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Chemistry of biotransformations

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POLYLACTIC ACID:
A BIODEGRADABLE THERMOPLASTIC POLYESTER

1. Abstract

Environmental, economic, and safety challenges have provoked scientists and producers to partially substitute petrochemical-based polymers with biodegradable ones; the project of bio-based plastics market is to reach 5.2 BEUR by 2030.

The general purpose of this review is to introduce poly-lactic acid (PLA), a compostable, biodegradable thermoplastic made from renewable sources. This renewable polyester has found applications in a wide range of products such as food packaging, textiles and biomedical devices. PLA production and modifications via different methods, like using modifiers, blending, copolymerizing, and physical treatments, are mentioned in this review; are described the most common strategies to modify the bulk properties of PLA like mechanical characteristics include copolymerization with other monomers and blending.

Mechanical and thermal properties of polylactic acid and copolymer are described.

PLA degradation (abiotic and biotic) are also discussed in details.

PLA applications like packaging and biomedical devices are discussed in details. In particular, polymer-based drug delivery systems are attracting interest for biomedical and, oncology-related applications due to interesting characteristics in terms of prolonged drug release.

Applications of nanomaterials in combination with PLA structures for creating new PLA nanocomposites with greater proprieties for food packaging are mentioned in this review.

The linkage of a 100% bio-originated material and nanomaterials opens new windows for becoming independent, primarily, of petrochemical-based polymers and, secondarily, for answering environmental and health concerns will undoubtedly be growing with time.

2. Introduction

2.1. Biodegradable polymers

Today, polymers and materials used for various products, consist of a variety of petrochemical-based polymers, metals, glass, paper, and board, or combinations hereof. The durability and degradability of packaging materials are 2 contradictory subjects; the 1st is desirable for packaging stability and protection for its contents during shelf life and the 2nd for its rapid degradation in the environment.[1] In particular, the problem of their degradation or incineration is a global problem for the whole ecosystem.

Synthetic biodegradable polymers are a class of polymers designed to decompose after their functional purpose is over. They might be an environmentally friendly alternative to conventional polymers such as polyethylene and polypropylene, which are non-biodegradable.

In addition to the ability of biodegradation into harmless constituents, biodegradable polymers could offer functional properties similar to that of conventional polymers such as polyethylene. Biodegradable polymers are a good option for applications that require short-term functional usage before disposal. In a disposal environment, biodegradable polymers start to degrade by the enzymatic actions of microorganisms such as bacteria, fungi and algae or non-enzymatic actions such as chemical actions. Biodegradation converts their polymer chains into CO2, CH_4, H_2O, biomass and other basic constituents.[2]

Target markets for biodegradable polymers include packaging materials, disposable nonwovens and hygiene products, consumer goods, agricultural tools and biomedical applications.[3] The most common synthetic biodegradable polymers are: polylactic acid, polycaprolactone, polyhydroxybutyrate, polybutylenesuccinate and polyethylene terephthalate; polyesters are an important class of biodegradable polymers.[2] The following two figures (fig.1 and fig.2) show the global production capacities of bioplastics.

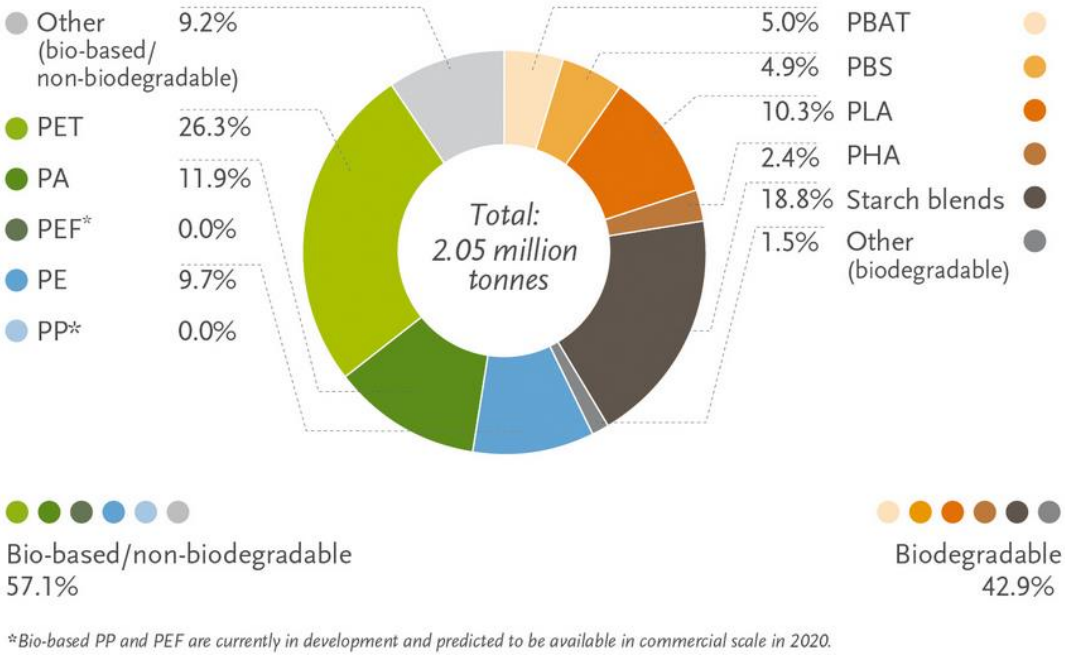


Fig.1–Global production capacities of bioplastics in 2017 (by material type)
Source: European Bioplastics, nova-Institute (2017)

