Mini Review

BIO Integration

# Classification and Medical Applications of Biomaterials–A Mini Review

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## Abstract

Biomaterials are natural, synthetic, or hybrid materials, which are used in medical devices or implants that are placed in contact with the human biological system to compensate for or restore diminished functions of the body. The field of biomaterials has rapidly developed to meet the ever-expanding needs in healthcare and medicine practices. Advancements in science and technology have enabled the fabrication and reengineering of biomaterials into useful medical devices or implants, such as heart valves, bone plates, hip joints, and cardiac pacemakers. Because biomaterials are placed in continuous close contact with the recipient's body fluids or tissues, the classification of available biomaterials is crucial for selecting safer and highly biocompatible materials. This review focuses on biomaterial classification, namely bioceramic, polymeric, and metallic biomaterials. Their medical applications, advantages, and disadvantages are discussed. Current trends in biomaterials involved in disease treatments, such as controlled drug delivery and cancer therapy, are additionally explored.



## Keywords

Bioceramic biomaterial, classification, medical application, metallic biomaterial, polymeric biomaterial.



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## Introduction

Biomaterials function in close contact with living tissue and may replace parts of a living system to augment, repair, or restore body function [1]. These materials can be derived from (i) natural sources, such as starch, chitosan, collagen, and bone; (ii) synthetic sources, in which a range of chemical reactions can be generated in a laboratory to produce biomaterials from not only metallic components but also polymeric and ceramic materials; or (iii) semi-synthetic or hybrid sources consisting of both natural and synthetic materials [1]. Biomaterials have diverse mechanical, biological, physical, and chemical properties that help them function properly and enable applications in or on the human body.

The field of biomaterials, particularly the development of biomedical devices and tissue engineering for human benefits, was established rapidly. Currently, thousands of biomedical devices and diagnostic products are being applied to facilitate the capability of human tissues or organs to regenerate after deterioration and restore normal bodily function [2]. More than 6000 types of medical devices have been listed in the Medical Device Product Classification Database regulated by the Food & Drug Administration's Center for Medical Devices and Radiological Health, to ensure their safety and effectiveness [3]. A variety of devices and materials, such as cardiac pacemakers, bone plates, artificial heart valves, nerve stimulators, and artificial knee joints, are currently being applied in the treatment of human disease or injury.

During the past two centuries, evidence of the use of biomaterials as implants and prostheses has been discovered on various Roman, Egyptian, Greek, and Etruscan human body parts, such as in skeletons or skulls, thus indicating that biomaterials have been used in or on the human body since ancient times [4]. The use of biomaterials dramatically accelerated after World War II. Many newly developed high-performance metal, ceramic, and particularly polymeric materials were developed, and have been used to construct medical devices to repair or replace damaged body parts or tissues [5]. Biomaterials can be classified in many ways according to their functionality in the human body and their material properties. This review highlights the classification of biomaterials and their applications in the medical field. Current trends in the use of biomaterials for disease treatments, such as drug delivery and cancer immunotherapy, are also discussed.

## Classification and medical applications of biomaterials

The functions of biomaterials in the medical field have markedly changed with advances in science and technology. The continual and ever-expanding practical needs in healthcare and medicine practices have significantly driven developments in the biomaterial field and its applications. Biomaterials can be classified in several ways, often according to their human body functionality and material properties [6]. First, biomaterials can be classified at the organ and system levels of the human body. For example, at the system level, the skeletal system can be repaired and restored with a joint replacement and bone plate; at the organ level, the human heart can be repaired and replaced by an artificial heart valve, total valve, and cardiac pacemaker. Second, biomaterials may be categorized according to the body parts treated. For example, an artificial hip joint and a kidney dialysis machine can be used to replace damaged or diseased body parts, whereas screws, sutures, and bone plates can assist in wound healing. **Table 1** reviews the classification of biomaterials in medical applications, according to organs, systems, and other parts of the body.

