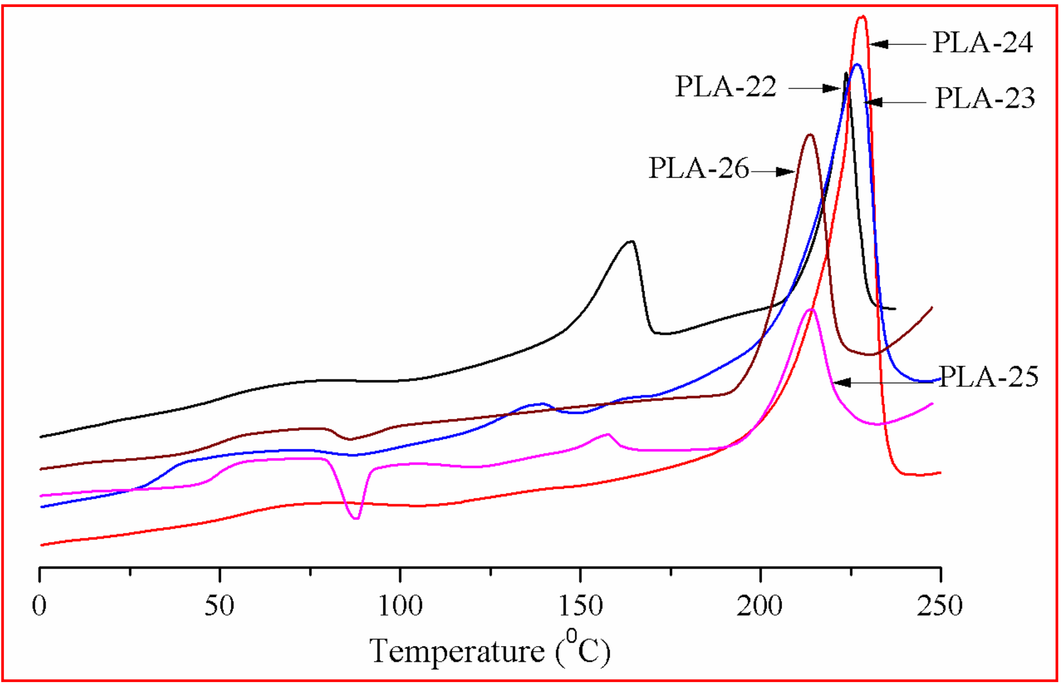

Fig. 3.33: Differential Scanning Calorimetry (DSC) of poly(lactide)s stereocomplex synthesized using cloisite modified catalyst showing melting points as well as glass transition temperatures respectively.

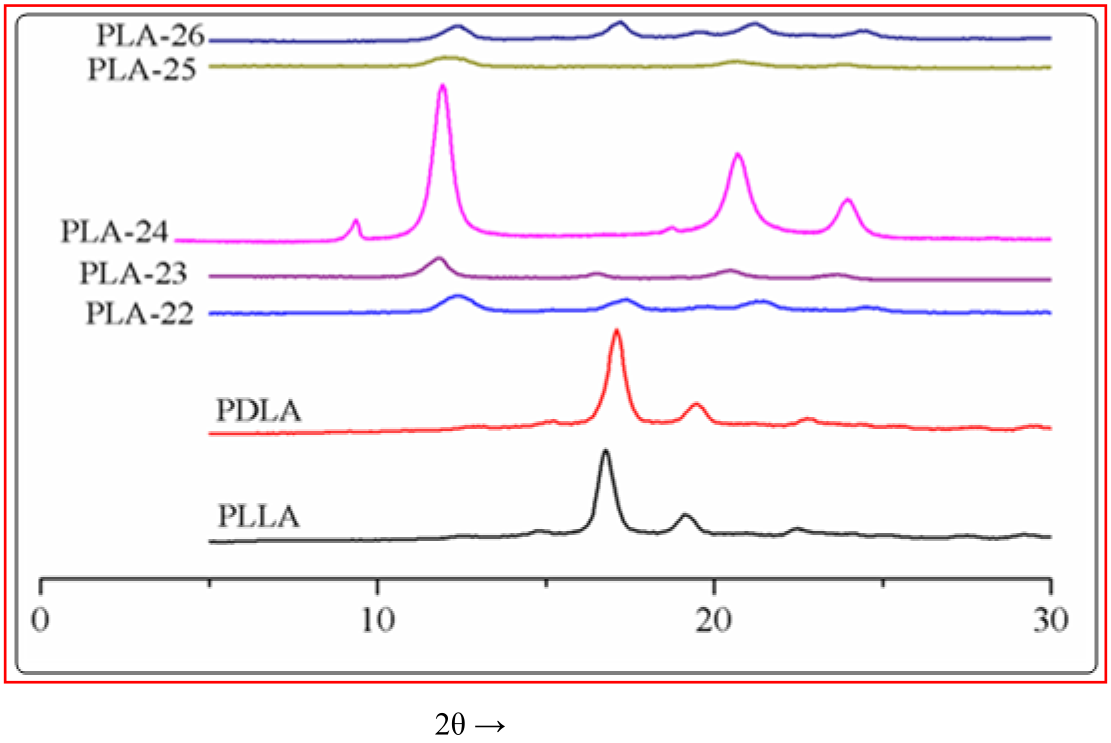

Fig. 3.34: Powder X-Ray Diffraction (XRD) patterns of poly(lactide)s stereocomplex.

Plasma studies: The PLA film prepared by stereocomplex (70:30) was treated with hydrogen plasma at various time periods. The particles in hydrogen plasma are hydrogen atoms, molecules and ions. Electronically excited particles can be expected to play only a minor role in the setup because their life times are too short. At a pressure of $2x10^{-4}$ bar, the concentration of molecular hydrogen is about $1x10^{-5}$ mol/l . The reactivity of molecular hydrogen is negligible on a polymer surface whether the surface is activated or not.

The reactor geometry (aperture and treatment chamber are two cylinders)) as well as the reactor material (stainless steel) are taken into consideration and the degree of dissociation in the active plasma zone is underestimated with 10%. The probability of the recombination on stainless steel has been reported by Melin and Madix.[119]

Using these mentioned data the concentration of atomic hydrogen at the sample position is estimated to be about 7% (~ $7x10^{-8}$ mole/l $\approx 4x10^{13}$ atoms/cm^3) of the concentration inside the active plasma zone. Thus, the hydrogen atom concentration is about 5 orders of magnitude higher than the concentration of hydrogen ions. Because of the low reactivity of molecular hydrogen and the low concentration of hydrogen ions, the atomic hydrogen is expected to be the only plasma particle that is able to react with the PLA polymers (stereocomplex) outermost surface. These particles however interact only with the polymers outer most surfaces.

SEM : Fig. 3.35 A, B, C represents the morphology of PLA-PDLA stereocomplex at various compositions (80:20, 70:30 and 50:50). fig. 3.35A and 3.35B shows that lamellae in the spherulites seem to organize in a unique manner which is quite different from PLA crystallization. Disk-shaped and spherical structures have been observed in the case of stereocomplex forming acetonitrile solution.

SEM of plasma treatment stereocomplex PLA polymers was shown in fig. 3.36 D, E and F. Topmost surface of PLA stereocomplex showed a regular honey comb structure at different intervals of plasma treatment. The difference in contact angles measure by contact angle measurement attributes the hydrophilic nature. The contact angles values of original stereocomplex PLA film and plasma treated one are 88 and 75^o respectively. As referred previously, the crystal structure of PLA/PDLA stereocomplex is trigonal, consisting of sub cells with two enantiomorphous, antiparallel chains. PLA and PDLA stems are arranged alternately taking 3_1 helical conformations in the stereocomplex. And vander Waals forces between the hydrogen of CH_3 and the oxygen of O=C of PLA chains with opposite configurations have been suggested to induce chain packing for stereocomplexation. Recently, according to FTIR analysis by Zhang et al.[23], the CH_3…O=C hydrogen bonding contributes to the interaction between chains in PLA/PDLA streocomplex and thus constitutes the driving force for the nucleation of stereocomplexation.

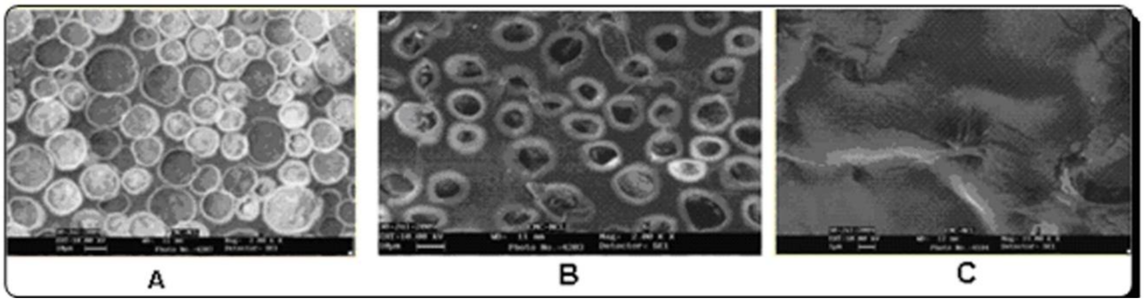

Fig. 3.35(A-C): E-SEM micrographs of the PLA/PDLA stereocomplex at different compositions (A: 80:20, B: 70:30, C: 50:50).

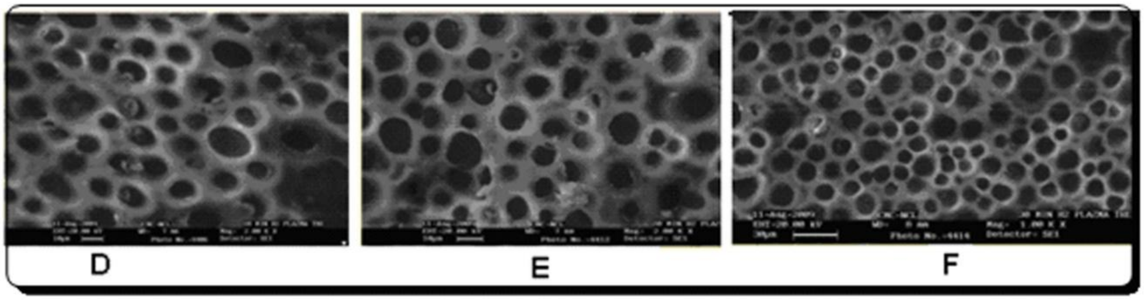

Fig. 3.36 (D-F): E-SEM micrographs of PLA/PDLA stereocomplex (70:30 after plasma treatment at various exposure times (D: 10 min, E: 20 min, F:30 min).

3.4 A Conclusion

The formation of stereocomplex was confirmed by TGA, DSC and XRD. SEM picture of sterecomplex at various compositions showed spherical morphology except 50:50 stereocomplex. Stereocomplex of 70:30 is treated with hydrogen plasma at various interval of time. A compact honeycomb structure having hydrophilic nature are obtained and confirmed by E-SEM and Contact angle measurement. The application of these new textures in the field of tissue engineering, wound dressing materials and preservation of bioactive agents are in progress.

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CHAPTER - 4

CHAPTER-4: SYNTHESIS AND CHARACTERIZATION OF HOMO AND COPOLYMERS OF ε-CAPROLACTONE USING CLOISITE MODIFIED CATALYST

4.1 Introduction:

Recently, there are enormous catalysts have been used for the polymerization of lactones.[1-4] Some studies of variable catalyst have also been carried out. The widely used catalyst such as salts or complexes of aluminium, tin or lanthanide ions for the polymerization of lactones, do not meet the above requirements. Zinc metal or its derivative was considered as a potential catalyst for lactones polymerization. Several difficulties have also been encountered. Zinc metal or zinc containing compound has been studied by several research groups with mixed results. Use of diethyl zinc catalyst during polymerization of lactones has caused technical problem because it is highly moisture sensitive and self-inflammable liquid.

Poly (ε-caprolactone) (PCL) belongs to the family of aliphatic polyesters has a unique position since it is biodegradable [5-6] and it is at the same time miscible with a variety of polymers, including poly (vinyl chloride) (PVC), poly(styrene-co-acrylonitrile), nitrocellulose, cellulose propionate and butyrate, poly (epichlorodrin), and bisphenolA polycarbonate.[7] In addition, PCL crystallizes very readily and cannot be quenched to a glass.

The biodegradability and lack of toxicity of PCL is of great interest for the controlled release of drugs from subdermally implanted polymer devices. In this environment, PCL has a useful lifespan around 1 year.

Poly (ε-caprolactone) shows low melting temperature (T_m~60 ^{0}C) and high decomposition temperature (T_d= 350 ^{0}C) and degrades very slowly due to its high hydrophobicity and crystallinity. It is known that block copolymerization allows combination of the chemical properties of the main components and physical properties of the resulted copolymers can be tailor made by adjusting the molecular weights and the composition of the constituting blocks. Though several strategies have been used for preparation of PLA and PCL, the particular convenient method to synthesize these polymers is the ring opening polymerization (ROP) of lactide/lactones and their functionally related compounds. The ring opening polymerization of lactide and ε-caprolactone give polymers with wider spectrum of properties than the polymers synthesized by copolymerization of the corresponding hydroxyacids, which have been reported in the literature. Such ring opened copolymers yield tough polymers with properties from rigid thermoplastics to elastomeric rubbers[8-9], with tensile strengths ranging from 0.6 to 48 MPa and also elongation. [10] The larger reactivity of lactide over ε-caprolactone leads to copolymers that are blocky, where the block lengths depend on the starting comonomer composition, catalyst [11] and polymerization temperature.

The copolymer of pure L-lactide with ε-caprolactone obtained by ROP contributes flexibility behavior because of the ε-caprolactone segment and high crystalline melting points from PLA blocks. Many metal complexes (e.g. Al [12], Li [13], Mg [14], Fe [15], Sn [16] and Zr [17] have been used as initiator/catalyst in the ROP of cyclic ester. β-diketiminato ligands have emerged as one of the most versatile ligands and these ligands are readily tunable to access derivatives containing a range of substituents around ligands skeleton. [18]

A highly efficient initiator (complexation of zinc with β-diketiminato ligands) for the ring opening polymerization of lactides and ε-caprolactone has been studied.[19] Zinc metal or zinc containing compounds were studied by several groups, [20-25] with mixed results. Diethyl zinc is a highly moisture sensitive and self-inflammable liquid which is inconvenient for up scaling and technical productions of polylactones, zinc powder needs to be removed by ultra filtration. Stannous octoate is a conventional catalyst for ROP of lactones. It has been well documented that in non polar solvents stannous octoate associates due to intra and inter molecular oxygen-metal coordinate bonds. The mean degree of association decreases significantly upon the increase of the dielectric constant of the medium or upon addition of suitable legends such as alcohols.

Stannous Octoate is used as a conventional catalyst for ring opening polymerization of ε-caprolactone. However, it has certain draw backs: (i) $Sn(Oct)_2$ is a viscous liquid and its quantitative addition for homogeneous mixing in ROP of lactides is achieved through dilution with some solvent. (ii) As such $Sn(Oct)_2$ allows forming some amount of octanoic acid during storage time. During ROP, the Octanoic acid reacts with alcohol and forms corresponding ester and also water. The formation of tin hydroxides, stannoxane are unavoidable when water is present or formed during initiation/ polymerization process. (iii) Kricheldorf et al. **[20]** have shown that the effective initiator for the polymerization of lactide above 120 ^{o}C was SnO instead of Sn(II) 2-ethylhexanoate. The difference in reaction rates and stability of the intermediate formed tin alkoxides has also been observed by using various natures of alcohols. (iv) $Sn(Oct)_2$ based initiators are a complex dynamic system which responds to all changes of the reaction condition by a change of structure and concentration of the active species.

Therefore, the clay modified solid tin catalyst was prepared for the first time to overcome all these encountered problems. The improvement of mechanical properties, flexural properties, heat distortion temperature and oxygen gas permeability of poly(ε-caprolactone) /montmorillonite nanocomposites in comparison with pure poly(ε-caprolactone) have been reported.

The present work highlights on synthesis and characterization of clay modified solid tin catalyst which has never been used as catalysts for the polymerization of ε-caprolactone most importantly solvent free process. Clay modified solid tin catalyst was selected because of easy handling and precise quantitative addition in polymerization reaction. The resulting homopolymers were characterized by ^{1}H-NMR, ^{13}C-NMR, Size Exclusion Chromatatography (SEC), Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning calorimetry (DSC), Thermogravimetric analysis (TGA) and MALDI-TOF-MS etc.

4.2 Materials and Methods

ε-Caprolactone (CL, Aldrich) was dried over calcium hydride (CaH_2, Aldrich) prior to polymerization. Cloisite-30B was purchased from southern clay and used after drying. Dichloromethane (DCM) and Methanol were purchased from SD-Fine Chemical India. The weight loss measured within 0-900 ^{0}C related to the water content varied in the range of 5.3–6.1 wt %. The average cation exchange capacity (CEC) was in arange 0.7–0.8 meq/g. Chloroform-D ($CDCl_3$, Aldrich) with isotopic purity of 99.9% containing 0.03% v/v of TMS was used as solvent for ^{1}H- NMR analysis.

4.2.1 Synthesis of clay modified catalyst: As discussed in 3.2.2 chapter 3

4.2.2 Polymerization:

ε-Caprolactone and clay modified catalyst (0.75 %) were weighed using dry box (model No-UniLabMBroun-MB-OX-SE-1, S.L.-7120) into a reactor ampoule having silanized glass walls (pretreated with Me_2SiCl_2). The break seal technique was used for all polymerization reactions. The sealed ampoule was completely immersed into a preheated fluidized sand bath reactor. All other polymerizations catalyzed by clay modified catalyst were performed analogously. The samples were used for ^{1}H-NMR. Molecular weight measurements, XRD and MALDI-TOF etc.

4.3 Analysis:

4.3.1 NMR: As discussed in chapter 3.

4.3.2 Molecular Weights: As discussed in chapter 3.

4.3.3 Thermogravimatric analysis (TGA): As discussed in chapter 3.

4.3.4 Differential Scanning Calorimetry (DSC): As discussed in chapter 3.

4.3.5 X-Ray Analysis: As discussed in chapter 3.

4.4 Results and Discussion:

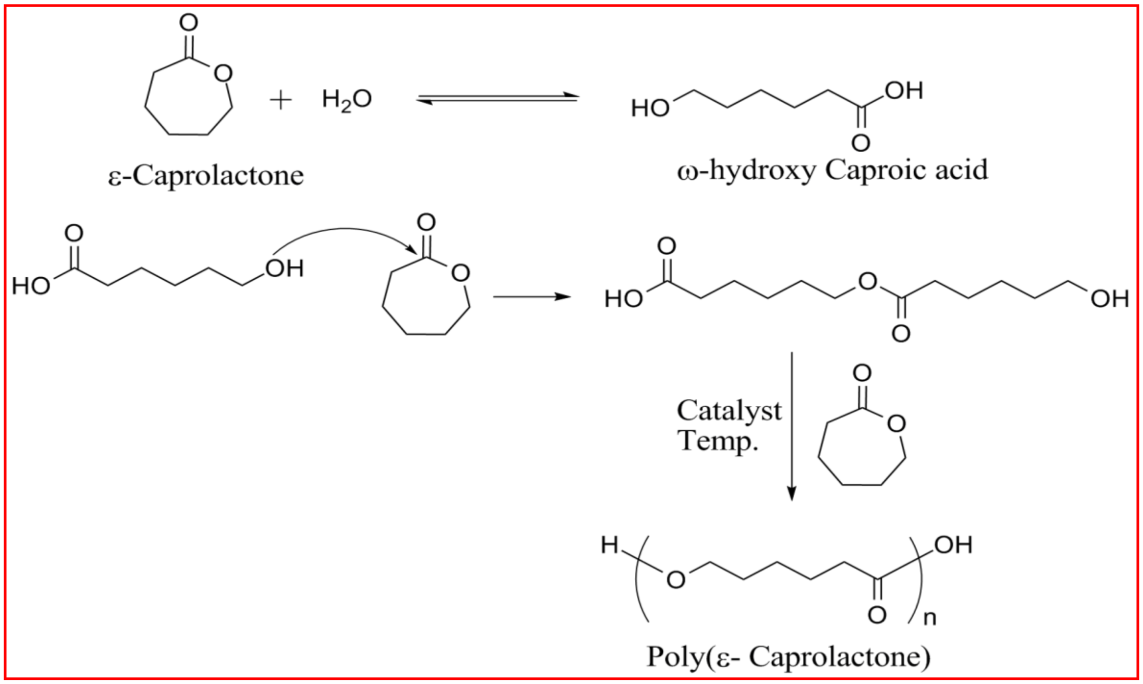
The rates of monomer conversion and increase of average molecular weight of prepared polymer were determined using nuclear magnetic resonance.The instantaneous monomer/polymer ratios were evaluated from relative intensities of peaks originating from ε-methylene protons. Obtained results are tabulated in Table 4.2.

In case of ε-caprolactone polymerization in the presence of solid cloisite modified tin catalyst, one can notice that increasing polymerization temperature caused an increase in the average molecular weight of polymer up to 220 ^{0}C as shown in Table 4.1.

Table 4.1: Effect of polymerization temperature on ROP of ε-caprolactone

Polymer	Time (hr)	Temp. (^{0}C)	M_n	M_w	D	T_m (^{0}C)	ΔH_m (J/g)
PCL-1	2	150	22400	35170	1.57	54.45	13
PCL-2	2	180	26800	42200	1.57	54.83	53
PCL-3	2	200	27800	44500	1.60	54.90	27
PCL-4	2	220	29000	46400	1.60	55.50	29

In ε-caprolactone/Cloisite catalyst ([M]/[I]) systems, the higher molecular weight of the final polymer was obtained at [M]/[I] =800. Discussing the polymerization of ε-caprolactone in the presence of clay modified catalyst and traces amount of water, it is reasonable to assume possible mechanism of polymer chain growth (Scheme 1).



Scheme 1: Polymerization of ε-caprolactone in the presence of clay modified catalyst.

This mechanism involves the formation of ω-hydroxycaproic acid as a product of ε-caprolactone hydrolysis. Table 4.1 illustrates polymerization of ε-caprolactone in the presence of clay modified catalyst at various polymerization temperatures ranging from 150 to 220 ^{0}C (PCL-1 to PCL-4). The molecular weight increased with increase of temperature as shown in fig. 4.1

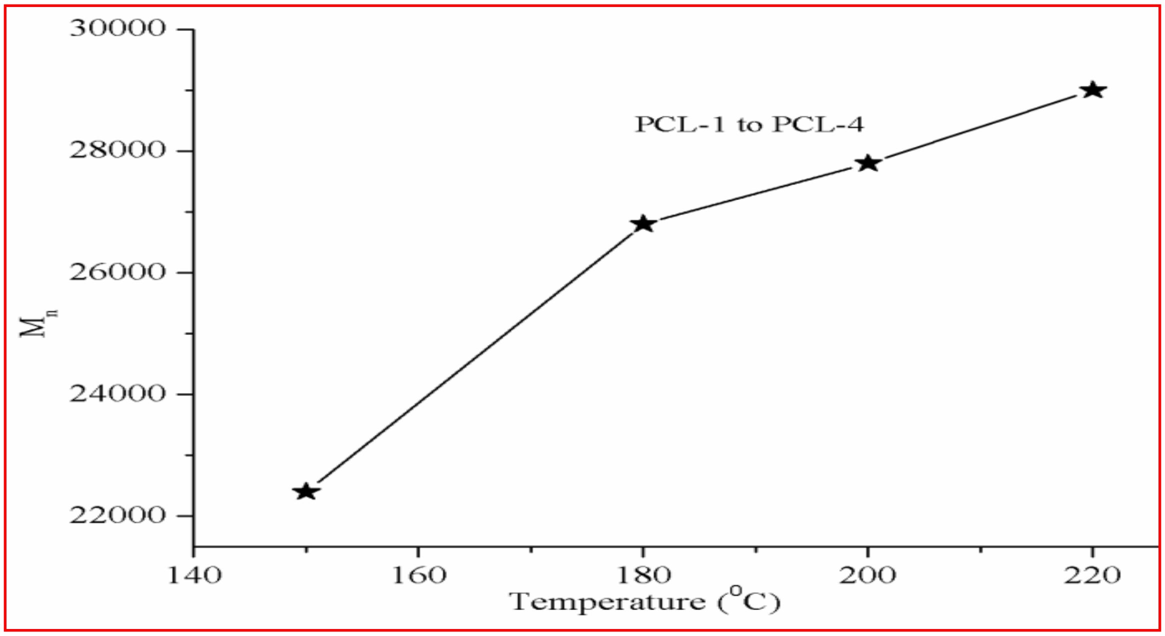


Fig. 4.1: Effect of polymerization Temperature on M_n of poly(ε-caprolactone).

Kiersnowski et al [25a] have made similar observations. Table 4.2 depicts the variation of reaction times at [M]/[I] is 200.

Table 4.2: Effect of reaction time on ROP of ε-caprolactone ([M]/[I]=200)

Polymer	M/I	Time. (hr)	Temp (^{0}C)	M_n	M_w	D	T_m (^{0}C)	ΔH_m (J/g)	Cry. (%)
PCL-5	200	0.5	180	13680	20770	1.51	55.61	230	32.59
PCL-6	200	1	180	16940	28500	1.68	66.01	281	32.75
PCL-7	200	2	180	26800	42200	1.57	66.13	067	36.69
PCL-8	200	3	180	26750	42800	1.60	66.62	380	31.31

The molecular weight steadily increased as the reaction times increase as shown in fig. 4.1 In the case of [M]/[I] systems, the traces of water present inside the silicate layers of solid cloisite modified catalyst.

The mechanism would involve hydrolysis of ε-caprolactone in the initial stage but the propagation of kinetic chain would occur by subsequent nucleophilic attack of hydroxyl end group of acid and stepwise addition of ε-caprolactone molecules. In the initial stage of polymerization, ω-hydroxycaproic acid is formed slowly by hydrolysis of lactone which is the rate determining step for the whole polymerization process.[26-27] Accordingly, it may be concluded that in the polymerization of ε-caprolactone in the presence of solid clay modified tin catalyst, the clay, acting as solid Lewis acid, catalyzes lactone hydrolysis and thus enhances polymerization rate. Discussing the problem of molecular weight lowering observed in [M]/[I] systems with increasing amount of silicate, the mechanisms of polymerization should also be taken under consideration. According to polymerization path (Scheme 1), traces amount of water would play its role in the initial (hydrolysis) steps only in the further stages water would be neither necessary nor produced as the reaction proceeds between the hydroxy acid and lactone only.

Table 4.3 depicts the variation of M_n with reaction times at [M]/[I] is 400 (PCL-9 to PCL-12), the molecular weight increased with respect to reaction time up to 2 hr and remain steady thereafter up to 3hr (fig. 4.2).

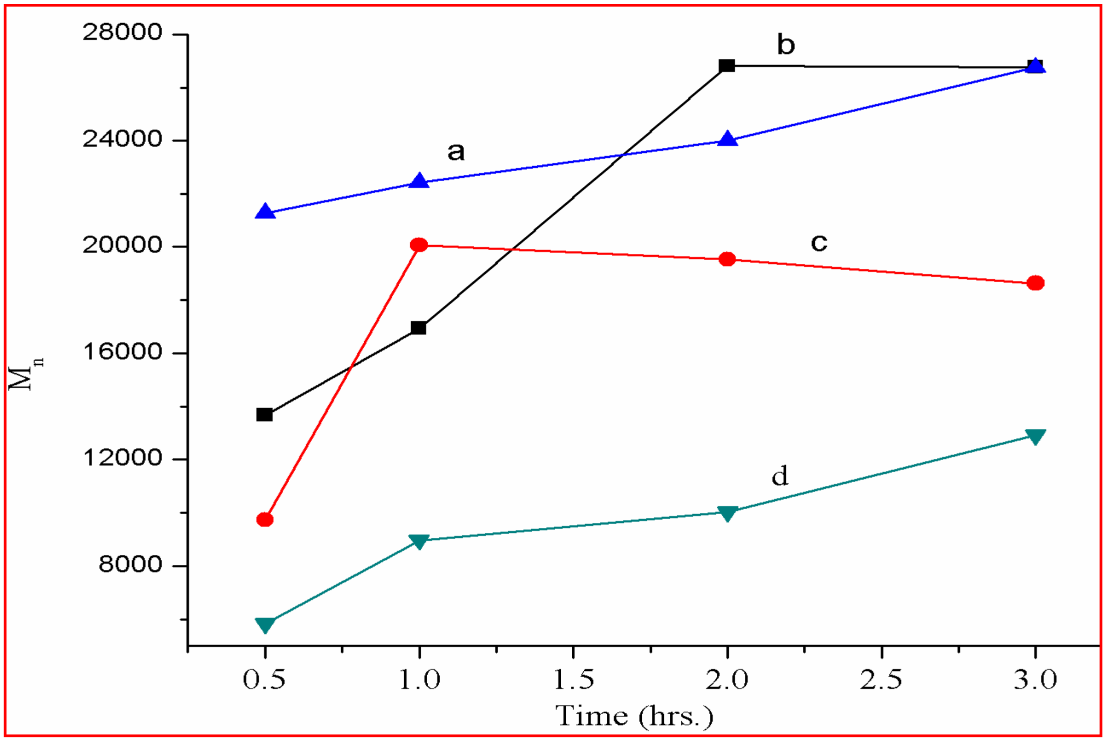


Fig. 4.2: Effect of polymerization time versus M_n at different monomer to initiator ratio ([M]/[I]): a(◀);[M]/[I]=200, b(■);[M]/[I]=400, c(●);[M]/[I]=800, d(▶);[M]/[I]= 1000.

Table 4.3 Effect of reaction time on ROP of ε-caprolactone ([M]/[I] =400)

Polymer	M/I	Time. (hr)	Temp (^{0}C)	M_n	M_w	D	T_m (^{0}C)	ΔH (J/g)	Cry. (%)
PCL-9	400	0.5	180	9770	14650	1.49	66	198	41.51
PCL-10	400	1	180	20078	34840	1.91	53	094	42.00
PCL-11	400	2	180	19540	36230	1.85	66	209	43.98
PCL-12	400	3	180	18630	38400	1.87	68	225	37.10

Table 4.4 illustrates the variation of M_n of (PCL-13 to PCL-16), [M]/[I] =800, with reaction times, the molecular weight increased with respect to reaction time up to 3hr as shown in fig. 4.2c.

Table 4.4: Effect of reaction time on ROP of ε-caprolactone ([M]/[I] =800)

Polymer	M/I	Time. (hr)	Temp (^{0}C)	M_n	M_w	D	T_m (^{0}C)	ΔH (J/g)	Cry. (%)
PCL-13	800	0.5	180	21280	27380	1.28	67	109	35.00
PCL-14	800	1	180	22420	29880	1.33	34, 46	5, 22	35.09
PCL-15	800	2	180	24000	31920	1.33	68	267	36.80
PCL-16	800	3	180	26570	50099	1.91	67	114	35.25

Similar trend was observed when M_n of (PCL-17 to PCL-20) [M]/[I] =1000 varies with reaction times, the molecular weight increased with respect to reaction time up to 3hr as shown in Table 4.5 and fig. 4.2d.

Table 4.5: Effect of reaction time on ROP of ε-caprolactone ([M]/[I] =1000)

Polymer	M/I	Time. (hr)	Temp (^{0}C)	M_n	M_w	D	T_m (^{0}C)	ΔH (J/g)	Cry. (%)
PCL-17	1000	0.5	180	5075	5840	1.15	63	147	34.71
PCL-18	1000	1	180	8973	10038	1.11	53, 63	10, 110	34.82
PCL-19	1000	2	180	10023	19570	1.95	56	74	39.96
PCL-20	1000	3	180	12930	24500	1.89	55	13	39.90

Bulk polymerizations of ε-caprolactone in the presence of solid cloisite modified tin catalyst resulted in relatively low molecular polymers as shown in Table 4.1. ^{1}H-NMR analysis of monomer (fig. 4.3a) and obtained polymers (fig. 4.3b) provided evidence of the formation a linear poly (ε-caprolactone).

ε-caprolactone: ^{1}H-NMR ($CDCl_3$) δ: 1.77 (m,β-CH_2 + γ-CH_2), 1.86 (m, δ-CH_2), 2.64 (m, α-CH_2),4.23 (m, ε-CH_2).

Poly (ε-caprolactone): ^{1}H-NMR ($CDCl_3$) δ: 1.36 (m,γ-CH_2), 1.63 (m, β-CH_2 + δCH_2), 2.30 (t, $3J_{HH}$ = 7.53; α-CH_2), 3.65 (t, $3J_{HH}$ = 6.60; ε *-CH_2), 4.02 (t, $3J_{HH}$ = 6.59; ε-CH_2).

As it can be noticed, signals of an equivalent group of protons recorded in lactones and polyester spectrum are well separated (their chemical shifts are significantly different). Due to low molecular weight of obtained polymers, in the spectrum of poly (ε - caprolactone), the signals marked with asterisk (ε*) originating from ε-protons in hydroxyl end groups are well visible. These properties were then used for investigation of polymerization kinetics.

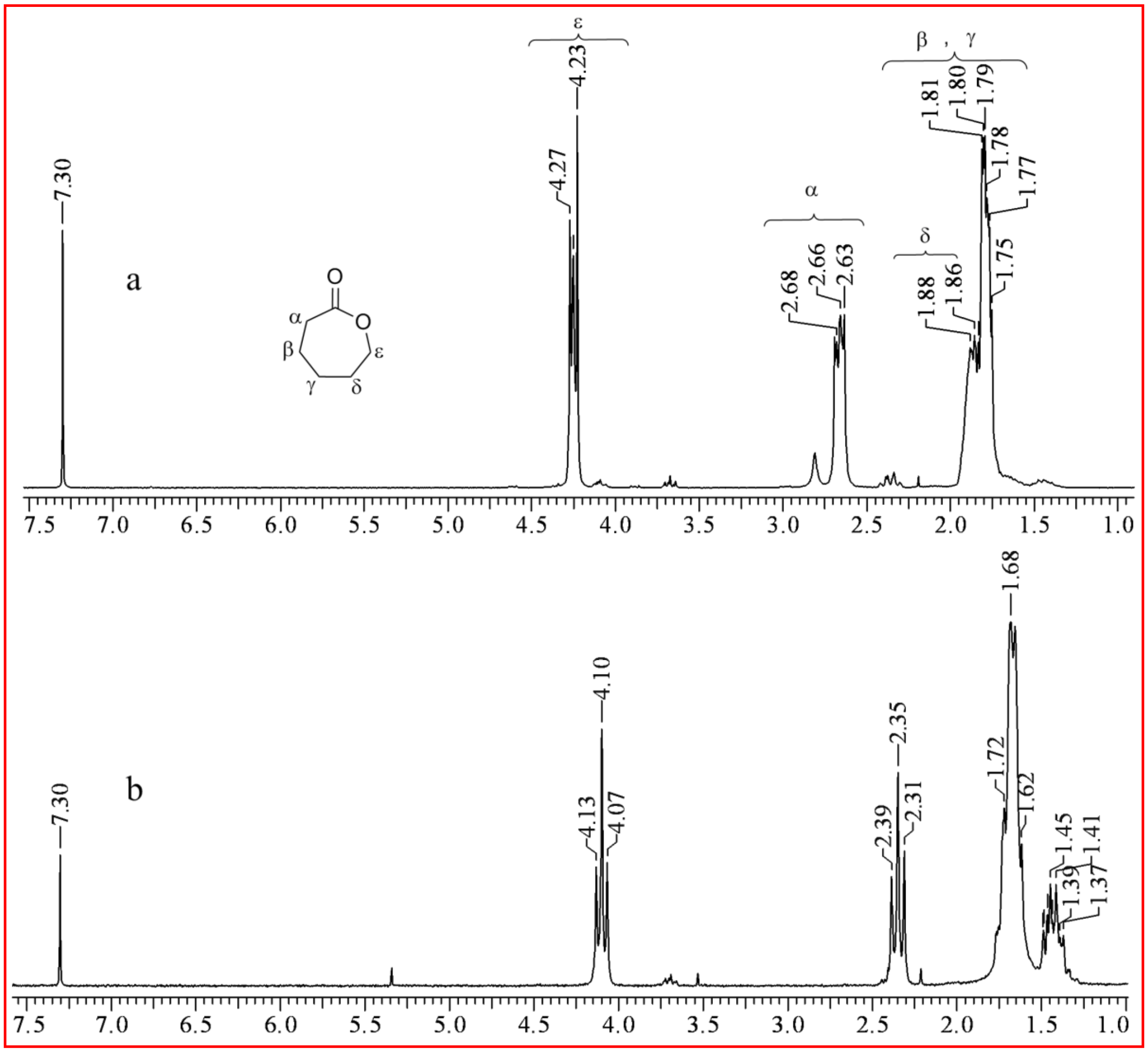


Fig. 4.3: a: ^{1}H-NMR of ε-caprolactone b: ^{1}H-NMR of poly (ε-caprolactone).

4.4.1 Nuclear Magnetic Resonance Spectroscopy (NMR): ^{13}C-NMR has been utilized as a useful tool for determining the number average molecular weight, M_n quantitatively. Besides end group analysis, this technique has also used in other quantitative analysis for determination of residual L-lactic acid, lactide formed due to unzipping of chain ends.[32-33] ^{13}C-NMR has also been used to study the crystallization and morphology,[34] and for direct observation of stereo defects in polymers.[35]

As it is typical of aliphatic polyesters, the carbonyl carbons exhibited the greatest sensitivity to chemical environment. Fig. 4.4 depicts the ^{13}C-NMR spectrum of each polymer in the series. It was observed for all polymers that degree of polymerization caused a pronounced effect on chemical shift. In general, as the degree of polymerization increased, main-chain and end-group resonances shifted upfield.

