

# Ring opening polymerization of lactide by using zinc proline catalyst

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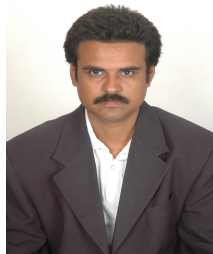
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Received: 16 June 2013, Revised: 16 July 2013 and Accepted: 21 July 2013

## ABSTRACT

Zinc salts of L-proline, D-proline were used in homopolymerization of L, L-lactide and D, L-lactide. Linear PLA oligomer with  $\bar{M}_n$  2900-3400 Da, can be prepared with zinc (L-proline)<sub>2</sub> catalyst. Less racemization were occurred in presence of Zn (L-proline)<sub>2</sub> than Zn (D-proline)<sub>2</sub>. The catalyst structure of Zn (L-proline)<sub>2</sub> and Zn (D-proline)<sub>2</sub> remains intact after polymerization. The zinc is bioactive molecule so these polymers prepared by using this catalyst are bioabsorbable. The resulting polymers were characterized by infrared spectroscopy (IR), size exclusion chromatography (SEC), differential scanning calorimetry (DSC), thermo gravimetric analysis (TGA), <sup>13</sup>C NMR, <sup>13</sup>C Cross Polarization /Magic Angle Spinning (<sup>13</sup>C CP/MAS) and MALDI ToF-MS. Copyright © 2014 VBRI press.

**Keywords:** Zinc proline; lactides; ROP; MALDI-ToF-MS; linear polymer.



Asutosh Kumar Pandey did his master from Banaras Hindu University in 2000. In 2003, joined National Chemical Laboratory Pune as a NET-JRF and finish Ph.D. in 2009, after that he visited France as a postdoctoral fellow in LCPM Nancy, Then after he got a postdoc position in University of Louisville KY USA. He published 34 International papers and his research interest is biomedical polymer synthesis characterization and applications.

## Introduction

In the recent year, there are enormous catalysts have been used for the polymerization of lactide and other lactones [1-4]. Some studies of variable catalyst have also been carried out. These catalysts are absolutely non-toxic, because they have been used and no adverse effect has been observed in polymeric product. Poly lactide (or poly lactone) polymer prepared using such catalyst does not require to be purified from the catalysts prior to a medical (implantation of various body parts and other accessories) or pharmaceutical application. The widely used catalyst such as salts or complexes of aluminum, tin or lanthanide ions for the polymerization of lactides or lactones, do not meet the above requirements. Zinc metal or its derivative was considered as a potential catalyst for lactides or lactones polymerization. Several difficulties have also been encountered. Zinc metal or zinc containing compound has been studied by several research groups with mixed results. Basic compound such as zinc oxide or

carbonate favors partial racemization of L-lactide and termination steps. Use of diethyl zinc catalyst during polymerization of lactide and lactones has caused technical problem because it is highly moisture sensitive and self-inflammable liquid. Zinc powder is removed from the poly lactones by ultra filtration. There are some literature reports about the use of organo-zinc in polymerization of lactide and lactones, but nothing is known about the toxicity of the legend, which does not belong to the human metabolism. Although numerous amino acids and their derivatives belong to the human metabolism, zinc salts of amino acids have rarely been used as catalysts for the polymerization of lactides and lactones [4].

Recently, poly (lactide) (PLA) and poly ( $\epsilon$ -caprolactone) (PCL) and their copolymer have attracted more attention in the fields of surgery, sustained drug delivery and tissue engineering [5-7]. These polymers have shown their potential applications in a variety of fields because of their biodegradability, biocompatibility and permeable properties. Poly ( $\epsilon$ -caprolactone) shows low melting temperature ( $T_m \sim 60$  °C) and high decomposition temperature ( $T_d = 350$  °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  $\epsilon$ -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  $\epsilon$ -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  $\epsilon$ -caprolactone obtained by ROP contributes flexibility behavior because of the  $\epsilon$ -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.  $\beta$ -diketiminato ligand 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  $\beta$ -diketiminato ligands) for the ring opening polymerization of lactides and  $\epsilon$ -caprolactone has been studied [19].

Zinc metal or zinc containing compounds were studied by several groups [20-25], with mixed results. Zinc oxide or carbonate favors partial racemization of L, L-lactide and termination steps. Diethyl zinc is a highly moisture sensitive and self-inflammable liquid. This is inconvenient for up scaling and technical productions of polylactides. Zinc powder needs to be removed by ultra filtration. Zinc bis (2, 2-dimethyl -3, 5-heptanedionate) gives high molecular weights, but nothing is known about toxicity of the ligand, which doesn't belong to the human metabolism. The present work highlights on zinc salts of amino acids, although numerous amino acids and their derivatives belong to the human metabolism, zinc salts of proline have never been used as catalysts for the polymerization of lactides. Zinc proline was selected because of its biocompatibility in comparison with other reported catalyst. Therefore, zinc salts of L-proline, D-proline were used in homopolymerization of L, L-lactide and D, L-lactide. The resulting copolymers were characterized by  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, size exclusion chromatography (SEC), infrared spectroscopy (IR), differential scanning calorimetry (DSC), thermo gravimetric analysis (TGA) and MALDI ToF-MS.

