



Review article

New emerging trends in synthetic biodegradable polymers – Polylactide: A critique

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Abstract

Polylactide (PLA), the biodegradable synthetic aliphatic polyester, has been studied extensively for a number of applications. With potential applications PLA represents its prospective utility in a number of growing technologies such as orthopedics, drug delivery, sutures, and scaffolds, and have further enhanced the interest of researchers in this novel area. Renewable resource generated monomers possess better mechanical properties and easy processability by conventional methods like thermoforming, injection, and blow molding with non-toxic degradation products, which have made it superior than the other conventional thermoplastics. In order to meet the different performance requirements, PLA can be synthesised by various methods using different catalysts. In this review a collection of more than 100 catalysts for the synthesis of PLA are mentioned, apart from this, efforts have been made to present an updated review on the various aspects of polylactide.

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Keywords: Polylactide; Polymerisation; Biodegradable; Catalysts

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1. Introduction

Biodegradable polymers have increasing interest over the past two decades in the fundamental research as well as in the chemical industry. Biodegradable in this connection means hydrolysable at temperatures up to 50 °C (e.g. in composting) over a period of several months to one year. Non-toxic degradation products are, of course, another important prerequisites for any potential application. The polyester and copolyesters of several α -, β - and ω -hydroxy acids have been used widely during the past 20 years. Many aliphatic polyesters possess these desirable properties, and among the numerous polyesters studies so far, polylactide (PLA) has proven to be the most attractive and useful class of biodegradable polyesters. This prominent role has several reasons. Lactic acid is easily obtained by a biotechnological process (usually based on the strain of a *lactobacillus*) from inexpensive raw materials [1]. PLA is a high strength and high modulus thermoplastic, which can be easily processed by conventional processing techniques used for thermoplastics like injection moulding, blow moulding, thermoforming and extrusion. For large-scale production, the polymer must possess adequate thermal stability to prevent degradation and maintain molecular weight and properties. Its degradation is dependent on time, temperature, low-molecular-weight impurities, and catalyst concentration [2].

A large number of investigations have been carried out on PLA and its copolymers in biomedical applications for resorbable medical implants [3–6] in the shape of rod, plate, screw, fibre, sheet, rod, sponge, beads for bone and tissue engineering, microsphere for drug delivery system [7], films or foils for wound treatment and for applications in agriculture like mulch films, slow release of pesticides and fertilisers. When PLA is used for orthopaedic and oral surgeries as fixation of augmentation devices, PLA of high molecular weight is needed to produce devices of high mechanical strength. On

the contrary, such high molecular weights are not necessary, when it is used as a carrier for drug delivery systems. In such pharmaceuticals applications, lactide copolymers of low molecular weights are generally preferred than high molecular weight, since shorter degradation time results in better release property. PLA degrades by simple hydrolysis of the ester bond and it does not require the presence of enzymes to catalyze hydrolysis. The degradation products of PLA are non-toxic to the living organisms [8], since lactic acid itself occurs in the metabolism. The major producers of PLA in the world are listed in Table 1.

2. Synthesis

2.1. Raw material

The monomer, i.e. lactic acid, can be synthesised by biological and chemical methods. However, biological method is generally preferred. It is based on the fermentation of starch and other polysaccharides, which are easily available from corn, sugar beet, sugar cane, potatoes, and other biomasses. The majority of the world's commercially produced lactic acid is by the bacterial fermentation. During

Table 1
Current producers of PLA

Company name	Location
Apack AG	Germany
BASF Aktiengesellschaft	Germany
Bio Invigor	Taiwan
Birmingham Polymers	USA, AL
Boeringer Ingelheim	Germany
Dow Cargill	USA, NB
Hycail B.V.	Netherlands
Mitsui Chemicals	Japan
Phusis	France
Polysciences Inc.	USA
Purac Biochem	Netherlands
Shimadzu Corporation	Japan

the fermentation process, the conditions like pH, temperature, atmosphere and in some cases the agitation are monitored closely to get the maximum yield with the purity of material.

2.2. Structure and property

Lactic acid (2-hydroxy propanoic acid) is the simplest hydroxy acid with an asymmetric carbon atom and exists in two optically active configurations. Both D- and L-enantiomers are produced in bacterial systems, thus lactic acid can be obtained by fermentation, selecting suitable microorganism, e.g. homo-lactic organisms such as various optimised or modified strains of *Lactobacilli* are used to produce stereoregular L-lactic acid. However, lactic acid obtained by the chemical process is a racemic mixture of D- and L-isomers (see Fig. 1).

However, the nomenclature of PLA prepared by different routes is full of contradictions in the literature, but generally polymers derived from lactic acid by polycondensation are generally referred to as poly(lactic acid) and the ones prepared from lactide by ring opening polymerisation as polylactide. Both types are generally referred to as PLA.

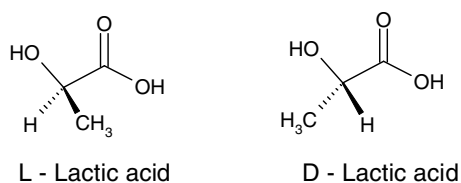


Fig. 1. Different isomeric forms of lactic acid.

2.3. Methods of synthesis

The polymerisation of PLA requires the monomer of high purity, since the impurities interferes with the course of reaction and reduces the quality of polymer. Functionalities like hydroxyl and carboxylic, water, etc. can be considered as impurities [9]. Hydroxyl impurities effect through the reactions of initiator formation, chain transfer, and transesterification resulting in an increase in the rate of polymerisation and lowering of molecular weight along with the broadening molecular weight distribution of the final polymer. Whereas, the carboxylic impurities affect through a deactivation reaction by making complex with the catalyst and reduce the rate of polymerisation. However, it does not show any considerable effect on the molecular weight of the final polymer. Generally, there are four methods used for the synthesis of PLA (see Fig. 2).

2.3.1. Direct polycondensation polymerisation

Lactic acid is polymerised in the presence of a catalyst at reduced pressure. The polymer obtained has a low molecular weight, because it is hard to remove water completely from the highly viscous reaction mixture; therefore a polymer of a molecular weight of a few ten thousands is obtained. The polymer of low molecular weight is the main disadvantage of direct polycondensation polymerisation and it restricts its use. Moreover, the stereoregularity cannot be controlled during the course of polymerisation. The polymer thus possesses inferior mechanical properties. So, this method is employed only if the polymer of low molecular weight is

