Chronological Review of the Catalytic Progress of Polylactic Acid Formation through Ring Opening Polymerization

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Authors' contributions

The reported research work was a multi-disciplinary, collaborative effort. Author SPD is the lead researcher and author of this manuscript. A detailed literature review and information regarding the ROP of lactide in the literature was conducted by author SPD as part of his doctoral thesis. Authors SPD, VM, HAA, JLB and KB contributed to the development of detailed study for the state-of-the art in the field of chronological development in the field of PLA processing. The author's contributed equally for making the manuscript more scientific and meaningful in terms of English language.

Review Article

ABSTRACT

The disposal of a large amount of polymer waste is one of the major challenges of this century. Use of bio-degradable polymers obtained from sustainable sources presents a solution to this problem. Poly lactic acid (PLA), a bio-degradable polymer, can be synthesized from sustainable sources as corn, starch, sugarcane and chips. Ring opening polymerization (ROP) of Lactide (LA) monomer using metal/bimetallic catalyst (Sn, Zn or Al) is the preferred method for synthesis of PLA. However, the PLA synthesized using such catalysts may contain trace elements of the catalyst.

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These catalyst traces are known carcinogens and as such should be (ideally) eliminated from the process. Use of the organic catalyst instead of metallic catalysts, may be one of the prominent solutions.

Organic catalysts require the higher energy of activation for the ROP reaction of LA. Such energy requirement can be achieved through the application of alternative energy during the reaction. Alternative energy sources such as LASER, Ultrasound and microwave are prominent options to implement and process the ROP of PLA. This paper is an effort to emphasize the chronological review and to establish the current state-of-the-art in the field of PLA research.

ABBREVIATIONS

PLA: Poly(lactic acid); PLLA: Poly Levo Lactic Acid; LA: Lactide; L-LA: Levo Lactic Acid; DL-LA: Dextro, Levo Lactic Acid; CA: Cellulose acetate; PA: Polyamide; PBS: Poly-butylene succinate; PP: Poly-propylene; PU: Poly-urethane; PET: Polyethylene terephthalate; HIPP: High impact polystyrene; PVC: Poly vinyl chloride; ROP: Ring opening polymerization; UFDA: U.S. Food and Drug Administration; AE: alternative energy; OMt-K10: Montmorilloniate-K10; DMAP: Di-alkyl-amino-pyridine; PPY: Polypyrrole; NHC: N-heterocyclic carbine; bvp4c: Boundary Value Problems; MINDO: Modified Intermediate Neglect of Differential Overlap; MO: Molecular orbital; B3LYP: Becke 3-Parameter (Exchange); Lee: Yang and Parr (correlation; density functional theory); UV: Ultra Violet; PCL: poly (ε-caprolactone); Rex: Reactive extrusion; LRP: living free radical polymerization.

1. INTRODUCTION

The disposal of a large amount of polymer waste mainly the daily use consumer product is one of the major challenges of this century. Use of bio-degradable polymers obtained from sustainable sources emerges as a promising solution to environmental waste. However, substituting traditional polymers derived from petroleum products with a bio-degradable polymer is not sufficient to overcome all the disadvantages of using petroleum based polymers. Large scale industrial production of biopolymers can introduce impurities into the finished product that can be toxic to the end user and harmful to the environment. For example, use of metallic or bimetallic catalysts for the synthesis of biopolymers may lead to industrial scale throughput, but it also creates some serious health issues like carcinogenic effect [1-9]. Hence, research efforts need to be directed to eliminate the use of such catalysts from the production process.

Ring opening polymerization (ROP) of LA monomer is one of the most preferred methods for synthesis of Poly(lactic acid) PLA. The state of the art techniques developed by Dubois et al., Witzke et al. and Yu et al. [8-11] for the ROP of LA is based on the metallic and bimetallic catalyst (Sn, Zn, and Al) in suitable solvents. This process leads to throughputs in the range of 30-40 kg/hr, making production scalable and cost effective. However, as the metallic and bimetallic catalysts were established to be carcinogenic, there is an urgent need to explore suitable alternatives.

The metallic catalysts aluminium isopropoxide $Al(OPr)_3$ zinc lactate ($C_6H_{10}O_6Zn$) and stannous octoate ($Sn(Oct)_2$) etc. typically used in the production of PLA result in the production of a nucleophile or electrophile, which initiates the polymerization process. Replacing the metallic catalysts with non-metallic catalysts or some other metal-free source makes the production 'inefficient' because of low activation capacity of non-metallic catalysts. As a result, the throughput obtained from such a process is well below the requirements for industrial scale production (30-40 kg/hr). Kamber et al. [5] Wang et al. [6] and Basaran et al. [7] etc. reported the use of organic/metal-free catalysts in the production of biopolymers. These studies conclude that although the ROP of LA is possible, the production rate was much less (2-3 kg/hr) compared to metallic one (20-40 kg/hr) for consumer product standard.

2. ROP OF MONOMERS THROUGH METAL/ORGANIC CATALYST

The basis of the ROP is opening the cyclic ring of monomers such as cyclic ether, amides

(lactams) and esters (lactones). Then the opened ring acts as an active centre where other monomers join to form a larger polymer chain through ionic propagation. ROP consists of a sequence of initiation, propagation and termination reactions [12]. Once the process is started by the initiator, monomers add to the active polymer chain and increasing the chain length. A wide variety of cyclic monomers has been successfully polymerized by using ROP such as cyclic olefin, amines, sulphides etc. The suitability of polymerization of cyclic monomer depends on both thermodynamic and reaction kinetic factors [12].

3. THERMO-DYNAMIC CONDITIONS FOR ROP OF CYCLIC MONOMERS

The thermodynamic factors such as binding energy, entropy, and enthalpy of bond breaking and formation process play a very significant role in determining the relative stability of cyclic monomer and linear polymer structures during the conversion of cycloalkanes to the corresponding linear polymer [13]. ROP is thermodynamically favourable to all except the 6-membered ring. The order of thermodynamically favoured cyclic structure is 3 > 4 > 8 > 5 > 7 atoms. The trend is a result of bond angle strain in 3 and 4-membered rings, eclipsed conformational strain in the 5-membered ring and trans-annular strain in 7 and 8-membered ring [12]. Thermodynamic parameters alone do not guarantee the polymerization of the cyclic monomer as shown in the case of the 6-membered ring. Polymerization also requires a favourable kinetic pathway to open the ring and undergo reaction. For nucleophilic or electrophilic attack by an initiator, existence of a heteroatom in the ring provides a suitable site resulting in further propagation by opening the ring. Such monomers polymerise when both thermodynamic and kinetic factors are favourable for the reaction [12].

