**Biodegradable Polymers: The Versatile Forever Material**

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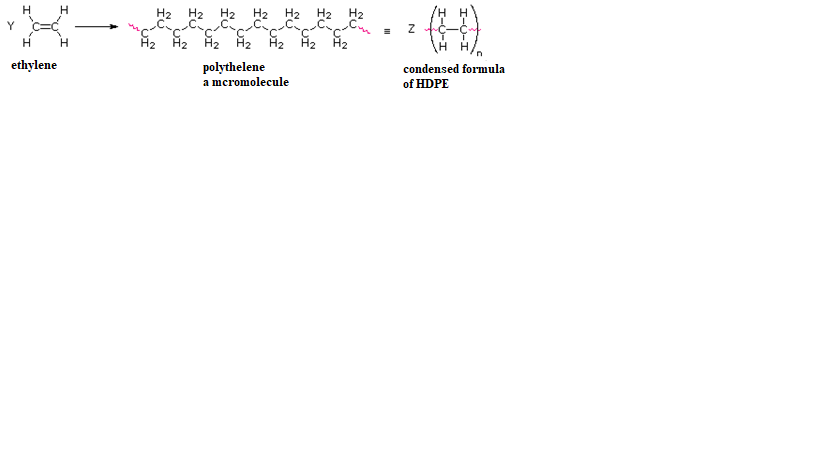
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**Abstract:** The macromolecules known as polymers are created by the chemical bonding of numerous smaller molecules, or repeating units, known as monomers. When exposed to air, water, soil organisms, and sunlight, plastics comprised of natural components like cellulose, starch, and hydroxycarboxylic acids disintegrate more rapidly than most polymers made of petroleum. These biodegradable materials can be composted, decomposed, and then put back into the ground as beneficial nutrients. Researchers and professionals from a broad spectrum of fields are highly intrigued in biopolymers since they represent a significant class of functional materials that are ideal for high-value applications. In order to solve a number of intricate issues pertaining to good health and wellbeing, interdisciplinary research is crucial to comprehend the fundamental and concrete aspects of biopolymers. There has been a significant amount of effort to substitute synthetic polymers with biodegradable materials, especially ones made from natural resources, in order to reduce the impact on the environment and reliance on fossil fuels. In this regard, numerous natural or biopolymer varieties have been created to meet the requirements of constantly expanding applications. Due to various special qualities, these biopolymers are increasingly being used in the pharmaceutical and medical sectors in addition to their current use in culinary applications. This chapter focusses on the application of these Biopolymers in the field of Medical Science, food and packaging industry and pharmaceuticals from time unknown to the present and stretching and strengthening towards the future.

***Keywords:*** *Biopolymers, Biodegradable materials, Cardiac Stent, Shape memory Polymer, Smart Polymers, Targeted Drug Delivery.*

1. **INTRODUCTION**

Chemists had severe suspicions about the existence of molecules with molecular weights larger than a few thousand before the early 1920s. Hermann Staudinger, a German scientist with experienced researching natural substances like rubber and cellulose, challenged this constrictive approach. Staudinger claimed that these compounds were composed of macromolecules with 10,000 or more atoms, as opposed to the conventional interpretation that these substances were collections of tiny molecules. He developed a repeating isoprene unit-based polymeric rubber structure (referred to as a monomer). Staudinger won the Nobel Prize in Chemistry in 1953 for his contributions to the field. The Greek roots poly (many), mono (one), and meros were used to create the phrases polymer and monomer (part). Most basic polymers have a recurring structural unit that not only represents the monomer(s) from which it was built, but also gives a clear way to depict these macromolecules in structures. This is shown by the equation below for polyethylene, which is possibly the simplest polymer. Here, ethylene (ethene) is the monomer, and high-density polyethylene is the name of the equivalent linear polymer (HDPE). HDPE is made up of macromolecules with molecular weights between 2\*105 and 3\*106 with n values between 10,000 and 100,000.



***Figure 1:*** *Chemical Formula for a typical polymer chain [1]*

If Y and Z are equivalent to moles of monomer and polymer, respectively, Z is around 10-5 Y. As ethylene is a stable chemical and acts as the polymer's synthetic precursor, it is given the name polyethylene rather than polymethylene (-CH2-)n. Since the atoms or groups found in those two free bonds depend on the chemical procedure employed for polymerization, they are typically not defined at the endpoints of the lengthy chain of carbons [1].

1. **CLASSIFICATION OF POLYMERS**

Polymers are broadly classified on the basis of the following characteristics:

1. Mode of Polymerization
2. Molecular forces experienced during the formation of the polymeric chain
3. Structure
4. Origin of source

The detailed classification has been shown in figure 2.

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***Figure 2:*** *Classification of Polymers*

1. **SOURCES OF POLYMER**

Polymers are available in two forms:  synthetic and natural. Scientists and engineers use petroleum oil to create synthetic polymers. Nylon, polyethylene, polyester, Teflon, and epoxy are some examples of artificial polymers. It is possible to isolate natural polymers from the ecosystem. They frequently consist of water. Silk, wool, DNA, cellulose, and proteins are a few examples of naturally occurring polymers.

