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Poly (lactic acid) as degradable resorbable polymer matrices in Biomedical Engineering: An overview

Ram Singh

Department of Applied Chemistry

Delhi Technological University, Delhi - 110 042

India

ABSTRACT

Polymers emerged as a boon in the advancement of modern medicine. The utilization of natural polymers for biomedical applications has been known for thousands of years but the application of degradable synthetic polymers is relatively recent. The field of biomedical engineering is shifting its focus towards degradable polymers in general and biodegradable polymers in specific. In recent times, due to substantial knowledge about the biocompatibility of degradable polymers, their specific applications in biomedical engineering become advantageous. This article provides a comprehensive coverage of the main advances published in recent years, outlining the synthesis, degradability and biomedical applications of poly (lactic acid).

Keywords**: Resorbable polymer, Biomedical Engineering, Degradation, Poly (lactic acid).

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1. INTRODUCTION

The polymeric material plays an important role in our everyday lives [1]. These materials have either replaced or trying to replace the traditional metallic materials in various utilities. Due to their light weight, durability and cost effectiveness, they are becoming essential for the economy of any country and also cover a large variety of consumer products [2]. The quantity of plastic produced annually increased rapidly. As per an analysis of European plastics production, demand and waste data (PlasticsEurope, Plastics – the Facts 2014/2015) the global plastic production reached a level of 299 Mt per year in 2013.

Every year new classes of polymeric materials with unique features and applications are being introduced. The upcoming and recent areas for polymeric materials are: (1) biomedical engineering [3], and (2) information and communications [4]. These two areas are based on the interdisciplinary aspect of polymer research and are attracting a great deal of attention [3,4].

The polymeric materials such as biopolymers play important role in biological processes. Biopolymers like deoxyribonucleic acid (DNA), ribonucleic acid (RNA), polysaccharides, enzymes and proteins are the essential components of life. These constitutes from molecular basis to whole life system of living organisms. The combined information from biology, chemistry, and applied fields like engineering, clinical practices gave strong foundation to modern medicine including biomedical engineering at both diagnostic and therapeutic level. Biomedical engineering is a strong bridge between medicine and engineering to provide solution for healthcare covering diagnosis, monitoring and therapy [5].

The field of biomedical engineering is shifting its focus towards degradable polymers in general and biodegradable polymers in specific. In recent times, due to substantial knowledge about the biocompatibility of degradable polymers, their specific applications in biomedical engineering become advantageous. This article provides a comprehensive coverage of the main advances published in recent years, outlining the synthesis, degradability and biomedical applications of degradable resorbable polymer, poly(lactic acid).

2. DEGRADATION OF POLYMERS

According to the IUPAC gold book, polymer degradation is defined as 'the chemical changes in a polymeric material that usually results in undesirable changes in the in-use properties of the material.' In general, degradation of the polymer leads to a decline of polymer properties [6]. The properties of a polymer or polymer-based product such as tensile strength, colour, shape, etc. changes under the influence of environmental factors like heat, light, chemicals or microorganisms etc. The researchers are actively involved in degradation of polymers or polymer-based product for the simple reason that they are getting accumulated in the environment due to their stability and high durability [7].

There are two possible pathways for the degradation of the polymeric materials: (i) abiotic and (ii) biotic pathways [8]. Sometimes both the pathways work together where one pathway changes a particular property and allow the other pathways to work efficiently. The abiotic degradation pathway is usually initiated thermally, photochemically or hydrolytically whereas biotic degradation pathways are initiated by the action of microorganisms such as bacteria, fungi and algae [9]. In most of the cases, the degradation of plastics starts from its surface which is exposed for attack by biotic and abiotic agents. When the degradation starts from surface, change in colour and roughness on the surface are the first visuals to be noticed [10]. The roughness allows the further degradation.