The third classification of biomaterials is based on to their material properties in three categories: bioceramic, polymeric, and metallic [22]. The vast variety of available biomaterials enhances the choice of materials for specific treatment purposes; for example, chemically inert metals may be chosen for high electroconductivity as electrodes in artificial organs and long-lasting restoration of lost body function. Nevertheless, biodegradable materials, such as sutures, can be used as a temporary framework for patients in whom function or lost tissue can be regenerated [1, 23]. Furthermore, some biomaterials, such as coronary and peripheral stents, are bioabsorbable and are used in cardiovascular implants. They are slowly eliminated from the body after fulfilling a function [24].

## Bioceramic biomaterials

Bioceramic biomaterials are fabricated from non-metallic and metallic elements held together by covalent and/or ionic bonds [25]. Oxides, such as aluminum oxide ($Al_2O_3$), magnesium oxide (MgO), and silicon dioxide ($SiO_2$), contain both non-metallic and metallic components, whereas ionic salts can form polycrystalline aggregates (such as ZnS, CsCl, and NaCl). Other common examples of ceramic materials are diamond and carbonaceous structures, which are usually covalently bonded. The strong covalent and ionic bonds between the ceramic elements make them hard, brittle, and stiff [26]. Consequently, the planes of atoms/ions in the ceramics do not easily slip past one another.

Ceramics and their composites have the potential to be used as medical devices to enhance or restore various parts of the body, owing to advances in science and technology. Consequently, various bioceramic devices or implants, including hip prostheses, bone grafts, and artificial tendons, have been developed for medical use. To be designated as bioceramics, the materials must have several important features after being placed in the recipient's body, including non-inflammatory, non-allergic, biofunctional, biocompatible, carcinogen-free, and non-toxic characteristics [27]. Furthermore, ceramics have been regularly used in dentistry applications, because they are relatively inert to bodily fluids such as saliva, and have aesthetically favorable appearance and excellent compressive strength [28]. Recently, bioceramics have shown immense medical applications in controlled drug delivery, gene therapies, and cancer therapies [29].

Bioceramics such as black pyrolytic carbons have been used in cardiovascular implants, particularly for blood interfacing applications such as heart valves. Although their unappealing color is a disadvantage, particularly in dental applications, pyrolytic carbons are simple to make and have acceptable biocompatibility in the human body [30]. They are also being used as composite implant materials and supporting components for tensile loading applications, such

**Table 1** Classification of Biomaterials in Medical Applications, on the Basis of Organs, Systems, and Other Parts of the Body

| Classification | | Examples | References |
|---|---|---|---|
| Classification of biomaterials in medical applications based on body organs | Eyes | Intraocular lenses | [7] |
| | Ears | Artificial stapes and cochlear implants | [8] |
| | Kidneys | Kidney dialysis machines | [9] |
| | Bladder | Catheters and stents | [8] |
| Classification of biomaterials in medical applications based on different body systems | Nervous | Nerve stimulators | [10] |
| | Circulatory | Artificial blood vessels | [11] |
| | Skeletal | Joint replacement and bone plates | [12] |
| | Muscular | Muscle stimulators and sutures | [13, 14] |
| | Respiratory | Tracheal stents | [15] |
| | Urinary | Catheters, stents, and kidney dialysis machines | [8, 9] |
| | Integumentary | Sutures, burn dressings, and artificial skin | [16, 17] |
| Classification of biomaterials in medical applications based on other body parts | Improve body parts' functions | Cardiac pacemakers | [18] |
| | Aid in healing | Sutures, screws, and bone plates | [12, 19, 20] |
| | Substitute for a broken part | Hip joint prostheses | [12] |
| | Assist in treatment | Catheters and drains | [8] |
| | Aid in diagnosis | Probes and catheters | [21] |

as artificial ligaments and tendons, mainly because of their highly biocompatibility with the human body and their high specific strength as fibers [30].

Three types of ceramics can be used to make implants: (i) resorbable or biodegradable (non-inert) ceramics, such as calcium phosphate and calcium aluminate, (ii) surface reactive or bioactive (semi-inert) ceramics, such as glass ceramics and hydroxyapatites, and (iii) non-absorbable (relatively inert) ceramics, such as alumina, zirconia, and carbons [31]. The medical applications of different bioceramics are listed in **Table 2**.

