

# BIODEGRADABLE POLYMERS: THE VERSATILE FOREVER MATERIAL

## Abstract

The chemical embracing multiple smaller molecules, or repeating units, known as monomers, results in the macromolecules known as polymers. Plastics made of natural materials like starch, dextrin and hydroxyl carboxylic acids degrade more faster than most polymeric materials manufactured from petroleum when bare to atmosphere, water, soil organisms, and daylight. 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 diminish the impact on the habitat 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 book chapter mainly emphasizes the application range of Biomedical polymers in the arena 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.

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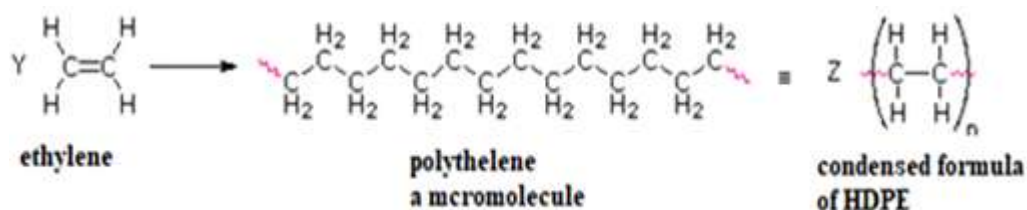
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## I. INTRODUCTION

Chemists had severe suspicions about the extent of molecules having large molecular weights, even larger than a few thousands preceding to early 1920s. A German scientist named Hermann Staudinger had experienced of researching towards innate substances like rubber and cellulose, challenged this constrictive approach. Staudinger argued that these chemicals were constituted of macromolecules with 10,000 or more atoms, as opposed to the common view that they were made up of little molecules. He fabricated a polymeric rubber structure applying repeated isoprene units (known as a monomer). Staudinger was a beneficiary of Nobel Prize winner in Chemistry in 1953 in recognition of his contributions to the discipline. Polymer and monomer (part) originated from the Greek roots poly (many), mono (one), and meros. 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  $2 \times 10^5$  and  $3 \times 10^6$  with n values between 10,000 and 100,000.



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

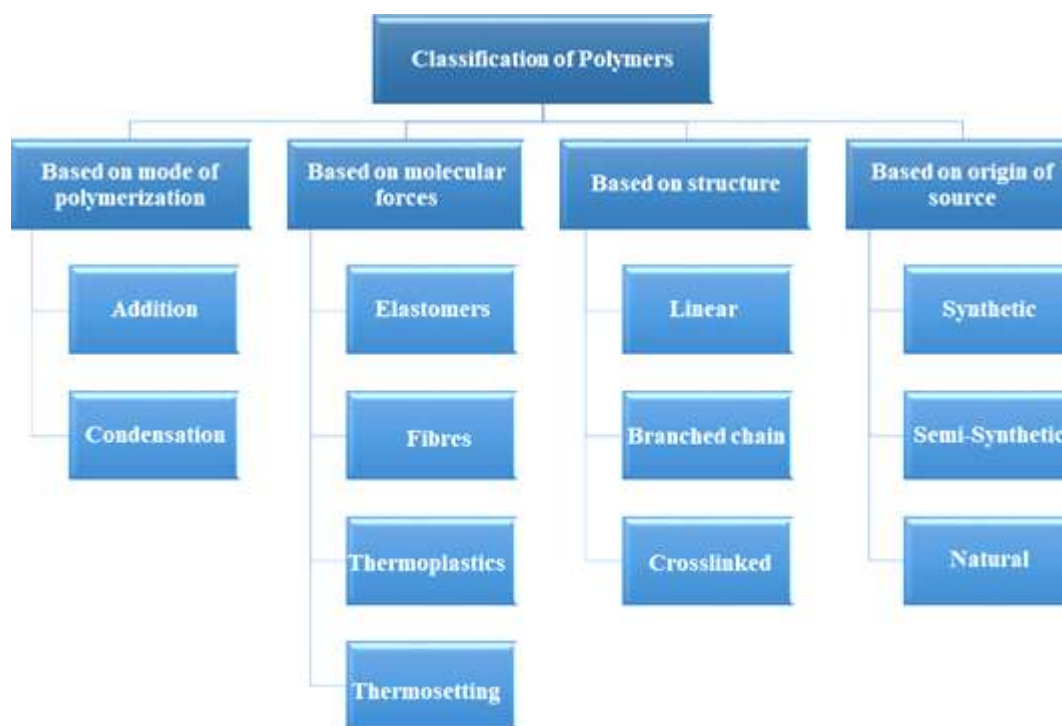
If Y and Z are equivalent to moles of monomer and polymer, respectively, Z is around  $10^{-5}$  Y. As ethylene is a stable chemical and acts as the polymer's synthetic precursor, it is given the name polyethylene rather than polymethylene  $(-CH_2)_n$ . Since the atoms or groups found in those two free bonds depend on the chemical procedure employed for polymerization, they are typically not defined at the endpoints of the lengthy chain of carbons [1].