4. ROP OF LACTIDE AND POLY-CONDENSATION OF LACTIC ACID FOR PLA SYNTHESIS

Based on the production rate and molecular weight, the two most efficient and common methods to produce PLA are polycondensation of lactic acid and ring opening polymerization of LA (Fig. 1). Poly-condensation involves removal of water of condensation by the use of solvent under high vacuum and high temperature. In general, it is the least expensive route, but in a solvent-free system, it is difficult to achieve high production rates (30-40 kg/hr). To manufacture a low to intermediate molecular weight polymer, the poly-condensation approach was used by Carothers and is still used by Mitsui Toatsu Chemicals Inc. [14,15].
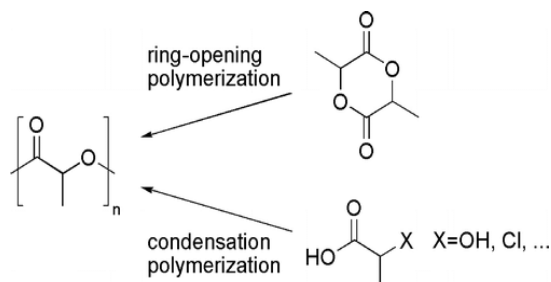

Fig. 1. Lactide and lactic acid monomer to form PLA polymer

The other efficient way to obtain PLA is the ROP of LA with suitable metal catalysts (tin, zinc, aluminium) in a suitable solvent [36]. Normally, the entropically favoured LA monomers are produced at the temperature below 180-200°C [19]. Based on cost and reaction time, ROP is preferred process for large-scale industrial production. Catalysts like Al(iOP)$_3$, $\underline{C_6H_{10}O_6\ Zn}$ and Sn(Oct)$_2$ have been studied to enhance the ROP reaction productivity [36]. To get the higher molecular weight, use of other coupling agents or esterification-promoting agents are required, which increase cost and complexity [36,37]. However, obtaining high molecular weight polyesters with good mechanical properties is not easy. Among them, stannous octoate (Sn(Oct)$_2$), approved by the U.S. Food and Drug Administration (UFDA), is the most widely used due to high LA polymerization feature [38].

4.1 ROP Mechanism of Lactide

ROP is generally initiated by the attack of ionic (anionic or cationic) initiator on the cyclic ring monomer to create an active site for further addition of monomer(s) [16-18,21,22]. Reaction involves the nucleophilic attack of monomer on the oxonium ion Fig. 2.

In the case of active species determination, Kricheldorf et al. [36] reported that tin halogenides were actually converted into tin alkoxide and behave as real active species. Several ring-opening polymerizations proceed as living polymerizations and polymer molecular

weight increases linearly with conversion and ratio of monomer to initiator [6]. ROP is the preferred way of polymerization because it results in polymers with high polymer molecular weight [7,20,24,29].
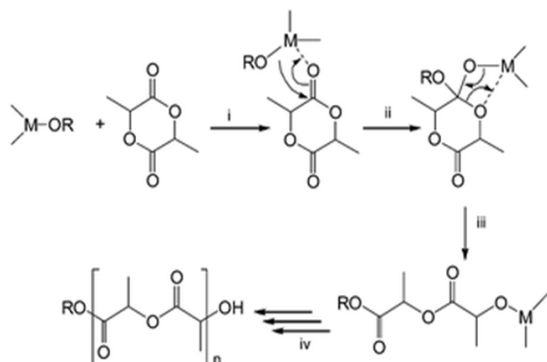

Fig. 2. Mechanism of ROP of lactide

5. CHRONOLOGICAL SCIENTIFIC RESEARCH DEVELOPMENT IN PLA SYNTHESIS FIELD

PLA as biocompatible and biodegradable class of polymer has garnered a lot of attention in past decades and has also resulted in industrial scale production at manufacturing units such as Nature work (USA) [33,39], Purac (Netherlands) [40], etc. In fact, the metal catalyst (in a suitable solvent) has been used for the synthesis of PLA for decades. Dubois et al. [41] in 1991 reported the mechanism of ROP of LA using Batch process and aluminium isopropoxide as a catalyst in toluene solvent. Witzke et al. [42] also reported reversible kinetics of L-LA in the oven-dried container using stannous octoate as a catalyst in toluene solvent, incidentally leading to an adverse effect (toxicity, irritation) on human health. Jennifer et al. [43] reported that $Sn(Oct)_2$ used in the polymerisation of LA is an irritant to the eyes, respiratory system, and skin. The different reaction stages involved in the polymerization of LA lead to the formation of impurities and side products. The use of $Sn(Oct)_2$ or another metal catalyst is also very toxic and hazardous for environment although lactic acid and LA are non-toxic in nature [8].

Apart from the catalyst, the reaction time is also an important factor which decides the production cost and quality of commercial PLA. The reported reaction completion time for ROP kinetics by Dubois et al. [8] and others was several hours (50-100). Mehta et al. [44] reported

the variation of the number average molecular weight of PLA with the time scale of 0-150 hours by using the experimental data from Dubois et al. Batch process [41]. Jacobsen et al. [2] and Banu et al. [9] using reactive extrusion for the polymerization of LA proposed the detailed study of ROP process. They observed that in initial few minutes the conversion rate reaches almost 95%, but if the process lasts longer, side reactions (like intermolecular trans-esterification and scission) can decrease the polymer molecular weight. For the estimation of monomer conversion and average molecular weight along the extruder, Banu et al. [9] reported the material flow and mixing by using the Ludovic® commercial simulator.

As mentioned earlier, the drawbacks of metal-catalyst have resulted in the growth of organo-catalysis as a prominent solution for ROP reactions. Basaran et al. [5] reported experimental technique detailing the synthesis and characterization of polylactide via the metal-free process. Consideration of Montmorlloniate-K10 (OMt-K10) as organic filler and acid catalyst for polymerization of LA opens a suitable source of catalyst application to overcome impurity caused by metallic catalysts [5]. The work proposed the use of OMt-K10 filler both as the catalyst and inorganic filler to prepare the biopolymer nano-composite of PLA. OMt-K10 has a catalytic proton, which can act as an acid catalyst for the polymerization process of LA. As mentioned earlier by several research groups an increase in temperature during the polymerization process, initiates several side reactions which decrease the molecular weight of the resulting polymer [37,43,45]. Basaran et al. [5] also verified the effect of temperature and found that beyond 180°C the reaction behaviour started changing and beyond a certain temperature range (180-200°C) the molecular weight started decreasing. Higher temperature like 185–190°C boosts unzipping and chain scission reactions and leads to the decrease of molecular weight as well as thermal degradation [47,48]. However, the basic principle of ROP process is still the backbone for all kind of new development and innovation in this field.

In the last few years, several research communities and groups have investigated the possibility to develop a technique through which the polymerization of LA becomes possible by using the metal- free or organic catalyst. Use of alternative energies such as microwave, LASER, and ultrasound source to achieve a precisely-

controlled and efficient continuous polymerisation of high molecular weight PLA in a twin screw extruder is currently being investigated. To implement the effect of the metal-free catalyst in the reaction mechanism, a proper understanding of reaction kinetics is needed. It is necessary to develop a theoretical mathematical model to check the suitability of parameters (time, concentration, temperature and rate constants) in reaction mechanism for LA polymerization.

6. REACTION MECHANISMS FOR PLA FORMATION USING ORGANIC CATALYSTS

To replace the effect of the metallic catalyst as a catalyst for ROP of LA and its adverse effects on the environment, in 2007 Kamber et al. [6] proposed very detailed review on the state of the art of effectiveness of organic catalyst related ROP reactions mechanism and the importance of the organo-catalytic ring-opening polymerization. The work examined several methods for initiate the ROP such as cationic, anionic, enzymatic and other organic ROP. The initial reaction scheme to understand the reaction for ROP of LA is mentioned in Fig. 3.
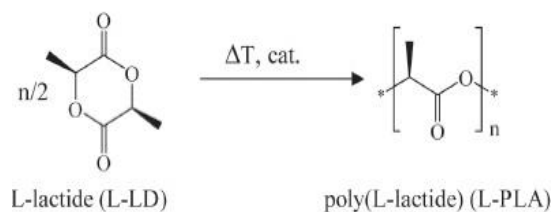

Fig. 3. PLA formation routes

The reaction scheme referred to in Fig.3. describes the reaction procedure well but does not give all the details by highlighting the intermediate steps which control and are ultimately responsible for the molecular weight distribution and the molecular weight of the macromolecules. Once the polymerization reaction starts, it goes on to a final stage with certain molecular weight. As a result, step growth or chain growth processes influence the reaction. The step growth process explains the details of ROP process by providing effective details of intermediate reactions and helps to control the molecular weight of process with the emergence of "living" polymerization or active site reactions [31,39,40,47].