Fabricating bioceramics as medical devices or implants provides several advantages. For instance, these materials are resistant to corrosion and can withstand high compression strength. They also demonstrate excellent benefits as bioactive/inert materials in the human body, such as in articulating surfaces subjected to loads and friction. However, the use of bioceramics as biomaterials is limited by their tendency to have low fracture toughness and low strength in tension. Therefore, a high force could cause them to shatter or crack [31]. In addition, their fabrication is challenging.

## Polymeric biomaterials

Polymers applied in biomaterials comprise naturally derived polymers and synthetic polymers, which are either biodegradable or non-biodegradable [41]. Naturally occurring polymers such as starch, collagen, and chitin are frequently used as biomaterials because they are biodegradable and easily obtained. In contrast, synthetic polymers are a mainstream polymer biomaterial widely used in prosthetic materials, dental materials, disposable medical supplies, and medical implants.

Most non-biodegradable synthetic polymers were initially created for non-medical purposes. However, their physical-mechanical qualities essentially identical to those of human soft tissues have led to their wide application as biomedical materials in or on the human body. Currently, many medical applications use various synthetic polymeric materials, including polypropylene, polyethylene, polymethylmethacrylate, polyethylenterephthalate, and polyurethane [41, 42]. The medical applications of these polymeric biomaterials are listed in **Table 3**.

Polymers are better biomaterials than metals or ceramics because of their ease of manufacturability in diverse forms such as fibers, films, sheets, and synthetic latex. Beyond that, they can be easily processed, have reasonable costs, and are available with desired physical and mechanical properties [48]. Several disadvantages of polymeric biomaterials include that they absorb water and protein in the human body; their surfaces are easily contaminated and difficult to sterilize; they are leachable compounds; they undergo biodegradation; and they are prone to wear and breakdown. In addition, the massive use of non-biodegradable polymers also poses challenges regarding environmental pollution and waste management [49, 50].

## Metallic biomaterials

Metals' excellent thermal and electrical conductivity make them among the most extensively used biomaterials [51]. They have been widely applied in artificial heart valves, including pacemaker leads and vascular stents [51, 52]. Moreover, load-bearing implants, such as hip and knee replacements, mostly use metallic biomaterials, because of their exceptional corrosion resistance and mechanical properties.

Beyond pure metal, alloys of metals with two or more elements are also frequently applied in producing biomaterials. These alloys are usually generated by surface modification,

**Table 2** Medical Applications of Bioceramic Biomaterials

| Types of Bioceramic Biomaterials | | Medical Applications | References |
|---|---|---|---|
| Resorbable or biodegradable (non-inert) | Calcium aluminate | Dental restorative products, orthopedic applications | [32] |
| | Calcium phosphate | Artificial bones, teeth, knees, hips, tendons, ligaments | [31, 33] |
| Surface reactive or bioactive (semi-inert) | Glass-ceramic | Bone augmentation and restoration | [34] |
| | Hydroxyapatite | Fillers, bone grafts, coatings for metal implants | [35] |
| Non-absorbable (inert) | Alumina | Dental and bone implants, hip prostheses | [36] |
| | Carbon | Heart valves, bone scaffolds, cartilage regeneration | [37, 38] |
| | Silicon nitride | Spinal fusion implants | [39] |
| | Zirconia | Hip joint replacement, tooth implants | [28, 40] |

**Table 3** Medical Applications of Polymeric Biomaterials

| Types of Polymeric Biomaterials | Medical Applications | References |
|---|---|---|
| Polypropylene | Hernia repair, blood oxygenator membranes, artificial vascular grafts, degradable sutures | [41, 43] |
| Polyethylene | Surgical implants, tendons, tubing for drains and catheters, acetabular liners | [41, 44, 45] |
| Polymethylmethacrylate | Artificial teeth, provisional crowns, bone cement | [41, 46] |
| Polyethylenterephthalate | Artificial vascular grafts, heart valves | [41] |
| Polyurethane | Wound dressings, breast implants, cardiac patches, drug delivery vehicles, vascular grafts, tracheal soft tissue | [41, 47] |


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such as coating with bioactive ceramics and polymeric thin films, or surface structuring, thereby enhancing corrosion resistance and increasing the material strength. Currently, three major material groups dominate the metallic biomaterials: pure titanium (Ti) or titanium alloys such as Ti-6Al-4V; stainless steel; and cobalt-chromium (Co-Cr) alloys [51, 53]. Several considerations that influence the selection of metals and alloys as biomaterials in medical applications are appropriate physical and mechanical properties, reasonable cost, corrosion resistance, and biocompatibility [54]. **Table 4** summarizes the medicinal applications of these three types of metallic biomaterials.