## II. CLASSIFICATION OF POLYMERS

Polymers are broadly categorised based on the following characteristics:

- Mode of Polymerization
- Molecular forces experienced during the formation of the polymeric chain
- Structure
- Origin of source

The detailed classification has been depicted in figure 2.



**Figure 2:** Classification of Polymers

### III. SOURCES OF POLYMER

Polymers exist in two types: synthetic and natural. Most of scientists and engineers employed petroleum oil to synthesize polymeric materials. Nylon, Polyethylene, polyurethane, polyester, Teflon etc. are the example of synthetic polymers. Naturally derived polymers can be extracted from the environment. They are frequently made up of water. Silk, wool, DNA, cellulose, protein etc. belongs to the naturally occurring polymers.

- 1. Natural Polymers:** Natural polymers can be extracted and are frequently found in nature. These polymers were produced using condensation or addition polymerization. Collagen, elastin protein and nucleic acids are classical illustrations of the countless natural polymers found in our bodies. Natural polymers are typically created by the release of water from condensation polymers as by-product. Certain naturally occurring polymers, including DNA and RNA, are crucial to all living things' ability to function [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].

Synthetic polymers are frequently detected in biomaterials employed as implantable materials, carrier for drug delivery systems, scaffolding materials for tissue engineering and/or hydrogels. Chemically synthesized polymers serve as a very extensive subcategory of substances for facilitating the manufacture of suitable biomedical materials as endogenous grafting material for osseous tissue regeneration. Based on their

exceptional water resistance property, biological compatibility, outstanding mechanical features, controllable degeneration rate, simplicity in scaffold fabrication, and low-cost, synthetic polymers are gaining a lot of attention in comparison to the limitations of biopolymers derived from natural sources.

Given their generally weak cellular associations, artificial polymers are typically surface modified or included into a system of composite material to strengthen the inherent cellular unity [4].

- 3. Semi-Synthetic Polymers:** These polymers originate from natural polymers via chemical transformation. Cellulose derivatives are available in two primary forms such as cellulosic ethers and cellulosic esters each form has its own set of physicochemical and mechanical properties. Viscous nature, surface reactivity, thermoplastic film characteristics, and cohesion against oxidation, thermal stability, and biodegradation are some of the important properties of cellulose by-products. In comparison, cellulose esters are normally water insoluble but have strong affinity towards film-making capabilities whereas cellulose ethers (such as methylcellulose, hydroxyethyl cellulose, hydroxypropyl methylcellulose, carboxymethyl cellulose, and sodium carboxymethyl cellulose) are water soluble [5]. These semi synthetic polymers typically serve as bioadhesives, gelling agents, thickening agents, as well as stabilising substances in cosmetic goods such as creams, shampoos, lotions, and gels. Starch, gelatin, agar, acacia, pectin, sodium alginate etc are the commonly used natural gelling agents and are less susceptible to microbial contamination [6].

