



Biomaterials at the forefront: A comprehensive review of patented biomedical applications

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ABSTRACT

Over the years, biomaterials have played a crucial role in mitigating the socio-economic burden of healthcare by significantly enhancing the diagnosis and treatment of injuries and diseases. Through collaborative innovations, newly developed biomaterials have not only contributed to saving lives and alleviating suffering but have also improved the overall quality of life. The burgeoning biomaterials market witnessed considerable expansion over the past decade owing to escalating demands for medical implants, increased prevalence of diseases among the geriatric population, and a rise in cosmetic and plastic surgeries. This growth trajectory indicates substantial potential for further expansion in the forthcoming years. Consequently, there has been a surge in requests for research and development of novel biomaterials for biomedical applications from governmental entities, academic institutions, and private enterprises, leading to a significant rise in the number of biomaterial patents issued annually. This study presents a comprehensive review of the escalating interest in novel biomaterial patents within the biomedical domain over the last decade, which has promoted stupendous technological advancements in orthopedics, dentistry, ophthalmology, and disease treatment. The promising outcomes of biomaterial-based research in the biomedical field pave the way for the emergence of smart biomaterials engineered through 3D and 4D printing technologies, capable of cell culturing, growth factor integration, and accurate emulation of complex body geometries. The future of biomaterials holds immense potential for transformative contributions to biomedical science and healthcare practice.

INTRODUCTION

The past decade has seen a remarkable upsurge of advancement and innovation in the health sector through the development of biomaterials [1,2]. With the increase in knowledge and understanding of the human body, biomaterials emerged with the ability to modify their properties to meet certain criteria and complement specific characteristics of the body, in contrast to previous materials having limited applications in the fields of aeronautics, electronics, and mechanical engineering [3,4]. The materials being exploited to innovate biomaterials

immensely include metals and alloys, natural and artificial polymers, ceramics (silica and inorganic mixtures), and hybrid biomaterials [5,6]. For instance, Figure 1 shows the global market of various biomaterials and depicts the abundance of growth opportunities in the global biomaterial and biomedical market based on material types and biomedical applications, respectively. The contribution of biomaterials is considered to be major in the orthodontics field, with the need for improved stents, valves, or grafts, especially for cardiovascular disease treatments [7–9].

The fabrication and utilization of biomaterials for biomedical applications include the invention of new biomaterials that resemble many body tissues (bones, tendons, skin, ligaments, teeth, and so on) [10,11]. For the material to be considered in the synthesis process, whether alone or in combination with biomolecules or synthetic materials, the following criteria ought to be met: (i) Biocompatibility.

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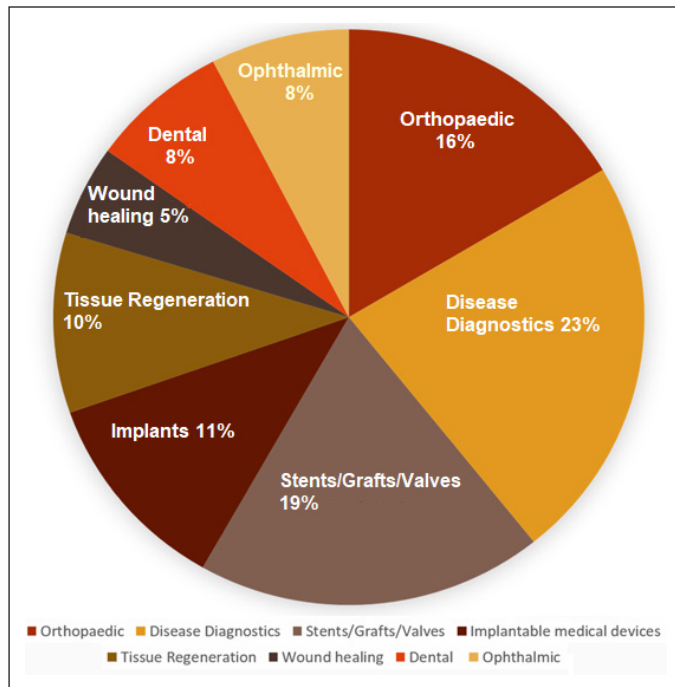


Figure 1. Global market share of biomaterials.

