A REVIEW ON DEVELOPMENT OF NANOPARTICLES BASED POLYMERIC BIOMATERIALS AND ITS MEDICAL APPLICATIONS

A PROJECT REPORT

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE AWARD OF THE DEGREE
OF

MASTER OF TECHNOLOGY
IN
INDUSTRIAL BIOTECHNOLOGY

Submitted by

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CANDIDATE'S DECLARATION

I, ALAA KHALID ABDELRAHMAN ABDALLA , Roll No's – 2K20/IBT/15. student of M.Tech (Department OF BIOTECHNOLOGY), hereby declare that the project Dissertation titled "A review on Development of Nanoparticles Based Polymeric Biomaterials and its Medical Applications" which is submitted by me to the Department of Biotechnology, Delhi Technological University, Delhi in partial fulfillment of the requirement for the award of degree of Master of Technology, is original and not copied from any source without proper citation. This work has not previously formed the basis for the award of any Degree, Diploma Associateship, Fellowship or other similartitle or recognition.

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CERTIFICATE

I hereby certify that the Project Dissertation titled "A review on Development of Nanoparticles Based Polymeric Biomaterials and its Medical Applications" which is submitted by Alaa Khalid Abdelrahman Abdalla, Roll No's – 2K20/IBT/15. Department OF Biotechnology, Delhi TechnologicalUniversity, Delhi in partial fulfillment of the requirement for the award of the degree of Master of Technology, is a record of the project work carried out by the students under my supervision. To the best of my knowledge this work has not been submitted in part or full for any Degree or Diploma to this University or elsewhere.

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ACKNOWLEDGEMENT

I wish to express our sincerest gratitude to Dr. Prakash Chandra for his continuous guidance and mentorship that he provided me during the project. He showed me the path to achieve my targets by explaining all the tasks to be done. He was always ready to help me.
I am grateful to Indian Council for Cultural Relation (ICCR) under the government of India, for the support throughout these studies I'm truly energetic about the entirety of my companions for their ideas and moral help during my visit in India.

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Abstract

Biomaterials are widely employed in a variety of medical applications, including surgical implants, healthcare equipment, medical instruments, and fittings. Biomaterials can also be used to enhance the appearance of the human body, such as breast implants or in piercings. Three things should be considered while developing new biomaterials: chemical composition, surface properties and structure. Natural and synthetic Nano engineered polymeric biomaterials are used in biomedical applications such as drug targetting and prolonged and controlled release. Nanocomposits prepared from natural polymers are biodegradable, low-to-no toxic and nearly biocompatible, making them popular in medicine. Biopolymer synthetic nanocomposites offer a wide range of uses. They can be modified by combining biomolecules in order to make them more biologically compatible and nontoxic to the body. Polymers, both synthetic polymers and environment friendly polymers, are widely used.

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CHAPTER ONE

INTRODUCTION

1.1 Polymers

Polymers are the most biomaterial that can be tailored to meet specific needs. They can be chosen based on features like mechanical resistance, degradation rate, permeability, solubility, and transparency, and their surface and bulk properties can be altered to improve them. Polymers used as biomaterials must be synthesized to have appropriate chemical, physical, interfacial and bio mimetic characteristics, that permits various specific applications [1].

1.2 Biocompatibility

The interaction between blood and tissues with polymers is determined by the localized area and purpose of use. Unless vascularization is essential to support living cells, the host organism's response is often adverse. Biocompatibility in blood-contact applications is mostly governed by unique interactions with blood and its components. The choice of biomaterial for applications that do not involve blood contact (such as dental procedures) is usually dictated by tissue biocompatibility [2]. In some cases, a material may be biocompatible in one use but not in another. Interfacial properties are generally important for impermeable solid devices since the material's surface is in direct contact with the biological medium. In such instances, the biological response is governed by the surface structure [3].

1.3 Types of polymeric biomaterials

Natural or synthetic polymers are the most common types of polymeric biomaterials.

1.3.1 Natural Polymers

Naturally available polymers are renewable resource that can be found in a wide range of environments. Natural polymers have a diverse spectrum of active groups and can be made via physical and/or chemical methods. Using developing nanotechnology, new biomaterials could be created from naturally occurring biopolymers [4, 5]. Biologically degradable, biocompatible, nontoxic, and environmentally friendly biomaterials can be made from naturally occurring and modified biopolymers. As a natural polymeric biomaterial, hyaluronic acid, starch, alginate, cellulose, chondroitin sulfate, chitosan, and other nanopolymers are often employed.

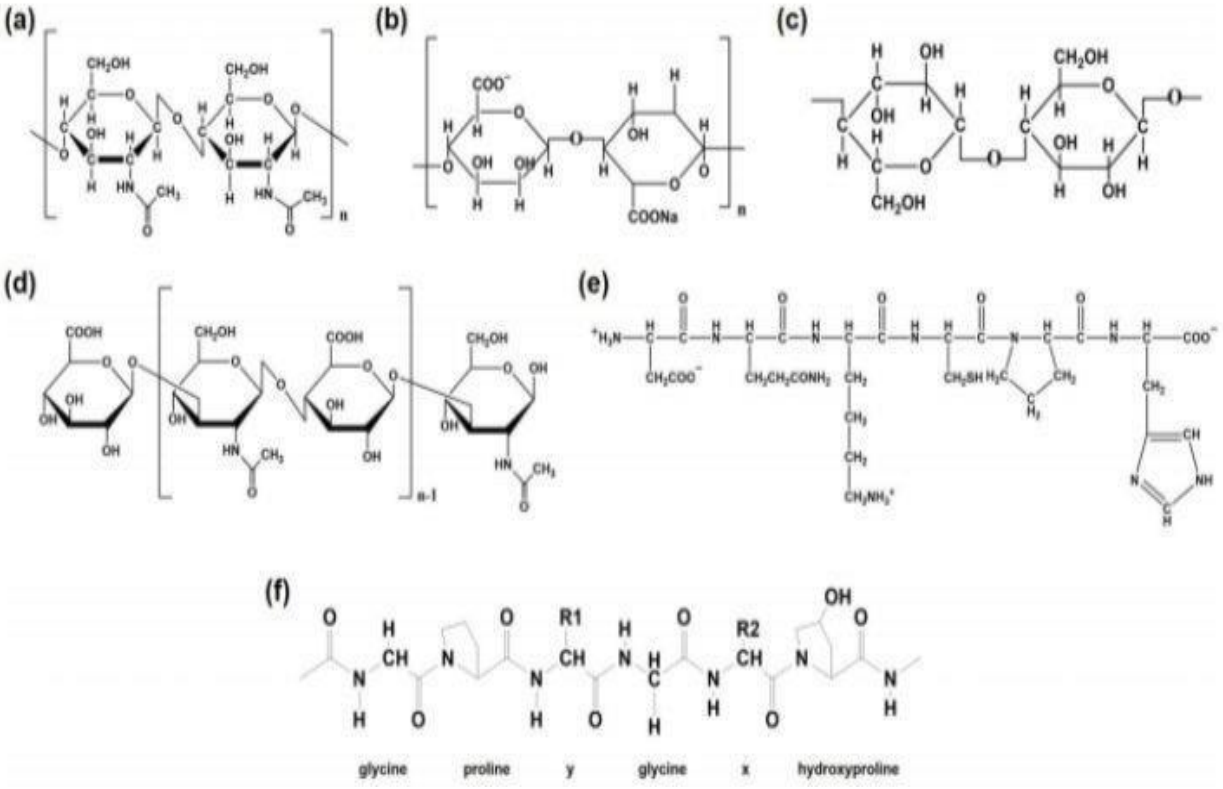

Figure 1.1

Natural polymers (a) Chitin, (b) Sodium alginate, (c) Cellulose, (d) Hyaluronic acid, (e) Gelatin, and (f) Collagen have different chemical structures.

