SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 4.
Issue: 3.
Page N. 156-163
Year: 2020

Review Article www.wjahr.com

BIO-DEGRADABLE POLYMER: VARIETY AND APPLICATION

Prof. S. K. Mahapatra[1], Malay Ranjan Mahanta*[2], Dr. B. Ray[2]

[1]IPT, Salipur, Odisha.
[2]GCP, Sambalpur, Odisha.

Received date: 28 March 2020 **Revised date:** 18 April 2020 **Accepted date:** 08 May 2020

***Corresponding author: Malay Ranjan Mahanta**
Gayatri College of Pharmacy, Sambalpur, Odisha.

ABSTRACT

Polymers have become an indispensable part of the drug delivery systems, be it be conventional drug delivery or novel drug delivery. They have drastically changed the mode of drug delivery by introducing lot of flexibility. Among the different types of polymers, biodegradable polymers have an edge over the non-biodegradable ones because of the advantage of obviating the need to remove the device after its depletion. The present article deals with variety of Such polymer with its Special Application.

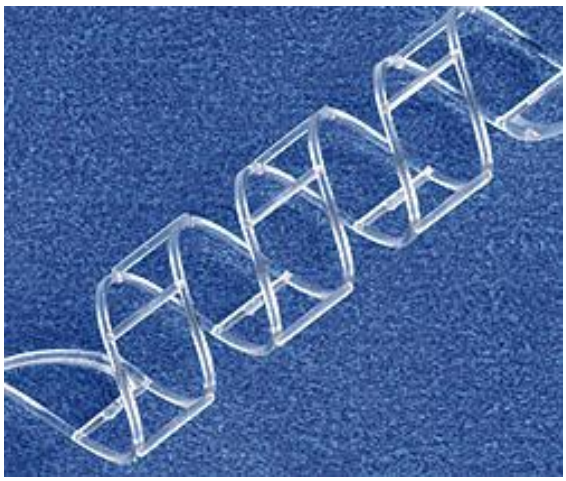
KEYWORD: Polymer, Poly lactide, Collagen, Chitosan.

1. INTRODUCTION

Polymers have become an indispensable part of the drug delivery systems, be it be conventional drug delivery or novel drug delivery. They have drastically changed the mode of drug delivery by introducing lot of flexibility. Polymers have taken a long stride from oral controlled release dosage forms to polymeric stents, implants, microchips etc.

The application of drug delivery is a valuable, cost effective life-cycle management resource. With more than 50 patents expiring by 2005, which includes a number of blockbuster drugs, pharmaceutical companies are recognizing drug delivery technology, which is based on the use of polymer, as a powerful strategic marketing tool to differentiate products. This enables them to extend product life cycle and remain competitive in the marketplace. By infusing drugs with new and innovative therapeutic benefits, drug delivery systems extend products profitable life cycle, giving pharmaceutical companies competitive and financial advantages and providing patients with improved medications. The growth rate for drug delivery systems is expected to increase 14% annually over the next five years.

Among the different types of polymers, biodegradable polymers have an edge over the non-biodegradable ones because of the advantage of obviating the need to remove the device after its depletion. In the first half of this century, research into materials synthesized from glycolic acid and other α-hydroxy acids was abandoned for further development because the resulting polymers were too unstable for long-term industrial uses. However, this very instability—leading to biodegradation—has proven to be immensely important in medical applications over the last three decades. Polymers prepared from glycolic acid and lactic acid have found a multitude of uses in the medical industry, beginning with the biodegradable sutures first approved in the 1960s. Since that time, diverse based on lactic and glycolic acid-and on other materials, including poly (dioxanone), poly (trimethylene carbonate) copolymers, and poly (ε-caprolactone) homopolymers and copolymers-have been accepted for use as medical devices. In addition to these approved devices, a great deal of research continues on polyanhydrides, polyorthoesters, polyphosphazenes, and other biodegradable polymers.