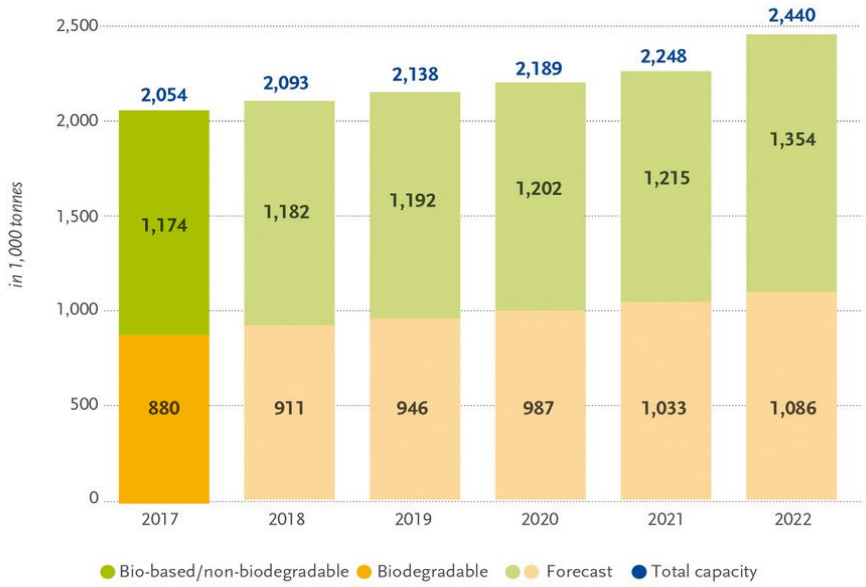
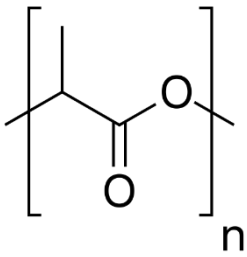


Fig.2–Global production capacities of bioplastics until 2022 (by material type)
Source: European Bioplastics, nova-Institute (2017)

2.2. Poly-lactic acid (PLA)



Poly(lactic acid) (PLA) as a biodegradable thermoplastic polyester has received increasing attention in the last years. This renewable polyester has found applications in a wide range of products such as food packaging, textiles and biomedical devices. Its major drawbacks are poor toughness, slow degradation rate and lack of reactive side-chain groups.[4]

PLA-based products had already been developed by the 1940s and 1950s, but their production became economically viable only 70 years later. This demonstrates the importance of optimizing the productivity and robustness of bioconversions to achieve cost-effective production.

In comparison to other biopolymers, the production of PLA has numerous advantages including: (a) production of the lactide monomer from lactic acid, which is produced by fermentation of a renewable agricultural source corn; (b) fixation of significant quantities of carbon dioxide via corn production by the corn plant; (c) significant energy savings; (d) the ability to recycle back to lactic acid by hydrolysis or alcoholysis; (e) the capability of producing hybrid paper-plastic packaging that is compostable; (f) reduction of landfill volumes; (g) improvement of the agricultural economy; and (h) the important ability to tailor physical properties through material modifications.[3]

Despite these excellent positive features, drawbacks such as brittleness and chemical inertness limit applications of PLA.

The development of PLA-based biomedical devices has gained increased interest due to the biocompatibility of this polymer. In the body, PLA degradation leads to lactic acid, an α-hydroxy acid already present in human metabolism.[5] For this reason, PLA is a useful material in clinical practice for tissue engineering, surgery, orthopedic devices and drug delivery.

The following graph show the trend of global PLA productions from 2011 to 2020.

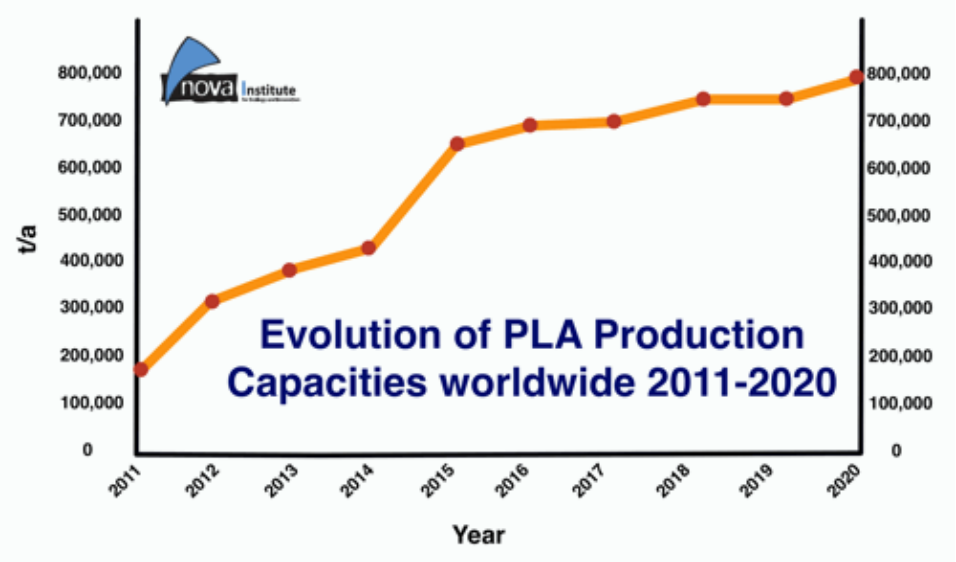


Fig.3–Evolution of PLA production capacities (t/a) from 2011 to 2020

3. Lactic acid and PLA production

Lactic acid (2-hydroxy propionic acid), the single monomer of PLA, is produced via fermentation or chemical synthesis. Its 2 optically active configurations, the L(+) and D(−) stereoisomers are produced by bacterial (homofermentative and heterofermentative) fermentation of carbohydrates.[1]