## Experimental

### Materials and methods

L, L-lactide,  $\epsilon$ -caprolactone, L-proline, D-proline and zinc acetate were purchased from Aldrich sigma USA, dichloromethane (DCM) and methanol were purchased from SD-Fine Chemical India.

### Synthesis of zinc proline catalysts

The catalyst zinc L-proline was easily synthesized by stirring zinc acetate  $\text{Zn}(\text{OAc})_2$  (1 equiv.), L-proline (2

equiv.) and triethylamine (2 equiv.) in methanol (Fig. 1A). The complex (white sluggish) was precipitated out from the methanolic solution and can be easily isolated. Zinc D-proline was prepared by using similar procedure. The spectroscopic data [26], the mononuclear zinc (proline) $_2$  was to be the prevailing species. FTIR also confirmed the structure before and after the complexation with proline.

$\text{C}_{10}\text{H}_{16}\text{N}_2\text{O}_4\text{Zn}$  (291.60), calculated, C 40.91, H 5.48, N 9.54 and found C 40.90 H 5.53 N 9.4. The crude product was recrystallized and  $[\alpha]_D^{20} = -53.68$  concentration 2.59/dl in water.

The complex was resulted from the reaction of zinc acetate with either (L or D) proline. The two L-proline molecules are coordinated to the zinc atom via their N and carboxylic O atom. The zinc atom is pentacoordinate, fifth coordination site being occupied by the symmetry related O (4') (symmetry code: (i) 2-x, y-1/2, -z) of a neighboring proline molecules, so that an infinite polymeric chain is generated. The polymer shows a helical structure along the 2<sup>1</sup> direction. The zinc coordination here is unique as most zinc amino acid complexes are hexadentate.

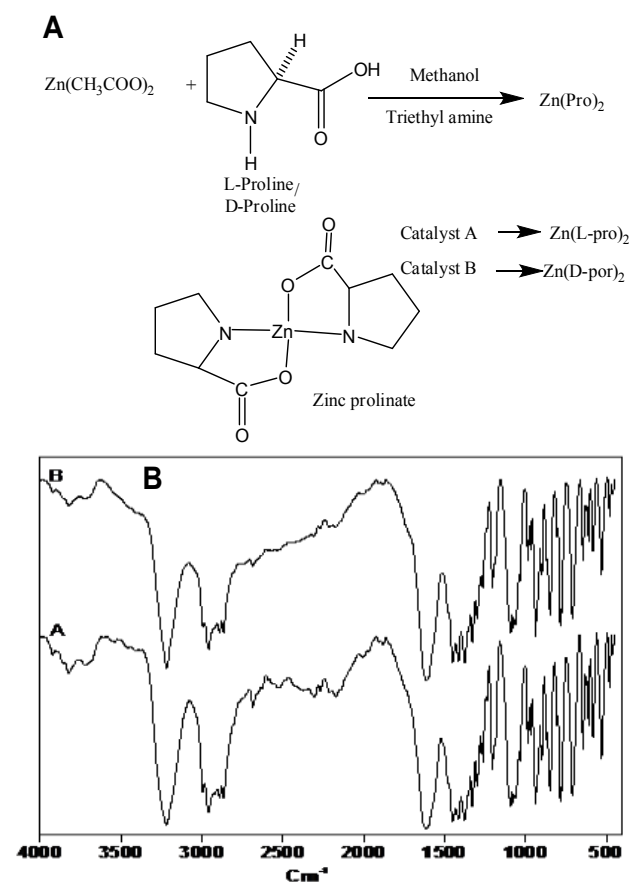


Fig. 1. (A) Synthesis of catalysts and (B) FT-IR spectra of (A) zinc L-proline and (B) zinc D-proline.

FT-IR (Fig. 1(B)) showed the N-H stretching at  $\sim 3750$   $\text{cm}^{-1}$ , C=O ketonic ( $\nu$  CO) =  $1590$   $\text{cm}^{-1}$  and antisymmetric and symmetric carbonyl stretching frequency at  $1720$  and  $1350$   $\text{cm}^{-1}$ . The stretching  $\nu$  (CO) and  $\nu$  N-H bands of L-proline after coordination with zinc appeared at  $3250$  and  $1550$   $\text{cm}^{-1}$ . The antisymmetric and symmetric carbonyl stretching frequency at  $1550$  and  $1350$   $\text{cm}^{-1}$  respectively.

