BIODEGRADABLE POLYMERS: PRODUCTION, PROPERTIES AND APPLICATION IN MEDICINE

SCIENTIFIC REVIEW PAPER

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ABSTRACT: Biodegradable polymers (biopolymers) represent materials of new generation with application in different areas of human activity. Their production has recently reached a commercial level. They can be divided according to the origin (natural and synthetic), according to the chemical composition, methods of obtaining, application etc. The use of biopolymers in medicine depends on their biocompatibility, mechanical resistance, and sorptive characteristics. Today, they are the most commonly used as implants in vascular and orthopedic surgery, for the production of materials such as catheters, products for gynaecology and haemodialysis, tooth reconstruction, etc. In pharmacy, they are used as a medicine matrix-carrier to allow controlled release of drug within the body. Within this review paper, the properties and methods of production of certain biopolymers such as polyglycolic acid (PGA), polylactide acid (PLA), poly-ε-coprolactone (PCL) and polybutylene succinate (PBS) will be described in detail, as well as their application in medicine and pharmacy.

KEYWORDS: polyglycolic acid (PGA), polylactide acid (PLA), poly-ε-coprolactone (PCL), polybutylene succinate (PBS)

INTRODUCTION

A biomaterial is defined as any natural or synthetic substance engineered to interact with biological systems to direct medical treatment.

Biomaterials must be biocompatible meaning that they perform their function with an appropriate host response [1]. Biodegradable polymers comprise ester, amide, or ether chemical bonds. In general, biodegradable polymers can be grouped into two large groups on basis of their structure and synthesis. One of these groups is agro-polymers, i.e. those derived from biomass. The other consists of bio polyesters, which are those derived from microorganisms or synthetically made from either naturally or synthetic monomers [2].

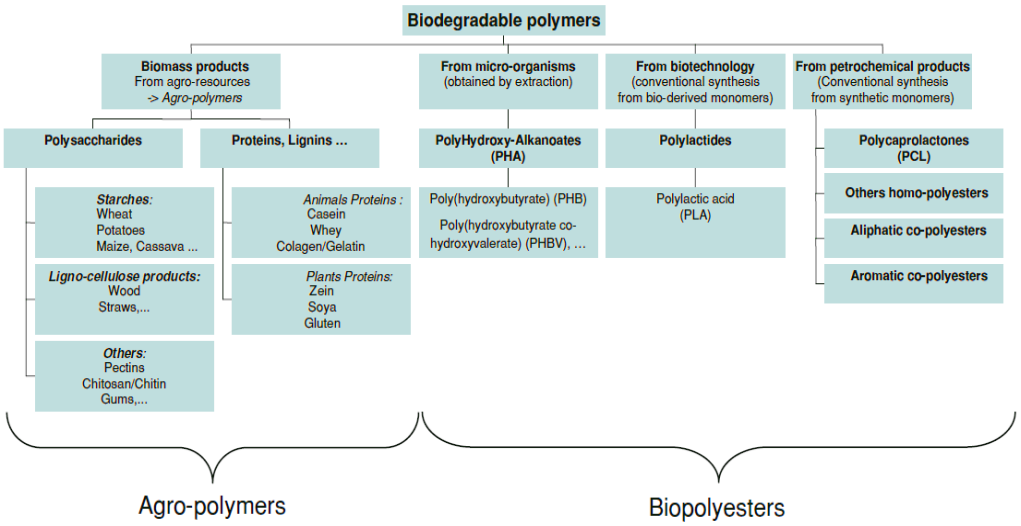

Figure 1. Classification of the main biodegradable polymers [3]

Biodegradable polymers represent a growing field. A vast number of biodegradable polymers (e.g. cellulose, chitin, starch, polyhydroxyalkanoates, polylactide, polycaprolactone, collagen and other polypeptides) have been synthesized or are formed in a natural environment during the growth cycles of organisms. Some microorganisms and enzymes capable of degrading such polymers have been identified. There are different classifications of biodegradable polymers, hereby is presented the classification according to the synthesis process, which is shown in Figure 1.

Polyesters are among the most used biodegradable plastics, given their hydrolysable ester bonds; therefore they represent a valid solution for biomedical applications. The properties of these materials strictly depend on the monomers used for their synthesis.

The aliphatic polyesters are almost the only high molecular weight biodegradable compounds and thus have been extensively investigated. Their hydrolysable ester bonds make them biodegradable. Aliphatic polyesters can be classified into two types according to the bonding of the constituent monomers. The first class consists of the polyhydroxyalkanoates. These are polymers synthesized from hydroxyacids, HO-R-COOH.