**2.1 Natural Polymers**

Natural polymers can be extracted and are frequently found in nature. These polymers were produced using condensation or addition polymerization. Proteins and nucleic acids are just two examples of the countless natural polymers found in our bodies. Water is a byproduct of the condensation of condensation polymers, which is how natural polymers are typically created. Certain naturally occurring polymers, including DNA and RNA, are crucial to all living things' ability to function [2].

**2.2 Synthetic Polymers**

Packaging for foods, cosmetics, and medications frequently uses synthetic polymers made from petroleum-based raw materials. Nevertheless, nondegradable synthetic polymer contamination of the environment is a severe concern spreading across the globe. As a result, the creation of packaging materials with novel functionality and reduced environmental impact is of great research interest [3].

Biomaterials utilised as implant materials, drug delivery systems, tissue engineering scaffolds, or hydrogels typically contain synthetic polymers to a certain degree. For the development of biomaterials as endogenous or donor graft material for bone tissue engineering applications, synthetic polymers constitute a very broad subfamily of materials. Synthetic polymers have drawn a lot of attention in the perspective of the limitations of biopolymers derived from natural sources because of their high water resistance, biocompatibility, excellent mechanical properties, controllable degradation rate, simplicity in scaffold manufacturing, and cost-effectiveness.

Synthetic polymers typically undergo a surface treatment or are incorporated in a composite material (e.g., natural polymers) to improve their cellular compatibility because of their generally weak cellular interactions [4].

**2.3 Semi-Synthetic Polymers**

These category of polymers are derived from natural polymers by chemical modifications. The two primary classes of cellulose derivatives are cellulose ethers and cellulose esters, which have various physicochemical and mechanical characteristics. A few of the features of cellulose derivatives include viscosity in solution, surface activity, thermoplastic film qualities, and stability against oxidation, heat, hydrolysis, and biodegradation. Contrary to cellulose esters, which are typically water-insoluble polymers but have good film-forming properties, cellulose ethers (such as methylcellulose, hydroxyethyl cellulose, hydroxypropyl methylcellulose, carboxymethyl cellulose, and sodium carboxymethyl cellulose) are soluble in water [5]. In cosmetic products such creams, shampoos, lotions, and gels, these semi synthetic polymers are primarily employed as gelling agents, bioadhesives, thickening, and stabilising agents. They have a lower sensitivity to microbial contamination than natural gelling agents such starches, acacia, sodium alginate, agar, pectin, and gelatin [6].

1. **BIODEGRADABLE POLYMER**

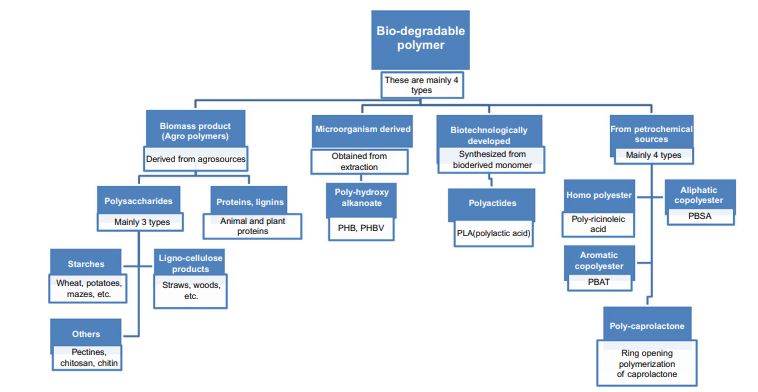
Since the inception of time, there have been biodegradable polymers. Under open air condition, all biopolymers, including polypeptides, cellulose, polysaccharides, chitin/chitosan, and natural rubber, degrade. The majority of polymers made from biological systems and bio-based materials, including plant and animal fats, vegetable oils, and plant extracts, are biodegradable. Poly(glycollic acid), developed in 1954, was the first synthetic biodegradable polymer manufactured by humans, despite its limited utility in everyday applications [7].

High molecular weight molecules represent a large field covered by biodegradable polymers. Differentiating between biodegradable polymers of natural and synthetic origin is typically useful. Native biodegradable polymers are the end product of a synthesis created over millions of years of evolution, creating materials specifically designed for various uses in nature. These biopolymers can be proteins, polysaccharides, nucleic acids, or lipids, and depending on the application, they exhibit entirely distinct properties. On the other hand, synthetic polymers are the outcome of just a century's worth of study and development [8].

**4.1 Types of Biodegradable Polymers**

For various biomedical applications, biodegradable polymers have drawn attention as a nanocarrier, scaffold, fibres, lenses, antibacterial dressing materials, gums, etc. There are around 200 different kinds of biodegradable polymers, both natural and man-made. The common biodegradable polymers used in many biological sectors have been compiled in this page. Moreover, this covers hydrogel, composites, copolymers, and polymer matrices, among many other things. The main factors taken into account for the development of innovative biomaterials are stability, degradation, mechanical behaviour, thermal characteristics, etc. [9].