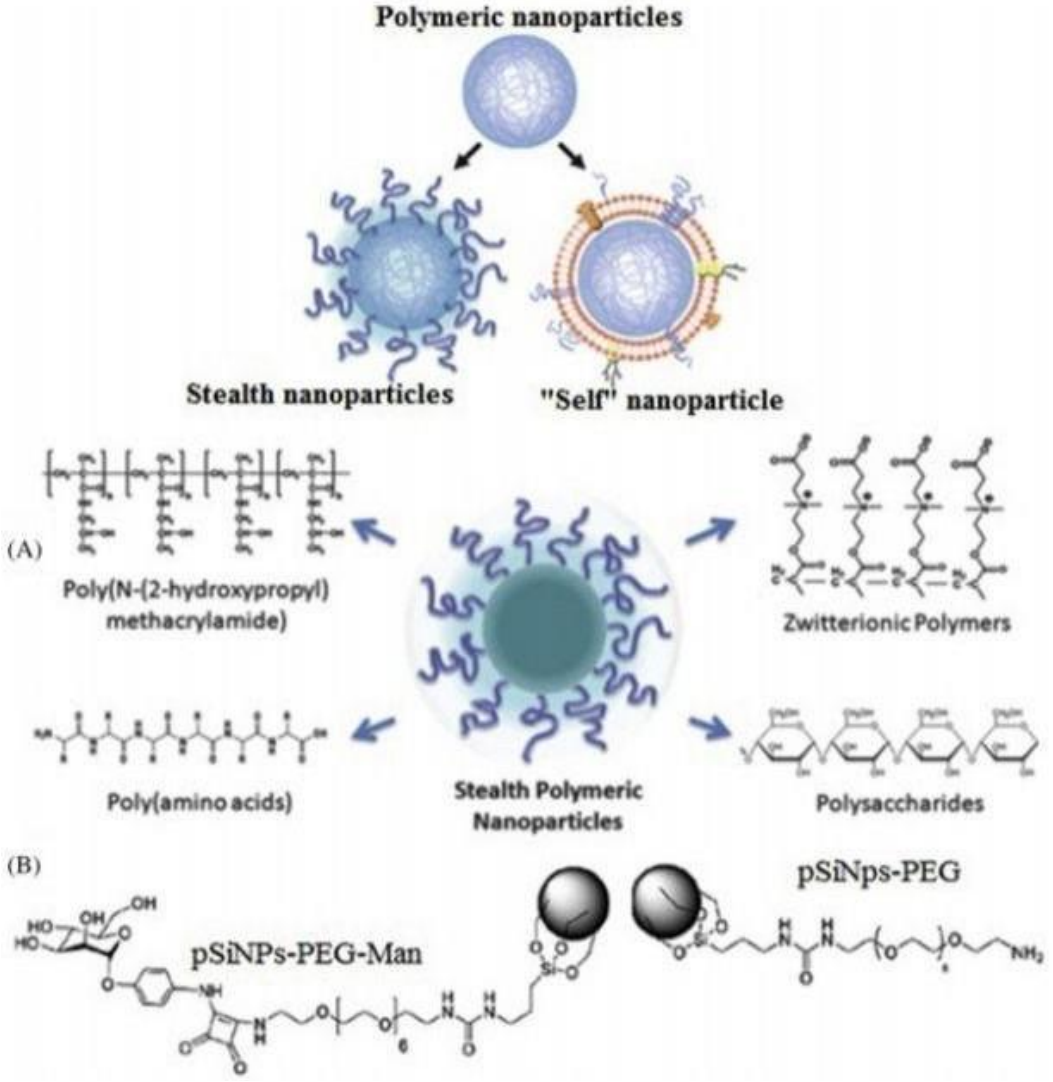

Figure 1.2

(A) Polymeric nanoparticles with hydrophilic polymers; (B) inorganic nanoparticles with hydrophilic polymers are examples of nanoparticle stealth functionalization.

Advantages of natural polymers

● Availability: polymers with natural origin are widely available in natural environments and can be simply extracted from natural resources (microbes, animals, or plants).
● Biocompatibility: as the natural polymers are derived from biological resources, hence they do not cause toxicity [6, 7].
● Biodegradable: Natural polymers are easily degraded by enzyme action inside the body of the human after they have served their purpose.
● Simple to modify: Natural polymers can be modified using chemical reactions to achieve a certain feature.

1.3.2 Synthetic Polymers

The synthetic polymers are synthesized in the laboratory under particular conditions; this process involves polymerization reaction that is carried out under the specified condition to produce a particular polymer of desired properties [8], such as poly(lactic acid), poly(glycolic acid), copolymer poly(lactide-co-glycolide), polyesters, polyurethanes, and poly(ethylene glycol) (PEG), lies in the controllable chemical, structural, and mechanical properties with minimal variations between the batches of synthesized nanomaterial.

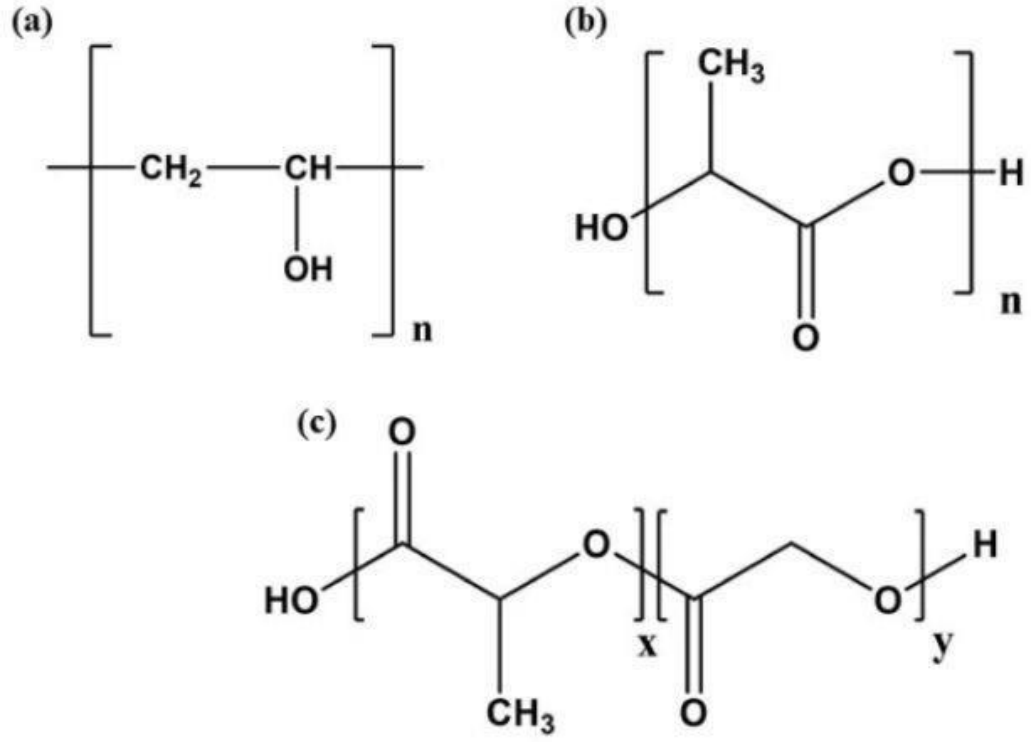

Figure1. 3

Synthetic polymers (a) Polyvinyl alcohol (PVA), (b) Polylactic acid (PLA), and (c) Poly(lactic-co-glycolic) acid have different chemical structures (PLGA).

Disadvantages of Natural Polymers	**Disadvantages of Synthetic Polymers**
● The extraction of natural polymers is difficult and expensive [9].	● Complication of synthesis processes and high cost is required [9].
● Natural polymers have a high variability rate.	●Toxic: Synthetic polymers are not biocompatible like natural polymers; they are toxic and must be synthesized in the lab.
● The structure of some natural polymers is complex.	● No biodegradable: Degradation of some synthetic polymers by the enzymatic action is not easily.

Table 1.1

1.4 Biodegradable polymers

The biodegradable synthetic polymers are used as biomaterials because their mechanical and physical properties can readily be adjusted by changing the preparation techniques and molecular structure [10]. Copolymers based on poly (glycolic acid) and poly (lactic acid) are ideal for tissue-cell-seeded constructs because they offer tuned degradability. A new type of biodegradable biomaterial33 is Polyphosphazenes , a unique backbone comprised of nitrogen and phosphorus atoms is used to characterize the polyphosphazenes .Unlike most other polymers, which have a carbon–carbon backbone, this one has a carbon–carbon backbone. Polymer characteristics can be adjusted by mixing this inorganic chemical structure with side-chain functional group. Different polymeric biomaterials can be used in catheters such as polyurethane (PU), polytetrafluoroethylene (PTFE) and silicone [11, 12].

Polymers applications

- Medicine and biotechnology.
-The cosmetics and food industries
- Biosensors.
- Applications include surgical devices.
-Ophthalmology.
- Supporting materials and implants (e.g. artificial organs)
- Cardiovascular.
- Drug-targeting systems with various routes of administration and its designing
- Wound Closure.
- Nerve Regeneration.

