Chapter 13
Biodegradable Polymeric Materials for Medicinal Applications

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1 Introduction

The design and development of biocompatible and biodegradable materials is a promising and challenging task in the fabrication of materials targeting medicinal applications. The 1982 Consensus Development Conference Statement of the National Institute of Health (NIH) defines a biomaterial as any substance (other than drug) or combination of substances, synthetic or natural in origin, which can be used for any period, as a whole or as a part of a system which treats, augments or replaces any tissue, organ or function in the body [1].

Biodegradable materials can be defined as those materials which modify their chemical and physical structure when these materials are in contact with the biological environment. If a material is biodegradable, then, by extending the right conditions and in the presence of microorganisms, fungi, or bacteria, it will ultimately break down to its basic elements and reverse back to earth. Preferably, these substances degrade without leaving any toxins behind. Biodegradation is a term used to designate the process of breakdown of a material by nature; however, in the case of medical purpose, biodegradation emphasized in the biological processes that cause a steady dissection of the material inside the living body. Biomaterials degradation is a very significant feature to contemplate when they are used for the medical purpose since their capability to function for a convinced application depends on the length of time that it is essential to keep them in the body. Biodegradation in a biotic environment may be defined as a gradual collapse of a material intervened by a specific biological activity. When materials are exposed to the body fluids, they may experience alterations in their physicochemical properties as a result of chemical, physical, mechanical, and biological correlations between the material and the neighboring

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environment [2]. A very crucial component in biodegradation is the interaction with the immune system and the specialized cells. An ideal biodegradable biomaterial should have degradation products that are non-toxic and easily metabolized and cleared from the body.

Frequently used biodegradable materials used in medicinal applications include ceramics, metal composites, and polymeric materials. Biodegradable polymers are designated as the "materials of today" [3]. In recent times, the biodegradable polymers have become highly significant in the field of biomaterials and tissue engineering, due to the unnecessary supplementary surgery to eliminate the implants or scaffolds. In medicine, biodegradable polymers offer the great capability for controlled drug delivery and wound management (e.g., clips, staples, adhesives, sutures, and surgical meshes), for orthopedic devices (ligaments, tacks, screws, pins, and rods), nonwoven materials and scaffolds for tissue engineering. The other important applications of biodegradable polymers embrace implantable large devices, in cardiovascular applications, intestinal applications, in dental applications, drug delivery systems, personal protection equipment, surgical instruments, biological liquids transfer and storage systems, artificial organs, carriers of cells or enzymes, microfluidic devices, biosensors, in vitro diagnosis tools, etc.

2 Classification of Biodegradable Polymeric Materials

The general classification of biodegradable polymers is schematically represented in Fig. 1. They are broadly classified in to natural, semi-synthetic, and synthetic based on their occurrence and synthetic strategies.

1. Natural polymers: These are the polymers which are derived directly from the natural sources
   (a) Polysaccharides (starch, cellulose, chitin and chitosan, hyaluronic acid, alginic acid, etc.).

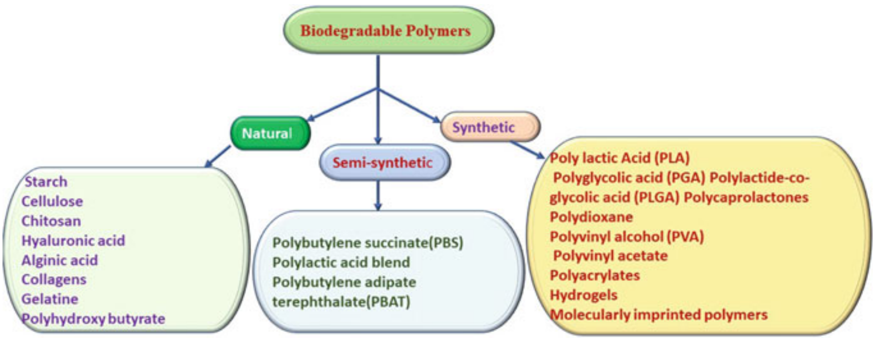


Fig. 1 Classification of biodegradable polymers. *Source* author

   (b) Polypeptides such as collagens, gelatine.
   (c) Bacterial polyesters, e.g., polyhydroxy butyrate.
2. Semi-synthetic polymers: These are the polymers in which raw material is obtained from nature, but polymerization takes place after some chemical modification.
3. Synthetic polymers: These are purely synthetic polymers derived from chemical synthesis.
   (a) Polymers having hydrolyzable backbone, e.g., polylactic acid copolymer (PLA), polyglycolic acid (PGA), polylactide-co-glycolic acid (PLGA), polycaprolactones, polydioxane, etc.
   (b) Polymers having carbon back bonds such as polyvinyl alcohol (PVA), polyvinyl acetate, polyacrylates, etc.

3 Commonly Used Natural and Synthetic Polymers

Natural biodegradable polymers are generally generated in nature by all living organisms. Even though the process of degradation of naturally occurring polymers is slow, they truly represent renewable resources since they are biodegradable. The extensively used natural polymers include polysaccharides, such as cellulose and starch. Other important classes of natural polymers are chitosan, gelatin, hyaluronic acid, collagen silk, etc. Their biodegradability, flexibility, and bioactivity make polysaccharides very promising natural biomaterials. The chemical structures of the commonly used natural, semi-synthetic and synthetic biodegradable polymers are shown in Fig. 2.

