International Journal of Engineering Applied Sciences and Technology, 2022
Vol. 6, Issue 12, ISSN No. 2455-2143, Pages 1-10
Published Online April 2022 in IJEAST (http://www.ijeast.com)

CHEMICAL COMPOSITIONS AND ANALYSIS OF BIOCOMPATIBLE MATERIAL(S), TECHNOLOGICAL ADVANCEMENT AND STANCE

Ajay Panwar,
Sr. Engineering Manager, Medtronic, California, USA

Jasdeep Shangari,
Manufacturing Engineer,
Zest Dental Solutions, California, USA

Abstract: **With the growing population, rising burden of disease and disability, there is an increase in demands for quality care and accessibility to medical devices and materials used in the manufacturing of these medical devices. However, not all materials can be used for this purpose. The biomaterials that can be used have specific properties and characteristics before they can be used to design health solutions and devices. To choose biomaterials for a particular purpose and manufacture medical devices, the first step is to determine the proper material that will serve the desired goal, the way it will be utilized and its capacity to fulfil the role. This review focuses on biomaterials, their types, uses, desired properties and pros and cons of every kind of biomaterial available. The review takes a deep dive into the five major types of synthetic biomaterials biocompatible polymers, natural biocompatible polymers, biocompatible metals, biocompatible ceramics, and biocompatible composites. It is also an in-depth look into how these materials are regulated, how their authenticity is tested and what new directions the biomaterials research is taking.**

Keywords: **Biomaterials, Biocompatible Materials, Medical Devices, Metals, Ceramics, Polymerics, Composites, Regulations, Technology**

I. INTRODUCTION

The use and popularity of biomaterials to enhance the quality of life are vital for the survival of many individuals, especially those affected by medical conditions that may otherwise limit the quality of life. Many types, variants, and qualities of these biomaterials are available and have a wide range of medical and non-medical applications. According to the definition, biocompatible or biomaterials are substances or a combination of substances that can be used for varying durations of time to replace or augment the body's tissues, organs, and functions. These biomaterials can be used independently or be a part of a system. Biomaterials are both natural and synthetic. These materials are compatible with the human body due to their properties that allow it to stay unchanged over long periods [1]. This means that these materials do not cause inflammation, damage, or cell death in the body. However, humans tend to react aggressively when foreign objects enter their bodies. This can start a cascade of reactions that cause adverse effects. Therefore, there are strict requirements for which materials can be used for medical devices and purposes.

Over time the applications of biomaterials have also evolved. Now, these can also be used for diagnostic purposes like gene arrays and biosensors, medical equipment like surgical tools and blood bags, therapeutic medications like implants and devices, and regenerative drugs like cartilage and tissue-engineered skin. The biocompatible materials can also be used in different body systems. For example, artificial tendons and ligaments, bone defects and fractures and joint replacements in the skeletal system can be built with the help of these materials. Similarly, artificial hearts and skin grafts can be constructed in the cardiovascular system, heart valves, vessel prosthesis, and organs. The utilization of biocompatible materials has also seen shifts with time. As more technological innovations have flooded the market, the research into biomaterials and their uses has expanded the knowledge base and applications for their use. During the third quarter of the 20th century, biomaterial research focused on inert biomaterials; these were the first-generation biomaterials that were primarily used to replace damaged tissues in the human body and provide structural support. During the 1980s and onwards, the subsequent period focused more on the commercial production of bioactive biomaterials. These materials included coatings that augmented the effectiveness and performance of the medical devices that used them. The latest phase during the 21st century has been concentrated on dealing with infections caused by biomaterials and toxicity and immunological responses in the human body after their application. This era also saw intensive research into biodegradable biomaterials and innovative biomaterials, which can minimize the shortcomings of permanent implants and have properties to emulate natural materials [2].

Types and Properties of Biocompatible Materials

Synthetic Biocompatible Polymers	Natural Biocompatible Polymers	Biocompatible Ceramics	Biocompatible Metals	Biocompatible Composites
• Synthetic Biocompatible Engineered Polymers • Synthetic Biocompatible Commodity Polymers	• Cellulose Polymers • Starch Compounds • Collagen • Other Natural Biocompatible Polymers	• Alumina • Porcelain • Hydroxyapatite • Zirconia • Other Ceramic Materials	• Precious Metals • Stainless Steel • Titanium • Other Biocompatible Metals	• Fibrous • Porous

Table 1. Types of Biocompatible Material [3,4]