(ii) Enhancing diffusion of metabolites/nutrients within cell or tissue. (iii) Prevention of reactive species. (iv) Avoid deleterious health effects. (v) Exhibiting stable chemical and biological plasma stability. (vi) Showing good bio-resorption or biodegradation kinetics. (vii) Promote *in vivo* characterization or compatibility [12]. Another rapid growth has been witnessed in hybrid biomaterials, which are an amalgam of different biomaterials with improved biocompatibility [13]. Such a characteristic enables them to mimic body tissues effectively and, in turn, prove their tremendous use in biomedical applications. For instance, the current success in treating bone defects requires hard tissue repair using metallic or ceramic biomaterials, which are biologically inert and possess resorbable capabilities [14]. Along with treating bone defects, biomaterials have various uses, including early detection and capture of tumor cells in blood samples and diagnosis and prognosis of many common diseases [15].

Biodegradable materials made of natural, synthetic polymers and hydrolyzable metals are indispensable components of implantable medical devices as they help generate a host immune response and are safely absorbed by the body after performing their function. These biodegradable devices eliminate the need for the removal of the device via secondary surgery and hence help avoid possible prolonged health perils associated with permanent devices [16]. Additionally, biomaterials have been found useful in tissue regeneration as scaffolds, helping to deliver cells, stimulate endogenous cells, furnish biological signals, and physically support the repair of tissues [17]. Biopolymers display characteristics that include regulating local angiogenesis and modulating the immune response to heal wounds [18]. Another area of biomedical applications whereby biomaterials have been found to be of enormous usefulness is in cornea repair and dental fixation issues. Biomaterial scaffolds are used to enhance cellular

function and tissue production. The enormous use of biomedical materials is clearly reflected by the idea of having a total of 50,392 patents with the keyword “biomedical” being granted in the past decade.

BIOMEDICAL APPLICATIONS OF BIOMATERIALS

Orthopedic applications

Considerable improvements that have taken place in the orthopedic field over the last decade include the services of hybrid biomaterials. For instance, calcium phosphate (CaP)/collagen composite prepared using a porous CaP ceramic (porosity 60%–95%) as the substrate and I-type collagen (concentration 5–20 mg/ml) as the toughening/reinforcing phase under vacuum negative pressure (0–10Pa) at normal temperature exhibit good biocompatibility, mechanical strength, and biological activity [19]. Additionally, bone repairing material was prepared using 60%–75% of bioactive glass (particle size of 212–425 μm), 25%–40% of PEG (polyethylene glycol), and 0%–15% of hydroxyapatite (particle size of 50–200 nm) display good stability, biocompatibility, and safety [20]. Another composite bone repair material invented using a porous block-shaped ceramic scaffold and a stabilizing polymer facilitates bone defect repair and selective regeneration of natural bone along with good resistance to mechanical stresses [21].

An injectable liquid metal bone cement has been proven effective in treating osteoporosis; a bone tumor for such cement has high curing speed, low solidification temperature, simple preparation process, and stable structures in *in-vitro* and *in-vivo* environments with an X-ray self-developing function [22]. Nevertheless, an improved bone formation device was found to be more stable [23]. Likewise, a malleable bone graft consisting of keratin, osteoconductive ceramic-based filler, and antibiotic was capable of self-assembling into fibrous microstructures, which in turn implicates better osteoconductive properties [24]. Poly-(diol citrates)-based (POC)/Hydroxyapatite (HA) composite material has good function as bone screws whereby it has shown improved mechanical properties of bending, compression, shear, tension, and torsion [25]. Hybrid intramedullary rods (intramedullary nails or bone nails), patented in 2019, are convenient implantable medical devices for orthopedic applications like fracture stabilization and fixation [26]. Figure 2 shows the biomaterials action in bone fracture. However, a modified intramedullary device, which can expand at one or both ends with the shaft of the device also expanding if required, performs as a finer apparatus for fracture repair [27].

Bio-ceramics have played a significant role in the development of novelties for bone applications. Ceramics’ porous body patent proved to be a good osteogenesis material [28]. Comic meat comprising artificial bone is excellent in quantity securement, shape following, shock resistance, and sanitary confirmation [29]. Another improved artificial bone used for sustained drug release along with implantation applications can be molded into various bone-shaped sizes according to the bone defect [30]. The note-worthy novel patents using bio-metals for bone applications include a composite device invented by Monaghan and Hoeman that combines porous metal and bone stimuli and promotes bone

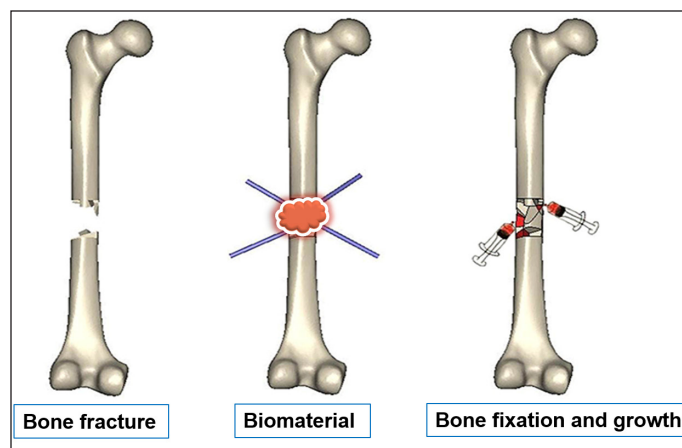


Figure 2. Biomaterial patents illustrating the applications in bone fracture.