4 Mechanisms of Biodegradation in Polymers

The degradation of polymeric materials inside the body occurs mostly by three general mechanisms, oxidation, hydrolytic, and enzymatic mechanism. The foremost significant organisms in biodegradation are fungi, bacteria, and algae. Natural polymers (i.e., proteins, polysaccharides, nucleic acids) are decayed in biological systems by oxidation and hydrolysis and biodegradable materials decompose into biomass, greenhouse gas, and methane. In the case of synthetic polymers, microbial consumption of its carbon backbone as a carbon source is required [4]. Polymer degradation within the living body could also be interpreted as an interaction between the organism tissue components and a polymeric material acting as a distant body at the implantation. The key compounds causing polymer degradation in our body are water, salt, trace elements, and the enzymes present in our body fluids [5]. Biodegradation of polymeric materials within the biological environment commences with the "biodeterioration" process. During this step, the polymeric materials are first disintegrated into smaller components by the action of microbial organisms and

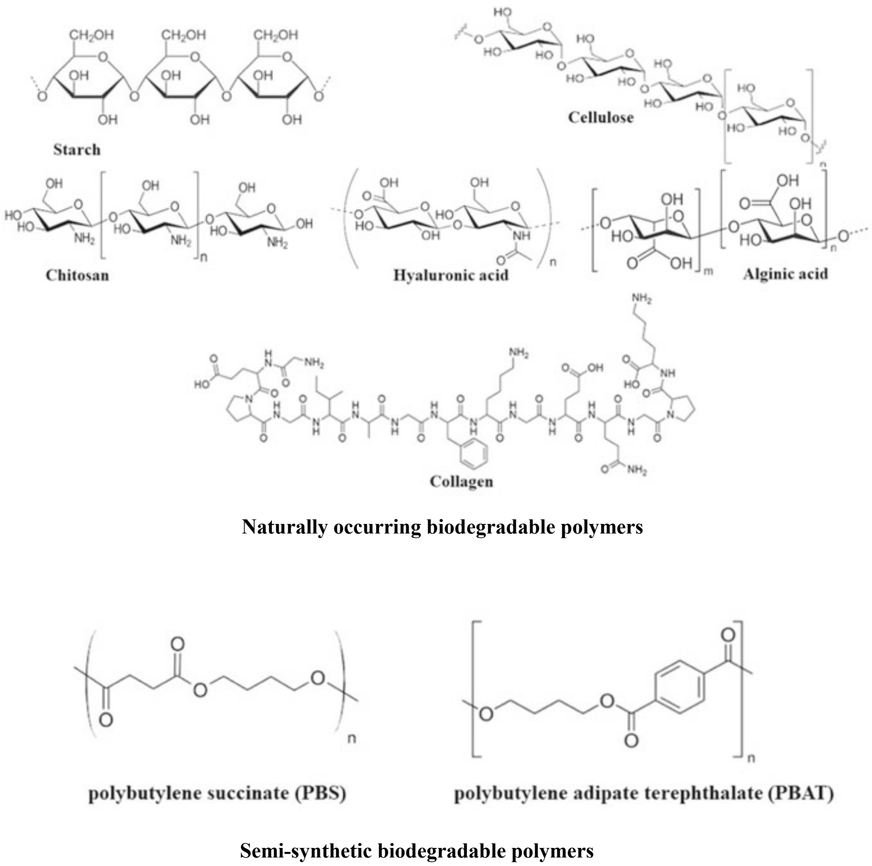


Fig. 2 Commonly used natural, semi-synthetic, and synthetic biodegradable polymers. *Source* author

abiotic agents present within the specific surroundings. Consequently, the polymeric backbones are cleaved by different hydrolytic enzymes (as well as other catalytic agents like free radicals) produced by various biodegrading microorganisms. This ends up in the progressive reduction of the relative molecular mass of the polymer. Several degradation products will be assimilated by the microorganisms resulting in mineralization of organic compounds and results in the generation of biomass [6]. Biocompatible polymers that change their properties in several physiological environments are extensively accustomed to design and develop smart drug delivery systems.

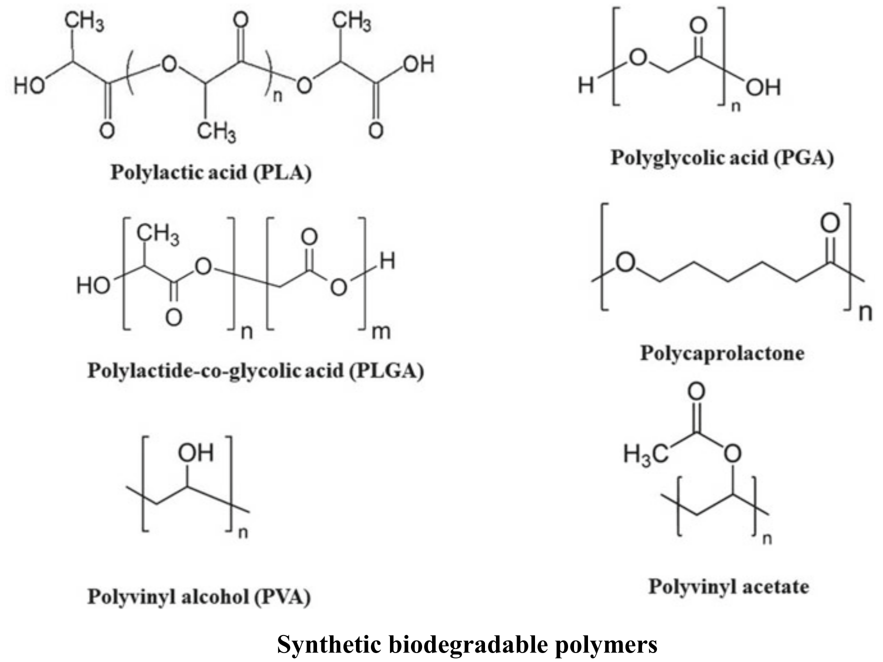


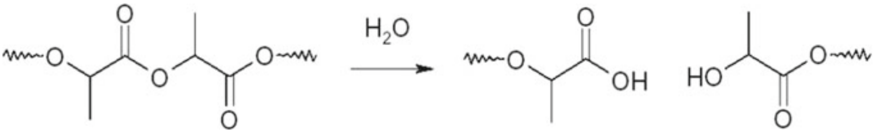
Fig. 2 (continued)

4.1 Oxidative Mechanism

One of the key degradation mechanisms of polymeric biomaterials that happens in our biological system is through the oxidative degradation process. This mechanism generally operates through the formation of highly reactive oxygen species (ROS) like superoxide (O^{2-}), per oxide (H_2O_2), gases (e.g., NO), and acid (HOCl) when the polymeric materials are exposed to the body fluids and tissues. The oxidative effect of those ROS may cause the fragmentation of the polymeric backbone and eventually ends up in their degradation. Also, in the presence of oxygen in air or water the formation of ROS is feasible and resulting in the assembly of hydroxyl free radicals ($OH^{\bullet}$) and singlet oxygen, which might deteriorate several critical biomolecules. For instance, superoxide could accelerate the degradation of aliphatic polyesters by the cleavage of ester bonds via the nucleophilic attack of O_2. It is also reported that polyurethanes are attacked initially by neutrophils which secrete reactive oxygen species (ROS) and HOCl, one among the foremost oxidative compounds [7].