Industrial lactic acid production utilizes the lactic fermentation process rather than chemical synthesis because the synthetic routes have many major limitations, including limited capacity due to the dependency on a by-product of another process, inability to only make the desirable L-lactic acid stereoisomer, and high manufacturing costs. The homofermentative method is preferably used for industrial production because its pathways lead to greater yields of lactic acid and to lower levels of by-products.[6]

NatureWorks® exclusively uses corn starch as raw material for lactic acid production via lactic fermentation. Many studies have been conducted to find other sources of carbohydrates for lactic acid production. Some agricultural products are potential substrates for lactic acid production include, cassava starch, lignocellulose/hemicellulose hydrolysates, cottonseed hulls, corn cobs, corn stalks and

many others. The use of a specific carbohydrate feedstock depends on its price, availability, and purity.[1]

Three ways are possible for the polymerization of lactic acid (fig.4):
(a) direct condensation polymerization; (b) direct polycondensation in an azeotropic solution; and (c) polymerization through lactide formation[1].
(a) The 1st method is based on esterification of monomers by the aid of some solvents and exudated water is removed using progressive vacuum and high temperatures. Obtaining high molecular weight polyesters with good mechanical properties via this method is not easy, although precondensates may be of interest for the preparation of biodegradable glues or lacquers, since the –OH and -COOH end groups allow cross-linking with suitable inorganic or organic multivalent additives.[7]
(b) Producing high molecular weight PLA polymers by direct polycondensation in an azeotropic solution and also application of some catalysts is more practicable.
The azeotropic solution helps to decrease the distillation pressures and facilitates PLA separation from the solvent by application of molecular sieves. The results identified by using improved experimental equipment, the proper complex catalyst, and solvent volume ratio, in order to obtain a molecular weight of PLA of 6.6 × 104.
(c) Polymerization through lactide formation is being industrially accomplished for high molecular weight PLA production. Lactide is a cyclic dimer formed by removing water under mild conditions and without solvent. L-lactide, meso (L, D) lactide, and D-lactide are products of L-lactic acid and D-lactic acid.[7]

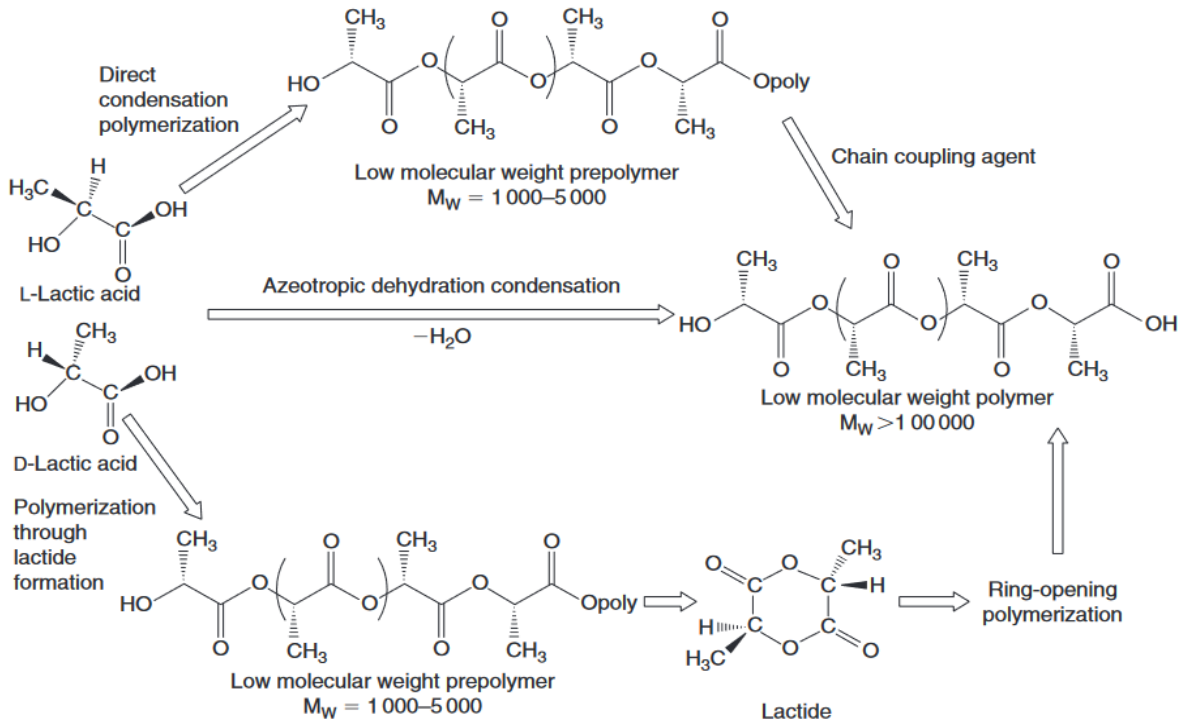


Fig.4–Synthesis methods for obtaining PlA high molecular weight

3.1. Enzyme-catalyzed polyester synthesis

Hydrolases, and in particular lipases were very successful in polyesters synthesis via two different step. Lipase catalyzes the polycondensation of lactic acid (AA-type monomers)[8] and the polycondensation of diacids (AA, BB-type monomers).[9]