The importance of biodegradable polymers as a "green" substitute for commercially accessible non-degradable polymers is growing. They are developing into a larger and larger area of study every day. Many forms of biodegradable polymers have been created, some of which are made in the natural environment as organisms are growing, such as cellulose, starch, polyhydroxy alkanoates, polylactide, polycaprolactone, collagen, and other polypeptides. Several biodegradable polymers are categorised as illustrated in Fig. 3 based on synthesis and processing [9].



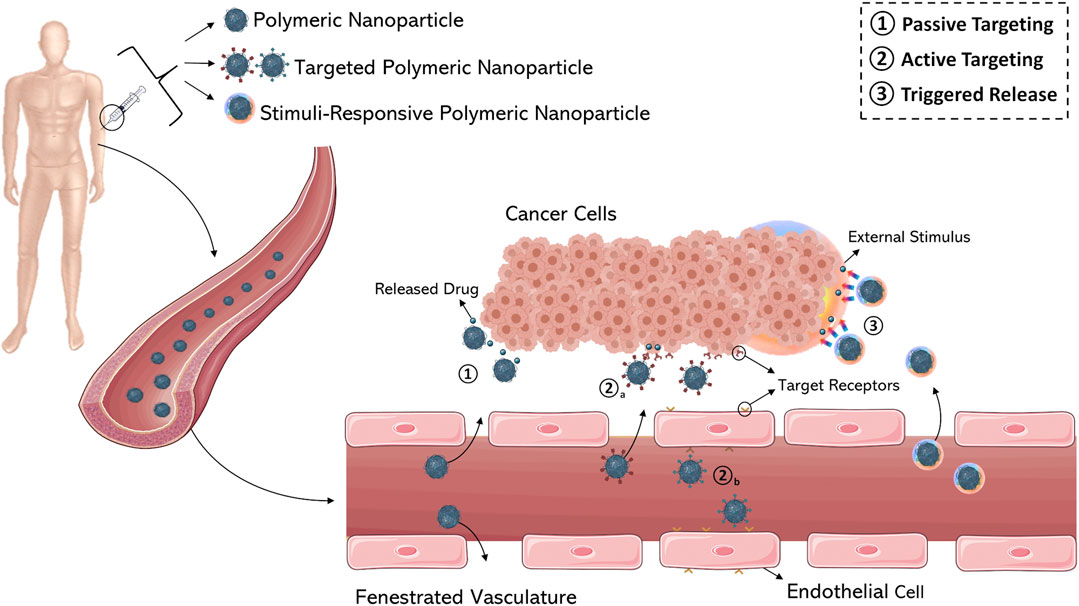
***Figure 3:*** *Classification of Biodegradable Polymers [9]*

**4.2 Applications of Biodegradable Polymers**

***4.2.1 Targeted Drug Delivery:*** Polymer use has grown increasingly significant in drug delivery systems. Various polymer-based system types are being researched continually for targeted tactics and for controlled release of active ingredients. The development of polymeric drug delivery systems uses biodegradable polymers as its preferred material due to their high biocompatibility and degradability features. By virtue of the hydrolyzable nature of the polymer backbone, canonical physiological cell processes result in the creation of non-toxic natural products that are consequently quickly removed. In order to choose the best polymeric material for a certain application and the chemical makeup of pharmaceuticals, biodegradable polymers can be derived from both natural and synthetic sources. In the realm of drug delivery, biodegradable polymers notably hyaluronic acid (HA), chitosan, and polylactic acid (PLA) are some of the most often utilised ones. In relation to the drug-loading strategy and the biological target, the size of polymers can vary, preventing fast clearance after intravenous administration, extending circulation half-life, while also increasing the likelihood of crossing a variety of biological barriers and preventing accumulation in capillaries and/or other organs. Due to the subcellular scale of systems, the use of biodegradable polymers modifies the pharmacokinetic characteristics of numerous active compounds. Polymer vectors can be created using various molecular arrangements, such as linear or branching, while adhering to various macromolecular structures, such as micelles or nanoparticles.

By altering the pharmacokinetic and pharmacodynamic effects the nanocarrier exerts, drug delivery within nanoparticles might improve therapeutic effectiveness. The passive targeting of nanoparticles, which is based on physical contact between the nanosystems and the tissue microenvironment, is partially responsible for these improvements (blood flow, lymphatic drainage, etc.).

As an alternative, tissue-specific ligand (antibodies, peptides, macromolecules, etc.) can be conjugated on the surface of nanoparticles to actively target them; these interactions cause a spatial concentration of nanoparticles in target tissues [10] (Figure 4).



***Figure 4:*** *Schematic representation of various drug targeting approaches (1–3). (1) Passive targeting of nanocarriers through fenestrated vasculature of tumor tissue by extravasation. Active targeting of cancer cells (2a) and (2b) tumor endothelium using ligand-modified nanocarriers. (3) Stimuli-responsive nanomedicines able to release the anticancer agent by internal or external triggers [11].*

***4.2.1.1 Passive Targeting***

Passive targeting takes advantage of the unique architectural and pathological defects of the tumour vasculature that encourage the accumulation of polymeric nanoparticles by convection or passive diffusion in the perivascular tumour zone [11]. The movement of big molecules over wide pores is referred to as convection. Diffusion, on the other hand, is characterised as a process of molecular transport across the cell membrane along the concentration gradient without consuming cellular energy and applies primarily to substances with a low molecular weight.