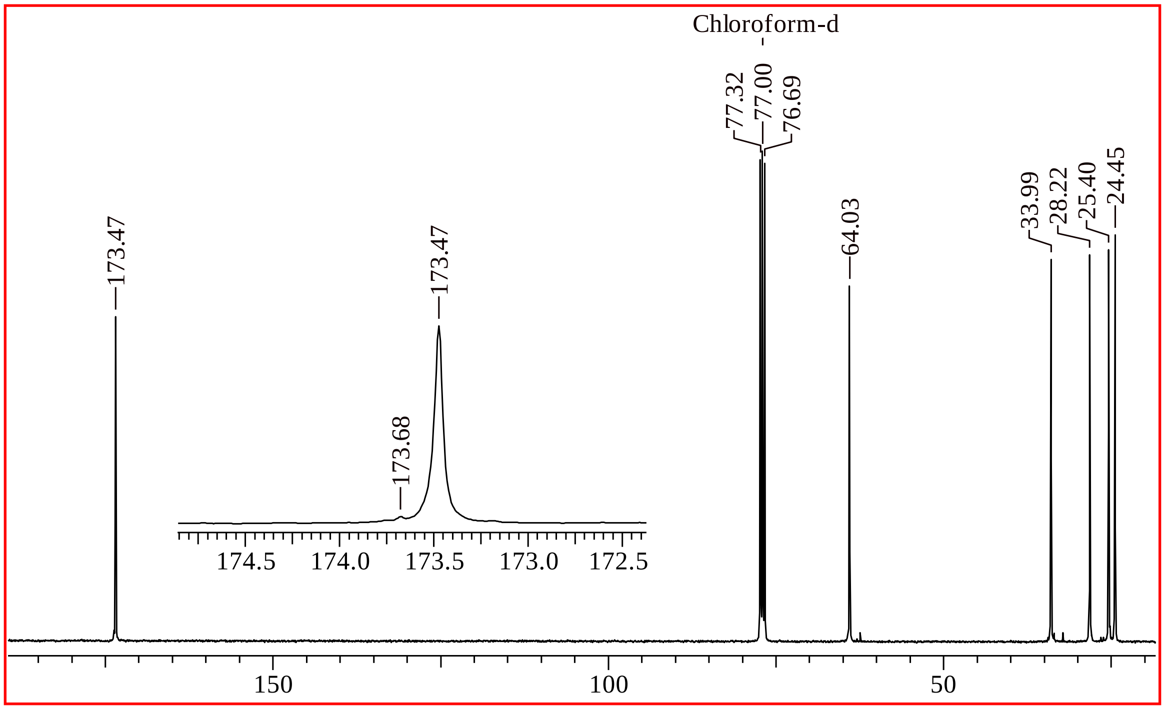


Fig. 4. 4: Quantitative ^{13}C-NMR of Poly(ε-caprolactone).

For the PCL-4 polymer, two distinct regions can be observed, one at 173.47 ppm due to ester carbonyl groups and the other at 173.68 ppm due to carboxylic acid end groups. The most intense signal at 173.47 ppm was attributed to the main-chain carbonyl carbons; the companion signal at 173.68 ppm has been assigned to the terminal carbonyl carbon nearest to the hydroxyl end group.

The effect of the terminal hydroxyl group is most strongly evident in the ε and a methylene region of the poly(ε-capro1actone) spectrum. The ε-methylene carbon resonances fall at 64.03 i.e., the range characteristic of carbon bonded to oxygen**.** In fig. 4.4, the spectrum shows the main-chain ε-methylene resonance at 64.03 ppm and, in addition, a small complimentary resonance at 62.2 ppm that has been attributed to the methylene carbon bonded directly to the hydroxyl group at the end of the polymer chain.

4.4.2 End-group analysis of poly(ε-caprolactone): Acid end group is indistinguishable from the main-chain ε-methylene groups. This is sensible since it is separated from the acid group by five covalent bonds. The most interesting region of the poly(ε-caprolactone) spectrum is that for the 6-methylene group, whose main-chain resonance appears at 28.2 ppm. The other two resonances, a main peak at 25.4 ppm that was assigned to the main-chain carbons and one peak at 24.4 ppm, were appeared.

4.4.3 Molecular weight determination: Table (4.1-4.5) show the ring opening polymerization of ε- caprolactone in presence solid cloisite modified tin catalyst. The homopolymers (PCL-1 to PCL-4) were prepared in presence of modified catalyst at various temperatures ranging from 150 ^{0}C to 220 ^{0}C, keeping fixed monomer to catalyst ratio ([M]/[I] =200). The yield and molecular weight increased monotonously up to 220 ^{0}C. The maximum yield obtained was 98 %, which is close to the realistic maximum. Because the conversion of ε-caprolactone cannot be higher than 98±1% due to thermodynamic reason. ε- caprolactone was prepared at 180 ^{0}C in 2hr and showed M_n and M_w values as 26800, 42200 Da and polydispersity as 1.57 respectively, which was obtained at [M]/[I] =200 ratio. The reaction temperature was chosen 180 ^{0}C because of molecular weight and narrow polydispersity as 1.57.

The molecular weights of ε-caprolactone increased with variation of reaction times in case of [M]/[I] ratio (200 and 400) and remain steady thereafter. Similar results have been observed using Zn L-lactate **[28]** catalyzed polymerization of 1, 4-dioxane-2-one polymerizing L-lactate in presence of Sn (II) Octoate **[29]** using highly active zinc catalyst for the controlled polymerization of lactide **[30]** and also other examples. The result of Zn L-prolinate catalyzed polymerization showed the η increased with increase in [M]/[I] ratio **[31]**. The molecular weights of ε-caprolactone increased with variation of reaction times in case of [M]/[I] ratio (800 and 1000) as shown in fig. 4.2c and 4.2d. The increase in the temperature resulted increase in molecular weight.

Young et al.**[31a]** mentioned that the bulk polymerization of ε-caprolactone initiated with a coordination-insertion type initiator at 204 °C, by following the viscosity as a function of polymerization time. Although the polymerization appears to proceed much faster, the shape of the ε-caprolactone reaction profile is comparable to fig. 4.2, also showing a maximum in polymer molecular weight. The SEC elugrams of the PCL polymer samples are shown in fig. 4.5. All molecular weight data correspond to polystyrene standards, with a refractive-index detector, and so are only apparent values. PCL-1 to PCL-4 polymers were prepared by ring opening polymerization with solid closite modified tin as a catalyst shown in Table 4.1.The M_n and M_w values increased with variation of polymerization time. PCL 5-8 were prepared at 180 ^oC with reaction temperature variation from 0.5-3 hr at the monomer to initiator ratio ([M]/[I]= 200). The M_n values increased from 22400 to 29000 Da and M_w values from 35170 to 46400 Da respectively. PCL-5 to PCL-8 polymers was prepared by ring opening polymerization with solid cloisite modified tin as a catalyst shown in Table 4.2. Fig. 4.5b showed the maximum increase of molecular weight (M_n=13680-26750, M_w =20770-42800) upto 2hr and remained almost constant up to 3hr. Fig. 4.5c showed the maximum increase of molecular weight (M_n=9770-20078, M_w =14650-38400) up to 1hr and remained almost steady up to 3hr fig. 4.5d and fig. 4.5e showed similar trend i.e. increase of molecular weight (M_n and M_w values) as the polymerization time progressed as shown in Table 4.4-4.5. An interesting observation was made in case of PCL-14 and PCL-18. The tailoring of the curves occurs due to low molecular weight fraction after 1hr polymerization time.

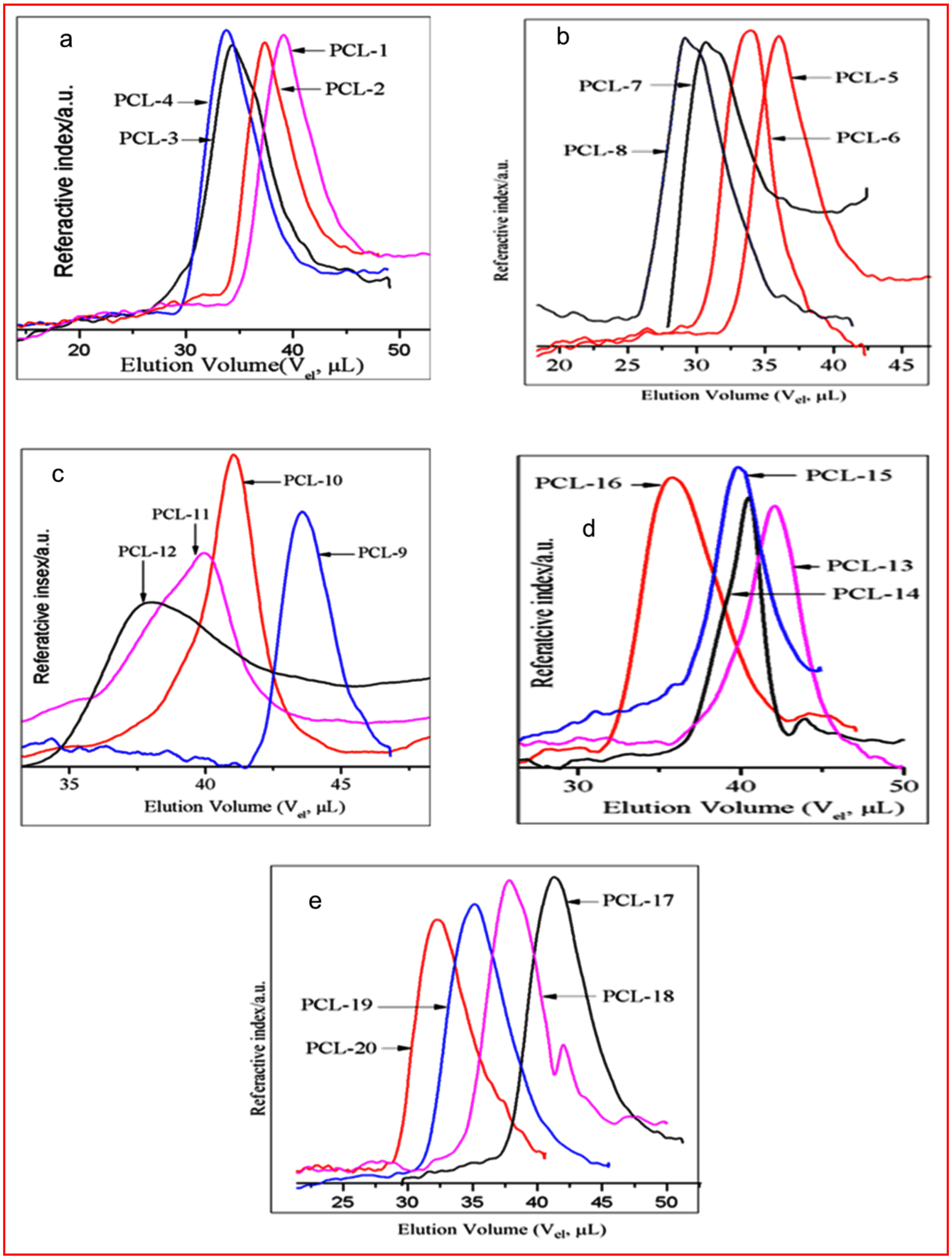


Fig. 4. 5: Size Exclusion Chromatography (SEC) elugrams of PCL (1-20).

4.4.4 Thermal Characterization: TGA was carried out to evaluate the degradation temperature of PCL. The results were obtained in the form of plot of temperature versus weight loss as shown in fig. 4.6a. The analysis results were obtained in the form of plot of temperature versus loss in weight (wt %) as shown in fig. 4.6b. Fig. 4.6a-b show few representative PCL polymers (PCL-7, 9, 14 and 18). Fig. 4.6a shows that there is no degradation of PCL polymers till 260 ^{0}C. The DTG curve was shown in fig. 4.6b and the degradation temperatures were tabulated in Table 4.6. The degradation temperature for PCL-7 is 326 ^{o}C whereas for PCL-9 is 348. PCL-14 and 18 showed two degradation temperatures at 345 and 419 ^{0}C respectively.

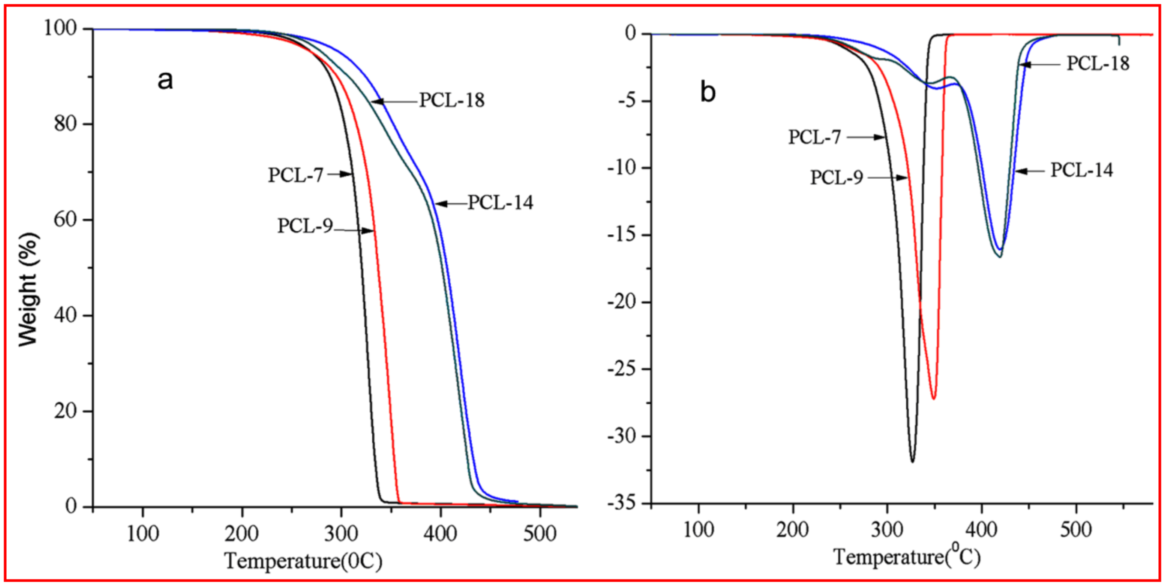


Fig. 4.6: Thermogravimatric analysis of PCL homopolymers.

Table 4.6: Degradation Temperature of PCL homopolymers

Polymer	Degradation Temperature (^{0}C)
PCL-7	326
PCL-9	348
PCL-14	350, 419
PCL-18	345, 419

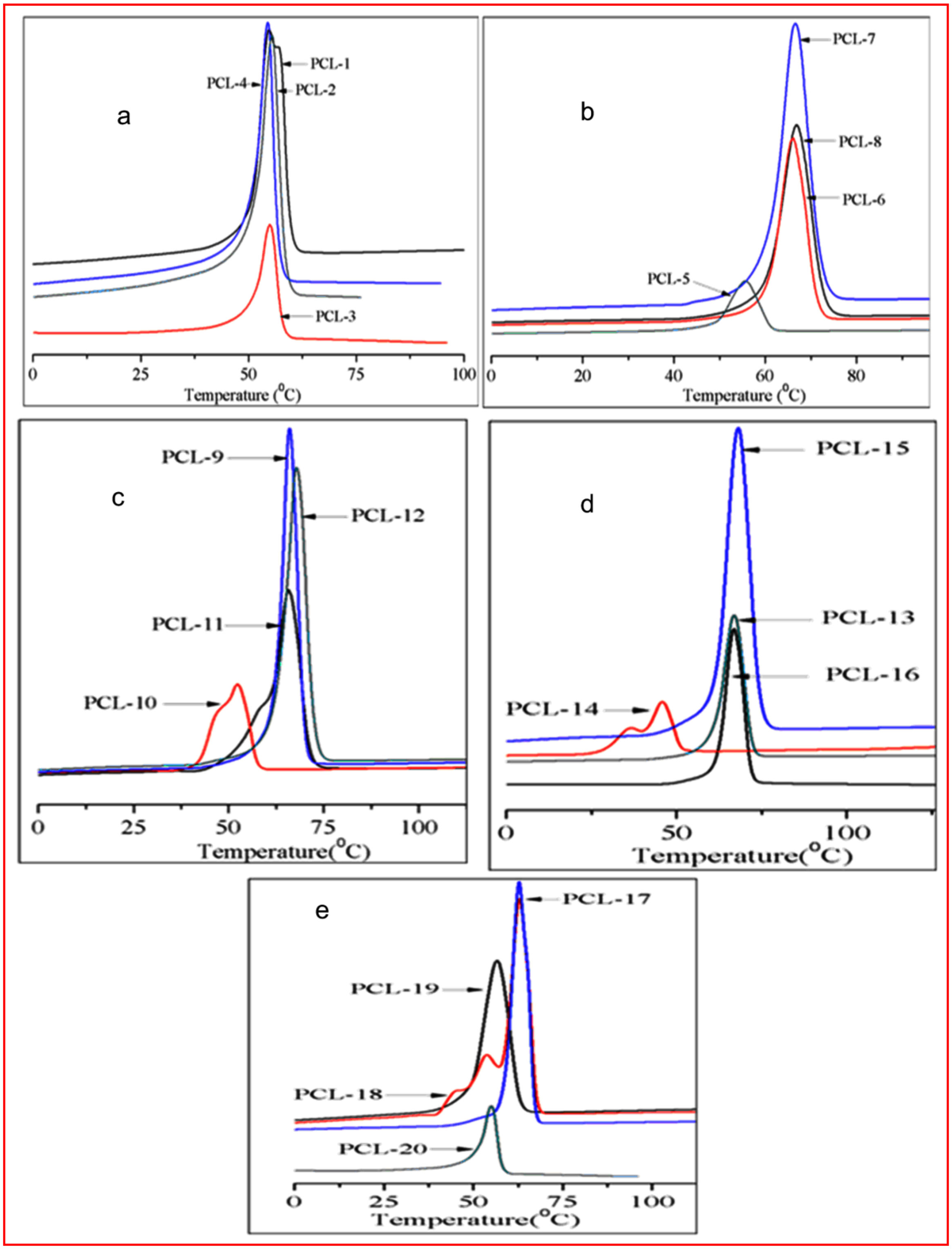


Fig. 4.7: DSC Thermogram showing melting temperatures(T_m) of PCL homopolymers.

DSC Analysis: The results of thermal characterization are shown in Table (4.1- 4.5) and thermograms are also shown in fig. 4.7. T_m varied from 34 to 68 ^{0}C for the polymers prepared with solid cloisite modified tin catalyst. Fig .7a and 7b showed a monotonic increase in T_m from 54 to 55.5 and 55 to 66 ^{o}C respectively. Almost similar trend was observed in case of fig. 4.7c-e except PCL-14 and PCL-18. Fig. 4.7c-e containing PCL-14 and PCL-18 showed two melting temperatures (34, 46 ^{o}C for PCL-14 and 53, 63 ^{o}C for PCL-18). PCL-14 and PCL-18 also showed two different types of molecular weights (lower molecular weight as well as high molecular weight PCL).

4.4.5 XRD:

In the case of XRD, measurements of the *d* spacing indicate an expansion (110) plane of the poly(ε-caprolactone) lattice, and all other planes such as (020) and (002) are invariant; this leads to the conclusion that only a parameter of the unit cell is changing. Therefore, the crystallinity percentage data obtained from XRD and DSC provide considerably different values.

WAXS analysis of the cloisite-30B and solid cloisite modified tin catalyst showed the peak at same position ($2\theta=4.8^o$) $^{\text{indicating}}$ that no intercalation had occurred. The degree of crystallinity increased up to 2 hr and steady thereafter as shown in fig. 4.8. The XRD spectrum (fig. 4.8) **shows** crystalline peaks. Pure PCL is a semi-crystalline material, which shows two crystalline peaks at about 23.8 and 21.5^o, indicating highly ordered chain folding characteristics. The less ordered amorphous in which the polymer chains are arranged. The d-spacing values were calculated using all the peaks and tabulated in Table 4.7. It was observed that the d-spacing values did not change substantially irrespective of variation of polymerization time, temperature and catalyst concentration etc.

Polymerization of ε-caprolactone initiated using solid cloisite modified tin catalyst. The driving force for chain growth in layer spacing must exceed the negative entropy effect accompanying polymerization in restricted space. The chains do not like to be in the interlayer since this is related to a dramatic decrease in the number of conformations for them. The effect has to be subdued by a tremendous driving force for chain growth, which would eventually lead to delaminating of the clay system. If the driving force for polymerization is too small (because of solid cloisite modified tin catalyst), the chain growth will cease, the chains remain small and unable to burst open the clay layers. According to the present investigations, neither delamination nor increase in d_{001} was observed, one may conclude that chains inside the interlayer regions of silicate are small due to unfavourable conditions for polymerization inside the gallery.

Energy minimization of poly(ε-caprolactone) has also provided an approximate polymer chain dimensions, which had then been used along with the known thickness of the silicate layers to predict layer spacings for various intercalation geometries. It has been determined that average minimal dimensions of polymer chain cross-section are 0.31 nm (in the C=O bond plane) and 0.18nm (perpendicular to the C=O bond plane). It may be concluded from the results that poly(ε-caprolactone) chains are flatly arranged (adsorbed) on each side of the silicate lamella.

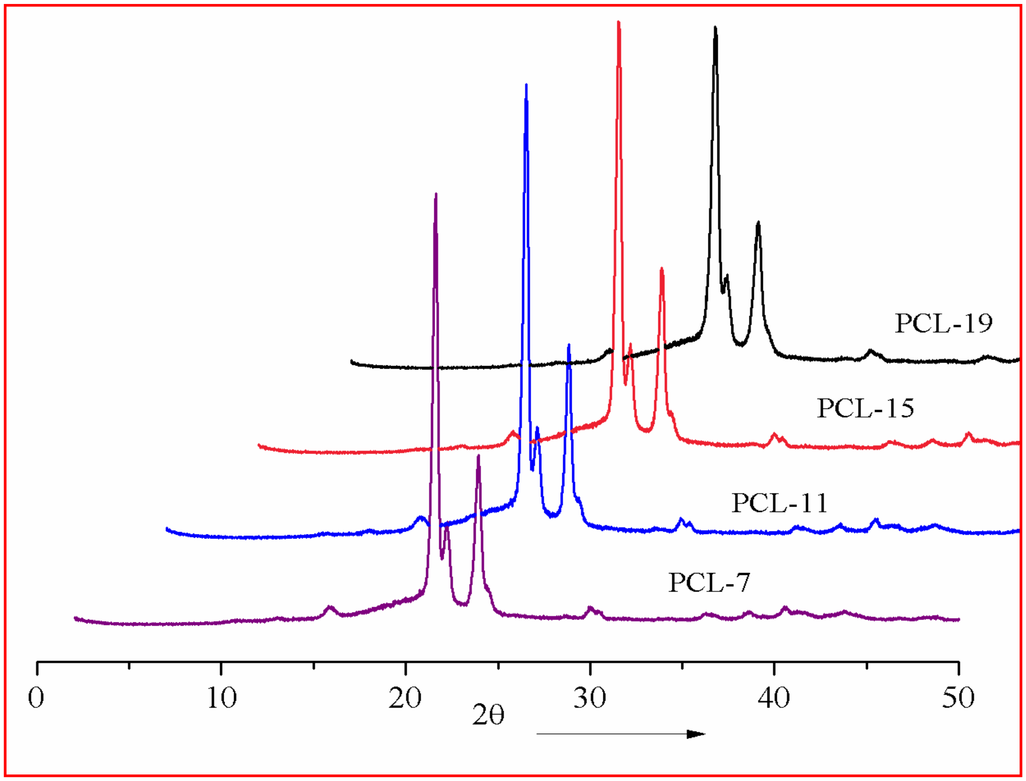


Fig. 4.8: Powder X-Ray Diffraction (XRD) of PCL homopolymers.

Table 4.7: Effect of [M]/[I] ratio of poly (ε-caprolactone) on d-spacing values

Polymer	2θ	d-sp	2θ	d-sp	2θ	d-sp	2θ	d-sp	2θ	d-sp
PCL-5	15.86	5.58	21.61	4.10	22.20	4.00	23.92	3.71	30.03	2.97
PCL-6	15.68	5.64	21.47	4.13	22.06	4.02	23.78	3.73	29.94	2.98
PCL-7	15.86	5.58	21.61	4.10	22.24	3.99	23.96	3.31	30.08	2.96
PCL-8	16.04	5.52	21.79	4.07	22.33	3.97	24.10	3.69	nd	-
PCL-9	15.77	5.61	21.52	4.12	22.11	3.73	23.83	3.73	29.89	2.98
PCL-10	15.86	5.58	21.52	4.12	22.11	4.01	23.83	3.71	29.94	2.98
PCL-11	15.67	5.43	21.54	4.23	22.23	4.19	23.85	3.58	29.94	2.97
PCL-12	16.04	5.52	21.83	4.06	22.38	3.73	24.10	3.64	30.30	2.94
PCL-13	14.18	6.24	15.77	5.61	21.61	4.10	22.24	3.99	23.96	3.71
PCL-14	15.58	5.68	21.38	4.15	21.97	4.04	23.69	3.73	nd	-
PCL-15	15.90	5.56	21.61	4.10	22.29	3.98	24.05	3.69	30.03	2.97
PCL-16	15.86	5.58	21.50	4.12	22.20	4.00	23.92	3.71	29.98	2.97
PCL-17	15.81	5.60	21.52	4.12	22.15	4.01	23.87	3.72	29.89	2.98
PCL-18	15.81	5.60	21.56	4.11	22.20	4.01	23.87	3.72	29.98	2.97
PCL-19	15.90	5.56	21.70	4.09	22.29	3.98	24.01	3.70	30.21	2.95
PCL-20	15.95	5.55	21.74	4.08	22.29	3.98	24.10	3.69	30.21	2.95

d-sp: d –spacing nd: not detected

4.4.6 MALDI-TOF-MS:

MALDI-TOF-MS has been employed for the determination of molecular weights and the nature of end group. Using ring opening polymerization reactions, only low-molecular weight oligomers and high molecular weight poly(ε-caprolactone) can be prepared. Fig. 4.9a depicts the MALDI-TOF mass spectrum of the PCL-9. As expected, the MALDI-TOF mass spectrum of the sample shows a series of intense molecular ion peaks ranging from a mass of 1070 to 4056 Da, which are assigned to sodiated adduct molecular ion of the type H- [O-CH_2-CH_2-CH_2-CH_2-CH_2-CO-]n-OH-Na^+. There is another series ranging from 1085 to 4056 Da, which are corresponding due to the potassiated adduct molecular ions, denoted by the structure H- [O-CH_2-CH_2-CH_2-CH_2-CH_2-CO-]n-OH-K^+.

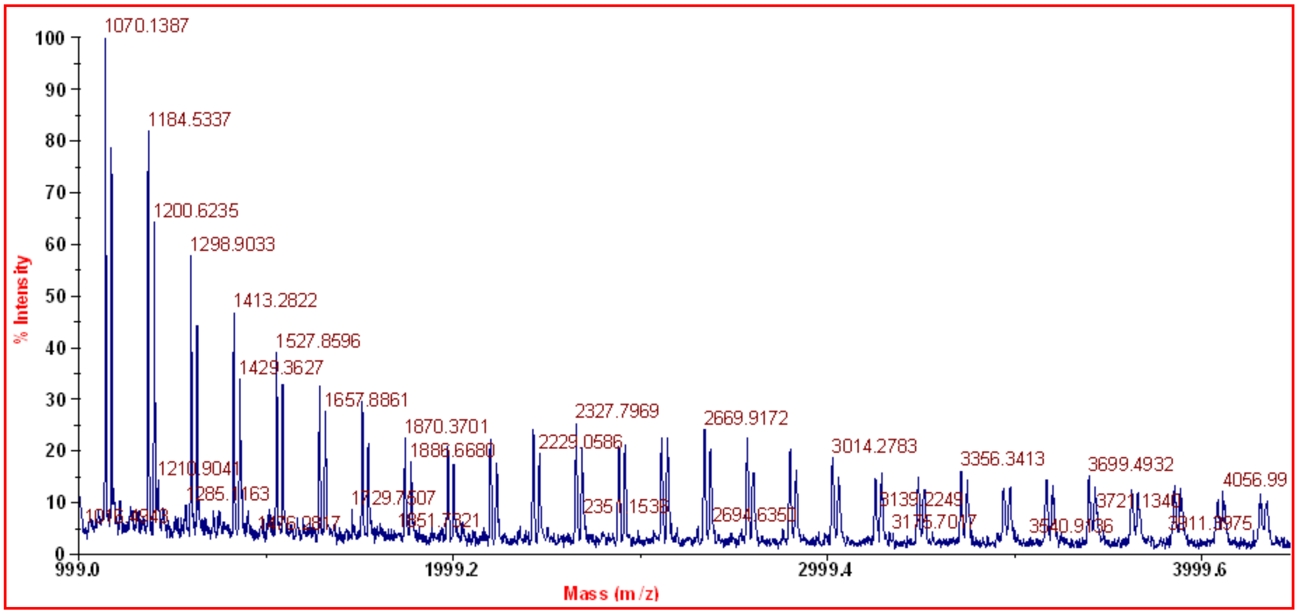


Fig. 4.9a: MALDI-TOF spectrum of PCL-9.

The MALDI-TOF spectrum of the PCL-14 and PCL-15 are presented in fig. 4.9b and fig. 4.9c. The most intense peak of the PCL-14 ranging from 1069 to 3927 Da, correspond to doped sodium ions of the linear oligomers with a mass of 114n +18+23 (n values varies from 9 to 37). The corresponding linear polymer doped with potassium ions can also be seen as peaks of mass 114n+18+39. fig. 4.9c depicts the MALDI-TOF spectrum of PCL-15. The most intense peaks, arising in the region from 1413 to 4273 Da, correspond to linear oligomers, doped with sodium ions (n varies from 12 to 37).

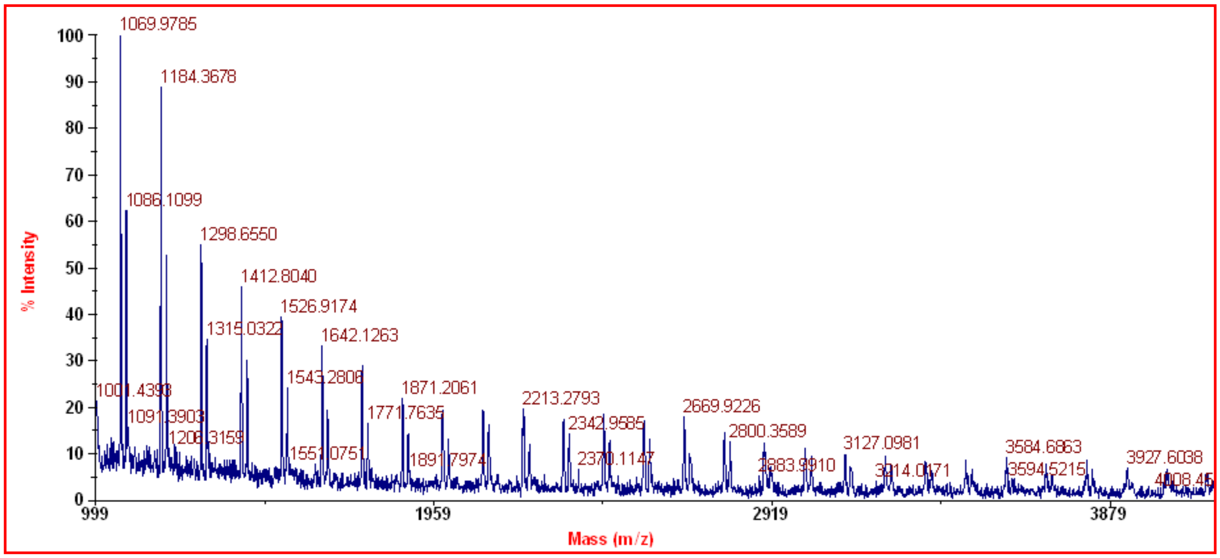


Fig. 4.9b: MALDI-TOF spectrum of PCL-14.

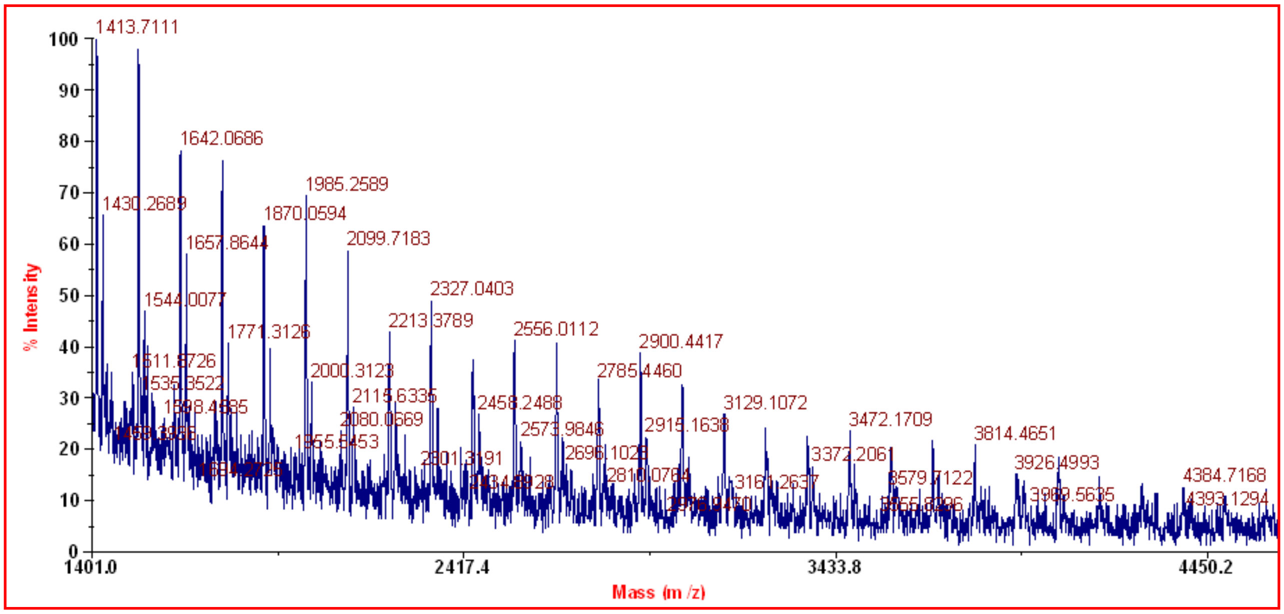


Fig. 4.9c: MALDI-TOF spectrum of PCL-15.

The doped potassium ion that appears in the same region is also of linear oligomers.

Fig.4.9d presents the MALDI-TOF mass spectrum of sample PCL-17. The oligomer contains chains terminated by OH on one side and COOH on the other. The MALDI TOF spectrum is dominated by a series of intense peaks ranging from a mass of 1070 Da to a mass of 6441 Da, corresponding to oligomers doped with Na^+ ions of type H- [O-CH_2-CH_2-CH_2-CH_2-CH_2-CO-]n-OH-Na^+; n values varying from 9 to 55 were detected , 23 being the mass number of sodium. The doped potassium ion that appears in the same region is also of linear oligomers. Fig. 4.9e depicts the MALDI-TOF mass spectrum of sample PCL-19. The MALDI-TOF spectrum is dominated by a series of intense peaks ranging from a mass of 1001 Da to a mass of 6683 Da, corresponding to oligomers doped with Na^+ ions of type H- [O-CH_2-CH_2-CH_2-CH_2-CH_2-CO-]n-OH-Na^+; n values varying from 9 to 65 were detected. The doped potassium ion that appears in the same region is also of linear oligomers.

These structure of prepared poly (ε-caprolactone) were confirmed as linear oligomers and contains hydroxyl and carboxyl groups at their chain ends.

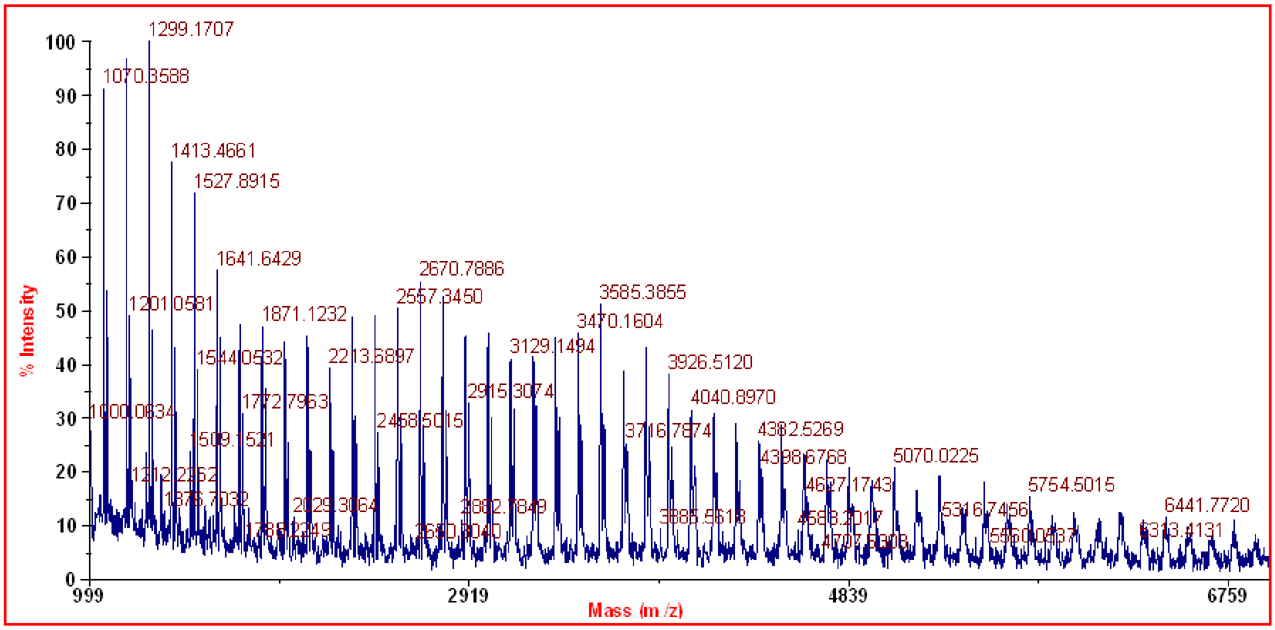


Fig. 4.9d: MALDI-TOF spectrum of PCL-17.

