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A Review on Biodegradable Polymers in Drug Delivery Systems and Biomedical Applications

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Abstract

Because they can improve biomedical uses and lessen environmental pollution, biodegradable polymers have become attractive substitutes for traditional plastics. Under the right environmental circumstances, these polymers are made to break down into non-toxic byproducts like carbon dioxide, water, and organic matter, reducing their long-term ecological effect. The research and large-scale manufacture of biodegradable polymers, including poly(lactic acid) (PLA), starch blends, polybutylene succinate (PBS), polybutylene adipate terephthalate (PBAT), and polyhydroxyalkanoates (PHAs), have advanced significantly in recent years.

Biodegradable polymers are essential as carriers in targeted and controlled drug delivery systems in the pharmaceutical

industry, allowing for precise drug release, lower dosages, and less adverse effects. Additionally, they are extensively employed in anticancer treatments, vaccine administration, and tissue engineering. Despite these benefits, there are still a number of issues, such as the lack of real-world degradation data, the need for harsh testing settings, and the effects of additives on safety and biodegradability.

The kinds, characteristics, and uses of biodegradable polymers are highlighted in this overview, with an emphasis on their importance for the environment and biomedicine. In order to guarantee their efficacy as sustainable substitutes in contemporary research and industry, it also highlights the necessity of thorough life cycle evaluations and realistic degradation studies.

Keywords: Biodegradable Polymers, Drug Delivery Systems, Controlled Release, Tissue Engineering, Poly(Lactic Acid) (PLA)

Introduction

We can use biodegradable plastics instead of recycled plastics, as they present different potential benefits and drawbacks. Due to their potential to address existing challenges, the development of biodegradable polymers has experienced a significant rise over the past several years. These polymers are also employed in tissue engineering and various medical applications. For more precisely targeted drug delivery to specific organs, they are used as carriers to transport and release drugs upon receiving a specific stimulus. This allows for lower drug doses and subsequently leads to fewer side effects. Biodegradable polymers decompose more efficiently and harmlessly compared to conventional non-degradable plastics, leading to a lower environmental footprint. To create more eco-friendly future and reduce plastics waste's impact on our planet, we can switch from traditional plastics to biodegradable alternative.

Unlike the bulk of industrial polymers, biodegradable polymers are designed to break down into organic matter, H₂O, and CO₂ when exposed to environmental conditions. This decomposition process ensures that they have a lesser impact on the environment. With growing awareness of plastic pollution, there's been a surge in demand for degradable plastics like compostable poly(lactic acid) (PLA). These plastics are now produced in large quantities. Over the past 20 years, the price of PLA has dramatically dropped from around \$1,000 per kg to just a few dollars per kg, making them as affordable as polystyrene. In addition to PLA, which represents 24% of global biodegradable polymer production, other significant types include starch blends (44%), biodegradable polyesters like PBS and PBAT (23%), and PHAs (6%). These materials are all manufactured on a large-scale manufacturing.

When reviewing primary research, the term "biodegradable" often appears in the title, but the actual studies frequently lack proof or degradation tests. Even when researchers study the degradation process, they often use extreme conditions (like high temperatures or very low/high pH values) or unrealistic environments (such as isolated microorganisms or enzymes), which don't reflect real-world scenarios. Biodegradable polymers are used to create sustainable alternatives to traditional plastics. Understanding their degradation mechanisms and byproducts in real-world conditions is crucial for developing effective drug delivery systems and other biomedical applications. It's also important to consider the impact of additives when conducting a life cycle assessment of biodegradable alternatives.

Biodegradable work by break down within living organisms, either through non-biocatalytic or biocatalytic, and produced by-products that are bio-friendly or inoffensive. To improve how drugs are absorbed, distributed, metabolized, and excreted in the body, while also reducing side effects, these polymers have shown significant benefits. Recent revolutions in the pharmaceutical field have focused on various areas, including controlled drug delivery systems (CDDS), sustained release drug delivery systems (SRDDS), vaccines, nucleic acid delivery, protein delivery, and anticancer drug delivery. These advancements have also attracted attention in tissue engineering and regenerative medicine. Such innovations aim to improve the efficacy, safety, and targeting of treatments, ultimately leading to better patient outcomes and enhanced therapeutic strategies.



