IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Biodegradable Polymers in Drug Delivery Systems: A Comprehensive Review

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Abstract

Because biodegradable polymers break down in the body into non-toxic byproducts, they are essential to the development of drug delivery systems (DDS). Because of this feature, they are especially well-suited for focused and controlled medication administration, which is crucial for effectively treating a variety of medical problems while reducing adverse effects. There are two sorts of polymers: synthetic and natural. Naturally occurring biodegradable polymers with a high degree of biocompatibility include chitosan and alginate, which are produced from biological sources. On the other hand, artificially produced biodegradable polymers such as polylactic acid (PLA) and polylactic-co-glycolic acid (PLGA) can be modified to display certain characteristics and rates of degradation, offering designers versatility for a range of uses. There exist three possible methods of breakdown for these polymers: enzymatic, hydrolytic, and oxidative. Enzymatic degradation happens when an enzyme cleaves the polymer, whereas hydrolytic degradation breaks down polymer chains by water interaction. Reactive oxygen species play a role in oxidative deterioration, notwithstanding its rarity. Biodegradable polymers have a wide range of uses in DDS, from hydrogels and implantable devices to nanoparticles and microspheres. By allowing for controlled and sustained medication delivery, these devices improve the effectiveness of treatment. Drugs, for example, can be encapsulated by nanoparticles to ensure targeted delivery and shield them from degradation until they reach the intended location of action. Notwithstanding their benefits, there are also issues, such as inconsistent rates of decomposition an d possible toxicity of byproducts.Subsequent investigations will concentrate on creating novel, cust omized biodegradable materials, boosting medication delivery effectiveness, and optimizing bioco mpatibility.All things considered, biodegradable polymers offer a viable path for creative medicatio n delivery methods that will enhance patient outcomes in contemporary medicine.

1.Introduction:

Although biodegradable polymers have made progress in drug delivery, there are still obstacles to overcome in order to achieve safe, effective drug release. Although the use of synthetic and genetically modified polymers is being investigated, worries regarding long-term toxicity and polymer retention in the body prevent their widespread application. The goal is still to ensure regulated medication release by carefully breaking down polymers, keeping biocompatibility in mind. This chapter will provide a summary of important synthetic and recombinant polymers, including information on their design, degradation, and state of study.[1-6] In regenerative medicine,

pluripotent cells show promise; nonetheless, a combination of cells, scaffolds, and signaling molecules is needed for tissue regeneration. Large bone abnormalities can be treated using a variety of techniques, including prosthetics and grafting, each of which has drawbacks such immunological rejection and problems. To address these problems, biodegradable polymers—a type of synthetic bone substitute—are being created. By serving as scaffolds, these materials encourage the regeneration of new bone and allow it to eventually replace the old one. This review concentrates on biodegradable polymers that are utilized in drug delivery for bone repair and as scaffolds.[7] Drug delivery systems (DDS) are technologies that maximize treatment efficacy and reduce negative effects by delivering medications to specified body regions. There are several ways to give them, including as transdermal, nasal, and oral. DDS has enabled targeted and regulated medication release that is independent of physiological variables throughout time, improving patient compliance and lowering toxicity. Innovative systems, like nanomedicine, use mechanisms like enhanced permeability and retention (EPR) for passive targeting in the treatment of cancer, while active targeting approaches with ligands and stimuli-responsive properties provide more specificity but are hindered by issues like lysosomal degradation and immunogenicity.[8-10]

2. Types of biodegradable polymers

2.1. Natural polymers

Natural polymers are present in a wide range of animals and are essential to biological processes. They are occasionally employed as food additives, such as guar gum and pectin, and include, among others, rubber, cellulose, starch, lignin, and chitin. Natural polymers can be made up of several monomer units, as in hemicellulose and lignin, or just one monomer, like glucose in cellulose. These polymers' compositions differ between various natural materials. Natural polymer examples are frequently described in scientific literature, along with their origins and structural properties.[11-12]

2.2. Synthetic Polymers

Natural and manmade biodegradable polymers are essential for medicinal applications because of their adjustable features and controlled decomposition. Tunable chemically, synthetic biodegradable polymers, especially polyesters like poly(amino ester)s (PAEs), have been produced for tissue engineering, bioimaging, medication and gene delivery, and other uses. Since their discovery in the 1970s, PAEs have drawn interest due to their biocompatibility, biodegradability, and capacity for functionalization for certain biomedical applications. Because of their sensitivity to pH, they can be modified to enhance drug loading, release profiles, and imaging capabilities, making them useful in the treatment of cancer and gene delivery. Additionally, PAEs have inherent fluorescence, which increases their potential for use in diagnostic settings.[13] Natural and manmade biodegradable polymers are essential for medicinal applications because of their adjustable features and controlled decomposition. Tunable chemically, synthetic biodegradable polymers, especially polyesters like poly(amino ester)s (PAEs), have been produced for tissue engineering, bioimaging, medication and gene delivery, and other uses. Since their discovery in the 1970s, PAEs have drawn interest due to their biocompatibility, biodegradability, and capacity for functionalization for certain biomedical applications. Because of their sensitivity to pH, they can be modified to enhance drug loading, release profiles, and imaging capabilities, making them useful in the treatment of cancer and gene delivery. Additionally, PAEs have inherent fluorescence, which increases their potential for use in diagnostic settings.[14-15]