The difference between the antisymmetric and symmetric stretching frequencies  $\nu$  (COO<sup>-</sup>), which is 168 cm<sup>-1</sup> and similar to the stretching frequency of M-O bond. Similarly IR spectra of zinc D-prolinate showed the frequency at 3250 cm<sup>-1</sup> and 1550 cm<sup>-1</sup>. The carbonyl antisymmetric and symmetric stretching frequency at 1680 and 1382 cm<sup>-1</sup> respectively.

#### Characterization

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<sup>-1</sup>).

Size exclusion chromatography: As Molecular weights (relative,  $\bar{M}_n$  and  $\bar{M}_w$ ) and polydispersity ( $\bar{M}_w/\bar{M}_n$ ) were determined with respect to polystyrene standards by size exclusion chromatography on a Thermo Finnigan Spectra Series AS300 machine at 25 °C by eluting PLA solutions of 10 mg/ mL concentration in CHCl<sub>3</sub>, with toluene as internal standard, through a series of five  $\mu$ -Styragel columns of pore sizes 10<sup>5</sup>, 10<sup>4</sup>, 10<sup>3</sup>, 500, and 100 Å<sup>0</sup>, respectively, and length 30 cm each. CHCl<sub>3</sub> 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.

Differential scanning calorimetry (DSC): Differential scanning calorimetric (DSC) measurements were made on a Perkin-Elmer thermal analyzer model DSC-7 in a nitrogen atmosphere. The measurements were run from -40 to 200 °C at a heating rate of 10 °C/ min and a cooling rate of 100 °C/ min. The glass transition temperature ( $T_g$ ) and crystallinity data were recorded from the second and first heating curves, respectively. Crystallinity values for different polymers were calculated from the heat of fusion. By integrating the normalized area of the melting endotherm, determining the heat involved, and rating it to the reference 100 % crystalline polymer (93.6 J/ g), the relative crystallinity of the polymer was assessed. In the present work, the relative degree of crystallinity is referred to as crystallinity, and  $T_m$  is the melting temperature.

Nuclear magnetic resonance spectroscopy (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 <sup>13</sup>C NMR measurements was 10 % by weight. Proton decoupled <sup>13</sup>C NMR spectra with NOE were recorded on a Bruker DRX 500 MHz NMR spectrometer working at 125.577 MHz for carbon-13. CDCl<sub>3</sub> served as solvent and TMS as internal standard for all <sup>13</sup>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.

<sup>13</sup>C cross polarization/magic angle spinning (<sup>13</sup>C CP/MAS): <sup>13</sup>C CP/MAS NMR spectra were measured with Bruker MSL-300 NMR Spectrometer (75.5 MHz) with <sup>13</sup>C CP/MAS accessory at room temperature (25 °C). The sample powder (200 mg) was placed in a cylindrical ceramic rotor and spun at 3 KHz. Contact time and repetition time were 2ms and 5s respectively. Spectral

width and data points were 27 KHz and 8 K, respectively. The 1H field strength was 2mT for both the CP and decoupling processes. The number of accumulations was 160-200. <sup>13</sup>C Chemical shifts were calibrated indirectly with reference to the higher field adamantane peak (29.5 ppm relative to tetramethyl silane ((CH<sub>3</sub>)<sub>4</sub>Si). The Hartmann-Hann condition was matched using adamantane in each case. The experimental errors for the chemical shifts were within  $\pm$  0.1ppm for broad peaks as described.

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 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 smoothed to reduce the spikiness by the average method; the smoothing filter moved along the collected data channels, adding together a number of channels and dividing by that number to give an average signal. This smoothing, however, did not eliminate or hide minor signals distinct from the baseline noise. The samples were dissolved in CHCl<sub>3</sub> (1 mg/ mL) and mixed with matrix (15 mg/mL of tetrahydrofuran) before being dried on the sample plate. 4-hydroxy cinnamic acid (CHCA) was used as the matrix. The sample plate was inserted in to the apparatus under a high vacuum (10-5 Pa).

## Results and discussion

The zinc salts of proline having two configurations (L- and D-) were prepared and used as potential catalysts of the polymerization of L-lactide and D, L-lactide. Zinc salt of L-proline should be compared with that of zinc D-prolinate in term of their structure. The catalysts can also be recovered by dissolving product (PLA) in dichloromethane and precipitating using deionised water because catalysts are water soluble. Zinc salts of L-proline and D-proline dried over P<sub>4</sub>O<sub>10</sub> and composition were rechecked by elemental analysis prior to further use.

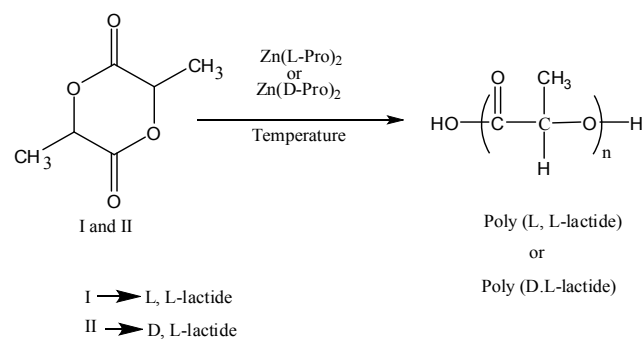


Fig. 2. Homopolymerization of L, L-lactide and D, L-lactide.