CHAPTER TWO

2.1 MEDICAL APPLICATIONS OF NANOMATERIALS

Medical applications are divided into four categories: diagnosis, medical devices, treatment, and tissue engineering.

2.2 POLYMERIC NANOMATERIALS

Polymer therapeutics is a type of polymeric nanoparticle which include: liposomes and polymeric drugs, polymer drug conjugates, polymer protein conjugates, polymeric nanoparticles, micelles, nanoshells, dendrimers, engineered viral nanoparticles, albumin-based nanoparticles, polysaccharide-based nanoparticles, polymersomes, polyplexes, or interpolyelectrolyte complexes for DNA delivery, polymer lipid hybrid systems, polymeric nonviral vectors, and inorganic (metallic, ceramic) nanoparticles modified with polymers using water-soluble polymers as a common core component [13].

2.2.1 Polymers as drugs

The natural polymers extracted from plants, animals, or seaweeds (polyanions and polysulfates) possess antiviral and antitumor activity. Modified polysaccharides, synthetic polypeptides, and some synthetic polymers are already used as drugs. These therapeutic agents have high molecular weight and functionality and are able to selectively recognize, sequester, and remove low-molecular-weight and macromolecular disease-causing species in the intestinal fluid [14,15]. The advantages of their use compared with traditional small-molecule drug products include longterm safety profiles, polyvalent binding interactions, they are able to sequester bile acids, phosphate, and iron ions, to bind toxins, viruses, and bacteria as well as polymeric enzyme inhibitors and fat binders as antiobesity agents. Functional polymers treat autoimmune disease and sickle cell anemia [16].

2.2.2 Polymeric nanoparticles

Polymeric nanoparticles are solid particles that are nanoscale in size and made up of natural or manmade polymers. There are two types of nanoparticles: nanospheres, which are matrix systems in which the drug is uniformly spread, and nanocapsules, which are reservoir systems in which the drug is situated in the core and is surrounded by a polymer membrane [17, 18]. These medicines are tagged on the surface of nanoparticle covalently or trapped inside the nanoparticle, depending on the production technique. Polymeric nanoparticles can control drug release by diffusing through the polymer matrix or degrading the matrix. They've been studied as drug delivery systems for tumor site-specific targeting and medication transport [19].

2.2.3 Polymers as a Contact Lens

A contact lens is prosthetics that is placed on the eye's cornea for medical, remedial, or aesthetic purposes. Contact lenses are worn by an estimated 125 million people around the world. High performance contact lens materials must have a variety of qualities, including:

(1) Good transmission of visible light
(2) tear-film wettability
(3) High oxygen permeability
(4) Resistance to deposition of components from tear-film, such as lipid, protein, and mucus
(5) Chemical stability
(6) Good thermal conductivity
(7) Ion permeability
(8) Amenability to manufacture

Contact lenses are made from a wide range of polymers, and their modulus of elasticity determines whether they are hard or soft [20, 21]. Poly (methyl methacrylate) (PMMA), a polymer commercially known as Plexiglas from which hard and soft lense materials are prepared, was used in the first generation of polymeric contact lenses. Bulk free-radical polymerization can be used to make PMMA, which can then be lathed into lens shape. It offers excellent optical qualities, including a higher index of refraction than glass, exceptional durability, and good resistance to component deposition from the tear film due to its hydrophobicity [22]. However, significant disadvantages like a lack of oxygen pemeation and a proclivity to alter the structure of the eye haves the use of PMMA contact lenses.

The addition of a highly hydrophobic siloxane to the copolymer reduces lens wettability, resulting in an increase in lipid deposition that is undesirable. To compensate for the loss of wettability, hydrophilic monomers like as methacrylic acid (MAA), 2-hydroxyethyl methacrylate

(HEMA), or N vinyl-2-pyrrolidone (NVP) are typically utilized as wetting agents in RGP lens formulation[32]. When Otto Wichterle invented poly (2-hydroxyethyl methacrylate) (PHEMA) in the 1960s, the contact lens business was permanently revolutionized. Soft contact lenses are typically formed of hydrogel, which are meshwork that retains much amount of water. The first PHEMA soft lens had a hydration content of 40% water. Despite the fact that it was more comfortable to wear than rigid lenses, PHEMA's low oxygen permeability was interfering with proper breathing [24, 25].

Increased hydrophilicity has the drawback of increasing protein binding to the lens, which can cause pain as well as other difficulties like bacterial adherence. Corneal desiccation can also be caused by hydrogels with high water content. In order to obtain superior oxygen permeability, researchers devised a unique kind of siloxane-containing hydrogel for soft contact lenses [26]. Siloxane-containing materials have significant oxygen diffusivity due to the complexicity of the siloxane groups (–Si (CH3) 2 – O–) chain length and mobility.

Siloxane materials are hydrophobic and thus prone to lipid accumulation, making them less pleasant to use with rubbery qualities.A functionalized siloxane macromere was created to compensate for these problems. [27] Focus Night & Day (lotrafilcon A) is a commercially available siloxane hydrogel based contact lens.

2.2.4 Polymeric Artificial Cornea

The cornea is the covering of frontal area of eye. It is the most important component of the ocular optical system, and it serves a variety of functions, including refracting light onto the retina to create an image and functioning as a protective barrier for the fragile inside eye tissue [28,29]. Corneal damage can result in vision loss, making it the second most prevalent cause of blindness in the world after cataracts. Transplantation of human donor corneas is the most generally approved treatment for corneal blindness. However, the scarcity of donor cornea tissues has necessitated the design and development of an artificial cornea substitute [30]. Keratoprostheses, or artificial corneas, come in a variety of shapes and sizes, ranging from entirely synthetic to tissue-engineered.

The following particular requirements should be met by a perfect artificial cornea:

(1) Transparent, having a smooth anterior surface and a curve that is acceptable.
(2) Ability to heal with the host cornea
(3) Flexibility and strength sufficient for surgical handling
(4) Suitable refractive index
(5) Biocompatibility.
(6) Avoidance of development of a retrocorneal fibroblastic membrane
(7) Ability to induce epithelial growth on the artificial cornea's anterior surface.

Early artificial corneas were constructed of a variety of hydrophobic polymers, including PMMA, nylon, poly (tetrafluoroethylene) (PTFE), polyurethane (PU), and poly (ethylene terephthalate) (Dacron)[31,32,33] . The design evolved from a button-like complete piece made of one material to the more common core and skirt arrangement, in which the core is made of one material and the skirt is made of other.The skirt is made of the same or a similar translucent material with good optical properties,a variety of materials to ensure host compatibility. Due of its exceptional optical qualities, PMMA is likely the most widely employed of these polymers, as detailed in the IOL section [34]. Despite the fact that PMMA is still used in artificial corneas, difficulties like retroprosthetic, endophthalmitis formation, extrusion, glaucoma, membrane, soft, hydrogel-based corneas are designed as a result of rejection.

The majority of the studies have focused on HEMA-based hydrogels. When the monomer is polymerized with less than 40% water, it forms a homogenous transparent hydrogel; when the water concentration is higher, phase separation occurs during polymerization, resulting in a heterogeneous and opaque hydrogel [35]. HEMA was used to create the first core-and-skirt hydrogel-based cornea, which is known as AlphaCor commercially. The core is made of translucent PHEMA with a decreased water content, while the skirt is made of phase-separated, macroporous opaque PHEMA [36]. Despite being a hydrophilic polymer, the water content of PHEMA is substantially lower than that of the natural cornea (783%). Because it enables nutrient transmission, high water content is crucial for the epithelium's integrity and survival. Various ways have been investigated in order to improve the water content of the artificial cornea [37]. Hydrogels manufactured from a homopolymer of poly (vinyl alcohol) (PVA), consists of 80% of water, are one example , and copolymerization of HEMA with an ionic acrylate MAA.Biomimetic hydrogels for artificial cornea have also been reported by several groups. Because type I collagen dominates the extracellular matrix of the cornea, it was employed to make a copolymeric hydro gel based on N isopropylacrylamide (NIPAAm), acrylic acid, N-acryloxysuccinimide, and collagen[38,39].

The designed hydrogel is simply a network made up of collagen that has been succinimide pendant-linked to acrylic acid and NIPAAm copolymers. This material has shown to have the necessary biomechanical qualities and optical clarity for corneal transplantation. In vivo animal investigations have revealed that the host corneal epithelium, stroma, and nerves can all regenerate successfully [40]. This substance is now undergoing clinical testing in humans to see if it may be used for therapeutic purposes. Artificial corneas have also been made with interpenetrating polymer networks (IPNs).

