Advancements in Biomaterials for Envisioning Healing and Function Restoration in Modern Medicine – A Review

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Abstract

The modification of human tissues to treat diseases is a highly intriguing interdisciplinary area of research in academia and the biotechnology industry. Three-dimensional (3D) biomaterial scaffolds play a crucial role in the morphogenesis of newly formed tissues by interacting with human cells. Both organic (natural) and synthetic (man-made) materials have been used to create polymer-based biomaterials. While simple polymeric biomaterials can provide the necessary mechanical and physical characteristics for tissue development, they often lack biomimetic qualities and effective interactions with human progenitor cells, hindering the production of fully functional tissues. The development of advanced functional biomaterials that respond to stimulation could be the next step in creating intelligent 3D biomimetic scaffolds. These scaffolds would actively interact with human stem cells and progenitors while maintaining structural integrity, thereby facilitating the rapid construction of functional tissues. This review explores various types of biomaterials, their design, methods of synthesis, and biomedical applications. It highlights the importance of smart biomaterials in transporting bioactive chemicals, mediating cell adhesion, and fabricating functional tissues to cure diseases, emphasizing the necessity for these materials to interact effectively with biological systems.

Keywords: Carbon dots, Ceramics, Extracellular matrix, Polymeric nanoparticles Smart materials, Tissue engineering, Regenerative Medicine, Polymers, Drug Delivery Systems

Significance | Biomaterials significantly enhance tissue repair and regeneration, offering innovative solutions in modern medicine and improving patient outcomes.

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1. Introduction

After a sickness or an injury, the process of regaining function and helping the body's natural healing can be significantly aided by using biomaterials in today's medical practice. In the field of medicine, biomaterials are utilised either as a scaffolding for healthy tissue or as substitutes for biological elements that are not functioning well. Both naturally occurring and artificial biomaterials can be utilized. Sutures made of animal sinew were the first biomaterials ever used in medical practise, and they originated in ancient Egypt (Brovold, 2018; Vince et al. 1991; Nanda et al. 2021). The contemporary study of biomaterials draws inspiration from various fields, such as medicine, biology, physics, chemistry, tissue engineering, and materials science. Over the last decade, various sectors, such as tissue engineering and regenerative

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medicine, have experienced substantial progress, leading to a rapid expansion of the whole field.

Biomaterials can be fabricated using a diverse range of materials, such as metals, ceramics, polymers, glasses, and even biological cells and tissue. Healthcare applications can utilize them through several means, including producing molded or machined components, applying coatings, and fabricating fibers, films, foams, and fabrics. Contact lenses, artificial hips, dental implants, and heart valves are all instances of such medical equipment (Megeed et al. 2002). The body can degrade and excrete some compounds once they have performed their role, while others degrade naturally over time. Some examples of biomaterials include metals, polymers, ceramics, and composites; others can be synthesized synthetically using a variety of chemical reactions. A composite is a type of biomaterial that combines multiple unique materials. This overview examines the several categories of biomaterials, their design, synthesis, and applications in biomedicine.

These applications encompass the delivery of bioactive chemicals and cell adhesion mediators and the development of functional tissues for disease treatment. The development and deployment of intelligent biomaterials are essential for interactions with biological systems. Biomedical equipment and living structures used or modified for medical purposes often perform similar functions to their natural counterparts but distinctly (Sofia et al., 2001; Ferry & Morrison, 1947). The heart valve is an instance of a function that is seen as predominantly inactive. In contrast, hydroxyapatite-coated hip implants exemplify a function that is considered highly bioactive and fulfills a more interactive role. Biomaterials are regularly used in dentistry, surgery, and drug delivery. For example, inserting a device into the body that includes embedded pharmaceutical items can allow for the sustained delivery of medication. This can be done with the help of devices that deliver drugs.