4.2 Hydrolysis

Hydrolytic degradation of polymers will be defined as the fission of chemical bonds in the polymer backbone by the attack of water to make oligomers and at last to corresponding monomers. This process occurs in polymers which are having water-sensitive active functional groups. Also, usually, these varieties of polymers possess heteroatoms within the main or side chains. Biodegradable polymers undergo hydrolytic bond cleavage to make water-soluble degradation products which will dissolve in an aqueous environment, leading to polymer erosion [8]. For instance, the degradation of the polymers through hydrolysis of ester bonds leads to the alteration of their chemical structure.



Usually, biodegradable polymers encompass hydrolyzable bonds such as glycosides, esters, orthoesters, anhydrides, carbonates, amides, urethanes, ureas, etc. The hydrolytic cleavage can be catalyzed by the presence of acids, bases, or salts. The acid-labile chemical bonds are stable at neutral pH but were degraded or hydrolyzed in acidic media. This unique property is having immense application in the development of drug delivery devices. The acid-labile functional groups include acetal, orthoester, hydrazine, imine, cis-aconyl bonds, etc. [9]. Important labile chemical bonds present in the main chain of the biodegradable polymers is shown in Fig. 3. During the process of hydrolytic degradation, initially, the hydrolytic cleavage of the main polymeric chains occurs and which in turn leads to a decrease in the molecular weight of the material. While degradation proceeds, the molecular weight of degradation products is reduced by further hydrolysis which allows them to diffuse from the bulk material to the surface and then to the solution, causing significant weight loss [10].

Examples of such synthetic polymers that are used in biomedical devices and drug delivery platforms include polylactic acid (PLA), polycaprolactone (PCL), poly (glycolic acid) (PGA), and polydioxanone (PDO).

4.3 Enzymatic Degradation

Polymeric biomaterials cast-off in the biomedical applications will be get tarnished in the body fluids and tissues by several enzymes either by the process of oxidation or hydrolysis. Enzymes are known for their biological catalytic activity, and they will accelerate the degradation reaction rates in living organisms without undergoing any permanent change. Generally, the degradation of polymers in the living

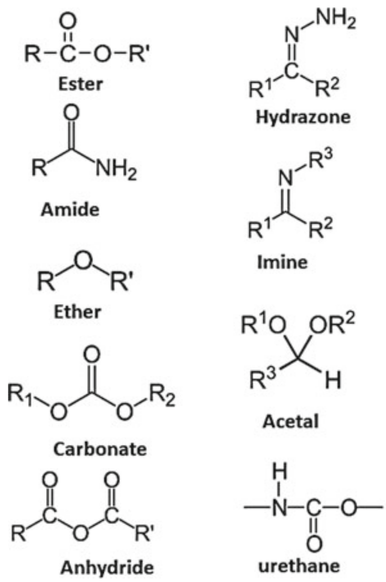


Fig. 3 Important labile chemical bonds present in the main chain of the biodegradable polymers. *Source* author

body may take place under the action of hydrolases and oxidases enzymes [11]. Hydrolases enzymes include proteases, esterases, glycosidases, and phosphatases, among others. For example, the degree of biodegradation of polyurethanes, in the presence of cholesterol esterase enzyme, is about 10 times higher than in the presence of buffer alone. Initially, the microorganisms will be attracted to the surface of the polymer and, the enzymes secreted by the microorganism converted the polymer macromolecule into their tiny components and eventually converted them into CO_2 and H_2O.

The mode of degradation mechanisms in the case of enzymatic process primarily occur through the diffusion of the enzyme from the bulk solution to the solid surface and are tracked by the adsorption of the enzyme on the substrate, resulting in the establishment of the enzyme–substrate complex. After the diffusion process, the enzyme-catalyzed hydrolysis occurs, and ultimately by the diffusion of the soluble degradation products from the solid substrate to the solution will occur. Enzymatic degradation of natural origin polymers proceeds through the action of specific enzymes.

Most materials employed for the fabrication of medical devices comprise synthetic polymers such as polyurethane, polyethylene, polypropylene, polystyrene, polyester, polycarbonate, polyvinyl chloride, polyacrylate, elastomers, fluoropolymers, silicone, or polyethylene terephthalate. For the construction of drug delivery devices, generally, polyacrylates, polyesters, isopropylacrylamides, poly(2-oxazoline)s, polyethyleneimine as well as naturally-based polymers (collagen and chitosan) and poly(ethylene glycol)s for hydrogels formulation are used [12].

5 Design Principles of Biodegradable Polymeric Materials for Medicinal Applications

The ultimate properties and function of the polymeric biomaterial are governed by its chemical, structural, and mechanical features of the polymer and how it will interact with the biological environment inside the human body [13]. The main principle behind the production of biodegradable polymer comprehends the introduction of weak linkages inside the polymeric backbone, in such a way that these linkages can easily be cleaved inside our body by the action of either temperature, pH, the concentration of the salt contents, the action of microbials or in the presence of highly reactive free radicals [14]. Thus, several synthetic strategies are adopted to formulate biodegradable polymers of varying degradation rates. The incorporation of functional groups such as carbonyl, ester, imine, acetal, hydrazone, etc., as a linking group in the main chain, which can be easily cleaved by chemical hydrolysis, aids the biodegradation process in a quite faster pathway.