3. Mechanism of polymer degradation rate

3.1. Hydrolytic degradation

Because they are affordable and long-lasting, plastics made from fossil fuels are widely used, yet they pose serious environmental problems. The price of these plastics is anticipated to increase as fossil fuel supplies decline. They also give rise to significant problems with air quality, pollution, and waste disposal. The methods of recycling and incineration are challenging and costly. Globally, the packaging industry is the primary contributor of plastic trash, with the textile and consumer product industries following closely behind.[16] When polylactic acid (PLA) is exposed to moisture, it breaks down, releasing soluble byproducts and losing molecular weight. Diffusion rates, the solubility of breakdown products, and water absorption are some of the variables that affect this process. Depending on the circumstances, PLA might deteriorate either at the surface or throughout the bulk. Research has demonstrated that while some additions, such as chain extenders, can slow down degradation, others, like ethanol and titanium dioxide (TiO2) nanoparticles, can speed it up.[17-19]

3.2. Enzymatic degradation

Polylactic acid (PLA) is broken down by enzymes such as lipase, esterase, and alcalase; the activity of these enzymes is affected by temperature, pH, chain stereochemistry, and crystallinity. Enzymes of the lipase, cutinase, and proteinase K types have all been thoroughly investigated for PLA breakdown. Plasmid-degrading bacteria usually colonize the surface to release enzymes that break down the polymer into monomers and lactic acid oligomers. Enzymes are essential in promoting the breakdown, which begins on the PLA surface and moves inside.[20-22] The sentence draws attention to the problems that synthetic plastic trash and surplus plant biomass—both of which are resistant to degradation—pose to the ecosystem. Plastics that have collected in landfills and the ocean are being investigated using similar techniques to break them down, just as microbes have evolved enzymes to break down plant polymers. The article makes the case that utilizing these microbes or enzymes to break down synthetic plastics would be a more environmentally friendly option than the present waste management techniques, which are inefficient and may even worsen the situation. Creating enzymes that can effectively break down artificial polymers is seen to be a crucial first step in solving the world's plastic waste issue.[23]

3.3. Oxidative degradation

Light is the main cause of damage to polymers, especially when it comes to processes like photodegradation and photo-oxidation, which start with light absorption. Particularly susceptible to degradation caused by ultraviolet (UV) light, synthetic polymers are impacted by UV light in the 290–400 nm range, mostly from sunlight. Because UV light easily breaks carbon-carbon bonds, photo-irradiation causes a variety of chemical groups to develop at the soft segments of polymers, where degradation takes place.[24]

4. Applications of electrospun cellulose acetate nanofibers in the drug delivery system

Because of their biocompatibility and biodegradability, cellulose acetate (CA) nanofibers are useful in drug delivery systems (DDS). When utilized as scaffolds, implants, or patches, they help with tissue engineering and localized therapy. These nanofibers, which are mostly made by electrospinning, improve drug loading and deal with problems like limited solubility and

bioavailability. Their high surface-to-mass ratio makes them ideal for a variety of uses, such as wound dressings and enzyme support, since it permits the controlled release of therapeutic substances. All things considered, CA nanofibers are a promising development in medication delivery technology.[25]

4.1 Nanoparticle_Based Drug Delivery System

Nanoparticle for targeted delivery, nanoparticles are preferred, with sizes ranging from 10 nm to 1000 nm. Particularly, those smaller than 200 nm are more easily able to flow through microcapillaries.Through the increased permeability and retention (EPR) effect, these carriers can be customized for particular drug release profiles, improving medication delivery to tumors. Local depots for long-term medication release are provided by biodegradable nanoparticles.[26] Two crucial nanocarriers for medication delivery are nanospheres and nanocapsules. Drugs are equally distributed in a matrix by nanospheres, whereas drugs are encapsulated in a polymer membrane by nanocapsules. For targeted delivery, nanoparticle.There aren't many medications based on nanoparticles that can be used to treat cancer because of various issues.Problems with Scaling Up: The majority of current technologies for fabricating nanoparticles are appropriate for lab-scale production; large-scale synthesis requires low-energy approaches. They are also more likely to aggregate because of their modest size. Material Variability: Chitosan is a common component whose characteristics and stability under various environmental circumstances are affected by variations in its molecular weight and purity. Toxicity and Biodistribution: The unique hazardous characteristics of nanoparticles make safety evaluations more challenging. If the medication that is encapsulated is hazardous, those that are between 50 and 100 nm in size may build up in the spleen and liver.Cytotoxicity: Because of their reactive surface groups, silica nanoparticles may be hazardous, requiring additional long-term safety research.[27-29]