Examples are poly(glycolic acid) or poly(lactic acid). Poly(alkene dicarboxylate)s represent the second class. They are prepared by polycondensation of diols and dicarboxylic acids. Examples are poly(butylene succinate) and poly(ethylene succinate) [4]. Application of biomaterials in therapy are various and some of these applications are aimed at replacing a lost function or an organ and request a therapeutic device made of biomaterials (prosthesis) for the rest of the patient's lifetime. Many other biomedical applications require a therapeutic aid for a limited period of time. Accordingly, it is desirable that the temporary therapeutic aid disappear from the body after healing in order to avoid the storage of any foreign materials.

Whereas permanent aids require biostable biomaterials, temporary aids should be preferably made of degradable or biodegradable compounds that can be eliminated from the body or to be bioassimilated after use.

Historically, biopolymers, i.e. polymers of natural origin such as polysaccharides and proteins, were primarily used as sources of wound dressings and suture threads either under their natural forms or after some chemical treatments. Because macromolecular compounds are usually biodegradable, i.e. degraded via biological processes, biopolymers are often regarded as suitable compounds to make bioresorbable therapeutic devices [5]. Biodegradable polymers that are often used as biomaterials are shown in Figure 2.

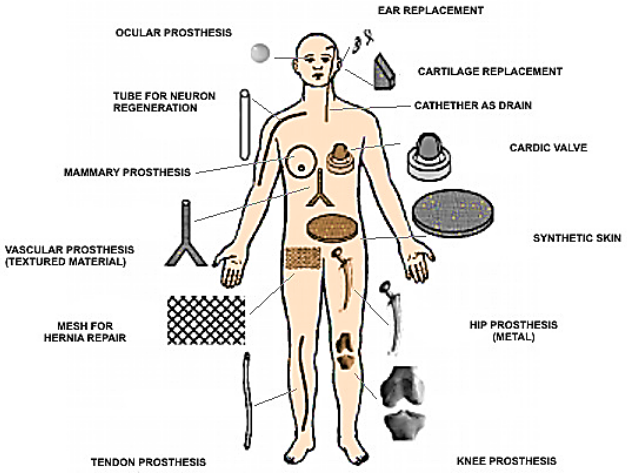

Figure 2. Biodegradable polymers used as biomaterials in human organism [7]

To be used as biomaterials, biodegradable polymers should have three important properties: biocompatibility, bioabsorbility and mechanical resistance. The use of enzymatically degradable natural polymers, as proteins or polysaccharides, in biomedical applications began thousands of years ago, whereas the application of synthetic biodegradable polymers dates back some fifty years. Current applications of biodegradable polymers include surgical implants in vascular or orthopaedic surgery and plain membranes. Biodegradable polyesters are widely employed as a porous structure in tissue engineering because they typically have good strength and an adjustable degradation speed [4]. Biodegradable polymers are also used as implantable matrices for the controlled release of drugs inside the body or as absorbable sutures [6].

SYNTHESIS, PROPERTIES AND APPLICATION OF SOME BIODEGRADABLE POLYMERS

Properties and methods of production of most common biopolymers: polyglycolic acid (PGA), polylactide acid (PLA), poly-ε-coprolactone (PCL) and polybutylene succinate (PBS) are described, as well as their application in medicine and pharmacy.

POLYGLYCOLIC ACID (PGA)

Polyglycolide or polyglycolic acid (PGA) is a biodegradable, thermoplastic polymer and the simplest linear, aliphatic polyester (Figure 3). PGA has been known since 1954 as a tough fiber-forming polymer [8]. Polyglycolide has a glass transition

temperature between 35-40°C and its melting point is reported to be in the range of 225-230°C. PGA also exhibits an elevated degree of crystallinity, around 45-55%, thus resulting in insolubility in water. The solubility of this polyester is somewhat unique, in that its high molecular weight form is insoluble in almost all common organic solvents (acetone, dichloromethane, chloroform, ethyl acetate, tetrahydrofuran), while low molecular weight oligomers sufficiently differ in their physical properties to be more soluble. However, polyglycolide is soluble in highly fluorinated solvents like hexafluoroisopropanol (HFIP) and hexafluoroacetone sesquihydrate that can be used to prepare solutions of the high molecular weight polymer for melt spinning and film preparation. Fibers of PGA exhibit high strength and modulus (7 GPa) and are particularly stiff [9].