A polymer mixture is cross-linked with other polymers, resulting in a two-polymer mesh is referred to as IPN. The major advantage with IPN is that it combines the beneficial properties of both polymers into the final material [41], A permanent and stable union of the PHEMA sponge skirt and the PHEMA core is provided by an IPN interdiffusion zone between the optical

core and the peripheral skirt, was the first application of IPNs in artificial cornea. More recent efforts focus on incorporating IPNs in the entire artificial cornea constructs [42].
To create a functioning artificial cornea in one design, The hydrophilicity and nutritional permeability of PNIPAAm are mixed with the mechanical strength, oxygen permeability, and transparency of PDMS. Another example is the IPN of a charged, weakly crosslinked polyacrylic acid with a neutral crosslinked poly (ethylene glycol) (PEG) (PAA) [43, 44]. The optical transparency, mechanical characteristics, and glucose diffusion coefficients of such IPNs were comparable to those of the natural cornea. Despite the fact that the majority of artificial corneas have demonstrated satisfactory biocompatibility in animal models, it is vital to guarantee that the materials are nontoxic, nonimmunogenic, nonmutagenic, and do not cause corneal opacification [45].

2.2.5 Polymeric Biomaterials used as an Orthopedics

Traditionally, orthopedic biomaterials have been primarily metallic, owing to their strong resemblance to bone tissue in terms of properties as an example high strength, fracture toughness and hardness . Polymers have long been utilized in orthopedics, and they are gaining popularity in the field of bone tissue engineering [45]. Polymers have traditionally been used in orthopedics for structural device attachment and under cyclic load-bearing conditions, as an example in knee and hip replacements. Despite the fact that there are hundreds of orthopedic applications on the market, only a few types of polymers, such as ultrahigh-molecular-weight polyethylene (UHM WPE) and PMMA, are dominant[46].

2.2.6 Polyethylene

UHMWPE are polymers with linear structure and molecular weight of 2 to 6 million molecules. UHMWPE is a common choice for the articulating surfaces of joint replacements such the hip, knee, ankle, and shoulder because of its fracture toughness, low friction coefficient, high impact strength, and low density [47]. Although UHMWPE has a number of appealing bulk and surface qualities, the viability of long-term radicals in the bulk as a result of the ionizing radiation used in the sterilization process can undermine these properties. These radicals can interact with oxygen, resulting in the formation of oxygen-containing functional groups and loss of surface and bulk characteristics, especially the rate at which particles are produced during the wear process [48].
The inflammatory reaction in the tis sues close to the implant has been attributed to an overproduction of wear debris. Granulomatous lesions, bone resorption, osteolysis, and implant failure will all result from this unfavorable tissue reaction. A number of additives,

Like the antioxidant -tocoferol and vitamin C, are being employed to prevent oxidation and improve surface characteristics in an effort to counteract oxidation. Because of the wear issue, UHMWPE is considered as vulnerable point in any total joint replacement. Highly cross-linked UHMWPE has been developed and used in joint replacement to improve wear resistance [49, 50]. UHMWPE is crosslinked by irradiating it with electron beam or gamma radiation, and then melting it to remove the free radicals created during the irradiation.

There is now a dispute about crosslinking and UHMWPE's clinical performance. Those in favor have demonstrated the effectiveness of strongly crosslinked UHMWPE in decreasing wear and periprosthetic osteolysis in complete joint arthroplasties [51]. According to the opposition, crosslinking improves wear resistance at the price of static mechanical qualities like as tensile and yield strength, as well as fatigue crack propagation resistance, which could decrease implant longevity, particularly in total knee arthroplasty[52,53]. Complete data on strongly cross-linked UHMWPE's ultimate long-term performance will help settle the scientific debate.

2.2.7 Polyacrylates

Charnley was the first to show the use of PMMA as a bone fixative. The liquid monomer MMA, a partially polymerized PMMA powder, an initiator (commonly dibenzoyl peroxide), an activator (N, N-dimethyl-p-toluidine), a radiopacifier (visible to X-rays) such as barium sulfate or zirconium oxide, and a copolymer to influence the mixing and handling of the cement are all included in the PMMA bone cement[54,55]. To prevent infection during implantation, an antibiotic (e.g., gentamicin) may be incorporated in the formulation. The contact between the activator and the initiator causes the polymerization to begin, resulting in a free radical that reacts with the monomer [56].

The hardened polymer allows the prosthesis to be firmly fixed in the bones. Even acrylic bone cements are frequently utilized in orthopedics; they have a number of disadvantages. Fat embolism could be caused by leftover monomer leaking into the body [57]. Because of the exothermic nature of the polymerization process, necrosis of the surrounding tissue is a possibility. Aseptic loosening, or loosening of the implant within the cement, is the most serious disadvantage. Mechanical and/or metabolic factors may contribute to aseptic loosening. Loading of the implant could cause cracks and structural loss of the cement on a mechanical level. Wear debris from the polyethylene component could move to the bone–cement interface and cause an inflammatory reaction, resulting in osteolysis and weakening of the implant interface biochemically [58]. A viable technique for improving PMMA attachment is to increase the cement's mechanical strength to avoid cement fracture. Researchers created bioactive glass ceramics, bone cement with better adhesive strength and compressive modulus than typical PMMA was created utilising a bisphenol-A-glycidyl dimethacrylate (bis-GMA)-

based resin entangled with bioactive glass ceramics.

Other alternative uses composites to reinforce PMMA with hydroxyapatite (HA) and bioactive glass, which provides strength, flexibility, and bioactivity. Polyethylmethacrylate (PEMA) and n-butylmethacrylate (n-BMA) monomers are used in the other acrylate bone cement. PEMA-n-BMA cement produces less heat during polymerization than PMMA cement, and the polymer has a low modulus and good ductility, which reduces the risk of fracture [59,60]. The PEMA-n-BMA cement has a high level of biocompatibility. However, creep has been discovered to be a problem with certain bone cements. Bioactive HA particles were used to improve creep resistance. Although HA increased the cement's bioactivity and creep behavior, it failed after a smaller number of cycles [61].

2.2.8 Polymeric Biomaterials in Cardiovascular

Heart valve prosthesis, stents, vascular grafts, indwelling catheters, ventricular assist devices, automatic internal cardioverter defibrillators,total implanted artificial heart, pacemakers, intraaortic balloon pumps, and other biomaterials have all been used to treat cardiovascular illnesses. [62.63]. Blood compatibility, or nonthrombogenicity, is a critical criteria for materials in cardiovascular devices; Specially blood interacting devices .Application-specific mechanical and surface characteristics are also required. The most often utilized polymers in cardiovascular applications are polyurethanes (PUs), polyethylene terephthalate (PET), and expanded PTFE (ePTFE).This section will go through each of the three polymers in detail, followed by a quick overview of other developing polymers for cardiovascular applications [64].

2.2.9 Polyurethanes

PUs is one of the most often used biomedical polymers in medical equipment that come into contact with blood. Hemodialysis bloodstream catheters, stents, pacemaker lead insulation, heart valves, vascular grafts and patches, left ventricular assist devices (LVADs), and other devices contain them [65]. By altering the structure and its molecular weight of the soft segment and coupling agents, PUs can be classified as segmented block copolymers with agood mechanical and blood interaction properties. In biological PUs, the urethane linkage, –NH–C (=O)–O–, can be produced in two steps. The first step is to create a pre polymer by end-capping macrodiol soft segments (such as polyether, polycarbonate, polyester, and polysiloxane) with diisocyanate. The prepolymer is then coupled with a low-molecular-weight monomer in the second step [66].

Because of its poor compatibility, the morphology of PUs containsof hard segments aggregating to forms structures that are distributed in a matrix created by the soft segments.

Because of their distinctive form, biomedical PUs have exceptional mechanical properties and biocompatibility.The resultant PU, for example, can be elastomeric or rigid depending on the respective molecular weights and quantities of the hard and soft segments [67,68]. The chemical composition of the chain extender can also be changed to customize the mechanical properties of PU. PUs made with aliphatic chain extenders are often softer than those made with aromatic chain extenders.