***4.2.1.2 Active Targeting***

The goal of the active targeting strategy is to promote a ligand's interaction with overexpressed receptors preferentially in tumour tissue while reducing interaction with healthy cells. It does this by conjugating, integrating, or adhering a ligand to the surface of a nanocarrier. For these reasons, either small compounds like folic acid and carbohydrates or macromolecules like peptides, proteins, antibodies, aptamers, and oligonucleotides have been utilised [12].

***4.2.1.3 Stimuli-Sensitive Polymeric nanoparticles (PNs) and Trigger Release***

Stimuli responsive systems encourage the release of pharmaceuticals in response to physical, chemical, or biological triggers as a result of the structural modification of the materials. According to Li et al. (2013) and Lim et al. (2018), triggers can be classified as internal stimuli (patho-physiological/patho-chemical condition), which include changes in pH, redox, ionic strength, and shear stress in the target tissues, and external stimuli (physical), which include temperature, light, ultrasound, magnetic force, and electric fields [13-17].

***4.2.2 Cardiac Stent:*** With newer generations of stents aimed at optimizing clinical outcomes, stent design is still evolving. With an emphasis on biodegradable polymers and stents and their potential advantages, this paper analyses various generations of stents. Comparing drug-eluting stents (DES) with bare-metal stents, DES reduces stent thrombosis (BMS). Yet, they are linked to a reduced rate of vascular repair and endothelialization as well as an increase in very long-term events (beyond 1 year). Several of these events (those lasting longer than a year) have been linked to persistent inflammation brought on by the polymer. By combining the advantages of reduced in-stent restenosis seen with DES and the advantages of reduced very-late stent thrombosis and myocardial infarction due to absence of polymer with bare-metal stents, biodegradable-polymer drug-eluting stents (BP DES) were developed to overcome this polymer related limitation of first-generation DP DES (BMS). However, the more recent generation of BP DES with ultrathin struts show promise in further reducing clinical outcomes when compared to second-generation DP DES. Earlier generations of BP DES demonstrated superiority over first-generation DP DES but at best were non-inferior to second-generation DP DES for clinical outcomes. It is yet unclear if this is because of the biodegradable polymer or the incredibly thin struts. The next generation of DES, which combines biodegradable polymer stents with ultrathin struts, has showed promise. However, more research and long-term follow-up are required to validate these outcomes [18].

DES are specialised vascular stents that provide regulated local medication delivery with the aim of reducing or preventing in-stent restenosis as a result of increased SMC proliferation [19,20]. Moreover, second- and third-generation DES currently use biomimetic polymers like phosphorylcholine (PC), poly(vinylidene fluoride)-hexafluoropropylene (PVDF-HFP), or the BioLinx polymer since they don't obstruct stent reendothelialization [21]. Beyond that, biodegradable polymers, such as PLA and poly(lactide-co-glycolide) (PLGA), were extensively investigated to enhance their characteristics and biocompatibility. DES are predicted to result in decreased stent-thrombosis since the polymeric coatings eventually deteriorate and turn into BMS. The next generation of DES with an even greater influence on endothelialization and arterial healing are the result of intensive work on stent development.

A different strategy to lessen hypersensitivity and late stent thrombosis involves utilizing no polymers at all. Drug elution from biodegradable polymers is one such strategy. Drugs were primarily integrated into microporous or nanoporous metallic stent surfaces in polymer-free DES that have been studied [22, 23]. The effectiveness and safety of polymer-free DES in clinical practise are now under discussion. Randomized controlled studies performed thus far either yield inconsistent findings or lack the necessary power to address the issue of their effectiveness and safety [24]. However, based on a lot of research, patients who receive durable polymer DES treatment have clinical results in terms of mortality, stent thrombosis, and long-term efficacy that are comparable to those of patients who receive polymer-free stent treatment [25, 26]. Nonetheless, it has been claimed that new generation DES have shown to be superior or noninferior to durable DES in terms of safety and efficacy [27, 28]. The CHOICE study could provide some insight into this matter [29]. As well as other cutting-edge, polymer-free drug reservoirs, biocompatible, polymer-based abluminal or dual, and side-selective coatings may be relevant [30, 31, 32]. Common Drug eluting stents are summarized in Table 1.