Fig 1: Global production capacities of biodegradable plastics in 2017

Degradation Mechanism

Biodegradable polymers are defined by the International Union of Pure and Applied Chemistry (IUPAC) as polymers that can break down through biological activity, resulting in a reduction in their mass. In the pharmaceutical field, other definitions specify that a biodegradable material must be broken down into organic matter, H₂O, and CO₂ during the biodegradation process. To tackle the issue of plastic waste accumulation in the surroundings, do we need to merely transform polymers into hydrosoluble compounds, or do we require complete crystallization into carbon dioxide, water, and biomass to ensure safety and effectiveness in drug delivery systems? Additionally, the duration required for the biodegradation process is crucial. The European Union has

recently proposed standardized rules for defining and labeling decomposable and biodegradable plastics. This is intended to allow for accurate sorting and to prevent false ecological claims.

In additionally, the process of polymer biodegradation can be separated into four steps:

1. **Biodeterioration:** Initial breakdown by environmental factors.
2. **Depolymerization:** Breaking down large polymer chains into smaller units.
3. **Bioassimilation:** Microorganisms incorporating the smaller units.
4. **Mineralization:** Conversion into inorganic substances like carbon dioxide, water, and biomass.

At the initial stage, a microbial biofilm forms, leading to the surface degradation of the polymeric material, which fragments into smaller particles. The microorganisms within the biofilm produce extracellular enzymes. These enzymes then stimulate the breakdown of the polymer chains into smaller units, such as oligomers, dimers, or monomers. The process where the small compounds produced are taken up by the bacterial cell and subsequently produce fundamental and peripheral metabolic intermediates is referred to as assimilation. In the final phase, these metabolites undergo mineralization, resulting in the formation and release of end products such as carbon dioxide (CO₂), methane (CH₄), water (H₂O), and nitrogen (N₂) into the environment.

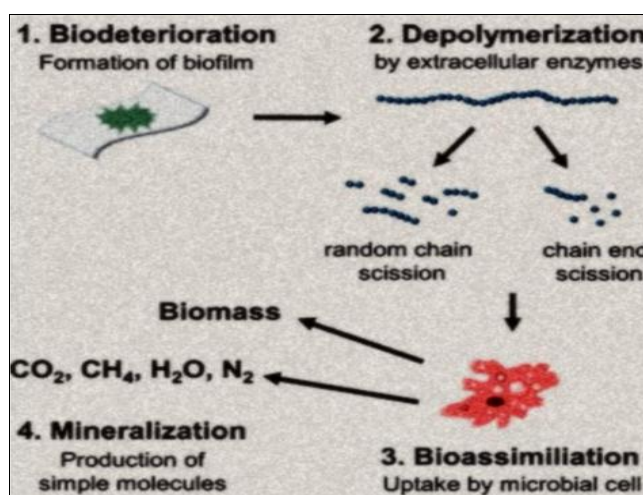


Fig 2: A diagram illustrating the various stages of biodegradation

Blends of Biodegradable Polymers

Starch-Based Blends

Starch is a low-cost, eco-friendly, and fully biodegradable material. Despite its eco-friendliness and low cost, starch's high sensitivity to water and comparatively weak mechanical properties limit its usage. Combining it with synthetic polymers may provide a solution. Numerous biodegradable molding plastic blends incorporating starch have been developed and in depth researched. Many studies focus on creating blends that combine starch with synthetic biodegradable polymers. The composition can be altered to tailor the material properties to fit the specific requirements of the application. Blending is a cost-effective alternative to developing new synthetic materials. These blends are designed to be more biodegradable than conventional synthetic plastics.

Starch-polyvinyl alcohol (TPS and PVOH) blends are

particularly noteworthy due to their excellent compatibility. Blends offer better tensile strength, elongation, and processability compared to pure TPS materials. Recent studies have examined their biodegradability. It has been found that the PVOH content significantly influences the rate of starch disintegration: higher amounts of PVOH slow down this rate.

Starch-PLA: Blending starch with PLA using traditional methods results in poor mechanical properties because of inconsistency. To enhance prolongation, flexibilizers or reactive agents can be incorporated during the expulsion process. Merging agents, such as cyanates, have also been utilized. The OH groups in starch can react with cyanate groups to form carbamate linkages, leading to synchronization of these systems. Additionally, the impact of starch coagulation was studied. Research has demonstrated that in PLA/gelatinized starch blends, starch acts as a nucleating agent, enhancing the crystallinity of PLA blends and significantly improving their mechanical properties.

Starch – PBS: Granular corn starch was blended with PBS. Increasing the starch content resulted in decreased lengthening at break and resilient strength. However, the addition of starch fillers greatly accelerated the degradation rate.

Others Blends

PHB and PHBV are known for their brittleness. To improve their mechanical properties, they are combined with other biodegradable materials. Adding nucleating agents results in the formation of smaller microcrystals, which in turn enhances the mechanical properties.

Furthermore, these properties are influenced by the processing situations, configuration, crystal arrangement, and glass transition temperature.