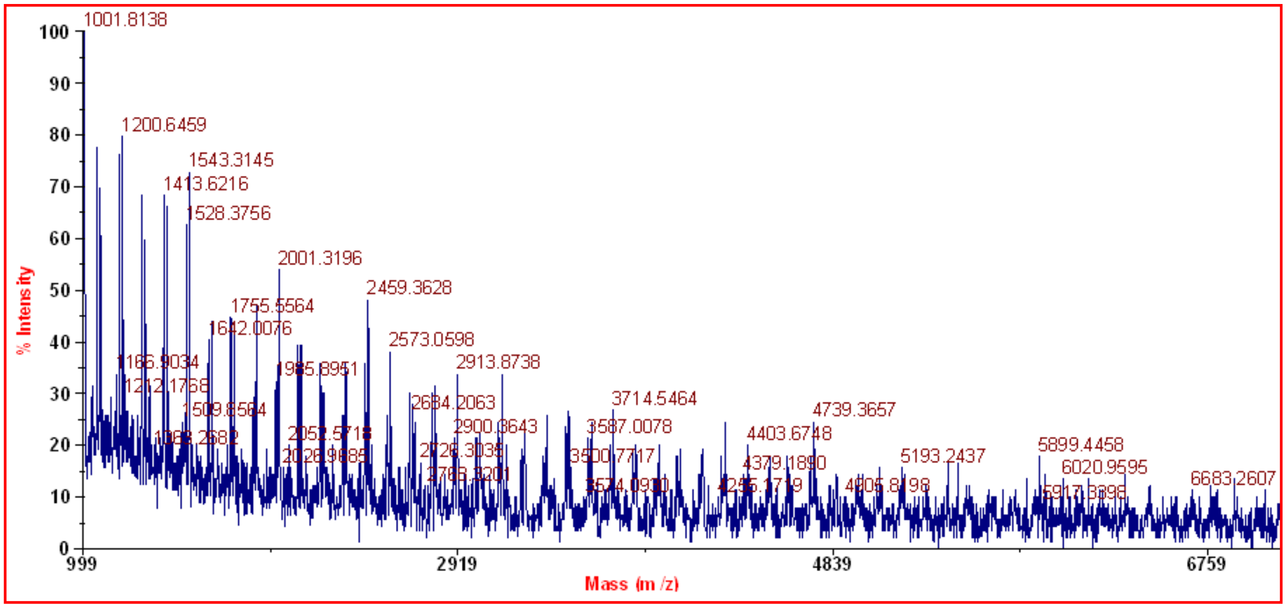


Fig. 4.9e: MALDI-TOF spectrum of PCL-19.

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COPOLYMERS OF ε-CAPROLACTONE WITH OTHER LACTONES USING CLOISITE MODIFIED CATALYST

4.1 A Introduction:

Copolymers of racemic β-butyrolactone ((R,S)-BL and ε-caprolactone (CL), have been synthesized by ring-opening polymerization initiated by sodium hydride (NaH).[1] Several titanium complexes based on aminodiol ligands were tested as initiators for the ring-opening polymerization of ε-caprolactone and rac-β-butyrolactone suggested that ring opening occurs through acyl-oxygen bond cleavage via coordination-insertion mechanism.[2] A series of copolymers has been prepared by ring-opening polymerization of ε-caprolactone and rac-β-butyrolactone using zinc lactate as catalyst. The copolymers appeared to be semicrystalline, the crystalline structure being of the PCL-type.[3] Jeffery Ben et al. demonstrated the utility of Group 4 metals for the well-controlled and stereoselective (ROP) of rac-β-butyrolactone (BBL) and their ability to form copolymers.[4] The polymerization of β-BL with the Zn catalyst system is demonstrated in a living fashion with a narrow polydispersity index, PDI = 1.01-1.10.[5] The neodymium-decorated silica converts the β-butyrolactone monomer into highly isotactic poly(β-hydroxybutyrate).[6]

The zinc alkoxide complex which contains alcohol acts both as coinitiator and chain transfer agent, proceeds smoothly under mild conditions is an efficient catalyst for both the solution and bulk ROP of racemic-β-butyrolactone to produce atactic poly(3-hydroxybutyrate) with moderate to high molar mass.[7] The ROP of racemic β-butyrolactone catalyzed by highly active chromium (III) salophen complexes gives poly(hydroxybutyrate) (PHB) with high molecular weight and with isotacticities of 60-70 %. The product is a biodegradable polymer material with mechanical properties that can be varied from crystalline to thermoplastic.[8] Dibutylmagnesium (Bu_2Mg) as initiator has been used both in bulk and in solution polymerization. Effects of molar ratio of initiator to monomer, reaction temperature and time on the monomer conversion and the polymer molecular weight and its distribution have been discussed.[9]

The poly(γ-butyrolactone) have been synthesized from low-cost monomer γ-butyrolactone. Poly(γ-butyrolactone) displays properties that are ideal for tissue engineering applications and the bacterially derived equivalent, poly(4-hydroxybutyrate) (P4HB), has been evaluated for such uses. The melting point of synthesized copolymer ranges from 53-60 ^{0}C. Poly(gamma-butyrolactone) degrades to give ε-hydroxybutyric acid which is a naturally occurring metabolite in the body and it has been shown to be bioresorbable.[10]

The biodegradation study of copolymers i.e. poly (rac-β-hydroxybutyrate-co-ε-caprolactone) synthesized using different distannoxane catalyst systems has been studied in detail. Results showed all these copolymers, synthetized from distannoxane catalysts, exhibit a high degree of biodegradation of around 75-88%.[11, 12] Atactic poly(R,S-3-hydroxybutyrate) has been synthesized by anionic polymerization of β-butyrolactone with potassium methoxide as an initiator. This completely amorphous polyester is capable of forming a crystalline inclusion complex with gamma-cyclodextrin adopting a channel structure.[13] Osanai Y et al. had performed lipase-catalyzed ring-opening polymerization of β-butyrolactone and polymer isolated in pure form by preparative supercritical CO_2 fluid chromatography.[14, 15] Copolymers poly(β-butyrolactone-co-ε-caprolactone) have also been synthesized by ROP using tetraisobutyldialuminoxane catalyst. The enzymatic degradability of these polymers has been studied in aerobic and anaerobic media.[16, 17]

Block copolymers of rac-β-butyrolactone and ε-caprolactone have been synthesized by combining the anionic polymerization of the first monomer with the coordinative ring-opening polymerization of the second one. The copolymerization yield is close to 100% and the molecular weight distribution of copolymers obtained is quite narrow less than or equal to 1.3.[18] Polymerization of β-butyrolactone has been studied in toluene with $Al(OPri)_3$ as an initiator. The ROP proceeded through a coordination-insertion mechanism at a very low rate. Well defined α-isopropylester ω-hydroxy, poly(β-butyrolactone)s are formed with a narrow molecular weight distribution at low monomer-to-initiator molar ratios.[19]

Thermomechanical tests of poly(L-lactide-co-ε-caprolactone) biodegradable shape memory polymer reinforced with pristine and functionalized multiwalled carbon nanotubes are reported.[20, 21] Casas M et al. obtained the copolymers of ε-caprolactone with a variable composition of a poly(L-lactide) a low polydispersity index (1.4-1.1) and number average molecular weight (20,000-35,000 g/mol).[22] The bulky substituents of homosalen complexes IPr_3Si-substituted homosalen-Al complex used for copolymerization of ε-caprolactone with L-Lactide (1:1).[23] The dimethylaluminum compounds have been used as initiators in the ROP of ε-caprolactone, L-lactide, and D,L-lactide.[24] Poly(L-lactide-co-ε-caprolactone copolymers with various L-lactide/ε-caprolactone mole ratios were prepared by the ring opening copolymerization of L-LA and ε-CL using nontoxic magnesium octoate as a catalyst in bulk. The results showed that a close relationship between copolymer crystallinity and the length of the copolymer sequence.[25]

Penta block poly(L-lactide-co-ε-caprolactone) with a central fluorinated segment and four PLA/PCL side chains was synthesized by sequential ring-opening polymerization (ROP) with stannous octoate catalyst forming a penta block structure with four polyester side chains. Reactions were carried out at 75 ^{0}C and low poly-dispersity indexes were obtained 1.34.[26] Copolymerization of mixtures of L-lactide and ε-caprolactone has been initiated by diphenylzinc. The temperature used varied between 50 and 120 ^{0}C. Copolymers were characterized by DSC and gel permeation chromatography. It has been observed that increasing reaction temperature, reaction time and concentration initiator is advantageous to the transesterification.[27] The formation of large-sized, well-oriented microdomains of poly(L-lactide)-b-poly(ε-caprolactone) has been successfully achieved by using different crystalline substrates including benzoic acid and hexamethylbenzene.[28] Hexakis[p-(hydroxylmethyl)phenoxy]cyclotriphosphazene has been employed in initiating the ring-opening polymerization of ε-caprolactone and L-lactide to produce star-shaped poly(L-lactide), poly(ε-caprolactone) and their block copolymer with cyclophosphazene cores. The GPC analysis showed narrow-distributed star-shaped polyesters were successfully synthesized with high yields.[29]

4.2 A Materials and Methods:

β-butyrolactone (Sigma Aldrich 98%), ε-caprolactone (Sigma Aldrich 99%), Ti(IV)butoxide (Sigma Aldrich 98%), Cloisite-15A (Southern Clay products)

Synthesis of copolymers: Were described in 3.2.5 B chapter 3.

4.3 A Analysis:

4.3.1 A ^{1}H- Nuclear magnetic resonance (^{1}H-NMR): As discussed in chapter 3.

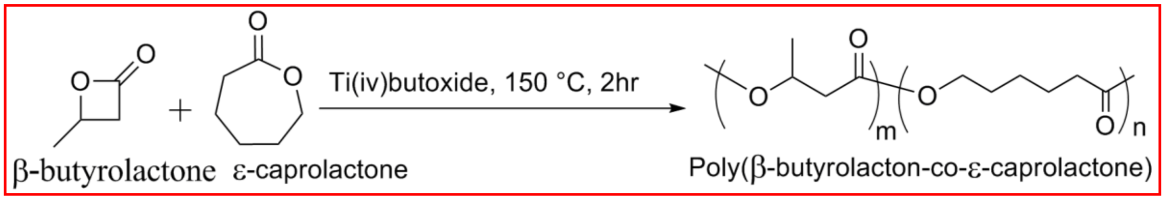
4.3.2 A Molecular weight: As discussed in chapter 3.

4.3.3 A Thermogravimatric analysis (TGA): As discussed in chapter 3.

4.3.4 A Differential Scanning Calorimetry (DSC): As discussed in chapter 3.

4.4 A Result and Discussion:

4.4.1 A Ring opening copolymerization: The reaction of β-butyrolactone(β-BL), ε-caprolactone (ε-CL) were carried out using Ti(IV)butoxide. β-BL, ε-CL and catalyst were taken in silylated glass reactor tube and sealed under vacuum. The resulting reaction mixtures were heated in a sand bath at a reaction temperature 150 ^{0}C. The resulting mixture was dissolved in trichloromethane and then was added to a mixture of diethyl ether and hexane to offer the white solid of the polyester. The yield is 96%.



Scheme 1: Copolymers of β-butyrolactone and ε-caprolactone.

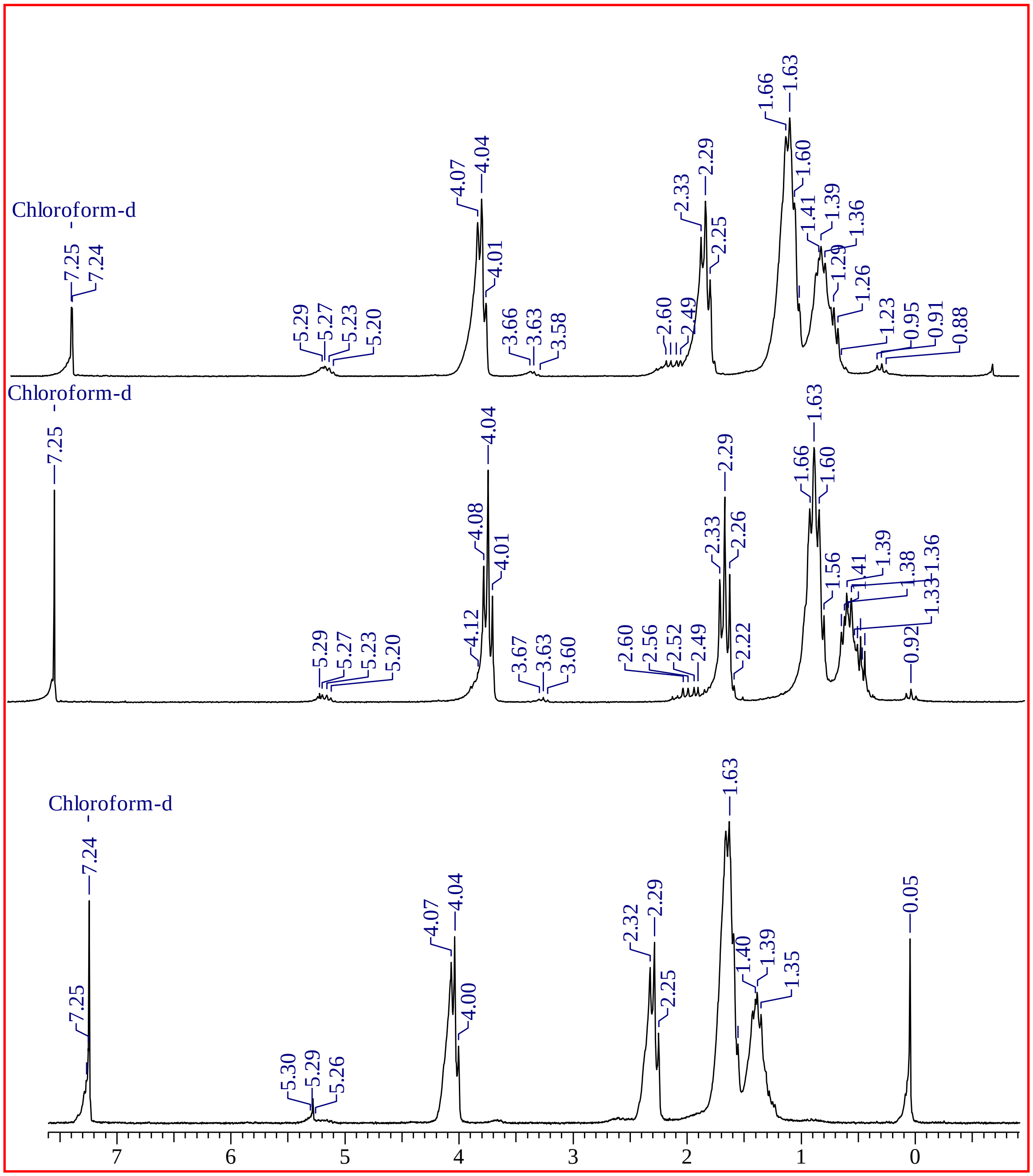


Fig. 4A.1: ^{1}H-NMR of copolymers.

4.4.2 A ^{1}H-NMR: ^{1}H-NMR (500 MH$_{z,}$ δ in ppm) CDCl$_3$. 1.20 -1.369 (m, 3H, CH$_3$ for 3H β-unit), 1.36-1.45 (m, 2H CH$_2$ for the 6-hydroxylhexanoate 6HH unit), 1.60-1.66(m, 4H CH$_2$ for the 6 H unit), 2.41-2.33 (m, 1H, CH$_2$ for the 3Hβ unit.), 2.53-2.67 (m, 1H CH$_2$ for the βHβ unit), 4.04-4.10 (m, 2H, CH$_2$ for the 6HH Unit, 5.20-5.32 (m, 1H, CH for the βHβ unit).

Table 4A.1: β-butyrolactone/ε-caprolactone copolymers using Ti (IV)butoxide catalyst (10 mol%) for 2 hr at 150 ^{0}C

Polym.	Ratio (Mol.) (BL:CL)	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	Deg.Temp. (^{0}C)
COP-1	10:90	10200	15500	1.5	33, 46	89	410
COP-2	20:80	13200	21200	1.6	32, 53	204	412
COP-3	30:70	16100	29300	1.8	62	196	413
COP-4	**40:60**	**23700**	**42200**	**1.7**	**46, 64**	**192**	**417**
COP-5	50:50	21600	33200	1.5	nd	nd	nd
COP-6	65:35	6810	13400	1.9	nd	nd	nd
COP-7	80:20	5330	4850	1.8	nd	nd	nd

BL= β-butyrolactone, CL= ε-caprolactone

A new series of biodegradable copolyesters of β-BL with ε-CL (COP-1 to COP-7) were easily prepared in presence of a catalytic amount of Ti(IV)butoxide in excellent yield (Table 4A.1). The molecular weight (M_w) was attained in range of 4850 to 42200 Da. Single T_g value and two melting endotherms were observed for COP-1, COP-2 and COP-4. The GPC traces of all copolymers were unimodal, but tailoring at the lower molecular weights in case of COP-1 and COP-2. Therefore all copolyesters turned out to be random copolymers with bulky chain segments. T_m and T_g values increased (fig. 4A. 2(a)) with decreasing the ε-CL values up to 60 in the copolyesters. The T_m values were not detected as the ε-CL ratio decreased from 60 to 10 in the range of -40 to 150 ^{0}C.

4.4.3 A Molecular weights: SEC of copolymers of β-BL and ε-CL was as shown in fig. 4A.2. COP-1 showed M_n and M_w as 10, 200 and 15, 500 Da respectively. COP-2 showed M_n and M_w as 13,00 and 21,200 Da, where as COP-3 and COP-4 showed unimodal with increment of M_n and M_w. The maximum molecular weight M_n and M_w were obtained as 23700 and 42, 200 Da. (40:60, BL:CL). As the proportion of BL was increased from 40 to 80, the molecular trend leveled up. This result may be attributed to low reactivity nature of β-butyrolactone.

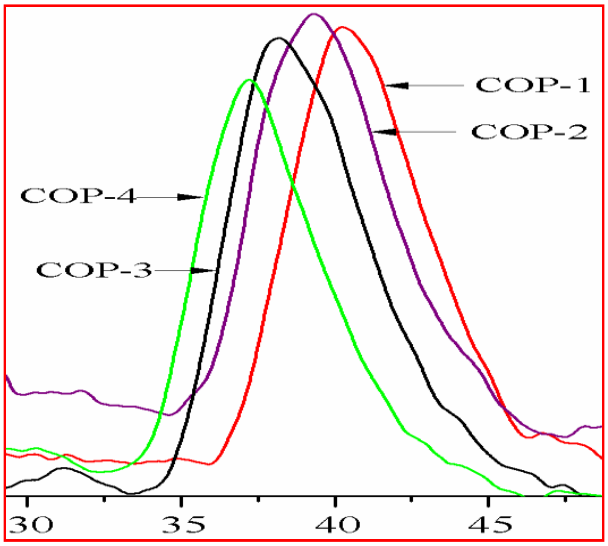


Fig. 4A.2: Size Exclusion Chromatography Poly(β-butyrolacton-co-ε-caprolactone).

4.4.4 A Thermal Properties of the Copolymers:

Thermal stability was evaluated by TGA and traces of the polymers are shown in fig. 4A.3 (b), decomposition temperature shown in Table 4A.1a whereas PCL-PBL copolymers exhibit an intermediate stability between both homopolymers and their stability decreases with content of ε-CL. In addition, the copolymers COP-1 and COP-2 show two stages of the degradation where the first one corresponds to a weight-loss comparable to the fraction in weight of the PBL in the copolymer as may be observed as 9.98 % similar observation was made for copolymer-2 where weight loss was calculated as 19.50 as incorporated in copolymer.

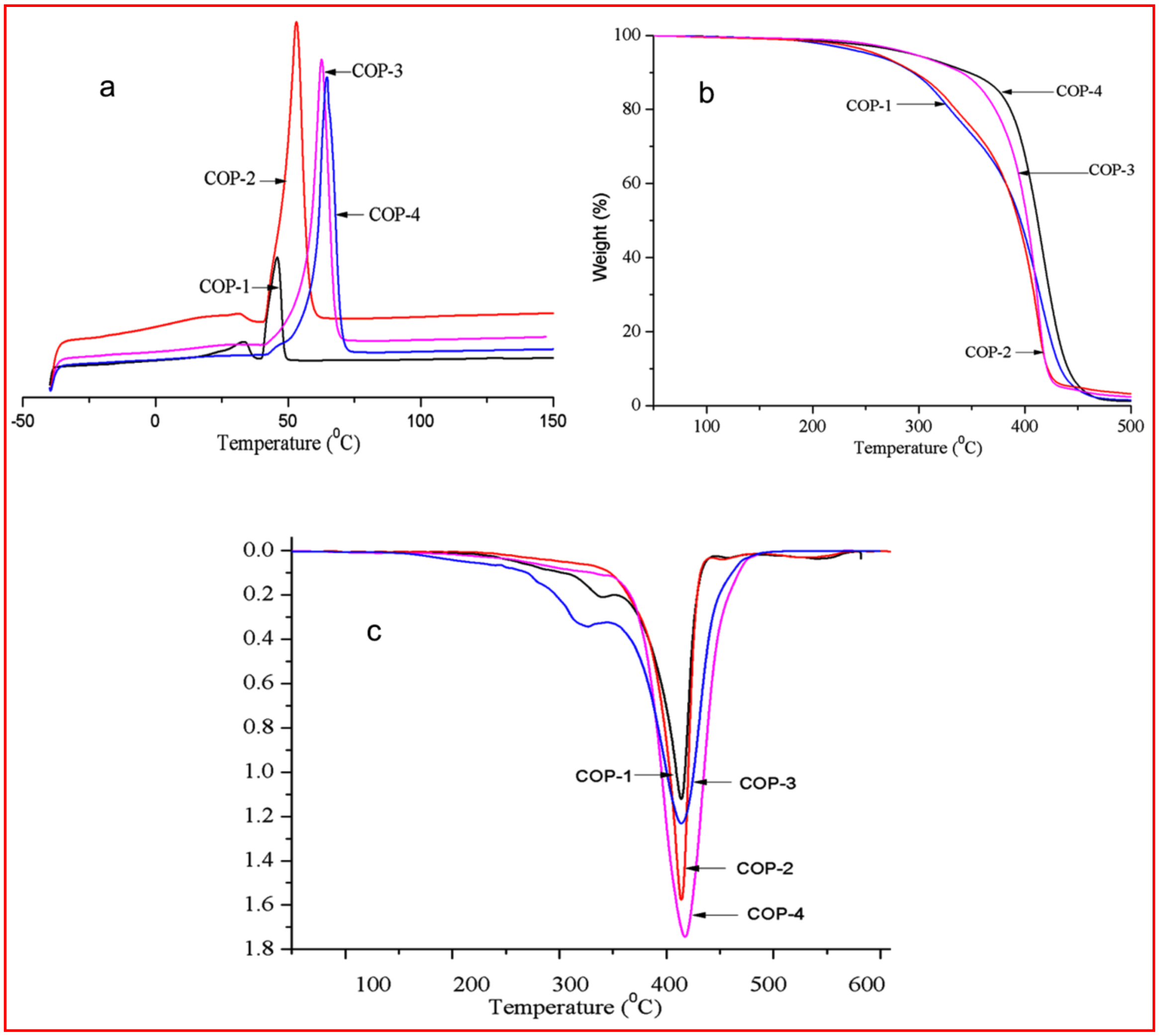


Fig. 4A.3: DSC (a) and TGA (b) of Poly(β-butyrolacton-co-ε-caprolactone) synthesized using Ti(IV)butoxide catalyst showing melting points.

4.4.5 A Coplymerization of β-butyrolactone-ε-caprolactone (40:60) in the presence of Cloisite-15A:

The composition of reaction mixture was selected from Table 4A.1 because of high molecular weights i.e. M_w =42,000. Cloisite-15A was selected for the study because it is organomodified clay. Cloisite-15A was incorporated along with two monomers (β-butyrolactone, ε-caprolactone). The polymerization condition was maintained at 150 ^{0}C and reaction time was 2 hr. The catalyst Ti(IV) butoxide was 10 mol% of the monomers. The weight of cloisite-15A was varied from 1 to 10 wt% of the monomers. The molecular weights M_n and M_w increased up to 8055 and 14080 Da respectively with the increase of clay up to 2 wt %. The molecular weight trend showed further decrement with increase of clay percent i.e. 3-10%. The traces amount of water present in the clay influenced the hydrolysis of lactones. According to polymerization reaction, water as required to play its role in the initial (hydrolysis) step only, the further stages water would be neither necessary nor produced as the reaction proceeds between the hydroxy acids and lactones only. The polymer chain in polymer will halt after complete monomer conversion. The GPC data shows clear increase in copolymers molecular weight after total monomer conversion. As the % of clay increased in the system, the molecular weight decreased.

The traces of water present in the clay gallery influences hydrolysis. Reaction at the beginning and enhances transesterification reaction in the later stage. Therefore it directly influences on molecular weights.

Thermogravimetric analysis (TGA): The Thermogravimatric analysis of COP-9 to COP-11 where shown in fig. 4A.4b and 4A.4c. The values were tabulated in Table 4A.2. The maximum decomposition temperature was observed as 310 ^{0}C in case of 2 wt% cloisite-15A incorporation.

Differential Scanning Calorimetry (DSC): Fig. 4A.4a shows DSC curves of COP-8 to COP-12. The melting temperatures showed 53 ^{0}C in the presence of 2 wt% clay decreased thereafter. It is obvious that intercalation of copolymer chain with clay is lower in comparison with high molecular of weight of β-butyrolactone-ε-caprolactone copolymers .Two T_m values are 37 and 53 ^{0}C. These copolymers showed two distinct T_m values which may be attributed to bulky nature of copolymers in presence of cloisite-15A. The same observation was made in COP-4 where two T_m values were 46 and 64 ^{0}C respectively in absence of cloisite-15A.

Table 4A.2: Effect of organomodified clay (Cloisite-15A) on COP-4

Polym.	Clay (Wt %)	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	Deg. Temp.(^{0}C)
COP-8	1	6410	10060	1.6	37, 43	016	nd
COP-9	2	8055	14080	1.7	37, 53	122	310
COP-10	3	7780	14040	1.8	37, 51	063	305
COP-11	4	7730	13000	1.6	38, 50	054	305
COP-12	10	5030	7350	1.5	37, 48	080	nd

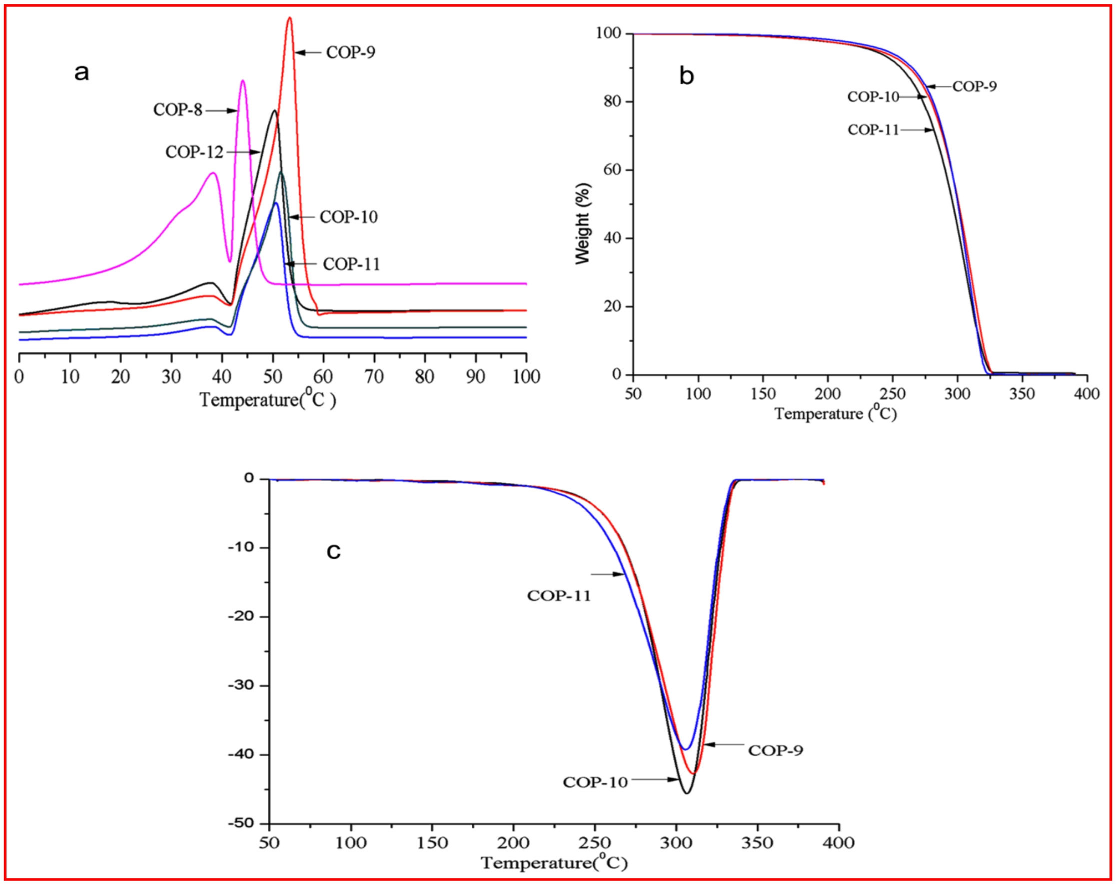


Fig. 4A.4: DSC(a), TGA(b), DTG(c) showing effect of Cloisite-15A on Poly(β-Butyrolacton-co-ε-caprolactone) synthesized using Ti(IV)butoxide catalyst showing melting points.

Table 4A.3: L-lactide/ε-caprolactone copolymers using Ti (IV)butoxide catalyst (10 mol%) for 2 hr at 150 ^{0}C

Polym.	Ratio (Mol.) (LA:CP)	M_n (SEC)	M_w (SEC)	PDI	T_m (^{0}C)	ΔH_m (J/g)	ΔCp (J/g ^{0}C)	T_g (^{0}C)
COP-13	90:10	14200	19900	1.4	136	23	20	22
COP-14	80:20	6890	14100	2.05	nd	nd	nd	nd
COP-15	70:30	5000	10500	2.12	nd	nd	nd	nd
COP-16	60:40	7510	9410	1.2	nd	nd	nd	nd
COP-17	50:50	2070	5360	2.6	nd	nd	nd	nd

LA- L-lactide, CP-ε-caprolactone

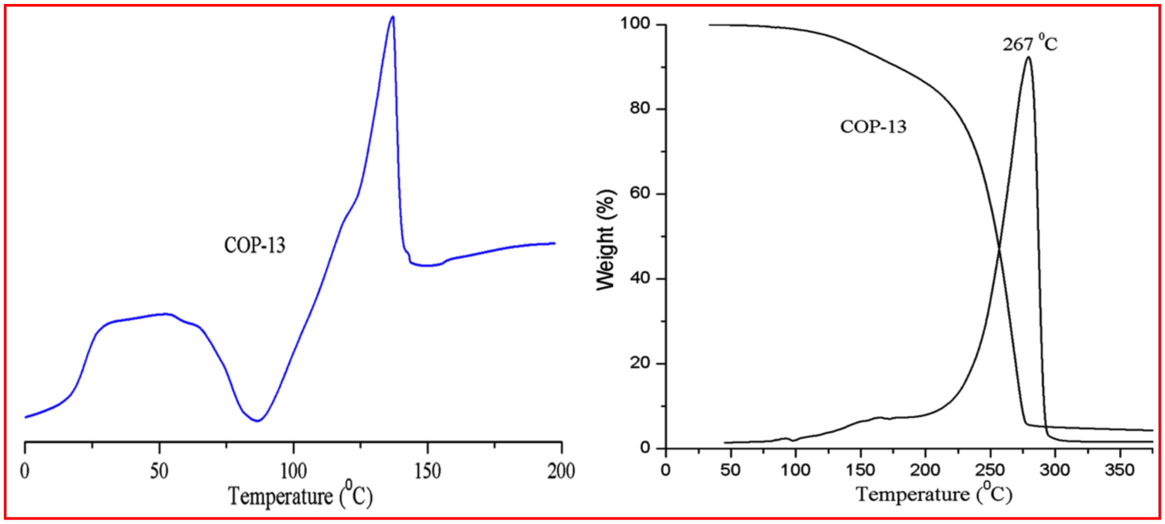


Fig. 4A.5: DSC and TGA of COP-13 showing melting and decomposition temperature.

In recent years, the current research on biomaterials has toured on copolymers of different types. Copolymer system exhibits a broad range of properties depending on the type and proportions of their constituent monomers. The hydrolyzable and biocompatible copolymers of ε-CL and LA have been of great interest for medical applications. Small amounts of elastic copolymers may be interest for nonmedical application as well as impact modifiers in brittle polyesters. ε-CL appears to be suitable comonomer for the preparation of diversified family of copolymers with mechanical properties ranging from elastomeric to rigid. The good elongation characteristics of elastomeric copolymers make them suitable for applications where elasticity and degradability are required in the same product.

The synthesis of ε-CL/LA copolymers has been widely studied in the literature. However, there is no report available for preparation of ε-CL/LA copolymer using Ti(IV)butoxide as a catalyst and ring opening polymerization technique.

Table 4A.2 illustrates the results of ε-CL/L-LA copolymers in compositions of 90:10, 80:20, 70:30, 60:40 and 50:50 (mol % in feed) using Ti(IV)butoxide as a catalyst. The copolymers appear to be random in nature because DSC trace shows a single glass transition temperature (T_g) at 22 °C and melting temperature (T_m) at 136 °C. Basically, the copolymers of ε-CL and LA were polymerized in bulk at 150 °C using Ti(IV)butoxide as the catalyst. Molecular weights and molecular weight distributions are presented in Table 4A.2. These copolymers differed greatly in appearance from plastic like to gummy according to the monomer composition. The conversions of the polymerizations were about 95-99%. The molecular weight trend decreased as ε-caprolactone proportion increased from 10 to 50. The M_w decreased from 19900 to 5360 Da. These results may be attributed to low reactivity of ε-caprolactone in comparison with L-Lactide. The copolymer (COP-13) is thermally stable up to 267 °C. DSC curve shows single T_g and melting temperature (T_m). The nature of the copolymer appeared as random because of single T_g and T_m i.e. 22 and 136 °C respectively.

4.5 A Conclusion:

Solid cloisite modified tin catalyst was prepared and characterized by several techniques such as ^{1}H, ^{13}C and ^{119}Sn NMR as described in Chapter III. The catalyst is solid and nonhygroscopic. The poly(ε-caprolactone) was prepared using ROP of ε-caprolactone using cloisite modified catalyst. The effects of kinetic and thermodynamic parameters were studied. The maximum molecular weight M_w was obtained as 42800 Da, where [M]/[I] was 200 at reaction temperature (180 ^{0}C) and time (3 hr). The maximum degradation temperature was obtained around 320 ^{0}C. The maximum T_m was obtained as 63 ^{0}C. The linearity of poly(ε-caprolactone) was confirmed by MALDI-TOF. The end group functionalities where hydroxyl and carbonyl groups. It is confirmed from the X-ray diffraction studies that poly (ε-cprolactone) chains are flatly arranged (adsorbed) on each side of the silicate lamella.

Copolymer of β-butynolactone/ ε-caprolactone were prepared at various composition 10:90, 20:80, 30:70, 40:60, 50:50, 65:35 and 80:20 using Ti(iv)butoxide as a catalyst. The maximum molecular weight was obtained as 42200 Da and distribution is 1.7. The maximum T_m was observed at 64 °C. The effect of organo modified clay was studied selecting a copolymer of (40:60) composition of β-butyrolactone and ε-caprolactone. The organo modified clay (cloisite-15A) was varied from 1 to 10 wt %. The maximum molecular weight was obtained as 14080 Da. The thermal decomposition temperature was around 305 °C. DSC results showed two melting's (T_{m}' s) with variation of clay (1 to 10 wt %).

Copolymer of L-lactide/ε-caprolactone were prepared using Ti(IV)butoxide. The composition were varied as 10:90, 20:80, 30:70, 40:60, and 50:50. The copolymers were confirmed because it showd single T_g in cases. The copolymers are random in nature.

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CHAPTER - 5

CHAPTER-5: SYNTHESIS AND CHARACTERIZATION OF THE LINEAR BIODEGRADABLE POLYESTERS VIA DEHYDROPOLYCONDENSATION ROUTE AND ROP OF MACRO CYCLIC LACTONES FROM RENEWABLE RESOURCES

5.1 Introduction:

In the dehydropolycondensation of L-lactic acid (L-LA) to poly (L-lactic acid) (PLA), small amounts of impurities are expected to play a major detrimental role. L-LA prepared by fermentation of biomass may contain impurities derived either from the fermentation step itself or from the separation and purification steps after fermentation. Several impurities, for example, methanol, ethanol, acetic acid, pyruvic acid, some dicarboxylic acids like oxalic, fumaric and succinic acids etc, have been reported to occur in the fermentation derived L-lactic acid.[1] The level as well as nature of impurities in the polymerization is believed to have a large effect on the final molecular weight by end capping either the hydroxyl or the carboxylic acid terminal of the growing polymer chain and thereby limiting the chain growth. It has been found that total level of interfering impurities should be less than 100 ppm in order to achieve high molecular weight PLA polymer.[2]

This chapter describes the effort to analytically detect and quantitate the level of impurities in the L-LA to be used for all polymerization reactions in the subsequent chapters. The L-LA obtained as an aqueous solution was esterifies with ethyl alcohol to form ethyl L-lactate. Both the L-LA aqueous solution and the ethyl lactate were analyzed by gas liquid chromatography (GC), High Performance Liquid Chromatography (HPLC), LC-MS.

Controlled ring opening polymerization (ROP) of L,L-dilactide (the dilactone of L-LA, alternatively called L-lactide) was also performed with $Sn(Oct)_2$) catalyst and measured amount of water as coinitiator, to produce linear PLA oligomers of well-defined number average molecular weight with carboxylic acid and hydroxyl end groups. These polymers were desired as model PLA oligomers for any L-LA that would be prepared in the work described in subsequent chapters. The carboxylic end groups were also quantitatively determined using ^{13}C-NMR spectroscopic technique, which in turn, was used to calculate the number average molecular weight.

12-hydroxystearic acid (12-HSA) or 12-hydroxyoctadecanoinc acid which is an aliphatic hydroxy-carboxylic acid has been polymerized into aliphatic polyester by self-condensation.[3] The homopolymer of 12-HSA, that is poly (12-HSA) (PHSA), is a colorless, viscous liquid. The presence of n-hexyl pendant (side chain) affects any parallel arrangement of the backbone polymer chains, which is essentially required for crystallization, although a similar polyester, poly (11-hydroxyundecanoate), which does not have such an aliphatic pendant is considerably crystalline even at low number average molecular weight. This is clear evidence of the fact that softness and amorphous property of PHSA is due to the n-hexyl side chain.