There are five main types of biomaterials depending on the chemical bonding. These include biocompatible polymers (synthetic & natural), ceramics, metals, and composites. Based on the type of chemical bonding (ionic, covalent, or metallic), these materials exhibit different properties. This means that the use of these materials in the body also differs. The different types of biomaterials and their subclasses include (Table 1) [3, 4]:

Synthetic Biocompatible Polymers

Synthetic biocompatible polymers are macromolecules made by humans and do not occur naturally. However, they represent a significant class of biomaterials used in various biomedical applications due to their low toxicity levels in biological systems, ease of manufacturing, post-processing, better shelf life, and superior physical and chemical properties. The reason for preferring synthetic biocompatible polymers over natural ones usually is the ease with which these materials can be changed and modified according to need. In addition, due to their artificial nature, these polymers can survive for years in biological systems without causing harm to the host [5,6].

Natural Biocompatible Polymers

The second primary class of biocompatible polymers is those macromolecular compounds that occur naturally within different living beings and organisms. These biopolymers are not manufactured or produced commercially but are sourced through living microorganisms. One of the prominent properties of these biopolymers is that they consist of repeating units bonded with each other through covalent bonds. Natural polymers can be found in several organisms, from microscopic to complex multicellular organisms like bacteria, fungi, algae, plants, and animals. These materials are favoured due to desirable properties like biodegradability, ability to be modified, and biocompatibility [5, 7, 8].

Biocompatible Ceramics

This type of biomaterial consists of inorganic solids. Biocompatible ceramics usually consist of metallic and nonmetallic elements bound with each other through ionic bonds. These compounds exist in crystalline and amorphous (non-crystalline) forms. Ceramics have excellent biocompatibility, are highly stiff, have high wear and tear compatibility, high strength, high corrosion resistance, and hardness. These materials have wide-ranging biomedical applications and include bio-inert ceramics like alumina, zirconia, and pyrolytic carbon. Another subtype of ceramics includes bioresorbable ceramics like calcium phosphates. Due to the high number of desirable properties of ceramics, particularly inertness, they are among the most sought-after biomolecules [9,10].

Biocompatible Metals

The most widely known biocompatible materials are metals. This type of biomaterial is indispensable due to its various applications in the medical field. Almost all metal biomaterials can be categorized as crystalline, i.e., with standard atomic arrangements. The biocompatible metals have high resistance to fracture, are tough, have better elasticity, strength, and rigidity than biocompatible polymers (synthetic and natural) and ceramics. Due to their excellent mechanical properties (Table 2), which are modifiable by dislocation and crystallization, these metals are used for multiple medical applications; for example, metals are used as load-bearing implants in orthopaedic, maxillofacial, and dental surgery. These are also used for making stents and stent-grafts for matters related to cardiovascular health [12, 13, 14]. The most common subtypes of biocompatible metals include titanium, titanium-based alloys, magnesium-based alloys, cobalt-based alloys, tantalum-based alloys, and stainless steel. Titanium is the most used metal when it comes to manufacturing medical devices. Its changing properties at different purity and chemical composition levels (Table 3) [1].

Materials	Young's modulus (GPa)	Ultimate tensile strength (MPa)	Fracture toughness (MPa)
CoCrMo alloys	240	900–1540	100
316L stainless steel	200	540–1000	100
Mg alloys	40–45	100–250	15–40
NiTi alloys	30–50	1355	30–60
Ti and Ti alloys	105–125	900	80

Table 2. Mechanical Properties of Some Loadbearing Metal Biomaterials [11]

Material	N	C	H	Fe	O
Grade 1	0.03	0.08	0.15	0.2	0.18
Grade 2	0.03	0.08	0.15	0.3	0.25
Grade 3	0.05	0.08	0.15	0.3	0.35
Grade 4	0.05	0.08	0.15	0.5	0.40

Table 3. Chemical Composition of Different Titanium Classes [1]

Biocompatible Composites

Composite materials are compounds that result when two or more different materials are combined. This category of biomolecules is usually famous for obtaining materials with better properties than their constituents. Biocompatible composites are made with a base material and reinforcement. For example, a polymer may be used for base material, which is reinforced with the help of carbon fibres. When two materials are combined in this way, the ultimate goal is to improve the produced biocompatible composite's mechanical strength, fatigue, and hardness [1].

Desired Properties of Biomaterials

Biomaterials are primarily used in medicine to help improve, treat, or substitute essential tissue organs or bodilyfunctions. This means that each biomaterial requires some specific properties to fulfil its role in the human body. Biomaterials are chosen based on the essential four elements for any position. These include the nature of the system, physiological specification, device architecture, and properties of the biomaterial used. To get the required results, the mechanical and chemical features of the biological systems are combined. In addition, the social and scientific parameters are also considered before processing any biomaterials. The following include the desired properties that make the biomaterials compatible in several body systems without causing harmful side effects [15,16].