Along with allografts, xenografts, and autografts, biomaterials also have the potential to serve as xenografts. Xenografts are transplanted organs from different species (Brovold, 2018; Vince et al., 1991; Nanda et al., 2021). It can be challenging to define biomaterial; however, the following is one attempt at doing so: The term "biomaterial" refers to "any material, natural or synthetic, that comprises all or part of a living structure or biomedical device that performs, augments, or replaces a natural function." Living things, as well as medical tools, contain biomaterials. Applied in medicine, the word "biomaterial" describes any substance altered for therapeutic intervention (Ferry & Morrison, 1947; Ghose et al. 2023). A heart valve is an example of a biomaterial with a beneficial function, and hydroxy-apatite-coated hip implants are an example of a biomaterial with an interactive function (the Furlong Hip, made by Joint Replacement Instrumentation Ltd. in Sheffield, is an example of a bioactive biomaterial; such implants can last for more than twenty years). An artificial kidney is an example of a biomaterial with advantageous and interactive properties. The pharmaceutical sector often utilizes biomaterials, particularly in drug administration. To do this, drug-impregnated structures are implanted so that medication can be slowly and continuously dosed (Peng et al., 2017).

Categories Of Biomaterials And Their Properties

Materials such as metals, polymers, ceramics, and composites can be extracted from the earth to generate biomaterials. Conversely, composites can be produced in the laboratory by employing diverse chemical processes. Adapting materials, which can be the original substance or biomedical technology specifically designed to perform the same function as the original or enhance it, is frequently required in medical applications. Hip replacements with hydroxyapatite coatings are bioactive, whereas a heart valve is passive. Biomaterials are commonly used in healthcare, dentistry, and drug delivery. A drug can be continuously released into the body by utilizing a structure that is infused with pharmacological substances, such as a drug (Brovold, 2018; Ghose et al. 2023). Another set of biomaterials are transplant materials, including xenografts, allografts, and autografts. In healthcare and dentistry, biomaterials are compounds interacting with biological fluids and cells. Although most people happen to come across biomaterials through tooth restorations, hip and knee replacements, and cardiovascular repairs depend more on them. Not only do these biomaterial implants improve the quality of life for the elderly with extended life expectancies, but they also assist an increasing number of younger individuals with cardiac disorders, traumas, or genetic disorders (Peng, et al. 2017; Jena & Chakraborty, 2021; Goswami, 2019)

Biomaterials play a crucial role in modern medicine by restoring function that has been lost due to illness or destruction. Biomaterials have numerous therapeutic applications, including maintaining, improving, and replacing biological tissue and functions. They can be either organic or man-made. The ancient Egyptians were the first people in history to utilise biomaterials; they created the first sutures from animal sinew. Recent advances in tissue engineering and materials science have also had an impact on the field of biomaterials research. Due to breakthroughs in regenerative medicine and other sectors, the field has grown rapidly during the past decade (Kim et al. 2017). Biomaterials can be made from inanimate matter like metals and plastics to organic materials like live cells and tissue. Moulded coatings, filaments, and textiles made from these materials can all be repurposed for use in healthcare. Contact lenses, dental implants, artificial hips, and artificial heart valves all fall within this category. Many of these medical aids break down naturally over time, and others can even be absorbed directly by the body (Goswami, 2019; Kim et al., 2017).

A biomaterial has following properties:

- It is a non-viable material or mixture. In other words, this stuff is incapable of evolving, expanding, or, to be honest, surviving.
- This material might be solid or liquid, and it can be naturally or artificially generated.
- The material is used to partially or wholly replace, regenerate, repair, or augment any organ, tissue, or biological component in terms of shape and function.
- The medicine is utilized to improve or maintain a person's quality of life.
- The substance is not a narcotic (Kim et al., 2017; Li Z, et al. 2005; Griffith and Naughton, 2002).

1.1. Design of biomaterials

A biomaterial is a material that is a non-viable substance meant to interact with living processes. The biomaterials' effective and reliable qualities allow them to be used in a physiological environment. These distinguishing features are provided by an appropriate blend of physico-chemical and biological capabilities in order to develop well-known biomaterials. Polymers, metals, composites, and ceramics are used to create these biomaterials in a novel way. The vast majority of biomaterials today were created independently or in conjunction with elements from these classes (Kim et al. 2017; Li Z, et al. 2005; Griffith & Naughton, 2002). Each material class has a unique atomic arrangement, resulting in a diverse set of structural, physical, chemical, and mechanical properties. As a result, these materials have a wide range of possible applications in the human body. The subsequent sections represent the material classifications (Naughton, 2002).