***Table 1:*** *Components and performance of current clinically approved DES.*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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| |  |  |  |  |  | | --- | --- | --- | --- | --- | | **Type** | **DES** | **Coating** | **Drug** | **Clinical performance** | | Durable | Taxus Express [33, 34] | SIBS | Paclitaxel | Superior to BMS in reducing ISR and TLR | | Promus Element [35] | PBMA/PVDF-HFP | Everolimus | Comparable to Xience-V | | Endeavour [36–38] | PC | Zotarolimus | Similar safety and efficacy as Taxus with higher ST; impaired polymer integrity | | Xience-V [39] | PBMA/PVDF-HFP | Everolimus | Prevents ISR and restores vasomotion, low ST | | Biodegradable | SymBio [40] | PLGA | Pimecrolimus/ Paclitaxel | No beneficial effect compared to Taxus | | Endeavour Resolute [27] | BioLinx | Zotarolimus | Noninferior in safety and efficacy trials compared to durable DES | | BioMatrix [41–43] | PLA | Biolimus A9 | reduced risk of CE compared to durable DES | | Polymer-free | Janus Flex [44] |  | Tacrolimus | Higher rates of TLR and ST in comparison with Taxus | | Yukon Choice [25, 26] |  | Sirolimus, Trapidil | Similar to Taxus, no beneficial effects compared to durable DES | |
| **SIBS:** poly(styrene-b-isobutylene-b-styrene) block copolymer, **PBMA**: poly(n-butyl methacrylate), **PVDF-HFP:** poly(vinylidene fluoride)-hexafluoropropylene, **PC:** phosphorylcholine polymer, **PLGA:** poly(lactide-co-glycolide), **BioLinx:** hydrophobic C10-polymer/hydrophilic C19-polymer/poly(vinyl-pyrrolidone) (PVP), and **PLA:** polylactide; **DES:** drug-eluting stent, **BMS:** bare metal stent, **ISR:** in-stent restenosis, **TLR:** target lesion revascularization, **ST:** stent thrombosis, and **CE:** cardiac events. |

***4.2.3 Scaffold for Tissue Engineering***

mechanical and biological attributes akin to native extracellular matrix is usually regarded as essential for designing live tissues (ECM). Prior to the regeneration of biologically functional tissue or natural ECM, they permit regulating cell adhesion, invasion, proliferation, and differentiation. The creation of composite or hybrid scaffolds that can serve as three-dimensional templates and artificial ECM environments is currently a problem in the field of bone regeneration. Here, we'll go through current processing techniques that successfully imitate cell-ECM interactions while achieving structural features that mirror the ECM on many levels. This will help to encourage the regeneration of mineralized tissues like bone [45].

To restore defects, chondrocytes are seeded into or onto biodegradable scaffolds in cartilage tissue engineering. The localised defects of the articular cartilage are almost exclusively repaired with the designed construct in cartilage repair. Engineered cartilage can primarily be utilised in head and neck reconstruction, including the treatment of abnormalities in the auricle, nose, and trachea, in addition to articular cartilage reconstructive applications. It is particularly difficult to achieve a suitable horizontal and vertical integration with the surrounding natural articular cartilage and subchondral bone during articular cartilage restoration. To avoid perifocal osteoarthritis (OA), the mechanical characteristics of the manufactured construct should ideally be comparable to those of the surrounding cartilage. Nonetheless, they are typically inferior at the time of implantation, depending on the implant's in situ maturation over time. The scaffold must additionally offer a setting that ensures the chondrogenic stability of the implanted chondrocytes. While it is advised that such an implant should be able to withstand inflammation, considerable clinical inflammation is clinically absent because it is a contraindication, much like OA or other forms of arthritis like rheumatoid arthritis (RA). Despite substantial advancements, no synthetic construct can perfectly duplicate the composition and characteristics of natural articular cartilage. The transplanted construct must either be strong enough to withstand a trimming in the operating room to be implanted in a defect-specific shape or be able to adapt to the defect because cartilage flaws come in a variety of sizes and are frequently irregular in shape [46].

Clinical use of engineered blood vessels, airways, heart valves, urinary tract, and other tissues is no longer regarded as science fiction because it is based on the traditional open systems tissue-engineering framework of cells sown onto biodegradable scaffolds. This technology is now available at the bedside for a restricted group of patients with challenging issues requiring surgical reconstruction thanks to a graded approach built on considerable background work by several disciplines testing these items in both small and big animal models [47].

***4.2.4 Food packaging***

In the contemporaneous food sector, food packaging plays a critical role. Technologies for new food packaging are being developed to satisfy consumer and commercial demands. Environmental awareness, changes in consumer lifestyles and the development of new fields of knowledge (such as nanotechnology or biotechnology) are driving forces behind the development of smart packages that can extend food shelf-life while maintaining and monitoring their safety and quality while also protecting the environment [48].

In food packaging, polymers are typically utilised as substrates and matrices. Synthetic undegradable polymers, such as high-, low-, and linear low-density polyethylene (HDPE, LDPE, and LLDPE), polystyrene (PS), polypropylene (PP), and polyethylene terephthalate (PET), are being used as packaging materials in the food packaging industry due to a lack of environmental awareness, cost, and technological limitations [49].

The market for biodegradable plastic packaging was valued at USD 4.65 billion in 2019, and it is anticipated to increase at a CAGR of 17.04% through the end of 2025, reaching a market value of up to USD 12.06 million. This growth is the result of different government measures to limit plastic waste as well as growing environmental concerns. In 2019, there were 2.11 million tonnes of bioplastic produced worldwide. By the end of 2024, it is anticipated that this number would rise to 2.43 million tonnes [50].

