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PROCESSING, DEGRADATION AND APPLICATIONS OF SYNTHETIC BIODEGRADABLE POLYMERS: A REVIEW

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ABSTRACT
Biodegradable polymers can either be natural or synthetic and they have been greatly applied across fields especially in medicals due to their bioabsorbability, biocompatibility and biodegradability. A lot had been achieved through the efforts of polymer scientist in using synthetic materials in human body and this is due to the versatility and biodiversity of the materials. Synthetic biodegradable polymers in general are of greater advantage over natural materials in that they can be tailored to give a wider range of properties and have more predictable lot-to-lot uniformity than materials from natural sources. Lately, there is a large increase in the use of these polymer materials in ecological applications, packaging, and pharmaceutics and even in agriculture. Hence, researchers have also intensified efforts to make these polymer based materials eco-friendly so as to reduce the pollution problems such as blockage of drainages and littering of the environment by these polymeric materials. In this review however, we will focus on synthetic biodegradable with emphasis on their mode of degradation, applications and processing conditions.

Keywords: *Biodegradable, bioabsorbability, pharmaceutics, eco-friendly and biodiversity*

1.0 INTRODUCTION

Biodegradation is the degradation of a material by environmental factors such as sunlight, temperature changes or the action of microbes. These microbes secrete enzymes both intracellularly and extracellularly which act on the polymer thereby subjecting the polymer to chemical reaction and degradation by polymer chain scission and oxidation. These processes of cellular metabolic reaction converts the biotic decomposition products into energy, water, carbondioxide and biomass as illustrated in Figure 1.1. This process converts artificial materials (synthetic biopolymers) into natural components which are non toxic to the environment.

Biodegradable synthetic polymers are therefore materials with the ability to function for a temporary period and subsequently degrade, under a controlled mechanism, into products easily eliminated in the body's metabolic pathways. In this way, biodegradability not only eliminates the risk of complications associated with the long-term presence of a foreign material and the need for a second surgery for implant removal, but also allows for improved healing, as viable tissue interacts and grows into the degrading construct as shown in Figure 1.2.

Since the early 1960s, several synthetic degradable polymer systems have been used as medical implant materials which include various polyesters, polyurethanes, polyanhydrides, polyacrylates, polyphosphoesters, and polydioxanone, among others. Biodegradable synthetic polymers offer a number of advantages over other materials for developing scaffolds in tissue engineering. The key advantages include the ability to tailor mechanical properties and degradation kinetics to suit various applications. Synthetic polymers are also attractive because they can be fabricated into various shapes with desired pore morphologic features conducive to tissue in-growth. Furthermore, polymers can be designed with chemical functional groups that can induce tissue in-growth. Biodegradable synthetic polymers such as poly (glycolic acid), poly(lactic acid) and their copolymers, poly(p-dioxanone), and copolymers of trimethylene carbonate and glycolide have been used in a number of clinical applications (Shalaby, 1988; Holland and Tighe, 1992; Hayashi , 1994; Kohn and Langer, 1997; Ashammakhi and Rokkanen, 1997). The major applications of these biopolymers include resorbable sutures, drug delivery systems and orthopaedic fixation devices such as pins, rods and screws (Behravesh et al., 1999; Middleton and Tipton, 2000). Among the families of synthetic polymers, the polyesters have been attractive for these applications because of their ease of degradation by hydrolysis of ester linkage, degradation products being resorbed through the metabolic pathways in some cases and the potential to tailor the structure to alter degradation rates.

1.1 CLASSIFICATION OF SYNTHETIC BIODEGRADBLE POLYMERS

Most of the biodegradable polymers studied belong to the polyester family. Among these, poly(α-hydroxy acids) such as poly(glycolic acid) (PGA), poly(lactic acid) (PLA), and a range of their copolymers have historically comprised the bulk of published material on biodegradable polyesters and have a long history of use as synthetic biodegradable materials (Shalaby, 1988; Holland and Tighe, 1992; Hayashi, 1994; Kohn and Langer, 1997; Ashammakhi and Rokkanen, 1997) in a number of clinical applications. These polymers have been used as sutures (Cutright et al., 1971) plates and fixtures for fracture fixation devices (Mayer and

Hollinger, 1995) and scaffolds for cell transplantation (Thomson et al., 1995b).

Below is a brief overview of these commonly used haliphatic polyester and other synthetic polymers.

1.1.1 Poly (glycolic acid) (PGA)

This is a rigid thermoplastic material with high crystallinity. It has a glass transition and melting temperatures of 36 and 225ºC respectively. Due to this high crystallinity, it is not soluble in most organic solvents; with the exceptions being highly fluorinated organic solvents like hexafluoroisopropanol. Processing techniques such as extrusion, injection and compression moulding can be used to fabricate PGA into various forms but its high sensitivity to hydrolytic degradation requires careful control of processing conditions (Mikos and Temenoff, 2000; Jen et al., 1999). The preferred method for preparing high molecular weight PGA is ring-opening polymerization of glycolide. The cyclic dimer of glycolic acid (Hollinger et al. 1997, Sawhney and Drumheller, 1998) and both solution and melt polymerization methods can be used. The common catalysts used include any of organo tin, antimony or zinc. The attractiveness of PGA as a biodegradable polymer in medical application is that its degradation product; glycolic acid, is a natural metabolite and one of its major application is in resorbable sutures although the degradation product glycolic acid is resorbable at high concentrations, which can cause an increase of localized acid concentration resulting in tissue damage. The ultimate fate of glycolic acid in-vivo is considered to be the conversion to carbon dioxide and water, with removal from the body via the respiratory system (Gilding, 1981).