Only a few references of macrolactonization of ω-hydroxycarboxylic acids, especially macrocyclic lactone formation from 12-HSA in presence of distannoxane type of catalysts, are available.[4, 5] Such lactonization is, however, reported to occur only in dilute systems or emulsions or microemulsions with or without the help of detergents. The low molecular weight homopolymers of 12-HSA(M_n= 5000 – 50,000) have found application in diverse fields for example, as an adhesion tuner and carrier material in ink-compositions,[6] as a softener in styrene-butadiene rubber,[7] and as a surface active agent in finished cotton-polyester mixed fabric and leather treatment.[8] Poly(12-hydroxystearic acid)-poly(ethylene oxide)-poly(12-hydroxystearic acid) triblock copolymer has been observed to be a very efficient polymeric surfactant for preparing oil in water microemulsions.[9]

The composites of homogeneous poly (ε-caprolactone) (PCL) with (R)-12-hydroxystearic acid (HSA) or N-carbobenzyloxy-L-isoleucylaminooctadecane (CIA) have been prepared mixing hot liquids of each component. The tensile moduli of both the composites were improved by the addition of CIA and HSA and showed high biodegradability as PCL.[10]

A dilactone, 13, 26-dihexyl-1, 14-dioxacyclohexacosane-2, 15-dione (12-HSAD), has been synthesized by lipase-catalyzed reaction of 12-hydroxystearic acid (12-HSA) in high yield and was subjected to the ring-opening polymerization with various catalysts to obtain poly(12-hydroxystearate) (PHS). The polymerization system of 12-HSAD showed an interesting polymerization behavior because of its large ring system.[11]

The monomers form a carboxylic cyclic dimer, and the secondary hydroxyl group promotes growth along the secondary axis.[12]

The enzymatic polymerization of 12-hydroxystearic acid (12-HSA) has been carried out with Lipase CA (R) in benzene to produce poly(12-hydroxystearate) (PHS) with a low molecular weight. When this polymerization was continued for a long, reaction time, the PHS once formed was depolymerized into a cyclic diester, 13,16-dihexyl-1,14-dioxacyclohexacosane 2,15-dione (12-HSAD). The preferential formation of cyclic diesters for 12-HSA was attributed to the structural requirements due to the bulky n-hexyl side groups stemming from the ring systems.[13]

A mixture of epoxidized soyabean oil (ESO), (R)-12-hydroxystrearic acid (HSA) and a photoinitiator for cationic polymerization in the ESO/HSA weight ratio 10/1 has been heated to 100 ^{o}C and gradually cooled to room temperature to give biobased gelatinous material.[14]

The polycondensation of 12-hydroxystearicacid, catalysed by *p*-toluene-sulphonic acid, obeyed simple second order kinetics for about 85% of the reaction and a tailing-off in degree of polymerization obtained. The constants K_v and α in the Staudinger viscosity/molecular weight relationship have been derived for poly 12-hydroxystearates.[3]

The poly-12-hydroxy stearic acid (PTHSA) has been synthesized and modified by esterification with pentaerythritol to obtain a polyol polymeric hyperdispersant (polyol-PTHSA.[15]

Vinyl 12-hydroxystearate was prepared from 12-hydroxystearic acid by vinyl interchange procedure with vinyl acetate. Vinyl 12-hydroxystearate was obtained by the treatment of this addition product with acid washed activated alumina in ether solution. Vinyl 12-hydroxystearate polymerized in an emulsion system at a pH of 7-8.5 with standard free radical initiation gave colorless solid polymer.[16]

The synthetic routes have been followed to prepare graft copolymers with long side chains containing acyl chloride terminal groups. In the first of these methods acryloxy aliphatic acyl chlorides were synthesized from 12-hydroxystearic acid and 10-hydroxydecanoic acid and then polymerized with other acrylate ester comonomers. In the second procedure, a prepolymers was formed by copolymerizing acryloyl chloride with acrylate esters. The prepolymer then was treated with 12-hydroxystearic acid or 9 (10) - hydroxymethylstearic acid to produce polymers with side chains having terminal carboxylic acid groups.[17]

Aliphatic polyesters constitute an important class of polymers because of their biodegradability,[18] and biocompability [19, 20] that enable their use in drug delivery systems, artificial tissues [21, 22] and commodity materials. Polyesters are commonly produced through either condensation or ring opening polymerization using various catalysts. [23, 24, 25, 26] Self-organization of condensation polymer is rare in the literature. Particularly, self-organization of amphiphilic polymers has resulted in assemblies such as micelle, vesicles, fibers, helical, superstructures and macroscopic tubes. These materials have potential application in areas ranging from material science to biological science. Thermo or pH sensitive polymer micelles [27, 28] and vesicles [29] , have been reported in which the nature of the functionality at the corona changes in response to the stimulus. A little attention has been paid to realize an environment-dependent switch from a micelle-type assembly with a lipophilic corona.[30] Here, we report a new class of aliphatic polyester superstructures that exhibit such properties.

Aleuritic acid has been used as a raw material for the synthesis of macrocyclic musk like lactones such as ambrettolide, civetone and exaltone. There is only one literature report of poly aleuritic acid, where aleuritic acid has been polymerized thermally and resulted insoluble product.[31] We demonstrate for the first time that the linear homopolymer of aleuritic acid (PAA) is obtained from aleuritic acid fig. 5.1. The change in the surface of the assembly is the amplified consequence of change in molecular level conformation with each polymer chain due to the presence of 9, 10-hydroxy group in each monomeric unit. These polymers with such properties could find use in the applications such as carriers for trafficking drugs and as components of smart adhesives. PAA is biocompatible and biodegradable polymer, which could find potential use in biological system.

Block copolymers are often used for a variety of supramolecular assemblies, in which the driving force involves the mutual immiscibility of the block and/or the immiscibility of one of the blocks in the bulk solvent. In case of poly (styrene-co-acrylic acid) block copolymers exhibit several interesting amphiphilic assemblies.[32, 33, 34, 35] We aimed to synthesize aliphatic polyester by polycondensation. The hydrophilic 9, 10-hydroxy functionality, the hydrophobic methylene moiety are stitched in the same polymer backbone. The methylene group's greater than five units in a polymeric chain show zigzag conformation in the polymer molecule.The thermal polymerization of aleuritic acid leads to insoluble product because both intra and intermolecular condensation are possible leading fast to the formation of fusible ethers, anhydrides, lactones and esters which ultimately become infusible and insoluble three dimensional network structures.

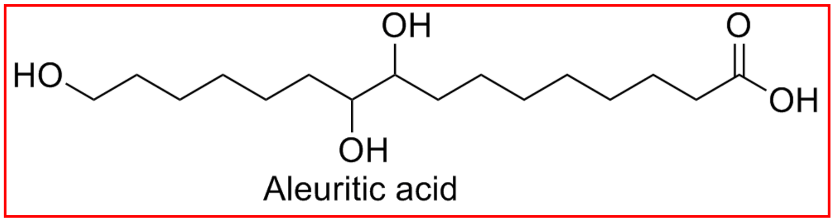


Fig. 5.1: 9, 10, 16-trihydroxy, palmitic acid (aleuritic acid).

These functional polymers can be post modified to crosslink the polymer, or to attach bioactive molecules such as peptides or drugs and have shown potential application in drug delivery systems and scaffold materials. The functional polyesters have tunable mechanical properties with in vivo degradability.[36] Polyesters syntheses have been explored by both chemical synthesis and enzymatic approaches. Several hydroxyl functional polyesters, [37, 38, 39, 40, 41], and poly (carbonate esters), have been synthesized.[42] Polymers with vicinal diols were prepared by chemical polymerization of L-lactide with protected sugars[43, 44] followed by deprotection.[45, 46, 47] Use of monomers, initiators with unsaturated bond enabled the introduction of epoxide groups by post modification reaction with m-chloroperbenzoic acid (m-CPBA), while treatment of allylic side chains with NMO/OsO_4 resulted in dihydroxylation of side chains.[48] Chemical polymerization of unprotected hydroxyl functional caprolactones,[49] and hydroxymethyl substituted 1, 4-dioxan-2-ones[50, 51] resulted in hyper branched structures with comparable molecular weights and degree of branching.

A variety of lactones were prepared in high yields at room temperature from the corresponding omega-hydroxycarboxylic acids using 2-methyl-6-nitrobenzoic anhydride in the presence of 4-(dimethylamino)pyridine.[52] Condensation of the dilithio-derivative of oct-7-yn-1-ol with 8-bromo-octanoic acid gives 16-hydroxyhexadec-9-ynoic acid which is semihydrogenated to *cis*-16-hydroxyhexadec-9-enoic acid. c*is*-and *trans*-hydroxylation processes then give *erythro*- and *threo*-9,10,16-trihydroxyhexadecanoic acids respectively.[53]

A mimetic polymer of plant cutin have been synthesized from 9,10,16-trihydroxyhexadecanoic (aleuritic) acid through a low temperature polycondensation reaction.[54]

A novel biodegradable polymer poly(aleuritic acid) (PAA) M_w=120,000) was prepared from aleuritic acid, which was obtained from renewable resources by using tin catalyst. Aleuritic acid (AL) was protected at 9, 10 position by dimethoxy propane. The protected AL (Pro.AL) was further polymerized to obtain linear protected polyaleuritic acid (PAL) by dehydropolycondensation. Effects of various kinetic and thermodynamic parameters were studied. After polymerization, the deprotection of PAL was carried out. The micelle and inverted micelle structure in polar and nonpolar solvents are highlighted.[55]

A number of new derivatives of aleuritic acid were synthesized and their antimicrobial activities studied using different strains of bacteria and fungi. All the compounds showed significant antibacterial and antifungal activities, at varying minimum inhibitory conc (MIC) values.[56] Z-(9)-Hexadecenal, an important pheromonal component, was synthesised from aleuritic acid, using novel procedure, resulting in improved yields. Microwave-assisted technique was also applied in the esterification of aleuritic acid, leading to shorter reaction times and 98% yield of methyl aleuritate.[57]

Synthesis of omega-chloro compounds obtained from aleuritic acid and its derivatives have been carried out and the known triphenylphosphine-carbon tetrachloride procedure has been found to be the most suitable for this purpose.[58]

The industrial process for manufacturing aleuritic acid from seed lac possesses certain problems like the long saponification period, need for reprocessing the crude product and the inevitable loss during this step. Some improvements are suggested to overcome these problems and get three aleuritic acid of 92% purity in an optimised yield of 23%.[59]

5.2 Materials and Methods:

5.2.1 Purification of Materials: L-lactic acid (L-LA) was obtained from PURAC chemical company, Holland, in the form of 88 % aqueous solution and was used as such, without any purification. Ethanol and benzene were both obtained from s.d. fine chemlimited, India. Ethanol was purified by distillation and dried on fused calcium chloride followed by magnesium ethoxide before use. Benzene was purified (free of thiophene) by stirring with 98 % H_2SO_4, washed with sodium bicarbonate and water, followed by drying first over fused calcium chloride and then over sodium metal. THF was dried over fused calcium chloride followed by calcium hydride (CaH_2). Trimethylsilyl chloride (TMSCl), acetone, 98 % H_2SO_4, sodium carbonate, fused calcium chloride and sodium metal were all obtained from S. D. Fine Chemicals, India, and used without purification. CaH_2 was procured from Aldrich Chemicals and was also used without any purification. L,L-dilactide was procured from Aldrich Chemicals and was used after recrystallization from dry THF. Doubled distilled and de-ionized water was used as co-initiator of ROP reactions. $Sn(Oct)_2$ catalyst was procured from Aldrich Chemicals and was freshly distilled before use.

12 hydroxystearic acid (Sigma Aldrich), Aleuritic acid (Fluka) used further without purification, p-toluenesulphonic acid (Fischer), Benzaldehyde dimethyl acetal (Sigma Aldrich), Camphor sulphonic acid (Sigma Aldrich).

5.2.2 Preparation of ethyl lactate from L-lactic acid: L-lactic acid was azeotropically dried with benzene (thiophene-free) without any catalyst, followed by removal of benzene under reduced pressure of 0.1 mbar at 60 ^{0}C (5 hr). The dry, waxy L-lactic acid (10 g) was esterified by refluxing in dry ethanol (50 mol/ mol of L-LA) with a few drops of 98 % H_2SO_4 as catalyst for 20 hr with intermittent (azeotropic) distilling out of ethanol and by-product water at every 4 hr. After 20 hr the whole reaction mixture was distilled up to dryness, so that all ethanol together. Further fractional distillation at the boiling point of ethanol and under atmospheric pressure removed ethanol and yielded 9.87 g (86 %) pure ethyl lactate.

5.2.2 a Prepolymer and L-Lactide formation from Purac Lactic acid using Nelson Reactor

Amount of Lactic Charged into the Reactor: 750 gm.

Procedure: L-Lactic acid was charged into the reactor vessel then temperature and vaccum conditions were varied as follows.

Lactic acid was heated under reduced pressure until dehydration and condensation in order to get prepolymer. The temperature is kept below 180 ^{0}C for the purpose of preventing the racemization of lactic acid. The lactic acid monomer, lactoyl lactic acid and water as a impurities collected while making prepolymer. The prepolymer and tin powder as a catalyst heated together and kept reaction mixture temperature 180 ^{0}C for the synthesis of lactide. The lactide vapor was cooled and collected.

Table 5.1: Time and temperature condition for prepolymer formation

Temperature (^{0}C)	Vacuum (mb)	Time (hr)
150	N_2 atmosphere	2
150	100	1.5
150	30	1.5
150	Full(-17.4)	1

Amount of water collected = 125 gram

Amount of Tin(Sn) Powder added to the prepolymer = 0.5 wt %

Table 5.2: Time and temperature condition for Lactide formation

Temperature (^{0}C)	Vacuum (mb)	Time (hr)
150	N_2 atmosphere	0.5
180	N_2	0.5
180	800	0.5
180	700	2.5
180	500	1
180	100	1
180	10	1
180	Full	7

5.2.2 b Purification of lactide:

Crystals of lactide were dissolved in ethyl acetate and precipitated using petroleum ether. Lactide crystal was dried under reduced pressure at 50 ^{0}C. Again lactide dissolved in sodium dry toluene for further purification till melting point in the range of 98-99 ^{0}C.

5.2.3. General procedure for ROP of L-lactide: As described in chapter 3.

5.3. Analysis

5.3.1. Gas liquid chromatography (GC): GC-analysis of L-lactic acid was done on Perkin Elmer GC Auto System XL-200 by injecting 0.1, 1 and 10 microliter injection volumes of the L-LA 88 % aqueous solution as such to a Perkin-Elmer BP-20 (polyethylene oxide, terephthalic acid treated) capillary column of 25 meter length by means of on-column injection procedure and comparing with the chromatograms of aqueous solutions of 4, 9 and 19 ppm (that is below 5, 10 and 20 ppm, respectively) concentrations each of methanol, ethanol, acetic acid, and pyruvic acid. The split ratio was 1:60, the detector was FID, the carrier gas was nitrogen with a pressure of 7 psi and the fuel for FID was hydrogen. Oven was isothermal at 50 ^{0}C for 30 min, followed by heating with a ramp rate of 5 ^{0}C/ min from 50 ^{0}C till another 30 min. The injector and detector were kept at 250 and 280 ^{0}C, respectively. Dicarboxylic acids, namely oxalic, fumaric and succinic acid did not elute through this column.

Ethyl lactate was analyzed under the same conditions, except that the column was Perkin-Elmer BP-21 (polysiloxane) and the injection was done in normal injection mode, where the sample evaporated inside the injector and went into the column in a gaseous form. Ethyl lactate chromatograms (corresponding to 0.1, 1 and 10 micro liter injection volumes) were compared with chromatograms of ethanolic solutions of 4, 9 and 19 ppm (that is below 5, 10 and 20 ppm, respectively) concentrations each of diethyl oxalate and diethyl succinate.

5.3.2. High Performance Liquid Chromatography: Quantification of impurities by HPLC is the process of determining the unknown concentration of a compound in a known solution. It involves injecting a series of known concentrations of the standard compound solution onto the HPLC for detection. The chromatograph of these known concentrations will give a series of peaks that correlate to the concentration of the compound injected.

The HPLC system employed for this work consisted of modular HPLC of WATERS make consisting of Pumps 3x515 HPLC High pressure pumps, Injector: 717-Autosampler, Detectors: 996 PDA [Photodiode Array Detector] 410 RI [Refractive Index Detector] and Millennium Software. The column used for impurity analysis was YMC (polar embedded, C_{18}). The chirality of 88 % L-LA aqueous solution was determined using MN-chiral 1 column. The chiral purity of 88 % L-LA aqueous solution was obtained as 99.9 %.

5.3.3. LC-MS: The LC-MS of L-lactic acid was analyzed in methanol solution using API Qstar Pulse.

5.3.4. Molecular weights: As discussed in chapter 3

5.3.5 ^{1}H-NMR Spectroscopic analysis were performed as described in 3.3.2b, chapter 3

5.3.6. Quantitative ^{13}C-NMR spectroscopic analysis: For NMR measurements, the samples were dissolved in Chloroform-d in 5 mm dia. NMR tubes at room temperature. The chemical shifts in parts per million (ppm) were reported up field with reference to internal standard chloroform-d at 7.25 ppm. The sample concentration for ^{13}C-NMR measurements was 10 % by weight. Proton decoupled ^{13}C-NMR spectra with NOE were recorded on a Bruker DRX 500 MHz NMR spectrometer working at 125.577 MHz for carbon-13. $CDCl_3$ served as solvent and TMS as internal standard for all ^{13}C-NMR measurements. Relative peak areas were proportional to the number of carbon atoms. Peak areas were calculated by deconvolution method using WIN-NMR software.

5.3.7. Thermal analysis (TGA, DSC): As discussed in chapter 3.

5.3.8. X-ray analysis: As discussed in chapter 3.

5.3.9 *FT-IR:* IR spectra were recorded as KBr pellets, on Perkin-Elmer Infrared Spectrometer Model 16PC FT-IR, using sodium chloride optics. IR bands are expressed in frequency (cm^{-1}).

5.4. Results and discussion:

5.4.1 Impurity detection and analysis in the L-lactic acid and ethyl L-lactate

5.4.1a L-lactic acid: The total level of impurities in the L-lactic acid 88 % aqueous solution was less than 30 ppm. Only methanol (< 5 ppm), ethanol (< 10 ppm) and acetic acid (< 10 ppm) were found to be present as impurities. Presence of L-lactide was also detected, but its quantification was not attempted because its formation inside the GC column was also possible, since L-LA is a thermally labile material. Some peaks, though with much tailing and disturbed baseline, which eluted after the L-LA remained unidentified. Although pyruvic acid was not found at all in the L-LA sample when injected, it was individually detectable up to the 4-ppm level from its own aqueous solution. So it was thus concluded that pyruvic acid was present in less than 5 ppm level in the L-LA sample and oxalic acid, fumaric acid and succinic acid were found < 5ppm.

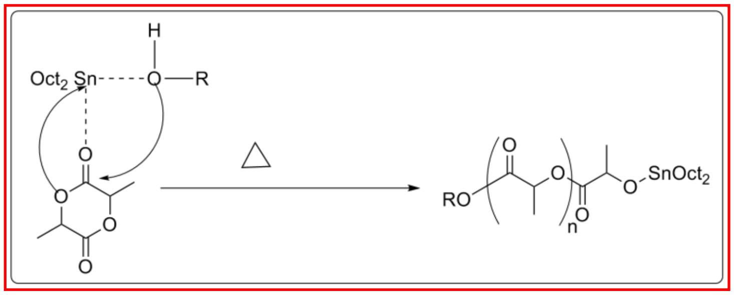
HPLC result shows the quantitative estimation of acid impurities present in L-LA 88 % aqueous solution. The quantitative results showed the presence of oxalic acid (28 ppm), pyruvic acid (174 ppm), acetic acid (1717 ppm) and succinic acid (388 ppm). The other acids for example, citric acid, itaconic acid, acotinic acid, propeonic acid, citraconic acid and buatyric acid are observed below the detection limit. The presence of fumaric acid was 0.6 ppm and other impurity are 6.6 ppm. Methanol and ethanol are observed below the detection limit. The purity (percentage) of L-lactic acid is 97.7 %. The chiral purity of L-lactic acid was examined in 1.5 molar solution of sodium hydroxide using at 20 ^{0}C. The specific rotation was obtained as -14.6.

The LC-MS result showed the presence of CH_3COOH---K^+ (100 Da), Lactoyl lactic acid---Na^+ (185 Da), trimer of lactic acid--- Na^+ (257 Da), trimer of lactic acid---K^+ (257 Da), tetramer of lactic acid- Na^+ (329 Da), pentamer of lactic acid---Na^+ (401), hexamer of lactic acid---Na^+ (473 Da), heptamer of lactic acid---Na^+ (563) and cyclic octameer of lactic acid---Na^+ (597 Da).

5.4.1b. Ethyl lactate: No impurities peaks were found in the ethyl lactate sample when injected (cut off time of 4 min given for ethanol) and there was only a single peak of ethyl lactate in the chromatogram. Impurities with boiling points less than that of ethanol had been removed at the time of removal of ethanol. However, any impurity with a boiling point higher than ethanol should remain in the sample after esterification. But the fact that no impurities were found implied that the peaks found after the L-LA peak during elution of the L-LA aqueous solution sample might be due to small oligomers of L-LA. The detection level of diethyl oxalate, diethyl fumarate and diethyl succinate was about 4 ppm, under the specified condition of anaysis. Thus it can be inferred that these impurities were present in less than 5 ppm concentration in the ethyl lactate sample.

The GC analysis thus could detect only three impurities, namely methanol, ethanol and acetic acid. Traces of L-lactide that was found could be either due to its presence as an impurity in the sample or its formation during the elution through the heated GC column, or both.

5.4.2. Synthesis and characterization of linear PLA oligomers of controlled number average molecular weight and with both carboxylic and hydroxyl end groups: Synthesis, by ROP of L-lactide: $Sn(Oct)_2$-catalyzed (initiated) ROP of lactonic monomers, including L-lactide, in presence of alcoholic coinitiators proceeds via a coordination-insertion mechanism of initiation and propagation.



Scheme 1: Ring opening polymerization of lactide.

In the present work, L-lactide was thoroughly dried under vacuum and all precautions were taken to avoid in trace of moisture during the reactions.[60, 61 , 62] Water was used as the coinitiator, so that carboxylic acid end groups instead of ester end groups as found in the Scheme 1 could be generated at the terminal of each PLA oligomer chain. The number average molecular weight and degree of polymerization M_n and DP_n, respectively, of PLA oligomers thus prepared were calculated as:

$$M_n = ([M] / [I]) \times M_L \times \text{conversion \%} \quad \text{and}$$

$$DP_n = ([M]/[I]) \times \text{conversion \%}$$

Where [M] = moles of monomer, [I] = moles of coinitiator (water) and M_L = molecular weight of L-lactide. Conversion was determined from yield of PLA oligomer.

5.4.3. Determination of molecular weights of oligomers: The achieved degree of polymerization and number average molecular weight was determined from the ratio of integral of the ester carbonyl carbon to that of the carboxylic acid carbonyl carbon in the ^{13}C-NMR spectrum, as shown in fig. 5.2.

Both theoretically calculated and experimentally obtained values of these parameters are organized in the data shown in Table 5.3, where samples 3.1 and 3.2 are the two PLA oligomers synthesized in this procedure with different [M]/[I] ratios and different Sn (Oct)$_2$ concentrations in proportion to the lactide monomer, to obtain oligomers of different degrees of polymerization and hence different number average molecular weights.

The theoretically calculated and experimentally obtained values of these parameters were found to be in very good agreement, thereby indicating successful use of water as a co-initiator in the ROP of L-lactide.

5.4.4. Thermal characterization (DSC) and powder XRD of oligomers: The thermal characterization data (melting point, T_m, and glass transition temperature, T_g) of the two oligomer samples are shown in Table 5.4 as well as in fig. 5.3 Both oligomers had similar values of T_m and T_g effect of DP_n on T_m is also evident from the result. The powder XRD patterns of the two oligomers are shown in fig. 5.4 where it can be found that the two polymers had almost identical patterns, as expected. The crystallinity values of the oligomers calculated from these XRD patterns are shown in Table 5.4 and they were also found to be similar.

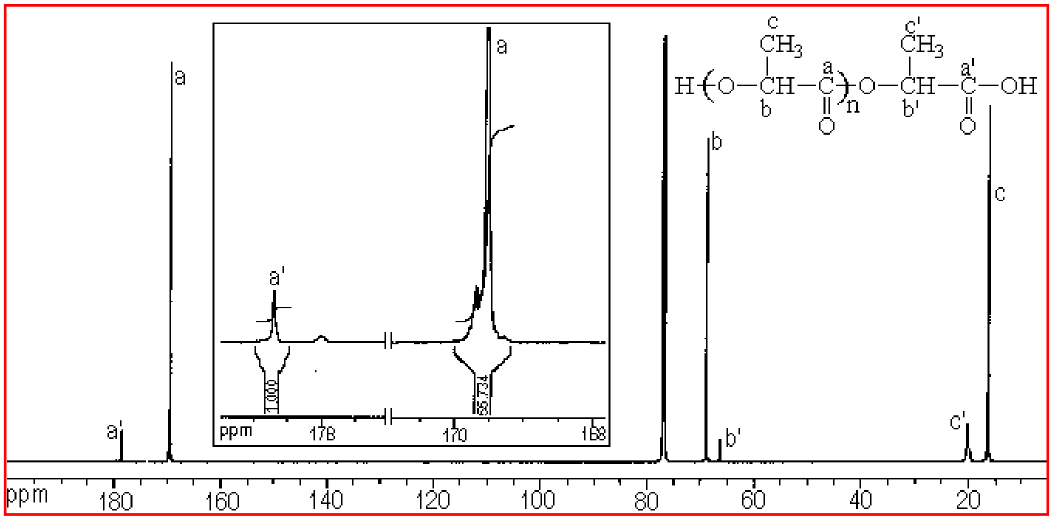


Fig. 5.2: ^{3}C-NMR spectrum of PLA oligomer 3.1 synthesized by ROP of L-lactide: inset showing ester carbonyl region (ester as well as carboxylic acid) as enlarged.

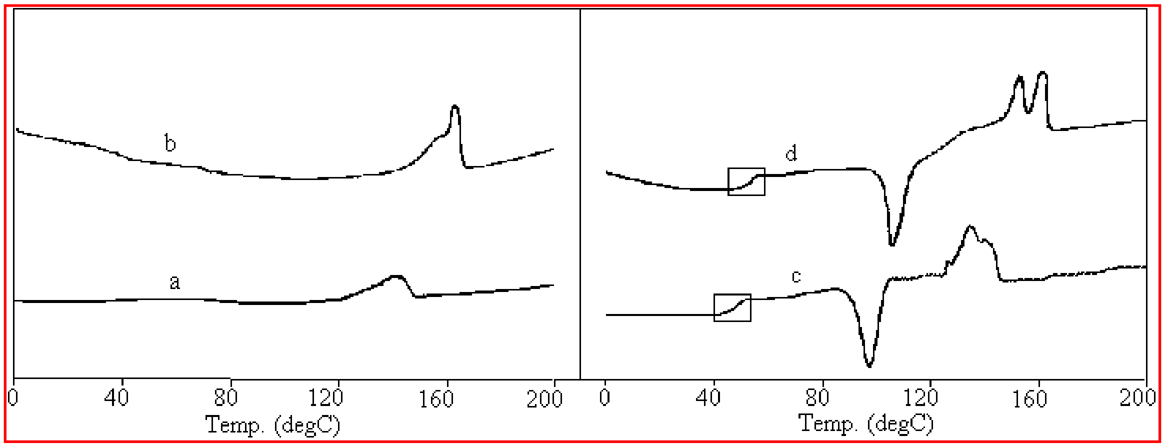


Fig. 5.3: Thermal characterization (DSC) first and second heating showing T_m and T_g, respectively of PLA oligomers: (a) 3.1, first heating; (b) 3.2, first heating; (c) 3.1, second heating and (d) 3.2, second heating.

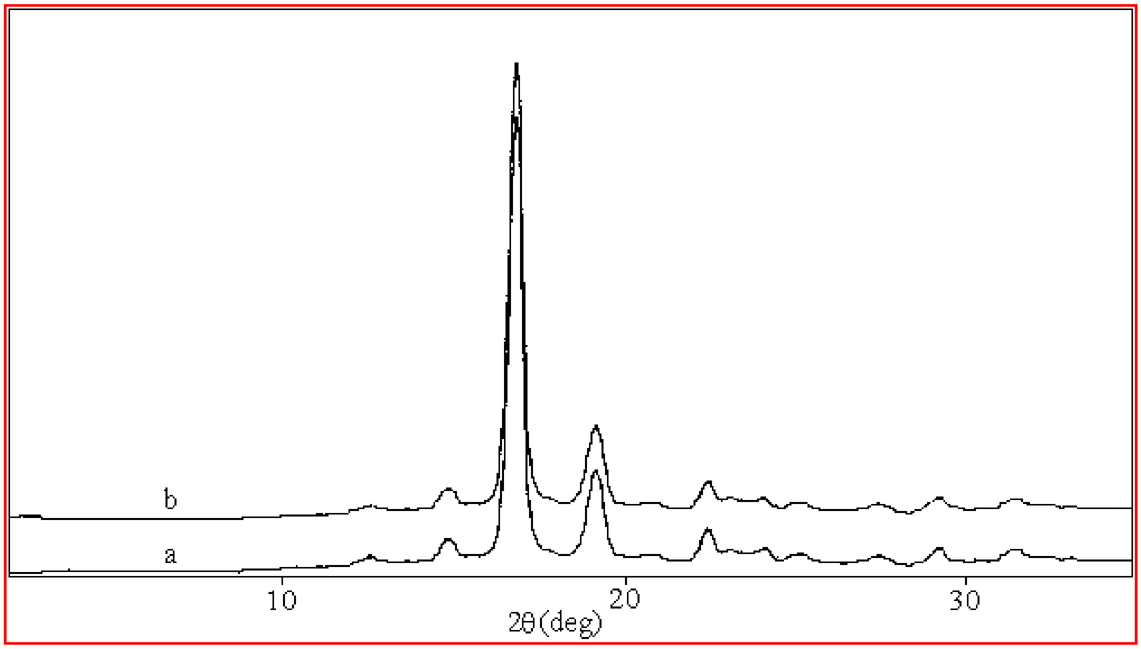


Fig. 5.4: Powder XRD patterns of PLA oligomers: (a) 4.1 and (b) 4.2.

Table 5.3: Number average molecular weights of the PLA oligomers synthesized by ROP of L-lactide with water as co-initiator and Sn $(Oct)_2$ as initiator.

PLA sample	[Lactide]/ [Sn(Oct)$_2$]	[Lactide]/ [H_2O]	Yield (%)	$DP_{n\ Cal}$	$DP_{n\ NMR}$	$M_{n\ NMR}$	$M_{n\ VPO}$
3.1	200	32	86	55	60	4320	4400
3.2	400	45	87	79	77	5544	5692

Table 5.4: Thermal characterization and crystallinity values of PLA oligomers synthesized by ROP of L-lactide.

PLA samples	T_g (°C)	T_m (°C)	ΔH_m ($J.g^{-1}$)	% Crystallinity from powder XRD
4.1	48	141	53.4	85.52
4.2	51	162	59.7	85.73

5.4.5 FT-IR 12- HSA:

Fig. 5.5 A shows FT-IR spectrum of 12-HSA. The peak at 1698 and 3206 cm^{-1} are due to carbonyl and hydroxyl group of 12-HSA. Apart from these peaks there are other peaks at 2849 and 1924 cm^{-1} due to C-H stretch of methane and methyl groups. The cyclized 12-HSA shows fig.5.5 B the disappearance of free carboxylic and hydroxyl groups at 1698 cm^{-1} and 320 cm^{-1} 6 and appears a strong peak at 1759 cm^{-1} due to cyclic ester group.

5.4.6 Procedure for Cyclization 12 HSA:

In a 500 mL, round-bottom, and three necked flask fitted with a condenser was placed a microemulsion consisting of 9.2 mL of H_2O, 84.1 mL of 2-propanol, and 101.3 mL of toluene. This microemulsion was made 8 x10^{-3}M in p-toluenesulfonic acid (Fischer). To the above solution was added an equal volume of a microemulsion of identical composition and 1 x 10^{-2} M in hydroxy acid over a period of 2 hr. After the addition was completed, the resulting mixture was heated at 65 ^{0}C for 12 hr. Removal of the solvent under vacuum afforded a light yellow solid which was crushed with pentane (3x100 mL) and filtered. The pentane solution was extracted with water (25 mL portions) until the water layer was no longer acidic, after which the pentane solution was dried over anhydrous magnesium sulfate. Removal of the solvent under vacuum afforded a light yellow solid. This solid was subjected to preparative layer chromatography or column chromatography with silica gel as solid support and hexane ether as eluent to afford pure lactone and 2-propyl esters which were identified by melting point, TLC, NMR, IR.

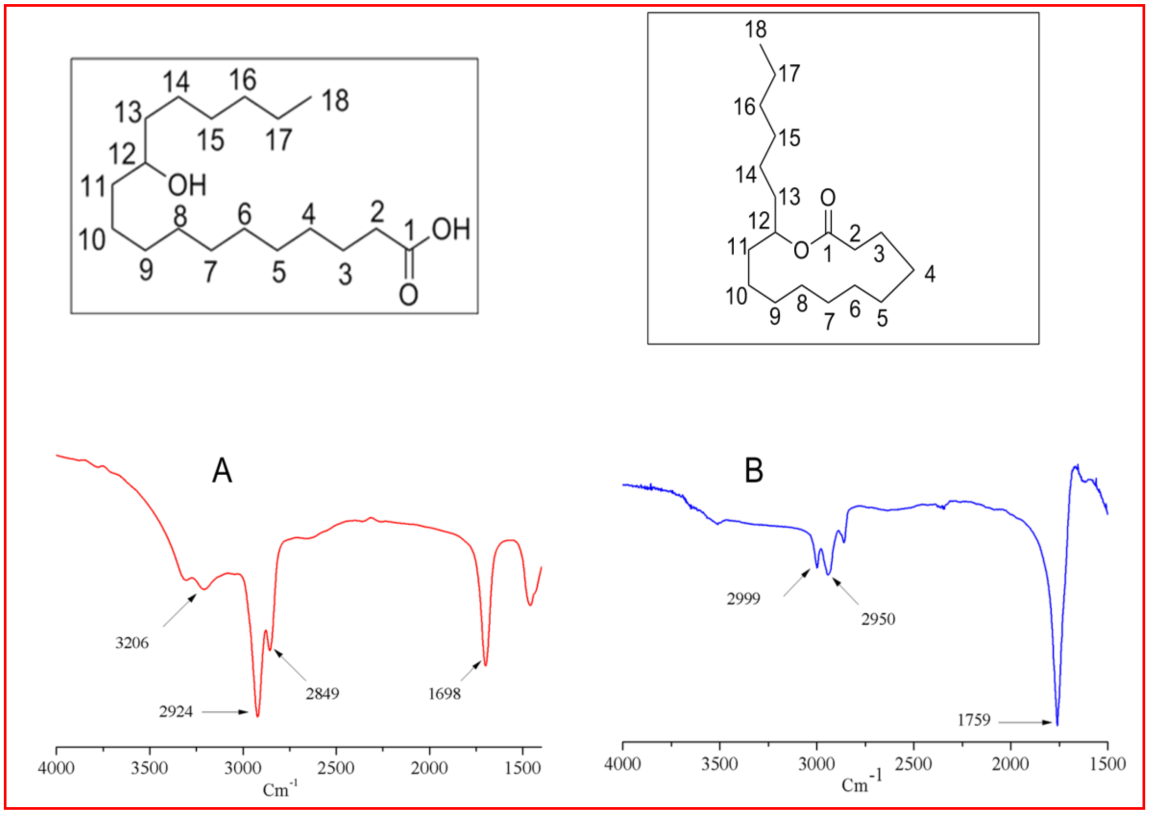


Fig. 5.5: FT-IR Spectra of 12-HSA and cyclic 12 HSA.

5.4.7 ^{1}H-NMR of 12-HSA, Cyclic 12-HSA:

^{1}H-NMR 12-HSA : δ(ppm, $CDCl_3$) 4.05-4.16(m,1H, H-12), 2.31-2.37(t,2H, H-2), 1.25 to 1.65(m,4H, H-11 and H-13,H-17), 0.84-1.209(t,3H, H-18)

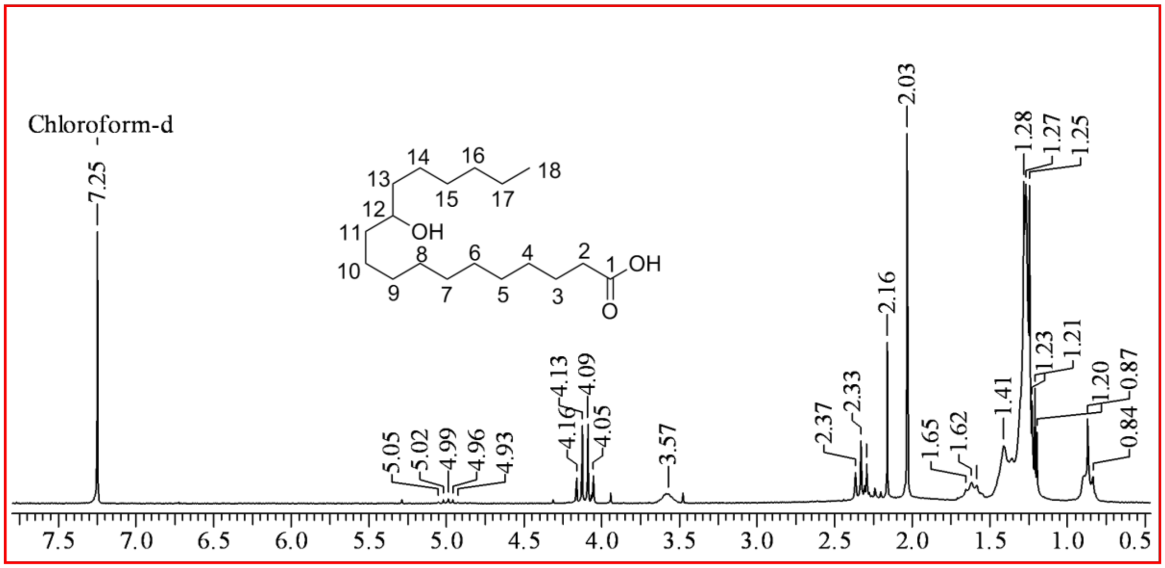


Fig. 5.6: ^{1}H-NMR of 12-hydroxystearic acid.