The enzymatic catalysis of the polycondensation shows many advantages over the conventional chemical catalysis. By using the enzymatic polycondensation process, the presence of strong acidic catalysts or high temperature, is not needed as in the chemical process.[11] Enzyme-catalyzed polyester synthesis is a perfect alternative for the use of organometallic catalysts, which are difficult to remove entirely from the produced polymers. These organometallic compounds are often toxic and thereby limiting the use of the produced polymers in biomedical applications.

Currently, PLA is synthesized via a two step process whereby fermentative lactic acid is oligomerized into lactides (fig.5), which are subsequently polymerized by the ring-opening process (ROP) using enzymes as catalysts into high molecular weight polymers.[10]

ROP has an important advantage over the polycondensation, whereas the molecular weight of the polymers can be controlled using the ROP by the initiator/monomer ratio while it can not be controlled in the polycondensation.

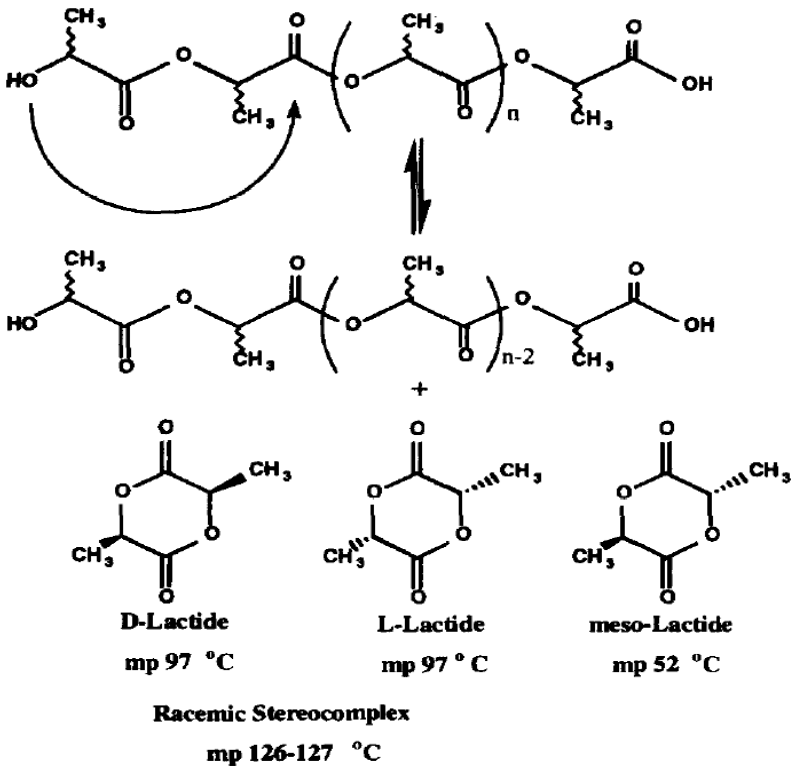


Fig.5–Lactide formation mechanism

3.2. Ring-Opening Polymerization of Lactones

Aliphatic polyesters, prepared by ring opening polymerization (ROP) of lactones and lactides, are versatile polymers having good mechanical properties, hydrolyzability, and biocompatibility. These attributes make them a leading candidate in biomedical and pharmaceutical industries as a resorbable implant material and a vehicle for controlled drug delivery.

The polymerization of lactones is generally carried out in bulk or in solution (THF, dioxane, toluene, etc.), emulsion, or dispersion. The temperature of bulk polymerization is generally in the range of 100-150 °C, whereas in solution polymerization, low temperatures have been used (0-25 °C) to minimize side reactions (inter- and intramolecular transesterfication).[8]

High molecular weight polyesters have only been obtained by using enzymatic or anionic ring opening polymerization.

The enzymatic ring opening polymerization (eROP) reaction can be divided into two steps: *initiation* where a nucleophile is needed for the ring opening of the lactone, and *prolongation* where the opened lactone act as a nucleophile, by its hydroxyl end group, for the ring opening of a new lactone unit.[12]

The anionic ring opening polymerization is initiated by the nucleophilic attack of a negatively charged initiator (alkali metals, alkali metal oxides, alkali metal naphthalenide complexes with crown ethers, etc.)[8] on the carbon of the carbonyl group or on the alkyl-oxygen, resulting in formation of linear polyester.

4. Mechanical and thermal properties of polylactic acid

Polylactic acid (PLA) belongs to a family of aliphatic polyesters and is considered biodegradable and compostable. PLA is a thermoplastic, high-strength, high-modulus polymer made from renewable resources as alternative to the conventional synthetic petrochemical-derived polymers such as polypropylene.

PLA has good mechanical properties, light weight, and it is easily processed on standard plastics equipment to yield molded parts, film, or fibers.