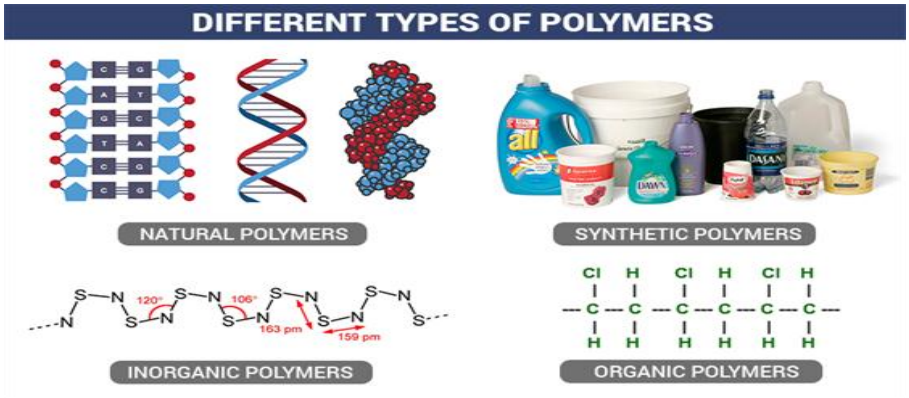


A biodegradable intravascular stent prototype is molded from a blend of polylactide and trimethylene carbonate.[1]

Types of Polymers

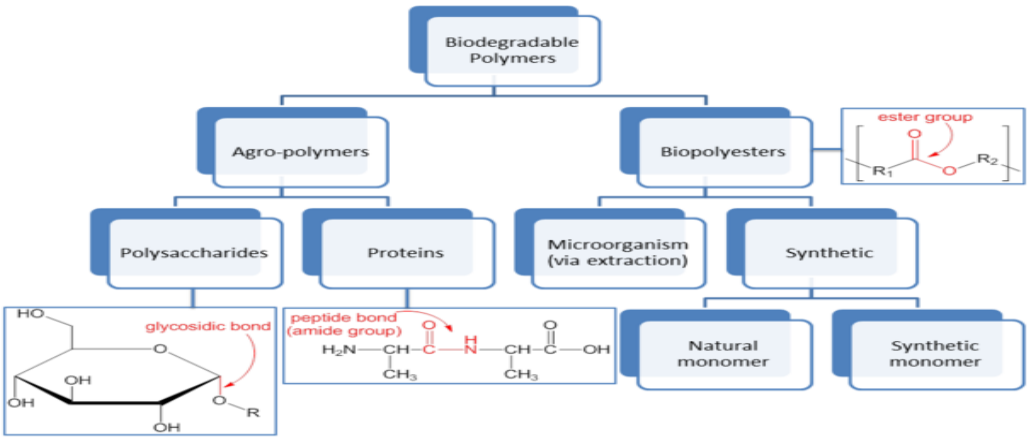
On the basis of the type of the backbone chain, polymers can be divided into

- Organic Polymers: Carbon backbone.
- Inorganic Polymers: Backbone constituted by elements other than carbon.



Polymers are most versatile class of materials and are widely used in pharmaceutical, medical, biomedical engineering, food, and cosmetic industry8,9. Biodegradable polymers are the youngest member of polymer family and find widespread use in drug delivery as they can be degraded to non-toxic monomers inside the body thus obviate the need to remove the drug delivery system (DDS). The introduction of the synthetic polymer based DDS led to heightened interest in the design and synthesis of novel biodegradable polymeric systems.[2,3]

2. Biodegradable Polymers



A variety of natural, synthetic, and biosynthetic polymers are bio- and environmentally degradable. A polymer based on the C-C backbone tends to be nonbiodegradable, whereas heteroatom-containing polymer backbones confer biodegradability. Biodegradability can therefore be engineered into polymers by the judicious addition of chemical linkages such as anhydride, ester, or amide bonds, among others.[4,5]

Advantages of biodegradable system in comparison to non-degradable system

- It does not require surgical removal even after it has delivered the drug contained in it.
- There break down products are natural, bio-compatible which overcomes the problem of toxicity.
- Release rate is less dependent on the drug properties.
- The release rate may be more steady with time.
- Biodegradable systems may be more suitable to the delivery of unstable drugs.