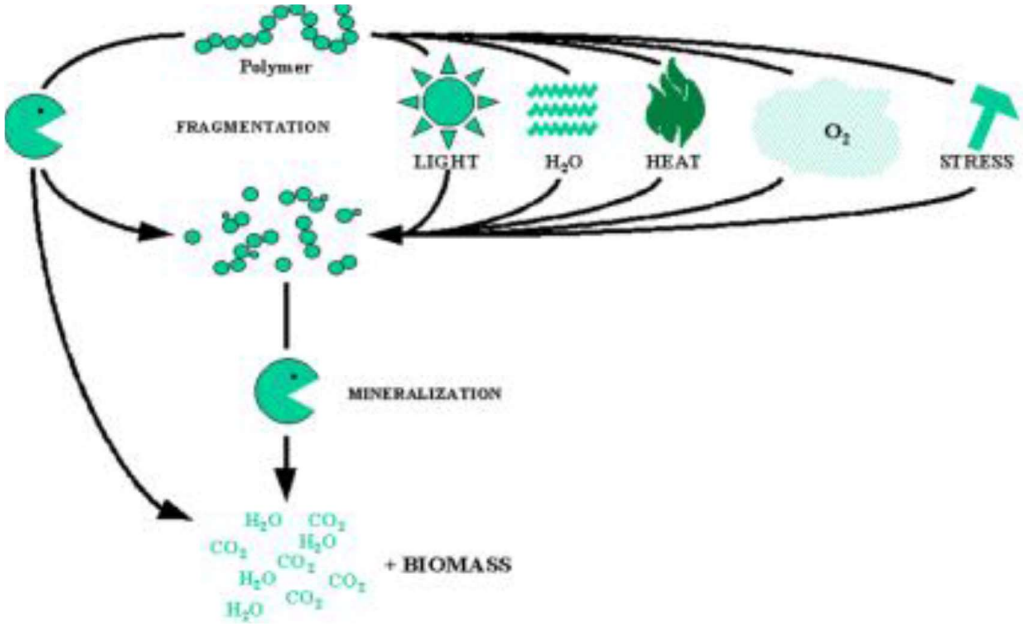


Figure 1.1: An insight into biodegradation of polymer (Andrej, 2012).

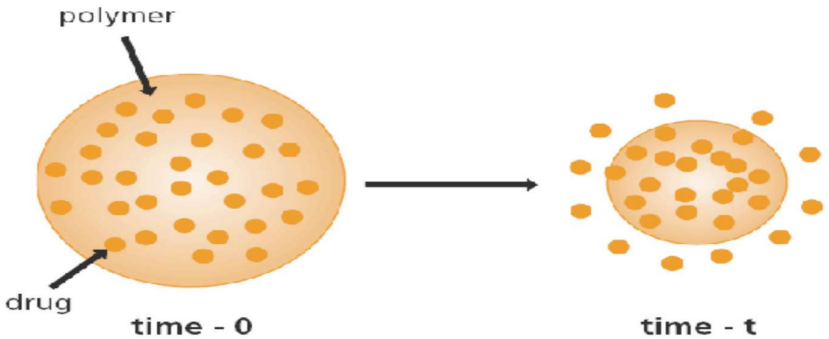
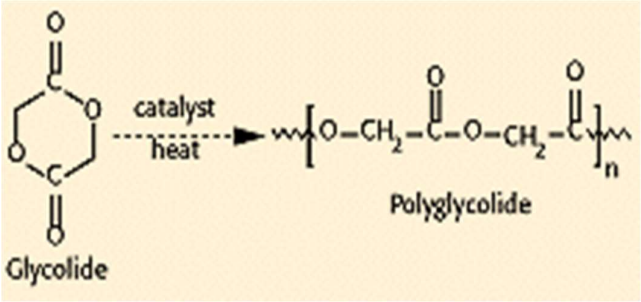


Figure 1.2: Polymer degradation at different time interval in a living system.



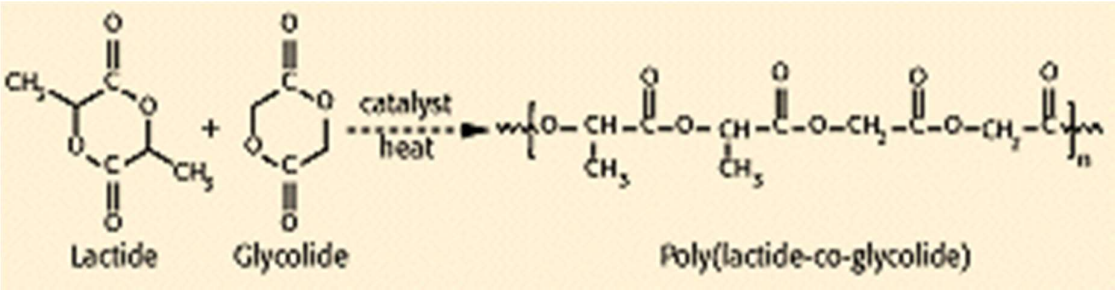
Ring polymerization of polyglycolide (PGA)

1.1.2 Poly (lactide) (PLA)

Lactide which is the cyclic dimer of lactic acid exists as two optical isomers, D and L. While the Llactide, is the naturally occurring isomer, the DL-lactide is the synthetic blend of D-lactide and L-lactide. The polymerization of lactide is similar to that of glycolide. The homopolymer of L-lactide (LPLA) is a semi crystalline polymer. PGA and LPLA exhibit high tensile strength and low elongation and consequently have a high modulus that makes them more applicable than the amorphous polymers for load-bearing applications such as in orthopedic fixation and sutures. Poly (DLlactide) (DLPLA) is an amorphous polymer having a random distribution of both isomeric forms of lactic acid and accordingly is unable to arrange into a crystalline organized structure. This material has lower tensile strength and higher elongation and much more rapid degradation time making it more attractive as a drug delivery system. Poly (L-lactide) is about 37% crystalline with a melting point of 175-178°C and a glass transition temperature of 60-65°C (Daniels et al., 1990; Agrawal et al., 1995). The degradation time of LPLA is much slower than that of DLPLA requiring greater than 2 years to be completely absorbed (Bergsma et al., 1995). Copolymers of L-lactide with glycolide or DL-lactide have been prepared to disrupt the L-lactide crystallinity thus accelerating the degradation process (Gilding and Reed, 1979; Shalaby and Johnson, 1994). PLA is more hydrophobic than PGA, and is more resistant to hydrolytic attack than PGA. For most applications the (L) isomer of lactic acid (LA) is chosen because it is preferentially metabolized in the body.

