Biodegradable Polymers

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Abstract Biodegradable polymers are a rapidly growing field driven by increasing concerns about plastic waste and its environmental impact. Polymers prepared from inexpensive and renewable raw materials might be the perfect alternative to plastics, and the properties like biodegradability and biocompatibility make them suitable for various biomedical applications. The biodegradability of the polymers is controllable by altering the monomer concentration and adding hydrolytically degradable groups in the polymeric backbone. These biopolymers can provide a safe and effective way of preparing devices/implantable materials for various biomedical applications. This chapter discusses biodegradable polymers, their synthesis, biodegradability, biocompatibility, along with their advantages and disadvantages for various biomedical applications, including drug delivery and tissue engineering.

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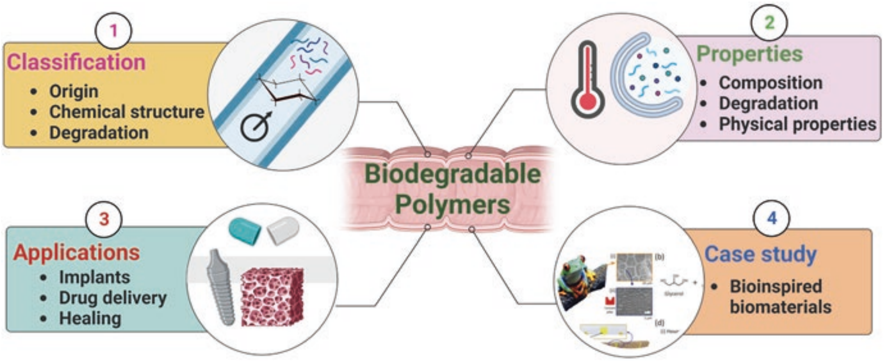
Graphical Abstract



Keywords Classification · Natural versus synthetic polymers · Degradation mechanisms · Biomedical applications

1 Overview

Polymer usage has soared dramatically over other materials due to various potential applications and the ease with which novel compositions with radically different properties can be designed. Modern alchemists have disassembled and repurposed hydrocarbons to create hundreds of compounds in the plastics family [1]. Synthetic chemicals, particularly petroleum-based products, are non-biodegradable and pose significant ecological risks, resulting in severe environmental contamination from waste buildup caused by manufacturing and incineration. For a period, the plastics industry seemed to be a boon and more beneficial to society, but its over usage resulted in devastating consequences on the natural environment and created a massive imbalance in the ecosystem. It is essential to explore alternatives like synthetic polymers to create a superior path in the form of natural polymers.

Recent decades have seen a rise in the need for environment-friendly products that encourage the development of biodegradable properties in past times. Biodegradable formulations are products or materials made from natural ingredients that readily degrade into non-toxic compounds when exposed to water, air, and microbes. These exposures will result in the breakdown of these materials into smaller components. They are typically made from renewable resources and are an alternative to conventional, non-degradable plastics. Biodegradable formulations can be incorporated into biodegradable plastics, agricultural products, and personal care products [2]. Biopolymers constructed from lipids, polysaccharides, DNA, and proteins are low cost and can be utilized from renewable raw materials. They also have a promising alternative to non-biodegradable plastic petroleum products [3].

Biopolymers market sales growth is very modest yet expanding. Due to their excellent biocompatibility and biodegradability properties, many of these materials are preferred over synthetic polymers in the medical, agricultural, engineering, and textile industries. Polysaccharides, like other biopolymers obtained from natural sources, have a wide range of possible applications due to their lack of toxicity and biodegradability. Among polysaccharides, cellulose is the most common polymer. Bio polysaccharides may be derived from a variety of sources, including plants (such as starch and pectin), animals (such as chitin/chitosan), and even microorganisms (e.g., bacterial cellulose). Hence, using microorganisms to manufacture biobased polymers has become more common. Silk is a biodegradable and biocompatible natural protein-based fiber, rendering it suitable as a biodegradable polymer. Silk fibers are intriguing for use in various applications, such as nanomedicine, and drug delivery systems, due to their distinctive features, which include high strength, flexibility, and biodegradability. Silk was developed as a suture material, which fueled the development of bio-based polymers [4]. DNA, the genetic material that carries the instructions for the development and function of all living organisms, has been explored as a potential biomaterial for various applications. One of the primary reasons DNA is being studied as a biomaterial is its ability to self-assemble into complex structures. Researchers have created various three-dimensional structures by manipulating the base-pairing interactions between DNA molecules, including nanostructures and scaffolds. These DNA-based structures have potential applications in drug delivery, tissue engineering, and biosensors. For example, DNA scaffolds can be used to support the growth of cells, while DNA nanoparticles can be designed to deliver drugs to specific target cells in the body [5].

The following are key characteristics of biodegradable polymers [6].

1.1 Composition

Biodegradable polymers are made from renewable resources such as corn, sugarcane, and potato. The most common biodegradable polymers include polylactic acid (PLA), polyhydroxyalkanoates (PHA), and starch-based polymers.

1.2 Degradability

The degradation rate can vary depending on the polymer composition and the environment in which it is exposed. Usually, the biodegradable property is calculated by the time required by the natural polymer to degrade completely into a relatively smaller compound. Microorganisms degrade natural polymers like cellulose, starch, and chitin rapidly. Whereas chemically derived biodegradable polymers like PLA and PHAs need specific environmental conditions, such as temperature, humidity, and oxygen, to affect polymer degradation. pH, moisture, and high-oxygen conditions may enhance biodegradable polymer degradation. The size of the polymer chain also plays a role in its degradability. Microorganisms can more easily break down smaller polymer chains.