Ti-6Al-4V is currently one of the most broadly used and desirable metallic biomaterials in medical applications, because of its outstanding properties: it is stronger, lighter, and more resistant to corrosion in the human body than stainless steel and Co-Cr alloys. However, Ti-6Al-4V has been reported to have issues in articulation surfaces in human bones, because it is less elastic and prone to wear and tear [58]. Moreover, the vanadium present in the alloy has the potential for adverse tissue and cytotoxicity reactions [59]. Over time, leached vanadium and aluminum can result in long-term neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease [60, 61]. The leached vanadium and aluminum ions in the human body also affect the respiratory and reproductive systems [59, 62]. Several recent studies have synthesized different coatings on Ti-6Al-4V alloys to increase their biocompatibility and corrosion resistance to the human body [63, 64].

Metals are beneficial as biomaterials because they possess corrosion resistance, wear resistance, and high strength. Furthermore, their ease of sterilization and fabrication, and their shape memory capabilities have led to their extensive use as biomaterials in medical applications. However, the drawbacks of using metallic biomaterials in the human body are their high modulus, cytotoxicity, easy corrosion, and metal ion sensitivity.

# Current trends in biomaterials in medical applications

The advancements in science and technology have shifted trends in biomaterial functions. Biomaterials have recently been applied in disease treatments including drug delivery into cells, cancer immunotherapy, cell regeneration, and antimicrobial treatment, among many others. Several types of biomaterials have been used in these applications, including polymer-based biomaterials, lipid-based biomaterials, and inorganic biomaterials.

## Polymer-based biomaterials

Hydrogels are polymer-based biomaterials widely used in disease treatment. Hydrogels may exist naturally or may be derived synthetically. Chitosan, fibrin, and alginate are examples of hydrogels of natural origin, whereas poly(vinyl alcohol) is an example of a synthetic hydrogel. Owing to their gelation properties, hydrogels have been used to carry DNAs, mRNA, proteins, or cytokines for disease treatments, such as in cancer immunotherapy and chemotherapy [65–70]. Interestingly, hydrogels' clinical potential in treating systemic sclerosis and inflammatory airway disease have recently been reported [71, 72], thus illustrating their promise in medical applications for treating other human diseases.

Micelles are another polymer-based biomaterial with important roles in drug delivery and cancer immunotherapy. Micelles are amphiphilic polymers assembled as nanosized particles that can deliver drugs to draining lymph nodes and therefore promote systemic drug administration. A recent study has constructed polypeptide-based micelles that regulate the tumor microenvironment and assist in inhibiting tumor cell metastasis [73]. Ren et al. [74] have also reported that micelles can be covalently bonded with chemically modified short peptide antigens to allow for effective delivery into dendritic cells for robust cellular immune responses (**Figure 1**), thus suggesting their potential in anti-cancer vaccine development and supporting their exploration as a component of cancer immunotherapy. Intriguingly, using micelles as a vehicle for ligand delivery in combination with chemotherapy drugs has recently been found to significantly increase selective immunogenic cell death in triple-negative breast cancer [75], an aggressive and deadly breast cancer type that lacks targeted therapy and has a poor prognosis because of high metastasis.

The blood-brain barrier (BBB) is a major challenge preventing effective systemic drug administration in the treatment of brain diseases. Lammers et al. [76] have demonstrated that poly(butylcyanoacrylate)-based microbubbles encased in ultrasmall superparamagnetic iron oxide nanoparticles can mediate and monitor BBB permeability in a mouse model. Another study in canines has reported that polymeric magnetite nanoparticles encapsulating chemotherapy drugs bypass[ing] the BBB and facilitate the delivery to intracranial tumors after infusion by convection-enhanced delivery [77]. The spatial control and bypassing of the BBB are critical for drug delivery in treating brain disorders such as brain tumors, Alzheimer's disease, and Parkinson's disease.