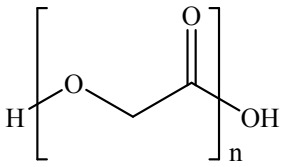

Figure 3. PGA structure

Synthesis. Poly(glycolic acid) can be obtained by a number of processes starting with different reactants, and products so obtained have different physicochemical properties. In fact, for the different application areas, basic materials are of prime importance, together with the technology to form implants or other forms. For instance, in the orthopaedic field, mechanical properties and design of the end product will be essential; to a lesser extent this will be the case in the pharmaceutical field, and so less attention needs to be paid to these aspects [10]. PGA can be obtained through several different processes starting with different materials: polycondensation of glycolic acid, ring-opening polymerization of glycolide and solid-state polycondensation of halogenoacetates. Polycondensation of glycolic acid is the simplest process available to prepare PGA, but it is not the most efficient because it yields a low molecular weight product. The most common synthesis used to produce a high molecular weight form of the polymer is ring-opening polymerization of "glycolide", the cyclic diester of glycolic acid (Figure 4).

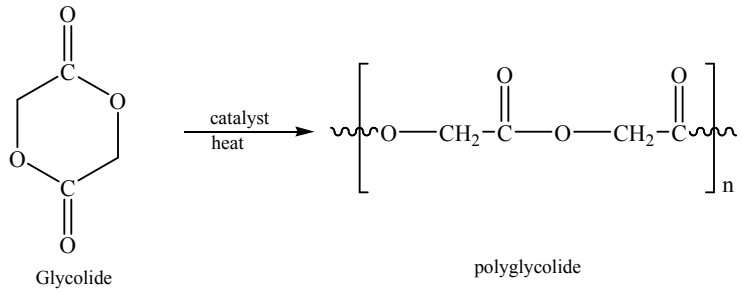

Figure 4. Ring-opening polymerization of glycolid In spite of its low solubility, this polymer has been fabricated into a variety of forms and structures. Extrusion, injection and compression molding as well as particulate leaching and solvent casting, are some of the techniques used to develop polyglycolide-based structures for biomedical applications. The high rate of degradation, acidic degradation products and low solubility however, limit the biomedical applications for PGA.

Therefore, several copolymers containing glycolide units are being developed to overcome the inherent disadvantages of PGA. Due to its hydrophilic nature, surgical sutures made of PGA tend to lose their mechanical strength rapidly, typically over a period of two to four weeks post-implantation. In order to adapt the materials properties of PGA to a wider range of possible applications, researchers undertook an intensive investi-gation of copolymers of PGA with the more hydrophobic PLA.

Polycondensation of glycolic acid is the simplest process available to prepare PGA, but it is not the most efficient one because it yields a low molecular weight product [11]. Briefly, the procedure is as follows: glycolic acid is heated at atmospheric pressure and a temperature of about 175–185°C is maintained until water ceases to distill. Subsequently, pressure is reduced to 150 mm Hg, still keeping the temperature unchanged for about two hours and the low molecular weight poly(glycolic acid) is obtained. 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. In the polycondensation system of PGA, two principal equilibrium exist, one is dehydration equilibrium for esterification [12]. The cationic-ring opening polymerization reaction of lactones has been achieved using alkylating agents, acylating agents, Lewis acids, and protic acids.

However, the quality of end product varies with the agents used. There are reports that polymers prepared using protic acid such as sulphuric acid and phosphoric, yield brittle and highly coloured polymers in high yield. While the polymers prepared using Lewis acids such as zinc chloride, ferric chloride, aluminium chloride, titanium tetrachloride, boron triflouride etherate, and antimony triflouride yield high molecular weight and high tensile strength PGA, especially antimony triflouride gave a tough and colourless almost quantitatively, whose reduced viscosity was higher than 0.7 [13]. Boron triflouride was moderately active at low temperature of 110°C.

Chemical and physical properties. Polyglycolide has a glass transition temperature between 35-40°C and its melting point is reported to be in the range of 225-230°C. PGA also exhibits an elevated degree of crystallinity, around 45-55%, thus resulting in insolubility in water [11].

PGA can be easily crystallized as spherulites and hedrites in a hedritic rosette. Braided sutures from melt-extruded, stretched, and heat-set PGA fibres were chosen for their high strength, excellent handling properties, minimal tissue reactivity, and a similar but more reproducible absorption rate than catgut, as comparing to nylon-4, poly(β-hydroxybutyric acid), poly(ethylene oxide), oxidized regenerated cellulose, and poly(vinyl alcohol) as absorbable sutures [14].

However, one of the two PGA polymorphs from ring-opening polymerization is readily degradable in the presence of moisture. In 1973, using the thermogravimetric gas evolution analysis together with kinetic study, It was confirmed that degradation of PGA was a first-order reaction mainly via an intramolecular ester interchange mechanism, as shown in Figure 5 [14].