1.3 Physical Properties

The physical properties of biodegradable polymers may differ depending on the source and the processing conditions. The glass transition temperature (Tg) of the polymer affects its mechanical properties and the stability of the payload (drug or other biomolecules) in the delivery system. Polymers with a high Tg tend to be brittle and have low flexibility, whereas polymers with a low Tg are more flexible and have a higher drug-loading capacity. The degree of crystallinity of the polymer affects its mechanical properties and the drug release rate. Highly crystalline polymers tend to have slower drug release rates compared to amorphous or semi-crystalline polymers. The surface area of the polymer affects its degradation rate and drug release rate. Polymers with a higher surface area tend to have faster degradation and drug release rates.

1.4 Applications

Biodegradable polymers are used in various applications. So, the design and properties of biopolymers should be varied based on their application and usage. They can be used as a substitute for conventional plastics in products such as bags, food containers, and disposable cutlery. Depending on the application, the properties of the biopolymer like its elasticity, durability, reliability, and sheer and tear stress level should be optimized.

2 Synthesis of Biodegradable Polymers

These polymers can be synthesized using polymerization techniques such as ring-opening polymerization, ring-opening copolymerization, and step-growth polymerization. Polycondensation is a reaction between two monomers to form a polymer chain, releasing a small molecule such as water as a byproduct. An example of a biodegradable polymer synthesized by polycondensation is polylactic acid (PLA). Copolymerization is the process of polymerizing two or more different monomers to form a copolymer, which can have unique properties compared to individual polymers. An example of a biodegradable copolymer is poly(butylene succinate-co-adipate) (PBSA). In addition, blending is a simple method of producing biodegradable polymers. It involves mixing two or more polymers to build a new material with improved properties. In the grafting technique, a biodegradable polymer is grafted onto another polymer to improve its properties. Other crosslinking methods are used to chemically bond the polymer chains to produce a three-dimensional network. This enhances the material's strength and stability. Different chemical and physical methods are used for modifying polymeric materials to improve their properties and performance. For example, adding hydrolytically degradable groups, crosslinking, and modifying the surface can enhance the biodegradability of the polymer[7].

Biodegradable polymers can be classified based on their origin, chemical structure, and degradation mechanisms.

2.1 Based on Origin

(a) Natural biodegradable polymers: These occur naturally in plants and animals. Examples include cellulose, chitin, and collagen.
(b) Synthetic biodegradable polymers: These are synthesized in the laboratory using petrochemicals or renewable resources. Examples include polylactic acid (PLA), polyglycolic acid (PGA), and polyhydroxyalkanoates (PHAs).

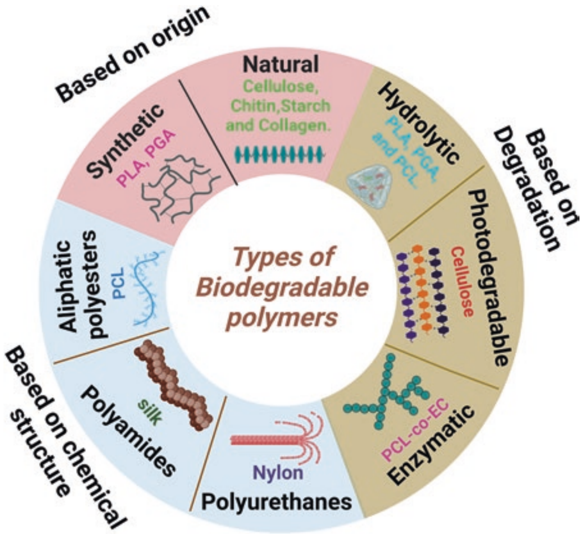
2.2 Based on Chemical Structure

(a) Aliphatic polyesters: These are polymers with ester bonds in their backbone structure. Examples include PLA, PGA, and poly(ε-caprolactone) (PCL).
(b) Polyurethanes: These are polymers formed by the reaction of isocyanates with polyols.
(c) Polyamides: These are polymers that have amide bonds in their backbone structure. Examples include nylon-2 and nylon-6.

2.3 Based on Degradation Mechanisms

(a) Hydrolytic degradation: These are polymers that degrade in the presence of water. Examples include PLA, PGA, and PCL.
(b) Enzymatic degradation: These are polymers that are degraded by enzymes. Examples include PHAs and cellulose.
(c) Photodegradable polymers: These are polymers that are degraded by exposure to light. Examples include poly(ε-caprolactone-co-ethylene carbonate) (PCL-co-EC) (Fig. 1).

Fig. 1 Broad classification of biodegradable polymer



3 Biodegradation Mechanism

Biodegradable polymers undergo degradation by different mechanisms. These biodegradable polymers may degrade by bulk or surface pathways, which are influenced by temperature, humidity, pH, and microbes.

3.1 Bulk Degradation

Bulk degradation of biodegradable polymers refers to the chemical or enzymatic processes that occur over the whole volume of the substance. Biodegradable polymers may degrade by hydrolysis, oxidation, or enzymatic degradation, resulting in the fragmentation of polymer chains into oligomers and monomers.

Hydrolysis is the most prevalent method for the bulk destruction of biodegradable polymers. The ester bonds in polymer chains are broken by water molecules, creating hydroxyl groups and carboxylic acids. This process may occur under various circumstances, including high temperature, acidic or basic pH, and in the presence of enzymes.

Oxidative degradation of biodegradable polymers entails the creation of carbonyl or carboxyl groups by the interaction of polymer chains with oxygen. This process may begin by exposure to ultraviolet light or ambient oxygen and can lead to the loss of mechanical characteristics and deterioration of the material.

Enzymatic degradation: Enzymes, such as lipases or proteases, accelerate the breakdown of biodegradable polymer chains, resulting in their enzymatic destruction. This process may occur in natural conditions, such as soil or water, where microorganisms can break down biodegradable polymers into smaller pieces that can then be digested.

Bulk degradation of biodegradable polymers is essential for controlling the material degradation rate and biocompatibility. By understanding the bulk degradation mechanism, researchers can design biodegradable polymers with tailored properties and degradation rates, making them suitable for a wide range of applications, such as drug delivery, tissue engineering, and environmental remediation.