Biocompatibility of Polyurethane is also influenced by its chemical structure of the chain extender and soft segment. Changes in the molecular weight of the polypropylene soft segments altered protein adsorption, according to early research by Lyman et al [69]. In the manufacture of biodegradable PUs, lysine diisocyanate and hexamethylene diisocyanate are chosen over aromatic diisocyanates, mainly due to the alleged carcinogenic characteristics of aromatic diisocyanates. Natural polymers, like chitin and chitosan, have been used as chain extenders to increase the biocompatibility of PUs in recent studies. PUs' main research focus has been and continues to be bio stability. The expected bio stability of PUs varies depending on the intended medicinal uses. Pacemaker lead covers, for example, should have superior Pus [70].

The following mechanisms are involved in the biodegradation of PU:

(1) Hydrolysis

(2) Enzymatic degradation

(3) Oxidative degradation, metal or cell catalyzed

(4) Surface cracking

(5) Calcification.

(6) Cracking due to environmental stress

The low hydrolytic stability of PUs with polyester soft segments is well known, while PUs with polyether soft segments evenly gets degraded by oxidation. More bioresistant PUs have been created over the years, guided by significant information gathered from thorough analysis of molecular pathways leading to PU biodegradation [71]. Polycarbonate macrodiols, polyether macrodiols with longer hydro carbon lengths between ether groups, and siloxane-based macrodiols are examples of these techniques. Bioresorbable polyurethanes, on the other hand, are gaining popularity as elastomeric tissue engineering scaffolds. Soft segments like polylactide or polyglycolide, polycaprolac tone, and polyethylene oxide are widely utilized in this type of PUs. Degradation is also programmed into the hard portions. Enzyme-sensitive connections have been included in the design [72, 73].

2.2.10 Polyethylene Terephthalate

PET belongs to the family of technical polyesters. It's a semicrystalline polymer that's used in synthetic fibers, as well as drinking and food containers. PET is frequently utilized in the medical industry as prosthetic vascular grafts, sutures, and wound dressings in both fiber and fabric form (commercially known as Dacron) [74]. PET is relatively stable in vivo despite the presence of a hydrolytically cleavable ester bond, owing to its high crystallinity and and non-water repelling. It is among the two clinically used biological materials for prosthetic vascular grafts. It's commonly employed in situations involving larger vessels (diameter > 6 mm). PET for vascular applications can be woven or knitted, depending on the porosity and mechanical properties of the graft [75, 76].Because woven grafts have less porosity than knitted grafts, the risk of transmural blood extravasation is reduced. Dacron vascular grafts are rigid and sturdy, not as flexible as natural arteries. This type of compliance mismatch has been linked to graft patency loss over a lengthy period of time (>6 months). The thrombogenicity of the PET graft is another serious consequence. Plasma protein will adsorb to the luminal and capsular surfaces when the graft comes into contact with blood, causing thrombus development and an inflammatory response [77, 78]. To produce the graft surface thrombo-resistant, various methods such as albumin passivation, fluoropolymer coating, hydrophilic polymer coating, adsorption of heparin albumin which are anticoagulant, and covalent coupling of antithrombotic substances have been tested.

2.2.11 PTFE Expanded

The other of the two main biomaterials for prosthetic vascular grafts utilised in clinical practise is EPTFE, widely known as Gore-Tex in the commercial world. EPTFE is used in surgical sutures and patches for soft tissue regeneration, such as hernia repair, in addition to being vascular. Extrusion, stretching, and heating processes are used to manufacture a microporous material with pore sizes ranging from 30 to around 100 micrometers [79]. EPTFE is extremely crystalline, hydrophobic, and stable, similar to PET. It has a very low coefficient of friction, which makes it very easy to handle. It has a lower tensile strength and tensile modulus than PET. Even while ePTFE graft compliance is lower than PET graft compliance, it is still too high when compared to PET graft compliance [80, 81].The graft failed to produce a full coverage of endothelial cells on the lumen side of the graft, according to reports. To solve this problem, one solution is to improve porosity in order to encourage tissue ingrowth .However, as previously said, avoiding blood element leakage needs a delicate balance. Carbon coating to boost surface electronegativity, impregnation with fibrin glue and attachment of anticoagulant or antithrombotic medicines to give growth factors that can promote endothelialization are some

of the other techniques of reduce surface thrombogenicity . Longer-term in vivo studies are needed to assess the true effects of these therapies [82]. The difficulty of small-diameter vascular healing has prompted research into alternative biomaterials that can match or even outperform autografts. In theory, such grafts will have mechanical properties that are very similar to those of natural tissues, but without the risk of persistent inflammatory reactions that are often associated with the presence of synthetic material. Poly (-hydroxyesters): poly (glycolic acid) (PGA), poly (lactic acid) (PLA), and its copolymers poly (lactic-co-glycolic acid) (PLGA); polycaprolactone; polyanhydride; polyhydroxyalkanoate; and polypeptide have all been employed to produce such constructs thus far [83, 84]. Several great evaluations on the current state of materials as scaffolding for vascular tissue engineering are available. Biodegradable stents are another cardiovascular application where polymers are expected to have a big influence. Stainless steel, cobalt–chromium, and Nitinol are the most common metals used in stents today. Long-term difficulties associated with metal stents, on the other hand, have encouraged research on a fully degradable alternative [85]. The polymeric stent must meet several critical requirements, the most important of which are mechanical qualities and degrading characteristics. In terms of deterioration, the degradation products should be biocompatible, and the process should last at least six months without jeopardising the device's structural integrity. The polymer should be able to endure deployment and blood vessel contractions in terms of mechanical properties. Both conditions are difficult, but they can be met if you have a strong understanding of the biology and the environment [86, 87].

2.2.12 Polymeric Biomaterials for Wound Closure

Sutures, adhesives, tapes, staples, and laser tissue welding are among options for closing surgical wounds. Sutures are the most commonly utilized procedure among these. Sutures are sterile threads that are used to approximate and retain tissue until the incision has healed sufficiently to bear mechanical pressures [88]. Sutures are characterized according to their origin: natural or synthetic; their performance: absorbable or non-absorbable; and their physical configurations: monofilament, braided, multifilament, or twisted. Suture polymers should, in general, provoke a low unfavorable biological response while still having fiber-forming rheological characteristics. The sutures must have a low tissue drag, high strength retention, and a secure knot. Coatings like tetrafluoroethylene improve lubricity and reduce tissue drag [89].

Polyamides, polypropylene (PP), polyesters lilke PET and polybutylene terephthalate (PBT), and, 1, 4-butanediol, and dimethyl terephthalic acid, polyether–ester based on poly (tetramethylene glycol) are among the synthetic polymers used to construct nondegradable sutures. Isotactic polypropylene is used to make the PP monofilament sutures. The PP

monofilament is treated to a number of post-pinning processes, including annealing, to improve crystallinity throughout preparation [90, 91]. PP sutures are highly resistant to hydrolytic degradation, although they can be heated oxidatively degraded. Due to its ionising radiation sensitivity,Radiation sterilisation, such as that from a cobalt-60 source, is commonly utilised, however PP sutures are normally sterilised by ethylene oxide or autoclave. PP suture has one of the lowest tissue responses in terms of performance.Sutures composed of polyamide are extensively used [92].

Monofilament, braided multifilament, and core–sheath configurations are all available with these polyamide sutures. To minimize tissue drag, braided multifilament nylon sutures are frequently coated (e.g., silicone coating). The sensitivity of the amide bond to hydrolytic breakdown in the nylon structure is linked to the observed decline in strength retention over time. The tensile strength of nylon sutures deteriorates at a rate of 15–25 percent per year [93, 94]. The tissue reaction to nylon sutures appears to be unaffected by their configuration, with braided and monofilament sutures evoking similar levels of reactivity. Sutures made of fluoropolymers as an example polyvinylidene fluoride (PVDF), PTFE, and copolymers of PVDF and hexafluoropropylene (HFP) have been developed and used to suture particularly sensitive and difficult tissues. PTFE is a heat-resistant material (Tm = 327°C) [95].

EPTFE fibres have morphology of nodules joined by thin crystalline fibres that influence tensile strength. The porosity of PTFE fibres has a direct relationship with mechanical qualities, biological reaction, and handling. Because of the microporous nature, ePTFE suture has a low bending stiffness, The porous structure, on the other hand, adds to the loss of strength. PVDF is a crystalline material as well. (Tm = 175°C) .PVDF sutures have excellent creep resistance and tensile strength retention. Surface stability has been established in morphological investigations, with no obvious evidence of bulk or surface fracture. PVDF sutures are prone to thermo-oxidative deterioration, however they can be sterilised quickly with radiation. PVDF elicits moderate tissue and cell response, a behavior similar to PP sutures [96, 97]. PVDF and HFP copolymer sutures were developed with the purpose of merging PVDF and PP's good handling properties and biological response into a single material. PVDF/ HFP sutures were also created to mimic the long-term stability of polyester sutures. Manipulation of the copolymer compositions can tune the strength, biocompatibilty, size, and handling of PVDF/HFP sutures.