2.1.1. Polymers

Polymers are employed in cardiovascular devices to replace and promote the growth of various soft tissues, and they might be helpful to for biomedical applications. Patients have received implants made of various polymeric materials. The aforementioned substances are currently being employed in a wide variety of medical applications, including but not limited to the following: heart valves, artificial hearts, vascular grafts, breast prostheses, dental materials, contact and intraocular lenses, fixtures for extracorporeal oxygenators, dialysis, and plasmapheresis systems, coating materials for medical products, surgical materials, and tissue adhesives, just to mention just a few. The makeup, arrangement, and structure of the macromolecules that make up a polymer define its qualities (Griffith and Naughton, 2002). Additionally, the flexibility of several applications needs the creation of polymers with suitable physicochemical, interfacial, and biomimetic properties in order to perform certain activities. It is necessary to synthesize these polymers in a variety of forms and compositions. In comparison to other types of materials, polymeric biomaterials have a number of advantages, including (i) their relative ease of secondary processing, (ii) their availability with the required mechanical and physical properties, (iii) their availability, and (iv) their relative affordability. In the medical sector, polymers of both natural and synthetic origin are used. Acrylics, polyamides, polyesters, polyethylene, polysiloxanes, and polyurethane are just a few examples of synthetic polymeric systems. Synthetic polymers frequently lack biocompatibility, leading to the development of inflammatory reactions following their application. Natural polymers may hold the key to a solution. Natural polymers in biomedical applications include chitosan, carrageenan, and alginate (Kim et al., 2017; Li Z et al., 2005; Griffith & Naughton, 2002).

2.1.2. Metals

Metal-based implant materials have a rich tradition of providing vital therapeutic value in the medical profession. Heavy tungsten alloys include stainless steel (316L), titanium and its alloys (Cp-Ti, Ti6Al4V), cobalt chromium alloys (Co-Cr), aluminium alloys, zirconium niobium, and zirconium niobium. Metals and metal alloys have also been employed in the medical area. A small selection of the numerous metal-based medical products that have been made possible by the quick development of biomaterials includes dental implants, craniofacial plates, and screws, pieces of artificial hearts, pacemakers, clips, valves, balloon catheters, medical devices and equipment, bone fixation devices, dental materials, medical radiation shielding products, prosthetics, and orthodontic devices (Griffith & Naughton, 2002; Kaushal et al, 2001; Giri et al., 2012). Although various materials can be employed in the biomaterial's creation process, metals are often the material of choice for engineers. This is because metals can be easily shaped into the ideal biomaterial. Metals are often chosen for use in biomedical applications due to their low cost, high corrosion resistance, high mechanical strength, and excellent biocompatibility.

***2.1.3.* Carbon Dots**

In addition, carbon dot/polymer composites are utilized in biosensing, bioimaging, and diagnostic applications to detect pharmaceuticals and genetic components (DNA or RNA). This is because CDs possess a broad UV absorption spectrum in addition to various physical, photothermal, mechanical stability, and chemical characteristics. Carbon nanopowder-derived C-dots have the potential to be used as extremely bone-specific bioimaging agents and medication carriers because of their distinctive characteristics. The notion of carbon-based nanoparticles has recently gained considerable advances and established new breakthroughs in biological applications, tissue imaging, and cancer treatments such as breast cancer suppression. Low-dimensional nanoscale materials are increasingly being researched in the medical field. Metallic quantum dots (QDs) got more attention than carbon-based CDs nanoparticles. However, CDs have distinct physicochemical and photophysical properties that can be advantageous in various preclinical and clinical studies. PEGpassivated CDs, for example, can provide biocompatibility and stealth in vivo. Such attempts can be used with other organic and inorganic substances to achieve desired biological outcomes (Peng et al., 2017; Jena and Chakraborty, 2021, Chandrapratap et al. 2024, Muntaha et al. 2024, Bhuneshwari et al. 2024, Lakhan et al. 2024). Various research has discovered that desirable CDs/polymeric nanostructures can be a possible contender for medicine and gene delivery in specific locations, such as a tumor. For an assortment of reasons, including their unique physicochemical and biological properties, the chemical composition agglomeration, and the solubility characteristics they possess, carbon nanomaterials such as nanotubes, graphene, and fullerene are of interest to both the scientific community and society. It is feasible that these attributes exert a more substantial influence on the target's biomolecules and cells (Goswami, Bhat, and Patnaik, 2019).