4.2 Nanosphere

Two crucial nanocarriers for medication delivery are nanospheres and nanocapsules. Drugs are equally distributed in a matrix by nanospheres, whereas drugs are encapsulated in a polymer membrane by nanocapsules.For targeted delivery, nanoparticle With an emphasis on tailored distribution to maximize therapeutic effects while reducing adverse effects and boosting patient compliance, the science of drug delivery has undergone substantial evolution. The use of advanced systems, such as controlled and sustained release techniques, has grown, especially with the use of polymer and microencapsulation technologies.The creation of PLGA microspheres for SAR 1118, which is intended to treat vascular eye problems, is one noteworthy use. In order to find polymers appropriate for varying degradation times—1, 3, and 6 months—and to maximize drug loading and release profiles, the study employed Design of Experiments. The outcomes demonstrated the potential of these microspheres for efficient drug delivery, with over 90% of SAR 1118 released within the required timeframes and minimal burst release (<20%) and efficient loading (15%–18%)[30-31]

4.3 Hydrogels

Three-dimensional networks of hydrophilic polymers with at least 20% water are called hydrogels; those with more than 95% water are superabsorbent. They can swell in water and contract when dry; the amount of swelling depends on the density of crosslinking and the hydrophilicity of the polymer. Chemical (covalent bonds) or physical (reversible non-covalent bond) crosslinking is how hydrogels

keep their structure intact. As demonstrated with sodium alginate and calcium ions, this reversibility enables physical gels to change between sol and gel states.Following the work of Wichterle and Lim on poly(2-hydroxyethyl methacrylate) (pHEMA), interest in the biomedical uses of hydrogels increased.[32-34]

4.4 Implantable Devices

Millions of patients benefit annually from surgical treatments utilizing implanted medical devices, which can either replace or augment biological structures, so improving their quality of life. Medical specialties that use implants include drug delivery systems, orthopedics, and cardiovascular therapy. Long-term drugs, implants, and innovative treatments are in greater demand as the prevalence of age-related disorders rises along with life expectancy. For example, degenerative joint illnesses affect almost 90% of adults over 40; as a result, the number of hip replacement surgeries performed has increased significantly from 152,000 in 2000. Comparably, the number of coronary stents used has increased dramatically; in 2004 alone, almost two million drug-eluting stents were implanted. Although tissue hyperplasia-related in-stent restenosis is still a concern, drug-eluting stents, which release specific medications to our body parts.[35-39]

5.Challanges In Biodegradable Polymers

Tablets formulations frequently employ direct-compression diluents such as chitosan, crystalline cellulose, and chitin, but each has drawbacks. Diffusion is the primary mechanism driving drug release from ethylcellulose (EC) matrix tablets, according to research, particularly for water-soluble medicines. Polymer relaxation and tablet erosion also play a role in less soluble medicines. Higher drug solubility has been shown to accelerate the rate of dissolution; at large drug loadings, diffusion is the main mechanism, but at lower loadings, polymer relaxation becomes more important.[40-42]

6. Future Directions

Drug delivery emerging technologies are developing quickly. By using microscopic channels and chambers, microfluidics (lab-on-a-chip) offers precise, site-specific medication delivery. Molecularly Imprinted Polymers (MIPs) help produce vaccines and drugs by selectively targeting molecules by imitating natural receptors. Though their mechanical strength needs to be improved, intelligent biomaterials, like adaptive hydrogels, respond to changes in the environment to control drug release. Despite difficulties with off-target consequences, CRISPR-Cas9 is being investigated for gene-editing-based medication delivery. Thanks to their distinctive fluorescence, quantum dots provide real-time drug tracking. Finally, the ability to create personalized, patient-specific drug delivery systems is made possible by 3D printing.[43-47]

7. Conclusion

To sum up, biodegradable polymers have become essential to the creation of sophisticated drug delivery systems, providing a reliable and effective way to administer medications. Because they naturally break down within the body, there is less need for surgery to remove them and there are less long-term negative effects, which makes them ideal for a variety of medicinal uses. These polymers increase patient compliance, decrease dosage frequency, and improve therapeutic efficacy by enabling regulated and prolonged drug release. Thanks to advances in polymer chemistry, it is now possible to precisely control the rate at which drugs release from polymers and target certain tissues or disease areas. Biodegradable polymers can be found in a variety of forms, such as

hydrogels, microcapsules, and nanoparticles, each of which has its own advantages. Modern drug delivery systems depend heavily on biodegradable polymers because they offer a viable and efficient means of delivering medications while the body breaks them down naturally, minimizing the need for surgical removal. The regulated and prolonged release of drugs made possible by these polymers enhances patient compliance and therapeutic results. Polymer chemistry has advanced to the point that its properties may be tailored, which makes it possible to use them in different drug delivery forms such as hydrogels and nanoparticles. Biodegradable polymers will become even more effective as research advances when combined with technologies such as nanotechnology, which will be crucial for the development of safe and customized drug delivery systems in the future.

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