3.2 Surface Degradation

Surface degradation of biodegradable polymers refers to the breakdown process primarily occurring on the material surface due to environmental exposure or physical pressures. Biodegradable polymers degrade by various surface degradation modes, including corrosion, erosion, abrasion, and microbial activity. When biodegradable polymers are exposed to an environment that induces chemical deterioration of the polymer chains, corrosion occurs. This may cause surface pits, fissures, or holes to emerge, leading to mechanical failure of the material. Exposure to acids, bases, or other reactive compounds may cause biodegradable polymers to corrode.

Erosion of biodegradable polymers happens due to mechanical forces acting on the material, such as fluid flow or impingement, causing the substance to be removed from the surface. Surface flaws or roughness may emerge as a consequence of erosion, affecting the mechanical qualities and performance of the material.

Abrasion of biodegradable polymers happens due to mechanical wear and tear, such as friction or rubbing, which may result in the loss of the surface material. Abrasion may cause surface scratches or grooves to emerge, altering the material's aesthetic and functional capabilities.

Microbial degradation of biodegradable polymers happens when microorganisms invade the material's surface and feed on the polymer chains. This may lead to surface flaws or changes in the material's surface chemistry and morphology.

When developing biomedical, environmental, or industrial materials, surface degradation of biodegradable polymers is also significant to address. Understanding the surface degradation processes allows researchers to design techniques to improve the material's resistance to deterioration and prolong its lifetime, making it more appropriate for various applications[8] (Fig. 2).

3.3 Characterization Techniques for Biodegradation

Many approaches, including chemical, physical, and biological methods, can be used to analyze the degradation and characterization of biodegradable polymers. The choice of technique is determined based on the type of polymer,

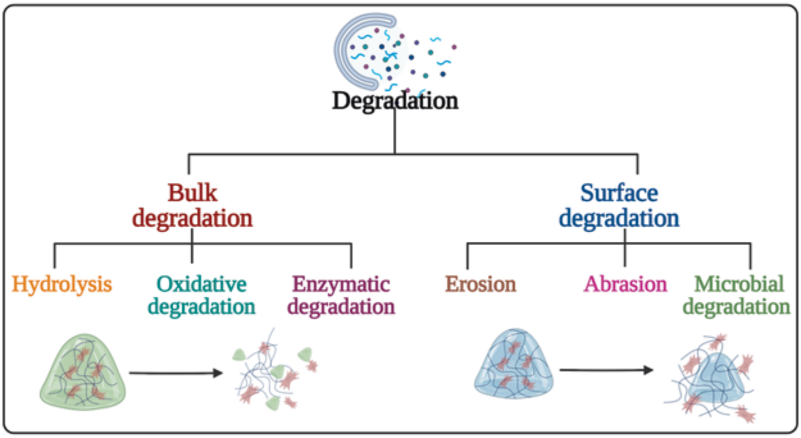


Fig. 2 Mechanism for degradation of biodegradable polymers

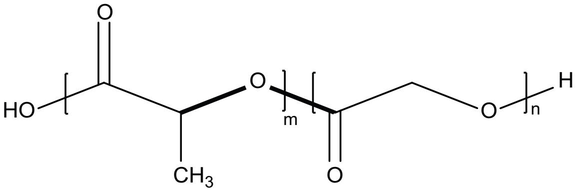
degradation process, and environmental factors. Spectroscopic techniques, such as Fourier transform infrared spectroscopy (FTIR) or nuclear magnetic resonance (NMR) spectroscopy, which can detect changes in the functional groups and chemical composition of the polymer chains, are chemical methods for monitoring the degradation of biodegradable polymers. Chromatography methods, such as gel permeation chromatography (GPC), may also assess time-dependent changes in the molecular weight and polydispersity of polymer chains. Mechanical testing, such as tensile testing or dynamic mechanical analysis (DMA), may identify changes in the mechanical characteristics of the material, such as tensile strength or elasticity, to monitor the degradation of biodegradable polymers. Thermal analysis methods, such as differential scanning calorimetry (DSC) or thermogravimetric analysis (TGA), may also be used to assess variations in the thermal characteristics of a material, such as its glass transition temperature or thermal stability. Monitoring the breakdown of biodegradable polymers biologically involves measuring the activity of microorganisms or enzymes in degrading the substance. For instance, respirometry may be used to assess the rate of microbial oxygen consumption as a metric of the polymer's biodegradation rate. The enzymatic breakdown of polymer chains may also be measured using lipase or protease assays. In addition to assessing the physicochemical qualities and performance of biodegradable polymers, characterization techniques may also be used to monitor their breakdown. Microscopy methods such as scanning electron microscopy (SEM) and atomic force microscopy (AFM) may be used to observe the surface morphology and topography of the material. Surface analysis methods, such as X-ray photoelectron spectroscopy (XPS) or contact angle measurements, may also be employed to analyze the material's surface chemistry and wettability [9].

4 Examples

4.1 Synthetic Polymers

PLGA (poly (lactic-co-glycolic acid) is a biodegradable and biocompatible polymer with extensive biomedical applications in tissue engineering and drug delivery. PLGA nanoparticles have been used to deliver various drugs, including small molecules, peptides, proteins, and nucleic acids. PLGA can encapsulate hydrophobic and hydrophilic drugs and be modified to release drugs in a controlled manner. The synthesized particles can be functionalized with imaging agents to visualize specific cells or tissues and monitor diseases. Additionally, in the scaffold configuration, it can be used to support tissue regeneration. They can be seeded with cells and implanted in the body to provide a temporary matrix for cell growth and tissue formation. PLGA nanofibers can be used to create tissue engineering scaffolds or wound dressings. They have a high surface area-to-volume ratio, allowing efficient drug delivery. The hydrolytic attack of the water molecules degrades the ester bond linkage in the PLGA polymer backbone.