#### General procedure for synthesis of PLA by ring opening polymerization

2g (0.0138 mmol) of lactide (L and D, L-lactide) was taken for each reaction and variable requisite concentration of zinc prolinate (L or D) was taken and polymerization was carried out in sealed glass reactor previously passivated

with trimethyl silyl chloride. Thermodynamic and kinetic parameters were altered to examine their effect on ring opening polymerization. The type of catalyst was also varied. The reaction scheme is shown in Fig. 2.

**Table 1.** Effect of temperature on ROP of L, L-lactide.

Polymer samples	Temperature (°C)	$\bar{M}_n$ (GPC)	$\bar{M}_w$ (GPC)	$T_g$ (°C)	$T_m$ (°C)	$\Delta H_f$ (J/g)	$T_c$ (°C)
L-1	150	850	2900	35.55	90.8	49.67	nd
L-2	180	3200	4200	34.12	144.13	39.63	70.08
L-3	195	5100	9200	55.15	138.99	29.69	103.29
L-4	210	4000	4600	21.31	124.93	18.38	nd
L-5	240	3800	4600	38.76	nd	Nd	nd

L, L-lactide, zinc L-prolinate catalyst,  $[M]/[C] = 675$ , time of polymerization 60 min and nd –not detected.

**Table 2.** Effect of  $[M]/[C]$  ratio on the polymerization (ROP) reaction of L, L-lactide.

Polymers samples	$[M]/[C]$	$\bar{M}_n$ (GPC)	$\bar{M}_w$ (GPC)	$T_g$ (°C)	$T_m$ (°C)	$\Delta H_f$ (J/g)	$T_c$ (°C)
L-6	337	4000	4700	51.66	146.85	21.1	105.2
L-7	405	4300	4900	35.15	132.09	23.0	106.5
L-8	506	4400	6200	42.28	139.28	20.7	95.3
L-3	675	5100	9200	55.15	138.99	29.7	103.3
L-9	1013	3400	8400	47.74	144.89	30.4	99.2

As all polymerization were conducted at 195 °C, monomer was L, L-lactide, zinc L-prolinate catalyst and time of polymerization time 60 min.

**Table 3.** Effect of reaction time on polymerization (ROP) of lactide.

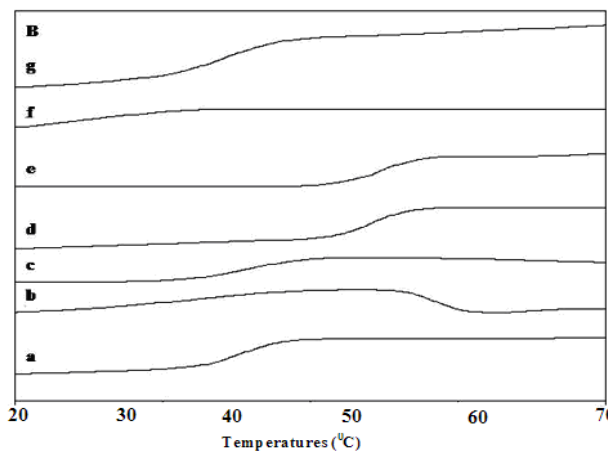
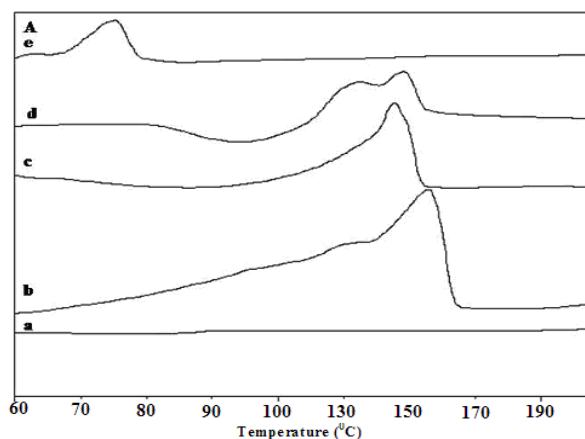
Sl. No.	Lactide	Catalyst	Time (min)	$\bar{M}_n$ (GPC)	$\bar{M}_w$ (GPC)	$T_g$ (°C)	$T_m$ (°C)	$\Delta H_f$ (J/g)	$T_c$ (°C)
L-10	L-LA	Zinc L-prolinate	30	4500	6500	16.24	110.02	15.26	68.77
L-11	L-LA	Zinc L-prolinate	90	4500	6600	49.75	133.69	17.09	nd
L-12	L-LA	Zinc L-prolinate	120	3600	6900	44.29	142.21	15.60	96.45
L-13	L-LA	Zinc D-prolinate	60	2500	5800	51.67	79.11	6.91	nd
L-14	D-LA	Zinc L-prolinate	60	1500	2700	20.65	Nd	Nd	nd
L-15	D-LA	Zinc D-prolinate	60	1341	2500	37.44	Nd	Nd	nd