1.1.3 Poly (lactide-co-glycolide) (PLG)

Using the polyglycolide and poly (L-lactide) properties as base materials, it is possible to copolymerize the two monomers to extend the range of homopolymer properties. Copolymers of glycolide with both L-lactide and DL-lactide have been developed for both device and drug delivery applications. It is important to note that there is no linear relationship between the copolymer composition and the mechanical and degradation properties of the materials. For example, a copolymer of 50% glycolide and 50% DL-lactide degrades faster than either homopolymer (Miller et al., 1977). Copolymers of L-lactide with 25-70% glycolide are amorphous due to the disruption of the regularity of the polymer chain by the other monomer (Gildy et al., 1979). Currently, only resorbable fixation devices made from homopolymer or copolymers of glycolide, lactide, caprolactone, *p*-dioxanone and trimethylene carbonate have been commercialized (Barber, 1998).



Synthesis of Poly (lactide-co-glycolide)

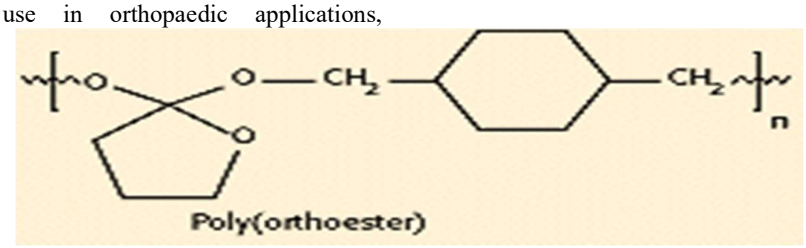
1.1.4 Polyanhydrides:

Polyanhydrides are among the most extensively studied classes of biodegradable polymers with demonstrated biocompatibility and excellent controlled release characteristics. Polyanhydrides degrades by surface erosion (Kohn and Langer, 1997) and their main applications are in controlled drug delivery. Polyanhydrides based drug delivery systems have been utilized clinically (Brem et al., 1995). Polyanhydrides are synthesized by dehydration of the diacid or a mixture of diacids by melt polycondensation (Domb and Langer, 1987). The dicarboxylic acid monomers are converted to the mixed anhydride of acetic acid by reflux in excess acetic anhydride. High molecular weight polymers are prepared by melt polycondensation of prepolymer in vacuum under nitrogen sweep. Polyanhydrides have limited mechanical properties that restrict their use in load–bearing applications such as in orthopaedics. For example, poly [1,6-bis(carboxyphenoxy) hexane] has a Young's modulus of 1.3 MPa (Leong et al., 1985; Uhrich et al., 1997) which is well below the modulus of human bone (40 to

60 MPa). To combine good mechanical properties of polyimide with surface-eroding characteristics of polyanhydrides, poly (anhydrides-co-imides) have been developed (Attawia et al., 1995; Uhrich et al., 1995), particularly for orthopaedic applications. Examples include poly [trimellitylimidoglycine-co-bis(carboxyphenoxy) hexane], and poly[pyromellitylimidoalanine co-1,6-bis(carboph-enoxy)-hexane] (Attawia et al., 1995; Seidel et al., 1996). These poly (anhydride-co-imides) have significantly improved mechanical properties, particularly compressive strengths. The degradation of these copolymers occurs via hydrolysis of anhydride bonds, followed by the hydrolysis of imide bonds. Photo cross-linkable polyanhydrides have also been developed for use in orthopaedic applications, particularly focusing on achieving high mechanical strength.

1.1.5 Polyorthoesters

Poly (orthoester)s (POE) constitute another family of polymers identified as degradable polymers suitable for orthopaedic applications. Heller and coworkers reported on the synthesis of a family of polyorthoesters that degrades by surface erosion (Ng et al., 1997). With the addition of lactide segments as part of the polymer structure, tunable degradation times ranging from 15 to hundreds of days can be achieved. The degradation of the lactide segments produces carboxylic acids, which catalyze the degradation of the orthoester (Ng et al., 1997).



Molecular structure of Poly (orthoester)

2.0 PROCESSING OF SYNTHETIC BIODEGRADABLE POLYMERS

Synthetic biodegradable polymers in general are of greater advantage over natural materials in that they can be tailored to give a wider range of properties and have more predictable lot-to-lot uniformity than materials from natural sources. They can be processed in similar ways to any engineering thermoplastic in that they can be melted and formed into fibers, rods and molded parts. The final parts can be extruded, injection molded, compression molded, or solvent spun or cast. Some of these processing techniques of synthetic biodegradable polymers are discussed below. They include:

2.1 INJECTION MOULDING.

Injection molding is one of the processing techniques for converting thermoplastics, and recently, thermosetting materials from the pellet or powder form into a variety of useful products (Ebewele, 1996). Forks, spoons, computer, television and radio cabinets, to mention just a few, are some of these products. Simply put, injection molding consists of heating the pellet or powder until it melts. The melt is then injected and held in a cooled mold under pressure until the material solidifies. The mold opens and the product is ejected. The injection molding machine therefore, performs essentially three functions viz:

I. Melt the plastic so that it can flow under pressure.
II. Inject the molten material into the mold.
III. Hold the melt in the cold mold while it solidifies and then eject the solid plastic.