The universal guidelines that have to be tracked while designing a biodegradable polymeric material targeting medicinal applications include an increased ratio of hydrophilic/hydrophobic ratio, selection of heteroatom-containing polymeric chain instead of the fully integrated carbon chain, branched-chain polymers, condensation polymers instead of addition polymers, replacement of macro-size polymers with lower molecular weight oligomers, lower surface area, water solubility, and purity. Another important design principle behind the biodegradable polymer includes the surface modification of polymeric chains, which can create meticulous densities of hydroxyl groups on the material surface, and then these groups can provide sites for the covalent attachment of specific biomaterials such as proteins or peptides [15]. In this case, the design of the materials is based on principles of surface segregation of a component with the lower surface energy. Thus, the surface science techniques can have a major role in the fabrication of biodegradable polymers, as evidenced by the application of these degradable polymers.

The prime factors which have to be taken into account during the design of biodegradable polymeric materials include

(1) The polymeric materials should not induce a sustained inflammatory response.
(2) possess a degradation time overlapping with their function.
(3) have suitable mechanical properties for their expected use.
(4) produce non-toxic degradation products that can be instantly resorbed or expelled and.
(5) include appropriate absorptivity and processability for proposed application [16].

Consequently, the biodegradable polymers should have the possibility to become part of new medical devices with precise and distinctive physical, chemical, and mechanical properties, such as electrical conductivity, optical properties, chemical reactivity, and mechanical strength [17]. In conclusion, the variables like the structure of the polymer, its chemical composition, distribution of the monomeric units, presence of functional groups, nature of main chain and side chains, structural configurations, molecular weights and polydispersity of the polymer, morphology, annealing effects, storage history, etc., might be considered while selecting and designing a biodegradable polymer. The synthesis of biodegradable polymers can be done by any one of the following synthetic reactions such as ring-opening, polycondensation, bulk synthesis, dehydrative coupling, transesterification, and polymerization.

6 Biomedical Applications of Biodegradable Polymers

An ideal biopolymer for a medicinal application should satisfy the following criteria.

- The mechanical properties of the material should match with the application and will remain sufficiently strong until the surrounding tissue is healed.
- It should not appeal an inflammatory or toxic response within the body
- The material should be metabolized in the body after satisfying its purpose, leaving no trace.
- The material should be easily processable into the final product form.
- It should have an acceptable shelf life and must be easily sterilized.

The important applications of biodegradable polymeric materials in medicine are schematically represented in Fig. 4. Beholden to their unique properties, biodegradable polymers now replace metals, alloys, and ceramics for use as biomaterials.

Biodegradable polymeric materials have been extensively used in various medical applications which include the applications focusing both in vivo and invitro studies over the past decade. The major important applications include the administration of pharmaceuticals and biomedical devices, controlled drug delivery systems, different forms of implants and devices for fracture repairs, ligament reconstruction, surgical dressings, dental repairs, artificial heart valves, contact lenses, cardiac pacemakers, vascular grafts, tracheal replacements and organ regeneration, implants in the blood vessels and as absorbable clinical sutures, etc. [18–20].

7 Drug Delivery Devices

The design and development of novel drug delivery systems lead to the development of novel biodegradable polymers with good biocompatibility and target specific capabilities. The oral drug delivery route is known as the golden standard for the consumption of drug administration. An ideal drug delivery device can be termed as a highly biocompatible material and will be releasing bioactive agents at the precise rate at the exact site and simultaneously maintaining the optimum level of drug to

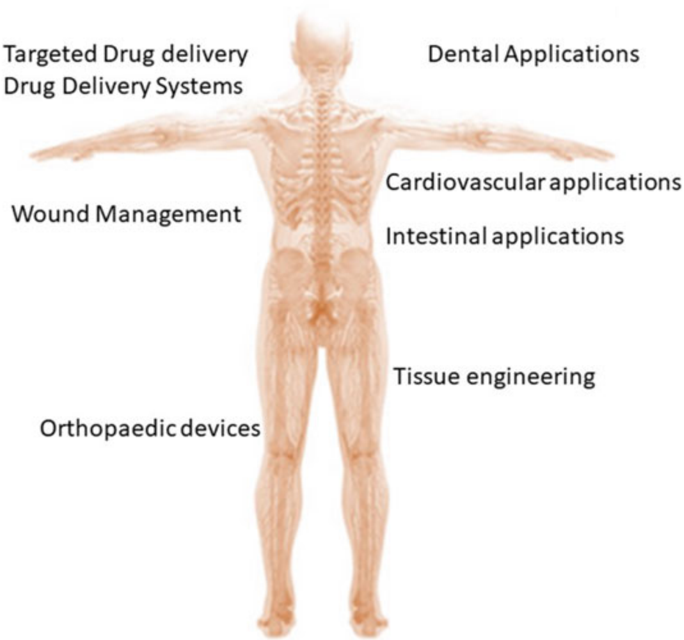


Fig. 4 Applications of biodegradable polymeric materials in medicine. *Source* author

avail maximum efficacy and minimize associated side effects [21]. Advanced materials used in drug delivery applications are either in the form of micro-/nanogels, microparticle/nano-particles, hydrogels or as imprinted polymers. Stimulus responsive nanomaterials which can be termed as intelligent or smart materials were found to be highly potential compared to the traditional drug delivery devices [22]. The most widely used biodegradable hydrogels include hydroxypropyl methyl methacrylate (HPMA), polyethylene glycol (PEG), polyglutamic acid (PGA), poly(L-lysine), polyethyleneimine (PEI), dextran, dextrin, chitosan, etc. [23]. Chitosan, a cationic polymer has been examined as an excipient in controlled delivery formulations and mucoadhesive dosage forms because of its gelling and adhesive properties. Chitosan can hypothetically be used as a drug carrier, a tablet excipient, delivery platform for drug formulations, disintegrate, and tablet coating [24].