Table 1. Biomaterial patents for orthopaedical applications.

Patent	Applications
JP2011219359A	A method for producing ceramics porous body
JP2011229518A	A production method of comic meat comprising artificial bone
CN103055352A	Calcium phosphate/collagen composite biologic ceramic material and preparation method
CN102488927B	Bone repairing material and preparation method
CN103251983A	Method for preparing spliced artificial bone-filled sustained release material with treatment effect
US8574611B2	Composite bone repair material using a porous block-shaped ceramic scaffold and a stabilizing polymer
CN103432624A	Injectable liquid metal bone cement, preparation method of injectable liquid metal bone cement, and special injection device for injectable liquid metal bone cement using liquid metal bone cement
JP 2014221427 A	Bone formation device for the repair of bone and its use
US 2015/0141333 A1	Keratin bio-ceramic compositions
S0169433215013045	Preparation of novel functional Mg/O/ZnO composite biomaterials and their corrosion resistance
US 9,566,156 B2	Composite device that combines porous metal and bone stimuli
US10610270B2	Hybrid intramedullary rods
EP 2 249 718 B1	Apparatus for fracture repair

regeneration and resorption [31]. The biomaterial patents for orthopedic applications are tabulated in Table 1.

Applications in diagnosis of diseases

Another widespread use of biomaterials, and specifically that of hybrid biomaterials, is found in the treatment of diseases and disorders. For instance, a matrix composed of a naturally occurring protein backbone cross-linked by a synthetic polymer is considered useful in treating a disorder caused by tissue damage. Moreover, the polymer linked to the denatured

fibrinogen releases a therapeutic portion of the fibrinogen in a pharmacokinetically regulated manner and thus helps treat the disorder [32]. Hybrid devices invented, consisting of naturally occurring polymers (collagen) and artificial ceramics (glass, hydroxyapatite, and so on), are used to boost the body's self-healing mechanism, which provides rapid healing of musculoskeletal injuries and degenerative diseases [33].

Hyaluronic acid-gold nanoparticles/protein complex, which is used to treat liver diseases, displays properties of stability, biocompatibility, biodegradability, and liver tissue-specific delivery [34]. Another dual-purpose thermosensitive poly (organophosphate)-superparamagnetic nanoparticle complex is considered suitable for the detection and treatment of cancer hyperthermia [35]. Also, the administration of PEGylated cysteine variants of IL-11 in the body stimulates platelet production and accelerates patient recovery from thrombocytopenia [36]. A composition containing biocompatible hydrogel encapsulating mammalian cells and anti-inflammatory drugs was proven effective in reducing fibrotic over-growth for at least 10 days after implantation [37]. Recent inventions using hybrid biomaterials include antibodies in combination with N-glycoside-linked sugar chains lacking fucosylation, which was found to be helpful in the diagnosis of many diseases. Moreover, the use of SBA-15 ceramics adsorbs antibiotics like vancomycin, linezolid, and rifampicin and can be used in the treatment of osteomyelitis [38].

With bio-metals and biopolymers being enormously utilized, it is evident to mention how interferon- β , which is delivered to the body with the help of aggregating metal (iron, copper, nickel, molybdenum, and tungsten) of concentration less than 500 parts per billion is used to treat multiple sclerosis [39]. A group in China invented a magnetosome formulation with transition metal formulation and chains extracted from magnetotactic bacteria for a similar magnetic irradiation antitumor therapy. Another application devised is the curcumin-conjugated nanoparticles made up of superparamagnetic iron oxide for noninvasive early detection of Alzheimer's plaques [40]. Similarly, an invention made use of gold nanoparticles or gold particles alone and was found to promote neurite outgrowth, hence treating and preventing neurological disorders [41]. Nitric oxide-releasing biodegradable polymers derived from 1,4 oxazepan 7-one and its derivatives have been verified useful for in situ-controlled delivery of additional bioactive agents and for treating various medical conditions (restenosis, aneurysms, and vulnerable plaque) [42]. Another invention demonstrated the use of intracellular stimuli-sensitive chitosan-graft-metformin prodrug in Type 2 diabetes combination therapy with improved lipid profile reversed the insulin resistance in obese mice and improved the fatty liver phenotype without toxicity [43]. Compositions comprising both hydrophobic and hydrophilic polymers have been shown to treat skin diseases and disorders. Certain naturally occurring and synthetic zwitter ionic polymers have been found to induce T regulatory (Treg) cells and exert immunosuppressive effects both in vitro and in vivo, which in turn help treat asthma and allergies. Potassium-binding polymers were used to treat ion imbalances like hyperkalemia [44]. Recent innovations using biopolymers include a biodegradable cationic polymer derived from the first cyclic carbonyl monomer (produced by ring-