Thermal compounding was used to prepare blends of PHBV and cellulose acetate butyrate. The thermal process did not cause transesterification or alter the atomic weight. Blends with less than 50% PHBV are indeterminate, whereas those with a higher PHBV content become semi-structured. With a high content of PHBV, it is only partially miscible with polysaccharide acetate butanoate.

Applications of Biodegradable Polymer

Biodegradable polymers can be handled using most standard plastics processing methods, although processing conditions and machinery may need to be slightly adjusted. Some of the processing techniques employed include parison molding, sheet extrusion, injection fabrication, and thermal molding. Biodegradable polymers have been primarily introduced in three key sectors: medicine, packaging, and agriculture. The applications of biodegradable polymers extend beyond pharmaceutical devices, such as matrices for enzyme inactivation and controlled-release systems, to also include therapeutic devices like temporary artificial limbs and reticulated structures for tissue engineering.

Packaging

In daily life, packaging is another crucial application of biodegradable polymers. To minimize waste, biodegradable polymers are frequently utilized. The physical characteristics of biodegradable polymers used in packaging

must vary according to the specific product being packaged and the storage conditions. Because of its availability and lower cost compared to other biodegradable polyesters, PLA is utilized for making lawn waste bags.

Additionally, PLA has moderate permeability to water vapor and oxygen, making it suitable for packaging applications such as bottles, mugs, and films. PCL is utilized in environmental applications such as soft compostable packaging.

Various polysaccharide-based biopolymers, including chitin, amylose, and dextran, have been explored for use in packaging films. Polysaccharide films are appealing materials for food packaging due to their low permeability. Films made from proteins and polysaccharides exhibit excellent mechanical and optical properties; however, they are highly sensitive to moisture. The latest trend in food packaging involves combining various biopolymers to enhance performance. Chitosan was applied as a coating in paper-based packaging to create an oil barrier. Studies indicated that chitosan coatings are effective fat barriers, but their treatment cost is relatively higher than that of commonly used fluorinated coatings. Chitosan-based films have demonstrated effectiveness in preserving food and hold potential for use as antibacterial packaging.



Fig 3: Biodegradable plastics used in packaging

Medicine and Pharmacy

Biodegradable polymers used as biomaterials need to be bioerodible, bio-tolerant, and mechanically resistant to be effective. In simpler terms, these materials must be safe for use in the body, able to be absorbed by the body, and strong enough to perform their intended function. Natural polymers like biomolecules and polysaccharides, which break down enzymatically, have been used in biomedical applications for thousands of years. However, synthetic biodegradable polymers have only been applied in this field for about fifty years.

Biodegradable polymers are also utilized as embeddable matrices to control the release of drugs within the body or as degradable sutures. Several commercial biodegradable medical products and their uses have been previously documented.



Fig 4: Biodegradable polymers used in pharmaceuticals

Agriculture

Resin films were initially used for plant house layering, overlays, and disinfection in the 1930s. Young plants are vulnerable to frost and need to be protected. Biodegradable cover films primarily function to retain moisture, raise soil temperature, and suppress weeds, thereby enhancing plant growth. Another application involves creating sowing strips. These strips contain evenly distributed seeds along with nutrients. In the realm of geotextiles, textiles made from biopolymers are used for filtration and drainage, along with the utilization of geogrids.

When starch comes into contact with soil microorganisms, it breaks down into harmless substances. This is why starch films are utilized as agricultural mulch films. The mechanical properties of biodegradable films remain stable when exposed to water and high temperatures. However, high doses of UV radiation negatively impact their elongation at break.

Conclusion and Future Perspectives

Biodegradable polymers often fall short of their claims of biodegradability, as it largely depends on the surrounding environment. The rates of biodegradation differ across environments due to varying levels of humidity, temperature, and microorganism concentrations. To create new polymers with improved biodegradation in natural environments, polymer scientists must collaborate with experts from other disciplines.

Simultaneously, it is essential to consider the key factors for biodegradation when selecting biodegradable polymers for specific applications. The polymer must break down in the environment where it is most likely to end up, as determined by risk assessments.

A universal polymer that degrades quickly in all ecosystems is unlikely, as the demands for specific applications, such as beverage containers, differ significantly from the need for rapid biodegradation in certain environments, like seawater. As a result, the creation of new biodegradable polymers based on life cycle or risk assessments becomes unavoidable.

Examples include biodegradable mulch films used in agriculture and drug delivery agents in biomedicine. Over

the past decade, numerous biodegradable polymeric drug delivery systems have been created for various applications, including enzyme immobilization, controlled drug delivery, gene delivery, targeted delivery, anticancer drug delivery, and vaccine delivery.

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