Enantiopurity is a key factor that affect PLA regarding its thermal properties.[13]

The homopolymers of LA enantiomers, P[(R)-LA] (PDLA) and P[(S)-LA] (PLLA), are crystalline polymers with a glass transition temperature (T_g) of about 61 °C and the melting point (T_m) of about 180 °C.[13] The stereocomplex of PDLA and PLLA has been achieved and its T_m has reached to 220 to 230 °C. Therefore, controlling the enantiopurity is crucial in regulating polymer properties.[14]

Generally, PLA is thermally unstable and exhibits rapid loss of molecular weight as the result of thermal treatment at processing temperatures. Different factors like particle size and shape of polymer, temperature, moisture, crystallinity, % D-isomer, residual lactic acid concentration, molecular weight, molecular weight distribution,

water diffusion, and metal impurities from the catalyst can have affect on the thermal properties and polymer degradation rate.[1]

Its thermal properties play an important role as they have an effect on the quality of polymers in aspects such as heat resistance and crystallization.

PLA and P(3HB) (polyhydroxybutyrate), for examples, exhibit transparent and opaque properties that are consistent with their glass transition temperatures (61°C and −7°C, respectively).[13]

The LA-based polymer P(LA-co-3HB)s exhibited increased T_g values at a range of −6 to 34°C, dependent on the LA fractions. On the other hand, P(LA-Co-3HB)s with 29 – 47 mol% LA displayed lower melting temperature and melting enthalpy (ΔH_m) compared to those of the P(3HB) and PLA homopolymers.[14] The lowered T_m may due to the copolymerization of different monomers that inhibited crystal packing of the polymer compared to the individual homopolymers. The lowered ΔH_m indicates a reduction of amount of the crystal.

Following table shows PLA properties in comparison with typical biodegradable polymer.

Table 1- Comparison of typical biodegradable polymer properties with LDPE, PS, and PET
Source: Clarinval and Halleux (2005).

	T_g (°C)	Tm (°C)	Tensile strength (MPa)	Tensile modulus (Mpa)	Elongation at break (%)
LDPE	−100	98 to 115	8 to 20	300 to 500	100 to 1000
PCL	−60	59 to 64	4 to 28	390 to 470	700 to 1000
Starch	–	110 to 115	35 to 80	600 to 850	580 to 820
PBAT	−30	110 to 115	34 to 40	–	500 to 800
PTMAT	−30	108 to 110	22	100	700
PS	70 to 115	100	34 to 50	2300 to 3300	1.2 to 2.5
Cellulose	–	–	55 to 120	3000 to 5000	18 to 55
PLA	40 to 70	130 to 180	48 to 53	3500	30 to 240
PHB	0	140 to 180	25 to 40	3500	5 to 8
PHA	−30 to 10	70 to 170	18 to 24	700 to 1800	3 to 25
PHB-PHV	0 to 30	100 to 190	25 to 30	600 to 1000	7 to 15
PVA	58 to 85	180 to 230	28 to 46	380 to 530	–
Cellulose acetate	–	115	10	460	13 to 15
PET	73 to 80	245 to 265	48 to 72	200 to 4100	30 to 300
PGA	35 to 40	225 to 230	890	7000 to 8400	30
PEA	−20	125 to 190	25	180 to 220	400

PGA = Poly(glutamic acid); PEA = Poly(ester amide).

5. PLA modifications

The special characteristics of PLA can make it a good fit for some applications but may also require modifications for some others.

There is an increasing interest in modifying polymer surfaces in order to improve properties like strength or flexibility, hydrophilicity, stiffness, barrier properties, thermal stability, production costs and/or creating reactive anchor groups for further functionalization. The latter includes for example covalent immobilization of bioactive compounds or decoration of nanoparticles for targeted drug delivery[15] while retaining the bulk properties.

The hydrophilicity of PLA, for example, is not appropriate for cell attachment on its surface and it is a biologically inert polymeric biomaterial that is not able to induce cell adhesion and tissue formation.[16] To improve the host−implant interaction of biomaterials, various modifications of PLA have been studied,[17] such as copolymerization with other functional and hydrophilic monomers or blending of PLA with other materials.[18] However, copolymerization and blending changes the bulk properties of PLA, and this is considered to be a drawback in many applications. Therefore, other kinds of modifications of PLA, such as surface modifications, has been the subject of attention. Indeed, surface functionalization are being applied in biomedical uses for improving polymer release properties.

This kind of modification of polyesters is usually achieved via wet chemistry,[19] photografting[20] or plasma treatment.[21]

Among the techniques employed for surface modification of biodegradable polymers, photografting is a useful tool with the advantages of low cost of operation, mild reaction conditions, and a permanent alteration of the surface chemistry.[22] Photografting employs a much lower energy than γ or electron beam irradiation, and this reduces the risk of possible degradation of the polymer.[15] Poly(acrylic acid) (PAA) has been covalently grafted onto the surface of degradable biomaterials including PLA by photografting. PLA has a much more hydrophilic surface after grafting with AA or

maleic anhydride, and the rate of degradation of PLA was enhanced as a result of the hydrophilic surface.[15]

The surface with functional groups could be used for the further covalent immobilization of bioactive molecules, such as gelatin, heparin, and nerve growth factor or vascular endothelium growth factor,[23] which could enhance cell adhesion and further regulate the cell behavior.