Polyethylene (PE), Polyethylene Terephthalate (PET), and Polyamides (PA) are non-biodegradable, bio-based plastics that together account for about 44% of the world's production of bioplastics. Almost 55.5% of the world's production of bioplastics is made up of biodegradable polymers like PLA, PHA, starch blends, PBS, PBAT, and others [51]. Asia (45%), Europe (25%), North America (18%), and South America (12%) are the regions that contribute most to the manufacture of bioplastics.

1. **SMART FUTURE: Being INTELLIGENT**

**5.1 Shape Memory Biodegradable Polymers**

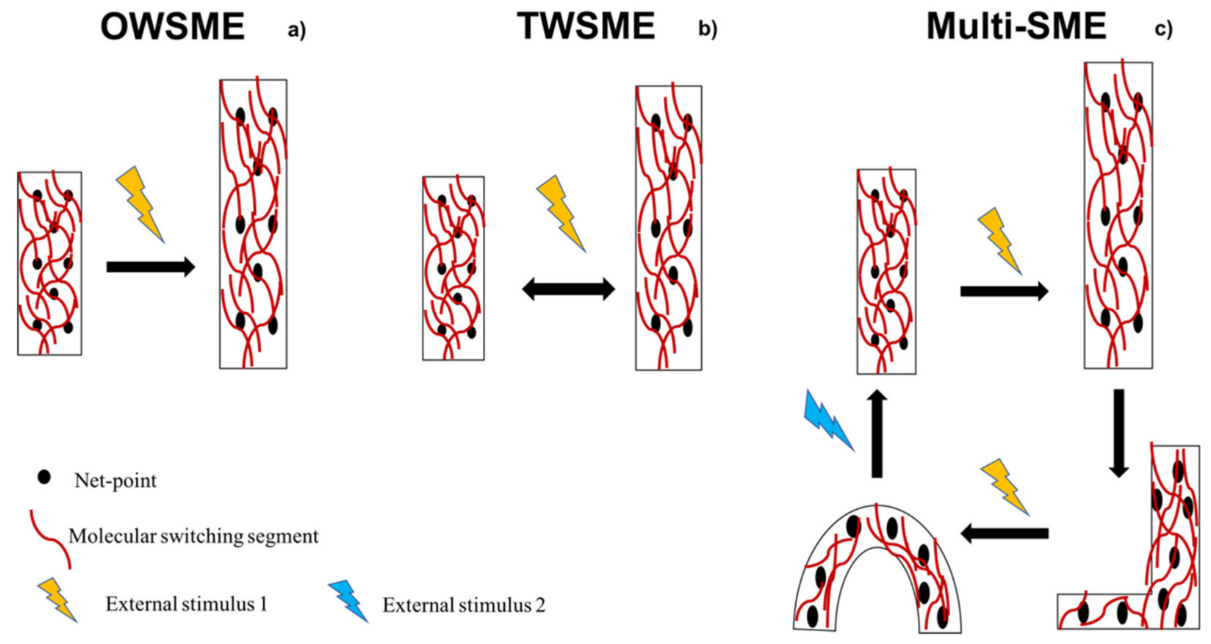
SMPs, or Shape Memory Polymers, have demonstrated a lot of potential in biomedical applications. Heat, UV light, and electricity are common shape recovery triggers, however they could be dangerous to people. Similarly, the inherent biocompatibility and convenient accessibility of water have made water-responsive SMPs important, particularly for in vivo applications. The known water-responsive SMPs, however, are few and quite complex. [52].

Shape-Memory Polymers (SMPs) are kind of smart that can change their size, shape, stiffness, and strain in response to a variety of external stimuli, including physiological ones like pH, body temperature, and ions concentration. These stimuli include heat, electric and magnetic fields, water, and light. SMPs have the capacity to recall their initial shape prior to triggered exposure and following deformation, in the absence of the stimulus, and to revert to that original shape on their own. Due to the advantages of nanofibers, such as their high surface area per volume unit, high porosity, small diameter, low density, desirable fibre orientation, and nanoarchitecture that mimics native extracellular matrix, SMPs nanofibers (SMPNs) have been investigated for biomedical applications more and more (ECM) [53].

Depending on the crosslinking type, shape-memory effect, macroscopic morphology, and triggering stimuli, there are numerous ways to categorise SMPs. SMPs are divided into two categories, physically crosslinked and chemically crosslinked. Chemically crosslinked SMPs have covalent links, whereas physically crosslinked SMPs have a network formed of noncovalent bonds. Shape-memory blocks, shape-memory foams, shape-memory fibres, and shape-memory films are some examples of SMPs that can be treated into various types of shapes [53]. According to their shape-memory effect (SME), SMPs may be divided into three categories: one-way shape-memory effect (OWSME), two-way reversible shape-memory effect (TWSME), and multiple-SME (Figure 5). The definitions of each category are provided below.

* OWSMEs: Materials lose their ability to change their shape, therefore an additional step is required to create a temporary shape before SMP regain its natural shape.
* TWSMEs: Materials that can alternate between their original and temporary shapes repeatedly without needing to be further reshaped. Reversible shape-memory effect (reversible SME) and reversible shape-memory polymers (reversible SMPs) are other synonyms for TWSMEs.
* Multiple-SMEs: Materials that display not just the original design, but also one or more additional temporary shapes. External stimuli enables them to change from one temporary shape to another, and more stimulation enables them to take their original polymer shape back [54].