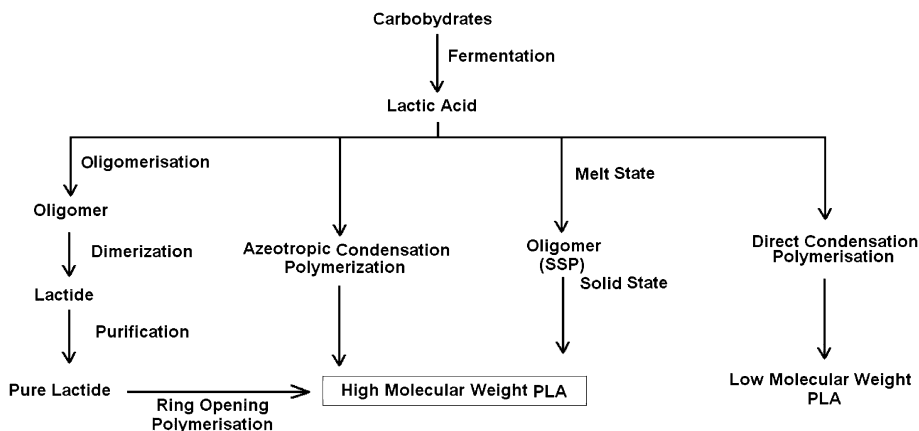


Fig. 2. Various routes of synthesis of PLA.

required. However, a polymer of high molecular weight can be obtained by the use of chain coupling agents. The coupling agent joins the polymer chain of low molecular weight to the chain of high molecular weight. Since, the self-condensation of lactic acid results in a low-molecular-weight polymer with an equimolar concentration of hydroxyl and carboxyl end-groups. Chain-coupling agents preferentially react with either the hydroxyl or carboxyl end groups of the polymer. With the use of a bi/multi-functional co-monomer, PLA can be modified to all hydroxyl or carboxyl end group. Hydroxyl terminated PLA can be synthesised by the polymerisation of lactic acid in the presence of a small amount of bi/multi-functional hydroxyl compounds such as 2-butene 1,4-diol, glycerol, or 1,4-butanediol, which leads to a preferential hydroxyl end-groups. This same concept can be used to synthesise carboxyl terminated PLA by using bi/multifunctional carboxylic acids such as maleic, succinic, adipic, or itaconic acid, leading to all carboxyl-end functional polymer [10–12]. PLA can also be post-reacted with acid anhydrides such as maleic or succinic acids to convert the hydroxyl group to a carboxylic end-group [12]. The reaction of bi/multi-functional PLA with a suitable coupling agent like di/polyacids or isocyanates to form copolyester or poly(lactic acid-co-urethane), respectively, results in an increase in the length of the polymer chain.

2.3.1.1. Azeotropic condensation polymerisation. High molecular weight PLA can also be synthesised azeotropically. In this approach, the problem of the removal of water is overcome by manipulating the equilibrium between a monomer and a polymer in an organic solvent and thus lactic acid is polycondensed directly into a polymer of a high molar mass. Ajioka et al. [13–15] synthesised PLA of high molecular weight by a one-step azeotropic condensation polymerisation of lactic acid by using an appropriate azeotropic solvent. It is a solution polymerisation technique, using a high activity catalyst and a low boiling organic solvent. Water as a by-product is removed azeotropically, whereas solvent is dried and recycled back in the reaction. This polymerisation technique allows a reaction temperature to be chosen below the melting point of polymer, and thus efficiently prevents depolymerisation and racemisation during polymerisation. It has been reported that a highly pure PLA with a molecular weight of upto 300,000 can be produced by this method [13]. Other research groups have also syn-

thesised PLA by Direct dehydration polycondensation [16–19].

2.3.1.2. Solid state polymerisation (SSP). This process involves heating a semi-crystalline, solid prepolymer (of relatively low molecular weight) in powder, pellet, chip or fibre form up to a temperature below the melting temperature with the simultaneous removal of by-products from the surface of the material either (by volatilising) under reduced pressure or with a carrier, for example, blowing inert gas [20]. Inert gas in SSP serves to remove the condensate from the reaction and inhibits polymer oxidation. This reaction essentially takes place in the amorphous region of the polymer, where all the reactive end groups reside. Therefore, the solid state polymerisation reaction has to be performed at a temperature above the glass transition temperature (to allow mobility of the end groups to react) and below the melting temperature [21]. Since the solid state reaction actually starts at much lower temperatures, compared to molten or solution state, the reaction temperature can range from sufficiently below the melting temperature to just 5–15 °C below T_m [22]. But the temperature of SSP for monomers must be high enough to facilitate chain growth but not so high that it leads to partial melting with simultaneous sticking, cyclisation or other side reactions. However, the time needed to reach a particular molecular weight is generally much longer than that in melt or solution, yet very high molecular weights can be achieved. In ordinary melt polycondensation of lactic acid, high temperature and high vacuum induce not only dehydration, but also favours back biting (inter and intramolecular transesterification) reactions, resulting in the decomposition of low molecular polymer into lactide and prevent the growing chain of PLA (see Fig. 3).

The advantages of SSP include low operating temperatures, which control over the side reactions as well as thermal, hydrolytic, oxidative degradations along with reduced discoloration and degradation of the product. SSP polymers often have improved properties, because monomer cyclisation and other side reactions are limited. There is practically no environmental pollution, because no solvent is required.

2.3.2. Ring opening polymerisation (ROP)

It was first demonstrated by Carothers in 1932 [23]. But the polymer of high molecular weight

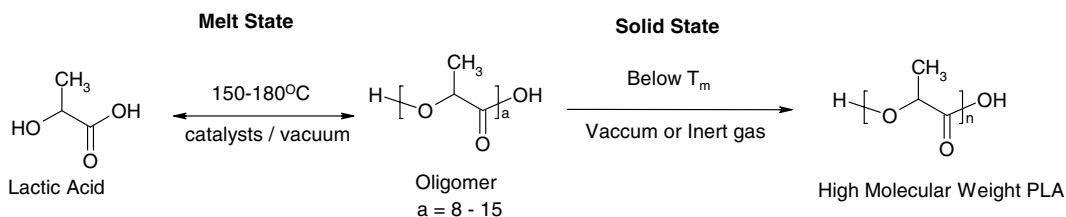


Fig. 3. Solid state polymerisation.

was not obtained until improved polymerisation technique was developed. The polymer prepared by ROP is the most commonly studied one due to the possibility of accurate control of chemistry and thus varying the properties of the resulting polymers in a more controlled manner, which broadens the application fields (see Fig. 4).

This method is usually employed for the synthesis of the polymer of high molecular weight with a high degree of stereo-regulation. By this method, polylactide is made by the polymerisation of their respective cyclic dimmers, i.e. lactide. Lactide is prepared from thermal cracking of low molecular weight PLA oligomer at high temperature and low pressure in the presence of catalyst. Lactide (3,6 dimethyl 1,4-dioxane 2,5-dione) is a six member cyclic dimer. Since lactic acid is found in two stereoisomeric forms therefore lactide is formed in three stereoisomeric forms viz. DD-, LL- and DL-lactides (Fig. 5). The crude lactide contains impurities like water, lactic acid and oligomers. These impurities

can interfere with the polymerisation reaction leading to the formation of polymer of low molecular weight with a higher degree of racemisation. Thus, the crystalline lactide is highly purified before the polymerisation. The ring-opening polymerisations of lactides may be classified by their four different reaction mechanisms and initiator types: anionic polymerisations, cationic polymerisations, coordination–insertion mechanisms. The first three are most prevalent and will be discussed here.