Wound closure during cardiovascular, neurological, and ocular procedures is the most common applications for PVDF/HFP sutures. These PVDF/HFP sutures are typically utilized as monofilaments with no coating. PET and PBT are two of the most regularly utilized polyester-based nonabsorbable sutures [98, 99]. There are other polyester-based sutures called polyetheresters that are manufactured from copolymers of poly (tetramethylene terephthalate) and poly (tetramethylene ether terephthalate). The condensation reaction of ethylene glycol and terephthalic acid produces PET. PET is a thermoplastic polymer with a

melting point of 265°C. Melt spinning monofilament fibers with varied profiles is possible thanks to PET's heat stability. The fibers are hot drawn during processing, which improves molecular orientation, crystallinity, and tensile strength. PET sutures are offered as coated or uncoated monofilament sutures on the market [100].

PET sutures retain their strength for an extended period of time. PET sutures have varying degrees of tissue reactivity. Due to the longer aliphatic section in the polymer structure, PBT sutures are often less brittle and stiff than PET sutures. Block copolymers of PBT and poly (tetramethylene ether) glycol terephthalate are used to make polybutester sutures (PTMG)[101,102]. The hard component of the copolymer is PBT, and the flexible segment is PTMG. These copolymers have elastomeric qualities due to incompatibility between the hard PBT and soft PTMG blocks. Polybutester sutures are appropriate for wounds prone to edema development because of their peculiar mechanical action.

Condensation or ring opening polymerization can be used to make PGA. The first absorbable sutures were PGA-based sutures. Coated or uncoated PGA sutures in a braided form are commercially available. Lactic acid, trimethylene carbonate, and -caprolactone were copolymerized with glycolide [103]. To make a random copolymer, glycolic acid was copolymerized with l- or dl-lactic acid. The composition of the glycolide-l-lactide sutures affects their performance. The concentration of crystallizable glycolide monomers determines the initial tensile strength and retention of the glycolide-l lactide sutured wound during the healing process. Copolymers based on dl-lactide do not show the same property dependence as copolymers based on l-lactide. Trimethylene carbonate has been copolymerized with glycolide to generate a triblock copolymer [104,105].

These sutures are supplied as monofilaments with no coating. The synthesis of segmented copolymers occurs when glycolide and caprolactone copolymerize. The soft and hard segments of these copolymers are formed by glycolide and -caprolactone, respectively. The ringopening polymerization of 1, 4-dioxanone-2, 5-Dione produces poly p-dioxanone (PDS). Melt spinning is used to make monofilament sutures [106]. A drawing procedure is used to improve the tensile strength and performance of the fibers. PDS has recently been copolymerized with PGA and PLLA to make sutures with a variety of characteristics. The current aim in wound closure suture research is to add additional functionality to the suture in addition to closing the wound. Controlling wound infection by producing antimicrobial sutures and accelerating wound healing by employing bioactive materials are two examples of these attempts [107].

2.2.13 Polymeric Biomaterials in Artificial Extracorporeal Organs

Before returning the blood to the circulatory system, these devices regulate the patient's blood outside of the body. Gas and heat exchangers, dialyzers, bioartificial livers, apheresis

devices, and other devices are examples of these devices. All of these technologies are intended to improve the material flow between body fluids and other fluids separated by a membrane [108]. Patients with acute liver failure are given bioartficial hepatic devices to help them. Hepatocytes in a bioreactor perform both exchange and synthesis roles in these devices or nonliving components remove toxins accumulated as a result of liver failure. These devices are used to help the patient until he or she receives a transplant. In the case of hollow fiber systems, natural or synthetic polymers such as collagen are used [109].

Through mass transfer operations, extracorporeal artificial organs maintain failing or compromised organ systems. A few examples include kidney replacement, hemodialysis, cardiopulmonary bypass (CPB), apheresis therapy, peritoneal dialysis, lung substitute and assist, and plasma separation [110]. The membrane is an important component of the extracorporeal artificial organ because it assists to separate the undesirable substance from the blood or plasma. Membranes utilized in these applications must have sufficient cellular and molecular interaction, compatible to blood. Membrane materials have long been prepared from natural and synthetic polymes. Cellulosic membrane is the most extensively utilized natural membrane. In the case of hemodialysis, early applications of cellulose membrane in the dialyzer used regenerated cellulose, that is, cellulose that had not been substituted with rich substances [111,112].

The membrane with high concentration of OH groups has been linked to complement activation, making it nucleophilic and vulnerable to protein deposition, notably C3b. Later study into the use of substituted cellulose for dialysis membranes, such as cellulose acetate and cellulose triacetate, where a fraction of the hydroxyl groups are replaced with acetate functionality in both cases, was sparked by this discovery [113]. By removing the active surface locations for complement protein interaction, these modified cellulose materials significantly reduced complement activation. Aside from chemically limiting complement interaction, steric hindrance techniques have also been investigated. To sterically limit the complement protein's reactions with the membrane, To replace the hydroxyl group, a bulky group such as benzyl substitution group or tertiary amine group was applied. Membranes for dialysis are now accessible. [114].

Synthetic membranes are less prone to complement activation than natural cellulosic membranes. The decreased level of topical nucleophiles for C3b adsorption is the cause for the better complement compatibility. Furthermore, certain synthetic membranes have a high negative charge on their surface, which allows them to absorb the activated cationic complement peptide (e.g., C5a) and reduce the inflammatory cascade that follows [115]. In comparison to cellulosic membranes, synthetic membranes have much bigger pore sizes and better hydraulic permeability. For high-flux applications, synthetic membranes are the best option. The greater pore size also enables for the elimination of intermediate molecules with

molecular weights of 500 to 2000 Da, which have been identified as bioactive and may have a biological effect. Most manufactured membranes are hydrophobic, which contributes to their hydrophobicity [116].

-Dental Implants/Cartilage Implants/Orthopedic Applications: Metallic implants, hyaluronic acid, chitosan, collagen, fibrinogen, and other naturally derived matrices have been used in bone tissue creation. However, the usage of these matrices has the disadvantage of being difficult to sterilize and eliciting an immunological response in the host. Synthetic polymers such as poly (a-hydroxy acid), polypropylene fumarate, polyethyleneglycol, and others have the benefit of being created with specific parameters, but they breakdown into hazardous components [117]. Bioactive glass, hydroxyapatite, porous coralline, tricalcium phosphate, and other bioactive inorganic materials are showing promise in bone tissue engineering.
They have the advantage of being able to be manufactured with specific characteristics, but they breakdown into harmful components. Bioactive glass, hydroxyapatite, porous coralline, tricalcium phosphate, and other bioactive inorganic materials are showing promise in bone tissue engineering. More effort is being done to improve the scaffold's bio-functionality by including osteinductive signals that can boost osteoblast growth on these scaffolds [118,119]. In cartilage tissue engineering, scaffolds prepare fron polymers of natural and synthetic materials are used. Agarose, alginate, chitosan, collagen, fibrin, and hyaluronan are examples of natural polymers, whereas synthetic polymers include poly (a hydroxy ester), polylactic acid (PLA), polyglycolic acid (PGA), and their copolymers, among others [120].

Dental implants that are intended for commercial use can be classified into two groups:

a . Implants that extend into the bone tissue are known as endosteal or endosseous implants.

b. The outer bone surfaces are in touch with the subperiosteal systems (Figs 3A and B).

Root forms (cylinders, screws) , transossious , blades (plates) or staples, or endodontic stabilizers are all endosteal implants that are implanted into the bone. However, superiosteal devices are bespoke shapes that are fitted to the bone surface. Furthermore, bone plates are implanted under the periosteum and secured with endosteal screws. Gold, platinum, iridium, and palladium are among the synthetic materials utilized in root form devices. Titanium and its alloys, aluminum oxide, and hydroxyapatite surface coatings are some of the other biomaterials or dental implants that are often employed [121].