^{1}H-NMR Cyclic 12-HSA: δ(ppm, $CDCl_3$): 0.88 (t, 3H, H-18), 2.30 -2.40 (t, 2H, H-2), 5.10-5.20(m, 1H, H-12), 1.28-1.65 (m, 4H H-11, H-13, H-17) , 1.28 methylene

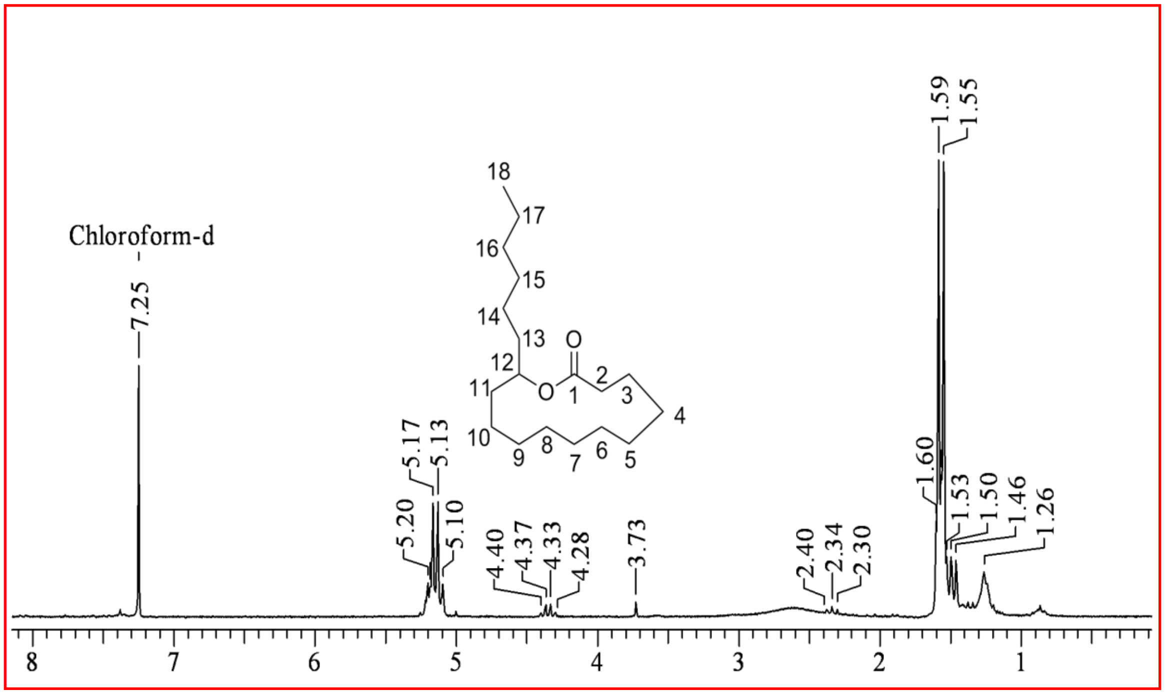


Fig. 5.7: ^{1}H-NMR OF cyclic 12-HSA.

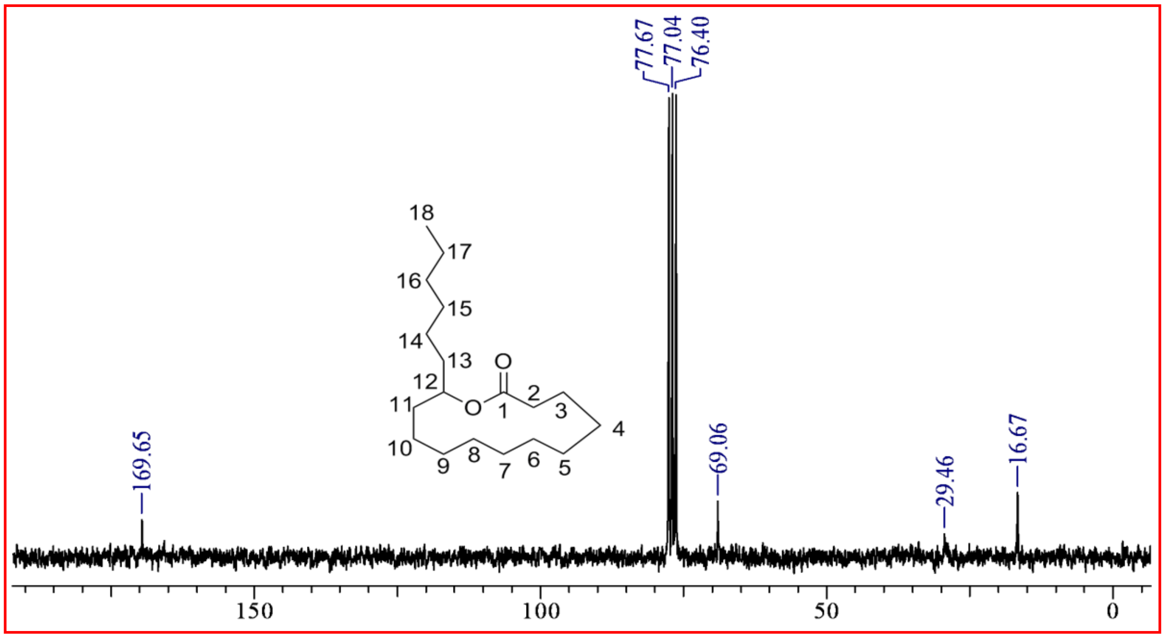


Fig. 5.8: ^{13}C-NMR of cyclic 12-HSA.

Characteristics ^{13}C-NMR Cyclic 12-HSA δ (ppm, $CDCl_3$). 169.65 (ester carbonyl), 69.06 (methine carbon i.e. - CH-), 29.46 and 16.67 (CH_2 and CH_3 carbon)

5.4.8 Synthesis of poly(12-HSA) homopolymer:

0.5 g (0.00177 moles) of cyclic 12-HSA and 0.00375 g (1x10^{-5}moles) solid modified tin catalyst were melted together dipping inside the sand bath after sealing the reactor. The glass reactor was previously passivated using 30% trimethyl silyl chloride in acetone, dried at 150 ^{0}C in an oven, cooled under dry argon atmosphere. The reaction mixture along with catalyst was inserted and vacuum was applied for several hr to remove traces amount of moisture. The reactor containing reaction mixture was sealed under vacuum. The reaction mixture was heated at three different temperatures i.e. 180, 200 and 220 ^{0}C respectively and polymerization was carried out for 1 hr. All polymers were transparent, colourless and viscous liquid, soluble in chloroform and methanol.The monomer and polymer being soluble in the same (both chloroform and methanol), any residual monomer couldnot be separated and homopolymer in this form was subjected to analysis.

Table 5.5: Homopolymers of Cyclic 12-HSA (12-Hydroxystearic acid) using cloisite modified catalyst (0.75wt %)

Polymer	Mole ratio (LA: C12-HSA)	Time (hr)	Temp (^{0}C)	M_n	M_w	PDI
HP-1	0:100	1	180	1097	2229	2.03
HP-2	0:100	1	200	1120	2290	2.04
HP-3	0:100	1	220	1160	2380	2.05

Table 5.6: Copolymers of Cyclic 12-HSA (12-Hydroxystearic acid) using cloisite modified catalyst (0.75wt %)

Polymer	Mole ratio (LA: C12-HSA)	Time (hr)	Temp (^{0}C)	M_n	M_w	PDI
COP-1	95:5	1	180	2191	5217	2.38
COP-2	85:15	1	180	1530	2570	2.40
COP-3	80:20	1	180	1169	1900	1.62
COP-4	60:40	1	180	1148	2380	1.48
COP-5	50:50	1	180	1129	1930	1.71

LA- L-Lactide, C12-HSA – Cyclic 12-Hydroxy stearic acid

5.4.9 Protection of aleuritic acid and cyliclization of protected aleuritic acid:

Camphor sulphonic acid was added at room temperature to a mixture of erythro-aleuritic acid and benzaldehyde dimethyl acetal. After reaction mixture has been stirred for 5 hr at 60 ^{0}C and 10 hr at room temperature, triethylamine was added. The reaction mixture was concentrated by evaporation of the solvent. The crude product was purified by column chromatography to get protected aleuritic acid as colourless oil.

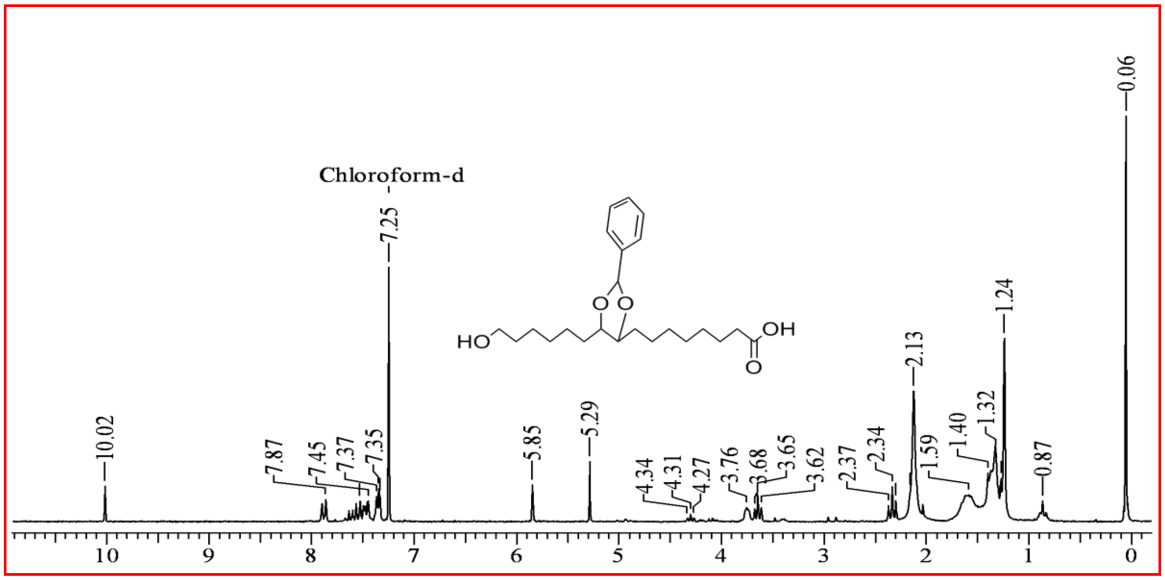


Fig. 5.9: ^{1}H-NMR of protected aleuritic acid.

^{1}H-NMR protected aleuritic acid: δ(ppm, $CDCl_3$), 3.76 (s,1-H), 3.62-3.68 (t,2H), 4.27-4.34(q,1H), 5.85 (s,1H), 2.34-2.37 (t,2H), 7.35-7.87, (m, due to aromatic protons).

5.4.10 Cyclization and polymerization of protected aleuritic acid:

The protected erythro-aleuritic acid (scheme 2) was dissolved in water and acetic acid. After having been stirred for 24 hr at room temperature, solid sodium hydrogencarbonate was added to the reaction mixture and the it was further stirred for 10 hr at 0 ^{0}C. The mixture was extracted with ethyl acetate and after evaporation of solvent compound is purified by coloumn chromatography.

Polymerization of protected aleuritic acid: Protected aleuritic acid and catalyst stannous stearate was taken into ampoule and procedure followed as discussed in 5.4.8

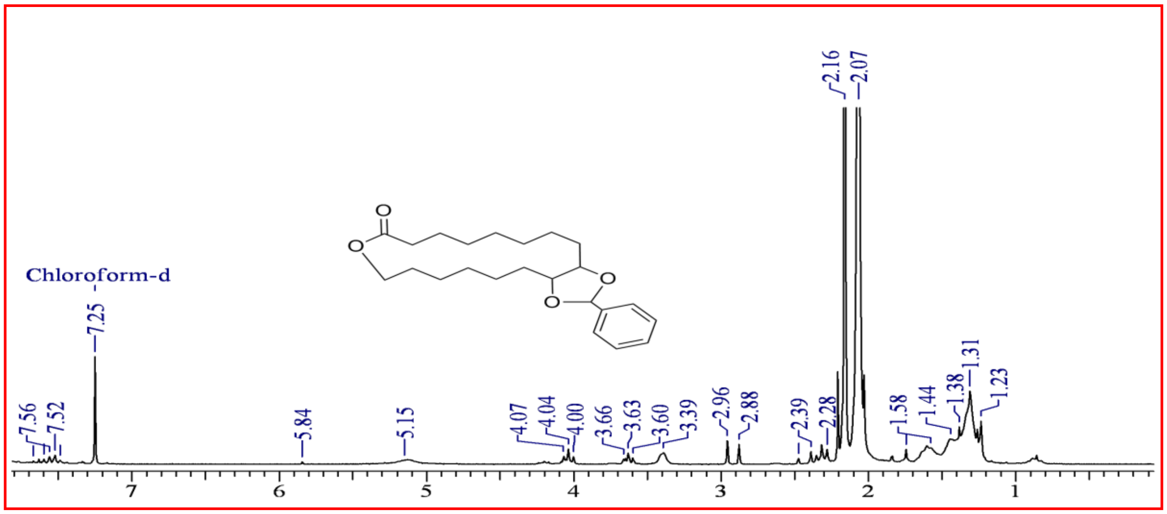
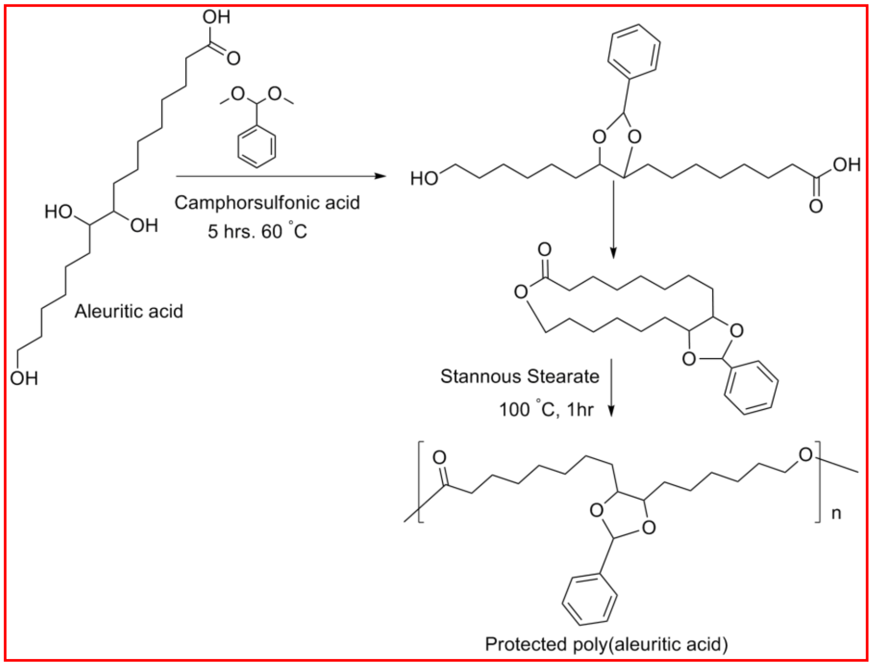


Fig. 5.10: ^{1}H-NMR of protected aleuritic acid lactone.

^{1}H-NMR: δ(ppm, $CDCl_3$), 7.52-7.56, (m, 5H), 5.84 (s, 1H), 4.00-4.07 (t, 2H), 3.39-3.66(q, 1H), 2.28-2.4 (t, 2H), 1.23-2.16 (m, due to methylene protons).



Scheme 2: Protection, cyclization and polymerization of aleuritic acid.

5.4.11 Determination of molecular weights of oligomers: The SEC elugram of the poly(aleuritic acid) polymer sample was shown in fig. 5.11. Molecular weight data correspond to polystyrene standards, with a refractive-index detector, and so are only apparent values. The number average molecular weight (M_n) and weight average molecular weight (M_w), PDI is recorded 2429 and 2933, 1.20 respectively. Fig. 5.11 shows GPC curve for polyaleuritic acid.

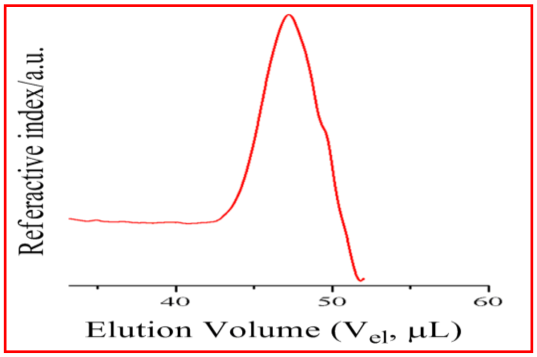


Fig. 5.11: GPC curve for protected poly (aleuritic acid).

5.5 Conclusion:

The impurities present in the L-Lactic acid were determined using HPLC technique. Poly(L-Lactic acid) was prepared using dehydro polycondensation. The structure of the polymer was confirmed by ^{1}H-NMR. The thermal properties and crystallinity were studied using DSC and XRD techniques. L-Lactides were prepared controlling temperature and vacuum. The L-Lactide was crystallized using ethyl acetate and finally recrystallized once again using dry toluene. The ROP of L-Lactide was also carried out and the polymer was characterized.

12-Hydroxy stearic acid (12-HSA) was used as a precursor for cyclic compounds of 12-HSA using literature procedure. The cyclic compound was characterized using mass spectra, ^{1}H and ^{13}C-NMR and the cyclic structure was confirmed. The homopolymers and copolymers with L-Lactide were prepared. The highest molecular weight in case of homopolymer was obtained as 2380 Da at 220 ^{0}C, reaction time 1 hr using cloisite modified tin catalyst. In case of copolymers the copolymer (95:5) showed maximum molecular weights i.e. 5200 Da. As the comonomer (cyclic 12-HSA) increased the molecular weight decreases with narrow distrubition. These results may be attributed to transesterification reaction.

Aleuritic acid was polymerized after protecting 9, 10 hydroxy groups using Dehydropolycondensation method. Here the cyclic compound of protected aleuritic acid was prepared, characterized by mass, ^{1}H and ^{13} C-NMR and the structure was confirmed. The ROP of cyclic aleurate was carried out using stannous stearate. The M_n, M_w and distribution 2420, 2933 and 1.20 respectively.

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CHAPTER - 6

CHAPTER- 6: SYNTHESIS AND CHARACTERIZATION OF PLA BASED ESTER-URETHANE, ESTER-ESTER AND ESTER-CARBONATE LINKAGES

6.1 Introduction:

Polyurethanes form a class of industrially useful materials because of their excellent properties. An isocyanate terminated prepolymers which are often reacted with diols,[1] diamines[2] and water.[3] Hydroxyl terminated polyesters[4, 5]are also starting material for many of the urethane polymers. A new kind of bio-based thermoplastic polyurethane based on PLA and poly(tetramethylene) glycol segments via chain-extension reaction of dihydroxyl terminated copolymer using hexamethylene diisocyanate (HDI) as a chain extender. Polydiols were synthesized through polycondensation of lactic acid and poly(tetramethylene) glycol in bulk.[6]

Polyurethanes have found a number of useful industrial applications in diverse areas such as coatings, adhesives, sealants, defoamers, and textile dyes.[7, 8, 9, 10, 11, 12, 13, 14, 15] In this area, biodegradable polymers such as polylactide, polycaprolactone, polycarbonate, poly (amino acid) have found interesting uses in biomedical application area such as drug delivery, stent, packing materials because of their relatively good mechanical properties, biodegradability and biocompatibility.[16, 17, 18, 19, 20]

PLA oligomers were prepared and converted into polyurethane with the addition of isocyanates.[21] Harkonen et al.[22] reported the synthesis of similar polyurethane’s with the treatment of a PLA polyol prepolymer with HDI in an inert atmosphere, but no exact description of the procedure has been given. Zhang et al.[23] had mainly used HDI and toluene diisocyanate (TDI) with PLA in solutions for 10-13 hr and/or some day at high temperatures and obtained yellow, stiff and fragile foam. Controlled release materials for urea are prepared by spray coating Urea granulates with lactic acid based homo- and co-polymers solutions.[24]

Borda et al.[5] showed that Stannous Octoate is better catalyst so far in comparison with other catalysts in ROP of lactones. However, it has certain drawbacks: (i) Stannous Octoate is a viscous liquid and its quantitative addition for homogeneous mixing in the reaction is achieved through dilution with some solvent (ii) As such Stannous Octoate allows the formation of some amount of octanoic acid during storage time. (iii) During reaction, Octanoic acid reacts with isocyanate group and forms amide linkage. Again, the formation of tin hydroxides, stannoxane is unavoidable when water is present or formed during reaction process. (iv) It has also been reported that the catalyst was effective for the polyurethane formation at 120 ^{0}C. The reactive species might be SnO in stead of Sn (II) 2-ethylhexanoate. (v) $Sn(Oct)_2$ based catalyst is a complex dynamic system which responds to all changes of the reaction condition by a change of structure and concentration of the active species.

Therefore, we have prepared tin modified solid cloisite catalyst for the first time to overcome all these above mentioned encountered problems. The catalyst structure is cyclic and its presence within the foam matrix will give a harder, more thermally stable structure. It is also well documented in the literature report that cyclic structure within the foam matrix is harder, more thermally stable structures. Poly (D, L-lactic acid) had been found to be amorphous in nature and contained both hydroxyl and carboxyl as the end groups. Therefore, both urethane and amide linkages had been observed.**[5]**

The literature report reveals that the mechanical properties are influenced by the functionality and the molecular architecture. Therefore, hydroxyl terminated Poly (L-Lactic acid) (PLA) oligomers were prepared from L-lactic acid and 2, 5-hexane diol using dehydropolycondensation method. Hydroxyl and carboxyl terminated PLA oligomers were also prepared using ring opening polymerization of L,L-lactide using stannous octoate as a initiator and water as a coinitiator.

The elastomeric properties of these materials are derived from the phase separation of the hard and soft copolymer segments of the polymer, such that the urethane hard segment domains serve as cross-links between the amorphous polyester soft segment domains.

The choice of chain extender, 2, 5 hexane diol behaves as soft segments in polyurethane polymers. The hard segments, which are formed from the isocyanate, L-lactic acid and chain extenders, are stiff and immobile, covalently coupled to the soft segments (2, 5 hexane diol), inhibit plastic flow of the polymer chains, thus creating elastomeric resiliency. The polyester urethane prepared by us can certainly contribute better mechanical properties such as high tensile strength, elongation, and tear resistance values according to its molecular architecture.

Literature report reveals that upon mechanical deformation, a portion of the soft segments are stressed by uncoiling, and the hard segments become aligned in the stress direction. This reorientation of the hard segments and consequent powerful hydrogen bonding contributes to high tensile strength, elongation, and tear resistance values.

Since there is no detailed study of polylactic acid esterurethane linkages reported in the literature, therefore we report the synthesis of a series of novel biocompatible and biodegradable poly (esterurethane) s (PEU) via *in-situ* melt polymerization of hydroxyl terminated poly(lactic acid) (diol) using tin modified solid cloisite-30B catalyst. PLA oligomers (containing both hydroxyl and carboxylic groups) and various isocyanates such as toluenediisocyanate (TDI), 4, 4'methylenebis (cyclohexyl diisocyanate) (HMDI), 4, 4'methylenebis (phenyl diisocyanate (MPDI), hexamethylene diisocyanate (HDI) were reacted to obtain polyesterurethane linkage. The effect of reaction temperature, time and novel cloisite modified catalyst were discussed. The present study will focus a better understanding of the synthesis of biodegradable and biocompatible polyurethane materials with improved properties, making them widely applicable.

High molecular weight lactic acid based polymers synthesized via hydroxyl terminated telechelic prepolymer using methylene diphenyldiisocyanate. All polymerizations have been carried out in the melt, using tin octoate as catalyst. With the increase in diisocyanate concentration, an increase in the T_g, M_w and was observed.[25]

A new kind of biodegradable polymers synthesized using ε-PCL, ethyleneglycol and isophorone diisocyanate.[26]

A high molecular weight biodegradable lactic acid polymer was successfully synthesized in two steps. First, the lactic acid monomer was oligomerized to low molecular weight hydroxyl-terminated prepolymer; the molecular weight was then increased by chain extension using 1,6-hexamethylene diisocyanate as the chain extender.[27, 28] Multiblock poly(ether ester urethane)s comprising of poly(lactic acid) poly(ethylene glycol) and poly(propylene glycol) segments were synthesized, and their aqueous solutions exhibited thermogelling behavior at critical gelation concentrations ranging from 7 to 9 wt%.[29, 30, 31]

Cooper T. et al. have synthesized linear poly(lactic acid) possessing a pendent carboxylic acid group via ROP of L- or D,L-lactide using bis(hydroxymethyl) butyric acids initiator and stannous octoate as catalyst (0.03wt%). Polymerizations were typically conducted in the bulk for similar to 3 hr at 130 ^{0}C.[32] Linear poly(urethane urea) containing a biodegradable soft segment and a hard segment built solely from methyl-2,6-diisocyanatehexanoate (LDI) where no chain extender is required. By having LDI in excess, together with a soft segment, and adding water in the vapor phase continuously creates amines insitu resulting in hard segments containing multiple LDI units linked via urea linkages. With a hard segment content between 12% and 18%, all of the materials showed very high elongation at breakage, ranging from 1600% to 4700%, and an elastic modulus from 2.1 to 140 MPa.[33]

Lactic acid polymers were synthesized from oligomers by the addition of highly reactive 1, 6- HMDI and 2,2'-bis(2-oxazoline) as chain extenders. The effects were studied of adding the extenders simultaneously and sequentially and in different amounts.[34] And the hydrolysis behaviour of these of lactic acid based poly(ester-urethane)s has been studied in a buffer solution of pH 7.00 at 37 and 55 ^{0}C. In the hydrolysis study, the effect on the hydrolysis rate of different stereo structures (different amount of D-units in the polymer chain) and the length of the ester units have been studied.[35] A series of polyurethane nanocomposites were synthesized from thermoplastic polyurethanes and two types of organically modified montmorillonites (OMMT) – Cloisite-10A and Cloisite-20A. It has been proven that the thermal stability and tensile properties of these new systems were higher when the organoclay was present within the polymer matrix. Moreover, these properties depend on both the OMMT loading and the type of gallery cations of the organically modified montmorillonites.[36]

Copolyesters of glycolic acid combined with sebacic acid and ethylene glycol have been synthesized in different molar ratios and their hydrolytic degradation was studied and correlated with their structures.[37] Hydroxyl functioned polyester synthesized from natural polyols and sebacic acid. Amphiphilic hydroxyl functioned polyester (HFP) can be used as compatibilizers for blends of starch and resins.

HFPs developed by condensation method by removal of water under N_2 atmosphere in the presence of dehydrative condensation catalyst used.[38] A novel injectable thermogelling poly(ester-anhydride) copolymer, methoxy poly(ethylene glycol) poly(sebacic acid-D,L-lactic acid)-methoxy poly(ethylene glycol) triblock co-polymer, was prepared by melt-condensation polymerization.[39] An injectable material for drug delivery a soft thermogel of poly(ethylene glycol)-sebacic acid polyester was synthesized. The polymer aqueous solution (25 wt%) undergoes 'clear sol-to-gel' transition as the temperature increases from 5 to 65 ^{0}C.[40]

Opaprakashit P. et al. synthesized lactic acid-based aliphatic/aromatic copolyesters using lactic acid dimethyl terephthalate and various diols by polycondensation technique. Effects of diol lengths and comonomer feed ratios on structure and properties of the resulting copolymers are investigated. Result showed an increase in diol length results in an increase in the copolymers molecular weight, and a decrease in T_g, T_m and crystallinity.[41]

Random copolymers of trimethylene carbonate (TMC) and ε-CL have been synthesized by ROP of TMC and CL in the presence of stannous octoate. The results showed that the molecular weight of the copolymers decreased with increasing ε-CL content and then increased. The decrease in the reaction temperature, polymerization time and catalyst content would increase the molecular weight of the copolymers.[42] The bioresorbable new terpolymers of L-lactide, glycolide, and trimethylene carbonate have been synthesized via ROP reaction of the cyclic monomers using Stannous octoate as initiator The glass transition temperature of the terpolymers changed from 33 to 51 ^{0}C with various compositions.[43]

The ROP of TMC initiated by water or n-pentanol and catalyzed by trifluoromethanesulfonic acid (HOTf) and methanesulfonic acid (MSA) has been investigated.[44] The copolymerization of trimethylene carbonate (TMC) and L-lactide (LLA)[45, 46] has also been carried out to improve the flexibility of PLA. The results showed that the composition of the copolymer is nearly the same as that in the feeding dose, and the molecular weight of the copolymer decreased with increasing TMC content. The decrease in the reaction temperature and polymerization time are able to increase the molecular weight, but the composition deviates from the feeding ratio.[47]

A series of bioresorbable polymers have been prepared by ROP of L-lactide DL-lactide, ε-CL) and TMC, using low toxic zinc lactate as catalyst.[48] Copolymer constituted by hard blocks of polyglycolide and soft segments derived from the copolymerization of glycolide and trimethylene carbonate was investigated because it is one of the most widely used for bioabsorbable surgical sutures.[49] **P**oly(5-methyl-5-methoxycarbonyl-1,3-dioxan-2-one-co-D,L-lactide) copolymers were synthesized by ROP. The results show that the yield and molecular weight of copolymers are significantly influenced by reaction conditions.[50]

New terpolymers of L-lactide, glycolide, and trimethylene carbonate with different compositions have been synthesized by ROP using zirconium (IV) acetylacetonate as initiator. The glass transition temperature of the terpolymers changes with various compositions from 12 to 42 ^{0}C. Terpolymers with high L-lactide content show a glass transition in the range of 38-42 ^{0}C.[51] Agarwal et al. have reported polymerization of TMC and its copolymerization with LA using the SmI2/Sm initiator. The reactions were carried out at different temperatures to optimize the reaction conditions.[52]

6.2 Materials and Methods.

4,4' Methylenebis(phenyldiisocyanate) (98%) , Toluene 2,4-diisocyanate, (95%), 4, 4' methylene biscyclohexyl isocyanate, (90%) , $Sn(Oct)_{2,}$ (95%) , Ph_4Sn(97%), Dibutyltin oxide (98%) were procured from Aldrich. Hexamethylene diisocyanate, (98%) and Cloisite-30B were purchased from Southern Clay respectively. L-lactic acid and L, L-lactide (purity higher than 99.5%) (prepared as per chapter no 5), 5, 5-Dimethyl-1, 3-Dioxan-2-one (Alfa Aesar), Terephthalic acid (Sigma Aldrich) All the materials were used without further purification. Polylactic acid was prepared condensation technique.

6.2.1 Synthesis and characterization of linear PLA oligomers of controlled number average molecular weight and with both carboxylic and hydroxyl end groups:

In a reactor vessel of glass, passivated using trimethylsilylchloride and fitted with a Dean and Stark type condenser, L-lactic acid (20 g, 0.196 M), as 88 % aqueous solution obtained from PURAC, xylene and tetraphenyl tin as catalyst.

6.2.2 Synthesis of diol-ended telechelic PLA Prepolymers:

In a reactor vessel of glass, passivated using trimethylsilylchloride and fitted with a Dean and Stark type condenser, linear PLA oligomers and 2,5-hexanediol were simultaneously with p-xylene for 6 hr and cooled to 50 °C under argon atmosphere, following which tetraphenyltin 0.2 wt% was added and refluxed in p-xylene for 15 hr. The xylene was finally evaporated and obtained polymer was dissolved in DCM (50 mL), precipitated into petroleum ether (250 mL), filtered, washed with petroleum ether and dried under reduced pressure at room temperature, and characterized.

6.2.3 Synthesis of clay modified catalyst: As discussed in chapter 3

6.2.4 Preparation of poly esterurethanes (PEU): The reaction of hydroxyl terminated PLA with isocyanates was performed in a two-necked reactor equipped with a reflux condenser, a stirrer. The reaction was carried out over the blanket of nitrogen atmosphere. The hydroxyl terminated PLA, equivalent amount of isocyanates and the modified clay catalyst were mixed thoroughly at requisite temperature and reaction time. The completion of the reaction was monitored by GC and IR. The optimum reaction time was found to be 0.5 hr. Therefore, all the ester-urethane reactions were carried out for 0.5 hr.

6.3 Analysis:

6.3.1 Molecular Weights: As discussed in chapter chapter 5.

6.3.2 NMR: As discussed in chapter 5.

6.3.3 Thermal Analysis: As discussed in chapter 5.

6.3.4 X-Ray Analysis: As discussed in chapter 5.

6.3.5 MALDI-TOF MS Analysis: As discussed in chapter 3.

6.3.6 Transmission Electron Microscopy Analysis (TEM): As discussed in chapter 3

6.4 Result and discussion:

Hydroxyl ended telechelic PLA polymer was prepared by dehydropolycondensation of L-lactic acid with 2, 5-hexane diol in presence of tetraphenyltin using xylene at 144 ^{0}C. The product was purified, characterized and used for the synthesis of PLA-based esterurethanes. The other telechelic PLA polymer was also prepared using stannous octoate as an initiator and water as a coinitiator by ROP method. To support the structure and functionality of the telechelic PLA polymer formed by dehydropolycondensation and ROP techniques, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR, GPC, DSC and XRD characterizations were performed. The results confirmed the desired structure and functionality of the telechelic PLA polymers which are the precursor of linear PLA-based ester-urethanes.

The reaction products of the hydroxyl terminated telechelic PLA polymers were shown in Scheme 1.

6.4.1 Synthesis of diol-ended telechelic PLA prepolymer **:**

Diol-ended telechelic PLA prepolymer was obtained from L-lactic acid and 2, 5-hexanediol (HDO) by polycondensation technique using xylene as a solvent and tetraphenyltin as a catalyst. ^{1}H-NMR (500 MHz,): δ (ppm, $CDCl_3$ at 7.25) 5.20 – 5.05 (qt, CH-a attached to ester in the repeating unit, extra shoulders due to different environments and/ or different degrees of polymerization), 4.65 – 4.60 and 4.55 (m and m, CH-b attached to ester, different environments), 4.25 – 4.12 (m, CH-b attached to terminal hydroxyl and CH-b attached to penultimate ester linkage, for those chains where HDO was at the end), 4.36 – 4.29 (qt, CH-a attached to terminal hydroxyl), 1.87 – 1.78 (m, CH_2-CH_2 due to HDO), 1.61 – 1.49 (d, CH_3-a), 1.22 – 1.49 (double d, CH_3-b + CH_3-b′). The diol-ended PLA telechelic was confirmed by ^{1}H-NMR (500 MHz) spectrum alone.

6.4.2 Determination of molecular weights of Oligomers:

Number average molecular weights of these oligomers were also determined by vapor pressure Osmometry (VPO). Both theoretically calculated and experimentally obtained values of these parameters are organized in the data shown in Table-6.1**(**where samples 1 and 2 are the two PLA oligomers synthesized in this procedure with different [M]/ [I] ratios and different Sn $(Oct)_2$ concentrations in proportion to the lactide monomer, to obtain oligomers of different degrees of polymerization and hence different number average molecular weights.

Table 6.1: Number average molecular weights of the PLA oligomers synthesized by ROP of L-lactide with water as co-initiator and $Sn(Oct)_2$ as initiator

PLA sample	[Lactide]/ [$Sn(Oct)_2$]	[Lactide]/ [H_2O]	Yield (%)	$DP_{n\ Cal}$	$DP_{n\ NMR}$	$M_{n\ NMR}$	$M_{n\ VPO}$
1	200	32	86	55	60	4320	4400
2	400	45	87	79	77	5544	5692

The OH end group concentration of the telechelic PLA prepolymer was determined by ^{31}P-NMR (shown in fig. 6.1**)** was found to be 2.49 x 10^{-3} M/g, and the number average molecular weight was calculated as 820, which matched closely with the values determined by SEC, as shown in Table 6.2.

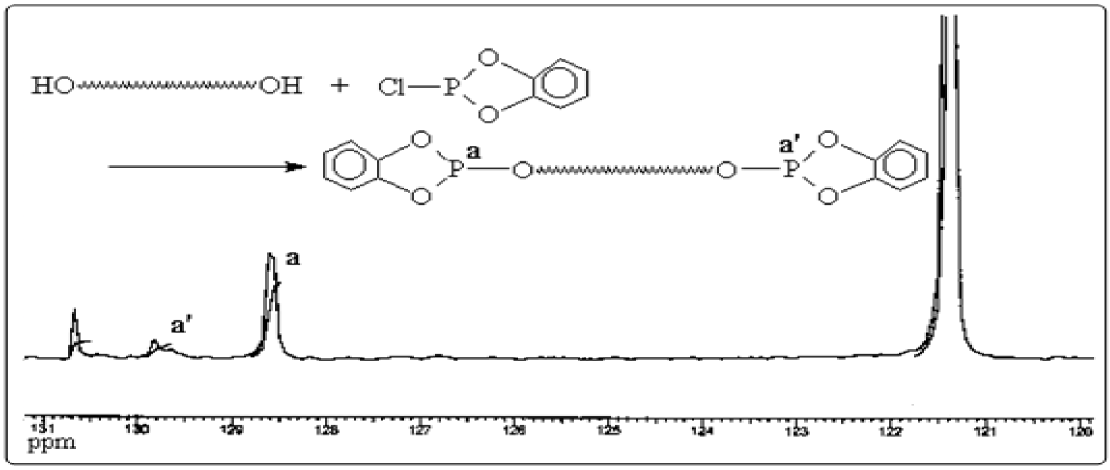
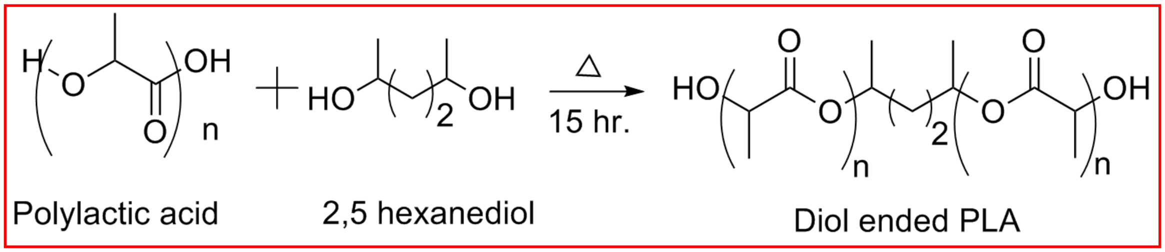


Fig. 6.1: ^{31}P-NMR spectrum of the diol-terminated telechelic PLA.