3. Composite Materials And Their Basic Considerations To Design

Composite engineering materials comprise two or more physically and chemically separate constituent materials that are correctly arranged or distributed and have physical properties that differ from the constituent elements. The matrix is a continuous bulk phase in composite materials, whereas the reinforcement is one or more discontinuous dispersion phases (Goswami, Bhat, and Patnaik, 2019). The reinforcement frequently outperforms the matrix in terms of quality. Aside from the matrix and reinforced phases, there is a third phase, the interphase between the matrix and reinforced phases. Since composites have unique properties and are frequently more robust than the basic materials they are formed from, they are used to solve complex problems when tissue in-growth is required. In recent years, the development of various biomedical composite materials has been the focus of scientific research because they offer novel alternatives to tissue load-bearing components. Composite scaffolds with porous structures made from blends of bio-glass particles and biodegradable fibers are one example of this (Goswami et al., 2019; Kim et al., 2017).biomaterials offer an alternate option to improve several unfavorable characteristics of homogeneous materials (metals or ceramics), even though metals and ceramics have drawbacks, including truncated biocompatibility and deterioration, as well as breakability and short rupture strength, respectively. A composite biomaterial's final composition is significantly influenced by the characteristics of the individual components. Linear expansion is a crucial factor to consider while creating composite biomaterials. When creating composites, it is usual practice to combine materials having comparable linear expansion constants. The goal of the implant may be defeated if the contact region (interface) between the reinforcement and matrix materials results in significant gaps via the contact surface due to different linear expansion constants between the component materials. Therefore, while choosing each component of the composite biomaterial, bone tissue engineers need to be more careful (Kim et al., 2017)

3.1. Ceramics

Another type of material used in the creation of biomaterials is ceramic. Because of its exceptional wear resistance, high compressive strength, and inert body, ceramics were chosen. They were also chosen for their outstanding formability in a variety of shapes and porosities. Heart valves, biocompatibility coatings for metallic implants, artificial knees, hip prostheses, bone grafts, dental and orthopedic implants, orbital and middle ear implants, and musculoskeletal system parts are all ceramic. Though less frequently than metals or polymers, ceramics are used to manufacture biomaterials. Ceramics have minimal applications due to their fragility and low tensile strength. Apatite had a significant influence on the creation of pottery (Griffith, Naughton, 2002; Shivani, Jashandeep, Singh, 2021). Calcium phosphate-based biomaterials, which are used in several ways throughout the body, cover every skeletal component. Some of its uses include dental implants, transdermic devices, the treatment of fractures and bone anomalies, total joint replacement, orthopedics, cranio-maxillofacial reconstruction, otolaryngology, and spinal surgery. Second, hydroxyapatite has been implanted to rectify bone abnormalities in load-free anatomical locations, including the middle ear and nasal septum. Bio-eye hydroxyapatite orbital implants and ceramic hydroxyapatite block implants are also made with hydroxyapatite. In addition to these applications, hydroxyapatite has been used as a coating material for implants made of stainless steel, titanium, and its alloys, as well as metallic orthopedic and dental implants, to aid in the bone attachment (Goswami, Bhat, and Patnaik, 2019; Kim et al., 2017). In this case, hydroxyapatite tightly adheres to the metal surfaces of the underlying bone structure. Contamination must be prevented at all costs, however. The failure of an implant and the significant difficulties it causes result from the ceramic layer delaminating from the metal surface.

3.2. Basic considerations to design

- While several devices and implants constructed from the materials above are being created to treat a wide range of medical conditions and injuries, the following fundamental concerns underpin the development of all biomaterials:
- Specifications according to which a biomaterial is developed. Accurately describing the biomaterial's intended environment and how that environment will influence the biomaterial's properties.
- Both the potential risks and benefits of using the biomaterial, as well as its expected lifespan, should be

thoroughly understood before its implementation (Kaushal, et al., 2001; Giriet al., 2012).