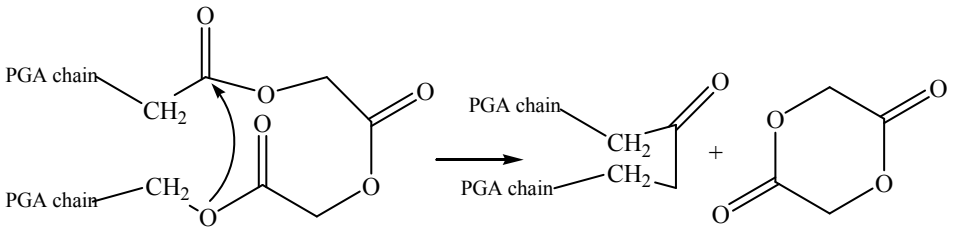

Figure 5. Intramolecular ester interchange mechanism of poly(glycolide) degradation (the intramolecular arrow indicates the direction in which the ester interchange occurs)

Application. Polyglycolide and its copolymers poly(lactic-co-glycolic acid) (PLA–PGA), poly(glycolide-*co*-caprolactone) and poly(glycolide-*co*-trimethylene carbonate) are widely used as materials for the synthesis of absorbable sutures. In most cases, PGA is copolymerized with other organic acids such as with PLA to make a PLA–PGA copolymer for improving its property. PGA–PLA copolymers have been known to be biodegradable and histocompatible for the past 40 years. Their physicochemical and biological properties have been found suitable, in many instances, for sustaining drug release *in vivo* for days or months. Microencapsulation technique is chosen frequently for its unique properties because microcapsules can be made using different traditional and nontraditional techniques containing core materials ranging from biological proteins to synthetic drugs. A biocompatible delivery system using poly(-DLlactide-*co*-glycolide) microspheres was developed as a controlled release antigen for parenteral administration. It offers several advantages in terms of immune adjuvanticity over other compounds. In contrast to other carriers, microspheres are more stable, thus permitting administration by the oral or parenteral route [14]. Because of PGA's rapid degradation and insolubility in many common solvents, limited research has been conducted with PGA-based drug delivery devices. Instead, the most recent research has focused on short-term tissue engineering scaffolds and the utilization of PGA as a filler material coupled with other degradable polymer networks [1].

PGA is often fabricated into a mesh network and has been used as a scaffold for bone, cartilage, tendon, tooth, vaginal, intestinal, lymphatic, and spinal regeneration. Although there has been research conducted into a wide range of applications, there exist significant issues with PGA. Rapid degradation leads to the loss of mechanical strength and significant local production of glycolic acid. Although glycolic acid is bioresorbable by cells via the citric acid cycle, high level of glycolic acid have been linked to a strong, undesired inflammatory response. In addition, PGA has mechanically failed as a biomaterial when used to facilitate colonic anastomosis formation and prevent intrapericardial adhesions [1].

POLYLACTIC ACID (PLA)

Polylactic acid or polylactide (PLA) is a biodegradable thermoplastic aliphatic polyester derived from renewable resources (corn starch, cassiva roots, sugarcane etc.). PLA is the most consumed biopolymer in the world (Figure 6) [15]. Polylactic acid belongs to the family of aliphatic polyesters commonly made from α-hydroxy acids, which include polyglycolic acid or polymandelic acid, and are considered biodegradable and compostable. PLA was discovered in 1932 by *Carothers (at DuPont)*. He produced a low molecular weight PLA by heating lactic acid under vacuum while removing condensed water. By ring-opening polymerization of the lactide, high-molecular PLA was synthesized. PLA was first used in combination with polyglycolic acid (PGA) and sold under name *Vicryl* in the USA in 1974 [16].

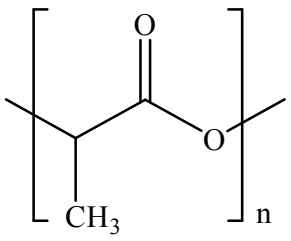

Figure 6. PLA structure

Synthesis. The basic building block for PLA is lactic acid, which was first isolated in 1780 from sour milk by the Swedish chemist *Scheele* and first commercially produced in 1881 [17]. The production of PLA is a multistep process which starts from the production of lactic acid, (2-hydroxy propionic acid), as single monomer of PLA, which is produced via fermentation or chemical synthesis and -ends with its polymerization. An intermediate step is often the formation of lactide. Polymerization of lactic acid can follow three main routes: direct condensation polymerization, direct polycondensation in an azeotropic solution and polymerization through lactide formation. Lactic acid can be manufactured either by carbohydrate fermentation or chemical synthesis, although fermentation predominates [18]. The majority of the world's commercially produced lactic acid is made by bacterial fermentation of carbohydrates, using homolactic organisms such as various optimized or modified strains of the genus Lactobacilli, which exclusively form lactic acid. The organisms that predominantly yield the L(+)-isomer are *Lactobacilli amylophilus*, *L. bavaricus*, *L. casei*, *L. maltaromicus* and *L. salivarius* [17].