Table 6.2: Results of Characterization of the Diol-ended PLA Telechelic Prepolymer

Oligomer Type	Synthesis Method	[η] (dL/g)	M_n (NMR)	M_n (VPO)	M_w (SEC)
Telechelic	Dehydropolycondensation of LLA with 2,5 hexane diol, HDO	0.085	820	830	1200

The telechelic PLA prepolymer was prepared form dehydropolycondensation of L-lactic acid (LLA) in presence of small amount of 2, 5-hexanediol, so that both ends of the telechelic contained similar, secondary hydroxyl groups as shown in Scheme 1. The M_n= 4300 and 5500 was used as a starting material for the preparation of ester urethane linkage. The polymerization procedure and characterizations such as ^{13}C-NMR, DSC, XRD were described in chapter no 5



Scheme 1: Synthesis of diol-ended PLA telechelic prepolymer.

All four types of diisocyanates i.e. toluene diisocyanate (TDI), bis (cyclohexyl diisocyanate), (HMDI), 4, 4’ methylene (phenyl diisocyanate) (MPDI) and hexamethylene diisocyanate (HDI) (fig. 6.2) and their reaction products of the hydroxyl terminated telechelic PLA polymers were shown in scheme 2. These products were soluble mostly in all chlorinated solvents. The dynamic light scattering measurements showed no particles larger 3nm. The results clearly focus the complete dissolution of the urethane polymers.

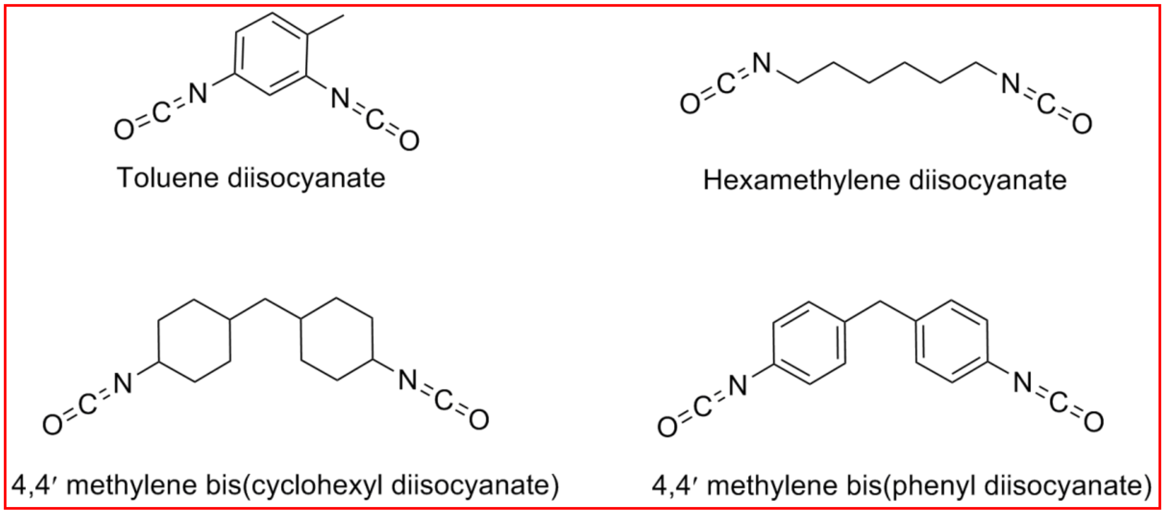
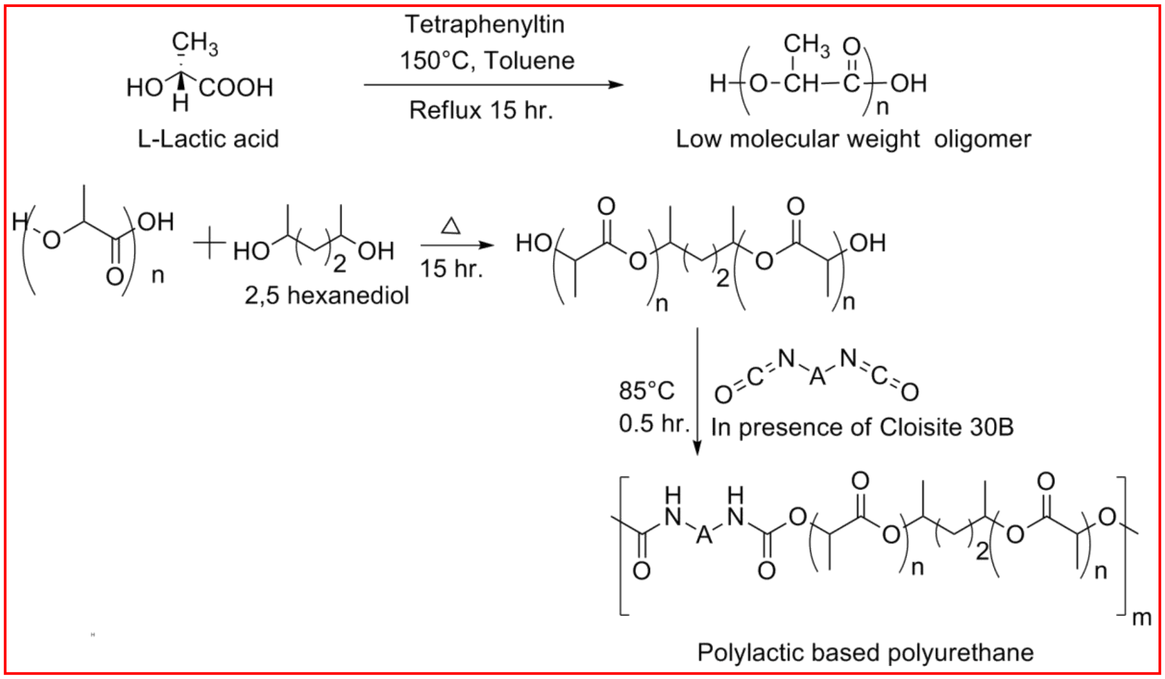


Fig.6. 2: Structures of isocyanates.



Scheme 2: Synthesis of ester-urethane linkage by degydropolycondensation.

6.4.3 Infra Red Spectroscopy(IR):

The IR investigations of TDI and all three products the PLA-TDI, PLA-HMDI, and PLA-MPDI) reactions were shown in fig. 6.3(a-d) and the spectra confirmed the completion of the reaction.

The infrared spectra of the poly(L-lactic acid) polymers showed characteristic absorption bands around 3400cm^{-1} (v_{OH}), 1740 cm^{-1}($v_{C=O}$) and intense absorption at 1100 cm^{-1}(v_{C-O}). fig. 6.3a showed the peak at 2266 cm^{-1}which is a characteristic peak of –N=C=O group. The disappearance of the peak at 2266 cm^{-1} due to –N=C=O group occurred in all the three respective spectra fig. 6.3(b**,** c and d) and the peaks due to esterurethane linkage appeared.

The structures of the prepared polyesterurethanes were established by studying their IR spectra. The infrared spectrum of the polyesterurethane (fig. 6.3 b, c, d) showed characteristic absorption bands around 3400 cm^{-1}(V_{NH}) and an intense absorption at 1100 cm^{-1}(v_{C-O}). The carbonyl absorption appeared as a strong band at 1740 for ester group.

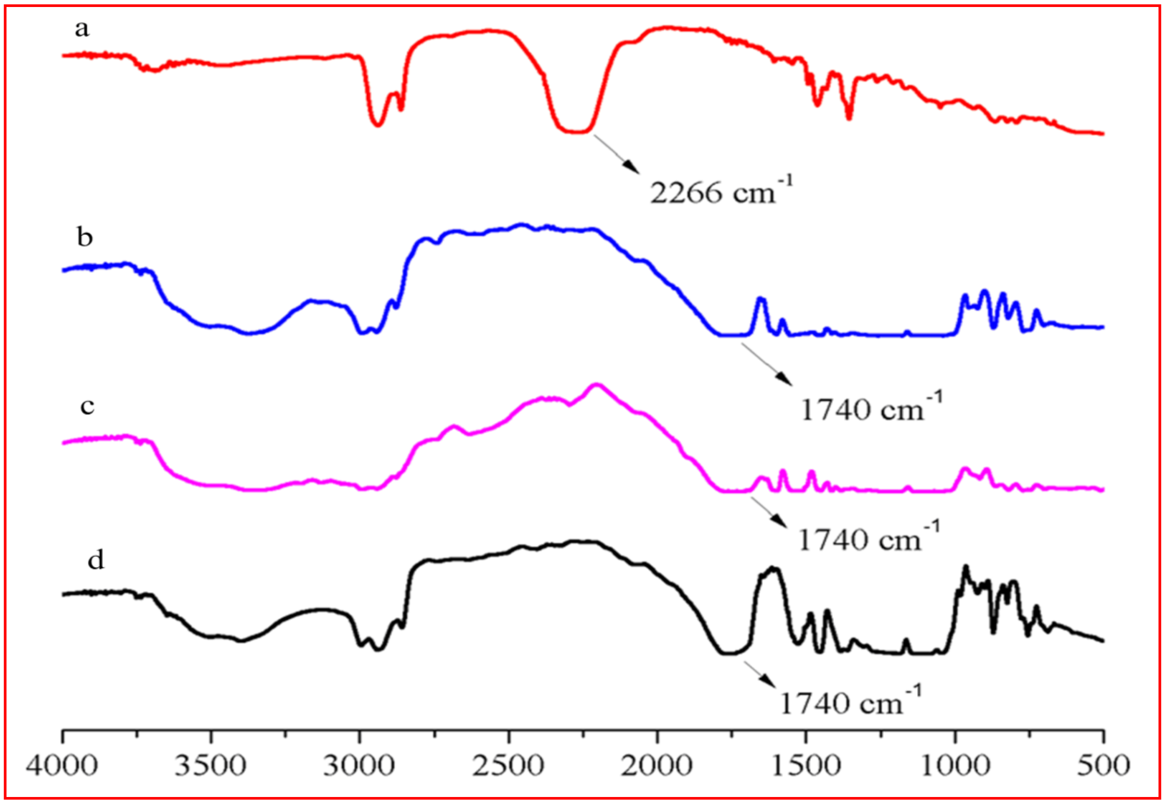


Fig. 6.3: Characteristic IR spectrum of the products obtained ; (a) TDI, (b) PLA-TDI, (c)PLA-HMDI, and (d) PLA-MPDI.

6.4.4 Nnclear magnetic resonance (NMR):

^{1}H-NMR (500 MHz): δ (ppm, $CDCl_3$ at 7.25) - The ^{1}H NMR spectra of the polyesterurethane (PLA-TDI) showed peak at 7.8-7.0 due to the aromatic protons and –NH groups. The peaks were appeared at 5.12 -5.18 (qt, -CH attached to urethane in the repeating unit, extra shoulders due to different environments and /or different degrees of polymerization), 4.37 -4.29 (qt, –CH attached to terminal hydroxyl), 2.4-1.9 (m, CH_3 attached to aromatic ring), 1.6-1.4 (d, CH_3 attached to CH) and 1.3 -1.19 (CH_3 attached to CH) respectively.

The ^{1}H-NMR spectra of the polyurethane (PLA- HMDI) showed at 7.8 and 6.72 ppm due to the NH groups. The peaks were appeared at 5.3 -5.1 (qt, CH attached to the urethane in the repeating unit, extra shoulders due to different environment and/or different degrees of polymerization), 4.96-4.7, (m, CH-b attached to ester) and 4.37-4.29 (qt, –CH attached to terminal hydroxyl group respectively. The peaks were appeared at

3.73 and 3.37 ppm are due to equatorial and axial hydrogen of cyclohexane ring respectively. The line width of peak calculated at 3.37 (axial-axial) is 10 Hz in comparison with peak at 3.73 (equatorial – axial and 4.8 Hz). The peaks were shown at 2.4 to 1.9 (m CH_3 attached to the cyclohexane ring), 1.6-1.4 (d. CH_3 attached to CH) and 1.3-1.11 (d, CH_3 attached to CH) respectively.

The ^{1}H-NMR spectra of the polyurethanes (PLA- MPDI) displayed bands at 7.7-7.0 due to protons of phenyl CH=CH and NH groups. The methylene attached to both aromatic rings appeared at 4.1-3.6 ppm. The peaks were aroused at 5.12 -5.18 (qt, -CH attached to urethane in the repeating unit, extra shoulders due to different environments and /or different degrees of polymerization), 4.37 -4.29 (qt, –CH attached to terminal hydroxyl), 2.4-1.9 (m, CH_3 attached to aromatic ring), 1.6-1.4 (d, CH_3 attached to CH) and 1.3 - 1.19 (CH_3 attached to CH) respectively.

6.4.5 Analysis by ^{13}C- NMR:

In this study, ^{13}C-NMR technique was used to determine the structure of polyester urethane using various isocyanates ranging from aliphatic, alicyclic and aromatic containing groups. The ^{13}C-NMR spectra corresponding to polyesterurethanes such as PU-1, PU-2 and PU-3, PU-4 are shown in fig. 6.4 (a, b) and 6.5 (a, b) respectively.

In the spectrum, PU-1(fig. 6.4a), the peaks appearing from 168.5 to 169.5 ppm are due to ester carbonyl groups. The peaks at 128.32 and 125.80 ppm are due to the presence of aromatic ring. The peak arises at 66.75 ppm is due to CH adjacent to hydroxyl end groups. The peak at 69.05 is due to CH group attached to ester linkage of the repeating unit of PLA. The peaks at 28.89 and 31.66 are due to methylene groups. The peaks at 19.77 and 16.67 ppm are due to methyl group attached to aromatic ring and methyl group attached to CH group of the repeating unit of PLA. The peak at 111 ppm is due to TDI protonated ring between urethane linkages. The peak arising at 101 ppm is due the CH attached to the urethane linkage.

^{13}C-NMR of PU-2 (PLA-HMDI) is shown in fig.6.5b. The peak arising at 169.64 ppm is due to ester carbonyl group. The peaks at 69.03 and 66.73 ppm are due to methine group attached to ester as well as alcohol respectively. The peaks ranging from 33.37 to 27.92 ppm are attributed to the methylene group of the cyclohexane ring. The peak at 20.48

ppm is due to the methylene group present between the two cyclohexyl rings. The peak at 16.65 is due to the methyl group present in the repeating unit.

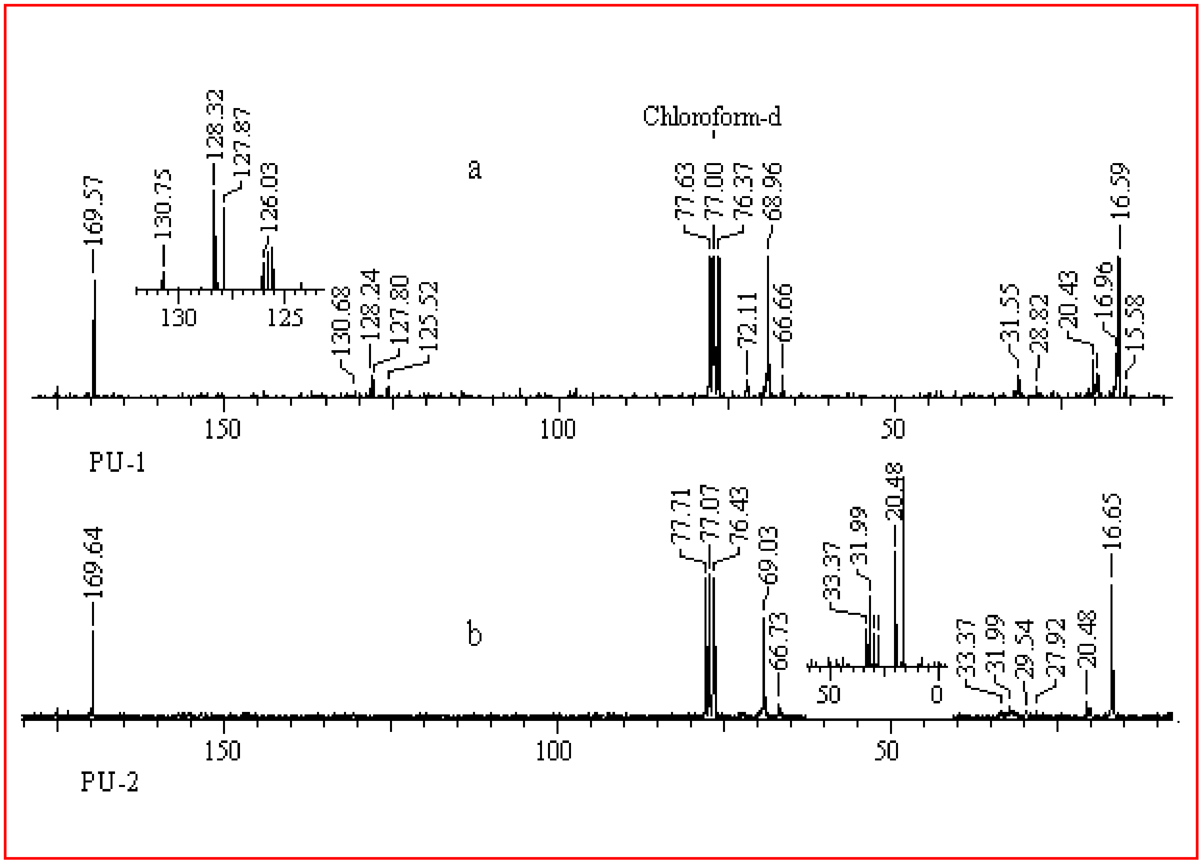


Fig. 6.4: ^{13}C-NMR spectra (500 MHz) of polyesterurethanes; (a) PU-1 and (b) PU-2.

^{13}C-NMR of PU-3 (PLA-MPDI) is shown in fig. 6.5. The peaks appearing from 119.08 to 129.42 ppm are due to aromatic region. The peak at 169.86 ppm is due to ester group of the repeating of PLA. The peaks at 69.07 and 16.67 ppm are due to the methine and methyl group of repeating group. The peak at 41 ppm is due to methylene group between two aromatic rings.

^{13}C NMR of PU-4 (PLA-HDI) is shown fig. 6.5 The peaks arising at 169.67, 69.08 and 15.66 ppm are due to ester carbonyl, methine and methyl carbon of PLA repeating unit. The peak at 66.78 ppm appears due to methine carbon attached to hydroxyl end group. The peaks ranging from 28.90-19.78 ppm are due to methylene groups.

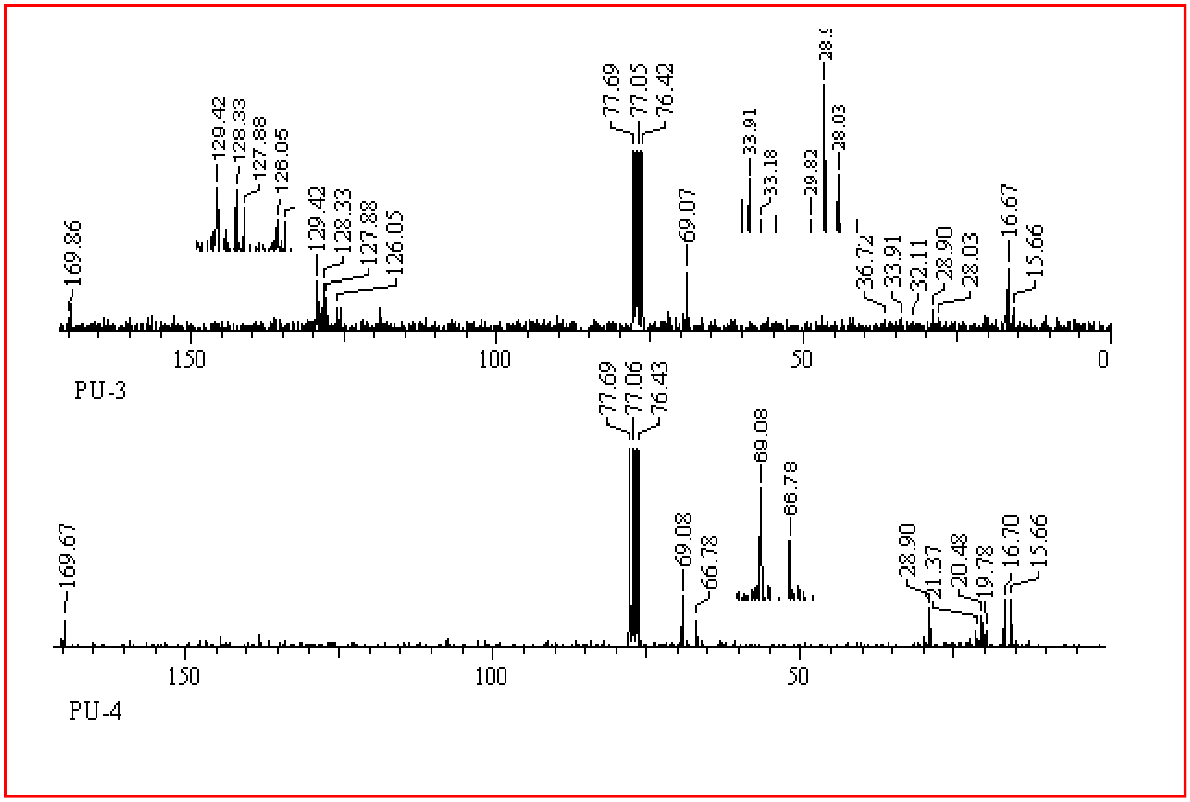


Fig. 6.5: ^{13}C-NMR spectra (500 MHz) of polyesterurethanes; PU-3 and PU-4.

6.4.6 Molecular Weights:

The results of characterization of the polyesterurethanes (PU-1 to PU-12) were tabulated in Table 6.3, 6.4 and 6.5 respectively. All polyesterurethanes are soluble in organic solvents and molecular weights data correspond to polystyrene standards, with a refractive index detector and so are only apparent values. PU-1, PU-2, PU-3 and PU-4 polyesterurethanes were prepared using telechelic polymer (diol ended PLA) with four different isocyanates i.e. TDI, HMDI, MPDI and HDI at 80 ^{0}C using reaction time (30 min.) in all the cases. PU-1 showed maximum weight average molecular weight M_w=8500 with number average molecular weight M_n=3900 with a molecular weight distribution (PDI~2.2). PU-2 showed M_w=5400, M_n=2400 and molecular weight distribution (PDI~2.2). PU-3 showed M_w=2600, M_n=1300 and molecular weight distribution 2.01 which are comparatively smaller than PU-1 and PU-2. PU-4 showed M_w=2200 with narrower distribution 1.5. A similar observation was made by Borda et.al[5] for TDI which contributed higher molecular weight polyesterurethane products in comparison with other isocyanates.

TDI is most industrially important diisocyanate although other types are now being developed and adopted industrially. Therefore, kinetic parameters were varied using TDI.

Table 6.3: Results of Characterization of the Polyesterurethanes from Diol-ended PLA Telechelic Prepolymer and Diisocyanate

Polymer	M_n	M_w	PDI	T_g (^{0}C)	T_m (^{0}C)	ΔH_m (J.g^{-1})
PU-1	3900	8500	2.17	27	77	0.90
PU-2	2430	5400	2.22	50	117	18
PU-3	1300	2620	2.01	13	144	18
PU-4	1450	2200	1.51	nd	nd	nd

It is apparent that the temperatures have greater impact on the molecular weight. Table 6.4 Illustrates the $M_{n,}$ M_w and MD values from PU-5 to PU-8 which were prepared using diol ended PLA with toluene diisocyanate. The following parameters were systematically investigated reaction time, reaction temperature and catalyst for the optimization of the reaction conditions. At the outset, the reaction time was varied. Low viscous liquid was observed till 25 min of reaction time. The product was formed in case of all four isocyanates, when the reaction time was increased gradually up to 30 min, optimized and kept constant for all reactions.

After the reaction time was fixed, the effect of the temperature was studied and the related results were shown in Table 6.4. With increasing reaction temperatures, the molecular weights also increased, but at higher temperature the molecular weights further decreased. The maximum molecular weight i.e.M_w=9000 was obtained at 100 ^{0}C.

Table 6.4: Effect of the Temperature on the PLA based Polyurethane Using Toluene Diisocyanate (TDI)

Polymer	Temp. (^0C)	M_n	M_w	PDI	T_g (^0C)	T_m (^0C)	ΔH_m $(J.g^{-1})$
PU-5	80	3870	8520	2.20	-12	77	0.90
PU-6	100	3810	8860	2.32	-9	59	7
PU-7	120	900	2480	2.75	-19	55	6
PU-8	140	996	2500	2.51	-19	56	4

A catalyst was always needed to speed up the reaction; the catalyst concentration of novel cloisite catalyst was varied from 1-4 wt%. The results were tabulated in Table 6.5. The highest molecular weight; M_w=11000 was obtained at 2 wt% catalyst. Thereafter, the molecular weight remained constant and the molecular distribution was obtained ~2 in all the polyester urethane polymers (PU-8 to PU-11).

Table 6.5: Effect of the Novel Cloisite Catalyst on the PLA Based Polyurethane Using Toluene Diisocyanate (TDI)

Polymer	Catalyst (wt %)	M_n	M_w	PDI	T_g (^0C)	T_m (^0C)	ΔH_m $(J.g^{-1})$
PU-9	1	3330	7000	2.10	-36	63	6
PU-10	2	5490	11400	2.08	-32	61	12
PU-11	3	4470	10890	2.43	-14	59	8
PU-12	4	5390	10600	1.96	-17	68	6

6.4.7 Thermal Characterization:

Thermal analysis of some polyurethanes showed that the polymers were stable up to 300-350 ^{0}C. TGA and DTG curves of polymers were recorded. These high thermal stability values obtained for the prepared polyesterurethanes are in agreement with those reported for polyester based polyurethanes.[20]

The results of the thermal characterization are shown in Table 6.3 and fig. 6(e-g). T_g varied from 27 to 13 ^{0}C for polyesterurethanes (PU-1 and PU-3). The decrease of T_g value in case of PU-3 is attributed to the incorporation of methylene group between two aromatic rings and resulted flexibility in the polymer chain and increase of mobility. The T_g value in case of PU-2 is 50^0C which is superior to PU-1 and PU-3. PU-2 polyesterurethane contains two cyclohexyl rings attached with methylene group. The cyclohexyl ring forms different conformation such as chair and boat form. The motion of the chair form experiences restriction in the mobility which enhanced the T_g value.

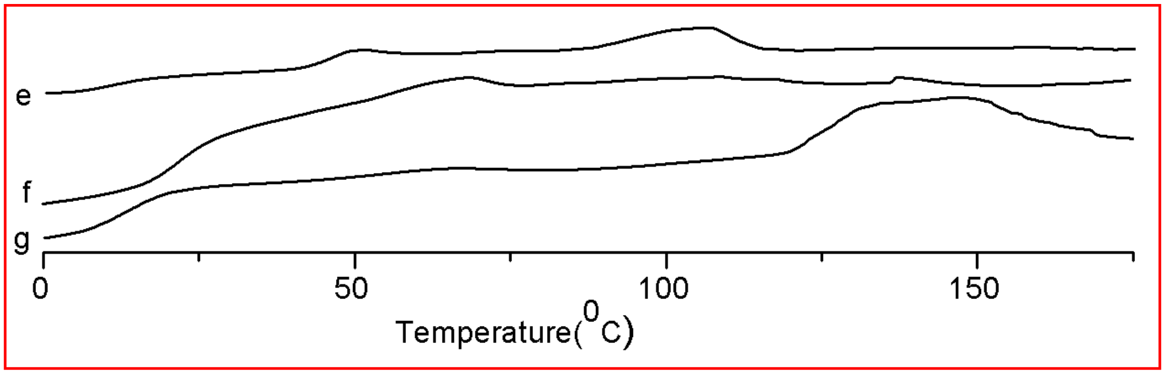


Fig. 6.6: DSC thermograms of polyesterurethanes; (e) PU-1, (f) PU-2 and (g) PU-3.

Table 6.4 shows the T_g values of PU-1 at four different temperatures i.e. 80, 100, 120 and 140 ^{0}C and the samples are designated as PU-5, PU-6, PU-7 and PU-8. T_g value is increasing by 3 ^{0}C by enhancement of reaction temperature from 80 to 100 ^{0}C. This may be interpreted as the molecular weight increased, T_g value also increased. The number of hard segment i.e. phenyl ring are more which results the restriction of polymer chain mobility. Therefore, T_g values in case of PU-7 and PU-8 are 19 ^{0}C because of low molecular weight.

6.4.8 XRD: The wide angle X-ray scans are shown in fig. 6.7. The crystalline structure of PLA has been investigated by XRD and found that four characteristic peaks appeared at $2\theta = 14.6^0$, 16.68^0, 19.14^0 and 22.27^0. [53] In case of PU-1 (fig. 6.7, X1) and PU-3 (fig. 6.7, X2), there is a single peak appeared at 18^0 is shown in fig. 6.7. The crystallinity may be attributed due to the lamellar superstructure as reveled by SAXS. [22] The peaks of PU-2 as shown in fig. 6.7 (X3) appeared at $2\theta = 17^0$, 19^0 and 32^0. The difference in θ values between fig.6.7 (X3) and PLA polymer clearly indicates the formation of different kind of crystallinity.

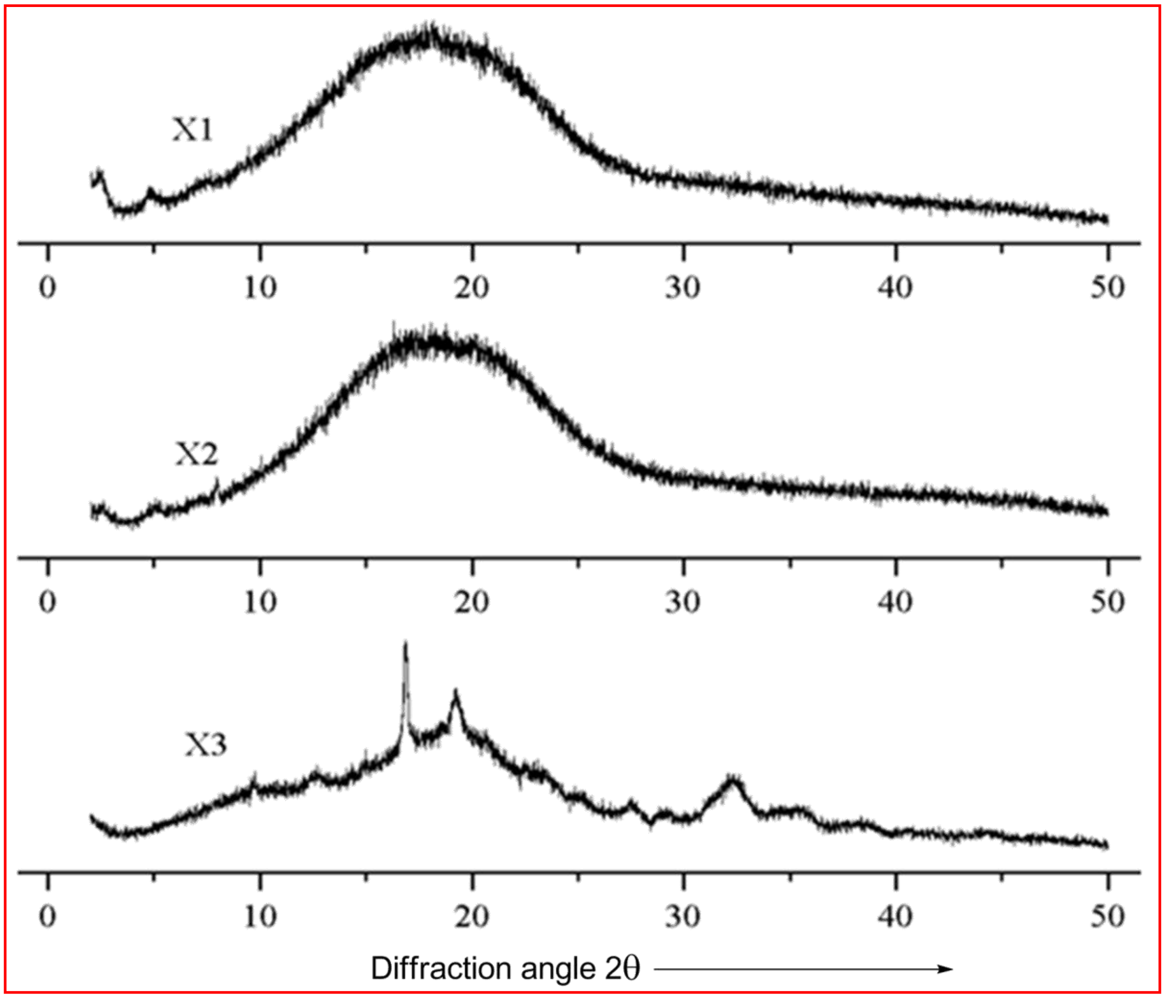


Fig. 6.7: SAXS diffraction patterns of polyesterurethanes: (X1) PU-1, (X2) PU-3 and (X3) PU-2.

6.4.9 MALDI-TOF MS-Analysis:

MALDI-TOF MS has been employed for the determination of molecular weights and the nature of the groups.[23, 53] With dehydropolycondensation reactions; only low molecular weight PLA can be prepared. Such oligomers were subjected to further reaction with various diisocyanates. The polyesterurethanes prepared during this study were subjected to MALDI-TOF MS analysis. The results of the analysis are shown in fig. 6.8 (a-d). Fig. 6.8a presents the MALDI-TOF mass spectrum of PU-1. The polyesterurethane contained chain terminated hydroxyl groups in both sides. The MALDI spectrum is dominated by a series of intense peaks ranging from mass 2000 to 6000 Da corresponding to polyesterurethanes doped with Na^+ ions of type.

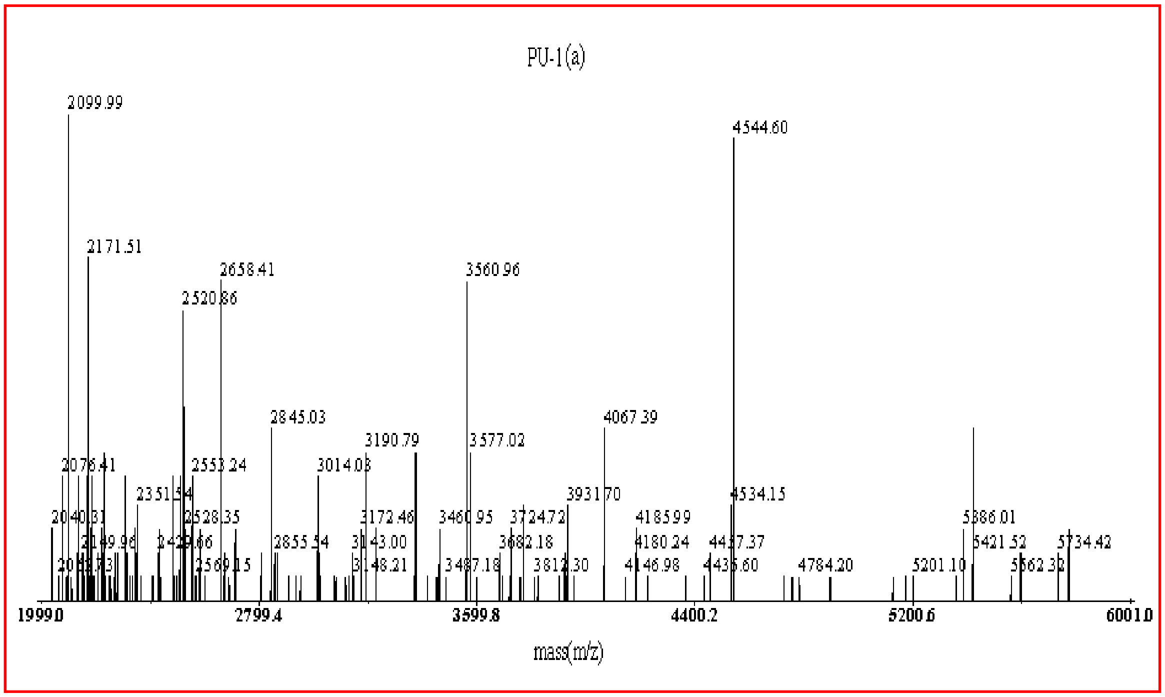


Fig. 6.8 a: MALDI-TOF spectra of polyesterurethane (PLA-TDI) (PU-1).

$\sim\sim\sim$[CO-NH-Φ-NH-CO-O]-[CH(CH_3)-CO-O]$_n$-[CH(CH_3)-(CH_2)$_2$-CH(CH_3)-[O-CO-CH(CH_3)]$_n$-OH-Na^+

(mass =72n+168+90+23); n values from 4 to 8 were detected, 23 being the mass no of sodium. The group also varies from 1 to 7. The symbol Φ represents the aromatic ring. The spectrum also displays other peaks of lower intensity, which desorbed as polyurethanes doped with K^+ ions. (K^+ adduct molecular ions, mass= 72n+168+90+39); see the peaks at 3190, 4897 in the inset.