Nafion, a common thermoplastic polymer utilised as SMPs in bulk film form, is an example of multiple-SME [53].



***Figure 5:*** *SMPs: (a) one-way (OWSME), (b) two-way reversible (TWSME) and (c) multiple-SME [53].*

***5.1.1 Biomedical Applications***

As static physical frameworks, tissue-engineered scaffolds have historically proved unsuitable for simulating the intricate dynamic behaviour of in vivo microenvironments.

With the use of SMPs, tissue regeneration scaffolds can be implanted with minimally invasive surgery while still promoting cell adhesion and proliferation [55].

Shape-memory scaffolds, particularly those in the form of nanofibers, have a high specific surface area and porosity, which make them very promising for application in tissue engineering. To create biomedical tissues that are suitable for simulating the complex dynamic behaviour of in vivo microenvironments, the most popular biocompatible and biodegradable SMPs are made from poly(-caprolactone) (PCL), polyurethane (PU), poly (D, L-lactide) (PDLLA), PVA, ethylene vinyl acetate copolymer (EVA), polymer blends, polymer composites, crosslinked polymers, and supramole materials.

Shape-memory feature was contributed to bone tissue engineering. It may also provide the opportunity to exert in situ mechanical stimulus to achieve greater efficacy in bone repair and regeneration, in addition to the capacity to enable minimally invasive surgical implantation. Due to their biocompatibility, tensile strength, and slow degradation rate, polylactides polymers, such as poly(L-lactide) (PLLA), poly(D-lactide) (PDLA), and poly(L-lactide) (PDLA), and PDLLA, have been widely employed as scaffolding materials for bone regeneration [56,57,58]. If appropriately programmed, polylactide polymers also have a SME. Polylactides were mixed and/or blended with other materials to achieve the desired toughness and Tg properties [59].

The main cause of death around the globe is cardiovascular disease. Treatment for vascular issues and endothelial cell dysfunction may involve artificial vascular grafts. To establish a proper regenerative process, however, a confluent endothelial monolayer must quickly grow on the lumen of a 3D structure [60]. A biocompatible shape-memory polymer and an electrospun nanofibrous membrane were combined to create novel shape-morphing scaffolds, enabling programmable deformation from planar shapes to small-diameter tubular shapes [61].

In order to close the lesion, cells, growth factors, and cytokines interact during the skin restoration process [62]. With the ability to hold their original shape in the midst of external stress, polymer wound dressings with shape memory feature can aid in the initial stage of wound healing by helping to seal open cracks. As a result, wound dressings with shape memory have a tremendous potential to speed up the healing of skin wounds [63,64].

***5.1.2 Effect of Shape memory on Sterilization***

Considering that sterilising treatments have the potential to change the features of scaffolds, the kind of SMP and the stimulus required to restore scaffold form must be taken into consideration while selecting the most suitable sterilisation procedure. Almost all polymer-based goods can be harmed by heat sterilisation, whether it be dry or steam heat, as heat can cause polymer breakdown or undesired crosslinking. Moreover, because SME can be changed, thermally sensitive SMPs cannot be sterilised by heat application. The two methods of sterilisation that are most frequently employed are gamma radiation and ethylene oxide (EtO).

The chemical sterilising technique ethylene oxide works by irreversibly alkylating cellular molecules that may contain amino, carboxyl, thiol, hydroxyl, and amide groups, which permanently suppresses cell metabolism and division. Regrettably, the potential lingering toxicity of EtO in the scaffolds is one of the main drawbacks of this sterilisation method. The maximum EtO residual concentration in medical devices after EtO sterilisation has been defined by the American National Institute for Occupational Safety and Health (NIOSH), with a suggested range of 10-25 ppm [65].

Since it operates at low temperatures and for brief periods of time, gamma irradiation is suitable for polymeric materials that are sensitive to heat. Yet, polymers are capable of undergoing a variety of chemical, mechanical, and morphological changes, such as chain scission breakdown of polymers or cross-linking of polymers, or even both. At the level of weak bonds, cleavage is seen together with bond breakage and a consequent drop in molecular weight. Large, fragile, and prone to deterioration three-dimensional networks are created through cross-linking. For instance, after exposure to gamma rays, PLA may experience morphological alterations, such as the development of rougher surfaces as a result of cleavage. After irradiation, PCL exhibits mechanical alterations, such as a rise in yield point [66,67].

**5.2 Smart Biodegradable Polymers**

The idea behind smart biomaterials is the use of polymers with built-in conductivity. Electrical conductivity responds very well to conducting polymers made of polypyrrole (PPy), polylactic acid (PLA), poly(3,4-ethylenedioxythiophene) (PEDOT), and polyaniline (PANI). The synthesis of biodegradable conducting polymers involves a number of techniques [68].