Fig. 4 explains the details of several mechanisms such as coordination-insertion mechanism,

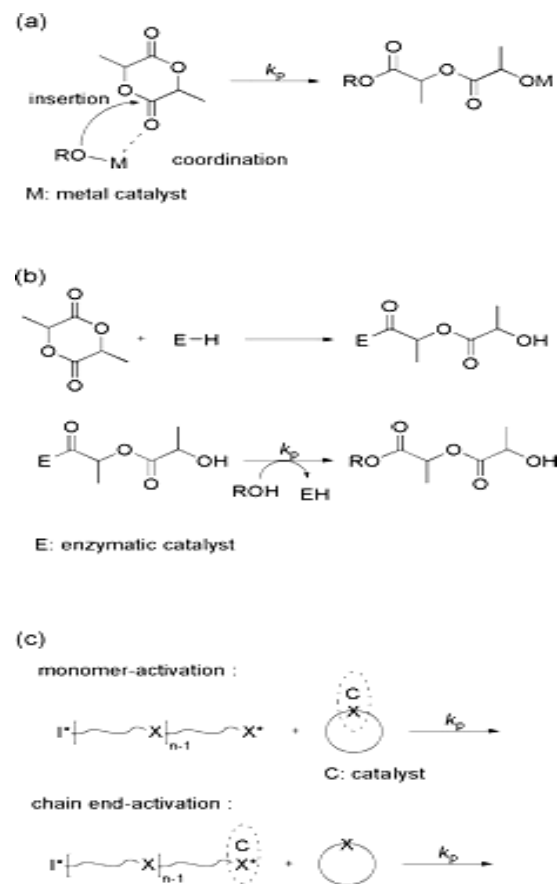activated monomer mechanism and monomer-activated mechanism versus chain end-activated mechanism.

Fig. 4. Different mechanism for ROP process

In general, the ROP of lactides follows the coordination-insertion mechanism [48]. This is different from usual cationic and anionic mechanism in which free ions or ion pairs are the charged propagating species and their counter-ion share a covalent bond [80]. The coordination-insertion mechanism is based on the coordination of the metal catalyst group with monomer ring and further attack of an alcohol group on the week site of monomer ring (Fig. 5). This mechanism shows better production yield and faster reaction times (20-60) min in ROP process [49]. There is also an alternative classification for enzymatic ROP known as an activated-monomer mechanism. In this process, the enzymes react with monomer and activate the monomer to enhance the polymer chain addition process [40]. The field of enzyme-catalysed ROP was demonstrated in the application of a lipase (a type of an enzyme

catalyst) for ROP of lactones by independent groups of Parmar et al. [35] Kobayashi et al. [40,] and Knani [34]. Enzymes show an effective stereo-active reaction and were extracted from renewable resources that can be easily recycled [9]. To define the role of a catalyst, classification of the catalytic process of ROP reactions either by chain end-activation or monomer-activation mechanism is crucial.

Several other ligands in organic and non-metallic catalysts are also capable of starting ROP of L (LA), such as pyridine, phosphine and carbines. The first organo-catalyst used in living ROP of Lactide (LA) was reported in 2001, using basic amines such as di-alkyl-amino-pyridine (DMAP) and poly-pyrrole (PPY) as trans-esterification catalysts [50]. DMAP was used successfully not only for trans-esterification but also for many other organic transformations such as alkylation, acylation, nucleophilic substitutions, etc [52]. Because of these properties, DMAP has been the centre of several reviews [51,53,54]. The Fig. 5 describes the mechanism for ROP of LA using a pyridine such as DMAP.
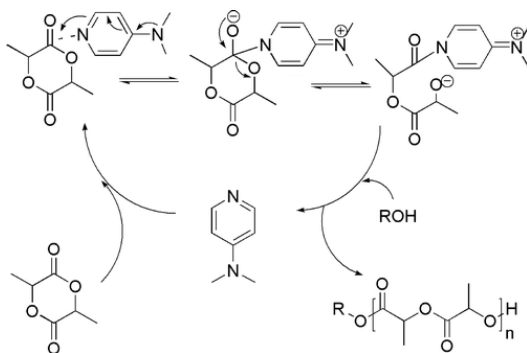

Fig. 5. DMAP acylation mechanism

In this series, phosphines are commonly known ligands in organometallic chemistry and homogenous catalysis. Phosphines are capable of mediating a wide variety of organic transformations including acylation reactions [52]. Several tertiary phosphines were used for trans-esterification catalysts of the ROP of Lactide (LA) [49]. In the presence of alcohol especially benzyl alcohol, phosphines were found to be an effective catalyst for ROP process of LA [38]. The phosphine catalysed polymerization process in dichloromethane (CH_2Cl_2) or toluene was slower and required high temperature $(90-100)°C$ in comparison to those catalysed by DMAP [55]. The activity of several phosphine ligand catalysts for (LA)

polymerization in decreasing order is as follows: tributylphosphine $(P(n-Bu)_3)$ > tert-Butylohosphine $((tert-Bu)_3)$ > dimethylphenylphosphine $(PhPMe_2)$ >methyldiphenylphosphine (Ph_2PMe) > triphenylphosphine (PPh_3) > trimethoxyphosphine $P(MeO)_3$. For nucleophilic-mechanism the suitability is based on more basic and nucleophilic-alkyl-substituted phosphines for the effective LA polymerization catalysts [44,56]. The mechanism is shown in Fig. 6.
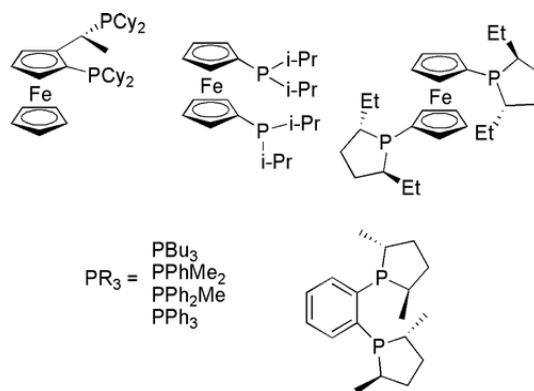

Fig. 6. Phosphine catalysis mechanism

Breslow introduced carbenes as a catalyst for polymerization, his studies steered researchers towards investigating the use of stabilized carbenes as the nucleophilic catalyst [57-59].