2.3.2.1. Anionic polymerisations. The anionic ring opening polymerisation is initiated when the nucleophilic anion of the initiator attacks the carbonyl group of the lactide, resulting in the cleavage of the carbonyl carbon and the endocyclic oxygen bond. This oxygen becomes a new anion, which continues to propagate [24,25], but highly nucleophilic initiators are so basic that they deprotonate the monomer and this leads to the racemisation. The highly active catalysts at high temperature

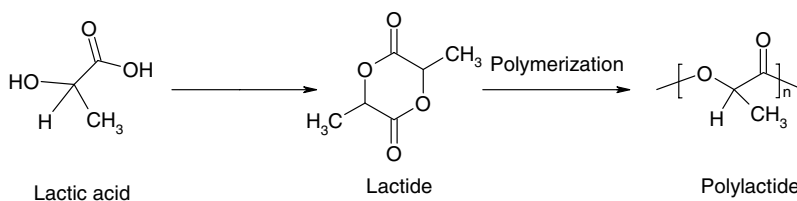


Fig. 4. Synthesis of PLA by ring opening polymerisation.

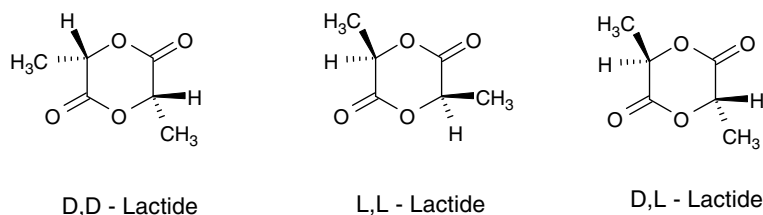


Fig. 5. Different isomers of lactide.

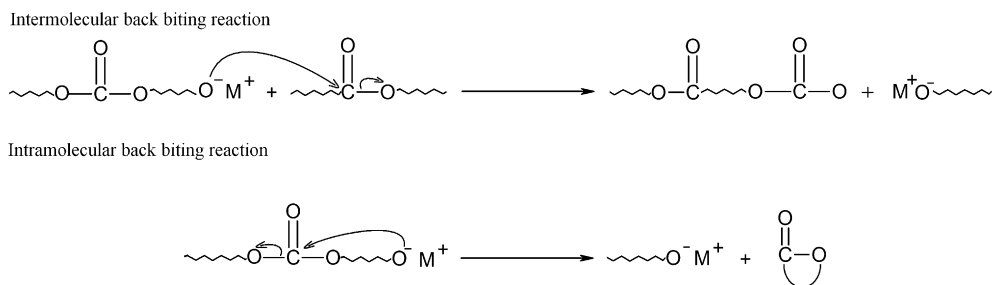


Fig. 6. Back biting reaction.

result in racemisation, back biting reaction (see Fig. 6) and other side reactions, which hinder the chain propagation. Therefore, it is very difficult to obtain the polymer of high molecular weight from this method. Example of anionic ring opening polymerisation initiators is alkali metal alkoxides (see Fig. 7).

2.3.2.2. Cationic polymerisations. Catalyst for the cationic ring opening polymerisation can be carbenium ion donors and a few strong acids such as triethyloxonium tetrafluoroborate, borontrifluoride, and trifluoroacetic acid [26]. The initiation step of cationic polymerisation occurs when the exocyclic oxygen of one of the lactide carbonyls is either

alkylated or protonated by the initiator, causing the resulting O–CH bond to become positively charged. Nucleophilic attack by a second monomer breaks this bond to create another electrophilic carbenium ion. The propagation step of this polymerisation repeats as nucleophilic attack by additional monomers continues until the polymerisation is terminated by a monofunctional nucleophile like water. In cationic polymerisation high temperature caused racemisation, since the second monomer attack at chiral centre propagating chain. However, the racemisation can be minimised at temperature $>50\text{ }^{\circ}\text{C}$ but at this temperature the rate of reaction is very slow [27] and does not yield high molecular weight polymer (see Fig. 8).

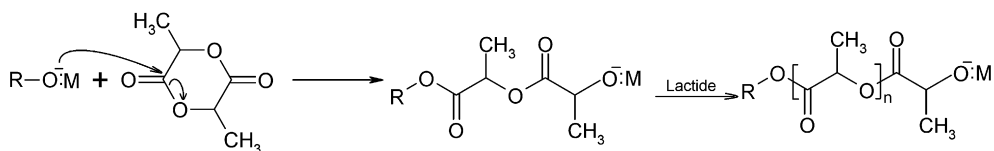


Fig. 7. Anionic ring opening polymerisation.

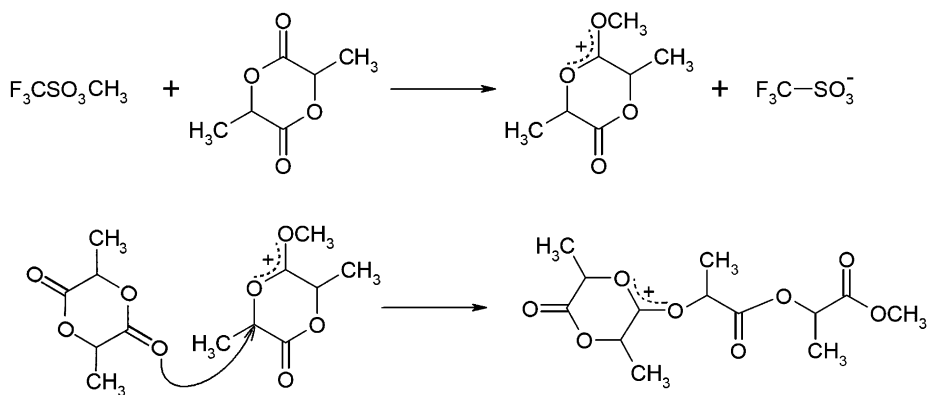


Fig. 8. Cationic ring opening polymerisation.

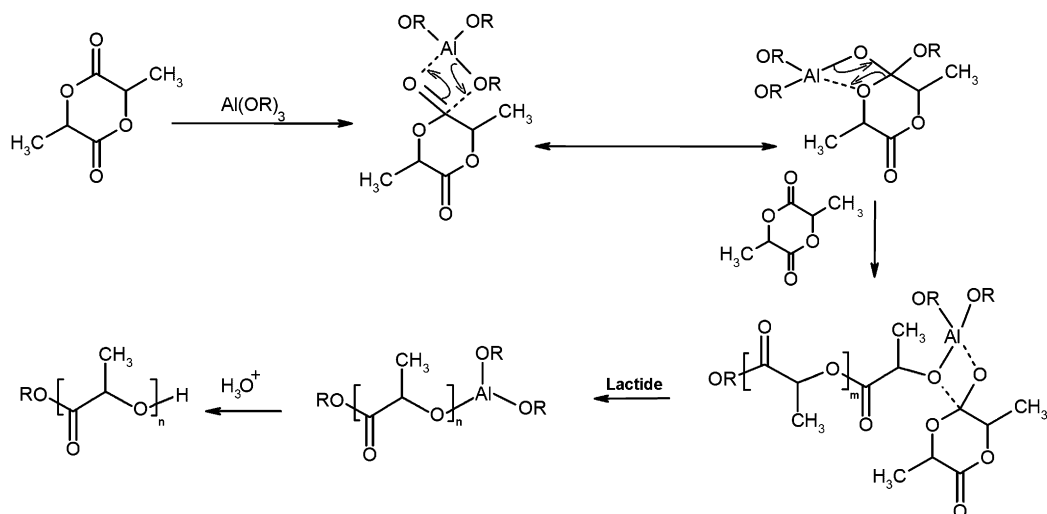


Fig. 9. Coordination insertion ring opening polymerisation.