- **Biocompatibility**

Biocompatibility indicates how well a biomaterial will gel in the biological system and perform its given function without causing any harm [17, 18, 19].

International Journal of Engineering Applied Sciences and Technology, 2022
Vol. 6, Issue 12, ISSN No. 2455-2143, Pages 1-10
Published Online April 2022 in IJEAST (http://www.ijeast.com)

- **Host response**

The host response varies based on the type of biomaterial used in medical devices and the final form used in its application. The response can range from standard to complex for naturally derived materials and typical for synthetic [20].

- **Non-toxicity**

One of the desired qualities of any biomaterial is its low toxicity or non-toxicity in human systems. However, inflammation, damage, or toxicity can cause serious adverse effects in the body and make any biomaterial with such properties unwanted [21,22].

- **Mechanical properties**

Due to their inherent structure and bonding, different biomaterials present different mechanical properties. Therefore, the usage of these biomaterials in different applications is based on these properties [23,24].

- **Corrosion, wear, and fatigue properties**

Some of the highly desired properties of biocompatible compounds include long-lasting durability for long durations of time. However, materials with short shelf lives may be preferred for applications like a quick biodegradable suture. In addition, the use of biomaterials depends on their wear and fatigue bearing capabilities [25,26,27].

- **Design and manufacturability**

Being cost-effective, accessible, sterilizable and easy to process make different biomaterials desirable [28,29]

Uses of Biocompatible Materials

Biomaterials serve as critical ingredients for several implants used in place of joints and other essential organs (Figure 1). These materials function by replacing or restoring the tissues or organs that have been injured. This way, biomaterials can help preserve the essence of life for patients. Here are some of the significant biomaterial groups, their use, and their potential advantages (Table.4) [30].

Biocompatible Polymers

Biocompatible polymers (synthetic + natural) are often used in prostheses, implants, removable medical supplies, and devices used for blood purification like hemofiltration and hemodialysis. These have also been utilized in drug delivery systems and treat bone-related problems. Polymers can easily be manufactured, processed, and are readily available. They are also highly cost-effective. Some of the most commonly used biocompatible polymers are polyvinyl chloride (used for making.

Bags to contain solutions and blood), polyethylene (used for making implants for bones), polypropylene (used for making disposable syringes and artificial vascular grafts), polymethyl methacrylate (used for making eye-related implants and blood pumps), polystyrene (used for making flasks and filter devices), polytetrafluoroethylene (used for making artificial vascular grafts and catheter), polyurethane (used for making packaging films), polyethylene terephthalate (used for making heart valves and implantable sutures), and polyethersulfone (used for making lumen tubing and catheters) [5,6,8].

Material	Uses	Advantages
Polymeric Biomaterials	Implants, veins, arteries, sutures, and artificial tendons	Have a low density and are easy to produce
Metallic Biomaterials	Plates and wires, dental implants, cranial plaques, joint prosthetics, staples	High resistance to wear and impact, Ductility
Ceramic Biomaterials	For the bone filling, medical equipment, medical tools, coatings	Have high resistance to corrosion, good biocompatibility, low electric and thermal conductivity, are inert
Composite Biomaterials	Implants, artificial joints, and heart valves	Are inert, have good biocompatibility, are corrosion resistant

Table 4. Uses and Advantages of Biomaterials [1]

Metallic Biomaterials

Due to their excellent electrical and thermal conductance, metallic biomaterials are used in several medical devices. These biomaterials have low acceptability to corrosion and are therefore used as tissue replacements like knee joints and total hip replacements. These can also be used for fixing

International Journal of Engineering Applied Sciences and Technology, 2022
Vol. 6, Issue 12, ISSN No. 2455-2143, Pages 1-10
Published Online April 2022 in IJEAST (http://www.ijeast.com)

vertebral columns and issues of the spinal cord. Other uses include bone fixing plates, catheter guide wires, dental braces, bridging wires, vascular stents, and cochlear implants [12].

Ceramic Biomaterials

Due to their inert, brittle, and complex nature, they have widespread applications. Some examples of ceramic biomaterials include alumina, bioglass, zirconia, tricalcium phosphate, and hydroxyapatite. In addition, the use of ceramic biomaterial includes porous spacers, crowns and bridges, femoral heads, porous coating for femoral stems, and bone screws and plates [10].