Figure 1 provides a schematic representation of the types of polymer degradation. The mechanism for degradation is by hydrolysis or enzymatic cleavage resulting in a scission of the polymer backbone. Macro organisms can eat and, sometimes, digest polymers, and also initiate a mechanical, chemical, or enzymatic aging.[5,6]

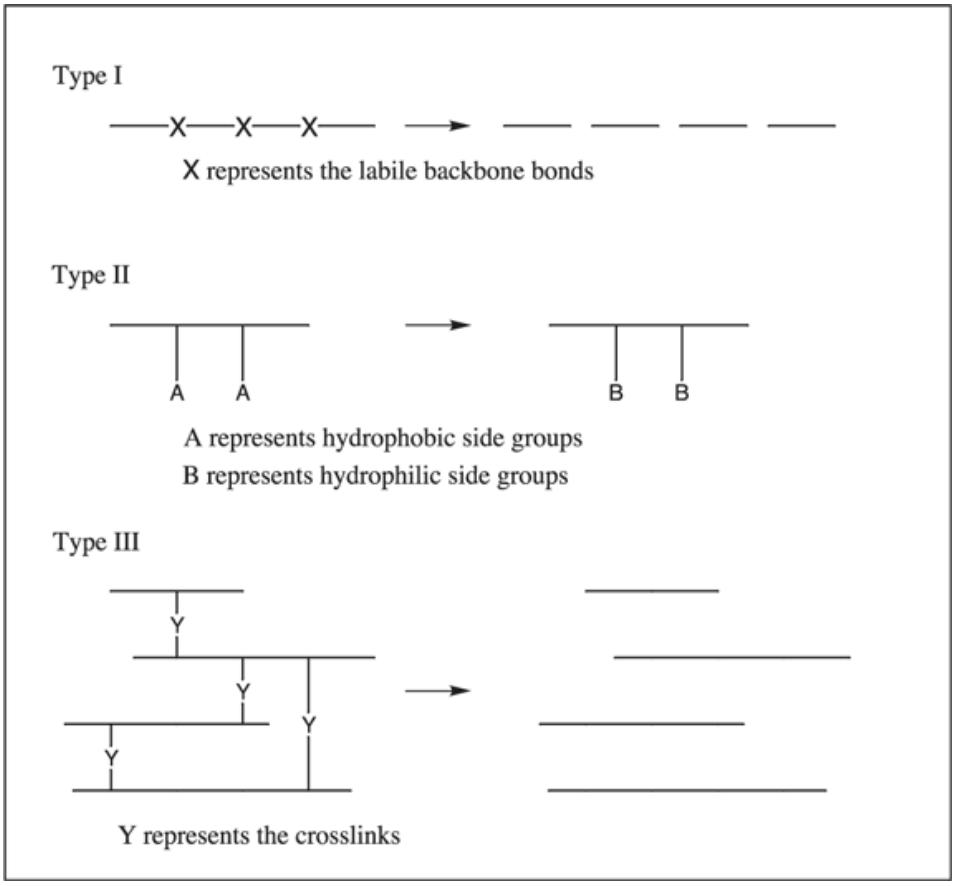


Figure 1: Schematic representation of the types of polymer degradation.

Biodegradable polymers can be either natural or synthetic. In general, synthetic polymers offer greater advantages than natural materials in that they can be tailored to give a wider range of properties and more predictable lot-to-lot uniformity than can materials from natural sources. Synthetic polymers also represent a more reliable source of raw materials, one free from concerns of immunogenicity.[7,8]

The general criteria for selecting a polymer for use as a biomaterial is to match the mechanical properties and the time of degradation to the needs of the application The ideal polymer for a particular application would be configured so that it:

- Has mechanical properties that match the application, remaining sufficiently strong until the surrounding tissue has healed
- Does not invoke an inflammatory or toxic response.
- Is metabolized in the body after fulfilling its purpose, leaving no trace.
- Is easily processable into the final product form.
- Demonstrates acceptable shelf life.
- Is easily sterilized

Biodegradation has been accomplished by synthesizing polymers that have hydrolytically unstable linkages in the backbone. The most common chemical functional groups with this characteristic are esters, anhydrides, orthoesters, and amides. We will discuss the importance of the properties affecting biodegradation later.[9,10]