The degradation of plastics is totally dependent upon the types of polymer, fillers, additives, dyes and pigments used. Due to this, different types of degradation pathways are effective for different polymeric materials. The important three ways for plastic waste management includes mechanical recycling, biological recycling and energy recovery. Every degradation pathways have its own advantages and limitations [11].

3. POLY(LACTIC ACID) (PLA)

Lactic acid (2-hydroxypropanoic acid) is a monomer of poly(lactic acid) (PLA). This monomer is chiral in nature and exists in two stereoisomeric forms such as L and D enantiomers which are *S* and *R* in absolute configuration, respectively. Chemical synthesis and fermentations are the two-important method for the production of this monomer. The sugers and starches on bacterial fermentation yields lactic acid in good amount [12,13]. The lactic acid polymerizes to give PLA. The PLA has melting point of 174-184°C and glass transition temperature in the range 55-59°C with a semi-crystalline nature [14].

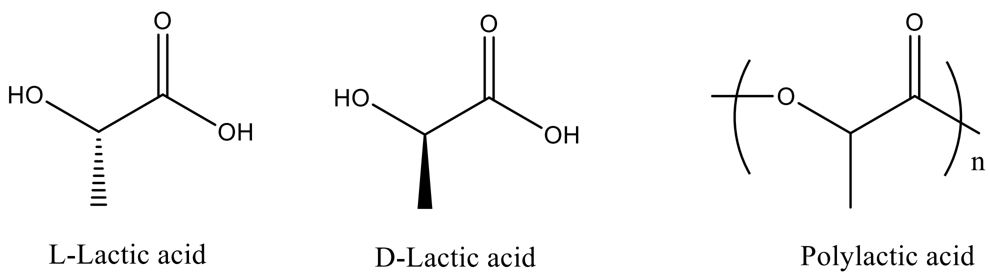

Figure 1. Chemical structure of lactic acid and polylactic acid

3.1 PLA SYNTHESIS

The PLA have been synthesized either by ring opening polymerization of lactide (Figure 2) or direct polycondensation of lactic acid. Lactide is a lactic acid cyclic dimmer. Usually, the direct polymerization method requires strong reaction condition

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[15-17] whereas ring opening polymerization method uses mild reaction conditions [18,19]. The outcome of the synthesis is dependent upon the applied temperature and pressure. The first ring opening polymerization was reported by Carothers in 1932 with low molecular weight [20]. Later with the modification of this methods, high molecular weight PLA have also been obtained followed by synthesis of high stereo-regulated PLAs [21].

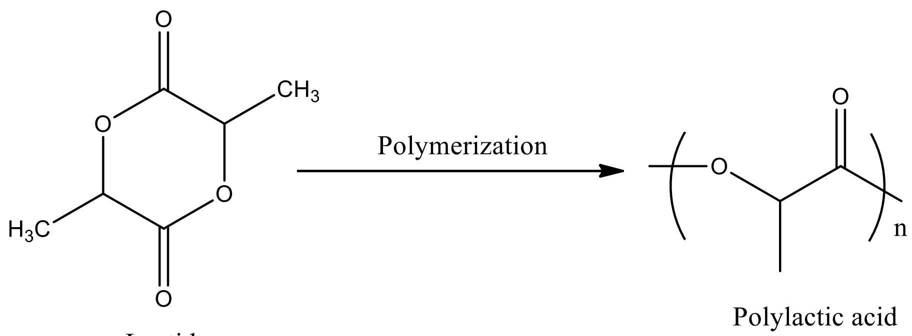

Figure 2. Ring opening polymerization of polylactic acid

The direct polycondensation of lactic acid to PLA usually takes place at reduced pressure and in the presence of a catalyst [21]. This method gives a low molecular weight polymer and hence restricts its applications. However, the low molecular weight PLA can easily be converted to high molecular weight polymer by using the coupling agents [22-24]. This method also has restriction towards the formation of stereo regular PLAs.