In the case of ROP, the use of different types of carbenes (unsaturated and saturated imidazolylidene and triazolylidene as the effective catalyst, have been investigated [60], [62]. The ROP depends on the nature of carbene and monomer. The reported rate of reaction was similar to one of the most active metal catalysts results from ROP of LA [52,61-63]. NHCs have higher nucleophilicity and basicity as compared to DMAP, which is responsible for the higher reaction rates. In the mechanism of polymerization of the lactones using carbene as the catalyst, the termination can be started by deactivation of the carbene introducing acetic acid, CO_2 or CS_2 which later forms the zwitterionic species i.e. a molecule with a positive and a negative charge and can be removed from the polymer by the precipitation process. In the nucleophilic mechanism, production of a zwitterionic intermediate is the key feature [64]. Nucleophilic attack of the carbene on the lactones creates zwitterionic species, followed by ROP of tetrahedral

intermediate to create the acyl-imidazolium alkoxide zwitterions [65]. Figs. 7 & 8 represent the mechanism of NHC catalysed ROP and formation of zwitterion.
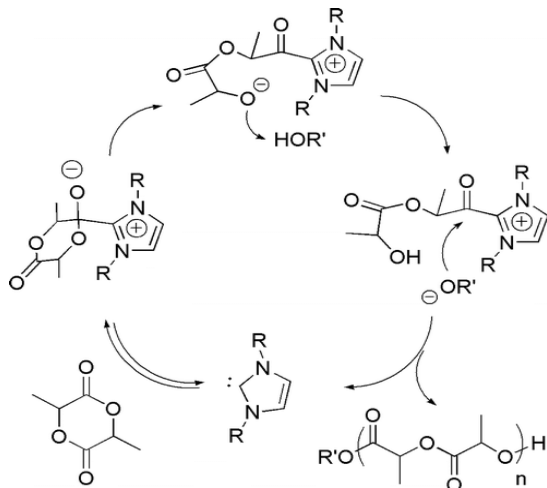

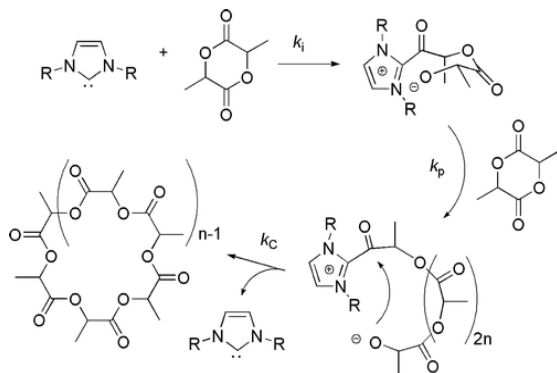**Fig. 7. Nucleophilic monomer-activated mechanism for ROP**

Fig. 8. Zwitterionic polymerization of LA

In 2013 Yan Wang et al. [7] contributed also in the field of organic catalysis of PLA by using NHC as a nucleophilic catalyst [10]. In their work, they investigated the influence of temperature, monomer/initiator molar ratio, monomer/catalyst molar ratio, monomer concentration, as well as polymerization time. In comparison with other catalysts especially the metal catalysts, carbine catalysts are inexpensive [55,66], highly active and nontoxic in nature. Imidazolium-based carbenes are a reliable alternative to the metal catalysts. The activity and efficiency NHC have illustrated as superior organo-catalysts for polymerization [67]. Recent methods proposed by Wang et al. [7] and several others, defines the suitability of carbene catalyst to exclude the complexity by isolating sensitive carbene complex and to provide polymerization details [58,67-72]. Parameters such as monomer/initiator molar ratio ([M]/[I]), monomer/catalyst molar ratio ([M]/[C]) and monomer concentration affect the molecular weight and polydispersity of polymerization process significantly. Both the monomer conversion and molecular weight of PLA increase with an increase of LA concentration up to the saturation point and then starts decreasing.

The decrease in molecular weight at higher concentration happens because the active monomer chain centre cannot react timely with the monomer owing to the increase in the systems viscosity. The monomer/initiator molar ratio has been examined in details by Wang et al. [7]. It was observed that the molar ratio was relatively critical to prepare high yield and high molecular weight—[11,12]. Because of the availability of less active centre in the polymerization system, the polymerization process cannot continue while decreasing initiator amount. Yet increasing initiator content can favour a large number of shorter polymeric chains, thus decreasing the molecular weight of PLA. The amount of catalyst also affects the formation of active species directly and thus the monomer conversion. Further the polymerization temperature and time also significantly affect the ROP of LA. It was also found that rise in temperature enhances the rate of intermolecular trans-esterification and thermal degradation reaction and causes the decrease in molecular weight of PLA, whereas below 15°C the polymerization reaction proceeds slowly [13].

6.1 ROP through Alternative Energies (Microwave, Ultrasound & Laser) Incorporation

Application of microwave heating to process chemical reactions has received increasing attention in the past few years. Due to its qualities such as high efficiency, the capability of uniform heating and reduced reaction time, the large number of chemical reactions, both organic and inorganic, undergo a significant increase in reaction speed due to microwave irradiation compared to the general methods for heat-irradiation such as furnace chamber and LASER heating etc. Microwave-assisted ROP of poly-lactide.

Microwave assisted ROP technology for LA emerges as a green method for chemical synthesis for PLA due to its high efficiency and homogeneous heating [71,75,76,78,79,96]. The first microwave-irradiated polymerization of D,L-LA (was reported by Liu et al. [73,74,77]).

Zhang et al. [73] polymerized successfully the D,L-LA by using ethanol, ZnO, SnCl$_2$ and Cat-A as catalyst applying continuous microwave irradiation in less than an hour. 36% yield has been reported on the final synthesis process. On the other hand compared to conventional heating with the same experimental setup, the negligible non-thermal effect of microwave irradiation was revealed. Based on chemical bonding studies, LA molecule contains two polar carbonyl groups which provide a suitable site of dielectric heating by absorbing microwaves, because of this fact Liu et al. [73] investigated the ROP of D,L-lactide (DLLA) considering micro-wave irradiation for PLA synthesis [18]. The rough reaction scheme of microwave-assisted ROP of LA is in Fig. 9.
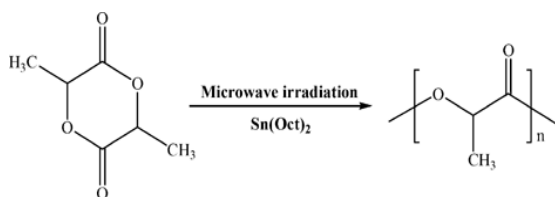

Fig. 9. Microwave-assisted ring-opening polymerization of lactide

For details in reaction procedure, a sample mixture of D,L-LA was prepared and mixed with Sn(Oct)$_2$ after that the reaction mixture was treated with three vacuum-argon cycles to get rid of solvent. The reaction mixture was then irradiated with power levels of 2.45 GHz through the microwave. The mixture irradiated with microwave then cooled down in dichloromethane and precipitated in methanol. The source of

microwave energy has been used as a pulse source to irradiate the mixture for short times. Further the weight ratio of the precipitate of polymer to the monomer was considered to determine the yield of the conversion of the amount of LA into PLA. The precipitate obtained was verified as P-DLLA by means of 1 H NMR spectroscopy and GPC test which were similar to those of an authorized PLA specimen. By measuring the weight average molecular weight (M_w) and yield of the resultant P-DLLA at varied time intervals, the effect of microwave energy on the ROP of DLLA was investigated at different power levels (170, 255, 340, and 510 W). With the help of detailed investigation, Liu et al. [73] proposed that the rate of polymerization step and the chain propagation of PDLLA were both enhanced significantly by an increase in the microwave power up to certain extant [94,95].