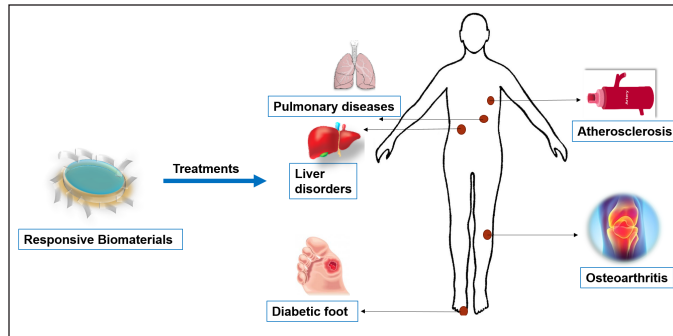


Figure 3. Biomaterial patents illustrate the applications in the treatment of various diseases.

opening polymerization). These polymers have low cytotoxicity and are capable of forming complexes with biologically active materials, making them helpful in gene therapeutics and drug delivery [45]. Cyclodextran-based polymers were also invented recently, and once conjugated with therapeutic agents, they help treat autoimmune, inflammatory, central nervous system, and cardiovascular diseases [46]. Figure 3 shows the biomaterial used in various organs. The biomaterial patents for diagnostic applications are tabulated in Table 2.

Applications such as stents, grafts, implants

Biomaterials have been extensively used for the fabrication of stents, grafts, and implants for a long time now, yet their use has massively increased over the past decade. A hybrid material of an anti-bacterial surface that can controllably release anti-microbial peptides was used for surgical implantation [47]. An injectable, moldable, tunable composite comprising of a thermosetting polymer, a ceramic-based bone-substitute/ bone-derived material (allo-, auto-, or xenograft origin), optional plasticizer (for more pliability), and therapeutic compounds were capable of becoming complex personalized bone grafts [48]. Bio erodible metal (Mg)/ceramic (HAp) stent made of a composite with uniform HA nanoparticles has enhanced strength, lower erosion rate, and promoted resorption [49]. A nanofiber-based electrospun composite material comprising fibroin was found viable as a heart valve replacement [50]. Recent patents include an implantable therapeutic delivery system made of a substrate, an inner polymeric coating surrounding the substrate, and an outer hydrogel coating with therapeutic agents, which are being tested for the treatment of type 1 diabetes [51].

A CaP-based ceramic with a selected dopant for manufacturing resorbable scaffolds shows controlled strength loss, ensuring long-term healing from surgeries such as spinal grafts [52]. Magnesium-based biodegradable biomaterials are particularly helpful as stents in the blood vessels of the body, whereby their formulation is based on the ability to achieve the desired mechanical characteristics while avoiding any toxic or undesirable side effects in the body [53]. Coatings that controllably release metal ions to create an anti-microbial zone and could be fine-tuned to enhance the galvanic release of the anodic metal are considered very versatile as they could be made into implants, patches, scaffolds, and strands [54]. An implant material comprising homogeneously distributed

Table 2. Biomaterial patents for therapeutic applications.

Patent	Applications
US 2011/0038828 A1	Matrix composed of a naturally occurring protein backbone cross-linked by a synthetic polymer
AU2011202152 A1	Method for delivering interferon- β
US 8,021,679B2	Nitric oxide-releasing biodegradable polymers as medical devices and coatings
US8163032B2	Devices and methods for treating defects in the tissue of a living being
ES2393602A1	Bio-ceramic materials for the treatment of osteomyelitis
WO2013176468A1	Liver-targeted drug delivery systems in the field of metal nanoparticles and preparing method
CN102811726B	Treatment of cancer or tumor induced by the release of heat generated by various chains of magnetosomes extracted from magnetotactic bacteria and submitted to an alternative magnetic field
US9017726B2	Biodegradable and thermos-sensitive poly(organophosphazene)-superparamagnetic nanoparticle complex and preparation
S0142961215007589	Biocompatible polymeric nano complexes as an intracellular stimuli-sensitive prodrug for type-2 diabetes combination therapy
EP2974717A3	Use of nano metal in promoting neurite outgrowth and treatment and prevention of neurological disorders
9233080	Compositions and methods for the delivery of agents
9265790	Zwitterionic immunomodulators for the treatment of asthma and allergy
US 10, 329, 337 B2	Method to increase the number of circulating platelets by administering pegylated cysteine variants of IL-11
US 2019 / 0254975 A1	Hydrogel-encapsulated cells and anti-inflammatory drugs
US10,485,821 B2	Ion-binding polymers and their uses
US 2020/0017593 A1	Method of producing antibodies with n-glycoside-linked sugar chains lacking fucosylation
US 2020/0046845 A1	Cyclodextrin-based polymers for therapeutic delivery
US 2020/0079901 A1	Biodegradable polymers, complexes for gene therapeutics, and drug delivery