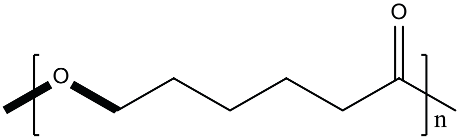
Degradable bonds: The by-products of degradation are lactic acid and glycolic acid, which are biocompatible and quickly eliminated from the body through the renal system.



PLGA structure

Polycaprolactone (PCL) is a biodegradable and biocompatible polymer with diverse applications in medicine, agriculture, and the environment. It is a thermoplastic aliphatic polyester that is synthesized from caprolactone monomers. It has been used in the medical field for scaffold preparation, drug delivery systems, and sutures. This polymer is also highly used in agriculture as a biodegradable alternative to synthetic plastics for mulch films, plant pots, and twine. In the environmental field, PCL has been used as a biodegradable alternative for plastic packaging, disposable tableware, and shopping bag products. Due to its biodegradability, biocompatibility, and versatility, PCL has attracted increasing attention as a promising material for broad applications.

Degradable bonds: Hydrolytic degradation of PCL takes place by breaking the ester bond in the structure.

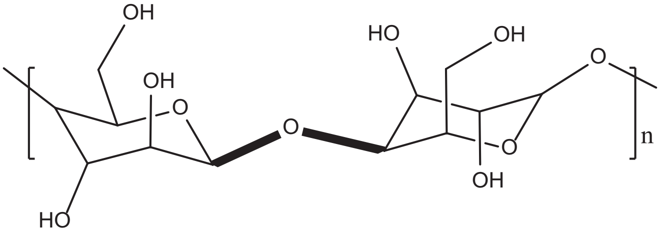


PCL structure

4.2 Natural Polymers

Cellulose is a natural, biodegradable polymer that has gained increasing interest in drug delivery and nanotechnology applications. Cellulose is abundant in nature and can be derived from various sources, including plants, bacteria, and algae. One of the most promising applications of cellulose in drug delivery is due to its unique physicochemical properties, including its high crystallinity and strong intermolecular forces that contribute to its strength and rigidity, while its hydrophilic nature and capacity to form hydrogen bonds with water molecules make it an efficient moisture absorber. In addition, the chemical stability and biodegradability of cellulose have led to its use in a wide range of biomedical applications. Cellulose-based drug carriers have several advantages, including high biocompatibility, low toxicity, and the ability to be easily modified with various functional groups to improve drug loading, stability, and release. Cellulose-based drug carriers can be synthesized in multiple forms, including nanofibers, nanoparticles, and hydrogels, and can be used to deliver a wide range of drugs, including small molecules, proteins, and nucleic acids. Moreover, cellulose-based nanomaterials have shown promising results in cancer therapy. Modified cellulose nanoparticles can target cancer cells, increasing drug concentration in the tumor tissue and reducing off-target effects.

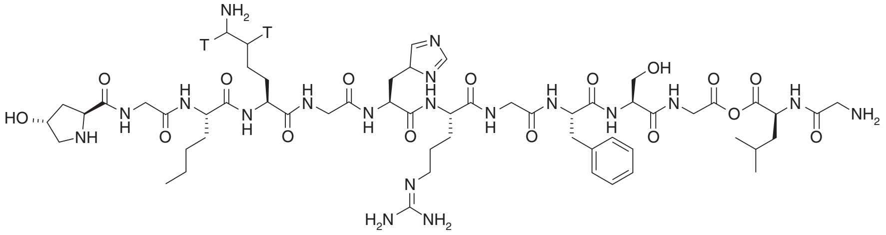
Degradable bonds: Cellulose degradation is done by hydrolysis of β-1,4-linkages in cellulose.



Cellulose structure

Collagen is a fibrous and most abundant protein in the human body. It plays a vital role in maintaining the structural integrity of many tissues, including skin, tendons, cartilage, and bone. It has a unique triple-helical structure composed of three polypeptide chains. The primary sequence of the polypeptide chains determines the specific type of collagen, of which there are over 28 types identified so far. Hydrogen bonds and covalent crosslinks between adjacent chains stabilize the triple-helix structure. Collagen-based nanostructures have recently received much interest because of their potential uses in medication delivery. Collagen nanoparticles can be functionalized with targeting moieties such as antibodies or peptides to target particular cells or organs. It may be used as a scaffold to aid tissue regeneration in various applications, including skin, cartilage, bone, and blood vessels. Because of its gelling and emulsifying capabilities, collagen is a food ingredient. It's used to make sutures, wound dressings, and artificial skin replacements, among other things. It's also employed in orthopedic procedures, including bone transplants and joint replacements. Since collagen-based nanoparticles may be functionalized to attach to specific cell types or tissues, they can be employed for targeted medication delivery.

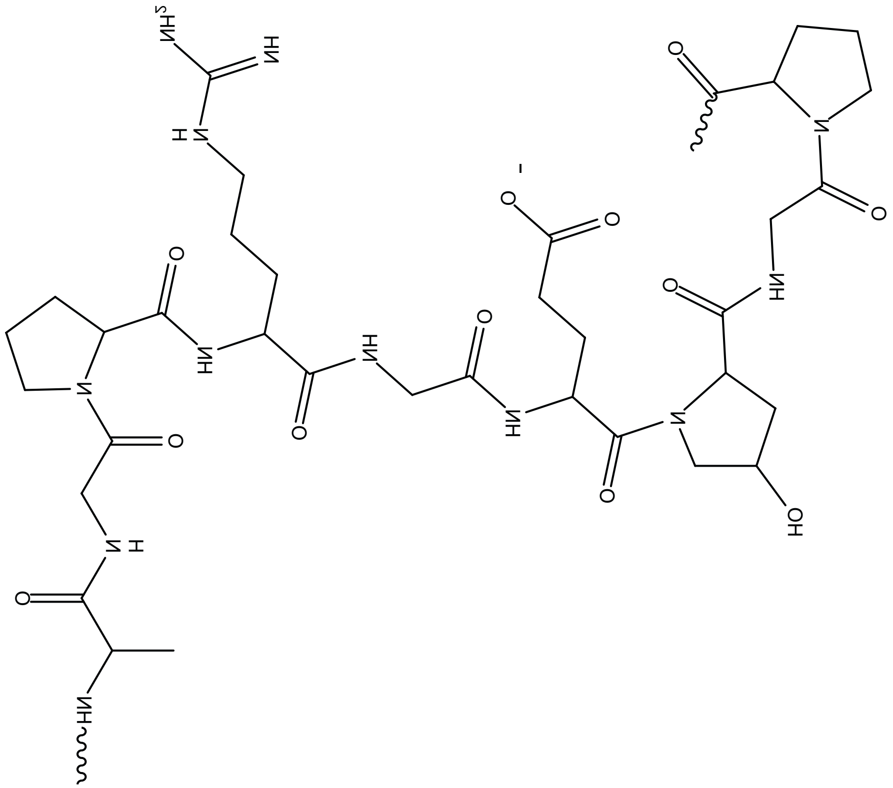
Degradable Bonds: Collagen can be degraded by heat, acids, and proteases, which disrupt the hydrogen bonds and crosslinks, leading to a loss of structure and function.