The spectrum displays peaks of higher intensity ranging from 2171 to 5600 Da corresponding to polyesterurethanes doped with H^+ ions of type

OH$\sim\sim\sim$[CO-NH-Φ-NH-CO-O]-[CH(CH_3)-CO-O]$_n$-[CH(CH_3)-(CH_2)$_2$ -CH(CH_3)-[O-CO-CH(CH_3)]$_n$-OH-H^1

(mass =72n+84+192m+1), where n values varies from 4 to 8 and m varies from 1 to 4, 1 being the mass number of hydrogen. fig. 6.8b shows the MALDI TOF spectra of polyesterurethane PU-2. The MALDI spectrum is dominated by a series of intense peaks ranging from a mass of 500 to mass 1300 Da, corresponding to polyesterurethanes doped with Na^+ of types

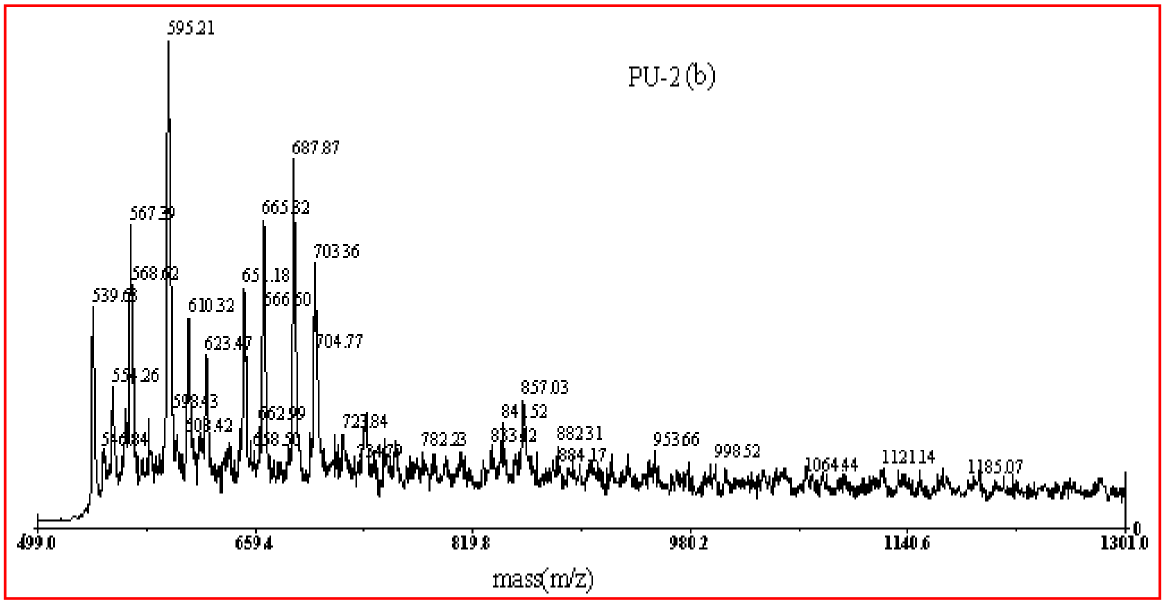


Fig. 6.8b: MALDI-TOF spectra of polyesterurethane (PLA-HMDI (PU-2).

$OH\sim\sim\sim[CO\text{-}NH\text{-}\Phi_1\text{-}NH\text{-}CO\text{-}O]\text{-}[CH(CH_3)\text{-}CO\text{-}O]_n\text{-}[CH(CH_3)\text{-}(CH_2)_2\text{-}CH(CH_3)\text{-}[O\text{-}CO\text{-}CH(CH_3)]_n\text{-}OH\text{-}Na^+$

(mass=72n+84=102+178+23), where n values varies from 3 to 8 and 23 being the mass number of sodium). Here Φ_1 represents dicyclohexyl methane group. The corresponding potassium ion doped peak appears at 533.6, 610 and 683.0 Da respectively. The two important peaks belonging to this series are observed, corresponding to polyesterurethanes of the same structure. (mass= 72n+84+280m+23) where n values varies from 3 to 8 and m varies from 1 to 2, 23 being the mass number of sodium.

Fig. 6.8c represents the MALDI-TOF mass spectrum of polyesterurethane prepared from PLA oligomers with 4, 4’ methylenebis (phenylisocyanate). The polyesterurethane contained chains terminated hydroxyl groups at both the chain ends.

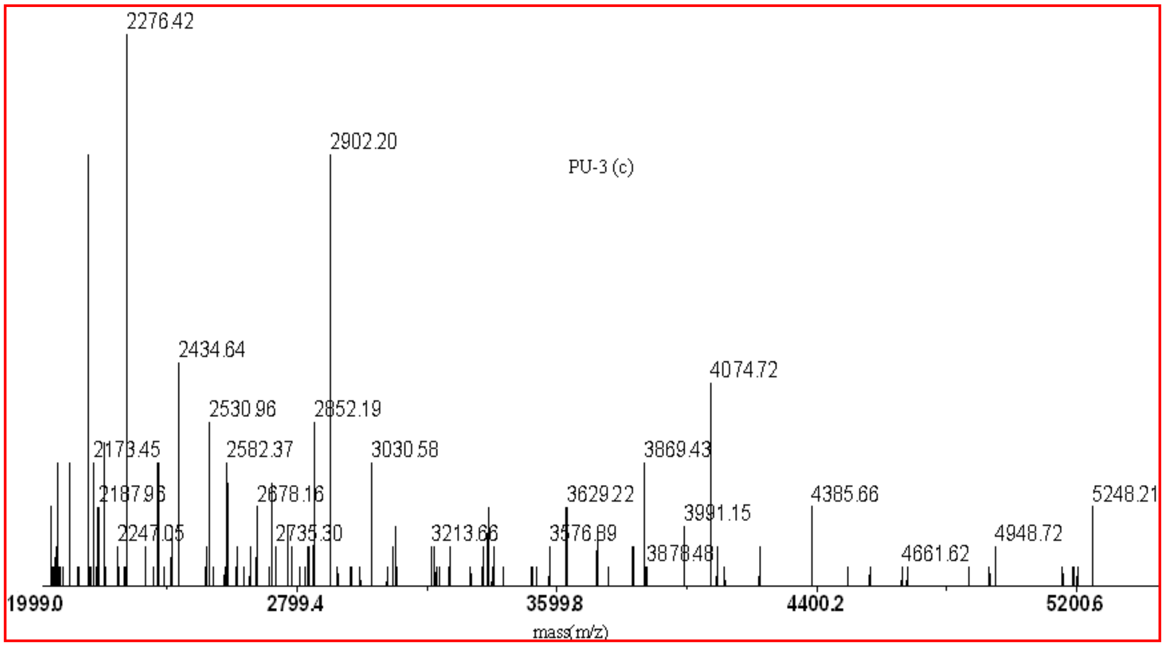


Fig. 6.8c: MALDI-TOF spectra of polyesterurethane (PLA-MPDI) (PU-3).

The MALDI is dominated by a series of intense peak ranging of 2050 to 4500 Da corresponding oligomers doped Na^+ ions of type

$OH\sim\sim\sim[CO-NH-\Phi_2-NH-CO-O]-[CH(CH_3)-CO-O]_n-[CH(CH_3)-(CH_2)_2-CH(CH_3)-[O-CO-CH(CH_3)]_n-OH-Na^+$

(mass =72n+84+102+166+23), where n varies from 1 to 4 and 23 being the mass number of sodium. Φ_2 represents biphenyl methane group. The corresponding peaks due to the polyester urethane doped with K^+ ions (K^+ adduct molecular ions, mass (72n+84+102+166+39), see the peak at 2188, 4075 and 4386 Da respectively. Fig. 6.9d depicted the MALDI TOF spectra of polyesterurethane of PU-4 prepared from hydroxyl terminated PLA with hexamethylene diisocyanates. The MALDI spectrum is dominated by a series of intense peaks ranging from a mass of 500 Da to a mass of 1100 Da, corresponding to oligomers doped with Na^+ ions of the type

$OH\sim\sim\sim[CO-NH-\Phi_3-NH-CO-O]-[CH(CH_3)-CO-O]_n-[CH(CH_3)-(CH_2)_2-CH(CH_3)-[O-CO-CH(CH_3)]_n-OH-Na^+$

(mass =72n+84+102+23), where n varies from 1 to 5 and 23 being the mass number of sodium. The corresponding additional peaks are due to the polyurethanes doped with K^+ ion (K^+ adduct molecular ions, mass= 72n+84+102+84+39), the peaks at 2187.9, 4074.7 and 4385.7 respectively.

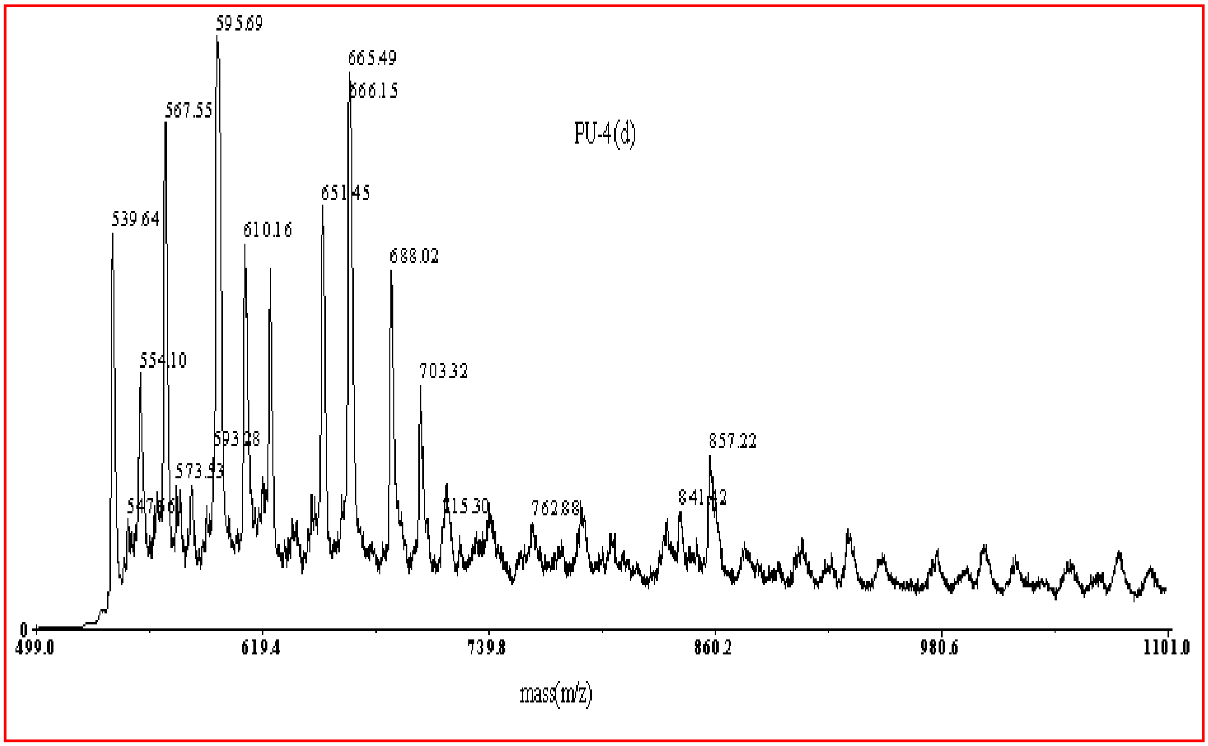


Fig. 6.8d: MALDI-TOF spectra of polyesterurethane (PLA-HDI) (PU-4).

6.4.10 Transmission Electron Microscopy (TEM:)

The thermal characteristic result showed the aggregation behavior of hydroxyl end groups, which was further examined by TEM shown in fig. 6.9 functionalized interfacial organic and polymer layers fabricated from molecular segments with different amphiphilicity, can be designed to act as a smart or switchable surface. These surfaces are capable of responding to very suitable changes in the surrounding environment such as pH, surface pressure and temperature, light and solvent quality. In the present system, PU-1, PU-2, PU-3 and PU-4 aggregate in isopropyl alcohol solvent and their structures are slightly different from each other. These structures are responsible for controlling physical properties in term of application such as drug delivery and biomimetic materials. PU-1, PU-2, PU-3 and PU-4 used in this study is hydroxyl terminated PLA and four different isocyanates, which were synthesized to obtain different poyesterurethanes. The M_n, M_w and polydispersity indices of the poyesterurethanes were estimated by gel permeation chromatography. T_g, T_m and ΔH values were calculated from DSC curves and illustrated in Table 6.3.

From the MALDI TOF spectrum, it was observed that all four poyesterurethanes contain hydroxyl terminated end group at both ends. Invariably, a single poyesterurethane polymer contains two hydroxyl groups. The hydrophilic and hydrophobic group will be placed on the opposite sides of the poyesterurethane backbone in isopropyl alcohol. Fig. 6.9 (a-d) showed the morphologies of the aggregates of PU-1, PU-2 and PU-4 in isopropyl alcohol. However, PU-3 showed the entirely different morphology in comparison with PU-1, PU-2, and PU-4 and showed précised narrow distribution of micelle-like aggregates in isopropyl alcohol. They consist of a hydrophobic units core covered with hydrophilic units (hydroxyl groups) forming corona. The hydrophobic units' core is covered with hydrophilic units forming the corona. Similar observation has been made by Lifeng Zhang et. al.[22]

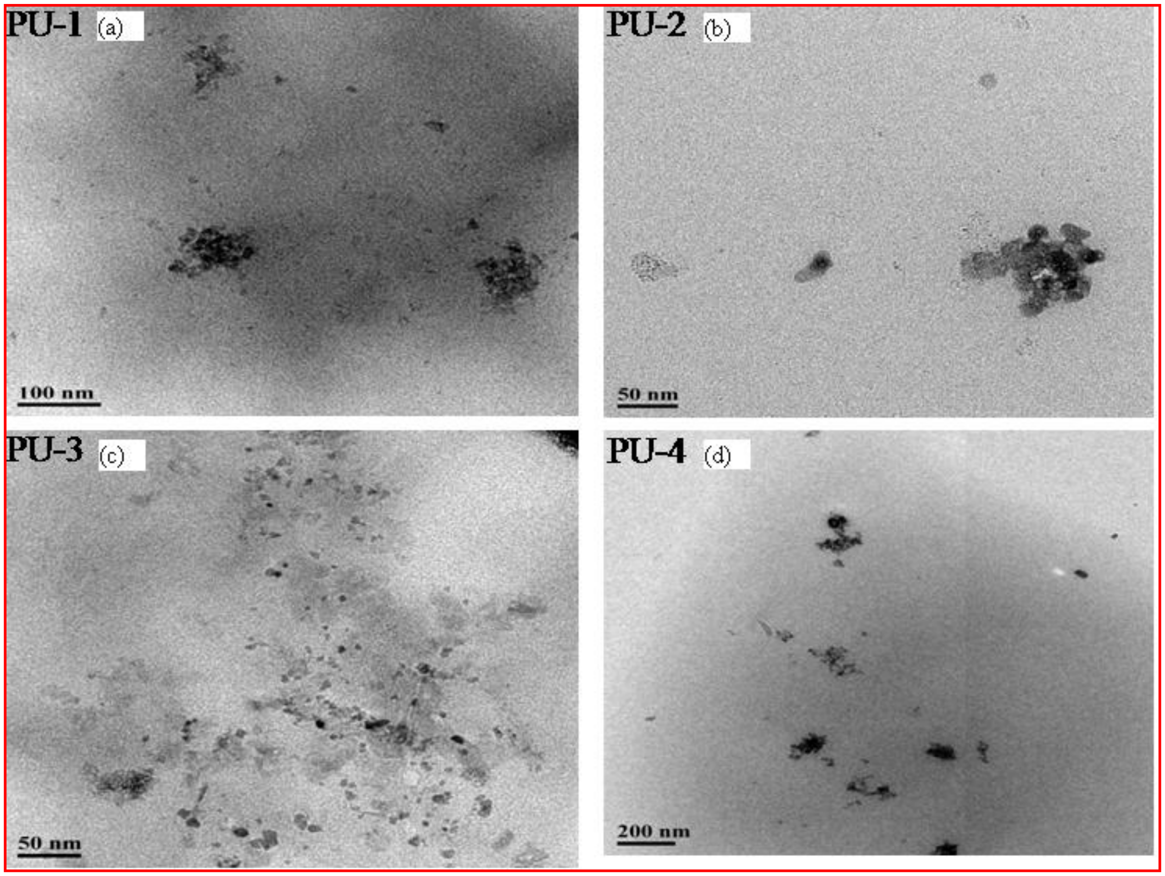


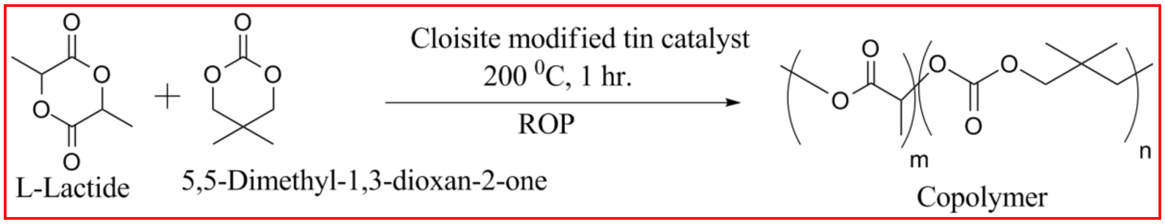
Fig. 6.9: TEM images of the micelle-like aggregates in isopropyl alcohol: (a) PU-1, (b) PU-2, (c) PU-3 and (d) PU-4.

The hydroxyl and carboxyl ended telechelic polylactic acid (PLA) oligomers were also subjected to a chemical reaction with above four isocyanates at similar reaction conditions as mentioned above. The obtained polyesterurethanes are mixture of linear and insoluble crosslinked products. In some of the reaction conditions, the insoluble crosslink products are around 30 %.

6.4.11 Ester-carbonate and ester-ester linkage:

Ester- carbonate:

Polycarbonate is a surface erosive biodegradable polymer material and has been used in drug controlled release systems and biomedical applications due to its good biocompatibility, favorable mechanical properties and elasticity. Therefore 5, 5-dimethyl-1, 3 dioxan-2-one (DTC) was polymerized using ROP technique in presence of cloisite modified tin catalyst. The resulted homopolymer was characterized using ^{1}H-NMR technique shown in fig. 6.10 A. The molecular structure of polymer was elucidated using ^{1}H-NMR spectra. No triplet at $\delta = 3.4$ ppm (characteristic peak of an ether group) could be detected, which demonstrated that no decarboxylation occurred during the ring opening polymerization.



Scheme 3: Copolymers constitute of L-Lactide and 5, 5-Dimethyl-1, 3-Dioxan-2-one

The copolymers of lactide and DTC were prepared using ROP at 200 °C for 1hr as shown in scheme 3. The catalyst used was 0.75%. The copolymer feed composition are 90:10, 80:20, 70:30, 60:40, and 50:50 respectively. The M_w of poly (DTC) and PLA are 13,700 and 75,000 Da respectively. The COP-1 showed M_n, M_w and dispersivity as 12,800Da, 20,900Da and 1.6 respectively. The decomposition temperature of P (DTC) is 261°C and T_m is 100 °C. The decomposition temperature of PLA is 300 °C. The values of T_g and T_m of PLA are 55 °C and 171 °C respectively as shown in fig. 6.12.

In case of copolymers, where the incorporation of second monomer i.e. DTC in lactide (LA) monomer. The decomposition temperature remained constant around 300 °C. The T_g value decreased by 8 °C in comparison with PLA and two T_m values appeared at 144 and 156 ^{0}C respectively. The T_g value decreased monotonically from 47 °C to 18 °C as the incorporation of DTC increased in the copolymer composition 90:10, 80:20, 70:30, 60:40 and 50:50.

Table 6.6: Synthesis of polycarbonate and its copolymers

Polymer	LA:DTC Feed ratio	M_n	M_w	PDI	T_g (^{0}C)	T_m (^{0}C)	Deg.Temp. (^{0}C)
Polyca.	0:100	6990	13700	1.9	-	100	261
PLA	100:0	45600	75000	1.6	55	171	300
COP-1	90:10	12800	20900	1.6	47	144, 156	304
COP-2	80:20	11800	19000	1.6	44	144, 157	300
COP-3	70:30	10700	18300	1.7	35	96	289
COP-4	60:40	16700	10100	1.6	28	76	287
COP-5	50:50	5430	10400	1.9	18	77	283

LA-L-lactide, DTC-5, 5-Dimethyl-1, 3-Dioxan-2-one.

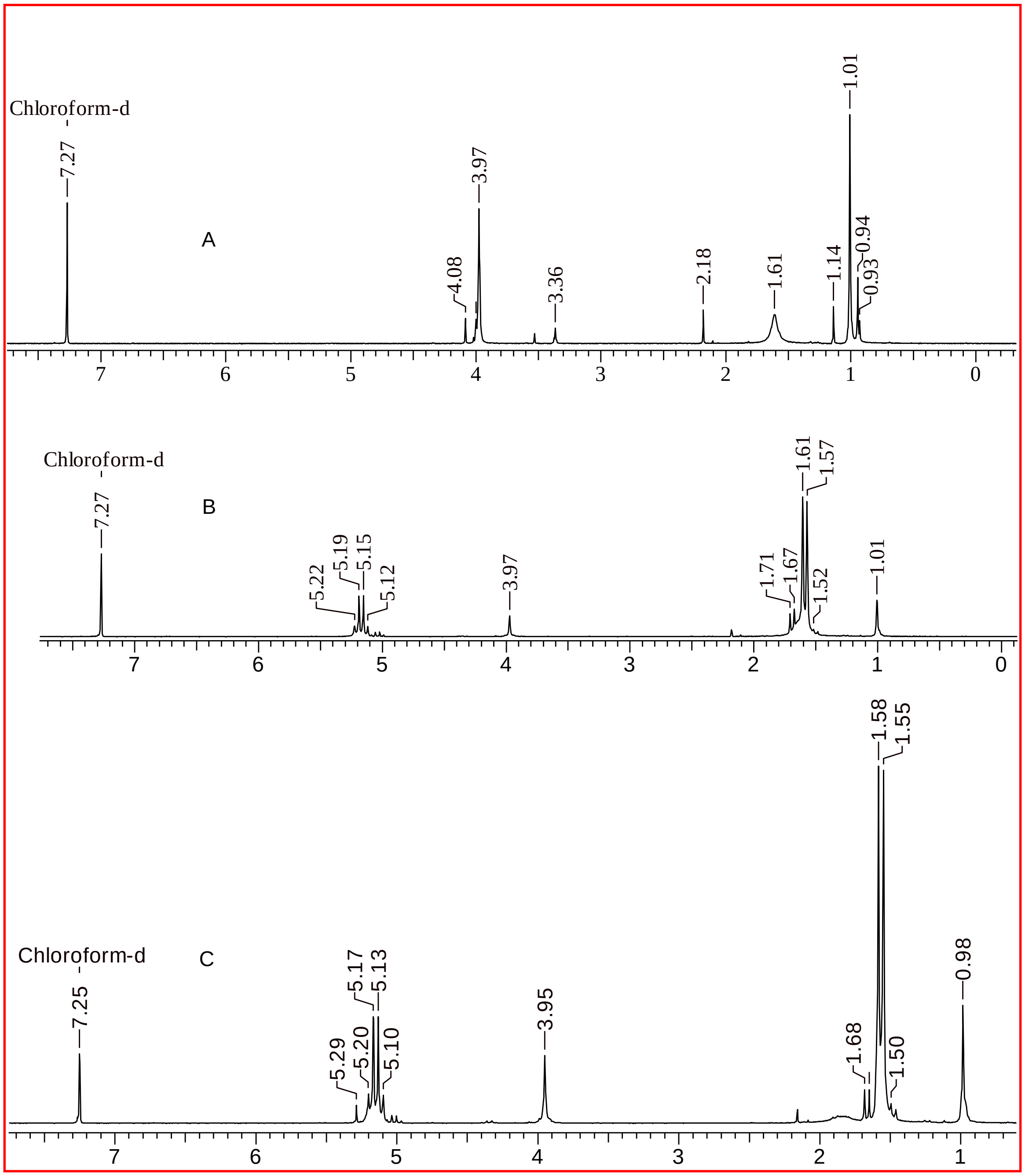


Fig. 6.10: ^{1}H-NMR A-Polyca. (homopolymer), B- COP-1, C-COP-2.

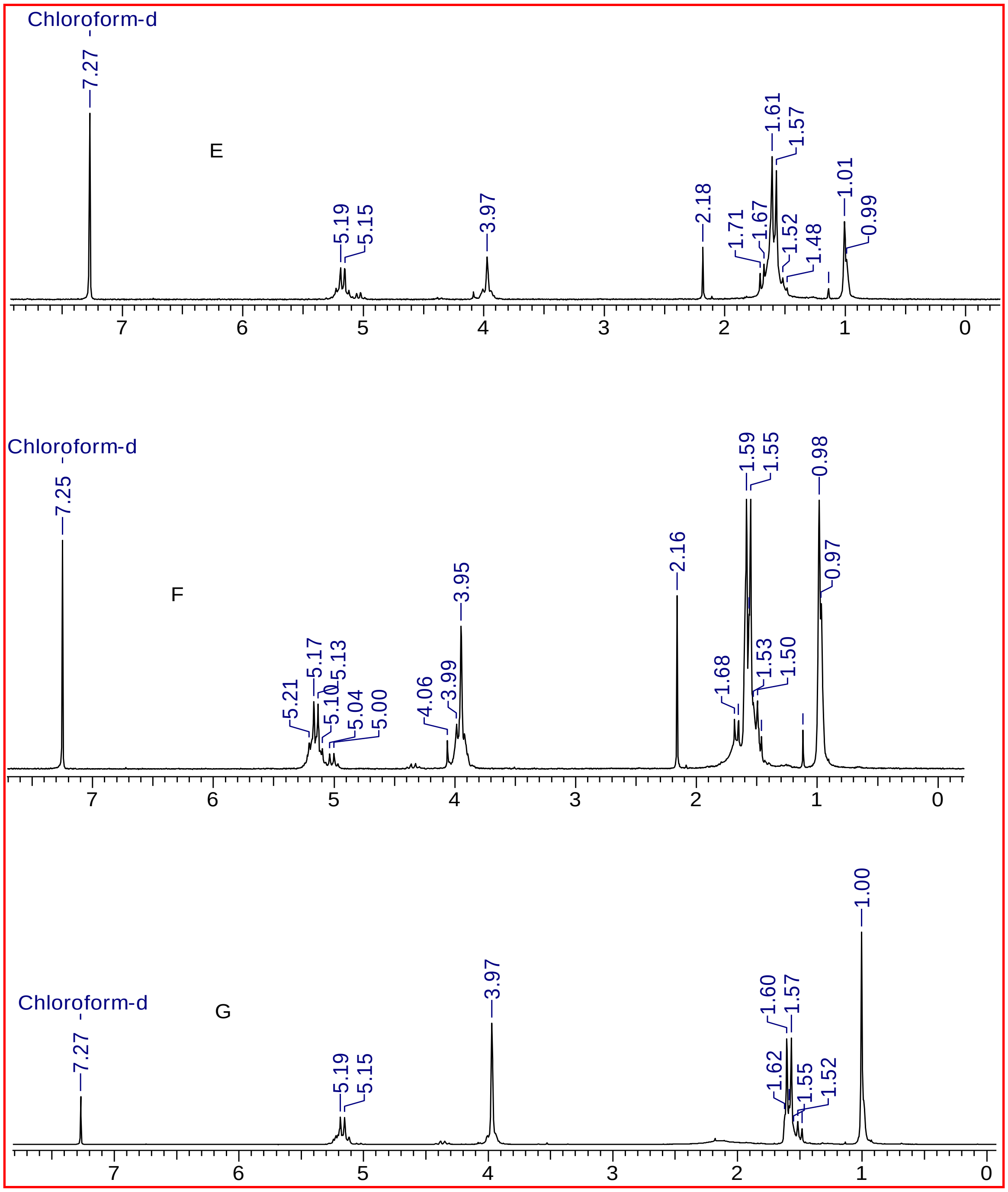


Fig. 6.10a: ^{1}H-NMR A-Polycarbonate (homopolymer), E- COP-3, F-COP-4, G- COP-5.

^{1}H-NMR of COP-1 and COP-2 were elucidated in fig.6.10 B COP-1 showed quartet peak at δ 5.15 ppm and doublet at δ 1.61 ppm. The peaks of DTC appeared at δ 3.9 ppm (OCH$_2$-) and δ 1.0 ppm (-CH$_3$ group. Similarly, COP-2 fig. 6.10 C showed quartet peak

(-CH-) at δ 5.17 ppm and doublet (-CH$_3$) at δ 1.58 ppm. The peaks at δ 3.4 ppm (-OCH$_2$-) and δ 0.98 ppm (CH$_3$) group. There is no evidence of ether linkage formation after removal of carbon dioxide, which generally occurs at δ 3.4 ppm. COP-1 and COP-2 again showed the absence of unreacted monomer (L-Lactide) and comonomer (DTC).

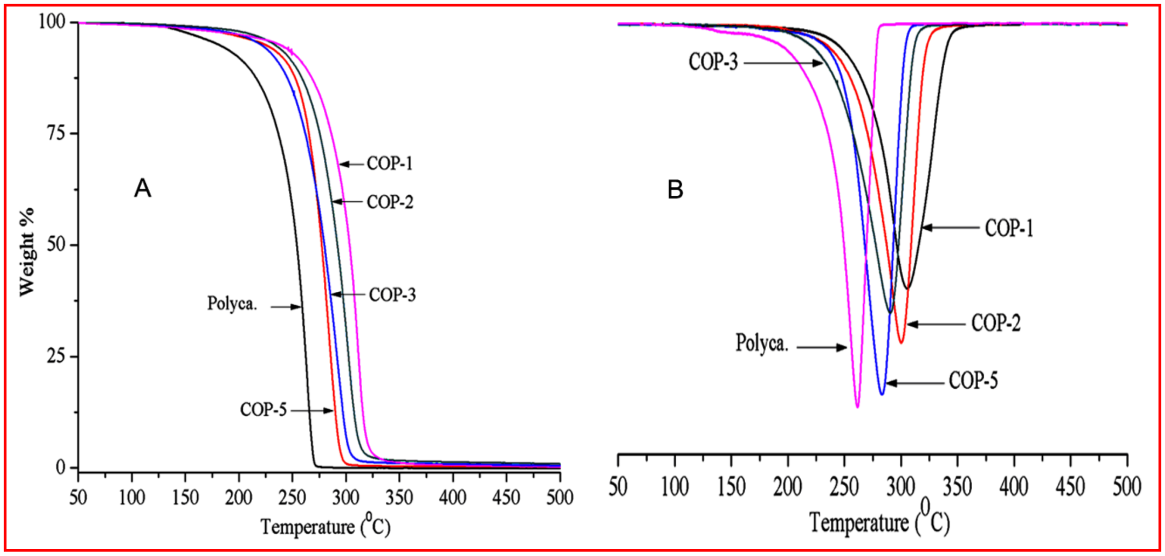


Fig. 6.11: Thermogravimatric analysis of polycarbonate and copolymers showing decomposition temperatures.

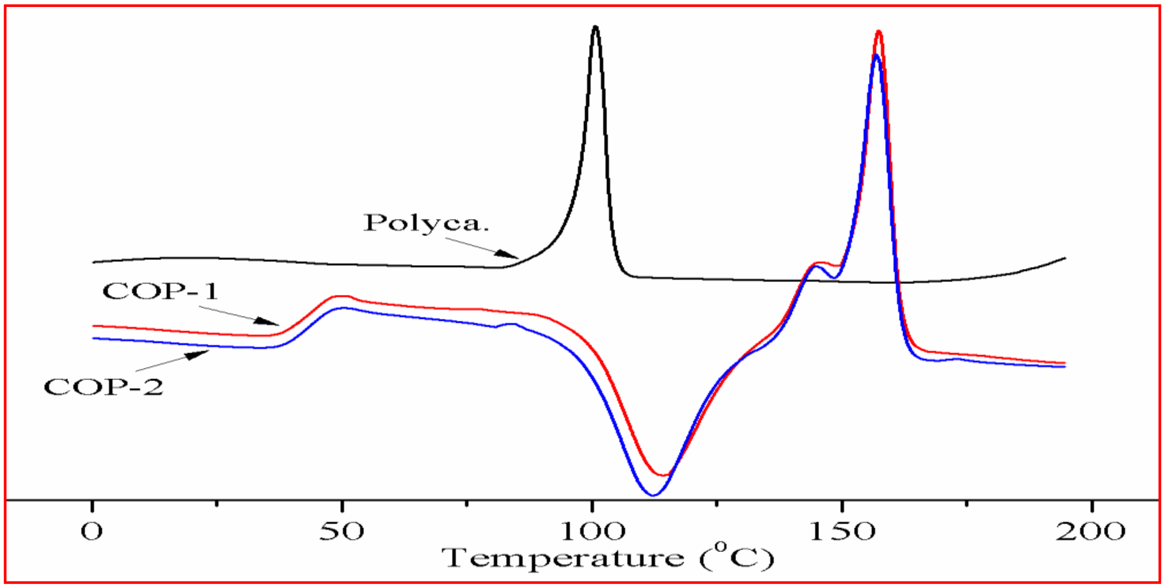


Fig. 6.12: DSC thermograms of polycarbonate and copolymers showing glass transitation temperature (T_g) and melting temperature (T_m).

The decomposition temperature (fig. 6.11) of Polycarbonate (DTC) is 261 °C and T_m is 100 °C. The single T_g and T_m were observed in case of COP-3, COP-4 and COP-5. The thermal stability is ~ 280 °C. The T_g value decreased from 35-18 °C and T_m values also showed a decline trend from 96 to 77 °C.

Ester-ester:

The ester-ester linkages were prepared using secondary hydroxyl terminated PLA telechelic polymer at both the end and sebacic acid. The dehydropolycondensation reaction was carried out in presence of tetraphenyltin catalyst (FDA approved) at 150 °C. The structure was elucidated from fig 15. The peaks due to methine carbon atom PLA as a quartet δ 5.17 ppm and methyl carbon doublet at δ 1.57 ppm. The quartet appeared at δ 4.37 ppm is due to CH group attached to COOH end group of PLA.

Fig. 6.13: ^{1}H-NMR ester-ester polymer (telechelic PLA and sebacic acid).

The methylene group of sebasic acid attached to COOH group appeared at δ 2.34 ppm as a triplet. The neighbouring methylene group appeared as multiplet at δ 1.6 ppm. The peak at δ 1.3 ppm is attributed to middle methylene group. The structure of polymer containing ester-ester linkage was confirmed from ^{1}H-NMR shown in fig. 6.13

Polymer containing ester-ester linkage was also prepared from hydroxyl terminated PLA telechelic polymer and terephthalic acid at 300 °C for 15 hr using dehydropolycondensation technique. ^{1}H-NMR spectrum was shown in fig. 6.14. The peak at δ 5.18 ppm appeared due to methine carbon (q) and at δ 1.59 ppm due to methyl carbon (d). The CH group attached to terminal group of PLA appeared at δ 4.34 ppm as a quartet. The aromatic peaks of phthalic acid unit appeared in the range of δ 7.25 ppm to δ 7.35 ppm. The peaks at δ 2.36 and δ 2.16 ppm are due to methyl groups. The structure of the polymer containing both aliphatic and aromatic ester groups was confirmed by ^{1}H-NMR.

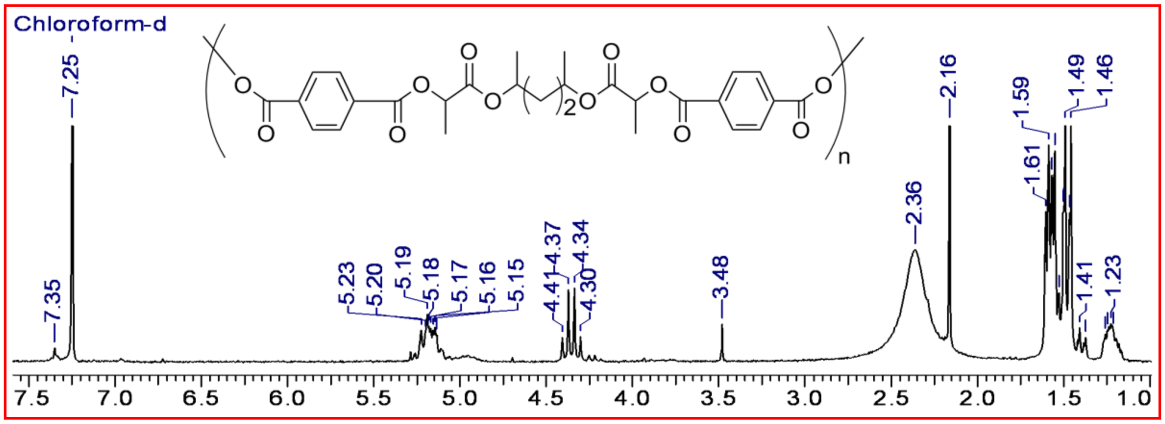


Fig. 6.14 ^{1}H-NMR ester-ester polymer (telechelic PLA and terephthalic acid).

6.5 Conclusion:

Hydroxyl terminated PLA oligomers were synthesized by the reaction of L-lactic acid with 2, 5-hexane diol via dehydropolycondensation technique. They were mainly characterized by ^{1}H, ^{13}C and ^{31}P NMR and confirmed that both ends contain secondary hydroxyl groups (CH (CH_3) OH). PLA oligomers containing both hydroxyl and carboxylic groups were also synthesized by the ring opening polymerization using stannous octoate as an initiator and water as a coinitiator and their structures were confirmed by spectral techniques. All the reactions were monitored precisely in a quantitative manner. The optimum reaction conditions were determined for the synthesis of linear PLA-based polyurethanes. The reaction time, reaction temperature, the concentration of modified cloisite catalyst was varied to obtain optimum result. The reaction time is much reduced in comparison with earlier literature report. The Tin modified solid cloisite catalyst had a fundamental impact on the molecular weight of the polyesterurethanes. The desirable linear polyesterurethanes were exclusively obtained from diol ended PLA oligomers and various aliphatic, alicyclic and aromatic diisocyanates.

The polyester-urethane product (~100 % yield) is white and completely soluble in organic solvents such as chloroform, N, N-dimethyl formamide etc. There is exclusively urethane linkage when diol ended PLA oligomers are used. The final telechelic polyurethane polymers contain hydroxyl groups at both ends. It can react with any telechelic polymer preferably containing isocyanate groups at both ends.