fluorescent nanodiamonds in a matrix of magnesium or a magnesium alloy shows increasing strength of the healing bone [55]. An improved form of this invention was designed recently, in which the stent has an additional coating of anti-inflammatory/anti-proliferative active agent [56]. Side-chain crystallizable polymers were designed as stents and are helpful in partially occluding a body cavity [57]. Stents comprising of biocompatible copolymers or homopolymers of 4-hydroxybutyrate and optionally poly-L-lactic acid and other additives are flexible, resistant to recoil and creep, and could be expanded and found applicable in coronary and urological diseases [58]. Bioactive composite made of thermoplastic

Table 3. Biomaterial patents describing the application of stents, grafts, and implants.

Patent	Applications
US20110046747A1	Anti-bacterial surface and method of fabrication
AU2011200350B2	Side-chain crystallizable polymers for medical applications
EP 1 959 025 B1	Magnesium-based biodegradable metal material
EP1991287B1	Polymeric, degradable drug-eluting stents and coatings
US8927004B1	Bioabsorbable substrates and systems that controllably release anti-microbial metal ions
US8992967B2	Poly (diol-co-citrate) hydroxyapatite composite for tissue engineering and orthopedic fixation devices
US20150273751A1	Bioactive composites of polymer and glass and methods
US9181636B2	Electrospun ceramic-polymer composite as a scaffold for tissue repair
US20150352248A1	Resorbable ceramics with controlled strength loss rates
9428588	Bio-hybrid material, production method
US 10, 219, 895 B2	Nanofiber-based graft for heart valve replacement
US 10, 299, 915 B2	Synthetic heart valves composed of zwitterionic polymers
US 2020/0139017 A1	Stent made of biodegradable magnesium alloy with magnesium fluoride coding and an organic coating
US 2020/0171095 A1	Implantable therapeutic delivery system

polyaryletherketone and combeite (bio-glass) showed enhanced mechanical properties with better bioactivity as compared to conventional screws [59]. An artificial heart valve invented recently includes a multiplicity of synthetic polymeric leaflets that help optimize the functionality of the heart valves during the life of the patient [60]. Table 3 summarizes biomaterial patents for stents/grafts/implant applications.

Applications for medical devices

Various biomaterial combinations have been utilized substantially for the fabrication of medical devices like the hybrid unitary surgical device consisting of two groups of devices, one of which had a pair of biocompatible, bioresorbable anchors while the second had extracellular matrix material, serving as tissue regenerating material [61]. Another would be the porous medical device made of continuous bioabsorbable polymer matrix and bio-ceramic fibers cast and used as a primary structure in medical devices with osteochondral applications [62].

Metallic microneedles made of an electrically conductive polymer layer and metal layer are useful in the transdermal delivery of macromolecules [63]. *In-vivo* biodegradable medical implants are the recent focus. These implants made from fine-grained metallic materials are rigid, stiff, and lightweight and have various stent applications [64].

Table 4. Biomaterial patents illustrating its application in medical devices.

Patent	Applications
US 7,871,440 B2	A unitary surgical device
US 2011/0020421 A1	Biodegradable polyphosphazenes containing pyrrolidone side groups
US 7,879,953 B2	Biobeneficial polyamide/polyethylene glycol polymers for use with drug-eluting stents
US 7.964.206 B2	A porous medical device and method for its manufacture
WO 2012/019145 A1	Radiopaque shape memory polymers for medical devices
US9220761B2	Alginate and alginate lyase compositions
9226764	Nano aggregates of molecular ultra-small clusters of noble metals and a process for the preparation
US9675790B2	Metallic microneedles
US 10,286,120 B2	<i>In-vivo</i> biodegradable medical implant comprising a microstructure-engineered metallic material