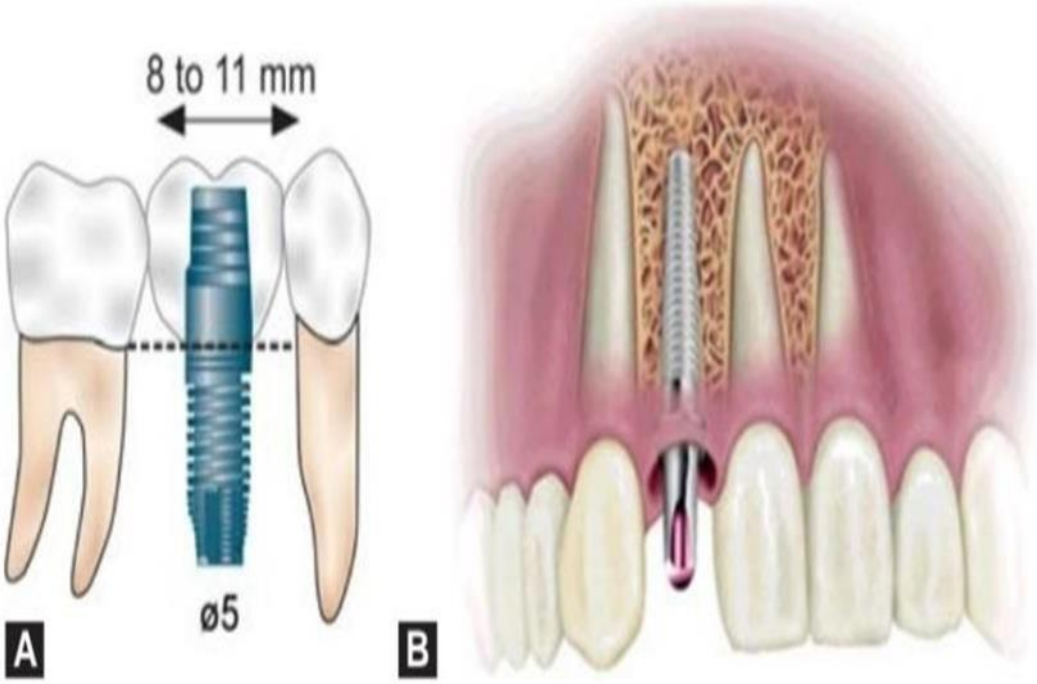

Figure 2.1:

(A) A contemporary dental implant and (B) dental implants those are osseous

2.2.14 Polymeric Biomaterials for Nerve Regeneration

Even though progress has been made in recent decades, properly repairing the damage so that lost neural system functions can be recovered remains elusive. There are two types of neural systems: the CNS and PNS. Guidance conduit, scaffolds with cell transplantation, and therapeutic administration has all been investigated for nerve regeneration in both the CNS and the PNS. The polymers employed in the nerve guiding conduit technique will be the subject of this section [122]. Axons, which are long structures that extend from the neuron cell body and conduct electrical signals, have long been thought to play a role in nerve regeneration. The nerve directing conduit is prepared to accomplish the following:

(1) The proximal nerve end's axons should be used to bridge the damage.
(2) Allow biomolecules released by damaged nerve endings to spread through a conduit.
(3) Scar tissue should not be allowed to invade the regeneration zone.

A standard nerve conduit should be semipermeable with directed surface features inside the conduit, electroactive, capable of dispersing bioactive substances, and capable of encouraging cell adherence and migration in order to achieve these objectives. Polymers are the best choice for nerve guidance conduit engineering because of their versatility. Nondegradable synthetic polymers such as silicone and ePTFE were employed in early studies. Although silicone nerve guiding conduit has been successful in bridging gaps as small as 10 mm, it has not been successful in supporting regeneration over bigger faults. As a result, the focus has turned to developing a biodegradable guide conduit in the future. The use of a biodegradable substance has the advantage of reducing long-term problems such as fibrotic reaction and nerve compression [123].

The material's degrading characteristics must meet the following criteria:

(1) The degraded product(s) should cause the least amount of tissue reactivity possible.

(2) The deterioration profile should mirror the axonal outgrowth profile in order for the guide conduit to provide enough mechanical support during regeneration.

Biodegradable poly (esters) like PGA, poly (caprolactones); polyphosphazenes; polyurethanes; and polyurethane (3-hydroxybutyrate), PLA, and PLGA. Electrically active polymers can give electrical signals have been used in guide conduit development since the publication of studies revealing that electrical charge affects neural spreading in vitro and promotes neuron regeneration in vivo. Piezoelectric polymers such as PVDF and its copolymer are among these polymers, as well as polymers like polypyrrole and its biologically modified compounds have conductive properties. Other electroactive polymers, such as polyaniline, may potentially enhance nerve growth, as tests with cardiac myoblast cells have showed promising results [124]. To support axonal growth, nerve guidance conduits can be empty or filled with matrix. Natural polymeric gel is a popular filler option. Ideally, Agarose , keratin ,methylcellulose, chitosan, hyaluronic acid, fibrin gels, alginate, collagen, and self-assembling peptide scaffolds are among the natural polymers studied. Agarose is a polysaccharide hydrogel that is thermally reversible. The temperature at which it gels can be altered by altering the functional groups connected to the sugar residues. Its fictionalization with other motifs to increase neurite

extension, as an example laminin-derived peptide sequences RGD, IKVAV and YIGSR. Fibrin is a natural wound-healing extra cellular component that appears early in the regeneration process. To reestablish hemostasis and induce tissue repair, it is generated by the blood coagulation cascade. The natural matrix formed in the guidance conduit spanning brief nerve gaps, where a fibrin cable is used, can be closely mimicked by using fibrin gels as the filler [125].

Polyamide, polydioxanone, PGA, catgut, polyglactin, poly (acrylonitrile-comethyl-acrylate), PLA, collagen, and other materials are used to make filaments. Recently, nerve guidance conduit materials research has progressed to a new level, with the traditional paradigm of passive material design being replaced by a new bioactive material design. To give the final biomaterial neuroactivity,Chemical messengers like neurotransmitters have been polymerized into the backbone of the polymer. Diglycidyl ester polymerized with dopamine to form a biological degradable substance with robust neurite outgrowth in vitro and biologically compatible to cells in vivo is the first example of this new type of polymer. Polysialic acid based hydrogel are another example of a novel bioactive polymer. Polysialic acid is a posttranslational alteration of neural cell adhesion that is dynamically controlled [126].