Collagen structureIpsum

Gelatin is a protein derived from the hydrolysis of collagen, which breaks down the protein into smaller peptides and amino acids. It has been used in tissue engineering due to its biocompatibility, biodegradability, and ability to form hydrogels. Hydrogels made from gelatin can mimic the extracellular matrix (ECM) of tissues and provide a supportive environment for cell growth and tissue regeneration. The physical and mechanical properties of gelatin hydrogels can be modified by changing the concentration of gelatin, the degree of crosslinking, and adding other components such as polymers or growth factors. Gelatin can be added to other polymers through blending, electrospinning, and crosslinking, among other methods. The properties of a polymer matrix can be enhanced by combining gelatin with polymers such as chitosan, polyethylene glycol, or polyvinyl alcohol. Additionally, gelatin has been chemically modified using different functional groups like methacryloyl or thiol, for example, to alter the material properties and provide additional means of crosslinking. In some cases, gelatin can also be used as a coating material to improve the biocompatibility of implantable devices, such as artificial joints or stents. Using gelatin coatings can reduce the risk of inflammation and rejection by the body's immune system. Due to its biocompatibility, low toxicity, and low cost, gelatin is a commonly used biodegradable polymer in the formulation of microparticles. It is advantageous for sustained drug delivery that the gelatin microparticles can be loaded with drugs and designed to deliver them over a specific time period. In addition, gelatin microparticles can be tailored to target specific sites within the body, thereby enhancing drug efficacy and minimizing adverse effects. Therefore, gelatin microparticles are a suitable option for applications involving drug delivery. Gelatin-based hydrogels can be used to deliver drugs topically to the skin. The hydrogel provides a moist environment that can enhance drug absorption, and the hydrogel's gel texture can help improve patient comfort.

Degradable bonds: Enzymatic degradation is the most common method for degrading gelatin, as it is a protein that can be broken down by enzymes such as proteases. During the process of enzymatic degradation, proteases break down the peptide bonds that hold the amino acid residues in gelatin together. This results in the cleavage of the protein into smaller peptides and eventually into individual amino acids.



Gelatin structure

5 Applications

Biodegradable polymers are a rapidly growing field driven by increasing concerns over non-biodegradable materials' adverse reactions, such as inflammation and tissue rejection, and they may require surgical removal if they fail or cause complications. In recent years, significant advances have been made in developing new biodegradable polymers and optimizing existing ones. The followings are some of the current research areas and future trends in the field of biodegradable polymer [10]. Researchers are actively developing new biodegradable polymers with improved properties such as increased strength, durability, and biodegradability. This is accomplished using new polymerization methods and techniques and incorporating biodegradable additives [2].

5.1 Medical Devices

Biodegradable polymers are an attractive option for medical device applications because they can be designed to degrade over time, eliminating the need for device removal and reducing the risk of long-term complications. Some examples of biodegradable polymers used in medical devices include:

1. Poly(lactic acid): PLA is derived from renewable resources such as corn starch or sugarcane. It has been used to make sutures, screws, pins, and plates that can be absorbed by the body over time.
2. Poly(glycolic acid): PGA is commonly used in medical devices such as sutures and tissue engineering scaffolds. It degrades rapidly in the body, releasing any drugs or growth factors that have been incorporated into the device.
3. Polycaprolactone: PCL has been used in surgical meshes due to its unique combination of mechanical properties and biodegradability. They are commonly used in hernia repair surgeries or designing scaffolds for bone regeneration, providing mechanical support to the damaged tissue and promoting new tissue growth.
4. Polyhydroxyalkanoates (PHAs): PHAs are a family of biodegradable polymers bacteria produce. They have been explored for use in orthopedic implants. PHA-based materials have been shown to support the growth and development of bone cells, making them suitable for bone regeneration applications. PHAs can also be processed into porous scaffolds that can be used to fill bone defects and promote the regeneration of new bone tissue.
5. Polydioxanone: PDO is used in surgical sutures, particularly for closing wounds requiring long-term support. PDO sutures maintain their strength for up to 180 days before breaking down in the body.

5.2 Drug Delivery

Biodegradable polymers can develop drug delivery systems, such as implants or microspheres, that can release drugs over a controlled period. This can improve the efficacy of the drugs and reduce side effects. These materials can be designed to dissolve over time in response to physiological conditions, releasing drugs in a controlled and sustained manner. This can be particularly useful in cases where it is desirable to avoid the accumulation of drugs in the body or where the drugs are required to be delivered directly to the site of an injury or disease. Biodegradable polymers formulate injectable drug delivery systems such as microparticles, nanoparticles, and implantable devices. These systems can provide controlled drug release over days, weeks, or even months, reducing dosing frequency and improving patient compliance. Biodegradable polymers can be functionalized with specific molecular groups that target specific cells or tissues, increasing the local concentration of drugs and reducing systemic side effects. Some examples of biodegradable polymers used in drug delivery include polylactide (PLA), polyglycolide (PGA), and copolymers of PLA and PGA (PLGA). These materials have been extensively studied and are well-established in drug delivery, with numerous FDA-approved products available on the market.