The following section presents an overview of the synthetic biodegradable polymers that are currently being used or investigated for use in wound closure (sutures, staples); orthopedic fixation devices (pins, rods, screws, tacks, ligaments); dental applications (guided tissue regeneration); cardiovascular applications (stents, grafts); and intestinal applications (anastomosis rings). Most of the commercially available biodegradable devices are polyesters composed of homopolymers or copolymers of glycolide and lactide. There are also devices made from copolymers of trimethylene carbonate and ε-caprolactone, and a suture product made from polydioxanone.

polyglycolide (PGA): Polyglycolide is the simplest linear aliphatic polyester. PGA was used to develop the first totally synthetic absorbable suture, marketed as Dexon in the 1960s by Davis and Geck, Inc. (Danbury, CT).[11]

Polylactide (PLA): Lactide is the cyclic dimer of lactic acid that exists as two optical isomers, d and l. l-lactide is the naturally occurring isomer, and dl-lactide is the synthetic blend of d-lactide and l-lactide. The homopolymer of l-lactide (LPLA) is a semicrystalline polymer.[12]

Poly (lactide-co-glycolide): Using the polyglycolide and poly (l-lactide) properties as a starting point, 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.

Poly (dioxanone) (a polyether-ester): The ring-opening polymerization of p-dioxanone) resulted in the first clinically tested monofilament synthetic suture, known as PDS (marketed by Ethicon).[13]

Poly(ε-caprolactone): The ring-opening polymerization of ε-caprolactone yields a semicrystalline polymer with a melting point of 59—64°C and a glass-transition temperature of —60°C . The polymer has been regarded as tissue compatible and used as a biodegradable suture in Europe. Because the homopolymer has a degradation time on the order of 2 years, copolymers have been synthesized to accelerate the rate of bio-absorption.[14]

Polyanhydrides have been synthesized via the dehydration of diacid molecules by melt polycondensation. Degradation times can be adjusted from days to years according to the degree of hydrophobicity of the monomer selected. The materials degrade primarily by surface erosion and possess excellent in vivo compatibility. So far, they have only been approved for sale as a drug delivery system. The Gliadel product, designed for delivery of the chemotherapeutic agent BCNU in the brain, received regulatory clearance from FDA in 1996 and is being produced by Guilford Pharmaceuticals, Inc. (Baltimore).[15,16]

Polyorthoesters: Polyorthoesters first investigated in the 1970s by Alza Corp. (Palo Alto, CA) and SRI International (Menlo Park, CA) in a search for new synthetic biodegradable polymers for drug delivery applications.

Polyurethanes (PU) represent a major class of synthetic elastomers that have been evaluated for a variety of medical implants, particularly for long-term implants. They have excellent mechanical properties and good biocompatibility. They are used in the fabrication of medical implants such as cardiac pace makers and vascular grafts.

Polyphosphazenes

The polyphosphazenes consist of several hundred different polymers with the general structure. Different polyphosphazenes are made by means of macromolecular substitution reactions carried out on a reactive polymeric intermediate, poly (dichlorophosphazene), (NPCl2)n. Although most polyphosphazenes are biostable, incorporation of specific side groups such as amino acid esters, glucosyl, glyceyl, lactate,or imidazolyl units can render polyphosphazenes biodegradable.[11]

Tyrosine-derived polycarbonates

Tyrosine-based polycarbonates have been reported as promising degradable polymers for use in orthopedic applications. These polymers possess three potentially hydrolysable bonds: amide, carbonate and ester. Studies have shown that the carbonate group hydrolyzes at a faster rate than the ester group, and the amide bond is not labile in vitro. Since the hydrolysis of the carbonate groups yields two alcohols and carbon dioxide, the problem of acid bursting seen in polyesters is alleviated.[17]

Natural polymers

Collagen: Because of its unique structural properties, has been fabricated into a wide variety of forms including meshes, fibers, sponge wound dressings, absorbable sutures and injectables for facial reconstructive surgery.