#### IV. BIODEGRADABLE POLYMER

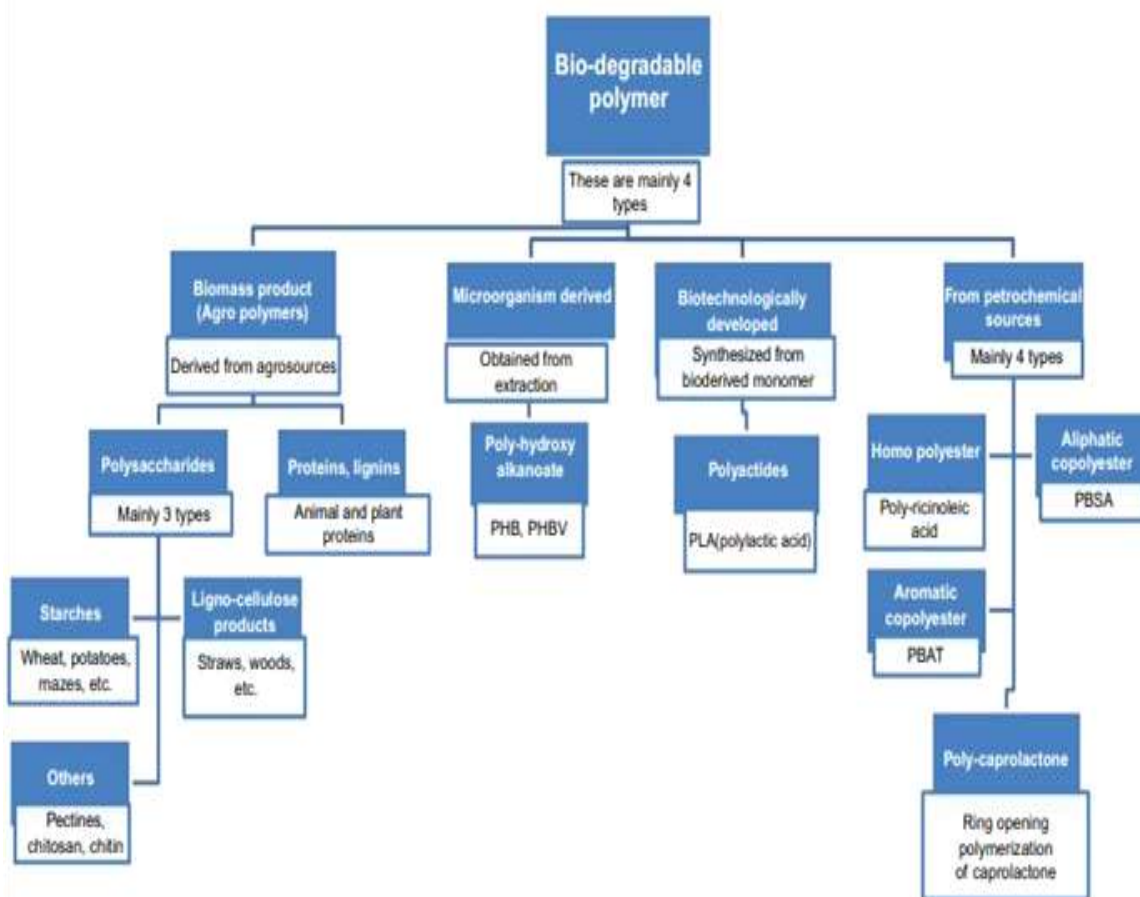
Since the inception of time, there have been biodegradable polymers. In open environment, all the biopolymers including polypeptides, polyesters, cellulose, polysaccharides, chitin/chitosan, and natural rubber can degrade easily. Most of the polymers made from biological origins and bio-based materials, including plant and animal fats, vegetable oils, and plant extracts, are commonly biodegradable. Poly-glycolic acid (PGA), first synthetic biodegradable polymers developed by humans in the year 1954, 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].

- 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 alkanooates, 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]