5.3 Tissue Engineering

Biodegradable polymers are used as scaffolds for tissue engineering, providing a supportive structure for tissue repair and regeneration. As the tissue grows, the polymer gradually degrades and is eventually replaced by the regenerated tissue. These polymers serve as scaffolds for tissue growth and repair and provide a supportive structure for cells to attach, grow, and differentiate. The properties of tissue engineering polymers, such as biocompatibility, mechanical strength, and degradation rate, can be tailored to suit the specific needs of different tissue sites. Some commonly used tissue engineering polymers include polylactic acid (PLA), polyglycolic acid (PGA), polycaprolactone (PCL), polyethylene glycol (PEG), polyvinyl alcohol (PVA), and alginate. These polymers can be processed into different forms, such as fibers, films, or porous scaffolds, to provide additional physical, mechanical, and chemical environments for cell differentiation and tissue regeneration (Fig. 3).

5.4 Wound Healing

Biodegradable polymers can be used as wound dressings to promote healing and reduce the risk of infection. The polymers can absorb excess fluids, provide a moist environment for the wound, and gradually degrade over time. There are several

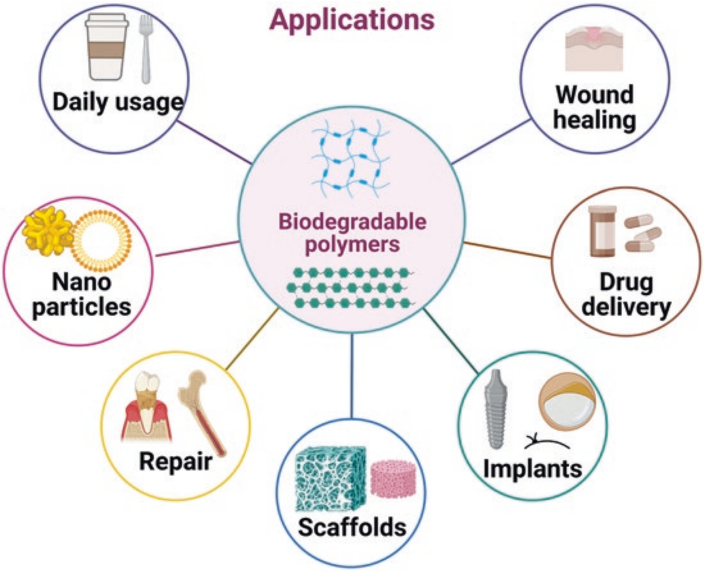


Fig. 3 Different kinds of biopolymer applications

types of biodegradable polymers used in wound healing, including polylactic acid (PLA), polyglycolic acid (PGA), and copolymers (PLGA). These polymers can be formed into various sizes and shapes based on wound severity and can be used as wound dressings and bio-bandages. In addition, these biomaterials promote external wound healing and show internal wound healing properties. The biodegradable nature of these polymers allows them to degrade gradually as the wound heals without leaving any foreign materials in the body for the long term. This reduces the risk of infection and other adverse effects and ensures the wound-healing process is not impeded. Some biodegradable polymers can release growth factors, antimicrobial agents, and other therapeutic agents to promote healing and prevent infections. Overall, biodegradable polymers have shown great potential for wound healing and have been used in various clinical applications with promising results. For example, internal intestinal and stomach wound can be healed using gelatin and other biobased polymers, these biomaterial helps in significant wound healing and avoid the risk of surgery and invasive stitches in the wounded regions.

5.5 Implant Materials

Biodegradable polymers have gained increasing attention in developing medical devices such as heart valves, stents, and nerve guides.

Heart Valves: Biodegradable polymers can be used to develop heart valves to replace damaged or diseased valves. This can eliminate the need for lifelong anticoagulation therapy, which is required for patients with mechanical heart valves. Polyglycolic acid (PGA), poly(glycerol sebacate) (PGS), and polylactic acid (PLA) are commonly used biodegradable polymers in heart valve applications.

Stents: Biodegradable polymers have been used to manufacture stents that slowly degrade over time, reducing the risk of complications such as restenosis and thrombosis. These stents are typically made from polymers such as polylactic acid (PLA), polyglycolic acid (PGA), and their copolymers. These materials have been shown to degrade within 6–12 months, leaving behind a more natural vessel structure.

Nerve guides are used to help damaged nerves regenerate. Biodegradable polymers are used as a scaffold-like structure that supports nerve growth and eventually degrades as the nerve heals. The polymer can be designed to release growth factors or other molecules that promote nerve growth and regeneration. Small tubes bridge gaps in damaged nerves and help regenerate nerve tissue. PGA tubes and poly(caprolactone) (PCL) are commonly used biodegradable polymers in nerve guide applications.

5.6 Biopolymeric DNA Vaccines

These are a type of vaccines that use genetic material to stimulate an immune response against a disease. They typically consist of a small piece of the DNA of the pathogen, such as a virus or bacterium, that causes the disease. The DNA is delivered into the body, usually via injection, and taken up by cells, where it is expressed and processed into viral or bacterial antigens. This stimulates an immune response, including the production of antibodies, that can recognize and neutralize the pathogen if it is encountered in the future. Biopolymeric DNA vaccines have several advantages over traditional vaccines, including the ability to be rapidly manufactured, their stability, and the fact that they do not carry the risk of infecting the recipient with the live pathogen. They have the potential to provide long-lasting protection against diseases. However, some challenges are associated with biopolymeric DNA vaccines, including their relatively low immunogenicity compared to traditional vaccines and the need for repeated dosing or adjuvants to enhance their effectiveness. Overall, biopolymeric DNA vaccines are an exciting new area of research and have the potential to provide a safe and effective way of preventing and treating a range of diseases.