Furthermore, for extending packaging and hygiene applications, a low molecular weight compounds have also been used as plasticizers for PLA, for example, oligomeric lactic acid, glycerol, triacetine, and low molecular weight citrates.[1]

5.1. Copolymers based on lactic acid units

A large number of macromolecular architectures of co-polymers based on lactic acid have been investigated.[24]

Most of them are biodegradable or/and biocompatible. These copolymers can be prepared by using units containing a specific functionalized structure, thus giving rise to complex structure with unique properties. Examples of these materials are branched polyesters and graft copolymers (star, hyper-branched polymers) which involve different macromolecular architectures associated with novel materials properties and applications.

5.1.1. Ring-opening copolymerization

Several heterocyclic monomers can be used as co-monomers with lactic acid in ring-opening copolymerizations; the most commonly used being glycolide (GA) for biomedical applications,[15] caprolactone (CL) and valerolactone.

The comonomer units can be inserted randomly or in block sequences.[24]

5.1.2. Modification by high energy radiations and peroxides

Radical reactions applied to PLA to modify its structure have been generated by peroxides or high energy radiation. Branching has been suggested to be the dominant

structural change in poly(l-lactide) (PLLA) with peroxide concentrations in the range of 0.1–0.25 wt% and crosslinking above 0.25 wt%.[25] The peroxide melt-reaction with PLA has been found to cause strong modifications of the original PLA properties. Irradiation of PLA causes mainly chain-scissions or crosslinking reactions, depending on the radiation intensity.

5.1.3. Graft copolymerization

Graft copolymers are often used as compatibilizers to improve the interfacial properties of blends or multiphase systems. Grafting reactions on a polymer can be induced chemically, by plasma discharge, or by radiation (UV, X-rays or accelerated electrons), the latter approach giving purer products at high conversions.

Plasma induced grafting is performed by introducing an organic vapour into a plasma of inorganic gases to modify the surface properties of a substrate.

The chemical modification of lactic acid-based polymers by graft copolymerization has been reported for the homopolymer of l-lactide and for copolymers with different l-lactide/CL contents.[24] Carbohydrate polymers (*e.g*. amylose) can be modified by grafting lactic acid chains on their OH groups. After amylose purification to eliminate residual butanol and water, amylose-graft-PLA is obtained by the ROP of purified lactide with bis-(2-ethylhexanoate) in toluene at 100°C for 20 h.

A recent study showed the interest of such a copolymer as a compatibilizer to improve the properties of starch/PLA blends to a better extent than the addition of peroxides or coupling agents (*e.g*. di-isocyanate) into the melt blend during the processing.

6. Degradation of PLA

Almost all the conventional plastics such as PE, PP, PS, and PVC are resistant to microbial attack; on the contrary aliphatic polyesters like PLA are readily degraded by microorganisms present in the environment.

6.1. Abiotic degradation

The main abiotic phenomena involve thermal and hydrolysis degradations during the life cycle of the material.

6.1.1. Thermal degradation

The thermal stability of biopolyesters is not significantly high, a fact that inevitably limits their range of applications. The PLA decomposition temperature is lies between 230°C and 260°C.[26] Recent studies concluded that the carbonyl carbon–oxygen linkage is the most likely bond to split under isothermal heating, as suggested by the fact that a significantly larger amount of carboxylic acid end-groups were found compared with hydroxyl end-groups.[26]

The reactions involved in the thermal degradation of lactic acid-based polymers can follow different mechanisms, such as thermohydrolysis, zipper-like depolymerization in the presence of catalyst residues, thermo-oxidative degradation and transesterification reactions which give simultaneous bond breaking and bond making.[27]

6.1.2. Hydrolytic degradation

PLA hydrolysis is an important phenomenon since it leads to chain fragmentation,[28] and can be associated with thermal or biotic degradation.

This process can be affected by various parameters such as the PLA structure, its molecular weight and distribution, its morphology (crystallinity), the shape of its samples and its thermal and mechanical history (including processing), as well as, of course, the hydrolysis conditions. Hydrolytic degradation is a phenomenon, which can be both desirable (*e.g*. during the composting stage) or undesirable (*e.g*. during processing or storage).

The hydrolysis of aliphatic polyesters starts with a water uptake phase, followed by hydrolytic splitting of the ester bonds in a random way. The amorphous parts of the polyesters have been known to undergo hydrolysis before their crystalline regions

because of a higher rate of water uptake. The initial stage is therefore located at the amorphous regions, giving the remaining non-degraded chains more space and mobility, which leads to their reorganization and hence an increased crystallinity.

In the second stage, the hydrolytic degradation of the crystalline regions of the polyester leads to an increased rate of mass loss and finally to complete resorbtion.[28] The explanation for this specific behaviour is an autocatalytic effect due to the increasing amount of compounds containing carboxylic end-groups. The degradation products in the surface layer are continuously dissolved in the surrounding buffer solution.[28] As expected, temperature plays a significant role in accelerating this type of degradation.

6.2. Biotic degradation

The biodegradation of lactic acid-based polymers for medical applications has been investigated in a number of studies *in vivo* and some reports can also be found on their degradation in other biological systems. The *in vivo* and *in vitro* degradations have been evaluated for PLA-based surgical implants.[29] *In vitro* studies have shown that the pH of the solution plays a key role in the degradation and that this analysis can be a useful predicting tool for *in vivo* PLA degradation.

Enzymes, such as proteinase K and pronase, have been used to bring about the *in vivo* PLA hydrolysis, although, enzymes are unable to diffuse through the crystalline parts. As expected, little enzymatic degradation occurs at the beginning of the process, but pores and fragmentation are produced, widening the accessible area to the different enzymes.