These functions must be performed automatically under conditions that ideally should result in a high quality and cost-effective part. Injection molding machines have two principal components to perform the cyclical steps in the injection molding process (Bryce, 1996). These are the injection unit and the clamp unit. While the injection unit melt the pellet or powder and then inject the melt into the mold, the clamp unit opens and closes the mold at appropriate times during the molding cycle; ejects the molded part; and provides enough pressure to prevent the mold from opening due to the pressure developed in the mold cavity as it is filled with the melt by the injection unit (Todd et al., 1994). Below is the schematic drawing of the major parts of an injection moulding machine.

2.2 EXTRUSION

Extrusion is a processing technique for converting thermoplastic materials in powdered or granular form into a continuous uniform melt which is shaped into items of uniform cross sectional area by forcing it through a die (Ebewele, 1996). Extrusion end products include pipes for water, gas, drains, and vents; tubing for garden hose, automobiles, control cable housings, soda straws; profiles for construction, automobile, and appliance industries; film for packaging; insulated wire for homes, automobiles, appliances, telephones and electric power distribution; filaments for brush bristles, rope and twine, fishing line, tennis rackets; parisons for blow molding. Extrusion is perhaps the most important plastics processing method today.

A simplified sketch of the extrusion line is shown in Figure 2.2. It consists of an extruder into which is poured the polymer as granules or pellets and where it is melted and pumped through the die of desired shape. The molten polymer then enters a sizing and cooling trough or rolls where the correct size and shape are developed. From the trough, the product enters the motor-driven, rubber-covered rolls (puller), which essentially pull the molten resin from the die through the sizer into the cutter or coiler where final product handling takes place (Richard, 1974)

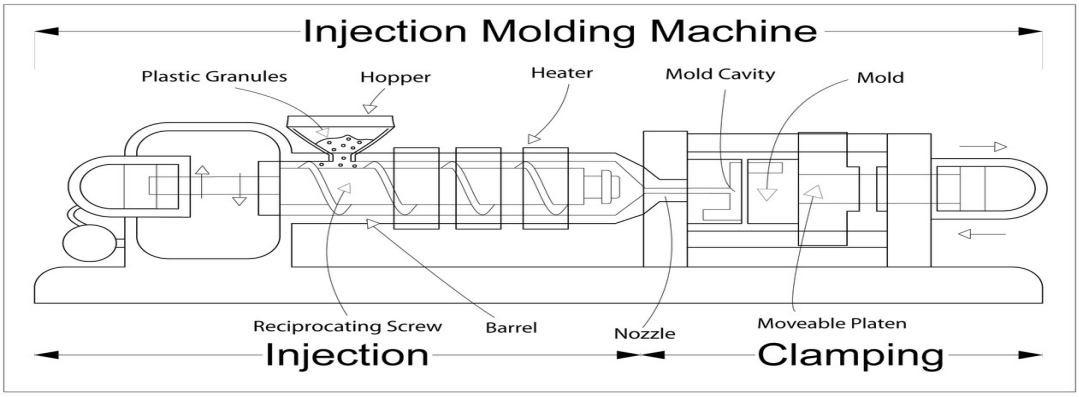


Figure 2.1: Schematic diagram of an injection moulding machine (Todd et al., 1994)

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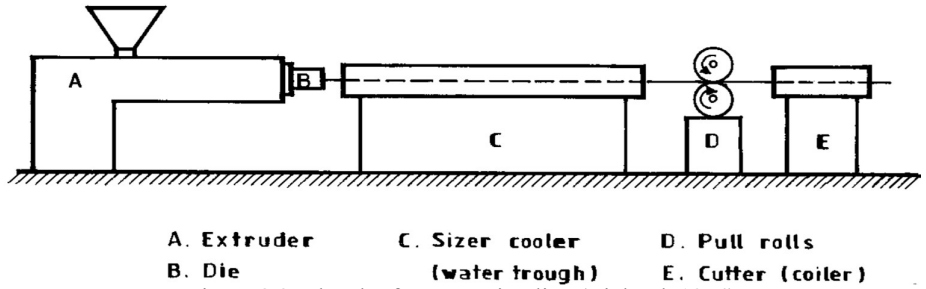

Figure 2.2: Sketch of an extrusion line (Richard, 1974)

2.3 COMPRESSION MOLDING

In compression molding, a pre-weighed amount of material is loaded into the lower half of a heated mold or cavity. The force plug (plunger) is lowered into the cavity, and pressure, which can range from 20 to 1000 tons, is applied to the powder. Under heat and pressure, the powder melts and flows into all parts of the mold cavity; the resin cross-links thus becoming irreversibly hardened. After an appropriate time, the mold is opened and the part is ejected while still hot (usually under gravity) and allowed to cool outside the mold (Ebewle, 1996). The machinery for compression molding is relatively simple, consisting essentially of two platens, which when brought together, apply heat and pressure to the mold material to form a part of desired shape. The platens move vertically, with the cavity usually mounted at the bottom so that molding material can be loaded into it (Ebewele, 1996).

One of the major advantages of compression molding is that it is relatively inexpensive because of its simplicity.

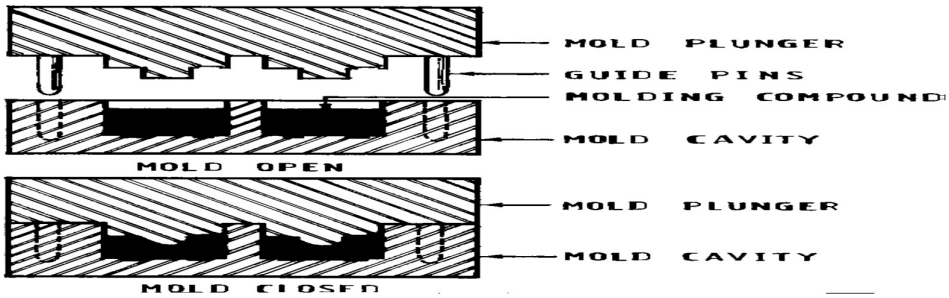

Figure 2.3: Schematic diagram of compression moulding showing material before and after Forming (Ebewele, 1996)

2.4 BLOW MOLDING

The basic principle of the blow molding process is to inflate a softened thermoplastic hollow preform against the cooled surface of a closed mold, where the material solidifies into a hollow product (Ebewele, 1996).