6.2 Ultrasound/Ultrasonic Facilitated ROP of Lactide

In literature, the use of UV and Ultrasound source is reported as an energy source for degradation of PLA chain. Work based on separation of PLA chain with their complex substituents called poly LA-co-glycolic acid using intense and targeted Ultrasound has also been reported in literature because of which, Ultrasound would be used as a relevant future AE source for ROP process to provide considerable bond breaking energy to initiate the polymerization reaction [81]. Deng et al. [83] and Oster et al. [84] demonstrated the application of UV source for surface grafting polymerization in detail. Fig. 10. Dubey el al. [96,97] and co-workers also reveals the benefit of using ultrasound source within the reaction process in great details. The implementation of ultrasound source highlighted the major benefits in the reaction process and reaction output.
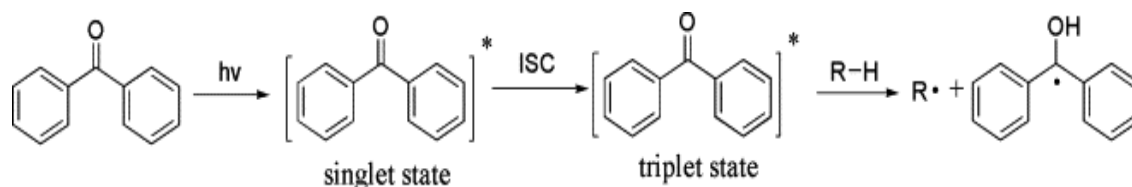

Fig. 10. Photo-grafting polymerization through UV radiation

6.3 ROP through Continuous Reactive Extrusion

There are several polymer processing techniques like melt-blending, polymerization, branching, grafting and functionalization. Reactive extrusion (REx) is a cost effective method for these techniques on account of its low cost production and processing techniques [85,86]. Important features of extrusion polymerization are as following,

- Melt processing can be carried out in the solvent free medium. So the product can be easily isolated.
- There is a continuous process which starts from monomer and gets completed with the formation of polymer or final product.
- Residence time and residence time distribution can be controlled
- Several extrusion streams can be incorporated while running process

There are several benefits of the extruders in different applications such as deciding the grade of the mixing, proper control and higher conversion output. The effectiveness of the extruder is controlled by the geometry of the screws which are used in the extruder [86]. Residence time, power input and the scale of mixing to form melt in the extruder all are controlled by the screw size, geometry and rotating speed.

Various types of high molecular weight biodegradable polymers are prepared by ROP of cyclic ester through extruder polymerization such as poly(ε-caprolactone) (PCL) Fig. 11, polylactides (PLAs) and other aliphatic–aromatic poly-condensates as poly(butylene adipate-co-terephtalate) [82]. By using reactive extrusion for ROP of several polymers at industrial level, it is possible to have control over polymerization, which is required to achieve desired molecular weights and suitable functional end groups [87].

Apart from PCL and PLAs, there are several other biodegradable aliphatic polyesters, for which traditional polycondensation method is used. One of such kind of polymer is poly(alkylene succinate) designed by Showa Denko, trademarked Bionolle® [88]. But due to relatively poor mechanical and high cost properties as compared to other polymers (polyethylene and polypropylene), the biodegradable copolyesters are still not very popular. It is possible to combine these biodegradable polymers with cheap inorganic (silicate type particles) or organic fillers (starch granules) to reduce the cost and to optimise the properties of aliphatic polyesters [86].

6.4 ROP of PLA using Continuous Extrusion Reaction

The current trend for the production of PLA at commercial level mostly supports the use of a continuous single-stage process reactive extrusion or twin screw extruder technology which satisfies both kinetic and thermal stability requirements [27]. For reactive extrusion polymerization, the use of purified form of LA is very significant. A mixture of D or L-LALA, stabiliser and the catalytic system is transferred continuously into a nitrogen purged material feeding unit. The crystalline powdery type LA is mixed with the catalyst such as stannous octoate dissolved in toluene. It is extracted later from the mixture using the vacuum. Design of the screw geometry widely influences the degree of mixing of PLA with other components and degree of mixing has huge impact on ROP of LA (Fig. 12).

The LA ROP proceeds through the 'coordination–insertion' mechanism by involving the cleavage of the particular oxygen-acyl cyclic ester monomer. It has been reported that the presence of one equimolar Lewis base such as triphenylphosphine along with 2-ethylhexanoic tin (II) salt ($Sn(Oct)_2$), significantly improves the LA polymerization rate. For the production of PLA the optical purity (D and L type) of the reagent lactic acid is crucial because small amounts of enantiomer impurity change the properties such as crystallinity or biodegradation rate of polymerization. Another factor which affects the properties of the polymer is the detection and removal of impurities during reaction because impurities can easily change the intermediate reaction and product [79,28]. Dubey et al. [96,97] also revealed the reaction kinetic details of ROP process for PLA formation by considering a combination of the metal catalyst and AE source in the extrusion reaction process. Fig. 13 represents the variation of conversion (X) and number average molecular weight $\overline{M_n}$ along the length of the screw (which in a continuous process can be correlated with time for the steady state) obtained with Ludovic® [92,93], taking into account the effect of the polymerization. These results correspond to the simulation of the experiment with these initial conditions: temperature (50-220)°C, AE source (250-600) W, screw speed 300-600 rpm. Similar curves have been generated for each reactive extrusion experiment.
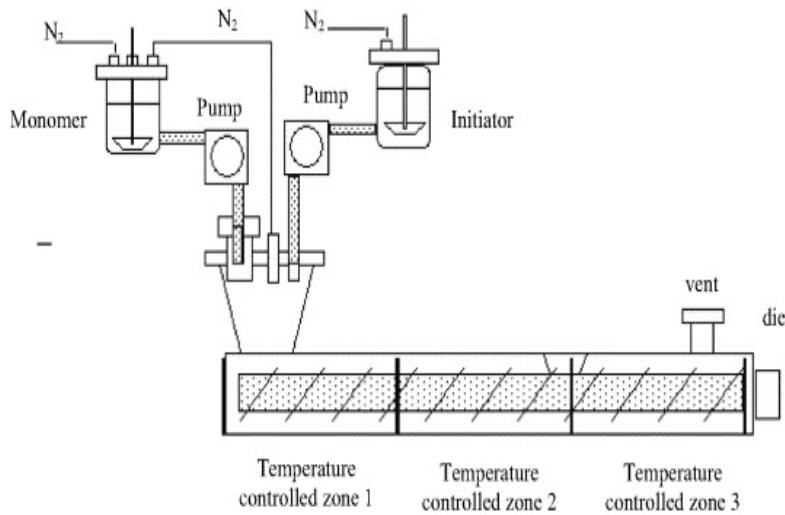
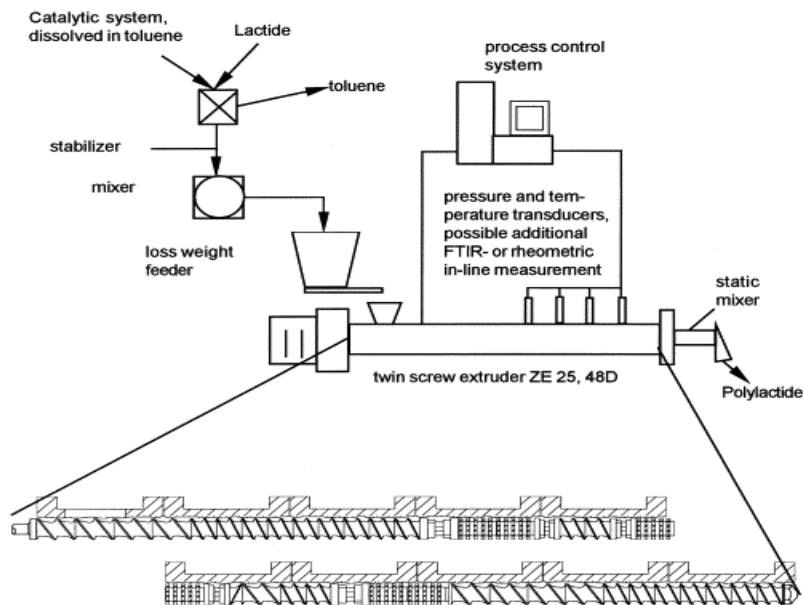**Fig. 11. Co-rotating twin-screw extruder for PCL polymerization**