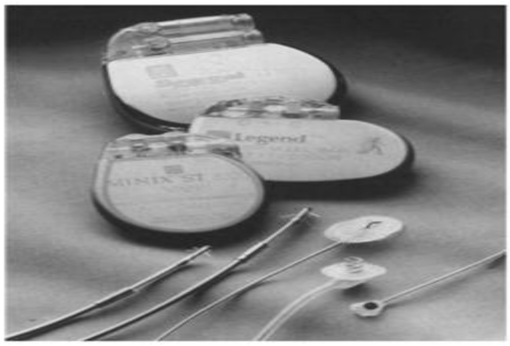
Composite Biomaterials

As composite biomaterials are made from merging other materials, they have different properties. Some of the standard applications of the composites include bone cement made from reinforced methyl methacrylate and polyethylene, composites for teeth filling, and orthopaedic implants with porous surfaces [1].

Risk and Side-Effects of Biocompatible Materials

There are several risks and side effects that are frequently associated with using biomaterials in human beings. It is significant to note that specific biomaterials can have distinct disadvantages when used for different functionalities (Table 5). However, all these biomaterials can cause some common adverse effects when used in therapeutic devices or implants. The following toxicities have been identified previously due to using biomaterial-based implants [22,34].

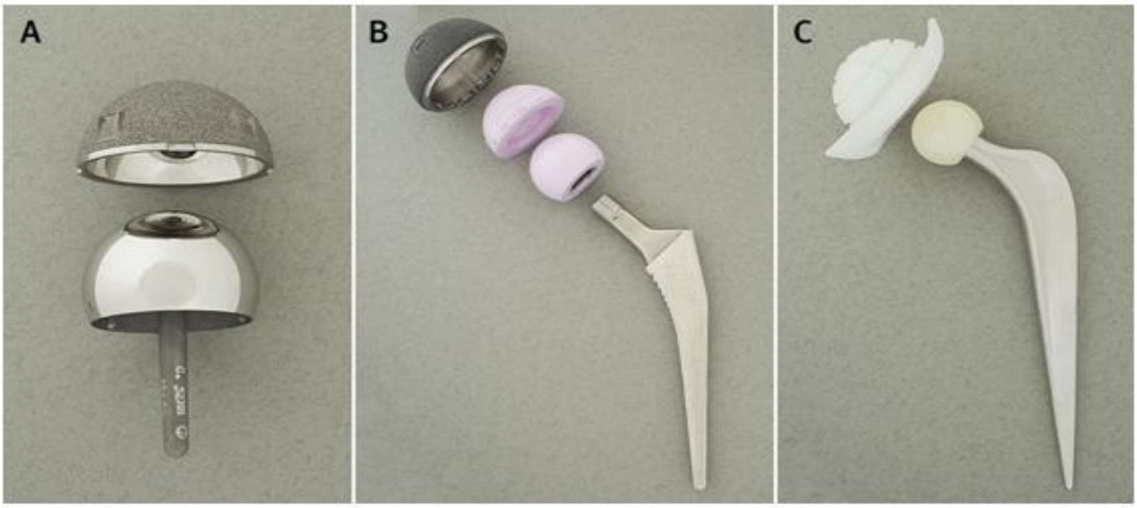
(1.a) silicone finger implant with metal grommets [31]



(1.b) components of pacemaker [32]

Table 5. Disadvantages of Using Biomaterials [1]

Material	**Disadvantages of Use**
Polymeric Biomaterials	Are easily degradable and have a low mechanical resistance
Metallic Biomaterials	Low resistance to corrosion, low biocompatibility, mechanical properties vary in different biological environments.
Ceramic Biomaterials	Are challenging to manufacture, difficult to reproduce specific properties, difficult to process, have a low impact strength
Composite Biomaterials	Difficult to reproduce or replicate



(1.c) represents (A) resurfacing implant; (B) ceramic-on-ceramic, large head, uncemented implant and (C) ceramic-on-polyethylene implant [33]
Figure 1. Uses of Different Biomaterials

Carcinogenicity
The ability to induce a local or systemic malignancy of the biomaterials is known as carcinogenicity. This becomes a particular concern when biomaterials are used in young patients with long life expectancy. The better the quality and safety index of biocompatible materials, the less is a chance that they can cause any carcinogenicity in the human body. Previously the use of metallic biomaterials has been associated with an increased risk of lymphatic and haemopoietic tumors in patients who have undergone total hip replacement. However, no cause and effect have been established. The current regulatory standards and procedures call for safety testing that can help evade such risks[34].