3.2 PLA IN BIOMEDICAL ENGINEERING

PLA is a thermoplastic polymer and has wide range of medical applications, first being used for mandibular fractures in dogs as sutures and rods [25-28]. The *in vivo* biodegradability, excellent mechanical and thermal properties and biocompatible character of this polymer makes it a suitable candidate for biomedical engineering [29-33]. This has been established that specific materials properties require for specific biomedical applications. The porous architecture with adequate porosity levels and mechanical strength are required for bone tissue engineering applications and hence L-PLA is a preferable biomaterial for the orthopaedic applications [34,35].

Different methods like phase separation [36], salt leaching [37], and gas-induced foaming [38] have been used by different groups to fabricate the polymer and control the porosity below 200 μm [39]. The other methods such as precise extrusion manufacturing (PEM) and thermally induced phase separation (TIPS) are used to produce highly porous scaffolds adequate for bone tissue engineering [39]. The TIPS is used on the composite skeleton of poly(L-lactic acid) (PLLA)/ hydroxyapatite (HA) to produce porosity as high as 95% with an improvement in the mechanical properties till 11 MPa for the composite. The pore sizes ranges from few microns to several hundred microns [39]. This composite skeleton of PLLA/HA showed good bonding to bone structure [40].

A biomaterial consists of D,L-PLA, HA, calcium carbonate ($CaCO_3$) and titanium (Ti) have been utilized to support weak bone in proximal femur [41]. This biomaterial possess an outer elastic layer of D,L-PLA, HA and $CaCO_3$ and an inner layer of Ti coated with PLLA and calcium salts [41]. This material has been designed in such a way as D,L-PLA degrade faster than PLLA and hence PLLA has enough time before degradation to provide the biocompatibility interface between the Ti and biological tissues to give the required mechanical stability [35,39]. The polylactide-co-glycolide (PLGA) has application in biomedical engineering due to its biocompatible, non-cytotoxic and non-inflammatory nature [35,42]. The PLGA is produced by the combination of lactic and glycolic acid in various compositions depending upon their utility. One of the important applications of this is in the field of orthopedics [43].

The PLLA has been used for tissue engineering field in variety of ways that includes scaffolds for bone, cartilage, vascular regeneration etc [44-47]. PDLLA is an amorphous polymer having Tg (glass transition temperature) less than PLLA due to the random presence of two isomeric monomers and hence has low molecular strength leading to its application where faster degradation in comparison to PLLA is required [48].

3.3 PLA DEGRADATION

The degradation of any polymer usually results in decrease in their physical properties and sometime changes in the chemical properties. The PLA cab be degraded to carbondioxide and water or till oligomers and monomers. The high molecular weight PLA is water insoluble in nature but during degradation the water penetration plays important role [49]. The hydrolysis of the ester group takes place with water leading to the formation of low molecular weight PLAs and oligomers. Sometimes the oligomers having carboxylic chain ends behave like autocatalysts for further ester hydrolysis [49,21]. The hydrolysis behaviour of PLAs has also been affected by their rigidity, stereochemistry, molecular weight etc [50,51]. The chemically recycling of PLA into its monomer is most widely used method which includes hydrolysis [51]. During hydrolytic degradation, the amorphous portion get first affected [52]. The inside matrix gets degraded faster than the surface [53]. The pH, solvent selection, temperature also have their impact on the degradation process [51].

4. SUMMARY

The biodegradable polymers obtained from renewable sources are always on the focus of research as they avoid the dependency on the fossil fuel-based non-biodegradable polymers. Polylactic acid (PLA) is considered as important potential biodegradable polymer due to its compatible chemical and physical properties for various applications including biomedical engineering. The PLAs are mainly synthesized either by ring opening polymerization of lactides or direct polycondensation of lactic acid. The PLAs also get converted into different types of composites and blends to improve the properties and utilized for different applications. The biodegradability of PLA can easily be initiated using the water which can easily diffuse into the matrix. There is great potential to use PLA and their different forms in biomedical engineering where this can replace other materials.

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