Figure 6 shows that during the composting stage, PLA degrades in a multistep process with different mechanisms.[30] Primarily, after exposure to moisture by abiotic mechanisms, PLA degrades by hydrolysis. First, random non-enzymatic chain-scissions of the ester groups lead to a reduction in molecular weight, with the consequent embrittlement of the polymer. This step can be accelerated by acids or bases and is affected by both temperature and moisture levels.[30]

Then, the ensuing PLA oligomers can diffuse out of the bulk polymer and be attacked by microorganisms. The biotic degradation of these residues produces carbon dioxide, water and humus (mineralization).

Studies on PLA-based multiphase materials have been carried out. Physical and morphological properties of the blend play an important role in its degradation behaviour, as in the case of their comparative study of the degradation of PLA with and without plasticized starch materials.[31]

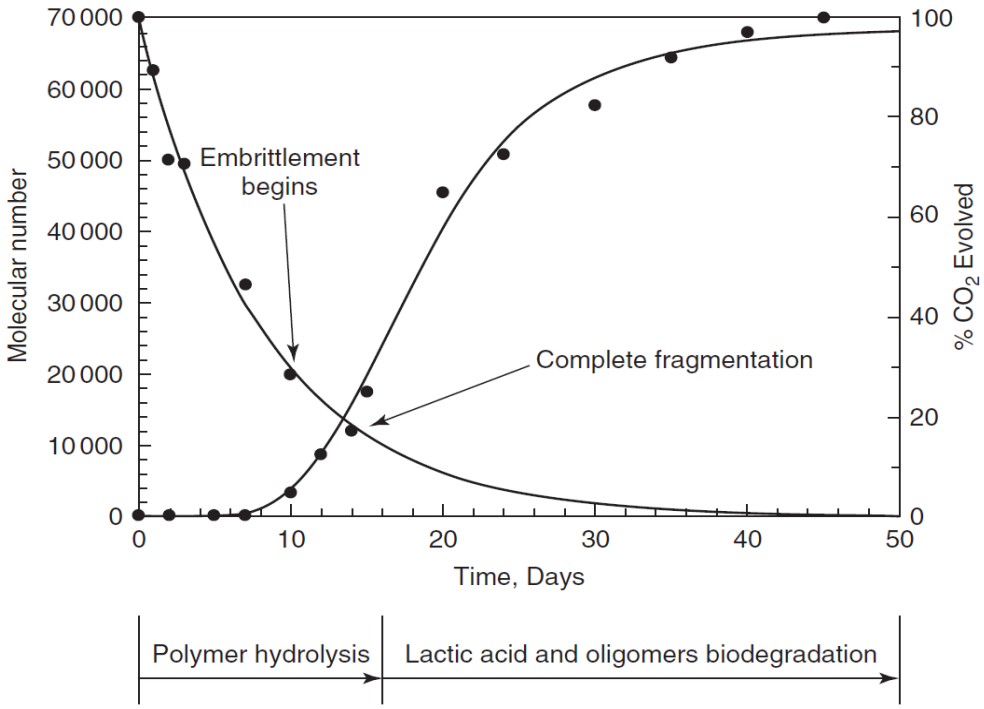


Fig.6–Abiotic and biotic degradations during composting stage

7. Applications

At present, PLA-based materials are mainly referenced on three different markets: the biomedical (initial market), the textile (mainly in Japan) and the packaging (mainly food, i.e. short-term applications). For instance, reported types of manufactured products are blow-moulded bottles, injection-moulded cups, spoons and forks, thermoformed cups and trays, paper coatings, fibres for textile industry or sutures, films and various moulded articles.[32]

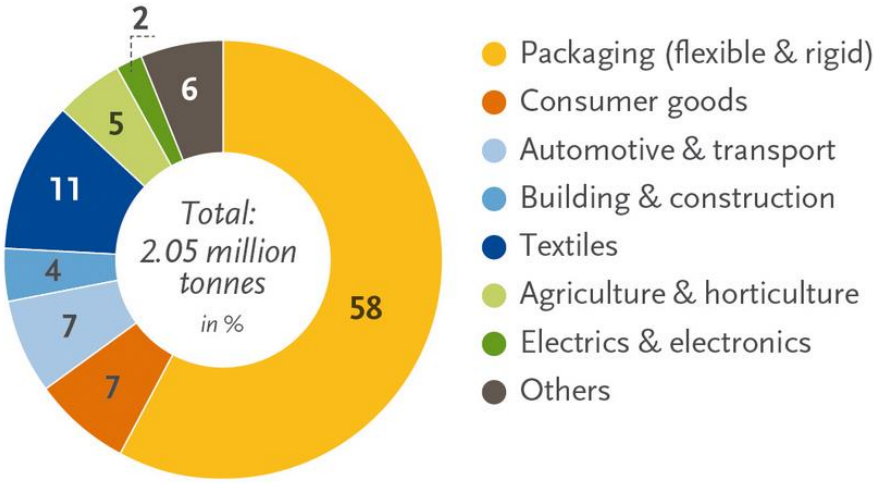


Fig.7–Global production capacities of bioplastics in 2017 (by market segment)
Source: European Bioplastics, nova-Institute (2017)

7.1. Packaging applications

Market studies show that PLA is an economically feasible material for packaging. With its current consumption, it is at the present the most important market in volume for biodegradable packaging.[33]