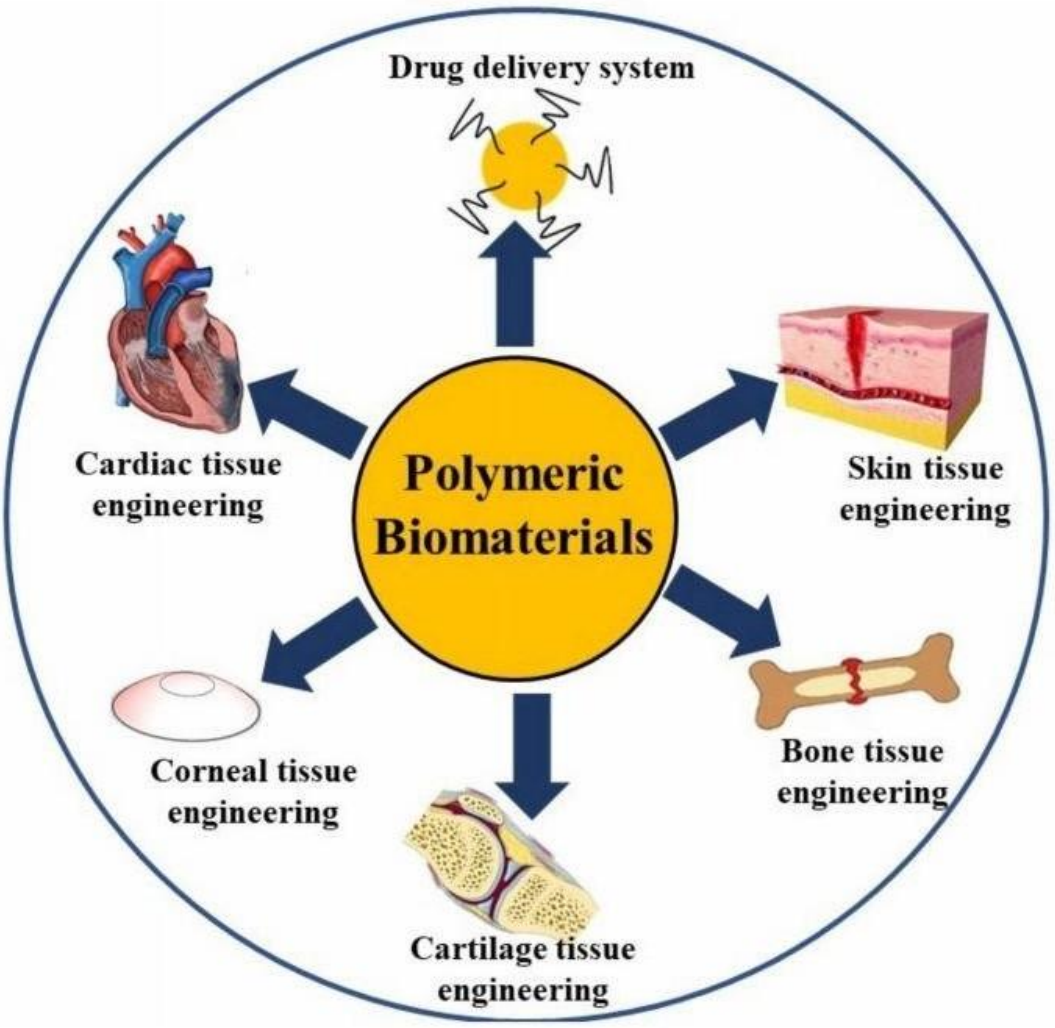

Figure 2.2

A diagram depicting the use of polymeric biomaterials in many biological fields.

CHAPTER THREE

3.1 APPLICATION OF NANOMATERIAL IN MEDICAL FIELD

3.1.1- NANOBIOSENSORS

Nanobiosensors are small, detectors of biological and chemical materials that can be used for patient testing at the point of treatment. .Piezoelectric polymers like PVDF and its copolymer are among these polymers Nanosensors based on fluorescence resonance energy transfer can detect low levels of DNA without the need for separation. To collect DNA targets, QDs are connected to DNA probes [127,128].used QDs to mark tumor vasculatures in live animals by combining them with a peptide. Different nanosystems are used to do in vivo cancer targeting and imaging. Solid nanoparticles can be utilized as contrast enhancers in ultrasonic imaging, allowing for the early detection of disease at the cellular level. QDs in Semiconductors [129].

3.1.2-TOOLS FOR NANOSURGERY/NANOROBOTICS

Nanosurgery/nanorobotics tools are being used for cancer early diagnosis and treatment [130]. Before being implanted, such a gadget must be biodegradable and its safety must be proved.

3.1.3-NANOORTHOPEDICS

Ceramic nanocomposites, nanomaterials, nanopolymers, carbon nanofibers, nanotubes, and nanocomposites improve the deposition of calcium-containing minerals on implants. On nanospaced materials like 3D nanofibrous scaffolds, proteins that promote particular osteoblast adhesion (such as fibronectin and vitronectin) adsorption and conformation are improved [131.132]. When compared to conventional materials, Because of their bigger exposed surface and better wettability, more proteins are attracted to nanophase materials that are close to the size of proteins (on the nanoscale). When vitronectin is adsorbed to nanophase materials rather than typical ceramics, the peptide sequence arginine-glycine-aspartic acid is more exposed, resulting in increased osteoblast cell adhesion to the proteins already adsorbed to the implants [133].

3.1.4-ANTIMICROBIAL NANOMEDICINE

Diagnostics, antimicrobial therapy, medication delivery, medical devices, and vaccinations are all part of antimicrobial nanomedicine, or the management of microbial infection [134]. MDR refers to the ability of some bacterial strains to develop or acquire resistance to multiple

antimicrobial agents. Methicillin- or vancomycin-resistant Staphylococcus aureus, for example. Clinically, MDR pathogens are sometimes incurable. Nanobiotechnology and nanomedicine are working on solutions for these issues. For bacterial diagnostics, antibiotic delivery, and medical devices, more than ten nanoparticle-based products have been marketed [135]. Nanomaterials can detect microbial diseases swiftly, sensitively, and selectively thanks to their unique physicochemical properties. The inherent proprieties of inorganic and organic can be used to combat antibiotic resistance by interfering with resistivity while having fewer coss reactivity and effect than antibiotics used conventionally, prevent microbial adhesion and infection, and act as antimicrobial agents. For microbiological diagnosis, magnetic, gold (Au), and fluorescent nanoparticles are utilized. Single-walled and multiwall carbon nanotubes and fullerene, cationic polymer and peptide based nanoparticle, metal (Ag, Te, Bi) and metal oxide (ZnO, CuO, TiO2, Al2O3, and CeO2) nanoparticles, and wound dressings are all examples of antimicrobial nanomaterials (as chitosan) . Biofilms and intracellular microorganisms are combated via nanoparticle-based antibiotic delivery, both targeted and nontargeted. Silver nanocrystals in Acticoat bandages [136,137] are particularly poisonous to bacteria in wounds. Nanoviricides, or virus-killing nanomedicines, are currently being developed. A nanoviricide is a substance that recognizes a particular virus particle, binds to it several times, neutralizes it, and then dismantles it. Influenzas, HIV, hepatitis C, and rabies are among the diseases targeted by this strategy [138].

3.1.5-Drug Delivery

Nanoparticles show great promise in drug delivery by altering drug molecules' bioavailability, pharmacodynamic properties and pharmacokinetic, to improve therapeutic delivery; due to a lack of appropriate and recognised solutions for precision targeting, controlled drug solubility and cell internalisation, and release, clinical translation has been delayed[139.140]. Drug-resistant tumor cells recycle the input of chemotherapeutic drugs via pumps identified as P-glycoprotein and multidrug resistance-associated protein; polymeric carriers, either for encapsulation or conjugation of the drug, can help reduce the out flux of drug for better cancer therapeutic performance [141, 142]. To combat multidrug resistance, Khdair et al. based on the natural polymer sodium alginate, developed a new type of multifunctional nanoparticle system. Photodynamic therapy for cancer therapy combines light with a cocktail of chemicals to treat cancerous tumors via three main mechanisms: inducing cell death via cytotoxic reactive oxygen species (ROS), activating an immune response against tumor cells via the inhibition of multidrug resistance pumps or damaging tumor vasculature [143,144]. In a mouse adenocarcinoma tumor model, single-dose tests of the combined chemotherapy and photodynamic therapy demonstrated significant improvements in drug accumulation and ROS production to inhibit tumor cell proliferation [145].

CHAPTER FOUR

CONCLUSION

Biomaterials are widely employed in a variety of medical applications, that incudes healthcare equipment, surgical implants, fixtures, , and medical instruments. Also they can be employed to enhance the appearance of the human body such as in breast implants or piercings. Three factors must be considered when designing new biomaterials: structure, chemical, surface characteristics and composition.

Natural and synthetic nanoengineered polymeric biomaterials are used in biomedical applications such as targeted sustained, drug delivery and controlled release.

Nanocomposites with natural polymers are biologically degradable, nearly biocompatible, and low-to-no toxic, making them popular in medicine. Biopolymer synthetic nanocomposites offer a wide range of uses. They can be modified by combining biomolecules in order to make them harmless to the body and more biocompatible. In the treatment of asthma, cancer, HIV, asthma, malaria, TB,and infectious disorders, both synthetic and natural polymers are commonly employed.

This review summarised recent breakthroughs in polymer-based biomaterials and their potential applications in medical fields such as surgical devices ,drug-delivery systems, implants and supporting materials (e.g. artificial organs), with various routes of administration and design, and more. Ophthalmology, Wound Closure, Cardiovascular, and Nerve Regeneration are some of the fields in which biosensors are used.

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CANDIDATE'S DECLARATION

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CERTIFICATE

I hereby certify that the Project Dissertation titled "A review on Development of Nanoparticles Based Polymeric Biomaterials and its Medical Applications" which is submitted by Alaa Khalid Abdelrahman Abdalla, Roll No's – 2K20/IBT/15. Department OF Biotechnology, Delhi Technological University, Delhi in partial fulfillment of the requirement for the award of the degree of Master of Technology, is a record of the project work carried out by the students under my supervision. To the best of my knowledge this work has not been submitted in part or full for any Degree or Diploma to this University or elsewhere.

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ACKNOWLEDGEMENT

I wish to express our sincerest gratitude to Dr. Prakash Chandra for his continuous guidance and mentorship that he provided me during the project. He showed me the path to achieve my targets by explaining all the tasks to be done. He was always ready to help me.
I am grateful to Indian Council for Cultural Relation (ICCR) under the government of India, for the support throughout this studies I'm truly energetic about the entirety of my companions for their ideas and moral help during my visit in India.

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