These strains yield high carbon conversions from feed stocks at standard fermentation conditions, pH range of 5.4 to 6.4, a temperature range of 38 to 42 °C, and a low oxygen concentration. The various types of carbohydrates that can be utilized in the fermentation depend on the particular strain of *Lactobacillus*. Most of the simple sugars obtained from agricultural byproducts can be used. These sugars include: glucose, maltose and dextrose from corn or potato starch; sucrose from cane or beet sugar and lactose from cheese whey.

Commercial fermentation is usually conducted in a batch process. Sugar concentrations of 5-10% are used, with the production rates of 2 grams of acid per 1 litre of broth per hour. Various methods of extraction of the produced acid have been developed. The major method of separation is based on calcium hydroxide addition to neutralize the fermentation acid and give soluble calcium lactate solutions, which is recrystallized and purified to give crude lactic acid.

Direct condensation polymerisation of lactic acid yields low-molecular-weight glassy polymer which is unusable for any application unless external coupling agents are used to increase the molecular weight of the polymer. Producing high molecular weight PLA polymers by direct polycondensation in an azeotropic solution application of catalysts is more efficient. The choice of catalysts and solvent volume percentages enabled the higher molecular weights of PLA up to 6.6×10^4 [19]. The third mechanism of producing PLA is to purify and ring-open polymerize (ROP) lactide to yield high-weight-average molecular weight (M>100.000) PLA (Figure 7).

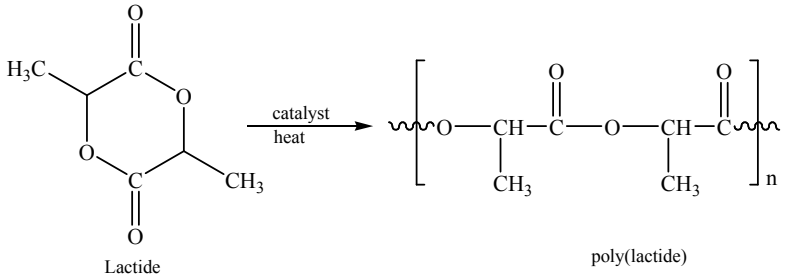

Figure 7. Synthesis of poly(lactide) (PLA)

The lactide method was the only method of producing pure, high-molecular-weight PLA until *Mitsui Toatsu Chemicals* commercialized the catalytic polymerization process in aprotic solvent, i.e., azeotropic dehydration condensation and obtained PLA with average molecular weights greater than 300.000 [20]. To increase the molecular weight, chain-coupling agents must be added, and it will preferentially react with either the hydroxyl or carboxyl groups. The condensed PLA can be modified to produce either all hydroxyl or all carboxyl groups. The PLA can also be treated with anhydrides such as maleic or succinic to convert the hydroxyl to a carboxylic end-group [21]. Various esterification–promoting adjuvants and chain-extending agents have been reported that can be used to increase the molecular weight of the PLA condensation products [22]. The use of chain-extending agents overcomes many of the disadvantages associated with esterification – promoting adjuvents. The azeotropic condensation polymerization is a method to obtain high-molecular-weight polymer without the use of chain extenders or adjuvents. The ring-opening polymerization of lactide was first demonstrated by *Carothers* in 1932, but high molecular weights were not obtained until improved lactide purification techniques were developed by *Du Pont* in 1954 [23]. Polymerization through lactide formation is being industrially accomplished for high molecular weight PLA production. Ring-opening polymerization of lactide can be carried out in melt or solution by cationic, anionic and coordination mechanisms, depending on the initiator utilized. The most considered active initiator for the L-lactide ring–opening polymerization is stannous octoate (bis-2-ethyl hexanoate, $SnOct_2$), which causes a low degree of racemization at high temperature. The choice of initiator system, co-initiator as chain control agent, catalyst concentration, monomer-to-initiator ratio, and polymerization temperature and time significantly affect the polymer properties. Properties such as molecular weight, degree of crystallinity, and residual monomer content, in turn affect the psychico-mechanical properties of polylactide and its copolymers [24].