Biodegradable polyphosphazenes containing pyrrolidone side groups, as studies show, are useful as drug delivery carriers, plasma expanders, and biocompatible coatings for medical devices [65]. Another medical device generated from type-one and type-two polymer coatings is used with drug-eluting stents [66]. Radiopaque-shaped memory polymers are in demand in the fabrication of medical devices. These polymers are chosen because of their sufficient resistance to water absorption and their ability to deform temporarily, facilitating insertion into vessels, lumen, and aperture/cavity [67]. Poly (vinyl alcohol) (PVA)-bacterial cellulose (15% PVA with 0.5% bacterial cellulose) nanocomposite was the first material stiffed with a very high modulus and used for the creation of a broad range of medical devices [68]. Table 4 reviews biomaterial patents for medical device applications.

Applications in tissue regeneration

After studying the applications of biomaterial patents in tissue re-growth/differentiation for a decade, it was shown that hybrid biomaterials are the most suitable for such use. That is to say, for example, a hybrid biological porous extracellular matrix scaffold prepared by suspension of extracellular matrix material in a liquid-forming slurry that coats a synthetic mat or through mixing or layering the slurry with a synthetic polymer solution was shown beneficial in repairing damaged or diseased tissue [69]. Another biomaterial utilized for *in vivo* tissue regeneration is the bioresorbable membrane, as it exhibits asymmetric osteoconductive behavior [70]. A composite made of bio-ceramics and degradable/nondegradable polymer was invented, displaying induction properties of repairing dentine [71] along with other biocompatible composites, including metal oxide and natural stem cells that hasten tissue and bone repair. The artificial component of the composite is porous and comprises ceria-stabilized zirconia, which provides a solid framework for cells to adhere to and regenerate the damaged tissue [72]. Biomatrix compositions constituting cross-linked lactoferrin,

single or synergistic with organic or inorganic components, are considered applicable for musculoskeletal tissue regeneration [73]. Another evident example would be implanted from bio-resorbable materials blended with biocompatible ceramics and glass, which help regenerate selected tissues and, in turn, treat tissue-related defects [33]. However, there are no significant novel patents utilizing bio-metals or biopolymers alone for the tissue regeneration application. Figure 4 shows biomaterial application in tissue growth. Table 5 summarizes biomaterial patents for tissue regeneration.

Applications in wound healing process

From the patent analysis of the decade, it has been observed that bio-polymers have been used considerably for wound healing. For instance, a multicomponent dressing with super-absorbing polymers absorbs the wound secretions while staying attached to it until the dressing is removed. This is evident in promoting efficient wound treatment [74]. Additionally, hemoglobin-based polymeric oxygen carriers for artificial blood substitutes having di-block copolymers as main components

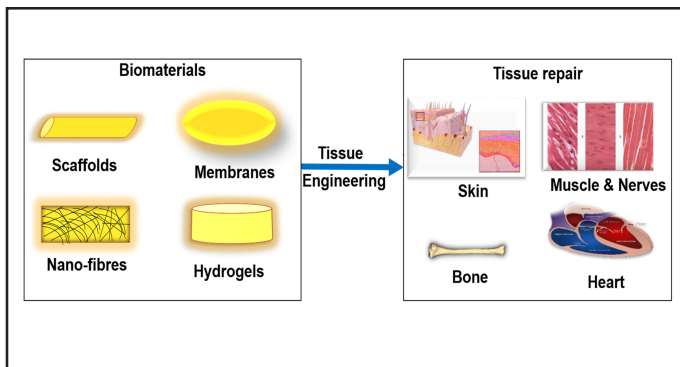


Figure 4. Biomaterial patents illustrating the applications in tissue growth/repair.

Table 5. Biomaterial patents describing the applications for tissue regeneration.

Patent	Applications
US 7,914,808 B2	A hybrid biologic/synthetic porous extracellular matrix scaffold
US 2011/0153029 A1	Bioresorbable and flexible membranes exhibiting asymmetric osteoconductive behavior in both faces
EP 2 388 023 A1	Composites based on bio-ceramics and biodegradable or non-biodegradable polymers containing antibiotics for tissue restitution
US8153158B2	Tissue substitutes comprising stem cells and reduced ceria
US8545927B2	Lactoferrin-based biomaterials for tissue regeneration and drug delivery for the formation of biomatrix
9233189	Hydroxyapatite tissue filler and its preparation
9283074	Devices and methods for treating defects in the tissue of a living being
9320776	Poly(thioketal-urethane) scaffolds and methods of use

display wound-healing applications [75]. Recent compositions having one or more elemental metals with nonconducting/semi-conducting materials as coatings hold pain-relieving and injury-healing characteristics [76]. Tissue engineering has emerged as a promising avenue for expediting wound healing, utilizing diverse biomaterials to facilitate the regeneration of damaged tissue. Notably, cerium oxide nanoparticles have garnered considerable interest owing to their diverse bioactivities. The integration of cerium oxide nanoparticles into polymer-based scaffolds tailored for wound healing has exhibited encouraging outcomes, accelerating the pace of the healing process [77,78]. Figure 5 shows the biomaterial application for the wound healing process. The biomaterial patents for wound healing applications are tabulated in Table 6.