Its characteristics as biomaterial offer several advantages: it is biocompatible and nontoxic in most tissues; it is readily isolated and purified in large quantities; it has well documented structural, physical, chemical properties and it can be processed into a variety of forms.[15]

Hyaluronic acids a linear polysaccharide found in the highest concentrations in soft connective tissues. It has been used in ophthalmic preparations to enhance ocular absorption of timolol.

Chitosan is a technologically important biomaterial. Chitin is the second most abundant natural polymer in the world after cellulose. Upon deacetylation, it yields the novel biomaterial Chitosan, which upon further hydrolysis yields an extremely low molecular weight oligosaccharide. Specifically, it is a biocompatible, antibacterial and environmentally friendly polyelectrolyte, thus lending itself to a variety of applications including water treatment, chromatography, additives for cosmetics, textile treatment for antimicrobial activity, novel fibers for textiles, biodegradable films, biomedical devices, and microcapsule implants for controlled release in drug delivery.[18,19]

Degradation

Once implanted, a biodegradable device should maintain its mechanical properties until it is no longer needed and then be absorbed and excreted by the body, leaving no trace. Simple chemical hydrolysis of the hydrolytically unstable backbone is the prevailing mechanism for the polymer's degradation. This occurs in two phases. In the first phase, water penetrates the bulk of the device, preferentially attacking the chemical bonds in the amorphous phase and converting long polymer chains into shorter water-soluble fragments. Because this occurs

in the amorphous phase initially, there is a reduction in molecular weight without a loss in physical properties, since the device matrix is still held together by the crystalline regions. The reduction in molecular weight is soon followed by a reduction in physical properties, as water begins to fragment the device (see Figure). In the second phase, enzymatic attack and metabolization of the fragments occurs, resulting in a rapid loss of polymer mass. This type of degradation-when the rate at which water penetrates the device exceeds that at which the polymer is converted into water-soluble materials (resulting in erosion throughout the device)-is called bulk erosion. All of the commercially available synthetic devices and sutures degrade by bulk erosion.[20]

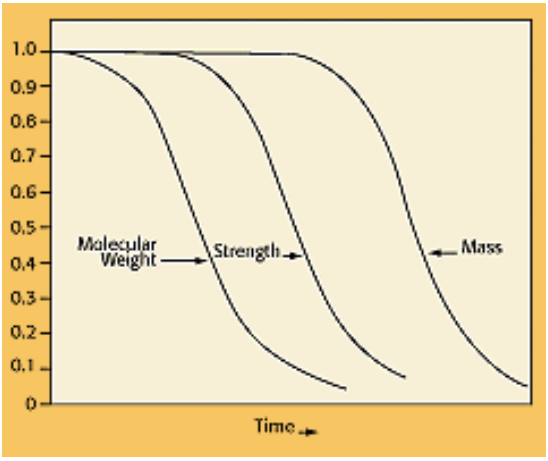


Figure 11: Generic absorption curves showing the sequence of polymer molecular weight, strength, and mass reduction.

Applications

In some cases—as, for example, polylactides, polyglycolides, and their copolymers—the polymers will eventually break down to lactic acid and glycolic acid, enter the Kreb's cycle, and be further broken down into carbon dioxide and water and excreted through normal processes. Degradation may take place through bulk hydrolysis, in which the polymer degrades in a fairly uniform manner throughout the matrix, as shown schematically in Figure.[21]

Polymer	Application and comment
	NATURAL POLYMERS
Proteins and protein-based Polymers	Absorbable, biocompatible, nontoxic, naturally available, typically elastic materials used as implants and in tissue engineering.
Collagen	Absorbable sutures, sponge wound dressing, drug delivery microspheres.
	From human and animal sources
Hyaluronic acid agent	Excellent lubricant, potential therapeutic