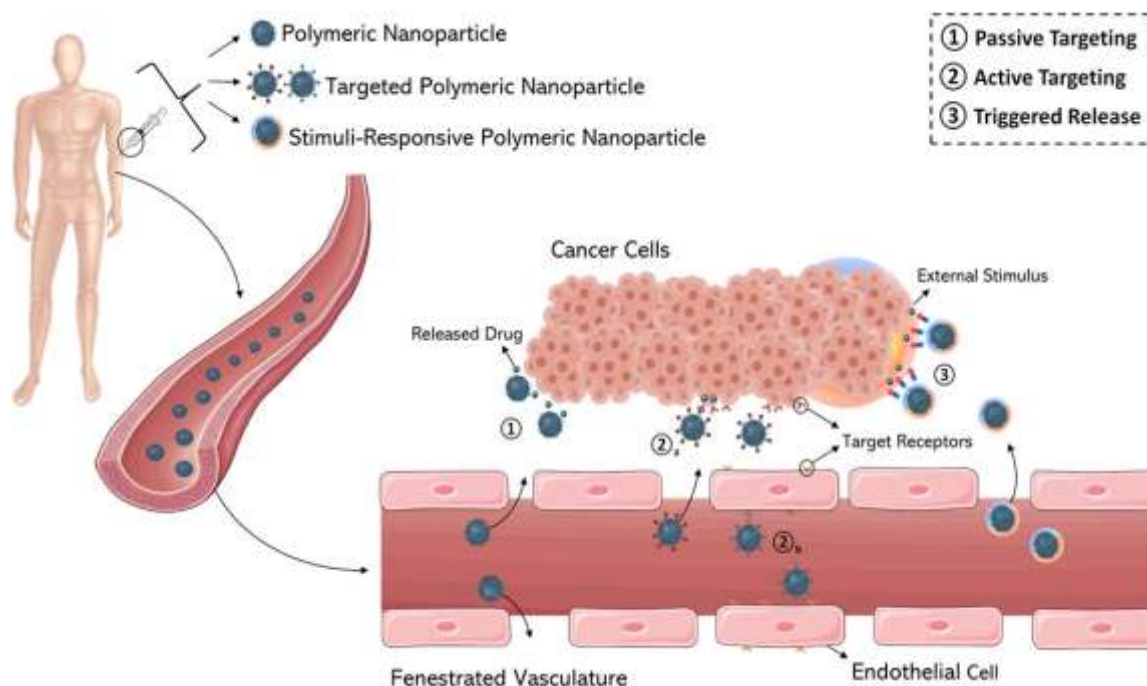
## 2. Applications of Biodegradable Polymers

- Targeted Drug Delivery:** Application of polymer has increased significantly in drug delivery systems. Various polymer-based system types are being researched continually for targeted tactics and for controlled release of active ingredients. Biodegradable polymers considered as most suitable materials for these systems due to their excellent bio-friendly and natural 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.

Drug distribution within nanoparticles may improve therapeutic effectiveness by modifying the kinetic and dynamic effects of the nanocarrier within the drug. The unflappable targeting of nanoparticles, is responsible for some of these changes (blood flow, lymphatic drainage, and so on).

To actively target nanoparticles, ligands of precise tissue (antibodies, peptides, macromolecules, etc.) can be conjugated with their exterior; these interactions result in a spatial concentration of nanoparticles in target tissues [10] (Figure 4).



**Figure 4:** Various drug targeting techniques (1-3) are depicted schematically. (1) Extravasation passively targets nanocarriers through fenestrated vasculature of tumour tissue. Cancer cells (2a) and tumour endothelium (2b) are actively targeted utilising ligand-modified nanocarriers. (3) Stimuli-responsive nanomedicines capable of releasing the anticancer drug in response to internal or external stimuli [11].

- **Passive Targeting:** Passive targeting takes leverage of the specific architectural and pathological deficiencies of tumour vasculature, facilitating the development of polymer based nanoparticles in the perivascular tumour zone through transmission or static diffusion [11]. Transmission or convection is the migration of large molecules through large pores. On the other hand, diffusion is a process of molecular shifting towards concentration gradient across the cell membrane that does not consume cellular energy and is applicable mostly to low molecular weight molecules.
- **Active Targeting:** The active or effective targeting technique strives to promote ligand engagement with overemphasised receptors in tumours while limiting engagement with healthy cells. It accomplishes this using conjugating, integrating, or attaching a ligand to a nanocarrier's surface. For these reasons, minor chemicals like folic acid and carbohydrates have been used whereas peptides, proteins, antibodies, aptamers, and oligonucleotides are executed as macromolecules [12].
- **Stimuli-Sensitive Polymeric Nanoparticles (PNs) and Trigger Release:** Stimulant responsive arrangement encourages the clemency of pharmaceuticals in return to physical, chemical, or biological stimuli as a result of the structural modification of the materials. According to literature, stimulus is mainly classified as internal stimulant that encompassing alteration of pH, redox, ionic strength & shear stress in the target tissues, and external stimulant which include thermal, optical, ultrasonic sound, magnetic force, and electric fields [13-17].
- **Cardiac Stent:** With the advent of new generations of stents which are aimed at optimizing clinical outcomes, stent design is still evolving. With an emphasis on organic polymers and stents and their prospectivel merits, this paper analyses various generations of stents. In comparison with bare-metal stents, drug-eluting stents (DES) significantly reduces the 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 procedures (beyond 1 year). Several of these events (those lasting longer than a year) have been linked to persistent inflammation brought on by the polymer. To minimize the polymer-related restriction involved in first-generation DP DES (BMS), biodegradable-polymer drug-eluting stents (BP DES) were developed by combining the advantages of reduced in-stent restenosis seen with DES and the advantages of reduced very-late stent thrombosis and myocardial infarction seen with bare-metal stents. When compared to second-generation DP DES, the most recent generation of BP DES with ultrathin struts shows potential in further reducing clinical outcomes. Earlier generations of BP DES outperformed first-generation DP DES but were not superior to second-generation DP DES in terms of 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 vascular stents that provide regulated local medicine with the goal of lowering or avoiding in-stent restenosis caused by enhanced SMC proliferation [19,20]. Furthermore, biomimetic polymers such as phosphorylcholine (PC), poly(vinylidene fluoride)-hexafluoropropylene (PVDF-HFP), or the BioLinx polymer are being used in second- and third-generation DES because they do not obstruct stent