6 Case Study I

6.1 *Bioinspired and Biodegradable Polymer-Based Adhesive Films [11]*

Main goal: Development of bioadhesives to address the limitations of traditional sealing methods, reducing the need for invasive procedures.

Biodegradable polymer: Poly (glycerol sebacate) (PGS).

Background: Researchers in the medical field are becoming more interested in using bioinspired and biodegradable polymer-based adhesive films because of their impeccable adhesion performance and ability to break down in the body without the need for further surgical procedures. Poly (glycerol sebacate) (PGS) can produce adhesive films of tunable soft microarchitecture because it is bioresorbable and leaves no residue. One research group has manufactured bioinspired oil-coated sticky film using PGS that can maintain adhesion to a wet surface by imitating a frog's toe pad and mucus. Unlike commercial acrylic-based glue, Raman and FTIR spectroscopy showed no liver surface spectra change following the PGS-based film removal. This film is capable of being made with bioinspired oil. Simple models based on the degree of esterification and the interfacial energy difference were utilized to define the parameters under which PGS patterned to construct frog-like adhesive designs. Reproducing the frog-like hexagonal microchannel and concave cup structures covered with aggressive glycerol oil led to a durable residue-free wet adhesion against a variety of non-flat soft organ surfaces, which was achieved by this oil-coated film's wet adhesion (Fig. 4).

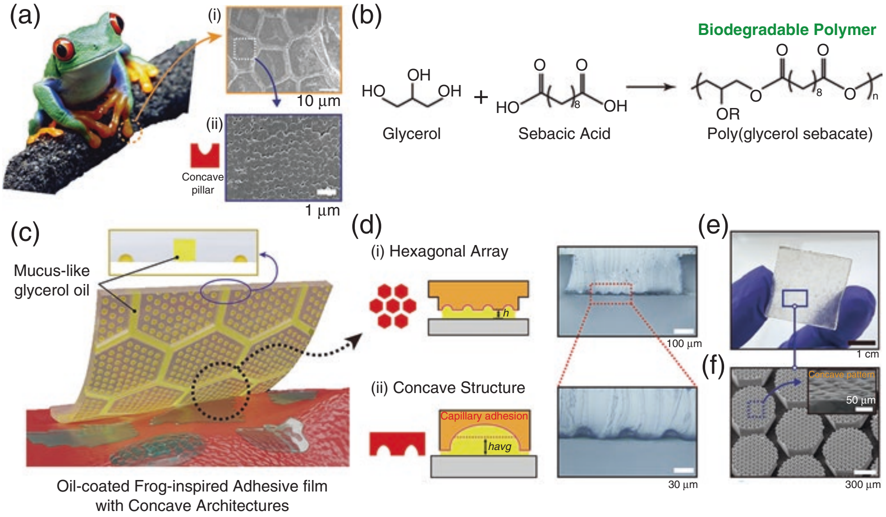


Fig. 4 Schematic illustration. (**d–f**), hierarchical structure of (i) hexagonal array and (ii) hemispherical concave cup enhanced the adhesion and friction forces by increasing the capillary interaction

7 Case Study II

7.1 *Bacteria-Responsive Biopolymer-Coated Nanoparticles for Biofilm Penetration and Eradication [12]*

Main goal: Development of multi-stimuli-responsive NPs to combat bacterial biofilms.

Biodegradable polymer: Gelatin, chitosan (CS), polyanion, hyaluronic acid (HA).

Background: Biofilm-associated bacterial infections are a major source of morbidity and death among patients globally. Biofilms are complex, three-dimensional bacterial communities encased in a matrix of extracellular polymeric substances (EPS) comprising proteins, polysaccharides, extracellular DNA, and lipids. These bacterial colonies are often seen on surfaces, including necrotic tissue and implants. Biofilms are associated with various illnesses, such as dental caries, urinary tract infections, burn wound infections, and diabetic foot ulcers. To tackle bacterial biofilms, the authors have developed a gelatin NP (GNP) drug delivery system that responds to the acidic environment of the biofilm and the presence of gelatinases and hyaluronidases. Here, the authors used layer-by-layer (LbL) self-assembly to attach a bilayer of the polycation chitosan (CS) and the polyanion hyaluronic acid (HA) to the surface of antibiotic-loaded GNPs. Each layer served a mechanical purpose. GNPs were loaded with the FDA-approved tetracycline antibiotic doxycycline (Doxy) since it is widely employed to treat V. vulnificus infections.

Indeed, they found that HA-CS-Doxy-GNPs displayed pH- and enzyme-responsive drug release characteristics and viability staining indicated severe membrane damage when HA-CS-Doxy-GNPs were applied to premade biofilms, suggesting that these nanoparticles had a high capacity to penetrate and eradicate V. vulnificus biofilms compared with free Doxy. In an ex vivo pig V. vulnificus infection model, these HA-CS-Doxy-GNPs similarly decreased bacterial load, lending credence to their potential for translation. Furthermore, fibroblasts, endothelial cells, and RBCs were all generally biocompatible with these NPs. Since these enzyme triggers and decreased pH are characteristics of many bacterial species, the multi-stimuli-responsive NPs platform may also demonstrate comparable antibiofilm effects against various biofilm-producing bacteria, including additional Gram-negative and Gram-positive bacteria. This adaptable drug delivery system could deliver a combination of drugs, such as those explicitly targeted at biofilms (e.g., antibiofilm peptides) or signaling molecules for infection detection, for efficient, all-encompassing infection treatment and detection (e.g., fluorescent dyes).