Commercially available PLA packaging can provide better mechanical properties than polystyrene and have properties more or less comparable to those of PET.[33]

Due to its high cost, the initial use of PLA as a packaging material has been in high value films, rigid thermoforms, food and beverage containers and coated papers. One of the first companies to use PLA as a packaging material was Danone (France) in yogurt cups for the German market. During the last decade, the use of PLA as a packaging material has increased all across Europe, Japan and the US, mainly in the area of fresh products, where PLA is being used as a food packaging for short shelf-life products, such as fruit and vege-tables. Package applications include containers, drinking cups, sundae and salad cups, wrappings for sweets, lami-nation films, blister packages and water bottles.[34]

Currently, PLA is used in compostable yard bags to promote national or regional composting programs. In addition, new applications such as cardboard or paper coatings are being pursued, for example, the fast-food market (cups, plates and the

like). However, to cater for a larger market, some PLA drawbacks must be overcome, such as its limited mechanical and barrier properties and heat resistance, and, in order to meet market expectations, the world production of PLA must be substantially increased.

7.1.1. Nanotechnology and PLA Food Packaging

The use of nanoparticles, such as micelles, liposomes, nanoemulsions, biopolymeric nanoparticles, and cubosomes, as well as the development of nanosensors aimed at ensuring food safety, are some novel nanofood applications. Nanoparticles can be used as bioactive compounds in functional foods.

Bioactive compounds that can be found naturally in certain foods have physiological benefits and might help to reduce the risk of certain diseases, including cancer. Omega-3 and omega-6 fatty acids, probiotics, prebiotics, vitamins, and minerals have found their applications in food nanotechnology as bioactive compounds.[34]

Nanotechnology is also applicable in food packaging in the form of elementary components of food packaging. This approach includes improving packaging performances like its gas, moisture, ultraviolet, and volatile barriers, increasing mechanical strength, decreasing weight, and increasing the heat resistance and flame retardancy of the packaging material.

Finally, nanoadditives, nanosensors, delivery and controlled release of neutraceuticals, antibacterial agents, self-cleaning packaging, and systems to monitor product conditions during transportation are other novel nano-approaches in food packaging.[35]

7.2. Biomedical applications

PLA has been widely studied for use in medical applications because of its bioresorbability and biocompatible properties in the human body. The main reported examples on medical or biomedical products are fracture fixation devices like screws, sutures, delivery systems and micro-titration plates.[36]

For examples, PLA-based materials are developed for the production of screws and plates for bone applications; this reducing the stress-shielding effect as the bone healing progresses. This is possible only if the plate loses rigidity in *in vivo* environment. To meet this need, researchers introduced resorbable polymers for bone plate applications. PLA resorbs or degrades upon implantation into the body, but most of its mechanical properties are lost within a few weeks.[37] To improve the mechanical properties, PLA is reinforced with variety of non-resorbable materials, including carbon and polyamide fibres. Carbon fibres/PLA composites possess very high mechanical properties before their implantation, but they lose them too rapidly *in vivo* because of delamination. The long-term effects of resorbed products, and biostable or slowly eroding fibres in the living tissues are not fully known, and are concerns yet to be resolved.[37]

Although PLA fibres are used in different textile applications, they achieved their first commercial success as resorbable sutures. One of the first commercially available fibre-formed bioresorbable medical products is based on copolymers of GA in combination with l-lactide (Vicryl).[9]

Fibres can be produced both by solvent and by melt-spinning processes and drawn under different conditions to orient the macromolecules.

Furthermore, micro and nanoparticles are an important category of delivery systems used in medicine, and the use of PLA is interesting due to its hydrolytic degradability and low toxicity. The most important properties of the micro and nanoparticles are the drug release rate and the matrix degradation rate which are affected by the particle design and the material properties.[38] Copolymers of GA and rac-lactide seem to be the most suitable combinations for use as drug delivery matrices.

The biodegradable polymeric delivery system, capable of providing a sufficient and localized radiation dose of a radiotherapeutic drug along with some chemotherapeutic agents to the tumor, can be utilized as an alternative to external beam radiotherapy. These biodegradable polyester have also been used to deliver peptide or protein drugs, which have unusual physicochemical properties, compared to low molecular weight drugs.[39]

Recent studies, finally, have been found that porous PLA scaffolds have potential reconstruction matrices for damaged tissues and organs.[37]

8. Conclusion

In this review has been introduced poly-lactic acid (PLA), a biodegradable thermoplastic polyester has received increasing attention in the last years. This renewable polyester founds applications in a wide range of products such as food packaging, textiles and biomedical devices in particular.

The most negative point of PLA was its price in comparison with petrochemical-based polymers. Today, optimization of lactic acid production processes, replacement of electricity energy by wind and solar energy for PLA production and increasing PLA demands, reduction of its price can be attained. The present PLA price is much lower than in previous years and it even will be considerably lower in the future because the global demand for biodegradable plastics will continue to increase by 30% each year and PLA will take a large part of this market.

According to its safety and biodegradability, the authors predict the substituting of many petrochemical-based polymers by PLA for almost all pharmaceutical and direct food contact packaging materials in the near future.

However, substituting petrochemical-based polymer with PLA in different sectors of application, which require determined properties like high-barrier properties or brittleness, is not often feasible unless some modifications are applied on the structure of PLA. With the help of nanotechnology many of its weakness compared to petrochemical-based polymer will be resolved.

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