reendothelialization [21]. Furthermore, biodegradable polymers such as PLA and poly(lactide-co-glycolide) (PLGA) have been widely researched to improve their properties and biocompatibility. Because the polymeric coatings eventually breakdown and transform into BMS, DES are expected to reduce stent-thrombosis. The next generation of DES will have a larger impact on endothelialization and arterial healing as a result of extensive stent development work.

The efficacy and safety of polymer-free DES in clinical use are now being debated. So far, randomised controlled trials have either shown inconsistent results or lacked the essential capacity to address the problem of their effectiveness and safety [24]. However, based on extensive research, patients who get durable polymer DES treatment have clinical outcomes comparable to those of patients who receive polymer-free stent treatment in terms of mortality, stent thrombosis, and long-term effectiveness [25, 26]. Nonetheless, new generation DES have been stated to be improved or equivalent to durable DES in terms of effectiveness and safety [27, 28]. The CHOICE study [29] could potentially able to provide some clarity on this particular problem. Biocompatible, polymer-based abluminal or dual, and side-selective coatings, as well as other cutting-edge, polymer-free drug reservoirs, may be beneficial [30, 31, 32]. Common Drug eluting stents are summarized in Table 1.

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

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/P VDFHFP	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/P VDF-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.

- **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 porous supporting network in cartilage bio-engineering. Localised articular cartilage abnormalities are usually always healed with the specified construct in cartilage repair. Engineered cartilage can primarily be used in head and neck reconstruction, including the treatment of auricle, nose, and trachea anomalies, as well as articular cartilage reconstructive applications. During articular cartilage repair, it is especially difficult to create a good horizontal and vertical integration with the surrounding native articular cartilage and subchondral bone. To avoid perifocal OA, the mechanical properties of the fabricated construct should ideally be equivalent to those of the surrounding cartilage. Nonetheless, depending on the implant's in situ maturation over time, they are often inferior at the time of implantation. 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].

- **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].

Polymers are commonly used as substrates and matrices in food packaging. Due to a lack of environmental awareness, cost, and technological limitations, 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 [49].

The global industry for biodegradable plastic packaging was assessed at USD 4.65 billion in 2019, with a CAGR of 17.04% expected by the fiscal year of 2025, achieving an estimated value of up to USD 12.06 billion. This increase is the result of several government initiatives to reduce plastic trash, as well as increased 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.