Orthodontic applications

Along with all the previous applications whereby biomaterials proved effective, bio-ceramics have been used substantially for dental applications. That is due to the fact that medical and dental biomaterials made from calcium silicate, calcium oxide, and CaP compounds are biocompatible, anti-bacterial, and capable of forming an effective seal for the filled cavity of teeth by setting efficiently in the root canal [79]. However, composite bio-ceramics with good mechanical strength and bioactivity were observed for dental implants [80]. For dental restorations, CeO₂-stabilized ZrO₂ ceramics, which have been recently formulated, are used due to their excellent mechanical properties [81]. Furthermore, Benzalkonium chloride compositions (hybrid biomaterials) were found

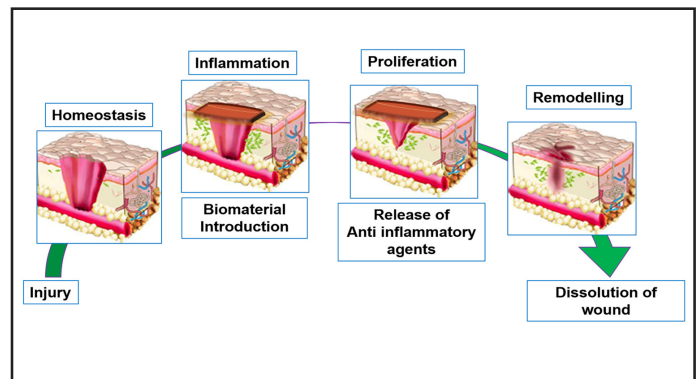


Figure 5. Biomaterial patents illustrating the applications in wound healing.

Table 6. Biomaterial patents and their applications in injury healing.

Patent	Applications
US 2011/0034894 A1	A multicomponent dressing for wound treatment on the human or animal body with the application of reduced pressure
25953204	An injectable, self-healing hydrogel to repair the central nervous system
9393344	Delivery system for functional nucleases
US 10,195,148 B2	Pain-relieving compositions comprising elemental metals

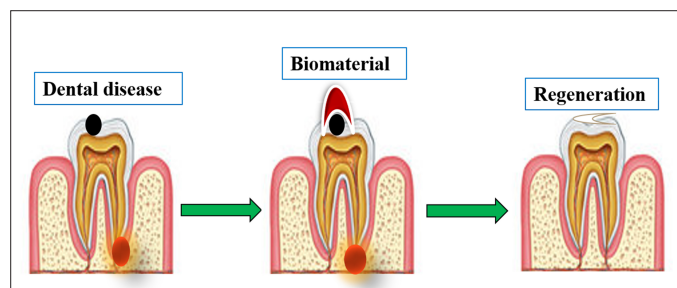


Figure 6. Biomaterial patents illustrating the applications in dental caries.

Table 7. Biomaterial patents for dental applications.

Patent	Applications
WO 2011/106089 A1	Benzalkonium chloride compositions for inhibiting the hydrolytic activity of endogenous matrix metalloproteinases in dental restorations
US8105086B2	Medical and dental biomaterial and method of use for the same
US20130150227A1	Composite bio-ceramic dental implant and fabricating methods
EP2694020A2	Oral care compositions
US 2019 / 0248709 A1	CeO ₂ - stabilized zro ₂ ceramics for dental applications
US 10,631,955 B2	Dental materials using thermoset polymers

to reduce bond strength degradation between the resulting dental restoration and the underlying tissue [82]. An oral care composition made from a coordination complex of metal cation (preferably zinc) was found to be effective in suppressing the activity of microbes responsible for oral cavities [83]. Recently, cross-linked polymer formulations have been invented for adjustment and re-positioning of teeth [84]. Figure 6 shows the application of biomaterials in dental carriers. The biomaterial patents for dental applications are summarised in Table 7.