### Molecular weight determination

**Table 1** shows the ring opening polymerization of L, L-lactide in presence of Zn (L-prolinate)<sub>2</sub>. The homopolymers (L-1 to L-5) were prepared in presence of zinc L-prolinate catalyst at various temperatures ranging from 150 °C to 240 °C, keeping fixed monomer to catalyst ratio. The yield and molecular weight increased monotonously up to 195 °C and thereafter became steady. The maximum yield obtained was 93 %, which is close to the realistic maximum. Because the conversion of L, L-

lactide cannot be higher than 96±1% due to thermodynamic reason. PLA was prepared at 195 °C in 1h and showed  $\bar{M}_n$  and  $\bar{M}_w$  values as 5100, 9200 Da and polydispersity as 1.8 respectively, which was obtained at 675 monomer to catalyst ratio. Polymers L-6 to L-9 are shown in **Table 2** varying  $[monomer]/[catalyst]$  ratios.

**Table 3** depicts polymers L-9 to L-13, which showed the effect of polymerization time. The maximum molecular weight was obtained at 2 h of polymerization time at 195 °C. Polymer L-3 and L-13 showed comparative results of the catalytic activity of Zn (L-prolinate)<sub>2</sub> and Zn (D-prolinate)<sub>2</sub> respectively.



**Fig. 3.** (A) DSC thermogram of PLA (a) L-5, (b) L-3, (c) L-9, (d) L-12 and (e) L-13 and (B) DSC thermogram of PLA (a) L-5, (b) L-3, (c) L-9, (d) L-12 and (e) L-13.

The results confirmed that Zn (L-prolinate)<sub>2</sub> is more reactive in comparison to Zn (D-prolinate)<sub>2</sub>. Similarly, catalytic activities of both zinc prolinate were studied in presence of the D, L-lactide. There were no remarkable effects of the catalyst in the polymerization reaction. The molecular weights of PLA polymers were low with narrow distribution. The molecular weight increased with the increase in  $[M]/[I]$  ratio and decreased thereafter. Similar results have been observed using Zn L-lactate [27] catalyzed polymerization of 1, 4-dioxane-2-one polymerizing L-lactate in presence of Sn (II) octoate [28] using highly active zinc catalyst for the controlled polymerization of lactide [29] and also other example. The result of Zn L-prolinate catalyzed polymerization showed

that  $\eta$  increased with increase in  $[M]/[I]$  ratio [30]. The increase in the temperature resulted increase in molecular weight. Polymer L-3 showed  $\bar{M}_n$  and  $\bar{M}_w$  values as 5100 and 9200 Da respectively and thereafter decreased with increase in temperature up to 240 °C.

#### Thermal analysis

The results of thermal characterization are shown in table. 1 to table. 3 and thermograms are also shown in Fig. 3a and 3b.  $T_g$  varied from 21.31 to 55.15 °C for the polymers prepared with Zn (L-prolinate)<sub>2</sub>. The melting temperature  $T_m$  of the polymers prepared with the Zn (L-prolinate)<sub>2</sub> catalyst increased from 110 °C to 142.2 °C, whereas polymer (L-13) prepared in presence of the Zn (D-prolinate)<sub>2</sub> showed  $T_g$  and  $T_m$  as 51.6 °C and 79.1 °C respectively. PLA prepared in presence of Zn (L-prolinate)<sub>2</sub> resulted less racemization in comparison with Zn (D-prolinate)<sub>2</sub>. The  $T_g$  obtained in case of D, L-lactide polymerization using Zn (L-prolinate)<sub>2</sub> imparts lower  $T_g$  than Zn (D-prolinate)<sub>2</sub>. The degree of crystallinity calculated from powder patterns is typically between 45 to 65 % except for few samples.