2.3.2.3. Coordination–insertion mechanisms. 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 catalysts contain free p or d orbitals of a favourable energy (Mg, Sn, Ti, Zr, Zn alkoxides), which possess a covalent bond between metal atom and oxygen atom and behave like weak Lewis acids [28]. 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 [25] [28]. The polymerisation 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 polymerisation variables allow for the control of molecular weights over a broad range. A high molecular weight is obtained by this method (see Fig. 9).

A large number of catalysts have been studied for the ring opening polymerisation of lactide. The effects on the properties like molecular weight, molecular weight distribution and racemisation of the PLA obtained have been mainly studied. The

different catalyst studied for the synthesis of PLA consists of different metals and their salts.

2.4. Catalysts for the polymerisation of lactide

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 alkylmetals and metal halides, oxides, carboxylates and alkoxides. Metal halides, oxides and carboxylates would act as lewis acid catalysts in ROP and are actually initiated with a hydroxyl containing compound such as water or ω -hydroxy acid. A large number of catalysts have been studied for the polymerisation of lactide for various applications, including biomedical applications, such as iron [29], Sn(Oct)_2 [30] SnCl_4 , $\text{Sn(C}_6\text{H}_6)_4$, Zinc lactate $[(n\text{-C}_4\text{H}_9\text{O}_2)\text{AlO}]_2\text{Zn}$ [31–33]. 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 was studied on the synthesis of PLA using dibutylmagnesium or

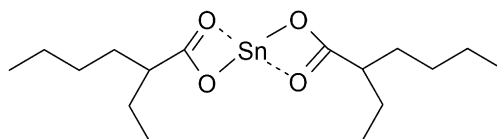


Fig. 10. Tin octoate.

Table 2
Catalysts used for the synthesis of PLA

S. no.	Catalyst	Authors	Reference
1	Cationic (<i>N</i> -heterocyclic carbene)silver	Samantaray et al.	[53]
2	Aluminium triflate	Kunioka et al.	[54]
3	Lithium alkoxide	Kricheldorf et al.	[55]
4	Aluminium triflate	Kunioka et al.	[56]
5	Alkoxide cationic polymerisation	Kricheldorf et al.	[57]
6	Cationic (<i>N</i> -heterocyclic carbene)silver	Samantaray et al.	[58]
7	Tetrakis Sn(IV) alkoxides	Kalmi et al.	[59]
8	Zinc aryloxides	Huang et al.	[60]
9	Calcium methoxide	Zhong et al.	[61]
10	Potassium <i>t</i> -butoxide and its 18-Crown	Sipos et al.	[62]
11	Titanium alkoxide	Kim et al.	[63,64]
12	Lanthanide alkoxide	Spassky et al.	[65]
13	Tributyl tin methoxide (Bu ₃ SnOMe)	Kricheldorf et al.	[63]
14	Dibutyltin methoxide (Bu ₂ Sn(OMe) ₂)	Kricheldorf et al.	[66]
15	Oxyethyl methacrylate aluminium trialkoxides	Eguiburu et al.	[35]
16	Aluminium isopropoxide	Philippe et al.	[67]
		Dubois et al.	[68]
		Philippe et al.	[69]
17	Magnesium and zinc alkoxides	Wu et al.	[70]
18	Dibutyltin dimethoxide	Stassin et al.	[71]
19	Aluminium alkoxide	Tina et al.	[72]
20	Anionic iron(II) alkoxides	McGuinness et al.	[73]
21	Ferric alkoxide	Wang et al.	[74]
22	Tin(II) butoxide	Kowalski et al.	[75]
23	(2-Methacryloxy) ethyloxy-aluminum trialkoxides	Eguiburu et al.	[76]
24	Cyclic tin alkoxide	Stridsberg et al.	[36]
25	Titanium biphenoxy-alkoxide	Umare et al.	[77]
26	Yttrium tris-(isopropoxyethoxide)	Simic et al.	[43]
27	Bis(trimethyl triazacyclohexane) peraseodymium triflate	Kohn et al.	[40]
28	Complexes of Cu, Zn, Co and Ni Schiff base	Sun et al.	[39]
29	Lithium diisopropylamide (LDA)	Luximon et al.	[38]
30	Butyl lithium and butylmagnesium	Kasperczyk et al.	[37]
31	Lithium chloride	Xie et al.	[34]
		Xie et al.	[34]
32	Dibutylmagnesium and butylmagnesium chloride	Kricheldorf et al.	[33]
33	Tin octoate (tin 2-ethylhexanoate)	Zhang et al.	[9]
		Kricheldorf et al.	[78]
		Umare et al.	[79]
		Leenslag et al.	[29]
		Leenslag et al.	[80]
		Vasanthakumeri et al.	[47]
		Nijkens et al.	[48]
		Kricheldorf et al.	[49]
34	Stannous(II) trifluoromethane sulfonate	Moller et al.	[81]
35	Triphenylphosphine and 2-ethylhexanoic acid Tin(II) salt	Degee et al.	[82]
36	Stannous octoate and zinc-initiated Polymerisation	Schwach et al.	[83]
37	Soluble tin(II) macroinitiator adducts	Storey et al.	[84]
<i>Metals</i>			
38	Zinc-bis(2,2-dimethyl-3,5-heptanedionato- <i>O,O'</i>)	Nijenhuis et al.	[85]
39	Zirconium(IV) acetylacetonate	Dobrzynski et al.	[86]
40	Iron	Stolt et al.	[28]
41	Zn, Pb, Sb, Bi, salts	Kricheldorf et al.	[87]
42	Phosphines (nucleophilic organic catalysts)	Myers et al.	[88]
43	Organoyttrium complexes	Yi Yang et al.	[89]

Table 2 (continued)