Table 1: Description of Biomaterials and its Merits and Demerits

Class of the Material	Merits	Shortcomings	References
Types of Polymers			
PTFE, silicones, Nylon,	Resilient Easy to fabricate	Not strong Deform with time, may degrade	(Ghose et al., 2021; Mckellop, Bradley, 1993; Edidin, Kurtz, 2000). Kumar et al., 2020); Dowson, Wallbridge, et al, 1985).
Metals		(Edidin, and Kurtz 2000; Kumar et al., 2020; Dowson, and Wallbridge, 1985; Radulovic, and Wojcinski 2014).	
Titanium, stainless steels, Co-Cr alloys, gold	Strong Tough, Ductile	May corrode High density	
Ceramics			
Aluminium oxide, Carbon dots. Hydroxyapatite	Highly biocompatible, Inert, high modulus Compressive strength Good esthetic properties	Brittle, Difficult to make, Poor fatigue resistance	(Radulovic and Wojcinski. 2014; Shekhawat *et al.* 2021; Shivani et al. 2021; Hernigou and Bouthors, 2016; Muster,1992; Hootman, et al. 2015)

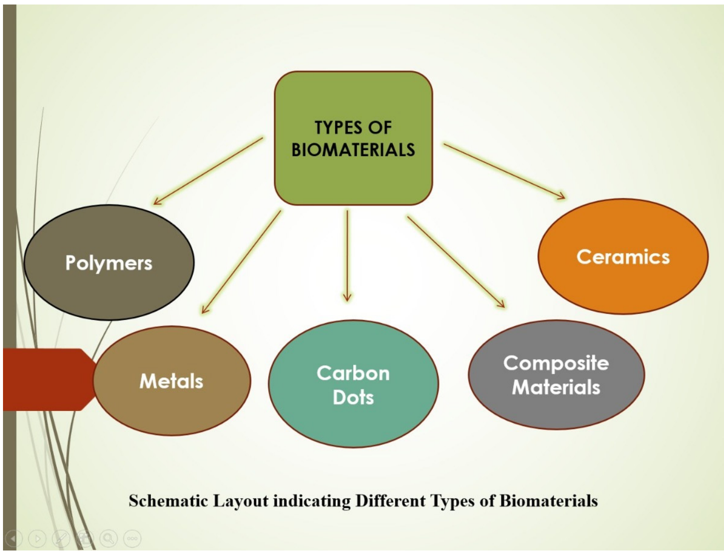

Figure 1. Types of Biomaterials.

4. Biomedical Applications Of Biomaterials

Implant materials made of metallic substances have a long history of playing an essential therapeutic role in medicine. Metals and metal alloys have been used in the medical field, including stainless steel (316L), titanium and its alloys (Cp-Ti, Ti6Al4V), cobalt-chromium alloys (Co Cr), aluminum alloys, zirconium niobium, and tungsten heavy alloys. The rapid development of biomaterials has allowed for the creation of a wide variety of metal-based medical products including dental implants, craniofacial plates and screws, pieces of artificial hearts, pacemakers, clips, valves, balloon catheters, medical devices and equipment, bone fixation devices, dental materials, medical radiation shielding products, prosthetics, and orthodontic devices. Biomaterials can be made from a wide variety of various substances. Engineers typically favor using metals as the primary material to construct the necessary biomaterial (Giri et al., 2012; Moran et al., 2014; Katari et al., 2014). This is because metals can be easily manipulated to create the desired biomaterial. Because of their outstanding biocompatibility, practical mechanical qualities, great corrosion resistance, and low cost, materials based on metal are frequently selected for use in biomedical applications. When a metal-based biomaterial is introduced into a biological medium, the material's surface may undergo changes and eventually degrade, producing several different byproducts. This releasing process makes it possible for cells or tissues to interact with the surface of the metal device. Because of this, current researchers are putting much effort into learning about the surface properties of metals to make materials that are safe for living things (Wagner et al., 2013; Lee, Singla, Lee 2001; Ghose et al., 2021). A detailed description of the classification of materials used for therapeutic purposes, as well as their advantages and disadvantages, is elucidated in **Table 1**.