Fig. 12. Twin screw extruder

7. INDUSTRIAL CONCERN AND CONTRIBUTION FOR PLA PRODUCTION

The market for biodegradable and common household consumable polymers, such as PET, HIPP and PVC, has been approximately around 200,000 tons in 2005, of which 50% was PLA. The demand for industrial production of biodegradable polymers instead of conventional petrochemical polymers increases many folds after the fact of environmental harm (landfilled) issues related to the petrochemical based polymers highlighted. Sven Jacobsen et al. [26] mentioned in an article mentioned that in the case of plastic waste, US alone produced 35 million tons of consumer polymers in 1998 whereas the corresponding figure of Europe and Asia were 34 million tons and 25 million tons. Since 2009, the total amount of plastic waste due post-consumer plastics which is plastic that can be "recycled" to reuse the material out of which they are made and to reduce the amount of waste going into landfills has been
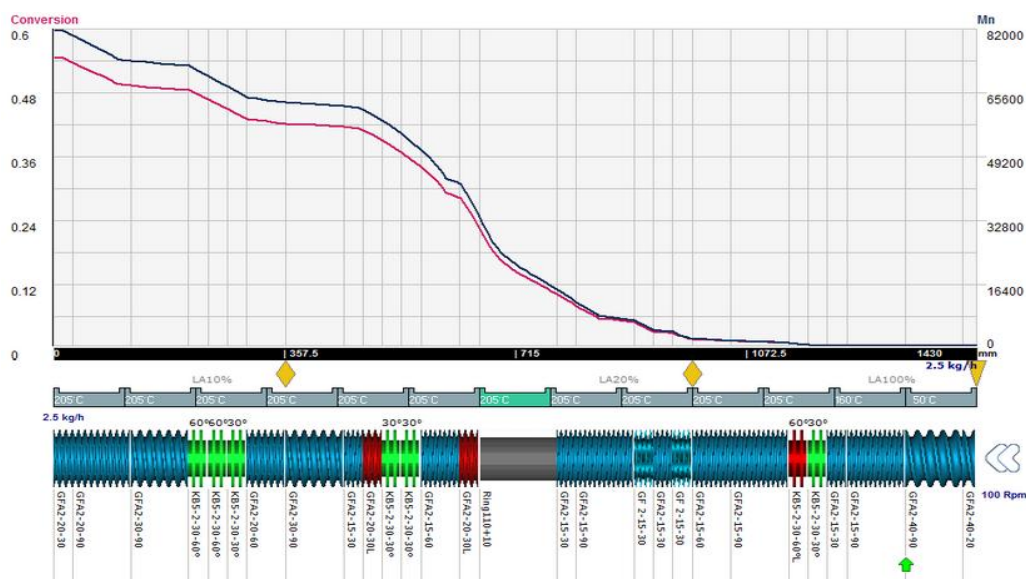
Fig. 13. (Mn)⁻(purple line) vs T & X (red line) vs T obtained with Ludovic® for T (50-220)°C, AE=250 W, 600 rpm

speeding in Europe but since 2011 it has remained the same, at about 25.2 million tonnes (2012). 77% of total waste was generated by the following seven countries: Germany, UK, France, Italy, Spain, Poland, and the Netherlands while the rest originated from the remaining 22 countries [89].

Commercial use of PLA has come into prominence in last 15 years because of its biodegradable and biocompatible nature and extensive application in the field of medical and clinical consumer products [46]. Lactic acids are the major component of the food-related application in USA and cover 85% of the commercial products [90]. The large production volume requires an economically viable manufacturing process. For large scale the metal-free and degradable commercial production, the continuous polymerization of PLA seems to be an essential and efficient way of production.

Based on quality and consumer requirements, several industrial processing methods such as reactive extrusion, injection moulding, injection stretch blow moulding, blown film, casting, thermoforming, foaming, fibre spinning, blending, batch process and compounding are employed to produce PLA [18,19,22]. The selection of initiator system, the catalyst concentration, monomer-to-initiator ratio, polymerization time and temperature change the property of the polymer. Initially, the ROP process of PLA was

carried out in a batch process which contains several vessels to mix the initiator and the catalyst with monomer at the certain temperature. The commonly used solvent for the batch process is toluene. In modern age for higher yield and cost effectiveness, PLA production is mostly based on the process of reactive extrusion process through twin screw extruder [9,38,86].

8. KINETICS AND THEORETICAL MODELLING OF ROP MECHANISM

In literature, several reaction mechanisms were proposed to describe the ROP process. To explain the interdependence of reaction parameters (monomer concentration, temperature, rate constants), reaction mechanisms were formulated by several groups in the form of ordinary differential equations [25, 30,32]. Different mathematical kinetic models have been proposed, but their number in comparison to experimental/empirical data is significantly less. To verify the experimental results theoretically, different groups adopted different mathematical techniques.

- Banu et al. [9] applied the least square method in their mathematical model to verify the reactive extrusion experimental work of ROP of LA using stannous octoate catalyst. The procedure was based on boundary value estimation function ''bvp4c'' using the software MATLAB.

11

- Ryner et al. [68] and Lavan et al. [22] used the hybrid density functional method B3LYP, a quantum chemistry calculation using Gaussian software to calculate the geometries and energies which govern the thermodynamical properties of ROP of LA.
- Yu, et al. [11,91] numerically solved the rate kinetics equation with the help of method of moments to verify the experimental work using stannous octoate as metallic catalyst. The method of moments is a technique for calculating estimators of the parameters that is based on matching the sample moments with the corresponding distribution moments.
- Dubey et al. [96] have solved the rate kinetic equations involved in ROP process of LA in the presence of the metal catalyst and AE source by using MATLAB tool.
- Dubey et al. [97] Revealed the reaction kinetic details of ROP process for PLA formation by considering the combination of the metal catalyst and AE source in the extrusion reaction process, which is one of its own kind of innovative work in this field.

In 2007 Mehta et al. [18] proposed detailed theoretical kinetic model of ROP of LA based on Dubois et al. [8] experimental work and results that were based on the use of aluminium isopropoxide as a catalyst. They formulated the reaction kinetics of RO of PLA in the form of different first order ordinary differential equations. The ROP of LA consists of three basic stages (eq. *1-3*) to complete the whole process that can be classified such as initiation, propagation, and termination [8]. The reaction mechanism is the following:

$$M + I \xrightarrow{K_0} P_i \qquad (1) \quad \text{(Initiation)}$$

$$P_j + M \xrightarrow{K_p} P_{j+1} \qquad (2) \quad \text{(Propagation)}$$

$$P_j + M \xrightarrow{K_t} M_j + P_1 \qquad (3) \quad \text{(Termination)}$$

Where M, I and P_j represent the monomer, initiator, and polymer chain of length j and K_0, K_p and K_t represent initiation, propagation and termination rate constants.

The work reported that ROP of LA proceeds through "coordination-insertion" mechanism. They found that the polymerization is normally "living" until a certain molecular weight is reached. Kinetics of the LA polymerization has been investigated at 70°C and it was found to be

first order [41]. In conclusion, the kinetics law proposed is mentioned below (4).

$$-\frac{d[LA]}{dt} = k_j[LA][Al(OPr)_3] \qquad (4)$$

Where [LA] and [Al(OPr)$_3$] represents the concentration of LA monomer and the catalyst. k_j stands for rate constant of the reaction.