Chitosan and its derivatives	Biocompatible, nontoxic, excellent gel- and film-forming ability, natural polycation. Widely used in controlled-delivery systems (e.g. gels, membranes, microspheres).
	SYNTHETIC POLYMERS
Aliphatic polyesters	
Poly (lactic acid), Poly (glycolic acid) And their copolymers	Used in sutures, drug-delivery systems and in tissue engineering. Biodegradable, often copolymerized to regulate degradation time.
Poly (hydroxy butyrate), poly (e-caprolactone) and copolymers	Biodegradable, used as a matrix for drug-delivery systems, cell-microencapsulation. Properties can be Changed by chemical modification, copolymerization and blending.
Polyamides (nylons)	Sutures, dressing, haemofiltration membranes.
Polyanhydrides	Biodegradable, useful in tissue engineering and for the release of the bioactive molecules.
Poly (ortho esters)	Surface-eroding polymers. Application in sustained drug delivery, ophthalmology.
Poly (cyano acrylates)	Biodegradable, depending on the length of the alkyl chain. Used as surgical adhesives and glues, potentially used in drug delivery.
Polyphosphazenes	Can be tailored with versatile side-chain functionality. Made into films and hydrogels. Applications in drug delivery.
Thermoplastic Polyurethanes	Good elastomeric properties. Can be tailored by varying the starting materials. Used in permanently implanted medical devices (prostheses, vascular grafts), catheters and drug delivery systems. Initial candidates for the artificial heart

Commercial Biodegradable Devices

Sutures: While comprising the lion's share of the total medical biodegradables market in 1995, this is a mature area not expected to grow rapidly in the future. About 125 million synthetic bioabsorbable sutures are sold each year in the United States. They are divided into braided and monofilament categories. Braided sutures are typically more pliable than monofilament and exhibit better knot security when the same type of knot is used. Monofilament sutures are more wiry and may require a more secure knot. Their major advantage is that they exhibit less tissue drag, a characteristic that is especially important for cardiovascular, ophthalmic, and neurological surgeries.[11]

Dental Devices: Biodegradable polymers have found use in two dental applications. Employed as a void filler following tooth extraction, porous polymer particles can

be packed into the cavity to aid in quicker healing. As a guided-tissue-regeneration (GTR) membrane, films of biodegradable polymer can be positioned to exclude epit.[22]

Orthopedic Fixation Devices: Orthopedic fixation devices made from synthetic biodegradable polymers have advantages over metal implants in that they transfer stress over time to the damaged area, allowing healing of the tissues, and eliminate the need for a subsequent operation for implant removal. helial migration following periodontal surgery.[23]

Intraoccular Implant

From the time of placement into the eye, the DDS delivers the drug at a controlled rate for the designed time interval that may range from days to months. After delivering the drug, the system degrades and is completely absorbed. No removal is required. Due to the system's built-in controlled and sustained release mechanism the drug concentration levels are non-fluctuating and can be designed to stay in the therapeutic range.[24,25]