The similar white product (~100 % yield) was obtained from hydroxyl and carboxyl ended PLA oligomers and diisocyanates compounds and soluble to some extent in organic solvents such as chloroform, N, N-dimethyl formamide etc. The urethane and amide linkage are observed when both hydroxyl and carboxyl ended PLA oligomers are used. However, around 30% crosslinked polyesterurethane products were obtained when PLA oligomers containing both hydroxyl and carboxylic groups reacted with various aliphatic, alicyclic and aromatic diisocyanates at identical condition. On the basis of the MALDI-TOF-MS, ^{13}C-NMR and IR investigations, the functionality of the various polyesterurethanes synthesized was determined, the presence of hydroxyl groups at the both ends were supported. TEM picture showed the morphologies of the aggregates of polyurethanes (PU-1, PU-2, PU-3 and PU-4) in isopropyl alcohol because of hydroxyl-hydroxyl self association.

This prepared polyester urethane has the advantages of good biocompatibility, simple preparation method, low preparation cost, environmental friendliness and suitability for industrial production, can be absorbed by human body, and has good application prospect in the field of medicine.

Poly ester carbonate linkages were prepared by ROP in presence of cloisite modified catalyst at 200° C for 1 hr. The highest molecular weight (M_w) was obtained as 20,000 Da and dispersity 1.6. The interesting result was observed from ^{1}H-NMR that there is no ether linkage formation after elimination CO_2 during reaction period. This catalyst is more advantageous than the catalyst reported in the literature. T_g value could be tuned by varying the molar feed ratio of DTC maintaining the thermal decomposition temperature 280 °C.

Poly ester linkages (aliphatic ester ester linkage and aliphatic-aromatic ester ester linkage) were designed and prepared. The hydroxyl terminated PLA and sebasic acid were reacted in the presence of tetra phenyl tin using dehydropolycondensation. The structure was confirmed by ^{1}H-NMR.

The hydroxyl terminated PLA and terphthalic acid were reacted at 300° C for 1 hr. The resulting polymer was purified, dried. ^{1}H-NMR spectra confirmed the structure of ester-ester polymer containing telechelic PLA and terphthalic acid.

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CHAPTER - 7

CHAPTER-7: APPLICATION OF BIOCOMPATIBLE AND BIODEGRADABLE POLYMER

7.1 Introduction:

The electrospinning technique gives the preparation of ultrafine fibers with diameters ranging from micron to nanoscale. The electrospinning is a new and efficient fabrication process that produced electrospun fibers using an external electric field to create an electrically charged jet of polymer solution or melt with simultaneous rapid evaporation of the solvent and leave a polymer fiber. The benefits of electrospinning process are simple equipment and cost effective process whereas requiring a long time to obtain enough fibers. The morphology of fibers depends on the process parameters, including the solution concentration, applied electric field strength, deposition distance, and deposition time and flow rate.

The electrospun mat of polylactide for controlled release of therapeutic concentration of dichloroacetate has been designed to suppress the cervical carcinoma in vivo.[1] Pitarresi et al. reported the production and characterization of electrospun scaffolds of the copolymer β-poly(N-2-hydroxyethyl)-DL-aspartamide-graft-polylactic acid proposed for a potential topical release of Ibuprofen.[2] PLA composites filled with electrospun nylon 6 fibers were prepared. This allowed to improve the mechanical properties and tune the degradation of the PLA matrix. The major effect of electrospun fibers on the matrix was that of modifying the semicrystalline framework, thickening the polymer lamellae.[3] Micro and nanofibrous electrospun PLA and PLA/poly (ethylene glycol) membranes containing different drugs i.e. diclofenac sodium, lidocaine hydrochloride, benzalkonium chloride, have been developed.[4] Poly(ethylene terephthalate-co-lactic acid) has been synthesized by employing polycondensation of mixtures of dimethyl terephthalate , lactic acid and ethylene glycol using $Sn(Oct)_2$ as a catalyst.[5]

Bundle membranes were made by electrospinning PLA, PLA/poly(ethylene glycol) using the ionic properties of diclofenac sodium, lidocaine hydrochloride , benzalkonium chloride and combinations thereof. The combination of the ionization of the drugs as well as the utilization of the multi-needle electrode allowed the successful preparation of bundle membranes.[6] The biodegradable nanofibers have been prepared by dissolving the acid form of Ibuprofen (from 1% to 10% by weight) in the same solvent as 75% polylactide, 25% poly-glycolide (PLGA) which gave rapid release of drug within the first 8 hr and then slower release over several days. Scaffolds with 10% Ibuprofen degraded within 6 days.[7] Novel fibrous materials of stereocomplex between high-molecular-weight PLA and diblock copolymers consisting of poly(L- or D-)lactide and poly(N, N-dimethylamino-2-ethyl methacrylate) blocks, respectively were prepared by solution electrospinning. Fibers with mean diameters ranging from 1400 to 1700 nm were obtained.[8] Inorganic nanosized layered double hydroxides modified with dodecyl sulfate (DS) ions were incorporated into semi-crystalline polylactide nanofibers non-woven membranes by combining a nanocomposite technique and the solution electrospinning process.[9] Bhattarai Shanta Raj et al. developed hydrophilic nanofibrous structure of PLA polymer in the form of nonwoven mat by electrospinning technique. Hydrophilicity of the PLA fibers was improved by adding small fraction of low molecular weight polyethylene glycol (PEG) into the electrospinning solution. Four different ratio types (100/0, 80/20, 70/30, and 50/50) of PLA/PEG.[10] To determine how the linear, random raised features produced by electrospinning affect proliferation and differentiation of osteoprogenitor cells, poly(lactic acid) and poly(ethylene glycol)poly(lactic acid) diblock copolymers have been electrospun with mean fiber diameters of 0.14-2.1 µm onto rigid supports.[11]

The microbial degradation of poly(-lactide), PLA in the soils has been focused.To enclose the part of microorganism in a real process of biodegradation and to understand surface morphology, decrease in molecular weights and thermal properties were examined. The tests were performed in soil i.e. in compost room temperature.

PLA nanocomposites based on organically modified montmorillonites at 5% w/w loading were prepared by melt blending using an internal mixer and then degraded in commercial compost. The addition of nanoclay was found to increase the PLA degradation rate, especially for the highest dispersed clay in the polymer matrix. Biodegradation by microorganisms isolated from the compost showed the bacterium Bacillus licheniformis as one of the responsible for PLA biodegradation in compost. It was also found that clays can influence the polymer bacterial degradation depending on their chemical structure and affinity of the bacterium towards the clay.[12] In order to improve PLA degradation, different layered silicate nanoclays has been added montmorillonites and fluorohectorites, without or with organic modifiers. Environment that contains a natural mixture of fungi and bacteria. Biodegradation studies of the biocomposites have been investigated in medium through morphological and weight loss studies.**[13]** The degradability of linear low-density polyethylene and poly(L-lactic acid) blend films under controlled composting conditions has been investigated according to modified aerobic standard test method.**[14]** PLA and thermoplastic starch blends with compatibilizer have been studied the biodegradation in the soil burial test The rate of biodegradation of the blends decreases with an increase in the content of compatibilizer.**[15]**

The *in vitro* degradation characteristics of microporous PCL and inulin/PCL materials in PBS at 37 ^{0}C have been monitored over 45 months. Microporous PCL demonstrated zero weight loss, minor changes in molecular weight characteristics.**[16]**

PLA and PCL nanocomposites have been prepared by adding 5 wt% of a sepiolite (SEPS9) and degraded in compost, leading to effective degradation. PLA and PLA/SEPS9 seem to be mainly degraded by a bulk mechanism, showing a significant level of polymer degradation, however the presence of SEPS9 particles partially delays the degradation probably due to a preventing effect of these particles on polymer chain mobility and/or PLA/enzymes miscibility. PCL and PCL/SEPS9 showed a preferential surface mechanism of degradation.**[17]** PLA undergoes degradation under aerobic composting conditions was described.**[18]** Tokiwa et al. emphasized mainly on microbial and enzymatic degradation of PLA.**[19]** The biodegradation of polylactide has been studied at different elevated temperatures in aerobic and anaerobic, aquatic and solid state conditions. Test showed that PLA was very slow at room temperature, but faster under thermophilic conditions. The clear effect of temperature on the biodegradability of PLA in the aquatic tests indicates that its polymer structure has to be hydrolyzed before microorganisms can utilize it as a nutrient source. The behaviour of PLA in the natural composting process was similar to that in the aquatic biodegradation tests.**[20]** The long-term tissue response and duration of degradation of self-reinforced poly-L-lactide (SR-PLA) multilayer plates in vivo were investigated. **[21]**

Duan et al. prepared a series of novel biodegradable polymer [polylactide (PLA)]-based nanocomposites using graphite nanosheets and multi-walled carbon nanotubes

(MWCNTs) by solution-blending technique and investigated dielectric properties, and electrical and thermal conductivities. Results obtained in this study indicated that significant improvements in thermal and electrical conductivities, thermal stability. concentrations, dispersion, and the resulted morphological structures.[22] Composites consisting of polylactide (PLA) and poly(ε-caprolactone) (PCL) filled with acid-oxidized multiwalled carbon nanotubes (A-MWCNTs) have been prepared through melt compounding with different ratio. An interesting change of electrical conductivity for PLA/PCL/A-MWCNT composites is observed, in which the maximum conductivity is observed for PLA/PCL/A-MANCNT composite with PLA/PCL ratio of 60/40.[23]

The synthesis of polymeric nanocomposites comprising of polylactide (PLA) and well-dispersed multiwalled carbon nanotubes (MWCNT) has been presented. The obtained PLA/MWCNT composites were characterized by low percolation threshold (0.25 wt. %) and a conductivity value of 5.10(-2) S/cm (with 1 wt. % of nanotubes, and conductivity 100 times higher than in the case of respective composites containing carbon black. These differences were attributed to the high aspect ratio of the MWCNTs and their high conductivity.[24] A series of polylactide/exfoliated graphite (PLA/EG) nanocomposites by melt-compounding and investigated, mechanical and electrical properties. The percolation threshold for electrical conduction of PLA/EG nanocomposites was found to be at 3-5 wt % EG, which is far lower graphite content than that 10-15 wt % of PLA/ natural graphite composites.[25] The preparation of multi-walled carbon nanotube (MWCNT)/PLA composites has also been described. High electrical conductivity can be achieved at a low carbon nanotube loading.[26] A novel electrically conductive biodegradable composite material made of polypyrrole (PPy) nanoparticles and poly(d,l-lactide) (PDLLA) was prepared by emulsion polymerization of pyrrole in a PDLLA solution, followed by precipitation. The electrical stability of the composite containing 5 wt% PPy was investigated in a cell culture environment for 1000 h with 100 mV DC applied voltage. Fibroblasts were cultured on the composite membranes and were stimulated with various DC currents. With the 1-17% increase in the PPy content, the conductivity of the composite increased by six orders of magnitude. The electrical stability was significantly better in the PPy/PDLLA composite than in the PPy-coated polyester fabrics.[27] DC and AC electrical conductivity of bionanocomposites based on the immiscible polymer blend poly(ε-caprolactone)/polylactide (PCL/PLA, w/w 70/30), loaded with multiwall carbon nanotubes (CNT), were studied in a wide frequency range, 10(-3) <= f <= 10(7) Hz from 143 to 313 K.[28]

7.2 Materials and Methods:

PLA (M_w=75000), (Prepared in our Lab) Azithromycin (Analytical standard, Sigma Standard), Dichloromethane (SRL), Domestic soil containing compost, Isobutrin (Isolated)

7.2.*1 Extraction of Isobutrin:* Isobutrin is ecofriendly sensitizer that is extracted from Butea monosperma (commonly known as "Flame of the Forest") flowers. Flowers were collected and dried in shadow after which were grinded to fine powder. The column chromatography was performed to extract the pure isobutrin using methanol and water system in which water was in trace amount.

7.2.2 Prepration of PLA solution for electrospinning:

PLA solution with concentration of 2 wt % was prepared using dichloromethane (DCM) as a solvent. PLA was dissolved in DCM using magnetic stirrer until the solution was cleared. Azithromycin drug (15%) were added to PLA solution.

7.2.3 *Biodegradation test:* Biodegradation was studied using domestic compost. The compost was made of dried leaves trees, soil from farm, and waste of cattle. The compost was kept wet during test. The PLA film was made using polymer hot press at 100 ^{0}C. The dimensions of the film were 1 cm x 1 cm and thickness was 0.1mm. The film was kept in contact with the compost. Film was removed at different interval of time for characterization.

7.2.4 *Pellet making procedure for electrical conductivity:* PLA, PCL solution was prepared in chloroform and isobutrin solution was prepared separately in dimethylformamide. Both solution mixed together uniformly using vertex for half an hour. Resulting mixture poured in petridish and kept in vacuum oven for two days at 40 ^{0}C. These material used for making pallet using polymer hot press at 100 ^{0}C. The volume resistance of samples was determined by using high resistance meter (Keithley 6517B). Then, the volume resistivity was measured by the relation ρ = R (A/L), ρ is the resistivity in Ω-cm, R is resistance in ohm, L is the sample thickness in cm and A is the cross sectional area (cm^2) of sample. The electrical conductivity was reported as the reciprocal of the volume resistivity.

7.3 Analysis

7.3.1 Molecular weights: As discussed in chapter 3.

7.3.2 Scanning Electron Microscopy (SEM): As discussed in chapter 3.

7.3.3 Differential Scanning Calorimetry (DSC): As discussed in chapter 3.

7.4 Result and Discussion:

7.4.1 Electrospinning: The experimental detail of electrospinning process is shown in fig. 7.1

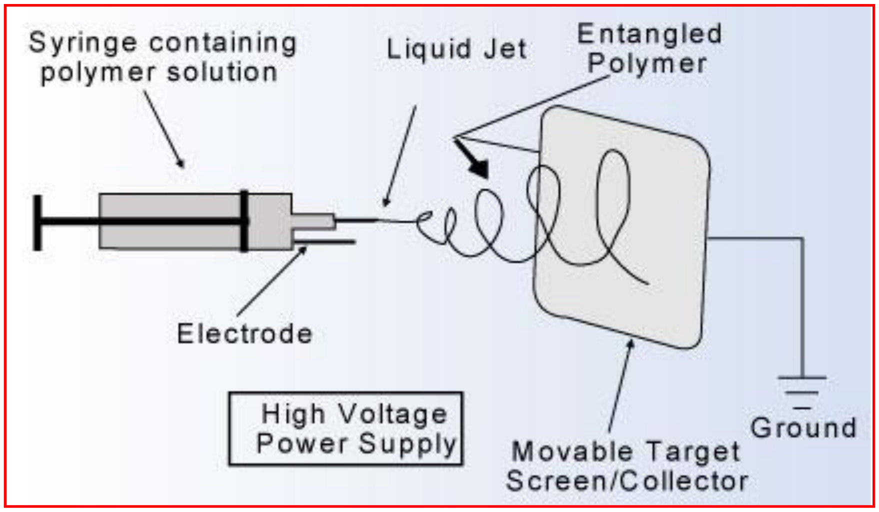

Fig. 7.1: Experimental electrospinning process.

The morphology of electrospun fibers of PLA was observed under Leica Cambridge Stereo scan Model 440 scanning electron microscope after gold coating by an ion sputtering with 15 mA for 15 min. of sample. The diameter of pure PLA fiber was found to be 469.88 nm, 860.51 and 630.41 nm, and the diameter of PLA with azithromycin drug was found to be 704.82 nm, 926.10 nm as shown in fig. 7.2

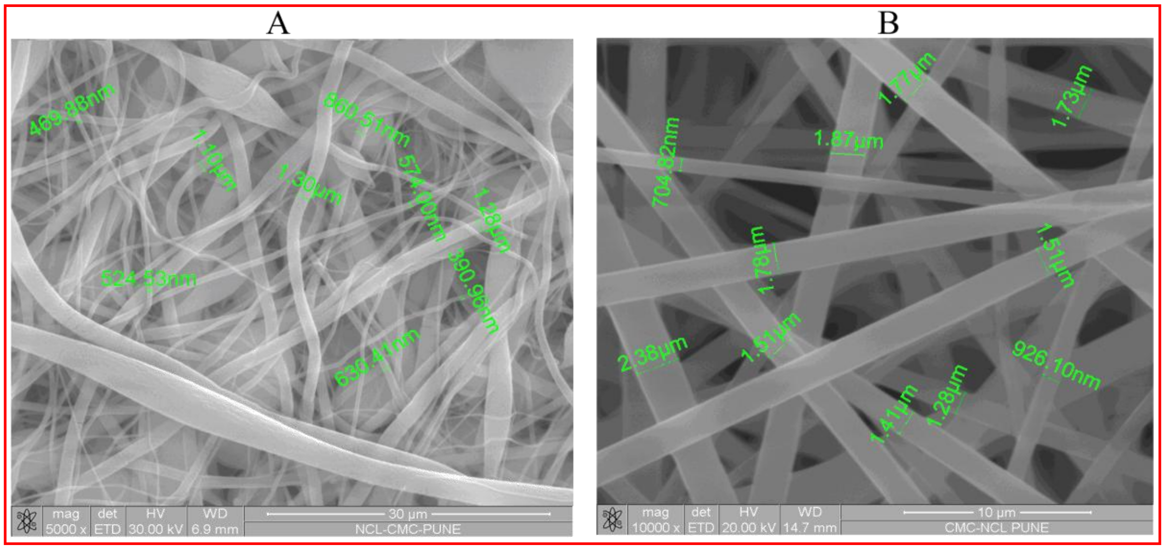

Fig. 7.2: SEM images of PLA electrospun A- without drug B-with Azithromycin drug.

7.4.2 Biodegradation Study: It has been observed that after 10 days there is a decrease in molecular weight of polymer matrix. This is due to the hydrolytic degradation of PLA matrix which gave lower molecular weights PLA chain. The molecular weight decreased from 75000 to 63700 within 10 days with lowering in melting point by 6 ^{0}C as shown in fig. 7.4. The changes in surface morphology of PLA shown in fig. 7.3.

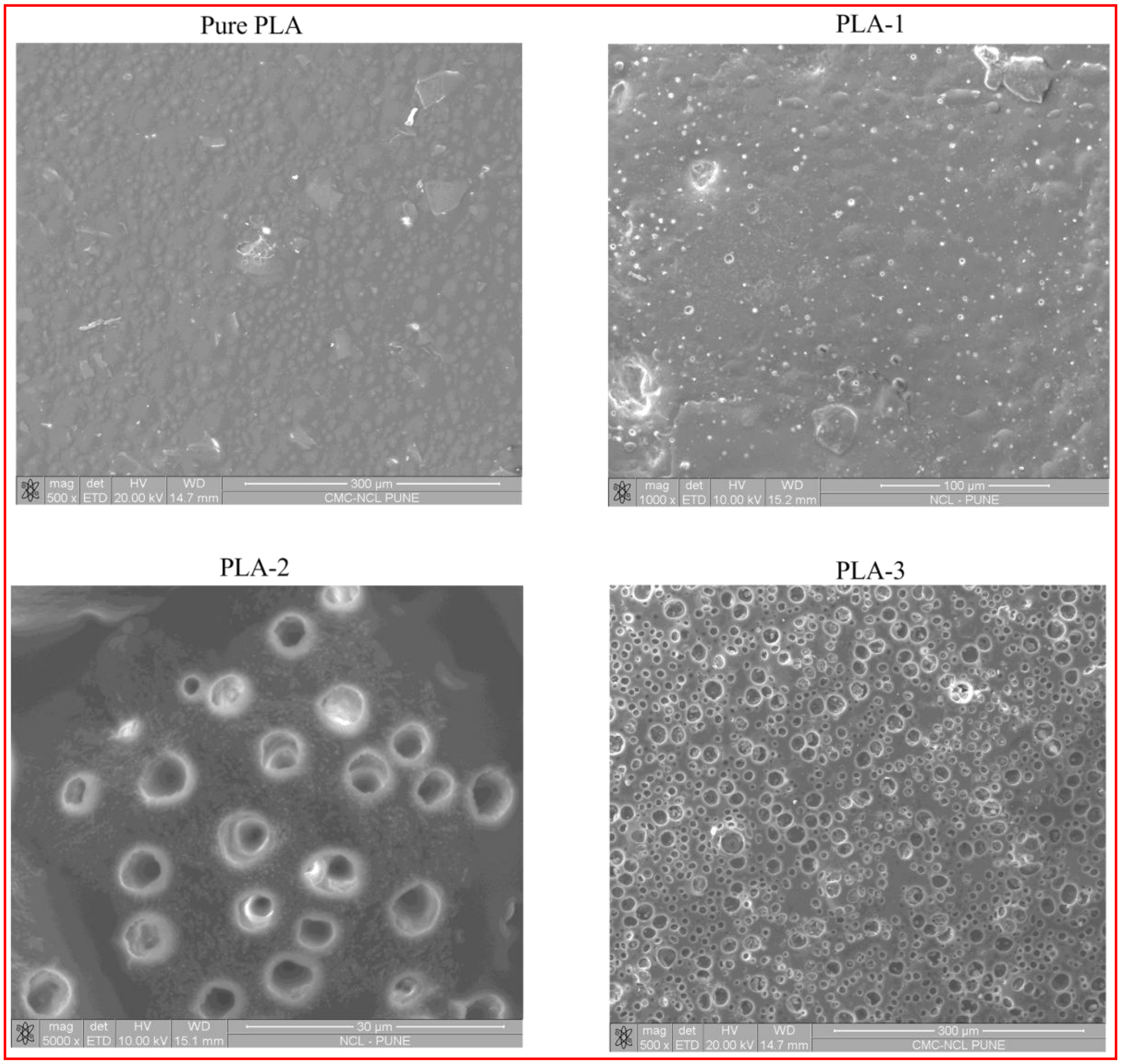

Fig. 7.3: Surface morphology of PLA before degradation (Pure PLA) and after degradation (PLA-1 to PLA-3).

7.4.3 SEM: Thus at different interval of times i. e. 10 days, 20 days and 48 days the change in molecular weight (Table 7.1) , surface morphology (fig. 7.3), melting temperature (fig. 7.4) occured. This is due to hydrolytic scission of ester group into an acid and an alcohol and thus low molecular weight polymer matrix converting into CO_2 and H_2O.

Table 7.1: Molecular weight and melting temperature of PLA after degradation

Polymer	Biodegradation Time (Days)	M_w	T_m (^0C)
Pure PLA	0	75000	171
PLA-1	10	63700	165
PLA-2	20	36000	162
PLA-3	48	22400	162

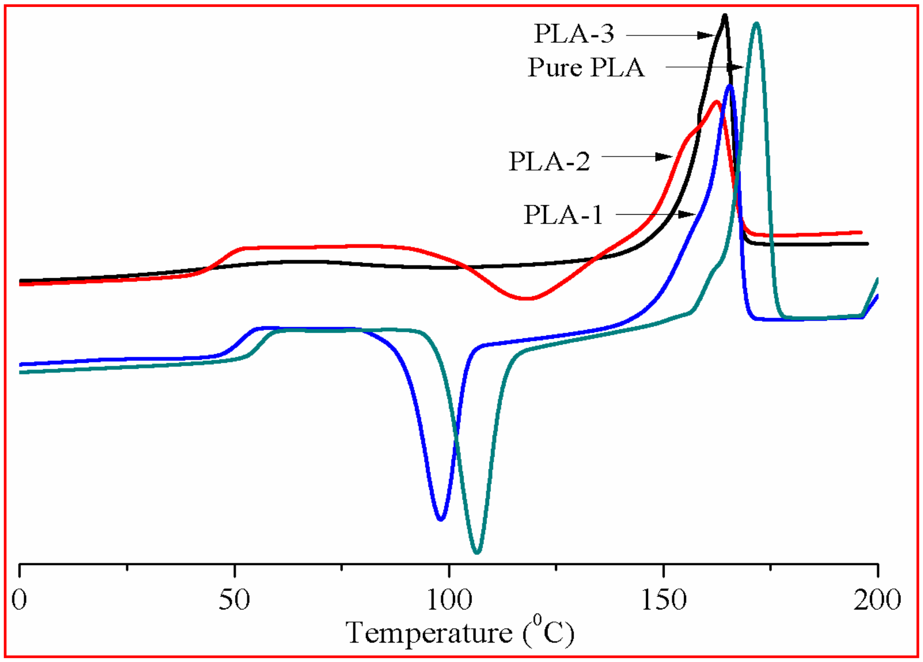

Fig. 7.4: DSC thermograms of PLA and degraded PLA.

7.4.4 Electrical Conductivity: Table 7.1 and Table 7.2 show the electrical conductivity of the PCL, PLA after mixing with isobutrin at different compositions. The electrical conductivity of pure PCL is 3.903×10^{-11}. The conductivity of the material increased i.e. 15.62×10^{-10} as the weight of isobutrin increased up to 60/40 composition. This may due to the physical interaction (non-covalent interactions) between PCL matrix and isobutrin. In case of PLA there was fluctuation of electrical conductivity result as depicted in Table 7.2. This showed less physical interaction (non-covalent interactions) between PLA matrix and isobutrin.

Table 7.2: Electrical conductivity of PCL/Isobutrin

PCL/Isobutrin (wt/wt)	Resistivity (Ω.cm)	Conductivity ($S.cm^{-1}$)
100/0	0.256×10^{11}	3.903×10^{-11}
90/10	0.158×10^{10}	6.293×10^{-10}
80/20	0.107×10^{10}	9.345×10^{-10}
70/40	0.103×10^{10}	9.689×10^{-10}
60/40	0.064×10^{10}	15.625×10^{-10}
50/50	0.412×10^{10}	2.422×10^{-9}

Table 7.3: Electrical conductivity of PLA/Isobutrin

PLA/Isobutrin (wt/wt)	Resistivity (Ω.cm)	Conductivity ($S.cm^{-1}$)
100/0	$0.0791 \mathrm{X} 10^{12}$	$12.642 \mathrm{X} 10^{-12}$
90/10	$0.2322 \mathrm{X} 10^{11}$	$4.30 \mathrm{X} 10^{-11}$
80/20	$0.095 \mathrm{X} 10^{12}$	$10.40 \mathrm{X} 10^{-12}$
60/40	$0.1225 \mathrm{X} 10^{11}$	$8.16 \mathrm{X} 10^{-11}$

7.5 Conclusion:

The PLA nonwoven nanofibers was fabricated using electrospinning. The antibacterial drug was added into it and fabricated nanofibers in nanometer range. Bacterial study showed good evident of killing bacteria in presence of drug inside the nanofibers. The biodegradable test was also performed. The degradation occured hydrolytically followed by enzymatically. The presence of bacteria is responsible for biodegradation converting PLA film to CO_2 and H_2O. PLA is an insulating polymer. The mechanical and conductivity properties were enhanced by incorporation of isobutrin, a naturally occuring compound.

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CHAPTER - 8

CHAPTER-8: SUMMARY AND CONCLUSION

8.1 Summary:

In the present work, poly (L-lactic acid) oligomers were synthesized, starting from L-lactic acid monomer obtained as 88 % aqueous solution. Monomer purity was determined by gas liquid chromatography and the total amount of impurities such as methanol, ethanol, acetic acid, pyruvic acid, fumaric acid and succinic acid were detected to be less than 30 ppm.

Linear PLA oligomers of controlled number average molecular weight and having both hydroxyl and carboxyl end groups were prepared as PLA oligomers by dehydropolycondensation and ring opening polymerization of lactide.

A range of PLA oligomers starting from linear to macro cyclic were obtained by dehydropolycondensation of L-lactic acid under various reaction conditions and using Lewis acid catalysts. Properties of the PLA oligomers were found to be more dependent on the polymerization temperature (140-190 ^{0}C) and also somewhat the nature of the catalyst. PLA oligomers are strictly linear in the polymerization temperature in to the temperature range (140-145 ^{0}C). Both linear and macro cyclic PLA oligomers were obtained in the range of 160-165 ^{0}C. Macro cyclic structures were predominant in the higher temperature (~190 ^{0}C). Incorporation of D-lactic acid units in the backbone due to racemization was also observed at 190 ^{0}C.

Clay modified tin catalyst was prepared and characterized using various techniques such as FTIR, ^{1}H-NMR, ^{13}C-NMR and ^{119}Sn-NMR. Linear PLA polymers were synthesized in presence cloisite modified tin catalyst using ROP technique. The prepared PLA polymer (M_w~75000) of both Poly (L-lactide)s and poly (D-lactide)s were used at various proportions to provide stereo complex. The surface modification was carried out by plasma treatment to obtain hydrophilic surface.

Homo and copolymers of ε-caprolactone were prepared in presence of cloisite modified tin catalyst. The kinetic and thermodynamic parameters were studied. Nano clays were incorporated to the polymer matrix (homo and copolymer) to obtain better thermal, mechanical and other properties.

Biodegradable polyesters were prepared by dehydropolycondensation route. Biodegradable macrocyclic lactones were prepared from naturally occurring hydroxy carbonyl acids such as 12-hydroxy stearic acid, Aleuritic acid etc. ROP of macrocyclic lactones were carried out and the copolymers were characterized using various techniques.

The precursor (PLA oligomers prepared by ROP) was used for ester-urethane, ester-ester and ester-carbonate linkage formations.

PLA films containing anti-inflammatory natural drug (isobutrin) were prepared and characterized. The biocompatible, biodegradable, non-woven PLA nanofibers for biomedical applications were fabricated using electro spinning. Antibacterial and biodegradation studies were carried out.

8.2 Salient achievements of the present work:

1) Although PLA polymers using stannous octoate catalyst have widely studied, the ring opening polymerization of lactones in presence of solid cloisite modified tin catalyst have not been carried out. **PLA and PDLA polymers using modified catalyst showed molecular weight and molecular weight distribution M_w/M_w as M_w~7 x 10^4 and 1.6 respectively. The maximum molecular weight M_w~ 185,000 Da of PLA was obtained. Stereo complexes of PLA and PDLA were prepared at various compositions. A compact honeycomb structure of the film (70:30 PLA: PDLA) stereo complex.**
2) There are few literature reports here and these regarding homopolymer of ε-caprolactone obtained. **Copolymers of ε-caprolactone with β- butyrolactone and L-lactide were prepared in presence Ti(IV)butoxide. Various clays were incorporated during *in situ* polymerization. A single T_g was observed in all set of copolymers at various compositions confirming the random distribution of comonomers in copolymer chain.**
3) There are few literature reports about poly aleuritic acid by enzymatic method. Poly (aleuritic acid) has also been carried out by condensation method and resulted infusible masses due to side reaction and cross linked reaction etc. **A linear poly (Aleuritic acid) with M_w= 120000 was prepared by dehydropolycondensation using protection and deprotection of 9 and 10**

hydroxy group. A macrocyclic ring of Aleuritic acid was synthesized after protection of 9,10 hydroxyl groups. Poly (aleuritic acid)s were prepared using ROP technique in presence of stannous stearate. The M_n, M_w and D are 2420, 2933 and 1.20 respectively. Cyclic structure of 12-HSA was synthesized. The monomer grade L-lactide was prepared. Copolymers of cyclic lactones of 12-HSA with L-lactide at various compositions were prepared and maximum molecular weight M_w~ 5200 Da was achieved.

4) Polyurethanes have found many applications such as coatings, adhesives, sealants, defoamers and textile dyes. Biodegradable polyester urethanes are used in biomedical application such as drug delivery, stent, packing materials because of their good mechanical properties, biodegradability and biocompatibility. Polyurethanes were prepared from diol ended PLA precursor and various isocynates (TDI, HMDI and HDI) at 80 °C using reaction time (30m). **The maximum molecular weight i.e. M_w=9000 Da was obtained at 100 °C. A linear polyurethane is formed if starting material is diol ended PLA. If the starting material is PLA containing both hydroxy and carboxyl groups, the obtained polyesterurethanes were a mixture of linear and 30% insoluble crosslinked products.**

Polyester carbonate was prepared by copolymerizing L-lactide with 5,5-dimethyl-1-3 dioxan-2-one at various compositions in presence of cloisite modified tin catalyst at 200 °C for 1 hr. **There was no ether linkage formation during copolymerization which is obvious in presence of other catalyst. The thermal properties such as T_g and T_m values can be tuned changing the compositions of comonomers. The maximum molecular weight was achieved as 20900 Da.**

Poly ester-ester was prepared using secondary hydroxyl terminated PLA telechelic polymer at both end and sebacic acid. **The structure of the poly ester-ester containing aliphatic as well as aromatic moiety was confirmed by ^{1}H-NMR**.

5) The application of PLA polymer in biomedical as well as other application is enormous. Isobutrin is generally recognized as an anti-inflammatory drug. **However, when it was incorporated in PLA matrix, it enhanced the**

conductivity. The nonwoven mat of PLA as well as PLA-Azithromycin was prepared using electrospinning technique. **The SEM showed that the electrospun fibers are of nanometer size. Biodegradation study of PLA films was performed inserting the films into the house made compost. The biodegradation study was carried out at different interval of time and SEM results showed there was a substantial degradation of PLA film after 48 days. The molecular weight M_w decreased from 75,000 to 22,400.**

Future directions:

High molecular weight PLA was prepared using solid cloisite modified tin catalyst. The application scope of PLA is limited because of its hydroscopic nature. In addition, the hydrophilic degradation rate of PLA for application in drug delivery purpose is slow due to its high crystallinity, which results in poorer soft tissue compatibility. In order to overcome the drawback of the PLA homopolymer, many kinds of comonomer i.e. glycolide unit was inserted in to PLA chain using the prepared catalyst. The application of poly(lactide/glycolide) (PLGA) in pharmaceutics and nanomedicine will be attempted. Processing of high molecular weight PLA finds difficulty because of its crystallinity. Several plasticizers have been tried. However the plasticizers are small organic molecules escape during processing. Therefore, 12-hydroxy steraic acid (12 HSA) was used as a precursor for preparing cyclic lactones of 12-HSA. The internal plasticization will be tuned using various proportions of composition of L-LA and lactones of 12-HSA.

Functionalization of aliphatic polyester is tedious. Therefore, aleuretic acid (AA) was used to prepared cyclic lactones of AA. After protecting 9, 10 hydroxyl group, the copolymerization will be attempted using different composition of L-lactide and cyclic lactones of AA. The prepared copolymers will have several applications. The hydroxyl group at 9, 10 positions will be free after deprotection and can be used for complexation with drug molecules, and also for ester bond formation.

Polyester urethanes were prepared. Injectible gel has attracted tremendous attention. Therefore, tridlock copolymers, poly (ethylene glycol-b (D, L-lactic acid-co glycolic acid)-b-ethylene (PEG-PLGA-PEG) will be prepared and coupled with hexamethylene diisocyanate. This polymer will show thermo-reversing gelatin, where sol-to-gel transition at lower temperature and gel-to-sol transition at higher temperature is targeted. Because it is the lower transition, sol to gel, which is more important because polymer will flow as a solution at room temperature while gel inside the body at body temperature. Novel bio-compatible, biodegradable hydrogel with controlled pore architectures will be synthesized for the applications in tissue engineering and CRT. Electrospun non woven nano-fiber of PLA and PLA with drugs was fabricated and characterized. The specific porogens (pore forming materials) will be developed using electro-spinning technique.

PUBLICATIONS

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Balaji S. Selukar, Asutosh K. Pandey, Smita S. Nande, Avinash Bansode, Baijayantimala Garnaik*****, **Journal of chemistry and Chemical Engineering 2012, 6, 54-60.**

2 Synthesis of Linear Polylactic Acid-Based Urethanes Using Tin modified Solid Cloisite-30B Catalyst, **Balaji S. Selukar** , Sharad P. Parwe , Kavita K. Mohite, Baijayantimala Garnaik*, **Advanced Materials Letters 2012, 3(2), 161-171.**

3 Synthesis and Characterization of Novel Value Added Biodegradable Poly(aleuritic acid) From Renewable Resources (shellac) and Invertible Amphilic Behaviors in Various Solvent, Asutosh K. Pandey, Smita S. Nande, **Balaji S. Selukar**, Baijayantimala Garnaik*, **e-Polymers 2010, 131, 1-12.**

4 Synthesis and Characterization of Poly(ε-Caprolactone) Using Solid Cloisite Modified Tin Catalyst, **Balaji S. Selukar**, Baijayantimala Garnaik*, **Journal of Polymer Chemistry, Chemistry Edition, 2012 (Manuscript under Communication).**

5 Ring-Opening Copolymerization of (R,S)β-butyrolactone and ε-caprolactone presence of Cloisite-15A Using Ti (IV)butoxide, **Balaji S. Selukar**, Baijayantimala Garnaik*, **Journal of Applied Polymer Science, 2012 (Manuscript under Communication).**

POSTER PRESENTATIONS IN NATIONAL AND INTERNATIONAL CONFERENCES

1 Attended **MACRO 2006**, an International Conference on Polymers for Advanced Technologies, 17-20, December 2006, **National Chemical Laboratory Pune, India.**

2 Presented a poster in International Symposium on Advanced Materials and Polymers for Aerospace and Defense Applications (**SAMPADA December 2008, Pune**)) entitled: "Unique template effects of fluorous distannoxane catalyst in transesterification of L- Lactic acids and poly lactate polymers." Balaji S. Selukar, Dnyaneshwar Rasale, Gundloori V. N . Rathna, Baijayantimala Garnaik.*

Best poster award-2nd Prize

3 Attended **MACRO 2009** Recent Advances in Polymeric Materials March 9-11, **2009, IIT Chennai**.

4 Presented a poster in Polymer Congress "APA" **December 2009 New Delhi** entitled: "Unique crystallization behaviour of poly (L actide) / poly (D Lactide) stereocomplex depending on ROP using novel clay modified metal catalyst." Balaji S. Selukar, Baijayantimala Garnaik.*

5 Presented a poster in **APSRT 2011 in IIT Khargpur** entitled: "Biocompatible, Biodegradable linear polylactic acid-based urethane with controlled hydrophobic to hydrophylic Group Ratio." Balaji S Selukar, Sharad P. Parwe, Kavita K. Mohite, Baijayantimala Garnaik.*

6 Presented a poster in **National Science Day 2011 in NCL**, Pune entitled: Synthesis of PLA using novel clay modified catalyst and its characterization, degradation and application in sustained drug release." Balaji S. Selukar, Sharad Parwe, Kavita Mohite, Swapnali Jadhav, Santosh Tupe, Baijayantimala Garnaik.*

7 Presented a poster in **National Science Day 2012 in NCL**, Pune entitled: "Synthesis and characterization of biodegradable and biocompatible copolymers." Balaji Selukar, Baijayantimala Garnaik*.