Packing is the major area of application of small to medium-size disposable blow molded products. Liquid foodstuffs are increasingly packaged in narrow neck plastic PET bottles. Blow molded containers are also used for cosmetics, toiletries, pharmaceutical and medical packaging and a variety of household products (Merril, 1995).

All of these techniques above are used in processing synthetic polymers and even synthetic biodegradable polymers.

3.0 DEGRADATION PROCESSES IN BIODEGRADABLE POLYMERS

The degradation of a biomaterial can occur at different stages of its preparation, during its storage. For instance, it was observed that the molecular weight of poly(*L*-lactide) decreased from 431,000 to 202,000 Da upon storage (Mainil-Varlet, et al., 1997). The conditions used during the processing and fabrication of polymeric materials may also lead to polymer degradation, consequently influencing their degradation behavior in vivo. Melt based techniques (injection molding, extrusion, compression molding) are performed at high temperatures and in the first two cases at high shear rates, which may cause some degradation of the material. The production of samples by injection molding leads to a partial material orientation, which is typically higher in the skin than in the core of the molding. The chain orientation across the sample upon processing may be responsible for a faster degradation in the center than in the skin (Mainil-Varlet, et al., 1997). In addition, it is very common to use additives (plasticizers, lubricants, antioxidants, salts, stabilizers) during the processing of polymeric materials, which will leach out after immersion and may enhance or inhibit the degradation process. Another aspect to be considered is the fact that biomedical materials need sterilization before being implanted. Sterilization can be performed using heat, steam, gas (ethylene oxide, EtO), or ionizing radiation, mainly γ or β. Each of these sterilization methods may have an effect on the material degradation, but sterilization by radiation requires high doses of high-energy radiation, resulting in some cases in polymer cross linking and degradation. γ - sterilization was shown to reduce significantly the molecular weight of poly(lactide–glycolide) polymers (Gopferich, 1996) but cold-cycle EtOH sterilization did not cause any changes in the molecular weight of polylactide (Mianil-Varlet, 1997). Materials exposed to the body fluids may undergo changes in their physicochemical properties as a result of chemical, physical, mechanical, and biological interactions between the material and the surrounding environment.

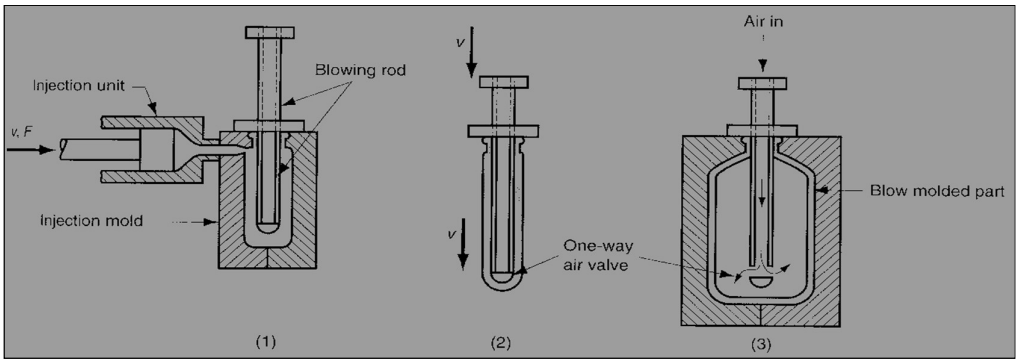

Figure 2.4. (1) Injection molding of parison, (2) stretching, and (3) blowing (Ebewele, 1996).

3.1 CHEMICAL AND ENZYMATIC OXIDATION

Polymeric biomaterials may be degraded by chemical and enzymatic oxidation when exposed to body fluids and tissues. It is well known that during inflammatory response to foreign materials, inflammatory cells, particularly leukocytes and macrophages are able to produce highly reactive oxygen species such as superoxide (O_2^-), hydrogen peroxide (H_2O_2), nitric oxide (NO), and hypochlorous acid (HOCl) (William and Zhong, 1994; Coleman, 2001 and Labow, 2002). The oxidative effect of these species may cause polymer chain scission and contribute to their degradation. Several studies have been carried out to assess the effect of oxygen species in the degradation of polymeric biomaterials (William and Zhong, 1994; Coleman, 2001; Labow, 2002; Lee and Chu, 2000). Lee and Chu, 2000; studied the role of superoxide in the degradation of absorbable sutures and found that O_2^- could accelerate the degradation of aliphatic polyesters by the cleavage of ester bonds via nucleophilic attack of O_2^-.

3.2 HYDROLYTIC DEGRADATION

This process occurs in polymers that have water sensitive active groups, especially those that take a lot of moisture. Polymers that have ability for hydrolytic destruction usually have heteroatom in the main or side chain. The scission of chemical functional groups by reaction with water is called hydrolysis. However, some polymers are very stable to this hydrolysis. Water absorbing plastics absorb water to varying degrees, depending on their molecular structure, fillers and additives which adversely affects both mechanical and electrical properties thus causing swelling (Siparky *et al.,* 1998). It is worthy of mention that exposing plastics to moisture at elevated temperature can lead to hydrolysis i.e. a chemical process that severs polymer chains by reacting with water. Thus, reducing the molecular weight and degrading the plastic.