Chemical and physical properties. Poly(lactic acid) exists as a polymeric helix, with an orthorombic unit cell. Due to chiral nature of lactic acid, several forms of polylactide exist. PLA is soluble in chlorinated solvents, such as benzene, tetrahydrofuran and dioxane [22]. The tensile properties of PLA can vary widely, depending on whether or not it is annealed or oriented or what its degree of crystallinity is. Polyactic acid can be processed into fibre and film on standard plastics equipment. PLA undergoes thermal degradation at temperatures above 200°C by hydrolysis, lactide reformation, oxidative main chain scission, and inter- or intramolecular transesterification reactions. PLA degradation is dependent on time, temperature, low-molecular-weight impurities and catalyst concentration [25]. Catalysts and oligomers decrease the degradation temperature and increase the degradation rate of PLA. Poly(lactic) homopolymers have a glass-transition and a melt temperature of about 55°C and 175°C, respectively. PLA have a very narrow processing window. The most widely used method for improving PLA processability is based on melting point depression by the random incorporation of small amounts of lactide enantiomers of opposite configuration into the polymer (i.e., adding a small amount of D-lactide to the L-lactide) [26]. High-molecular-weight poly(lactic acid) is a colourless, glossy, stiff thermoplastic polymer with properties similar to polystyrene. The amorphous PLA is soluble in most organic solvents (tetrahydrofuran, THF), chlorinated solvents, benzene, acetonitrile and dioxane [17].

Application. PLA has potential for use in a wide range of applications. It is used as a buffering agent, acidic flavouring agent, acidulant and bacterial inhibitor in many processed foods. PLA is growing alternative as a „green" food packaging polymer. Due to the larger thermal processing ability compared to other biomaterials like polyethylene-glycol, polyhydroxyalkanoates (PHA) and poly α-caprolactone; the processing of PLA can be achieved by film casting, extrusion, blow molding and fiber spinning [27]. The major PLA application today is packaging (70%); the estimation for 2020 shows the increase of other applications especially in biomedicine.

Commercialized PLA products demonstrate the fact that PLA is not being used solely because of its degradability, nor because it is made from renewable resources; it is being used because it functions very well and provides excellent properties at a competitive price [28]. Applications of PLA are limited by several factors such as low glass transition temperature, weak thermal stability and low toughness and ductility [29].

A large number of investigations have been performed on the blending of PLA with various polymers, such as: thermoplastic starch, poly(ethylene oxide), poly(ethylene glycol), poly(ε-caprolactone), poly(vinyl acetate), poly(butylene succinate) etc. Low molecular weight compounds have also been used as plasticizers for PLA, for example, oligomeric lactic acid, glycerol, low molecular citrates etc. [30].

The choice of polymers or plasticizers that are to be used as modifiers of PLA is limited by the requirements of application. The final properties of these blends depend on the chemical structure of the original components, the mixing ratio of the constituent polymers, the interaction between the components and the processing steps to which they are then subjected. PLA is also used in biomedical applications, with various uses as internal body components, interference screews in ankle, knee and hand; tacks and pins for ligament attachment; rods and pins in bone, plates and screews for craniomaxillofacial bone fixation [31] and also for surgical sutures, implants and drug delivery systems [32]. This is based on their advantages over nondegradable biomaterials with respect to long term biocompatibility. PLA offers biodegradability, biocompatibility and thermoplastic process ability, and it is used as surgical implant material and drug delivery systems, as well as porous scaffolds for the growth of neo-tissue [33]. Tissue engineering is a technique whose concept was introduced in 1988 by the reconstruction of the biological tissues using biomaterials. Three dimensional porous scaffolds of PLA have been created for culturing different cell types used in cell based gene therapy for cardiovascular diseases, muscle tissues, bone and cartilage regeneration [34].

Different surface modification strategies, such as physical, chemical, plasma and radiation induced methods for creating desirable surface properties of PLA biomaterials. PLA fibres are used for ligament and tendon reconstruction and stents for vascular and urological surgery. One application of PLA in the form of injectable microspheres is for temporary fillings in facial reconstructive surgery, as well as embolic material in trans catheter arterial embolization [35].

Microspheres and microcapsules have been applied in drug delivery systems (DDS). Release of drugs from these systems is based on several mechanisms that include diffusion and polymer degradation (hydrolysis or enzymatic degradation) [36]. Erosion, diffusion and swelling are one of the ways by which polymeric drug release occurs. In the encapsulation process of many drugs, PLA and their copolymers have been utilized in nanoparticle form [37]. Different methods were used to obtain nano-particles, such as solvent evaporation, solvent displacement, salting out and emulsion solvent diffusion [38]. PLA nano particles have been tested in human skin revealing that they can propose the active sites into hair follicles which makes them a stellar candidate as a drug delivery layout [39].