One resolution is to design pharmaceutical polymers that endure physiochemical changes in retort to environmental incentives such as temperature, pH, electric or magnetic field, enzymes, solvent polarity, etc. The stimuli-responsive biodegradable polymers, which can release the drugs at the desired site with respect to the change in pH or temperature are of potential applications in cancer drug delivery devices since the cells around the cancer cells normally have a lower pH value between 5 and 6 and a higher temperature ~42 °C because of the increased metabolic activity near the cancer cells.

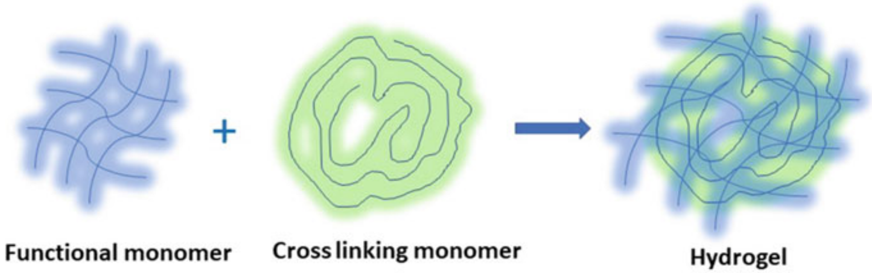


Fig. 5 Schematic representation of formation of hydrogels. *Source* author

An important category of stimuli-responsive cross-linked polymers are hydrogels. These polymers are centered on hydrophilic, water-soluble oligomeric or polymeric chains that have been bonded to each other to establish a covalent network. The synthesis of a hydrogel-based drug involves the crosslinking of linear polymer or simultaneous polymerization of monofunctional monomers and crosslinking with polyfunctional monomers. Usually, polymers containing hydroxyl, amine, amide, ether, carboxylate and sulfonate as functional groups in their side chain are explored for the synthesis of hydrogels [25]. The synthesis of a hydrogel is schematically shown in Fig. 5.

Controlled drug release systems based on molecular imprinting strategy is an advanced drug delivery system and have gained much recognition in recent years. Molecularly imprinted polymers are artificial polymers with recognition binding sites which are able to recognize a target analyte or its structural analogues from a complex. Molecularly imprinted polymers are prepared by the co-polymerization of functional and crosslinking monomers in the presence of the imprint molecule. The functional monomers initially forms a complex with the target molecule and following polymerization; the functional groups are apprehended in location by the highly cross-linked polymeric structure. Subsequent ejection of the imprint molecule exposes the binding sites that are correlative in size and shape of the analyte. Thus, a specific molecular memory is launched in to the polymeric matrix proficient of rebinding the targeted analyte with high specificity and selectivity [26–28]. The synthetic strategy adopted for a molecularly imprinted polymer is shown in Fig. 6.

8 Surgical and Orthopedic Devices

Biodegradable polymers are extensively used in surgical devices such as implants, suture materials, and staples, which are the major domain of polymers in general surgery. These materials for surgical purposes are mainly concerned in diverse areas such as in orthopedics and traumatology, maxillofacial surgery, vascular surgery,

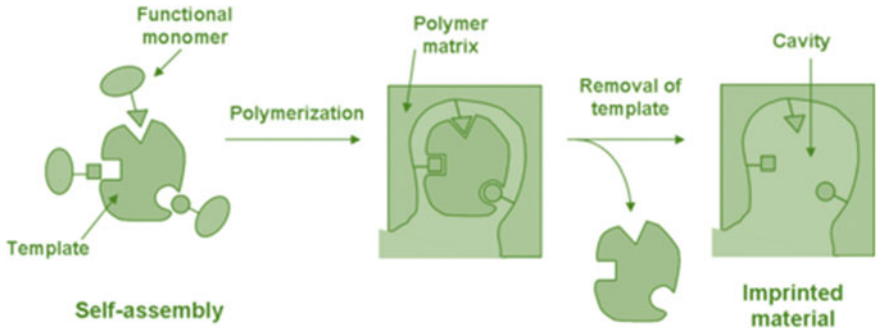


Fig. 6 Synthetic strategy for a molecularly imprinted polymer. *Source* author

microsurgery, neurosurgery, etc. [29, 30]. The suture materials will provide artificial fiber support until the natural fiber (collagen) is synthesized in our biological system. The important parameters that must be considered in surgical suture materials depend on tensile strength, friction/trauma to tissue, degradability, and the stability of knots. Degradable biological suture materials are fabricated with collagen-based materials, catgut, silk or cellulose (cotton). Synthetic materials widely explored are PGA, a copolymer of a small amount of lactide with glycoside (PGA/PLLA), etc. Recently, several clinical studies have been published using PGA, PGA/PLLA and PDS sutures or bands in the repair of tendons, ligaments and dislocations of joints. Reinforced composites of PGA and PGA/PLLA-polylactide/polyurethane (PLLA/PU) composites are widely employed for artificial skin and vascular prosthesis [31–33]. Many biodegradable materials, such as poly(P-hydroxybutyrate), poly(valerolactone), poly(p-dioxanone) and poly(amino acid), have been considered as potential candidates for the fixation process, and the most important ones employed in surgery are poly(L-lactide) (PLLA), polyglycolide (PGA) and their copolymers [34].

The emerging applications of biodegradable polymers in orthopedic applications comprised of in the fabrication of fixation devices, which in turn include pins, rods, screws, tacks, and ligaments. In orthopedic treatments, the effective use of a bone morphogenic protein will catalyze the healing process after a fracture or may help to avert osteomyelitis following surgery. Most of the commercially available biodegradable devices are polyesters composed of homopolymers or copolymers of glycolide and lactide. There are also products made from copolymers of trimethylene carbonate, e-caprolactone and polydioxanone. Synthetic biodegradable polymers explored in orthopedic devices have advantages over metal implants and reduce the need for a consequent operation for implant removal. These polymeric materials have found immense applications where lower-strength materials are adequate, such as in the fixation screws of the ankle, knee, hand areas as interference, tacks, and pins for ligament attachment and meniscal repair, suture anchors, and rods and pins for fracture fixation.