Hydrolytic degradation can also be harmful and helpful in many cases, for example: hydrolytic chain scission of the ester linkage of polyester is the fastest and the most "harmful" degradation process, as it causes a considerable reduction in the molecular weight and in the mechanical properties of the polymer but the polymer degradation is useful for Controlled Drug Delivery System (Siparky *et al.,* 1998). For most biodegradable materials, especially synthetic polymers, passive hydrolysis is the most important kind of degradation. The hydrolysis in this case could be divided into enzymatic and non-enzymatic hydrolysis as shown below.

3.2.1 NON ENZYMATIC HYDROLYSIS

Polymer hydrolytic degradation may be defined as the scission of chemical bonds in the polymer backbone by the attack of water to form oligomers and finally monomers. In the first step, water contacts the water-labile bond, by either direct access to the polymer surface or by imbibition into the polymer matrix followed by bond hydrolysis. Hydrolysis reactions may be catalyzed by acids, bases, salts, or enzymes (William and Zhong, 1994). After implantation, the biomaterial absorbs water and swells, and degradation will progress from the exterior of the material toward its interior. All biodegradable polymers contain hydrolysable bonds, such as glycosides, esters, orthoesters, anhydrides, carbonates, amides, urethanes, ureas, etc. (Ratner, 1996; Gopferich, 1996 and William and Zhong, 1994). Polymers with strong covalent bonds in the backbone (like C-C) and with no hydrolysable groups require longer times to degrade (Ratner, 1996 and Hasirci, 2001).

3.2.2 ENZYME-CATALYZED HYDROLYSIS

Enzymes are biological catalysts, i.e., they accelerate the reaction rates in living organisms without themselves undergoing any permanent change. In fact, in the absence of enzymes, most of the reactions of cellular metabolism would not occur. Hydrolysis reactions may be catalyzed by enzymes known as hydrolases, which include proteases, esterases, glycosidases, and phosphatases, among others. This class of enzymes comprises cell-derived proteins that are responsible for the catalysis of several reactions in the human body. For example, hydrolytic enzymes are present in the plasma and interstitials in the brush border membrane and lumen of the gastro-intestinal tract and in the tubular epithelium of the kidneys, where they ensure the efficient hydrolysis of different substrates to facilitate absorption of nutrients and solutes (Shalaby and Park, 1994).

In this sense, it is expected that some of these enzymes may play an important role in the degradation of biomaterials by catalyzing their hydrolysis. It has been shown that the degree of biodegradation of polyurethanes, in the presence of cholesterol esterase enzyme, is about 10 times higher than in the presence of buffer alone (Santerre, 1994). This fact may explain the higher in vivo degradation rates of some biomaterials when compared with in vitro experiments. While some enzymes catalyze only one reaction involving only certain substrates, others are not very specific. This indicates that the degradation of synthetic polymers may also occur by enzymatic hydrolysis.

3.3 BIODEGRADATION BY MICRO ORGANISM

Extracellular and intracellular depolymerases enzymes are actively involved in biological degradation of polymers. During degradation, exoenzymes from micro organisms break down complex polymers yielding short chains or smaller molecules, e.g., oligomers, dimers, and monomers, that are smaller enough (water soluble) to pass the semi-permeable outer bacterial membranes and then to be utilized as carbon and energy sources (Gu, 2003). This initial process of polymer breaking down is called depolymerization. When the end products are inorganic species, e.g., CO_2, H_2O, or CH_4, the degradation is called mineralization. When O_2 is available, aerobic micro organisms are mostly responsible for destruction of complex materials with microbial biomass, CO_2, and H_2O as the final products. In contrast, in the absence of O_2 i.e. under anoxic conditions, anaerobic consortia of micro organisms are responsible for polymer deterioration.

4.0 APPLICATION OF SYNTHETIC BIODEGRADABLE POLYMERS

The significance of the application of synthetic biodegradable polymers cannot be over emphasized. Their application cut across many aspects of human endeavours. These include but not limited to automotive industry, agriculture, packaging and medical applications. Many materials that have been developed and commercialized are applied in more than one of these categories.

4.1 Biomedical Application of Synthetic Biodegradable Polymers

Polymers with controlled biomedical degradation characteristics can be used as an important part of tissue engineering and drug delivery therapies. Many types of natural and synthetic biodegradable polymers have been investigated for medical and pharmaceutical applications. While use of natural polymers, such as cellulose and starches, is still common in biomedical research, synthetic biodegradable polymers are increasingly used in pharmaceutical and tissue-engineering products. Synthetic polymers can be prepared with chemical structures tailored to optimize physical properties of the biomedical materials and with well-defined purities and compositions superior to those attainable when using natural polymers. Some of these biomedical applications of synthetic biodegradable polymers include (Nairs and Laurencin, 2007);

4.1.1 Medical devices

Synthetic biodegradable polymers have attracted considerable attention for applications in medical devices, and will play an important role in the design and function of medical devices. The general criteria of polymer materials used for medical devices include mechanical properties and a degradation time appropriate to the medical purpose. In addition, the materials should not evoke toxic or immune responses, and they should be metabolized in the body after fulfilling their tasks (Nairs and Laurencin, 2007). According to these requirements, various synthesized biodegradable polymers have been designed and used. Some of the synthetic biodegradable polymers that have been used or show potentials in selected fields are summarized below (Shalaby and Burg, 2003).

4.1.1.1 Drug-eluting stents (DES)

DES have been widely used as a default treatment for patients with coronary artery disease. Biodegradable polymers are always used as a biodegradable and bioresorbable coatings on stents to control the release of drugs (Kukreja et al., 2008). One of such stents coated

with polyurethane was used as drug control layers as reported by (Radeleff et al., 2009).

Besides being used as biodegradable coatings, biodegradable polymers are also candidate materials for fully biodegradable stents (Wykrzykowska et al., 2009) because of their suitable properties for controlled drug release and good mechanical performance to prevent stents from deforming or fracturing.