Systemic Disease
Another consideration while using any biomaterial is the question of injury to one or more organ systems due to its presence in the body. For example, metal implants corrosion can release ions linked to an increased risk of systemic toxicity. However, this risk can be evaded with the help of extensive research, pre and post biomaterial usage in test subjects, and conducting long term studies in human recipients [22].

Hypersensitivity
There have been reported allergic reactions and hypersensitive to biomaterials, especially metallic biocompatible materials. This kind of hypersensitivity reaction can manifest as contact dermatitis on the skin or inflammation inside the body. Testing, meeting regulatory standards, and following correct procedures during transplant is essential to evade such risks. However, some materials can still sensitize the body and cause an immune reaction. Other adverse reactions associated with hypersensitivity in humans include pain, swelling, and even draining sinuses [34].

Quality Testing & Regulatory Standards
Quality testing can evaluate the biocompatibility of medical devices that use biomaterials. A set standard is material characterization, where the different properties of material used in medical devices can be evaluated with help of tests. These tests can help rule out adverse reactions like carcinogenicity, sub-chronic toxicity, dermal irritation, skin sensitization, cytotoxicity, and intracutaneous reactivity. Three main domains of testing related to biomaterials have been identified. These include biocompatibility testing with the help of in-vivo implantation and other studies, safety testing of the finished device, and efficacy testing of the product.

International Journal of Engineering Applied Sciences and Technology, 2022
Vol. 6, Issue 12, ISSN No. 2455-2143, Pages 1-10
Published Online April 2022 in IJEAST (http://www.ijeast.com)

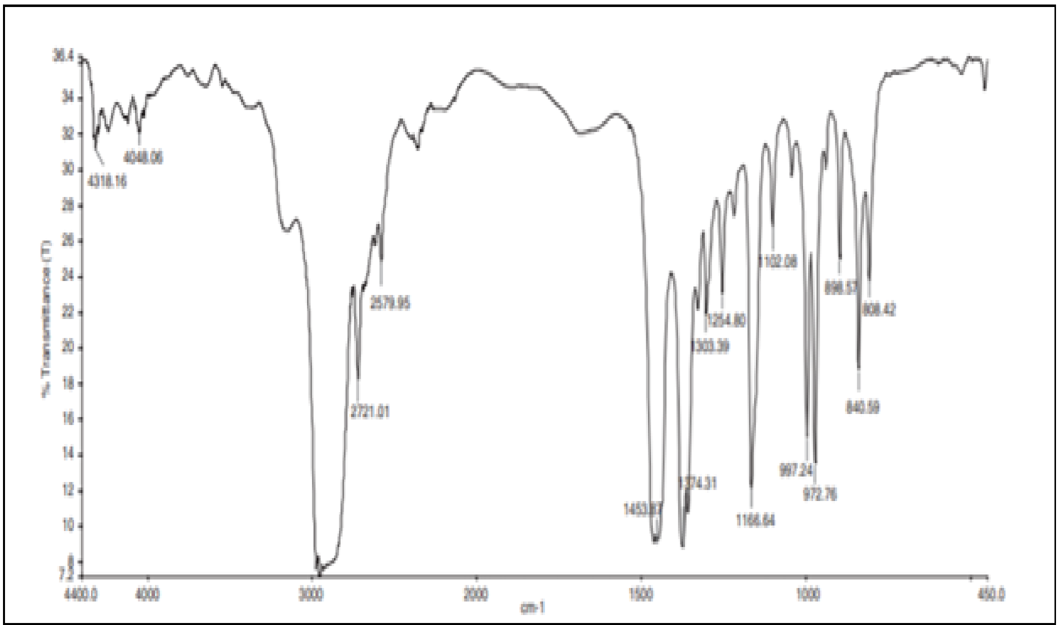


Figure 2. IR Analysis of Polymeric Biomaterials. The x-axis represents the frequencies or wavelengths [38]