## V. SMART FUTURE: BEING INTELLIGENT

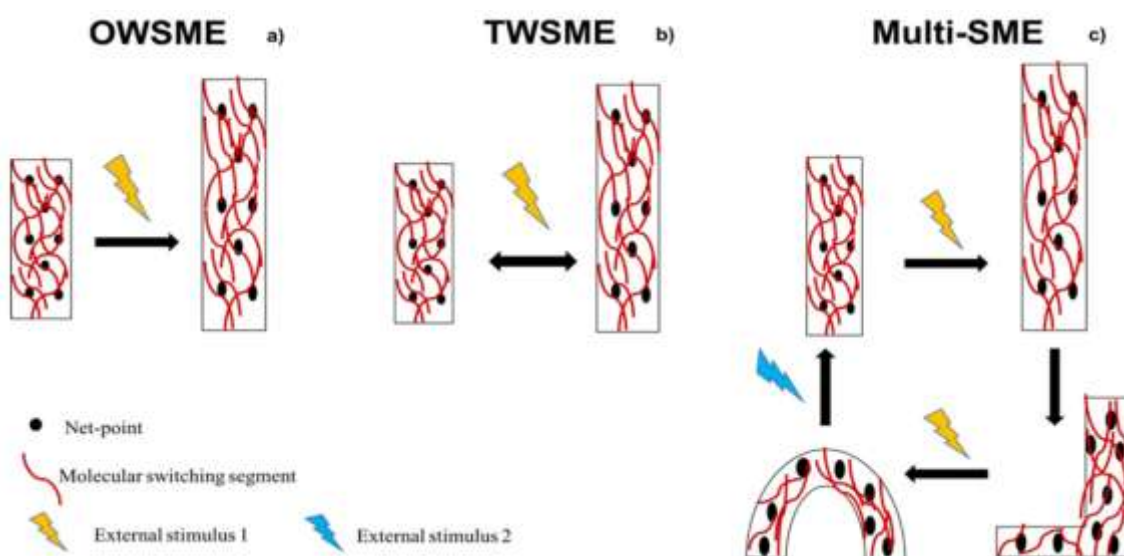
1. **Shape Memory Biodegradable Polymers:** SMPs, or Shape Memory Polymers, have demonstrated a lot of potential in biomedical applications. Heat, UV light, and electricity are common shape recovery triggers, however they could be dangerous to people. Similarly, the inherent biocompatibility and convenient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

Shape-Memory Polymers (SMPs) are intelligent polymers that may alter their size, shape, stiffness, and strain in accordance with external stimuli such as hydrogen ion concentration, body temperature, and ion density. Thermal, electrical and magnetic fields, water, and luminosity are some common instances of stimuli. In the absence such triggering factors, SMPs can recall their initial shape before the induced stimulation and following deformation and revert to that original shape on their own. It has been investigated and observed that SMP nanofibers reflects potential application in Biomedical domain and more (ECM) owing to the benefits associated with nanofibers, such as their substantial superficial area per unit volume, high porous nature, meagre diameter, low density, desirable fibre arrangement, and nanoscale architecture that

simulates innate extracellular layers. [53]. SMPs are classified in a variety of ways based on their type of crosslinking, effect of shape-memory, perceptible morphology, and stimulating events. SMPs are classified into two types: physically and chemically crosslinked. Chemically crosslinked SMPs have covalent linkages, whereas physically crosslinked SMPs have a noncovalent bond network. SMPs that may be processed into varied shapes include blocks, foams, fibres and films [53]. SMPs are categorized based on their shape-memory effect (SME): one-way shape-memory effect (OWSME), bilateral bidirectional shape-memory effect (TWSME), and multiple-SME (Figure 5). The features of each category are provided below.

- **OWSMEs:** These category of polymers loses 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 enable them to change from one temporary shape to another, and more stimulation enables them to take their original polymer shape back [54].

Nafion, a typical thermoplastic polymer employed in bulk form of films as an SMP, is a prime instance of multiple-SME. [53].



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

- **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 bonding and propagation [55].

Shape-memory scaffolding, which are particularly nanofibers, possess an exceptionally effective surface area and permeability, rendering them highly intriguing for the purpose of tissue culture and bioengineering. The most commonly used biocompatible and biodegradable SMPs for creating biomedical tissues, suitable for simulating the complex dynamic behaviour of in vivo microenvironments are poly( $\epsilon$ -caprolactone) (PCL), polyurethane (PU), poly(D, L-lactide) (PDLLA), PVA, ethylene vinyl acetate copolymer (EVA), polymer blends, polymer composites, cross-linked polymers, and supramole materials.