S. no.	Catalyst	Authors	Reference
44	Zn salts and Zn(II) L-lactate	Kricheldorf et al.	[32]
45	Aluminum/Schiff base	Tang et al.	[90]
46	[5-Cl-Salen]Alome	Cameron et al.	[91]
47	Influence of various metal salt (Plzm or not)	Kricheldorf et al.	[92]
48	Aluminium Schoff's base complexes	Jhurry et al.	[93]
49	Yttrium(III) arylamidinates	Aubrecht et al.	[94]
50	Zirconium and hafnium aryloxide	Hsieh et al.	[95]
51	Gold(I)	Ray et al.	[96]
52	Yttrium(III)	Chamberlian et al.	[97]
		Drysdale et al.	[41]
		McLain et al.	[42]
53	Zn lactate	Schwach et al.	[98]
54	Yttrocene complexes	Beckerle et al.	[99]
55	Zinc amino acid salts	Kricheldorf et al.	[100]
56	Guanidinium	Li et al.	[101]
57	Zinc(II), complexes	Dumitrescu et al.	[102]
58	Samarium(III) complexes	Dumitrescu et al.	[102]
59	Tin(II) complexes	Dumitrescu et al.	[102]
60	Ferrous acetate	Stolt et al.	[103]
61	Strontium-based initiator	Tang et al.	[104]
62	Germanium	Finne et al.	[105]
63	Tetraphenyltin	Kohn et al.	[106]
64	Fe(II) lactate and Fe(II) salts	Kricheldorf et al.	[107]
65	Zinc metal and zinc lactate	Schwach et al.	[108]
66	Organomagnesium complexes	Chivers et al.	[109]
67	Bimetallic zinc	Bukhaltsev et al.	[110]
68	Yttrium(III) complexes	Chamberlain et al.	[111]
69	Aluminum isopropoxide trimer or tetramer	Kowalski et al.	[112]
70	Zn and Al	Bero et al.	[113]
71	Yttrium tris(acetylacetonate)	Ford et al.	[125]
72	Yttrium tris(2,2,6,6-tetramethylheptane dionate)	Ford et al.	[125]
73	Scandium tris(2,2,6,6-tetramethylheptane dionate)	Ford et al.	[125]
74	Yttrium octoate	Ford et al.	[125]
75	Scandium tris(hexafluoroacac)	Ford et al.	[125]
76	Yttrium bis(2,2,6,6-tetramethylheptane dionato)dimethylaminoethoxide	Drysdale et al.	[126]
77	Yttrium bis(2,2,6,6-tetramethylheptane dionato)isopropoxide	Drysdale et al.	[126]
78	Tetra(phenylethynyl)tin	Lahcini et al.	[114]
79	Sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al)	Li et al.	[115]
80	Dimeric aluminum chloride complexes	Doherty et al.	[116]
<i>Rare earths</i>			
81	Rare earth 2,6-dimethylaryloxide	Zhang et al.	[117]
82	Lanthanum isopropoxide	Save et al.	[118]
	Lanthanum Isopropoxide		[119]
83	Rare earth coordination catalyst for polymerisation	Zhang et al.	[120]
84	Rare earth tris(4- <i>tert</i> -butylphenolate)s	Yu et al.	[121]
85	Rare-earth tris(4- <i>tert</i> -butylphenolate)	Yu et al.	[122]
86	Chiral Schiff's base/aluminium	Spassky et al.	[123]
87	Organoacid rare earth compounds	Deng et al.	[124]
88	Lanthanum tris(acetylacetonate)	Ford et al.	[125]
89	Lanthanum bis(2,2,6,6-tetramethylheptane dionate) (2-ethylhexanoate)	Ford et al.	[125]
90	Lanthanum tris(2,2,6-trimethyloctan-3,5-dionate)	Ford et al.	[125]
91	Lanthanum tris(<i>t</i> -butyl-acetoacetate)	Ford et al.	[125]
92	La[MeC(O)CHC(O)Me] ₂ (2-ethylbutyrate)	Ford et al.	[125]
93	La[Me ₃ CC(O)CHC(O)CMe ₃] ₂ (2-ethylhexanoate) ₂	Ford et al.	[125]
94	La[Me ₃ CC(O)CHC(O)CMe ₃] ₂ (2-ethylhexanoate)	Ford et al.	[125]
95	Anhydrous lanthanum tris(acac)	Ford et al.	[125]
96	Lanthanum tris(acac) · 3H ₂ O	Ford et al.	[125]

(continued on next page)

Table 2 (continued)

S. no.	Catalyst	Authors	Reference
97	[Lanthanum bis(2,2,6,6-tetramethylheptane dionato) isopropoxide	Drysdale et al.	[126]
98	Tris(d,d-dicampholymethanato) europium	Ford et al.	[125]
99	Cyclopentadienyl rare-earth complex	Tao et al.	[127]
<i>Miscellaneous</i>			
100	Lipase-catalyzed	Matsumura et al.	[128]
		Dong et al.	[129]
101	Bismuth tris(2,2,6,6-tetramethylheptane dionate)	Ford et al.	[125]
102	Cerium tris(trifluoroacetyl acetate)	Ford et al.	[125]
103	Praseodymium tris(hexafluoroacetate)	Ford et al.	[125]
104	Di-iodo-samarium-1-benzyl- <i>n</i> -octyloxide	Drysdale et al.	[126]
105	Microwaves	Zhang et al.	[130]
106	Magnesium aryloxides	Shueh et al.	[131]
107	Phosphorous compound	Yasuhiro et al.	[132]
108	Titanatranes	Youngjo Kim et al.	[133]
109	Tetracoordinated aluminum complexes	Emig et al.	[134]
110	Creatinine	Wang et al.	[135]

butylmagnesium chloride [34]. It was found that PLA of molecular weight in the order of 3×10^5 with almost complete optical purity was obtained. When lithium chloride [35] was used with ethylene glycol (EG) and α -D-glucopyranoside (MGlC) as initiator, the polymer of higher molecular weight was obtained. Different research groups have worked on a number of catalysts such as oxyethyl methacrylate aluminium trialkoxides [36], cyclic tin alkoxide [37], butyl lithium and butylmagnesium [38], lithium diisopropylamide (LDA) [39], complexes of Cu, Zn, Co and Ni Schiff base [40], bis(trimethyl triazacyclohexane) praseodymium triflate [41], yttrium [42,43], and yttrium tris-(isopropoxyethoxide) has been found to be very reactive initiators for the polymerisation of (D,L)-lactide in dichloromethane solution [44]. Aluminium alkoxides proceed through the coordination/insertion mechanism, and are reported to give controllable molecular weights with narrow distributions and minimum racemisation [45,46]. It was found that there was no transesterification at temperatures less than 150 °C, which yields polymers with narrow molecular weight distribution [28]. The standard catalyst for the synthesis of high molecular weight polylactides is Sn(II) (2-ethyl-hexanoate) [47–49]. This catalyst has several advantages over the others, such as solubility in organic solvents and molten lactide, stability on storage, and free polymerisation upto 180 °C. Moreover, it has been approved by FDA (Food and Drug Administration) and therefore it is getting attention for the synthesis of polymer for food packaging and biomedical applications (see Fig. 10).

Several rare earth compounds have also been studied for the ring opening polymerisation of lactide like rare earth phenyl compounds such as triphenyl yttrium, triphenyl neodymium and triphenyl samarium [50]. It was observed that when triphenyl yttrium was used as catalyst, a higher molecular weight polymer was obtained at lower monomer/initiator ratio. A co-ordination–deprotonation–insertion mechanism was suggested when 2-methyl phenyl samarium [51] was used as a catalyst and acyl–oxygen cleavage mechanism was suggested in the case of lanthanide tris (2,4,6-trimethylphenolate)s [52] as a catalyst (see Table 2).