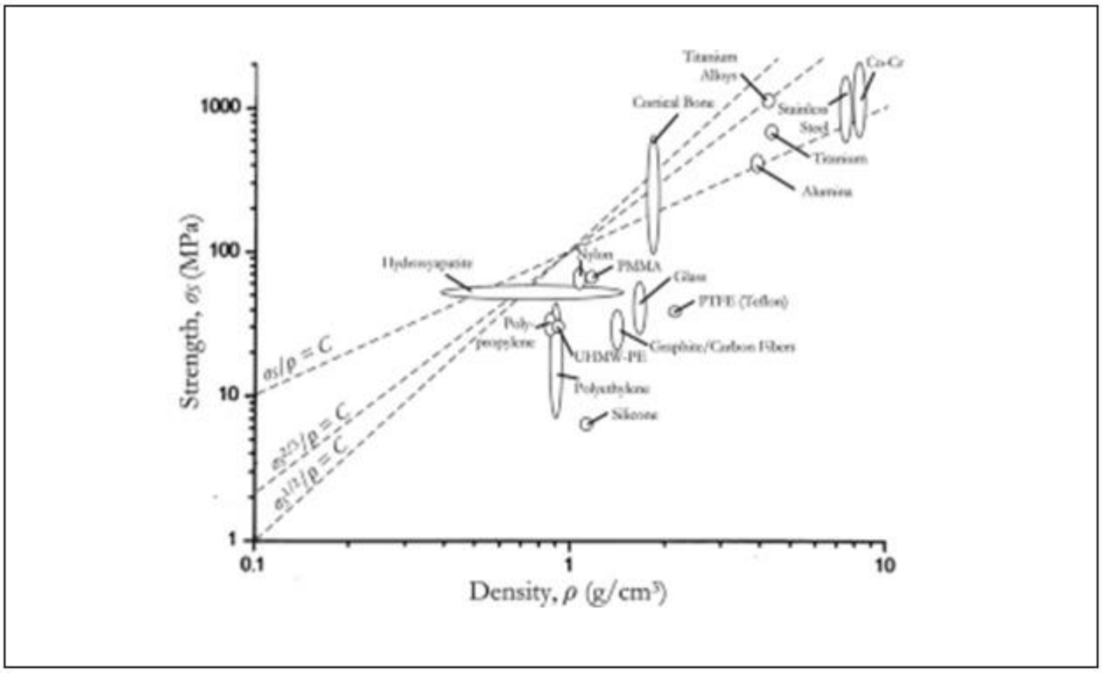


Figure 3. Strength and Density of Different Biomaterials [39]

Properties of the used material determine the efficacy of the device and its performance. The most used analysis is Infrared (IR) which is used to test out polymeric chemicals and compounds. The IR spectrum for any material used in the medical device is the set standard for determining characteristics of the material used. During the test, infrared energy is passed through an extremely thin layer or film biomaterial. During and after this, the amount of energy that was absorbed at different wavelengths is measured. When the two factors- wavelength and absorption are charted against each other in a table, this provides the characteristics of the material (Figure 2) [38]. Other tests include thermal testing, molecular weight, strength, and density testing of the biomaterial (Figure 3) [39].

The standards set for testing are often referred to as guidelines. The major followed guidelines for biomaterials testing come from International Organization for Standardization (ISO). There are other parallel regional and national testing standards provided that ensure better safety and efficacy. Table 6 shows different types of testing standards set for biomaterial safety in medical devices [35, 36, 37].

Other organizations and guidelines involved in quality standard procedures include ASTM International, European Conformity Marking, US Pharmacopeial Convention, International Council for Harmonization, and International Medical Device Regulators Forum.

New Directions in Biocompatible Material Development

The field of biocompatible materials is ripe for research and finding new materials that can be used for similar purposes. Here are some of the future directions where biomaterials research can achieve great success [40,41].

For biocompatible metals, this means developing biologics that can initiate desired responses, have improved engineering properties like (wear, fatigue, and corrosion resistance), development of high load bearing materials, forming templates for bone or tissue regeneration, and implants of smaller sizes. Whereas there is more likely to be more research into developing composite and polymer biomaterial due to their ease of use and versatility of use going forward. Previously ceramics were left untouched due to their difficult mechanical properties, but now with advancing technology that is no longer the case. Future of ceramic biocompatible materials include modification of bioglass, bioceramics, and optimizing their properties for better use and utility [40,42].

A new interest has also been developed in self-healing biomaterials and how to develop new biomaterials that have properties of healing. Mechanical failure of medical devices may be combated with help of such materials. A special focus has been to develop self-healing biomaterial that could be used for implants that are damage through cyclic loading patterns. Such materials can extend implant lifetimes. These materials may also be used for benefits in other field like aerospace engineering and development of construction material [43].

II. CONCLUSION

There is a growing need to develop new materials that can be used to replace tissue or support essential functions in the human body. This need is being met by the hundreds of biomaterials that have been developed over the years. However, these materials are not perfect and have some side effects and disadvantages for use. Among the developed biomaterials, the essential function is served by those used as implants. These implants originate from five primary types: synthetic biocompatible polymers, natural biocompatible polymers, biocompatible metals, biocompatible ceramics, and biocompatible composites. Due to their intrinsic characteristics and properties, these materials can be used alone or in sync to fulfil essential functions in medical devices and other implants.