Ophthalmic applications

Biomaterials have aided in the formulation of ocular lenses for retinal rectification. A dual-purpose pressed porous Si-PCL (polycaprolactone) composite implant exhibited enhanced ocular cell attachment and growth with its absorbable surface for drug loading [85]. Another improved implant made of a solid metal ring, a solid polymer shape, a mesh polymer shape, or a combination of both is used for the correction of myopia and hyperopia [86]. Furthermore, a recent invention useful for treating corneal defects is the Inter alia, a novel biocompatible, easy-to-handle, light-cross linkable, and bio-adhesive that integrates between the collagen matrix of the cornea and sclera [87]. Corneal transplantation remains the predominant form of transplant globally, serving to ameliorate visual impairment resulting from severe corneal damage. However, transplantation has inherent risks, including immune-mediated responses leading to rejection and the potential transmission of diseases from the donor tissue. Furthermore, the process of organ or

Table 8. Biomaterial patents for ophthalmic applications.

Patent	Applications
US 2011/011120 A1	Preparation of anti-microbial contact lenses with reduced haze using swelling agents
26277579	A novel pressed porous silicon-polycaprolactone composite as a dual-purpose implant for the delivery of cells and drugs to the eye
US9532902B2	A minimally invasive method and an apparatus for restructuring the retina
EP 3 291 976 B1	Method for producing contact lenses with durable lubricious coatings
WO2020051133A1	Light-activated adhesive scaffold
EP 3 028 692 B1	Ophthalmic compositions containing a synergistic combination of two polymers
WO2009135068A1	Artificial Cornea

tissue transplantation encounters multifaceted cultural, ethical, and legal challenges. Keratoprosthesis, such as Boston KPro and osteo-odonto-keratoprosthesis, offers a surgical alternative to traditional donor transplantation, albeit with varying success rates. While materials and designs of keratoprotheses differ, poly(methyl methacrylate) commonly serves as the primary material due to its stability and biocompatibility [88,89].

Other innovations include silicone hydrogel contact lenses with a well-constructed coating that possesses a water-gradient structural configuration with a soft and lubricious surface [90]. Bio-metals are also employed to produce contact lenses that obstruct the growth and adhesion of bacteria or other microbes on their surface [91]. An ophthalmic composition containing a synergistic combination of two polymers suitable enough for topical ophthalmic administration was invented recently [92]. Biomaterial patents for ophthalmic applications are tabulated in Table 8.

FUTURE TRENDS

Researchers are currently pursuing automated generation via computer-aided transfer processes (bioprinting) of structurally assembled and biologically working products from live cells, biomolecules, and biomaterials (mainly hydrogels and shape memory polymers, bioceramics, and biometals) with explicate 2D or 3D constructions (bio-fabrication). These biomaterials developed with the help of bioprinting techniques are known as Bioinks and can recreate complicated tissue properties like shape, vasculature, and specific functionalities, facilitating 4D printing of innumerable potentials and applications in the biomedical field [93]. Researchers are also working to design biomaterials that have the potential to mimic the dynamic and heterogeneous characteristics of the endemic extracellular matrix. Photoresponsive biomaterials are being exploited thoroughly due to their capabilities of site-specific therapeutic delivery *in vivo* and 4D modulation of synthetic cell culture platforms to mimic the complexity of the human body *in vitro* [94].

CONCLUSIONS

Biomaterials have been a key element in the fabrication of devices with humongous biomedical applications. The

growing interest in biomaterials comes from patent analyses over the past decade. With the versatility of biomaterials, the interest in research for the manipulation of these materials and the number of inventions coming up every year has been on a significant rise. However, one of the drawbacks of these inventions, as seen in most patents, is the ambiguous explanations of the mode of action of the biomaterial for a particular application. Without a clear understanding of the mode of action of the material, it becomes difficult to compare, rank the products, or classify them as novel or an advancement of prior similar products.

The next generation of biomaterials is expected to be more accurate both structurally and functionally, with improved biocompatibility with the human body. With 3D and 4D printing technologies, we hope to see drastic innovations in tissue engineering and regenerative medicine. The “omics” technologies and artificial intelligence-based approaches can also be of great use when it comes to understanding and generating biomaterials applicable to regenerative medicine. With advanced technologies and biomaterials, it is promising to be able to achieve regeneration of the whole tissue/organ within the next decade. Bio-fabricated skin/cartilage/vascular/cardiac patches and peripheral neural grafts may be made available in the clinics in the next 5–10 years. Also, with the ability to detect, biomaterials are capable of treating or rectifying many diseases, including cancer. Photoresponsive biomaterials are currently limited to being applicable in transdermal patches, yet with a combination of optogenetics and photoresponsive biomaterials. It is possible to have control over 4D cell fate. The future awaits more innovative and exciting inventions of biomaterials that would drastically revolutionize the biomedical field.

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All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

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