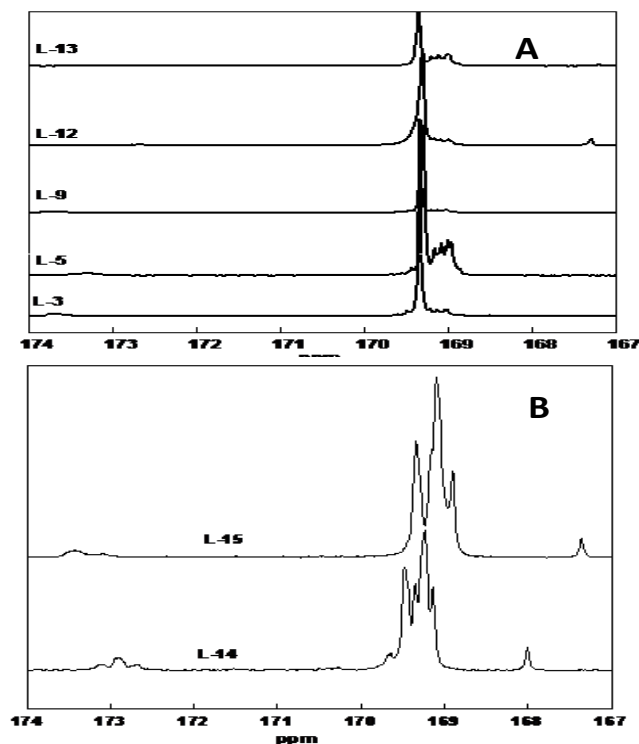


Fig. 4 (A). <sup>13</sup>C NMR spectra (500 MHz) around carbonyl (ester), carbonyl (acid) and carbonyl (lactide) areas of PLA oligomers L-3, L-5, L-9, L-12 and L-13 and (B). <sup>13</sup>C NMR spectra (500 MHz) around carbonyl (ester), carbonyl (acid) and carbonyl (lactide) areas of PLA oligomers L-14 and L-15.

#### Nuclear magnetic resonance spectroscopy (NMR)

<sup>13</sup>C NMR has been utilized as a useful tool for determining the number average molecular weight,  $\bar{M}_n$  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 [31]. <sup>13</sup>C NMR has also been used to study the

crystallization and morphology [32], and for direct observation of stereo-defects in poly (L-lactide) [33]. In the present study, <sup>13</sup>C NMR was used to determine the end groups, residual lactic acid, lactide and stereosequence of poly (lactic acid) s in PLA samples. The PLAs were prepared by changing various parameter such as catalyst concentration, polymerization time, reaction temperature variation etc, and are shown in Table 1 to 3. The spectrum of L-3, L-5, L-9, L-12 and L-13 are depicted in Fig. 4 (A). The peaks appearing from 169.23 to 169.70 ppm are due to ester carbonyl groups and peaks arising from 172.9 to 173.4 ppm are due to carboxylic acid end functional groups. The accuracy of DP<sub>n</sub> estimate, which was same in two consecutive NMR measurements. There is a peak at 167.2 ppm is due to lactide in the polymers and calculated for samples as L- 12 and L-13 are 1.2 and 0.8 respectively.

Fig. 4(B) shows the <sup>13</sup>C spectra of L-14 and L-15. The peaks arising from 169.13 to 169.72 ppm and 168.9 to 168.7 (L-16) ppm appearing are due to ester carbonyl groups. The peaks arising from 172.9 to 173.4 ppm are due to carboxylic acid end functional groups. There was a peak at 167.9 (L-14) and 167.3 (L-15) ppm due to lactide in the polymers and was estimated 2 %.