The shape-memory feature has aided bone tissue manufacturing. In addition to the ability to provide minimally invasive surgical implantation, it may provide the possibility to apply in situ mechanical forces to gain greater effectiveness in bone repair and regeneration. Polylactides polymers, such as poly(L-lactide) (PLLA), poly(D-lactide) (PDLA), and poly(L-lactide) (PDLA), and PDLLA, are generally exploited and explored for the purpose scaffold development for bone regeneration because to their biocompatibility, durability, and slow degeneration rate [56,57,58]. Polylactide polymers have a SME if properly programmed. To attain the requisite toughness and T<sub>g</sub> characteristics, polylactides were combined and/or compounded with other materials [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 biodegradable shape-memory polymer and an electrically spun membrane comprised to nanoscale fibres were coupled to construct novel shape-morphing scaffolds that allow for programmable deformity from planar to small-diameter tubular geometries [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 very preliminary stage of wound healing by helping to seal open cracks. As a result, wound dressings with shape memory have a tremendous probability to speed up the healing of epidermal wounds [63,64].

- **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, heat responsive SMPs cannot be sterilised by thermal treatment. The two methods of sterilisation that are most frequently employed are gamma radiation and ethylene oxide (EtO).

Ethylene oxide is a chemical sterilising treatment that works by irreversibly alkylating biological molecules that may contain amino, carboxyl, thiol, hydroxyl, and amide groups, permanently suppressing 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 sterilisation has been defined by the American National Institute for Occupational Safety and Health (NIOSH), with a suggested range of 10-25 ppm [65].

Gamma irradiation is beneficial for polymeric materials responsive to heat since it works best at low temperatures and for shorter periods of time. Polymers, on the other hand, can undergo a variety of chemical, mechanical, and morphological modifications, such as chain scission breakdown or cross-linking, or even both. Cleavage is noticed at the level of weak bonds, along with bond breakdown and a subsequent loss 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].

- 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].

Adaptive polymers have a distinctive ability to adapt to minor environmental changes by undergoing large transformations. Smart materials, stimuli-responsive materials, and environmentally conscious materials are all terms used to describe these materials. Small changes in the environment generate fast 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 found to produce these changes in polymer physical properties [69-73]. At the macroscopic level, the changes are observable as precipitate development, phase separation, or, in the case of hydrogels, 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]:

- Intelligent pH sensitive polymers
- Smart thermosensitive polymers
- 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.

## VI. CONCLUSIONS

A fast developing field is the design of targeted drug delivery approach utilizing both natural and synthetic polymers. It makes use of the impressive delivery method that infections and mammalian cells have developed, which includes discriminatory intending and sustained dissemination through evading immune systems. The potential for the biomimetic and bioinspired systems to overcome any problems with polymeric drug delivery is quite promising. The design and development of biocompatible and bioactive copolymers as well as dendrimers for the remedy of cancer, particularly their application as carriers towards effective anti-cancer medications like cis-platin and doxorubicin, will have been successful. Dendrimers are intriguing new porous polymeric structure for drug delivery systems because

of their special qualities, which includes higher degree of branching, numerous-valence, globular topology, and precise molecular weight.

SMPs have clearly achieved important architectural advancements, spawning fresh approaches and biomedical applications. With a growing emphasis on knowing SME and biological reactions on polymeric substances, substantial research has been carried out to establish structural design principles that can customise polymer modifications for wide range of applications. Shape memory polymer nanocomposites (SMPNs) in particular are gaining popularity by virtue of their fast catalytic response, resilience property, light weight, simple manufacturing, and inflecting designs. SMPs, particularly in healthcare industry, have demonstrated a potent fibrous architecture excellent for directing cell arrangement and differentiation, regulating medication administration, and ensuring porous architecture. Nevertheless, there persists a number of challenges that must be addressed. Capricious micro/nanostructured SMPs should be investigated in detail for developing scaffolds that operate better and persist longer. When comparing various shape-memory characters, TWSME is shown better result over OWSME. Thermo-responsive SMP fibres are the most researched due to their many applications; however, for specific biomedical applications, a more accurate transition temperature range is still required because various temperatures are in fact activated during inflammation, infection, or other pathological conditions.

For innovative medical devices, bio-friendly and biodegradable SMPs with suitable mechanical attributes could be created. For *in vivo* testing in animal model, a huge, cumbersome equipment might be temporarily implanted inside the body using minimally invasive surgery before being extended to their final shape to fit as needed. One of the major challenges in endoscopic surgery is that the tying a knot using surgical tools and degradable 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 already been created with concurrent capabilities for small invasive operation and quick bone regeneration.

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