## Lipid-based biomaterials

Liposomes are lipid-based biomaterials that are highly successful and commonly highlighted in disease treatments.

**Table 4** Medical Applications of Metallic Biomaterials

| Types of Metallic Biomaterials | Medical Applications | References |
|---|---|---|
| Pure titanium (Ti) and titanium alloys (Ti-6Al-4V) | Conductive leads, screws, joint prostheses | [55] |
| Stainless steel | Vascular stents, fracture plates, guide wires | [56] |
| Cobalt-chromium (Co-Cr) alloys | Dental apparatus, artificial cardiac valves, joint replacement, screws, fracture plates | [57] |

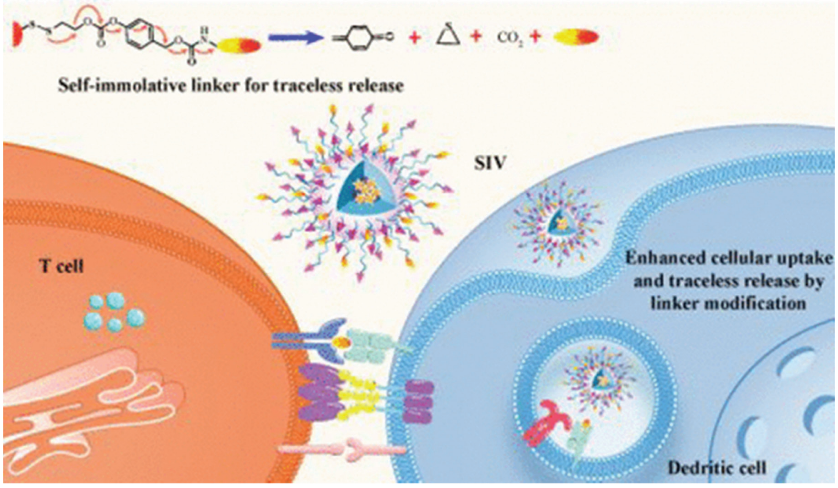


**Figure 1** A system for delivery of short peptide antigens to dendritic cells for strong T-cell responses, on the basis of block copolymers chemically modified with a hydrophobic and self-immolative linker. The micelles effectively capture antigens and adjuvants via a covalent bond after modification [74]. Reproduced with permission from the American Chemical Society, 2022.

They are spherical vesicles made of phospholipid bilayers that encapsulate various types of therapeutic drugs. Hydrophilic drugs are enclosed within the center aqueous region, and hydrophobic drugs are entrapped within the lipid bilayers [78]. These features make liposomes an effective biomaterials for disease treatments. Since 1986, many liposome products have been licensed for medical applications, such as delivering chemotherapy drugs for cancer treatments, encapsulating inactivated viruses for vaccination purposes, delivering antibiotics for antimicrobial therapy, delivering painkiller drugs for pain management, and even hormone therapy [79]. Furthermore, several investigations have shown that liposomes might be used in cancer immunotherapy and as nanocarriers of imaging agents to improve clinical diagnosis and treatment [80–84]. In a rat glioma model, targeted ultrasound technology has been used to temporarily permeabilize the BBB with doxorubicin hydrochloride drugs contained in long-circulating pegylated liposomes [85]. This exciting finding provides insights into future drug delivery into the brain. Recently, liposome-based mRNA vaccines for COVID-19 have been developed by Moderna and Pfizer/BioNTech, exploiting the excellent ability of liposomes to protect mRNAs against degradation by nucleases in the blood circulation and allow the mRNAs to easily enter the cytoplasm of cells through endocytosis [86].

## Inorganic biomaterials

Gold nanoparticles are an inorganic biomaterial that has been extensively studied in disease treatments. According to Li et al. [87], the use of gold nanorods in photothermal