4.1.1.2 Orthopedic devices

In the 1960's, poly (glycolide) was used to prepare completely biodegradable and bioresorbable sutures. Since then, poly (glycolide), poly(lactide) and other materials such as poly(dioxanone), poly(trimethylene carbonate), PCL and poly [d,l-(lactide-co-glycolide)] have been widely used for medical devices (Meddleton and Tipton, 2000). Orthopedic devices made from biodegradable materials have advantages over metal or non degradable materials. They can transfer stress over time to the damaged area as it heals, allowing of the tissues, and there is no need of a second surgery to remove the implanted devices. Many commercial orthopedic fixation devices such as pins and rods for bone fracture fixation, and screws and plates for maxillofacial repair are made of PLLA, poly(glycolide) and other biodegradable polymers (Meddleton and Tipton, 2000 and Peltoniemi et al., 2002).

4.1.1.3 Disposable medical devices

In the 21st century, environmental factors concern all manufacturing industries. Many disposable medical devices, such as syringes, injection pipes, surgical gloves, pads, etc., are usually made of non-degradable plastics, resulting in serious environmental and economic issues. PLA, poly(glycolide), poly[d,l-(lactide-co-glycolide)] and PCL are all biodegradable. Therefore, they are promising materials for use in disposable medical devices meeting environmental friendly requirements. These biodegradable polymers have been used to prepare some disposable medical devices and will likely have a widening commercial application (Hutmacher et al., 1996; Ratner, 2004).

4.1.2 Surgical Use*:* Most of the applications of synthetic biodegradable polymers are for surgery and the largest and longest use is for suturing. Commercial polymers used for this purpose include polyglycolide, which is still the largest in volume production, together with a glycolide-L-lactide (90:10) copolymer (Gilding, 1981; and Benicewicz and Hopper, 1991). The sutures made from these glycolide polymers are of braid type processed from multi-filaments, but synthetic absorbable sutures of mono-filament type also at present are commercially available.

4.1.3 Pharmaceutical Use:

In order to deliver drugs to diseased sites in the body in a more effective and less invasive way, a new dosage form technology, called drug delivery systems (DDS), started in the late 1960's in the USA using polymers. The objectives of DDS include sustained release of drugs for a desired duration at an optimal dose, targeting of drugs to diseased sites without affecting healthy sites, controlled release of drugs by external stimuli, and simple delivery of drugs mostly through skin and mucous membranes. Polymers are very powerful for this new pharmaceutical technology. If a drug is administered through a parenteral route like injection, the polymer used as a drug carrier should be preferably absorbable, because the polymer is no longer required when the drug delivery has been accomplished. Therefore, biodegradable polymers are widely used, especially for the sustained release of drugs through administration by injection or implantation into the body. For this purpose, absorbable nanospheres, microspheres, beads, cylinders, and discs are prepared using biodegradable polymers (Lewis, 1990; Leong, 1991 and Asano et al., 1990).

4.1.4 Use for Tissue Engineering:

Tissue engineering is an interdisciplinary field that applies the principles of engineering and life sciences towards the development of biological substitutes used to restore, maintain or improve tissue functions (Langer and Vacanti, 1993; and Place et al., 2009). The main purpose of tissue engineering is to overcome the lack of tissue donors and the immune repulsion between receptors and donors. In the process of tissue engineering, cells are cultured on a scaffold to form a natural tissue, and then the formed tissue is implanted in the defect part in the patient's body. In some cases, a scaffold or a scaffold with cells is implanted in vivo directly, and the host's body works as a bioreactor to construct new tissues (Place et al., 2009).

A successful tissue engineering implant largely depends on the role played by three-dimensional porous scaffolds. The ideal scaffolds should be biodegradable and bioabsorbable to support the replacement of new tissues. In addition, the scaffolds must be biocompatible without inflammation or immune reactions and possess proper mechanical properties to support the growth of new tissues.

4.1.5 Gene delivery

Gene delivery has great potential for treating various human diseases (Merdan, 2002). Recently, non viral vectors have been proposed as safer alternatives to viral vectors for gene delivery (Cook et al., 2005). However, many carriers are non-degradable and the risk arises of accumulation in the body, especially after repeated administration. Furthermore, most cationic polymers show high cytotoxicity because of adverse interactions between the cationic polymers and the membranes when the gene carriers cross certain barriers to enter the cells (Wong et al., 2007) causing loss of cytoplasmic proteins, permeabilization of cellular membranes and collapse of the membrane potential (Fischer, 2003).

Design requirements for gene delivery systems include the ability to (I) package therapeutic genes, (II) gain entry into cells, (III) escape from the endo-lysosomal pathway, (IV) affect DNA/vector release, (V) travel through the cytoplasm and into the nucleus, and (VI) enable gene expression (Wong et al., 2007).