REFERENCE

1. John C. Middleton and Arthur J. Tipton page, [1].
2. Baker, R. W., Controlled Release of Biologically Active Agents, John Wiley & Sons, New York, 1987.
3. Sayed, H.A. and Price, J.C., Tablet properties and dissolution characteristic of compressed cellulose acetate butyrate microcapsules containing succinyl sulfathiazole, Drug Dev. Ind. Pharm, 1986; 12: 577.
4. Lucas N., Bienaime C., Belloy C., Queneudec M., Silvestre F, Nava-Saucedo J.E. Polymer biodegradation: mechanisms and estimation techniques.Chemosphere, 2008; 73: 429442. doi:10.1016/j.chemosphere.2008.06.064. [PubMed] [CrossRef] [Google Scholar].
5. Willett J.L. Mechanical properties of LDPE/granular starch composites. J.Appl. Polym. Sci., 1994; 54: 16851695. doi:10.1002/app.1994.070541112. [CrossRef] [Google Scholar]
6. Gil ES, Hudson SA. Stimuli-reponsive polymers and their bioconjugates. Prog. Polym. Sci., 2004; 29(12): 1173–222. [Google Scholar]
7. Schmaljohann D. Thermo- and pH-responsive polymers in drug delivery. Adv. Drug Deliv. Rev., 2006; 58(15): 1655–70. [PubMed] [Google Scholar]
8. Colombo P, Bettini R, Santi P, Peppas NA. Swellable matrices for controlled drug delivery:gellayer behaviour, mechanisms and optimal performance. Pharm. Sci.Technol. Today., 2000; 3(6): 198–204. [PubMed] [Google Scholar]
9. Mayersohn M. Principles of drug absorption. In: Florence AT, Siepmann J, editors. Modern Pharmaceutics. 5th ed Informa Healthcare; New York, 2009; 23–80. [Google Scholar]
10. Schmaljohann D. Thermo- and pH-responsive polymers in drug delivery. Adv. Drug Deliv. Rev., 2006; 58(15): 1655–70. [PubMed] [Google Scholar]
11. Nair L.S., Laurencin C.T. Biodegradable polymers as biomaterials. Progr. Polym. Sci., 2007; 32: 762–798. doi: 10.1016/j.progpolymsci.2007.05.017. [CrossRef] [Google Scholar]
12. Maharana T.,Mohanty B.,Negi Y.S. Melt-solid polycondensation of lactic acid and its biodegradability. Progr.Polym.Sci., 2009; 34: 99124. doi:10.1016/j.progpolymsci.2008.10.001. [CrossRef] [Google Scholar]
13. Yang K.K., Wang X.L., Wang Y.Z., Huang H.X. Effects of molecular weights of poly(p-dioxanone) on its thermal rheological and mechanical properties and *in vitro* degradability. Mater. Chem. Phys., 2004; 87: 218–221. doi:10.1016/j.matchemphys.2004.05.038.[CrossRef] [GoogleScholar]
14. Mochizuki M., Hirami M. Structural effects on biodegradation of aliphaticpolyesters. Polym.Adv.Technol, 1997; 8: 203. doi:10.1002/(SICI) 10991581(199704)8:4<203::AIDPAT627>3.0.CO;2-3.[CrossRef] [Google Scholar]
15. Chandra R., Rustgi R. Biodegradable polymers. Progr. Polym. Sci., 1998; 23: 1273–1335. doi:10.1016/S0079-6700(97)00039-7.[CrossRef] [Google Scholar]
16. Tokiwa Y., Suzuki T. Hydrolysis of polyesters by lipases. Nature, 1977; 270: 76–78. doi:10.1038/270076a0. [PubMed] [CrossRef] [Google Scholar]
17. H. Wieser, Chemistry of gluten proteins, Food Microbiology 24, 2007; 115–119.
18. Gao C., Stading M., Wellner N. Plasticization of a protein-based film by glycerol: A spectroscopic,mechanical, and thermal study. J. Agric. Food Chem, 2006; 54: 4611–4616. doi:10.1021/jf060611w.[PubMed] [CrossRef] [Google Scholar]
19. Song Y.,Zheng Q.Improved tensile strength of glycerol-plasticized gluten.Bioresour.Technol, 2008; 99: 76657671. doi:10.1016/j.biortech.2008.01.075.[PubMed] [CrossRef] [Google Scholar]
20. Tamada JA, Langer R. Erosion kinetics of hydrolytically degradable polymers. Proc. Natl. Acad.Sci. USA., 1993; 90(2): 552–56. [PMC free article] [PubMed] [Google Scholar]
21. Park K, Shalaby W, Paark H. Biodegradable Hydrogels for Drug Delivery. Technomic; Lancaster, PA, 1993. [Google Scholar]
22. R.H. Roydhouse, Introduction to Polymers, in *Dental Materials: Properties and Selection*, W.J. O'Brien, Quintessence, Chicago.Google Scholar, 1989.
23. Agrawal, C.M., Niederauer, G.G., Micallef, D.M. and Athanasiou, K.A., Chapter 30: The use of PLA-PGA polymers in orthopaedics, in

Encylopedic Handbook of Biomaterials and Bioengineering. 1995, Marcel Dekker: N.Y., 2081–2115. Google Scholar

24. Mostafavi N, Ataei B, Nokhodian Z, Monfared LJ, Yaran M, Ataie M, et al. Toxoplasma gondii infection in women of childbearing age of Isfahan, Iran: A population-based study. Adv Biomed Res., 2012; 1: 60. [PMC free article] [PubMed] [Google Scholar]