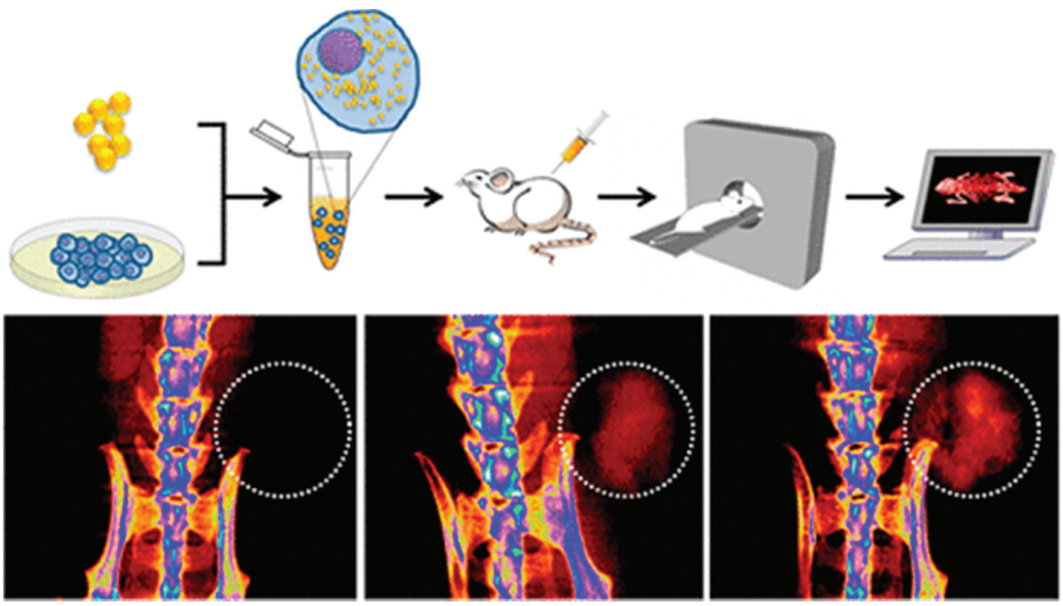

**Figure 2** T-cells were transduced to express a melanoma-specific T-cell receptor and labeled with gold nanoparticles as a computed tomography contrast agent to examine the distribution, migration, and kinetics of T-cells [89]. Reproduced with permission from the American Chemical Society, 2015.

therapy in combination with chemotherapy enhances cancer treatment efficiency and modulates the tumor microenvironment. Another study has found that radioisotope-labeled gold nanoclusters allow for the activation of dendritic cells and subsequently induce long-term anti-cancer immunity in a mouse model, by eliminating primary tumors and suppressing distant-tumor development [88]. Furthermore, gold nanoparticles have been found to aid in effective imaging by coating with cancer-specific T-cell receptors as a computed tomography contrast agent, thereby allowing for easy observation of T-cell migration, distribution, and kinetics under imaging (**Figure 2**) [89]. Although most research remains in animal-trial stages, gold nanoparticles appear to have great potential in human cancer treatment.

Another inorganic biomaterial, silica nanoparticles, also have anti-cancer properties after being doped with elements such as calcium, magnesium, and zinc [90]. These doped mesoporous silica nanospheres have been found to increase $CD4^+$ and $CD8^+$ T-cells in the spleen and stimulate an anti-cancer immune response. In addition, Kakizawa et al. [91] have found that silica nanoparticles coated with specific amino acids and incubated with dendritic cells and ligands induce the production of crucial cytokines, such as IL-1 and IFN, thereby implying that silica nanoparticles might be used as a carrier for cellular immunotherapy. Moreover, silica nanoparticles have been widely used in creating vaccines against bacteria and viruses such as *Mycoplasma hyopneumoniae*, hepatitis B, and most recently, SARS-CoV-2 [92–95]. These vaccinations, however, remain in pre-clinical stages.

## Conclusions and outlook

This review discussed the classification of biomaterials and their medical applications. Developments in biomaterials have led to the fabrication and reengineering of various highly promising medical devices or implants to restore the functions of the human body. Bioceramic, polymeric, and metallic biomaterials are beneficial to humankind. Nonetheless, their application poses challenges, such as environmental pollution and substantial waste disposal resulting from the massive use of non-biodegradable synthetic polymeric biomaterials. Most recently developed biomaterials used in drug delivery and cancer therapy remain in early stages of development, facing hurdles relating to biocompatibility, biosafety, and toxicity. Thus, new biomaterials that are environmentally friendly and highly biocompatible with the human body will have enormous potential in medical applications.

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## Competing interests

The authors declare that they have no competing interests.

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