4.1. Biomaterials in dental

Polymeric biomaterials have diverse uses in the fields of dental and biomaterial prostheses. They are used for craniomaxillofacial reconstruction, which involves repairing anomalies in the midface, orbit, temporomandibular joint, and cranial structures. Polymeric biomaterials, such as polyetheretherketone (PEEK) and BioHPP, are now under development as substitutes for metals and metal alloys in dental applications. These materials possess exceptional esthetic and physical-mechanical properties, which make them very suitable for dental prostheses. Polymethyl methacrylate (PMMA) is extensively used in prosthetic dental applications, specifically for producing artificial teeth, denture bases, and dentures. PEKK biomaterials exhibit significant potential for dental applications, such as tooth restorations, crowns, bridges, denture frames, and dental implants. Dental polymers should be biocompatible, safe for oral tissues, and free of poisonous or allergic chemicals. The most commonly utilized polymer in prosthodontics is polymethyl-methacrylate resin (PMMA) (Heboyan et al., 2023).

4.2. Biomaterials in orthopedic

In orthopedics, sodium alginate hydrogel is a helpful material for tissue engineering, and poly (2-oxazoline) is a valuable material for bone implants. A wide range of adhesive combinations is required to provide strength for orthopedic applications such as bone therapy, wound healing, and tissue adhesion. When orthopedic biomaterials are introduced into the human body, they perform various biological tasks, such as tissue replacement or repair of bone, cartilage, ligaments, and tendons, and guided bone regeneration. As a consequence, the selection of biomaterials must ensure compatibility with the specific requirements of the application, taking into account the harsh environment of the human body and the unique biological traits the biomaterial must possess, in addition to the standard mechanical, chemical, and physical properties (Navarro et al., 2008).

4.3. Biomaterials in cardiovascular systems

Polymer-based synthetic biomaterials are used for (A) pericardial repair with expanded polytetrafluoroethylene, or Gore-tex®; (B) vascular grafts with polyethylene terephthalate, or Dacron®; and (C) polyurethane in leads. Metal-based synthetic biomaterials are employed in heart valves (D) and coronary stents (E). Numerous biomaterials are employed to repair and replace injured cardiac tissues. The biomaterials are categorized into two distinct groups: synthetic and natural. Metals and polymers are two distinct categories of artificial substances employed in cardiovascular applications. Biological sources, such as human donors or collected animal tissues, provide natural resources. A new class of composite materials has arisen to capitalize on the strengths of synthetic and natural materials while minimizing their shortcomings (Lam et al., 2012).

5. Conclusion

Innovative biomaterials may adapt to changes in physiological parameters and exogenous stimuli, and they significantly impact many facets of modern medicine. Innovative materials can help to advance promising medicines and enhance the treatment of chronic diseases. We highlight recent breakthroughs in designing and implementing intelligent biomaterials for tissue engineering, drug delivery systems, medical devices, and immunological engineering. In recent years, there has been an increase in interest in natural polymers based on proteins or polysaccharides due to the multiple applications they can have in biomedicine. These materials offer various possible applications due to their chemical stability, structural plasticity, biocompatibility, and widespread availability. Potential uses include tissue engineering, medication delivery, and wound healing. We provide an overview of the therapeutic applications of biomaterials in dental, orthopedic, and cardiovascular systems that are now using these naturally occurring materials. On the contrary, this review aims to assess the current state of the art and the future possibilities of so-called "smart biomaterials" from the perspective of translational science and, more specifically, clinical research. In order to facilitate the transition of intelligent biomaterials from the laboratory to the clinic, our objective is to identify and, investigate, and investigate which scientific discoveries and innovations will be of assistance.

Author contributions

S.S., A.N., R.N.S., B.R.J., R.S.D., A.P., and P.P. planned, wrote, and conceptualized the study concept and design. Authors A.S. and B.N.R. collected and analyzed the advanced literature and handled referencing. All authors reviewed and approved the final manuscript.

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Competing financial interests

The authors have no conflict of interest.

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