Middleton et al. [35] has compiled a review of the synthetically biodegradable polymers offered in orthopedic devices. The other important categories of biodegradable polymeric materials include polyaryletherketones (PAEKs), which are progressively utilized as biomaterials for orthopedic, trauma, and spinal implants. Polyether ether ketones (PEEK) are used in trendy settings for spinal implants, femoral stems, bearing materials for hip and knee replacement, and hip resurfacing. Polyurethane (PU) biomaterials have been investigated for compatible orthopedic-bearing materials. Silicones, synthetic polymers, are broadly used in health care and orthopedic applications. The most common orthopedic applications of silicone are hand and foot joint implants [36].

Bioabsorbable polymers like polyglycolic acid (PGA) is used in the fabrication of pins and screws. Polylactic acid (PLA) is also used in a variety of implants including pins, rods, tacks, screws, and plates. Extensively explored implants in orthopedic devices are made from the copolymers of PLA and PGA. Other bioabsorbable materials used are poly(orthoesters), poly(glycolide-co-trimethylene carbonate), poly (p-dioxanone), poly(ε-caprolactone) (PCL), poly (hydroxybutyrate) (PHB), and PHB hydroxy valeric acid, etc.[37]. PDS has also been effectively used in tissue regeneration and fracture repair applications [38]. Composites produced using calcium phosphates and collagens are believed as the most biomimetic system for bone substitute and re-forming applications. Chitosan and collagen incorporated chitosan composite micro-granules can be effectively utilized as bone substitutes. Chitosan membranes engineered with silica xerogels also have been appraised for applications in the bone regeneration process [39–41].

9 Wound Dressings

A perfect wound dressing should accomplish the healing of the wound with infinitesimal time and cost-effective. It should possess qualities such as simple and painless to apply, antimicrobial, maintains a moist wound environment, and requires minimal dressing modifications and protecting the wound. Biodegradable and antimicrobial wound dressing will decrease the indisposition by diminishing interaction during wound care, eradicating the need for repeated dressing shifts and dispensing drugs that can reduce the risks of infection. Due to the advancement in the field of synthetic biodegradable polymers, the wound management system has been modernized in several corridors in recent times [42–46]. Numerous investigations have detailed the use of polymers in dressings and in medical devices for prospective advancement in regulating the wound healing process.

Natural polymer films such as alginate, fucoidan, silk sericin, keratin, chitosan, and hyaluronic acid are widely exploited in wound dressing procedures. Chitosan and chitosan coupled with hyaluronic acid were found to be excellent wound healing systems that have been used for the development of dressing for skin ulcers. Polymeric forms like films, foams, hydrogel, or hydrocolloids are the major configurations in the wound management process. Polyurethane (PU) is utilized in numerous semi-permeable dressings owing to its ability to furnish great fences and penetrability to oxygen [47]. Hydrocolloids are polymers having inherent hydrophilic characteristics due to the occurrence of many hydroxyl groups. The hydrocolloids can be developed either synthetically or naturally. The important category of hydrocolloids used in wound healing applications is generally polysaccharides. Agar, alginate, pectin, gelatin, etc., are examples of natural hydrocolloids. The current flea market for hydrocolloid dressings explored its uses in healing diabetic foot ulcers [48].

Hydrogels synthesized using crosslinked polymers (hydrophilic), for example polyvinylpyrrolidone, polyacrylamide, and polyethylene oxide, are also having widespread use in wound dressing applications. Hydrogels are employed as wound dressings in the form of elastic films or amorphous gels. Also, poly(lactide-co-glycolide) (PLGA), polyethylene glycol (PEG), polyurethane (PU), polycaprolactone (PCL), etc. are the other important category of synthetic biodegradable polymers employed [49–51] in wound dressing fabrication. Polymer blend solution of poly(lactic-co-glycolic acid) and poly(ethylene glycol) (PLGA/PEG) sprayed with a portable airbrush were found to be inherently adhesive polymer fibers and can accumulate on and heal the wound. Recently, Mir et al. [52] reported the effective usage of silver salts incorporated (PLGA/PEG/Ag) as a sprayable and antimicrobial wound dressing agent.

10 Dental Applications

Current advances in biodegradable polymers have led to the development of novel materials for dental applications and have extended their use in protective, rejuvenating, and regenerative treatments. The utilization of biomaterials in dentistry is more broadened similar to other medical fields in terms of both quantity and quality. Polymers derived from natural sources have been applied in oral and maxillofacial surgery as extra-cellular matrix (ECM) substitute in skeletal muscle, bone, and periodontal regeneration [53]. The natural biodegradable polymers explored in dental applications include chitosan, collagen, hyaluronic acid, and alginate. The most frequent synthetic biodegradable polymeric materials employed for periodontal regeneration are poly(lactic acid) (PLA), polyglycolic acid, (PGA, polylactide-co-glycolide (PLGA), polycaprolactone (PCL), etc. Polylactic acids are utilized for dental pulp and dentin restoration, and bioactive polymers are explored in advanced drug delivery systems. PLGA is used in a variety of dental applications ranging from creating screws for bone fixation, handling periodontal pathogens, and generating buccal mucosa or indirect pulp-capping procedures. PLGA can also be utilized for periodontal treatment, antibiotic delivery, and in the forms of PLGA implants, disks, and dental films [54]. Also, gel composite fabrics of PLGA can be used in bone regeneration, The other important category of biodegradable polymeric materials normally used in dentistry is polyethylene (PE), polymethyl methacrylate (PMMA), polycarbonate (PC), polyethylene glycol (PEG), polydimethylsiloxane, polyurethane (PU), poly(ε-caprolactone) (PCL), polypyrrole(PPy), hexamethyl disilazane (HMDC), N-isopropyl acrylamide, N-test-butyl acrylamide and hydrogels of different natural and synthetic polymers. Recently, Agata Szczesio-Wlodarczyk et al. [55] reviewed the dental composites based on methacrylate resins. Hydrogels based on micro-cellulose (MC), chitosan, and its composites, the natural well-known polymer gelatine, and its combination with hydroxyapatite (HA) were also explored in dentistry.