3. Properties of PLA

Poly(lactide) is well known for its good processability, biocompatibility; biodegradability (mainly by simple hydrolysis). PLA can be quite different in chemical and physical properties because of the presence of a pendent methyl group on the alpha carbon atom. This structure causes chirality at α carbon of lactic acid and thus L, D and DL isomers are possible. Poly(L-lactic acid), poly(D-lactic acid) and poly(DL-lactic acid) are synthesised from L(–), D(+) and DL-lactic acid monomers, respectively. A wide range of degradation rates, physical and mechanical properties, can be achieved varying its molecular weights and composition in its copolymers.

PLLA has a melting point of 170–183 °C and a glass-transition temperature of 55–65 °C [132–138] while PDLLA has (T_g) 59 °C [139]. Density of

Table 3
Mechanical properties of PLA (Naturework™ Cargill Dow)

	2002D	2100D	PLA resin
Specific gravity	1.24 D792	1.30 D792	1.24 D792
Melt index, g/10 min (190°C/2.16 K)	4–8 D1238	5–15 D1238	10–30 D1238
Clarity	Transparent	Opaque	–
Tensile strength at break psi (MPa)	7700 (53) D882	8100(56) D638	7000 (48) D638
Tensile yield strength, psi (MPa)	8700 (60) D882	9000 (62) D638	–
Tensile modulus, kpsi (GPa)	500 (3.5) D882	500(3.5) D638	–
Tensile elongation, %	6.0 D882	3.0 D638	2.5 D638
Notched izod impact, ft-lb/in (J/m)	0.24 (12.81) D256	0.37 (19.8) D638	0.3 (0.16) D256
Shrinkage	Silimar to PET	–	–

PLLA is 1.25–1.29 g/cc and for PDLLA is 1.27 g/cc [140]. The solubility of lactic acid based polymer is highly dependent on the molar mass, degree of crystallinity and other co-monomers present in the polymer. Good solvents for enantiomerically pure poly(L-lactide) are chlorinated or fluorinated organic solvents, dioxane, dioxolane, furan and for poly(DL-lactide), in addition to the previously mentioned ones are many other organic solvents like acetone, pyridine, ethyl lactate, tetrahydrofuran, xylene, ethyl acetate, dimethylsulfoxide, *N,N*-dimethylformamide and methyl ethyl ketone. Typical non-solvent for lactic acid based polymers is water, alcohols like methanol, ethanol, propylene glycol and unsubstituted hydrocarbons like hexane, heptane, etc.

PLLA is crystalline whereas PDLLA is completely amorphous biodegradable polymer. Because of the crystallinity, poly(L-lactide) of same molecular weight has better mechanical properties than poly(DL-lactide). PLLA has more ordered and compact structure and hence it has better mechanical properties and longer service time. However, the annealed PLLA has better mechanical properties than un-annealed PLLA [141], because of higher degree of crystallinity resulted by annealing. Whereas degree of crystallinity depends on many

factors, such as molecular weight, thermal and processing history, and the temperature and time of annealing treatments. The calculated values for the heat of fusion of 100% crystalline PLLA have been reported 135–203 J/g [142,143] in different literature.

The mechanical properties of PLA can be varied to a large extent ranging from soft, elastic plastic to stiff and high strength plastic. With the increase of molecular weight the mechanical properties also increase. With the increase of molecular weight of PLLA from 23k to 67k, flexural strength increased from 64 to 106 MPa but the tensile strength remains the same at 59 MPa [141]. In the case of poly(DL-lactide) when molecular weight is increased from 47.5k to 114k [141] tensile and flexural strength increased 49–53 MPa and 84–88 MPa, respectively. The various properties of PLA are listed in Tables 3 and 4 [144].

Since the mechanical properties of PLA are mainly dependent on its molecular weight, there are several methods to determine its molecular weight like GPC, light scattering, osmometry, etc., but the simplest one is the viscosity measurement. The viscosity molecular weight of PLA is found by using Mark-Houwink equation

Table 4
Mechanical properties of PLA (LACEA Mitsui Chemicals)

		PLA		Commodity plastics		
		Standard	IRG ^a	GPPS	PET	PBT [145]
Tensile strength	[MPa]	68	44	45	57	56
Elongation at break	[%]	4	3	3	300	–
Flexural strength	[MPa]	98	76	76	88	–
Flexural modulus	[MPa]	3700	4700	3000	2700	2340
Izod impact	[J m ⁻¹]	29	43	21	59	53
Vicat softening point	[°C]	58	114	98	79	170
Density	[kg m ⁻³]	1.26	1.48	1.05	1.4	–

^a Impact resistant grads.

$$[\eta] = K \times M_w^a$$

where ' M_w ' is the molecular weight of the polymer, ' K ' and ' a ' are constants for a particular polymer/solvent/temperature system. Mark-Hauwink equation for the different conditions are given as follows:

When chloroform was used as a solvent at 25 °C [146]

$$[\eta] = 5.45 \times 10^{-4} M_w^{0.73} \text{ poly(L-lactide)}$$

$$[\eta] = 2.21 \times 10^{-4} M_w^{0.77} \text{ poly(DL-lactide)}$$

When chloroform was used as a solvent at 20 °C [147]

$$[\eta] = 7.4 \times 10^{-5} M_w^{0.87} \text{ poly(L-lactide)}$$

$$[\eta] = 1.32 \times 10^{-3} M_w^{0.58} \text{ poly(DL-lactide)}$$

When THF was used as a solvent at 37 °C [51].

$$[\eta] = 1.04 \times 10^{-4} M_w^{0.75} \text{ poly(DL-lactide)}$$

When ethyl acetate was used as a solvent at 25 °C [148]

$$[\eta] = 1.63 \times 10^{-4} M_w^{0.73} \text{ poly(DL-lactide)}$$

$$[\eta] = 1.58 \times 10^{-4} M_w^{0.78} \text{ poly(DL-lactide)}$$

3.1. Degradation

PLA is water insoluble when its molecular weight is sufficiently high. But when PLA is subjected to degradation, water penetrates the bulk of the polymer matrix and hydrolysis on the ester group takes place preferentially by attacking at the chemical bonds in the amorphous phase, converting long polymer chains into shorter one, ultimately to low molecular weight water soluble oligomers and monomers [138]. Water soluble oligomers thus formed escape from the matrix into the surrounding aqueous medium. Degradation causes an increase in the number of carboxylic chain ends, which are known to autocatalyse the ester hydrolysis. As the aging time increases, soluble oligomers which are close to the surface can leach out before total degradation, whereas those which are located well inside the matrix remain entrapped and contribute totally to the autocatalytic effect. The hydrolysis mechanisms and behaviours of PLA are affected by numerous factors, including the materials and the hydrolysis media. In polylactides the diffusion coefficients of the soluble oligomers depend primarily on factors like molar mass, degree of swelling of the matrix, macromolecular conformation, rigidity,