The most famous and used materials for such functions are biocompatible metals. These include titanium and titanium alloys. But these metals are not without their problems and can cause toxic effects in the body when not used correctly or used for long durations. Therefore, it is significant to find and develop newer metals that have more biocompatibility with human tissues and the body (mechanically and chemically). The other popular rising biomaterials are ceramics. This is their inert nature and excellent properties that can be used alone or combined with other materials to form composite biomaterials for different uses. The formed composite is often better and has more biocompatible properties than its components. Polymers are a particular interest group as they have tremendous and widespread applications due to ease of availability, production, and diversity. There are endless possibilities to explore the field of biomaterials further to help create better resources to deal with disease, trauma, and diagnostics. The most critical area of work is finding new biomaterials and improving the biocompatibility of those already being used.

III. REFERENCES

[1]. Kiradzhiyska DD, Mantcheva RD. Overview of Biocompatible Materials and Their Use in Medicine. Folia Med (Plovdiv). 2019 Mar 1;61(1):34-40. doi: 10.2478/folmed-2018-0038. PMID: 31237853.
[2]. Reinwald, Y., Shakesheff, K., &Howdle, S. (2011). Biomedical devices. Porous Polymers, 323, 357.
[3]. Biocompatible Materials - Industry Market Research, Market Share, Market Size, Sales, Demand Forecast, Market Leaders, Company Profiles, Industry Trends and Companies including Dow Chemical, BASF and PolyOne. (2014). Retrieved 27 March 2022, from https://www.freedoniagroup.com/Biocompatible-Materials.html
[4]. Bronzino, J. D., & Peterson, D. R. (2014). Biomedical engineering fundamentals. CRC press.
[5]. Shalaby, W. (2012). Polymers as biomaterials. Springer Science & Business Media.
[6]. Gunatillake, P. A., Adhikari, R., &Gadegaard, N. (2003). Biodegradable synthetic polymers for tissue engineering. Eur Cell Mater, 5(1), 1-16.
[7]. Balaji, A. B., Pakalapati, H., Khalid, M., Walvekar, R., & Siddiqui, H. (2018). Natural and synthetic biocompatible and biodegradable polymers. Biodegradable and Biocompatible Polymer Composites. Duxford: Woodhead Publishing, 3-32.
[8]. Mogoşanu, G. D., & Grumezescu, A. M. (2014). Natural and synthetic polymers for wounds and burns