Smart polymeric materials have the unique ability to react to modest environmental changes by making significant changes. These materials are referred to as smart materials, stimuli-responsive materials, or environmentally conscious materials. Little environmental cues cause quick and reversible changes in the microstructure of smart polymers. Temperature, pH, solvent or ionic composition, electric field, light intensity, and the addition of certain ions are just a few of the stimuli that have been shown to cause these modifications in the physical properties of the polymers [69–73]. The changes are visible at the macroscopic level as precipitate development, phase separation, or, in the case of hydrogels, as magnitude variations.

These effects are intrinsically reversible, implying that when the trigger is taken away, the system can return to its initial state. These transitions are triggered by a variety of common stimuli, such as the neutralisation of charged groups by a pH shift or the addition of a polymer with an opposite charge, changes in hydrogen bonding efficiency brought on by an increase in temperature or ionic strength, and the disintegration of hydrogels and interpenetrating polymer networks [74].

Throughout the past two decades, the employment of functional polymers has increased significantly. These polymers react as desired to changes in temperature, pH, magnetic or electric fields, or other conditions. The field of smart polymeric materials, which are being specifically designed for use in biotechnology and medicine, has recently experienced exponential expansion. For many different uses, various smart biopolymer kinds have been developed.

They are categorised according on the nature of the stimuli and the capabilities of the polymers [74]:

1. Intelligent pH sensitive polymers
2. Smart thermosensitive polymers
3. Stimuli responsive intelligent polymers

The term "pH-sensitive polymers" refers to polymers with ionizable functional groups that react to changes in pH. Since these polymers have acidic (carboxylic or sulphonic) or basic (amino salts) groups in their structure, they can take or release protons in reaction to pH variations [75].

Thermosensitive polymers are advanced polymers that react to temperature changes by altering their microstructural characteristics. In drug administration systems and biomaterials, these polymers are the most researched, utilised, and safest [74]. The potential to distribute hydrophilic and lipophilic pharmaceuticals, site-specific drug delivery, avoiding hazardous organic solvents, and prolonged release features with decreased side effects are some of the benefits of temperature sensitive polymeric systems. On the other hand, these also show a number of drawbacks, including high-burst drug release, a lack of polymeric system biocompatibility, and a steady reduction of the system's pH due to acidic degradation [76,77].

When exposed to different stimuli, even small ones sometimes have a positive effect on stimuli responsive polymers. These intelligent polymers are further subdivided into light-sensitive, electrically-sensitive, magnetically-sensitive, and stimuli-responsive polymers [74].

Smart polymers are easy to shape and colouring, strong, resilient, non-thrombogenic, biocompatible. A very significant part of medication delivery is played by these smart biopolymer characteristics. They keep the medicine stable, are simple to make, effective nutrition carriers for the cells, and can be modified with cell adhesion ligands. Moreover, they can be injected in vitro as a liquid to form a gel at body temperature. For example, to create excellent formulations with poor solubility pharmaceuticals as a carrier for drug delivery, some hydrophobic medications, like paclitaxel, were solubilized using thermo-sensitive polymers.

1. **CONCLUSIONS**

A fast developing field is the design of drug delivery systems based on both natural and synthetic polymers. It makes use of the impressive delivery method that infections and mammalian cells have developed, which includes selective targeting and sustained circulation by evading immune systems. The potential for the biomimetic and bioinspired systems to overcome any problems with polymeric drug delivery is quite promising. The development of biocompatible and biologically relevant copolymers and dendrimers for the treatment of cancer, particularly their usage as carriers for effective anti-cancer medications like cis-platin and doxorubicin, will have been successful. Dendrimers are intriguing new scaffolds for polymeric drug delivery systems because of their special qualities, which include their high degree of branching, multi-valence, globular topology, and well-defined molecular weight.

It is clear that SMPs have made significant architectural development, inspiring novel techniques and biomedical applications. With a rising focus on comprehending SME and biological reaction to polymeric materials, extensive work has been done to identify network design principles that can tailor polymer chemistries for a range of purposes. Because to their faster stimulus response, good adaptability, low weight, simple processing, and modulating architectures, shape memory polymer nanocomposites (SMPNs) in particular draw a lot of interest. SMPs, in the form of micro/nanofibers, particularly in the biomedical industry, shown a dynamic fibrous structure ideal to direct cell regulation and differentiation, regulate drug administration, and ensure scaffolding. However, there remain a number of issues that need to be resolved. In order to create scaffolds that work better and last longer, reversible micro/nanostructure SMPs should be further researched. TWSME is favoured above OWSME when comparing different shape-memory effects. Due to their many applications, thermo-responsive SMP fibres are the most researched; however, for specific biomedical applications, it is still necessary to programme a more accurate transition temperature range since different temperatures are actually registered during inflammation, infection, or other pathological conditions.

For innovative medical devices, biocompatible and biodegradable SMPs with suitable mechanical properties could be created. In the case of animal testing, huge, bulky devices might be temporarily implanted into the body using minimally invasive surgery before being extended to their final shape to fit as needed. One of the challenges in endoscopic surgery is tying a knot using tools and sutures to close an incision or open lumen. Several applications for the SMPs have been discovered in tissue engineering. A shape memory polymer-based bioactive porous scaffold has been created with simultaneous capabilities for minimally invasive surgery and quick bone regeneration.

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