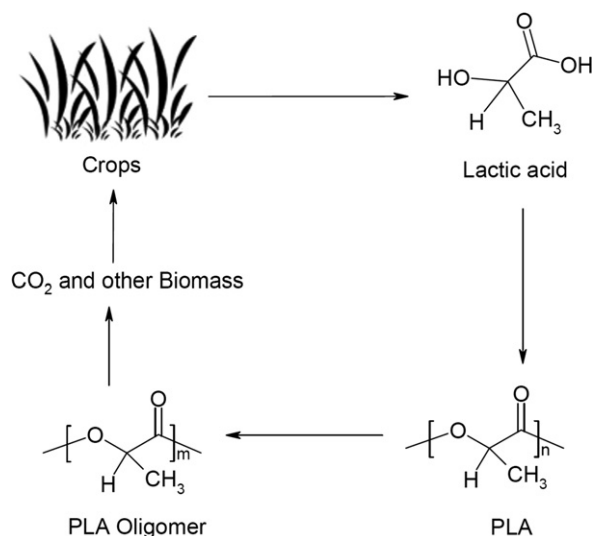


Fig. 11. Life cycle of PLA.

chemical structure, molecular weight, molecular weight distribution impurity/monomer residue, stereochemistry, chain mobility and crystallinity [149]. The crystalline domain is more resistant than amorphous, to biodegradation. The hydrophobic and hydrophilic characters of the polymeric chain noticeably affect the biodegradation process. The release of the soluble carboxyl-terminated oligomers depends on their solubility in the surrounding aqueous medium and thus factors like pH, ionic strength, temperature and buffering capacity become important (see Fig. 11).

A number of properties of polymer deteriorate during degradation, e.g. molecular weight, molecular weight distribution, surface morphology, mechanical properties crystallinity, etc.

3.1.1. In vitro studies

Different research groups have studied the degradation of PLA under various environments like in controlled environment in soil and in microbial culture of *Fusarium moniliforme* and *Pseudomonas putida* [150] in alkaline medium [151] in sea water [152], compost microorganisms [153], hydrolytic degradation [154–159] in buffer at pH 6.5 [160] with lauric acid [161], electron beam [162] enzymatic degradation [163]. However, the most commonly used method, for studying the biodegradation for medical application, is the degradation in phosphate buffer saline solution at 37 °C. In this method, the samples of equal size and weight are placed in a degradation medium (i.e. pH 7.4 phosphate buffer)

Table 5
Degradation of PLA

Degradation type	Authors	Reference
Soil, microbial culture of <i>Fusarium moniliforme</i> and <i>Pseudomonas putida</i>	Torres et al.	[196]
Alkaline medium	Cam et al.	[197]
Compost microorganisms	Hakkarainen	[198]
Sea water	Tsuji et al.	[199]
Hydrolytic degradation	Grizzi et al.	[200]
	Tsuji et al.	[201,202]
	Li et al.	[203]
	Duek et al.	[204]
	Wiggins et al.	[205]
Buffer at pH 6.5	Laitinen et al.	[206]
Lauric acid	Annette et al.	[207]
Electron beam	Loo et al.	[208]
Enzymatic degradation	Kurokawa et al.	[209]

equal to 100 times the sample weight, and all the flasks are allowed to swing at same temperature at 37 °C. After predetermined degradation period, samples are taken out, washed many times with distilled water, and vacuum-dried for 1–2 weeks at room temperature until a constant weight is obtained (see Table 5).

Weight loss and water absorption of samples are evaluated by the percentage of weight loss (WL%) and water absorbed (WA%) is deduced from the equation

$$W_L \% = \frac{(W_0 - W_r)}{W_0} \times 100$$

where W_0 , and W_r are the initial weight and the residual weight of the same carefully dried, partially degraded specimen, respectively. The amounts of absorbed water are deduced from the equation

$$W_A \% = \frac{(W_s - W_r)}{W_r} \times 100$$

where W_s is the weight of the swollen specimen after wiping the surface with paper.

3.2. Blends

PLA possesses excellent mechanical properties and can be slowly broken down into non-toxic metabolites by bio-organisms. The desired properties to be a biodegradable polymer include the degradation kinetics, initial mechanical properties, and

a balanced course of time between the degradation and its strength change, which are dependant on the application part of the biodegradable polymer and the environment to which it was exposed during or after their practical use. However, the ranges of its application are somewhat limited because of the difficulty in controlling the hydrolysis rate, poor hydrophilicity as well as the high rigidity and crystallinity. To overcome these problems; various blends of PLA with other biodegradable polymers have been studied, e.g. starch, chitosan, polyethylene glycol (PEG), poly(ϵ -caorolactone) (PCL), etc. Blending of starch, which is an abundant and cheap biopolymer with PLA, can reduce the cost for the resulting blend, but the mechanical properties of the blend decrease significantly with increasing starch content and the moisture. PLA is a brittle material with low possible elongation, and the addition of starch into such an already brittle material results in even more brittle material. Also, the blend of plasticised PLA with thermoplastic starch shows a small degree of compatibility with the decrease in mechanical properties drastically [164]. The blend shows the similar behaviour with hydrophobised starch [165]. Poly(vinyl alcohol) (PVOH) [166] has been used to enhance compatibility and improve the mechanical properties of PLA-starch blend; at a concentration above 30 wt% it forms a continuous phase with simultaneous increase in the tensile and impact strengths. Other compatibilising agents like methylenediphenyl diisocyanate (MDI) have also been used to improve the compatibilisation of PLA/starch blends. Addition of 0.5% of MDI improves the interfacial adhesion of the blend with higher tensile and greater elongation. At 45 wt% of starch, the blends showed smooth structure and highest tensile strength and percentage elongation [167]. However, the moisture in starch reduces the compatibilisation of the blend [168]. Compatible blends of PLA starch upto 50% can also be obtained by reactive blending; using 1% reactive agent results in blend with 1000–1400 N/cm² of tensile strength and about 40–80% elongation [169].

Chitosan is considered to be one of the most promising biopolymer used in tissue engineering, wound healing, drug delivery agents, blood anti-coagulants, scaffolds, burn treatment. A biopolymer should have properties like biodegradability, biocompatibility, antibacterial property, and it should neither cause inflammation to human tissue nor induce antibody from the immune system [170]. Because of these properties, it has been used with

PLA. PLA and its copolymers have high initial strengths, while the natural products like chitin and its derivatives like chitosan possess low mechanical strength but exhibit excellent cell adhesion [171]. However, PLA was readily resorbed by living tissues, yet high crystallinity and low hydrophilicity of PLA reduce its degradation rate, which results in poorer soft tissue compatibility. The melt blending of PLA and chitosan results in reduction in tensile strength and elongation, whereas there is an increase in the modulus, without showing any appreciable miscibility [172]. Similar results were obtained when PLA and chitosan were solution blended using chloroform and acetic acid as solvent [173]. However, the miscibility and intermolecular hydrogen bonding [174] were shown when PLA and chitosan were blended by solution–precipitation method.