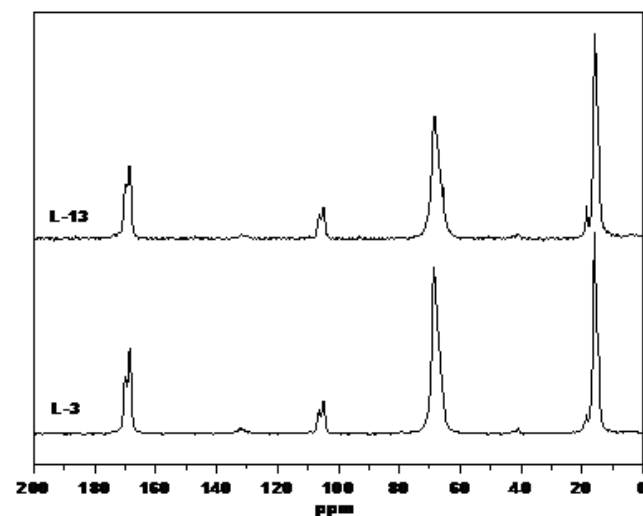


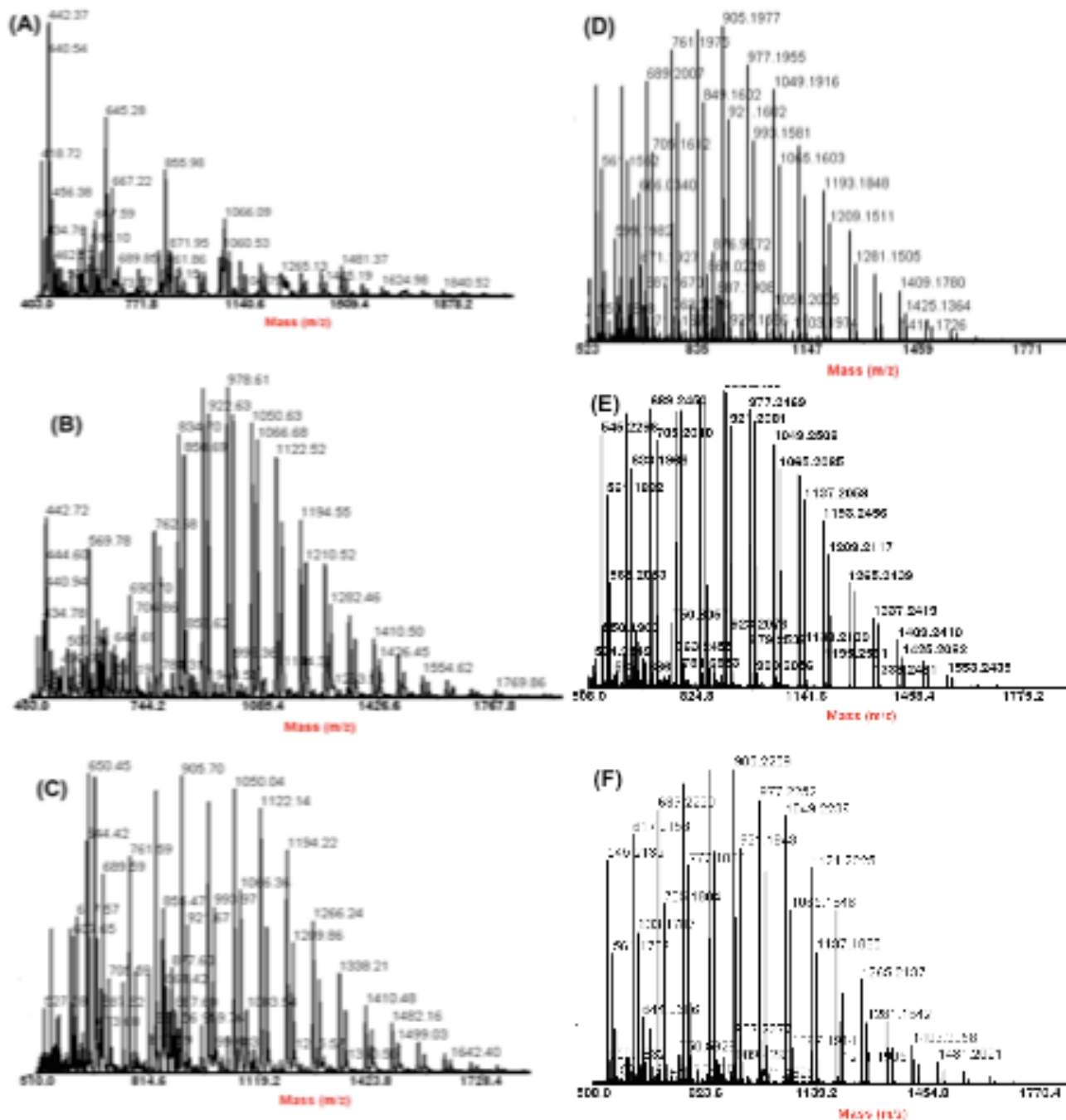
Fig.5. <sup>13</sup>C CP/MAS (300 MHz) L-3 and L-13.

#### <sup>13</sup>C cross polarization /magic angle spinning (13C CP/MAS)

The <sup>13</sup>C NMR spectrum of L-3 and L-13 are shown in Fig. 5. The peaks at 109.1 and 110.5 ppm which correspond to C-2 carbon of the complex catalyst structure.

#### 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 PLA can be prepared. Therefore polymers were prepared during this study was subjected to MALDI-ToF MS analysis and are shown in Fig. 6 (B) to 6 (F). Polymer L-3 (Fig. 6(A)), showed peaks ranging from 689 to 1840 Da corresponding to sodiated adduct molecular ions H- [O-CH (CH<sub>3</sub>) CO-]<sub>n</sub>-OH-Na<sup>+</sup> (mass=72n+18+23); n found to be varying from



**Fig. 6.** (A) MALDI ToF-MS of L-3 oligomers, (B) MALDI ToF-MS of L-5 oligomer, (C) MALDI ToF-MS of L-9 oligomer, (D) MALDI ToF-MS of L-13 oligomer, (E) MALDI ToF-MS of L-14 oligomer and (F) MALDI ToF-MS of L-15 oligomer.

9 to 25, 23 being the mass number of sodium. The series ranging from 490 to 1497 Da corresponding potassiumated adduct molecular ions of type H- [O-CH (CH<sub>3</sub>) CO-]<sub>n</sub> OH-K<sup>+</sup>.

**Fig. 6 (B)** depicts the MALDI-ToF mass spectrum of the L-5. As expected, the MALDI-ToF mass spectrum of the sample shows a series of intense molecular ion peaks ranging from a mass of 618 to 1769 Da, which are assigned to sodiated adduct molecular ion of the type H- [O-CH (CH<sub>3</sub>) CO-]<sub>n</sub> OH-Na<sup>+</sup>. There is another series ranging from

706 to 1498 Da, which are corresponding due to the potassiumated adduct molecular ions, denoted by the structure H- [O-CH (CH<sub>3</sub>) CO-]<sub>n</sub> OH K<sup>+</sup>. The peaks ranging from 784 to 1215 Da correspond to oligomers of the structure H- [O-CH (CH<sub>3</sub>) CO-]<sub>n</sub> OCH<sub>2</sub>CH<sub>3</sub>, with a molecular mass 72n+46+23. The MALDI-ToF spectrum of the L-9 and L-13 are presented in **Fig. 6 (C)** and **Fig. 6 (D)**. The most intense peak of the L-9 ranging from 617 to 1626 Da, correspond to doped sodium ions of the linear oligomers with a mass of 72n+18+23 (n values varies from 8 to 22).