To validate their theoretical model based on Dubois et al. [41] they proposed a set of ordinary differential equations (ODE) to consider the role of each reaction parameter in reaction kinetics. The mass balance equations for batch reactor were written for the above kinetic reaction (eq. 1-3) as follows (eq. 5-9):

$$\frac{d[M]}{dt} = -[M]\{k_0[I] + \sum_{j=1}^{n} k_j[P_j] + \sum_{j=1}^{n} k_{tj}[P_j]\} \qquad (5)$$

$$\frac{dy[I]}{dt} = -k_0[I][M] \qquad (6)$$

$$\frac{d[P_1]}{dt} = k_0[I][M] - k_1[P_1][M] + \sum_{j=2}^{n} k_{tj}[P_j][M] \qquad (7)$$

$$\frac{d[Pj]}{dt} = [M]\{k_{(j-1)}[P_{j-1}] - kj[P_j] - k_{tj}[P_j]\}, \; j > 1 \qquad (8)$$

$$\frac{d[M]}{dt} = k_{tj}[P_j][M], \quad j \geq 1 \qquad (9)$$

Where: [M], [I] and [P_j] represents the concentration of monomer, initiator and polymer chain of length "j", and k_0, k_j and k_t represent the rate constant of initiation, propagation and termination reactions.

Mehta et al. [8] solved the above ODE rate equation by using multiple-step Euler method and verified the model with the help of Dubois et al. [41] experimental report [12]. For modelling the process, the maximum polymer chain length was considered to be 5000 repeating units. This was based on observations of experimental results [8]. In order to compare the output of the simulation at several monomers to initiator ratio with experimental data, the number average molecular weight (M_n) was calculated using the following expressions (10):
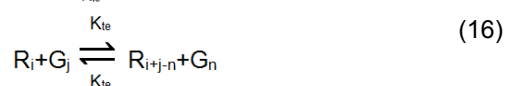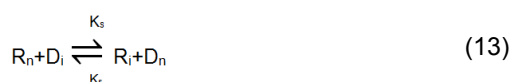
$$M_n = \frac{\sum_{j=1}^{n} j \cdot ([P_j] + [M_j])}{\sum_{j=1}^{n} ([P_j] + [M_j])} \qquad (10)$$

The comparison of the variation of number average molecular weight (Mn) versus time is in Fig. 14.

Although the ROP of LA can be carried out using several catalysts, in order to obtain PLA in a

continuous process using reactive extrusion, the bulk polymerisation has to be completed in a very short time (few minutes), which would be the residence time of the extrusion process. Therefore, ROP of LA using stannous octoate $Sn(Oct)_2$ as the catalyst was selected because $Sn(Oct)_2$ promotes fast LA polymerisation which results in higher molecular weight. However, when $Sn(Oct)_2$ is used, side reactions (like trans-esterification and random chain scission reactions) occur even during any other melt processing [7].

In 2009 and later on in 2011 Yu et al. [91] proposed a model which considered $Sn(Oct)_2$ as a catalyst and 1-dodecanol as co-catalyst at a temperature range between 130 and 180°C to start the ROP of LA monomers [11,91]. Different monomer-to-catalyst and cocatalyst-to-catalyst ratio to investigate the proper reaction mechanism of ROP process were performed [11]. "Ester interchange" reactions, also called trans-esterification and non-radical random chain scission, were additionally considered to the previously proposed reaction mechanism of Mehta et al. [91]. The reaction scheme proposed is shown in equations 11-19. In the reaction mechanism equation 11, 12 and 13 represent initiation, propagation and termination reaction. Equations 14, 15 and 16 represent the trans-esterification reactions. The reactions 17, 18 and 19 represent random chain scission.

$$C + D_n \underset{K_{a2}}{\overset{K_{a1}}{\rightleftharpoons}} R_n + A \tag{11}$$

$$R_n + M \underset{K_d}{\overset{K_p}{\rightleftharpoons}} R_{n+2} \tag{12}$$

$$R_n + D_i \underset{K_s}{\overset{K_s}{\rightleftharpoons}} R_i + D_n \tag{13}$$

$$R_i + R_j \underset{K_{te}}{\overset{K_{te}}{\rightleftharpoons}} R_{i+j-n} + R_n \tag{14}$$

$$R_i + D_j \underset{K_{te}}{\overset{K_{te}}{\rightleftharpoons}} R_{i+j-n} + D_n \tag{15}$$

$$R_i + G_j \underset{K_{te}}{\overset{K_{te}}{\rightleftharpoons}} R_{i+j-n} + G_n \tag{16}$$

$$R_i \underset{K_{de}}{\overset{K_{de}}{\rightarrow}} R_{i-k} + G_k \tag{17}$$

$$D_i \underset{K_{de}}{\overset{K_{de}}{\rightarrow}} D_{i-k} + G_k \tag{18}$$

$$G_k \underset{K_{de}}{\overset{K_{de}}{\rightarrow}} G_{k-j} + G_j \tag{19}$$

Where: ka_1, ka_2 are the activation rate coefficients, k_p, k_d are the propagation rate coefficients, ks is the chain-transfer rate coefficient, k_{te} is the trans-esterification rate coefficient and k_{de} is the random chain scission reaction rate coefficient;

C is the catalyst, $Sn(Oct)_2$, A is octanoic acid (OctOH) produced by the catalyst, R_i represents the active polymer chains with length "i", D_i represents the dormant polymer chains with length "i", G_j represents the terminated polymer chains with length "j" and M the monomer.

To consider the effect of several reaction parameters on the proposed reaction mechanism, reaction equations 11-19 were formulated into mathematical equations (eq. 20-25) which show the variation of several parameters with time.

$$\frac{d[C]}{dt} = -k_{a1}[C]\mu_0 + k_{a2}[A]\lambda_0 \tag{20}$$

$$\frac{d[A]}{dt} = k_{a1}[C]\mu_0 - k_{a2}[A]\lambda_0 \tag{21}$$

$$\frac{dM}{dt} = -k_p M\lambda_0 + k_d(\lambda_0 - R_1 - R_0) \tag{22}$$

$$\frac{d[Rn]}{dt} = k_{a1}[D_n][C] - k_{a2}[R_n][A] + (1-\delta_{n,0})(1-\delta_{n,1})(k_p[R_{n-2}][M] - k_d[R_n]) + k_d[R_{n+2}] - k_p[R_n][M] - k_s[R_n]\mu_0 + k_s[D_n]\lambda_0$$
$$- k_{te}\{[R_n](\lambda_1 - \lambda_0 + R_0) - (1-\delta_{n,0})\lambda_0 \sum_{j=n+1}^{\infty}[R_j] + (1-\delta_{n,0})(1-\delta_{n,1})(n-1)[R_n]\lambda_0 - (1-\delta_{n,0})\sum_{i=0}^{n-1}[R_i]\sum_{k=n+1-i}^{\infty}[R_k]$$
$$+ [R_n](\mu_1 - \mu_0 + D_0) - (1-\delta_{n,0})\lambda_0\sum_{i=n+1}^{\infty}[D_i] + [R_n](\gamma_1 - \gamma_0 + G_0)$$
$$- (1-\delta_{n,0})\lambda_0 \sum_{i=n+1}^{\infty}[G_i]\} - kde\,(n-1)[R_n] + kde\sum_{i=n+1}^{\infty}[R_i] \tag{23}$$