Due to high strength it is possible to create 3D structures for bone fixation in the forms of plates, pins, screws and wires. Three dimensional (3D) electrowave fibrous scaffolds is a possibility tissue engineering device for bone renewal. PLA and its copolymers are utilized in wound management, such as surgical sutures, healing dental extraction wounds [40].

PLA can be blended with other monomers, such as glycolic acid, and such copolymer is used in drug release. PLA is often mixed with starch to increase biodegradability and to reduce its price and to increase the water absorption.

POLY (Ε-CAPROLACTONE) (PCL)

Poly ε-caprolactone, PCL is one of biodegradable and biocompatible polymers, which have received significant attention because they are environmentally friendly and are extensively used in biomedical applications. PCL structure is shown in Figure 8.

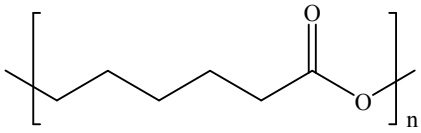

Figure 8. PCL structure

Synthesis. Poly (ε-caprolactone) PCL is synthesized by polymerization of hydroxy acids, HO-R-COOH, or by ring-opening-polymerization of cyclic monomers, -R-COO-. PCL is prepared by the ring opening polymerisation of the cyclic monomer (ROP) of ε-capro lactone (ε-CL) using ammonium heptamolybdate as a catalyst at 155 °C. It is composed of five methy lenes [$(CH_2)_5$] and an ester functional group as the repeating unit (Figure 9) and was studied as early as the 1930s.

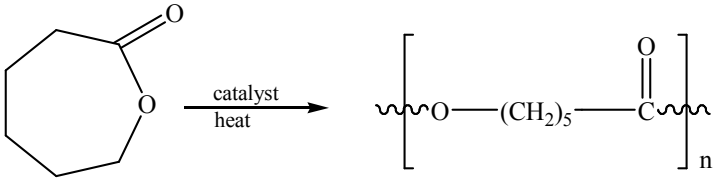

Figure 9. Synthesis of poly(ε-caprolactone) (PCL)

PCL and its derivatives are polymers that have been of great interest in the pharmaceutical industry as matrices for medical formulas. Recently a wide range of catalysts for the ring opening polymerization of caprolactone has been reviewed. Catalysts such as stannous octoate are used to catalyze the polymerization and low molecular weight alcohols can be used to control the molecular weight of the polymer. There are various mechanisms which affect the polymerization of PCL and these are anionic, cationic, coordination and radical. Each method affects the resulting molecular weight, molecular weight distribution, end group composition and chemical structure of the copolymers [41]. The obtained PCL was purified by dissolution into chloroform and precipitated ion with methanol, finally being isolated by vacuum filtration [42].

Chemical and physical properties. PCL is a semicrystalline aliphatic polymer that has a slow degradation rate 12-24 months. It has a low glass transition temperature at -60°C, a melting temperature at about 60°C, and a high thermal stability [43]. PCL has been shown to be degraded by the action of aerobic and anaerobic microorganisms that are widely distributed in various ecosystems [44]. The biodegradability of PCL can be increased by copolymerization with aliphatic polyesters [45]. PCL is soluble in tetrahydrofuran, chloroform, methylene chloride, carbon tetrachloride, benzene, toluene, cyclohexanone dihydropyran and 2-nitropropane and only partially soluble in acetone, 2-butanone, ethyl acetate, acetonitrile and dimethyl fumarate [46]. Recently, other studies have considered the fabrication of PCL nanofibres using less harmful solvents, like formic acid. In fact, formic acid is relevant for the reduction of the fibre diameter [47]. PCL is degradable in several biotic environments, including river and lake waters, sewage sludge, farm soil, paddy soil, creek sediment, roadside sediment, pond sediment, and compost [48]. The degradation times of PCL varies with molecular weight, crystallinity degree and morphology [49].

Application. Due to PCL's very low in vivo degradation rate and high drug permeability, it has found favour as a long-term implant delivery device. Current research is being conducted into the development of micro- and nano-sized drug delivery vehicles, but the degradation rate (2–3 years) is a significant issue for pure PCL products to be FDA approved for this use. PCL and PCL composites have been used as tissue engineering scaffolds for regeneration of bone, ligament, cartilage, skin, nerve, and vascular tissues [1]. A recent advancement using PCL hybrid scaffolds has been used in interfacial tissue engineering [1].