The corresponding linear polymer doped with potassium ions can also be seen as peaks of mass  $72n+18+39$ . **Fig. 6 (D)** depicts the MALDI-ToF spectrum of L-13. The most intense peaks, arising in the region from 545 to 1425 Da, correspond to linear oligomers, doped with sodium ions ( $n$  varies from 7 to 19).

The doped potassium ion that appears in the same region is also of linear oligomers. The peaks ranging from 599 to 959 Da, correspond to cyclic oligomers doped with sodium ions ( $n$  varies from 8 to 13). The doped potassium ions that appear in the same region are also of the cyclic oligomers. This confirms that few macrocyclic oligomers were present in this sample.

The peaks ranging from 1283 to 1427 Da, corresponding to linear oligomers zipped with catalyst molecule with sodium mass of  $72n+36+23$  in the middle. The peaks are of the HO-(-CH(CH<sub>3</sub>)COO)<sub>n</sub>-Zn-O-Zn-O(COCH(CH<sub>3</sub>)<sub>n</sub>-OH-Na<sup>+</sup>) type that is linear polymer molecules. **Fig. 6 (E)** presents the MALDI-ToF mass spectrum of sample L-14. The oligomeric 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 560 Da to a mass of 1497 Da, corresponding to oligomers doped with K<sup>+</sup> ions of type H- [O-CH (CH<sub>3</sub>)CO-]<sub>n</sub> OH-K<sup>+</sup> (mass= $72n+18+39$ );  $n$  values varying from 7 to 20 were detected, 39 being the mass number of potassium. The peak ranging from 545 to 1553 Da corresponding to oligomers doped with Na<sup>+</sup> ions of type H- [O-CH (CH<sub>3</sub>) CO-]<sub>n</sub> OH-Na<sup>+</sup> (mass= $72n+18+23$ ),  $n$  values varying from 7 to 21 were detected, 23 being the mass number of sodium. There is another series ranging from 573 to 861 Da corresponding to oligomers doped with Na<sup>+</sup> ions of type H- [O-CH (CH<sub>3</sub>) CO-]<sub>n</sub> OC<sub>2</sub>H<sub>5</sub>-Na<sup>+</sup> (mass= $72n+46+23$ ),  $n$  values ranging from 8 to 11 were detected, 23 being the mass number of sodium. This peak most likely appears in the spectrum because of the presence of impurity ethanol, which reacted during polymerization and formed chain ends of PLA. The peaks ranging from 779 to 1427 Da corresponding to a new structural formula, HO- [CH (CH<sub>3</sub>) CO-]<sub>n</sub> Zn-O-Zn-(OCO-CH-CH<sub>3</sub>)-OH. These chains have residual catalyst attached in the middle of the polymer chain. This result confirmed that a small amount of catalyst dissociates during polymerization reaction. **Fig. 6 (F)** shows the MALDI spectrum of polymer L-15. The most intense peaks belonging to this series, corresponding to oligomers doped with Na<sup>+</sup> ions of type H- [O-CH (CH<sub>3</sub>) CO-]<sub>n</sub> OH-Na<sup>+</sup> (mass= $72n+18+23$ );  $n$  values ranging from 7 to 20 were detected, 23 being the mass number of sodium. These peaks of linear oligomers doped with potassium ions that appear in the same region are also observed.

#### Mechanistic discussion and catalytic response

Zinc proline formed polymer and showed  $\alpha$ -helical structure. Zinc atom showed trigonal bipyramidal geometry and the pyrrolidine rings adopted envelope conformations [26]. The zinc atom is pentacoordinate, the fifth coordination site being occupied by symmetry related oxygen atom of a neighboring molecule to generate an infinite helical structure along the 2, direction. Lactide molecule behaves like ligand and replace L-proline molecule and forms complex with zinc atom.

## Conclusion

The structure and properties of low molecular weight PLA oligomers produced by ring opening polymerization were determined in term of the nature of the catalyst, polymerization time, and temperature. Results showed that linear PLA oligomers with  $\bar{M}_n$  2900-3400 Da, can be prepared with zinc (L-proline)<sub>2</sub> catalyst. The failure to obtain high molecular weight polymers in bulk can be attributed to the competitive formation of small amount of macrocycles. A small part of catalyst dissociate during the course of polymerization. Less racemization were occurred in presence of Zn (L-proline)<sub>2</sub> than Zn (D-proline)<sub>2</sub>.

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