dressing. International journal of pharmaceutics, 463(2), 127-136.
[9]. Goffard, R., Sforza, T., Clarinval, A., Dormal, T., Boilet, L., Hocquet, S., & Cambier, F. (2013). Additive manufacturing of biocompatible ceramics. Adv. Prod. Eng. Manag, 8, 96-106.
[10]. Sikalidis, C. (Ed.). (2011). Advances in Ceramics: Electric and Magnetic Ceramics, Bioceramics, Ceramics and Environment. BoD–Books on Demand.
[11]. Bazaka, O., Bazaka, K., Kingshott, P., Crawford, R. J., & Ivanova, E. P. (2021). Metallic Implants for Biomedical Applications.
[12]. Balakrishnan, P., Sreekala, M. S., & Thomas, S. (Eds.). (2018). Fundamental Biomaterials: Metals. Duxford, UK: Woodhead Publishing.
[13]. Asri, R. I. M., Harun, W. S. W., Samykano, M., Lah, N. A. C., Ghani, S. A. C., Tarlochan, F., & Raza, M. R. (2017). Corrosion and surface modification on biocompatible metals: A review. Materials Science and Engineering: C, 77, 1261-1274.
[14]. Manam, N. S., Harun, W. S. W., Shri, D. N. A., Ghani, S. A. C., Kurniawan, T., Ismail, M. H., & Ibrahim, M. H. I. (2017). Study of corrosion in biocompatible metals for implants: A review. Journal of Alloys and Compounds, 701, 698-715.
[15]. Kiran, A. S. K., & Ramakrishna, S. (2021). An Introduction to Biomaterials Science and Engineering. World Scientific.
[16]. dos Santos, V., Brandalise, R. N., & Savaris, M. (2017). Biomaterials: Characteristics and properties. In Engineering of Biomaterials (pp. 5-15). Springer, Cham.
[17]. Williams, D. F. (2008). On the mechanisms of biocompatibility. Biomaterials, 29(20), 2941-2953.
[18]. Black, J. (2005). Biological performance of materials: fundamentals of biocompatibility. Crc Press.
[19]. Williams, D. (2003). Revisiting the definition of biocompatibility. Medical device technology, 14(8), 10-13.
[20]. Santavirta, S., Takagi, M., Gómez-Barrena, E., Nevalainen, J., Lassus, J., Salo, J., &Konttinen, Y. T. (1999). Studies of host response to orthopedic implants and biomaterials. Journal of long-term effects of medical implants, 9(1-2), 67-76.
[21]. Autian, J. (1975). Biological model systems for the testing of the toxicity of biomaterials. In Polymers in medicine and surgery (pp. 181-203). Springer, Boston, MA.
[22]. Tekade, R. K., Maheshwari, R., & Jain, N. K. (2018). Toxicity of nanostructured biomaterials. In Nanobiomaterials (pp. 231-256). Woodhead Publishing.
[23]. Lv, S., Dudek, D. M., Cao, Y., Balamurali, M. M., Gosline, J., & Li, H. (2010). Designed biomaterials to mimic the mechanical properties of muscles. Nature, 465(7294), 69-73.
[24]. Wang, L., Wang, C., Wu, S., Fan, Y., & Li, X. (2020). Influence of the mechanical properties of biomaterials on degradability, cell behaviors and signaling pathways: current progress and challenges. Biomaterials Science, 8(10), 2714-2733.
[25]. Teoh, S. H. (2000). Fatigue of biomaterials: a review. International journal of fatigue, 22(10), 825-837.
[26]. Blackwood, D. J. (2003). Biomaterials: past successes and future problems. Corrosion reviews, 21(2-3), 97-124.
[27]. Niinomi, M. (2007). Fatigue characteristics of metallic biomaterials. International Journal of Fatigue, 29(6), 992-1000.
[28]. Ranđelović, S. (2018). Manufacturability of biomaterials. In Biomaterials in Clinical Practice (pp. 633-658). Springer, Cham.
[29]. Zhu, Y., & Wagner, W. R. (2019). Design principles in biomaterials and scaffolds. In Principles of Regenerative Medicine (pp. 505-522). Academic Press.
[30]. Pandey, E., Srivastava, K., Gupta, S., Srivastava, S., & Mishra, N. (2016). Some biocompatible materials used in medical practices-a review. International journal of pharmaceutical sciences and research, 7(7), 2748-2755.
[31]. Alnaimat, F. A., Owida, H. A., Al Sharah, A., Alhaj, M., & Hassan, M. (2021). Silicone and Pyrocarbon Artificial Finger Joints. Applied Bionics and Biomechanics, 2021.
[32]. Davis, J. R. (2003). Overview of biomaterials and their use in medical devices. Handbook of materials for medical devices, 1-11.
[33]. López-López, J. A., Humphriss, R. L., Beswick, A. D., Thom, H. H., Hunt, L. P., Burston, A., ... & Marques, E. M. (2017). Choice of implant combinations in total hip replacement: systematic review and network meta-analysis. bmj, 359.
[34]. Rubin, J. P., &Yaremchuk, M. J. (1997). Complications and toxicities of implantable biomaterials used in facial reconstructive and aesthetic surgery: a comprehensive review of the literature. Plastic and reconstructive surgery, 100(5), 1336–1353.
[35]. Schuh, J. C., & Funk, K. A. (2019). Compilation of international standards and regulatory guidance documents for evaluation of biomaterials, medical devices, and 3-D printed and regenerative medicine products. Toxicologic Pathology, 47(3), 344-357.
[36]. Bollen, L. S., & Svendsen, O. (1997). Regulatory guidelines for biocompatibility safety testing. Medical Plastic and Biomaterials, 4, 16-20.

[37]. Di Silvio, L. (Ed.). (2008). Cellular response to biomaterials. Elsevier.

[38]. Albert, D. E. (2012). Material and chemical characterization for the biological evaluation of medical device biocompatibility. In Biocompatibility and performance of medical devices (pp. 65-94). Woodhead Publishing.

[39]. Lam, R. H., & Chen, W. (2019). Biocompatible Material Selection. In Biomedical Devices (pp. 243-266). Springer, Cham.

[40]. Narayan, R. (Ed.). (2009). Biomedical materials (Vol. 1). New York, NY, USA:: Springer.

[41]. Narayan, R. J. (2010). The next generation of biomaterial development. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences, 368(1917), 1831-1837.

[42]. Punj, S., Singh, J., & Singh, K. (2021). Ceramic biomaterials: Properties, state of the art and future prospectives. Ceramics International, 47(20), 28059-28074.

[43]. Brochu, A. B., Craig, S. L., & Reichert, W. M. (2011). Self-healing biomaterials. Journal of Biomedical Materials Research Part A, 96(2), 492-506.