PCL nanofibres show viscoelastic properties. It could be that higher molecular weight PCL results in softer nanofibres. These different values suggest that different nanofibre properties can be achieved by varying the preparation methods. The mechanical properties of electrospun PCL nanofibres do not closely mimic any of the natural or electrospun protein fibres. However, they seem to come closer to fibrin fibres and electrospun fibrinogen fibres, rather than collagen fibres [50]. PCL fibres may have suitable mechanical properties for various applications in biomedical and tissue engineering including blood vessels, skin grafts, and tendons. Viscoelastic properties have been found to depend on the age of the fibres. Younger fibres could be pulled to a greater strain before permanent deformation than older fibres. This is an important property for determining how long a scaffold made from these single fibres can be stored before the mechanical properties are significantly altered. The relaxation times and total and elastic moduli also show age-relate dependencies. This dependence on age gives a better understanding of how PCL degrades over time, from a mechanical perspective. Combining these findings with PCL's bioresorbable properties will allow for better fabrication of specific bioengineered scaffolds and devices [50].

POLY(BUTYLENE SUCCINATE), PBS

Polycaprolactone (PCL), and poly(butylene succinate) (PBS) are petroleum based, but they can be degraded by microorganisms. PBS degrading microorganisms are widely distributed in the environment, but their ratio to the total microorganisms is lower than PCL-degraders. PBS structure is shown in Figure 10.

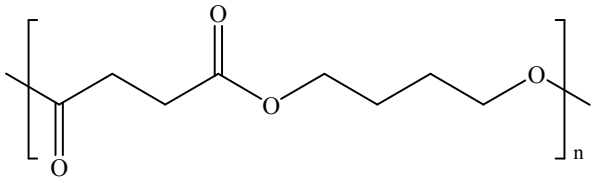

Figure 10. PBS structure

PBS is nowadays one of the most appealing biodegradable polymer because it is fully sustainable, commercially available and exhibits a good balance of thermal and mechanical properties [51]. PBS also referred to as polytetramethylene succinate, is a biodegradable thermoplastic polyester resin. PBS exhibits good thermal and mechanical properties that are comparable with those of widely used polymers such

as polyethylene and polypropylene, with high melting points of 112-114 °C. The favourable properties coupled with ease of processing have resulted in emergence of a variety of application areas across diverse end use industries for PBS. Efforts are channelized towards developing bio-based PBS from bio based 1,4 butanediol and succinic acid. Succinic acid is one of the two primary intermediates used to manufacture PBS, and is a building block chemical in the production of 1,4-butanediol (BDO). Although diglycollic acid has a similar structure to succinic acid, it possesses ether-oxygen in molecules and thus, thermal, mechanical and biodegradable properties are different [52]. Biodegradable plastic like PBS has conventionally been made using petroleum-based feedstock but it moved the packaging industry a step in the right environmental direction. Mechanical properties are comparable to polypropylene and low-density polyethylene (LDPE) [44]. PBS is synthesized from dicarboxylic acids (e.g., succinic and adipic acid) and glycols (e.g., ethylene glycol and 1,4-butanediol) [53]. Synthesis of PBS is presented in Figure 11.

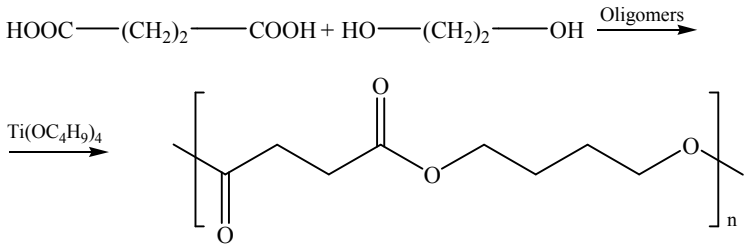

Figure 11. Synthesis of PBS

It has high flexibility, excellent impact strength, and thermal and chemical resistance. However, its high cost and other properties such as elastic modulus, tensile strength, gas barrier properties, and melt viscosity for further processing, restrict its extensive application [54].

CONCLUSIONS

Biodegradable polyesters have been intensively investigated in the last two decades because of their biodegradability and superb physical properties. The biodegradable polymers are indispensable in drug delivery due to their unrivalled physicochemical properties. These physicochemical properties have a significant effect on the drug delivery system, as well as on the pharmacological effect. Currently, a wide range of degradable polymers exist that hold potential as biomaterials. As a result, the market of these environmentally friendly materials is in rapid expansion. Utilization of polymers as biomaterials has greatly impacted the advancement of medicine and pharmacy. Biopolymers with desired physical, chemical, biological, biochemical and degradation properties can be designed, and a wide range of these novel materials have been investigated for biomedical applications. The field of degradable polymeric biomaterials will continue to progress since these new materials present the great challenge to sophisticated multidisciplinary research as well as to their economic technological production.

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