Polymeric materials (PMs) and polymeric films (PMFs) have extended its horizons in medicine and dentistry. PMs and PMFs are tapped in dentistry owing to their advanced antimicrobial, drug delivery properties, and corrosion resistance [56]. Novel techniques include the use of antibacterial polymer coatings for inhibiting bacterial growth on artificial tooth surfaces in other dental materials and dental composite kits increasing the restoration's longevity. Examples of such antibacterial coatings include copolymers of acrylic acid, alkyl methacrylate and polydimethylsiloxane copolymers, pectin-coated liposomes, and carbopol. PMFs like acrylic acid copolymers are employed as a dental adhesive. Innumerable polymeric films were found to be protecting the teeth against erosion by preventing the direct contact of the acidic environment in the oral cavity with the teeth. Beyer et al. [57] analyzed the proficiency of a polymer-modified citric acid solution of propylene glycol alginate to reduce tooth erosion. Chitosan is also found to be an excellent candidate for the protection against erosion and enamel demineralization process and can be attributed to its ability to form a protective multilayer on the tooth surface in the presence of mucin from saliva [58]. For controlled drug release applications, different pectin-coated liposomes and polymers such as polycarbonate micelles have also been employed. Also, polycarbonate, blended with polyethylene glycol (PEG) and antimicrobial agents were explored in controlled drug release applications. Travan et al. [59] reported an antimicrobial nanocomposite containing lactose-modified chitosan incorporated with Ag-NPs and polymerized PMMA in the dental industry.

Biomimetic titanium surfaces smeared with nanohydroxyapatite (n-HA) and poly(lactic-co-glycolic acid) (PLGA)/collagen nanofibers have been analyzed for dental and bone-implant surfaces to improve osseointegration [60]. Biocompatible modified polymeric films have been coated on NiTi alloy wires to increase corrosion resistance and improve mechanical properties [61].

11 Cardiovascular Applications

Biodegradable polymeric materials are extensively explored in numerous areas in cardiovascular applications. These applications mainly focused on drug delivery, stent and graft preparation, fabrication of artificial valve, and tissue regeneration [62]. Treatments for cardiac ailment include tactics ranging from medicines to surgical intrusions. Popular surgical treatments encompass skirting the injured tissue like bypass grafts, or substituting them, as in heart transplants. Frequent biodegradable polymers that include both natural and synthetic ones have been used to control cells that are related to cardiovascular tissue engineering applications. The natural polymers embrace cellulose, hyaluronic acid (HA), chitosan, collagen, gelatin, etc. Synthetic biomaterials explored in cardiovascular applications principally involve polymers, metals, or a combination of both the synthetic biodegradable polymers and mainly embrace poly(glycolic acid) (PGA), poly(lactic acid) (PLA), poly(ε-caprolactone) (PCL), poly(ethylene glycol) (PEG), polyhydroxyalkanoate (PHA), and their copolymers [63]. Typical synthetic biopolymers that have been used for myocardial tissue engineering include polyglycolic acid (PGA), polylactic-l-acid (PLA), polylactic glycolic acid (PLGA), and polyurethane. Polyurethanes (PUs) are typically utilized in cardiac pacing leads as an insulator. PU is also being examined as a substrate in cardiac stem cell therapy and durable devices to biodegradable scaffolds [64]. The cytocompatibility of synthetic polymers can be improved by different chemical modification processes.

Polytetrafluoroethylene (ePTFE) is one of the popular polymeric material employed in routine cardiovascular applications due to its superior material performance. These characteristic features of ePTFE have made it an excellent selection for producing shunts, renovation, and valve repair and have even been used for casing implantable devices to minimize inflammation [65]. Polyethylene terephthalate (PET), PET, is recommended for fabricating vascular grafts. Polymers, possessing the inherent properties such as biodegradation, drugs releasing capacity, or biomimicking, are of great concern in the development of cardiovascular implants.

Biocompatible and bioabsorbable polymeric stents have enticed much consideration as substitutes to metal stents. Endovascular stents have become the most reliable medical devices for treating coronary artery diseases. The stents overcome the limitations and drawbacks of bypass surgery and balloon angioplasty by enabling scaffolding, widening, and supporting the blocked vessels. Also, these types of stents displayed many advantages like short duration of post-stenting, avoid chronic inflammatory processes as well as the ability of the vessel remodeling. Moreover, bioresorbable stents are recommended for tracheomalacia treatment in infants because removal surgery is not necessary. Thus, the advanced progress in the field of polymeric materials makes the stent-based polymers as an attractive tool in cardiovascular medicine. Cardiovascular tissue engineering techniques embrace injectable biomaterials, cell therapies, and artificial organ fabrication. Injectable materials mostly employed in cardiovascular applications are hydrogels composed of alginate, fibrin, chitosan, collagen or matrigel and self-assembling peptides generally in the form of nanofibers. Injectable polymeric materials formerly engendered interest due to their biocompatibility, the capability to offer advantageous chemical surroundings, and their potential non-invasive delivery routes [66].

Biodegradable polymers are not only intended for stents but also effectively utilized as a drug carrier in drug-eluting stent (DES). Generally, polymers employed as stent platforms and coating matrices for drug-eluting stents (DES), are vascular stents that allow the delivery of antiproliferative drugs to inhibit vascular smooth muscle cell (SMC) growth. Biomimetic polymers, such as phosphorylcholine (PC), poly(vinylidene fluoride), and hexafluoropropylene (PVDF-HFP), do not interfere with the stent and are presently explored in the second- and third-generation DES [67]. Integrating a biocompatible polymeric coating with poly(L-lactic-acid) (PLA) is one of the most predominant approaches to reduce the bio-corrosion of biodegradable metals and maintaining their biocompatibility. Polymeric coating can normalize the metal corrosion by isolating it from the corrosive environment or by conquering the dissolution of metal or equivalent cathodic reaction. Polymeric coating can control the metal corrosion by isolating it from the corrosive environment or by suppressing the dissolution of metal or corresponding cathodic reaction. Incorporating a polymeric coating not only can act as a corrosion barrier, but also it can be encumbered with drugs that can be released in controlled amounts to prevent post-surgery inflammations or restenosis [68].