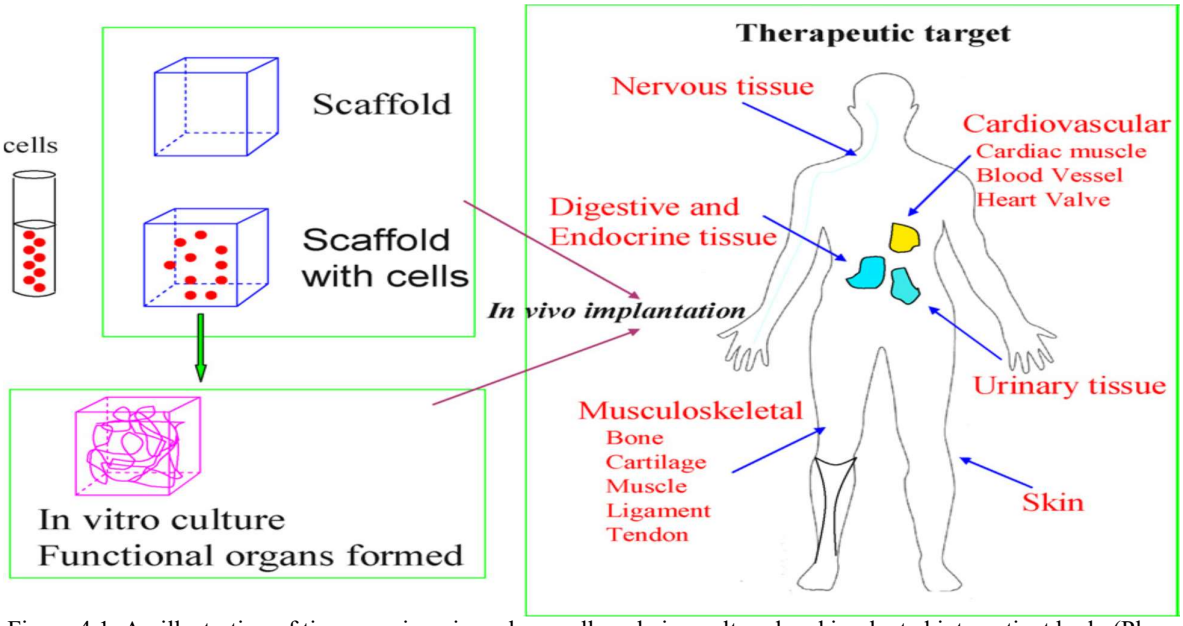

Figure 4.1: An illustration of tissue engineering where cell are being cultured and implanted into patient body (Place et al., 2009).

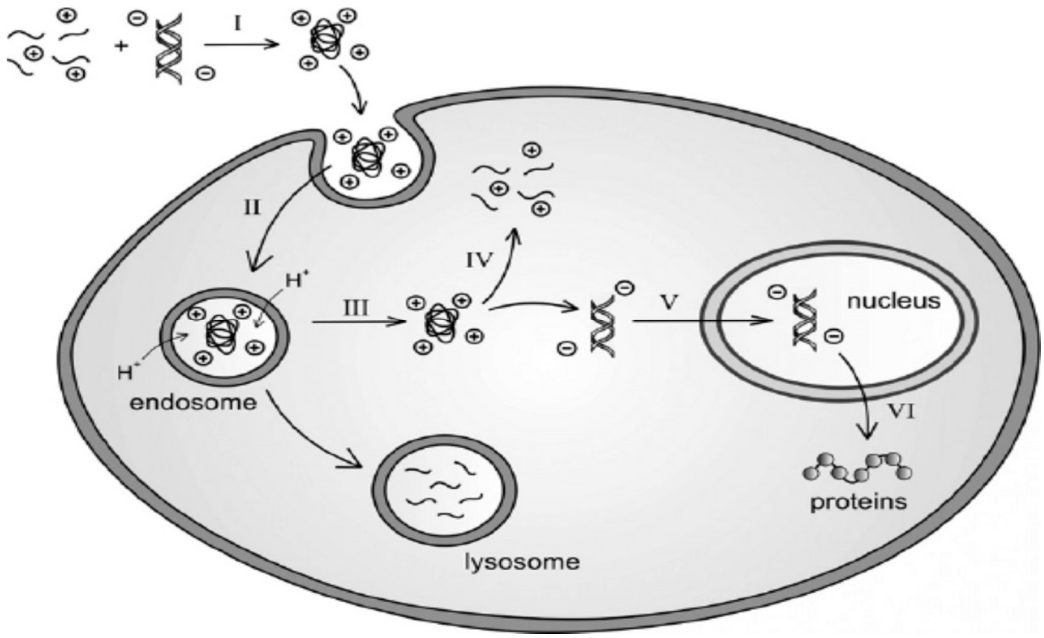

Figure 4.2: An illustration of barriers to gene delivery (Wong et al., 2007) and Fischer, 2003).

4.2 Agricultural Application

One of the major areas of application of synthetic biodegradable polymers in agriculture is mulching (Feuilloley, 1999). Mulching is a current operation that consists of covering the soil with a film in order to improve cultural condition such as:

I. Protection against weed and cost reduction for weed killing.
II. Limitation of moisture evaporation and
III. Protection against plant diseases

4.3 Industrial Application

Industrially, synthetic biodegradable polymers are used in producing packaging materials and even in compostable bags. These help to solve the environmental problem of blockage of waterways and even littering the environment since the material will degrade on its own by virtue of the biotic factors such as light, rainfall, temperature, pressure (Andreopoulos, 1994).

4.4 Ecological applications

The other major application of biodegradable polymers is in plastic industries to replace biostable plastics for maintaining healthy environments. The first choice for processing of plastic wastes is reuse, but only some plastic products can be re-used after adequate processing, and many of them are very difficult to recycle. In this case, wastes are processed by landfill or incineration, but these processes often pollute the environments. If biodegradation by-products do not exert adverse effects on animals and plants on the earth, biodegradable plastics can be regarded as environmentally friendly or ecological materials. Therefore, much attention has been focused on manufacturing biodegradable plastics which, however, should address several requirements. They are to be low in product cost, satisfactory in mechanical properties, and not harmful to animals and plants when biodegraded (Boustead, 1998; Bastioli, 1998; Chua and Yu, 1999).

CONCLUSION

Synthetic biodegradable polymers in general are of greater advantage over natural materials in that they can be tailored to give a wider range of properties and have more predictable lot-to-lot uniformity than materials from natural sources. When compared to biologically derived biodegradable polymers, synthetic biodegradable polymers do not have immunogenicity, rather it is easier for them to be chemically modified and functionalized. Functionalization of synthetic biodegradable polymers has extended the application scope for these biomaterials and has greatly promoted the development in the biomedical field. In view of these developments, numerous synthetic biodegradable polymers are available and still being developed for sustained and targeted drug delivery applications since they have proven their potential for the development of new, advanced and efficient drug delivery system and capable of delivering a wide range of bioactive materials.

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