$$\frac{d[Dn]}{dt} = -k_{a1}[D_n][C] + k_{a2}[R_n][A] + k_s[R_n]\mu_0 - k_s[D_n]\lambda_0 + k_{te}(1-\delta_{n,0})\sum_{i=0}^{n-1}[R_i]\sum_{k=n+1-i}^{\infty}[D_k]$$
$$- k_{te}(1-\delta_{n,0})(1-\delta_{n,1})(n-1)[D_n]\lambda_0 - k_{de}(n-1)[D_n] + k_{de}\sum_{i=n+1}^{\infty}[D_i] \tag{24}$$

$$\frac{d[Gk]}{dt} = k_{te}(1-\delta_{n,0})\lambda_0 \sum_{i=n+1}^{\infty}[G_i] - k_{te}(1-\delta_{n,0})(1-\delta_{n,1})(n-1)[G_n]\lambda_0 - 2k_{de}(1-\delta_{n,0})(1-\delta_{n,1})(n-1)[G_n]$$
$$+ 2k_{de}(1-\delta_{n,0})\sum_{m=n+1}^{\infty}[G_m] + k_{de}(1-\delta_{n,0})\sum_{k=n+1}^{\infty}[R_k] + k_{de}(1-\delta_{n,0})\sum_{k=n+1}^{\infty}[D_k] \tag{25}$$

Equations 20-22 are the material balances of the monomeric species present in the kinetic model equations 11-19. Equations 23-25 are population balances of all active, dormant and terminated chains, respectively, considering reversible activation, propagation, chain transfer, intermolecular trans-esterification, and the newly developed irreversible termination, random chain scission [11].

In order to compare the output of the developed kinetic model at several monomers to initiator ratio with experimental data, Yu et al. [91] calculated the number average molecular weight (Mn) for different initial conditions [11]. The variation of Mn versus time (Fig. 15) shows the significance of several stages of reaction mechanism. The initial variation up to 0.01 h

shows the dominance of initiation process on rate of reaction. At 0.02h propagation starts and at the saturation point 0.1h shows the termination state of the ROP process [11]. The final stage includes all the side reactions, trans-esterification and scission which suffice the termination reaction at the end.

A detailed model of L-LA polymerization at different temperature using $Sn(Oct)_2$ as the catalyst and 1-dodecanol as cocatalyst was developed. The model considered the effect of inter and intramolecular transesterification reactions. The validation of the model was carried out by comparison with experimental data at the different monomer to catalyst ratio and catalyst to cocatalyst ratio. The reaction responsible for the decrease of molecular weight
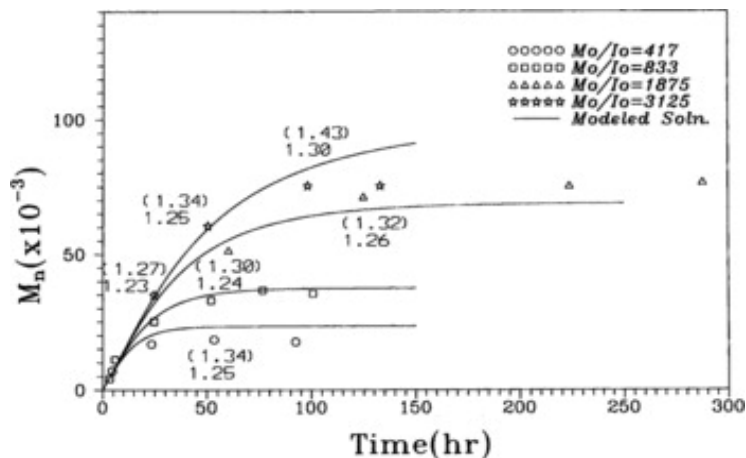

Fig. 14. A comparison of experimental [41] and modelling results (number average molecular weight) for the polymerization of (D, L)-Lactide. The solid lines are the solutions obtained from the model and points are the experimental values
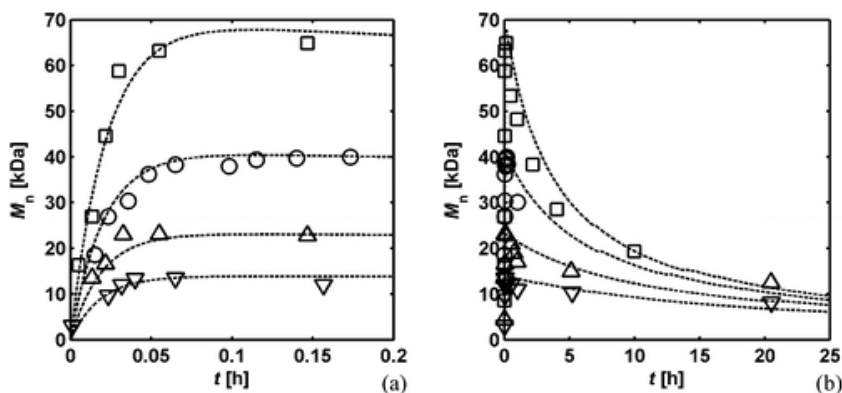

Fig. 15. Number average weight (Mn) for ROP of LA with $Sn(Oct)_2$ and 1-dodecanol at 180ºC, $[M]_0/[C]_0$=10000 and $[OH]_0/[C]_0$= 20 □ 34, ○60, △ 100,▽ experimental results in dots and simulated results with dashed lines

at high temperature is mentioned at random chain scission. Satisfactory prediction of MWD was achieved when both transesterification and random chain scission were included in the kinetic scheme. The overall average errors of the model predictions at the different condition in comparison to experimental data are well below 5%.

9. CONCLUSION

Synthesis of PLA from LA monomers through ROP process using the metal catalyst is the standard industrial process and it leads to throughputs of up to 20 kg/hr Although PLA can boast of its eco-credentials, it can be toxic. The health and environmental hazards may emanate from traces of the metal catalyst that are left behind in the polymer after the polymerisation of PLA. In order to produce non-toxic PLA, the metal catalyst can be replaced with organic and/or metal-free catalyst. Several studies have explored this possibility, but unfortunately, they obtained low conversion rates and PLA with low molecular weight. Also, the maximum throughput was about 2-3 kg/hr, much lower than the industrially sustainable/commercially viable rate of 20 kg/hr.

For the production of safer and cleaner PLA polymer from lab scale to industrial scale, further investigations will be required which includes large-scale computational simulation too. Research which involves the experimental and theoretical investigation of PLA synthesis considering the non-metal and alternative energy in the reaction seems to be an effective mechanism to focus on. Theoretical modelling and simulation are useful to provide an estimate of the throughput and help to plan the experimental/industrial production accordingly.

Groups such as InnoREX consortium (www.InnoREX.eu) are performing detailed step by step investigations of above-defined mechanism to achieve highly precise, controlled and large scale synthesis of PLA through the reactive extrusion process. The group is working on considering the impact of replacing the metal catalyst with organic one as well implementation of AE sources in the reaction process. To achieve this target lab scale experiments and mathematical simulation model to verify the output of the reaction are being performed. To consider the impact of AE sources and to study

the production quality/market demands of PLA (Medical, Electronic & Food Packaging), several industrial partners also involved in InnoREX group. The InnoREX group is not the only one interested in a safer and no-toxic method to prepare PLA. Many experts from industries like Purac and Nature-work limited are also trying to develop a novel reactor concept using continuous, highly precise and controlled metal-free polymerisation of PLA.

ACKNOWLEDGEMENT

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
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