The degradation kinetics and brittleness of PLA can be improved using the biodegradable polymers having a lower glass transition temperature like poly (ϵ -caprolactone) [PCL] or polyethylene glycol (PEG). But PLLA with a higher molecular weight is usually immiscible with PCL, the resulting morphology of PLLA/PCL blends becomes coarse and adhesion strength becomes poor, thus desirable mechanical properties are not anticipated [175,176]. However, the compatibility of the blend is observed by reactive compatibilisation [177]. When low molecular weight PCL-b-PEG copolymer is used as compatibiliser, improvement in the mechanical properties of the PLA/PCL blend is observed, however, the thermal properties show that PEG phase of the block copolymer is miscible with PLA but the PCL phase is still immiscible with PLA [178]. The addition of bisphenol-A enhances the miscibility of the immiscible PCL/PLLA binary blend and at higher concentration it forms miscible blends at room temperature [179]. Blends of PLA/PHB by melt show miscibility in lower molecular weight region but in higher molecular weight region it shows phase separation [180]. However, at moderate molecular weight PLA/PCL blends were immiscible when made by solution blending and miscible when melt blended [181].

With an increase in the PEG component in the PLA/PEG blend, a depression in the melting point is observed. The compositions of PLA and PEG give rise to different miscibility and crystallisation behaviours of the blend. PLA/PEG blends are miscible in the amorphous phase due to the difference in crystallisation temperature of PLA and PEG. The

desired mechanical properties are achieved in quenched PLA/PEG blends at upto 30 wt% PEG. However, these blends are not stable at ambient temperature and the attractive mechanical properties are lost over time. The ageing results crystallisation and phase separation [182]. However, above 50% PEG an increase in modulus, because of increased crystallinity of PEG is observed [183]. In the PLA/PEG blend, PEG with a methyl end group exhibits greater interaction with PLA than hydroxyl end group [184].

4. Applications

PLA is a biodegradable thermoplastic because, of its good mechanical property, biodegradability and non-toxicity degradation products, it is being used for number of application from biomedical to conventional thermoplastics. PLA has been used in the field of sustained drug delivery system, before 1980 protein based drug such as insulin and growth hormones were produced by extraction from tissue and few such drugs were in wide clinical use. With the advent of molecular biology, protein could be made synthetically and introduced into cells. A major driving force in the development is needed to deliver therapeutic agents directly to the circulatory system, which is important to the drugs that undergo significant inactivation by the liver. PLA and its copolymers have been used for applications like drug delivery system [185–192], protein encapsulation and delivery [193–195], development of microspheres [139,196–203], hydrogels [204], etc. In fracture fixation, metal devices are generally used to align bone fragments into close proximity, and control the relative motion of fragments so that union can take place. However, complete healing of the bone depends on its bearing normal loads, which is prevented as long as the device bears part of the load. Furthermore, sudden removal of the device can leave the bone temporarily weak and subject to refracture. However, in the case of PLA based devices, degradation reduces in cross-section area as well as the elastic modulus and the load is transferred gradually to the healing bone and after the complete degradation the device will be completely absorbed, and a second surgical procedure is not necessary. PLA based fracture device has considerably lower tensile modulus than metal fixture device, but it can be improved by careful attention by fabrication using high modulus fibre reinforcement. PLA has been used for application like biodegradable/bioabsorbable fibrous articles

for medical applications [205,206], orthopaedics screw [207]. The commercially available devices are BioScerw[®], PHUSILINE[®] and SYSORB[®] interference screw, BIOFIX[®] and PL-FIX[®] pins. The other biomedical applications of PLA include the development of scaffolds [208], biocomposite material [209,210], sutures [211–215], prosthesis, etc. Moreover, low molecular weight PLA is used for tissue engineering [216–219].

Since, the mechanical properties of high molecular weight PLA are comparable to other commodity thermoplastics like polystyrene and PET, and therefore it has large opportunities to replace these polymers for numerous applications. But its high cost has prevented it from being used in other spheres. But now latest technological advances have given rise to PLA that are commercially viable and can compete with petrochemical plastics. Recent advances in the production process of PLA together with improvement in the material properties have also opened up a promising outlook in the sector of fibres and nonwovens, films, thermoformed and injection moulded articles. PLA finds its application in a number of growing applications, such as injection moulded articles, fibres, textile, and packaging. Injection moulded articles have the moulding shrinkage of about 02–04% of the mould size, or almost the same level as for polystyrene. The mould is therefore recommended same as that for PS. Articles have transparency equivalent to or higher than PS and PET. Fibres of PLA made by thermal spinning possess physical properties similar to PET and nylon. Moreover, PLA is aliphatic polyester and does not contain any aromatic ring structures. Hence, moisture regains and wicking properties are superior to those of PET, and garments made from PLA or with wool or cotton are more comfortable with silky touch. Being a non-flammable polymer, the fibre shows improved self extinguishing characteristics [220–222]. Fibres can either be manufactured by solvent or by melt spinning processes. The fibres prepared by solvent spinning usually have higher mechanical properties than the fibre prepared by thermal spinning, because of the thermal degradation during melt spinning [223].

PLA possesses high transparency and is an excellent material for packaging. PLA is an inherently polar material due to its basic repeated unit of lactic acid. This high polarity leads to a number of unique attributes such as high critical surface energy that yields excellent printability. Another benefit of this polar polyester polymer is the resistance to aliphatic molecules such as oils and terpenes. Apart from this,

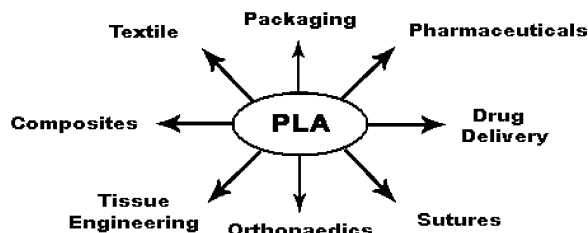


Fig. 12. Application of PLA.

PLA possesses stiffness, clarity and twist retention, low-temperature heat sealability, as well as an excellent combination of barrier properties including flavour and aroma barrier characteristics. Non-oriented films can easily be moulded by vacuum of pneumatic process into transparent containers and trays (see Fig. 12).

PLA also finds applications in agricultural films, degradable rubbish bags, thermoformed trays for fruits and vegetables, disposable plates and cups, toys, cutlery, fibre composites [224], PLA layered silicate nanocomposites [225–230], home furnishing and household articles. In agriculture for applications like mulch films, temporary replanting pots, delivery system for fertilisers and pesticides.

5. Conclusion

PLA and its copolymers offer the prospective applications in a number of fields like orthopedics and pharmaceuticals. Research is needed for the deliberate synthesis of PLA using proper catalyst and monomer, to get tailored property in respect to degradability and strength for a particular application. Moreover, there is a great potential to use PLA polymers in a number of unexplored applications by replacing the conventional polymer, where it can contribute a significant role in the form of composites, copolymers and blends to get different properties for different applications. But the cost of PLA is still higher than those of other plastics. There is a surge of research in the area to develop the technology to produce PLA at a lower cost. By improving the synthesis and properties using optimum catalysts system, we can further augment this polymer.

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