In parallel to cardiovascular applications, a large number of biodegradable polymers are effectively employed in intestinal applications such as colon-specific drug delivery, its formulation aspects, and in the fabrication of stents.

12 Tissue Engineering Applications

Tissue engineering is an effective pathway for the fabrication of biological alternatives that repair, retain, or enhance the proper functioning of tissues. It can be described as a tool by which we can assess the structure–function relationship of individual tissues. In tissue engineering, biomaterials have to be designed to substitute or regenerate completely (or partly) the injured tissue. The biomimetic materials will act as a three-dimensional matrix as a scaffold in the regeneration process. An essential role for biomimetic materials is to furnish a three-dimensional matrix as a scaffold and guaranteeing the preservation of cells and signals for redeveloping the tissue or organ [69]. Creating physiologically functional artificial tissues and organs is an essential requirement of tissue engineering, and technological advancements in tissue engineering repeatedly strengthen its progress. Several synthetic and natural biodegradable polymers and their composite materials have been cast-off to engineer scaffolds for bone tissue engineering, nerve rejuvenation, controlled drug release, dental structure regeneration, guided tissue regeneration (GTR), strengthening of dental composite, bone and cartilage rejuvenation [70]. Nano-configuring of biomaterial scaffolds from nanoparticles, nanocomposites, and organic–inorganic hybrid polymer materials has also exhibited progress in organ regeneration and tissue engineering applications.

The most frequently explored synthetic polymers for tissue engineering include aliphatic polymers, poly(lactic acid) (PLA), poly(glycolic acid) (PGA), poly(lactic-co-glycolide) (PLGA), poly(ε-caprolactone) (PCL), poly(p-dioxanone), copolymer soft trimethylene carbonate and glycolide. These materials are smart biomaterials to construct scaffolds and have been widely applied with favorable results in regenerative medicine.

Blends of D-PLA and L-PLA (PDLLA), PLA, PGA, and PLGA have been utilized clinically to cure patients facing damaged or lost organs or tissues. Natural biopolymers encompass polysaccharides (e.g., starch, alginate, chitin/chitosan, hyaluronic acid derivatives) or proteins (e.g., soy, collagen, fibrin gels, silk) [71–74]. These materials operate as fundamental prototypes for cell connection and expansion owing to their intrinsic biocompatibility. Collagen and fibrin have been widely probed in cardiac tissue engineering due to its ability of natural interaction with cells inside the human body. Biodegradable synthetic polymers that have been effectively employed for myocardial tissue engineering include polyglycolic acid (PGA), poly(lactic acid) (PLA), polylactic glycolic acid (PLGA) and polyurethane. polyurethanes have also marked its potential applications in dermal regeneration. Poly(ε-caprolactone) (PCL) is an appealing material when long-term implants are preferred. Another group of thermoplastic polymers that have been developed recently for tissue engineering includes multi-block copolymers comprising poly(ethylene oxide) (PEO) and poly(butylene terephthalate) (PBT) (PEOT/PBT)). Fascinating class of other degradable materials explored in tissue engineering is polyphosphate-esters (PPEs), polyphosphates), polyanhydrides (PAs) and polymorpho-esters (POEs).

The augmentation of precursors like polyols and macromonomers based on polyesters emerged as novel candidates in injectable and situ curable polymer formulations. Poly(propylene fumarate) is an example of an injectable polymer system used in tissue engineering applications Polyurethanes also offer many advantages in the design of injectable and biodegradable polymer compositions.

Recently hydrogels have revolutionized the field of tissue engineering where they are engineered as scaffolds to monitor the growth of new tissues. The design and application of biodegradable hydrogels have significantly enhanced the prospective power of hydrogel materials in the biomedical field and facilitated the advancement of exciting materials focused on tissue engineering applications. Examples of hydrogel-forming polymers of natural origin are collagen, gelatin, fibrin, HA, alginate, and chitosan, and the synthetic polymers are PLA, PPF-derived copolymers PEG derivatives, and PVA [75]. Nanofibers have also emerged as scaffolds for musculoskeletal tissue engineering, which include bone, cartilage, ligament, and skeletal muscle, skin, vascular, neural tissue engineering. Natural polymers and synthetic polymers explored as a fibrous scaffold in biomedical applications. For the fabrication of nanofibers includes collagen, gelatin, chitosan, HA, silk fibroin, PLA, PU, PCL, PLGA, PEVA, and PLLA-CL.

13 Conclusions

The design and development of biodegradable polymers is an emerging area in the field of medicinal chemistry. The fabrication of newer and newer smart materials targeting human cells is highly demanded in the current scenario. The mechanistic aspects of degradation, its sustainability in the human physiological conditions, and the longevity of the materials are the major concerns and challenges to the researchers in this area. Certainly, the present area must be explored in different dimensions of human life that persist on the planet earth. The filed tissue engineering, fabrication of implants, artificial valves and stents, and artificial organs, bioabsorbable wound healing devices are among the few in the category of biodegradable materials. By adopting the natural mechanisms of degradation, the naturally biodegradable polymeric materials can be derivatized and by the incorporation of nanomaterials, the mechanical strength and the corrosion resistance of the composite materials can be enhanced. The synthetic materials widely explored can be fine-tuned and can be configured to newer formats to meet the advanced applications such as in the development of novel drug delivery devices, stimuli-responsive targeted drug delivery applications, antibacterial and anti-viral agents, biodegradable safety equipment, etc. We hope by the advancement of newer technologies and the emergence of novel materials, applicatisons of biodegradable polymers will surely open broad horizons in the medicinal field.

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