8 Future Perspective

Without a doubt, using biodegradable polymers in biomedicine has enormous potential. Drug delivery gene transfection, protein transport, bioimaging and diagnostics, tissue engineering, and biomedical devices are some of the current biomedical applications that use biodegradable polymers. There are a significant number of other biomedical applications as well. In addition to exhibiting their unique properties, which are application specific, they can be easily incorporated with additional required properties. In addition, BPs have several unique benefits, including degradability, compatibility, nontoxicity, and intelligent responsiveness to a range of physiological stimuli, demonstrating significant potential in various applications within biomedicine and agriculture. BPs have a bright and fruitful future ahead of them. Even though much ground has been covered, many challenges remain. Existing BPs still have suboptimal mechanical characteristics, forcing the progress of more complex polymers. Second, despite the reality that many systems made of non-degradable polymers and metals have been used in a wide range of applications, the biomedical use of BPs has not been fully realized due to their high cost of initial production and instability in vivo. This is in contrast to the widespread use of systems made of non-biodegradable polymers and metals. In recent years, many promising and multi-functional biopolymers have been reported, and they show more significant properties than traditional implants and methods. This shows that more research and new polymerization methods must be explored to develop pathbreaking novel biopolymer compounds.

Questions

1. Which option is correct for blending in the context of biodegradable polymers?
   (a) Grafting a biodegradable polymer on another polymer
   (b) Mixing two or more polymers to build a new material with improved properties
   (c) Chemically bonding polymer chains together to create a three-dimensional network
   (d) Polymerizing two or more different monomers to form a copolymer
2. Which of the following is an example biodegradable polymer?
   (a) Polylactic acid (PLA)
   (b) High molecular weight polyethylene
   (c) Polypropylene
   (d) Polyvinylchloride

3. Which monomers are used to synthesize PLGA?
   (a) Poly-L-lysine and glycolic acid
   (b) Lactose and glycine
   (c) Lactic acid and glycolic acid
   (d) Lactic acid and glycine
4. Which of the following methods increases the material's strength and stability?
   (a) Ring-opening polymerization
   (b) Introduction of hydrolytically degradable groups
   (c) Grafting
   (d) Crosslinking
5. Which of the following is the protein-based polymer?
   (a) Polybutylene terephthalate
   (b) Silk
   (c) Polyethylene terephthalate
   (d) Polylactic acid
6. Which polymer is indigestible by humans?
   (a) Gelatin
   (b) Starch
   (c) Cellulose
   (d) Chitosan
7. Implantable medical devices prepared with biodegradable and biocompatible polymers have the following properties except.
   (a) It has minimal risk due to biodegradation and biocompatibility
   (b) No need to remove the implant by surgery
   (c) Produces harmful byproducts
   (d) Does not produce immunogenic responses
8. Why biopolymers are used in drug delivery?
   (a) It releases drugs all at once
   (b) It releases drugs in a controlled manner
   (c) It can release drugs at the targeted site
   (d) Both b and c
9. What are biodegradable polymers?
   (a) The polymers which do not degrade at all
   (b) The polymers do not degrade by enzymes and bacteria
   (c) The polymers degrade by enzymes, and bacteria and produce harmless byproducts
   (d) The polymers prepared from bacteria that do not degrade

10. What is the role of the scaffold in tissue engineering?
    - (a) To create non-degradable artificial tissue
    - (b) To support the cell attachment, growth, and differentiation
    - (c) To prevent body from absorbing tissue
    - (d) To make new tissue

Explanations

1. Poly lactic acid is a biodegradable polymer that is derived from resources like sugarcane, and corn starch. it has properties like high strength, stiffness, and good thermal properties.
2. In the context to biodegradable polymers, the term "blending" describes the process of combining two or more distinct polymers to create a composite material with improved properties. Strength, stiffness, thermal conductivity, and biodegradability could all be improved by this process.
3. Lactic and glycolic acid are used as the monomers in a ring-opening polymerization (ROP) reaction to synthesize PLGA. A catalyst, like stannous octoate, and a co-initiator, like benzyl alcohol, are used in the reaction to start the polymerization process. The ratio of lactic acid to glycolic acid controls the properties of PLGA, increasing glycolic acid proportion increases degradation rate, biodegradability, and hydrophilicity.
4. Crosslinking is the process of chemically linking or more polymer chains together to create a three-dimensional network structure. This process can increase the stability and strength of a material by preventing the sliding of chains and increasing the intermolecular forces between the chains.
5. Among the given options, two polymers, polyethylene terephthalate (PET) and polybutylene terephthalate (PBT) are synthetic polymers made up of chemical reactions of synthetic monomers and they are non-biodegradable. Polylactic acid (PLA) is a biodegradable polymer made up of starch, and silk is only a protein-based natural polymer produced by silkworms, is it composed of two proteins sericin and fibroin.
6. Human digestive system can digest simple sugars like, glucose and fructose. The beta 1,4 glycosidic bond present in cellulose cannot be broken down by human digestive enzymes such as amylase.
7. Implantable medical devices prepared with biodegradable polymers would degrade in physiological conditions with time and form harmless byproducts, and there is no need to remove these implants by surgical procedure.
8. Biopolymers are biodegradable and biocompatible, which minimizes chances of toxicity and immune response to the delivery system, additionally, these polymers can be engineered to enhance the drug loading capacity, control release, and targeted delivery.

9. A scaffold is a three-dimensional structure used in tissue engineering those functions as a guide for the growth of new tissue. The scaffold gives cells a framework to stick to and arrange themselves on, directing the growth of new tissue and encouraging regeneration. it mimics the ECM of tissue which supports cell attachment, growth, and differentiation.
10. Biodegradable polymers are polymers that can be degraded naturally by enzymes, microorganisms, and other natural processes into harmless byproducts such as water and carbon dioxide. On the other hand, non-biodegradable polymers are a class of polymers that cannot degrade by these processes and can withstand this environment for many years. Some examples of biodegradable polymers are polylactic acids, polylactic acids, gelatin, and polyvinyl alcohol. In the given example (c) is the only option that defines a biodegradable polymer.

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