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Bioceramics for Hard Tissue Engineering Applications: A Review

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Abstract

The bioceramics are using as a substitute for hard tissue engineering since 1960. A compelling way to deal with hard tissue engineering aims to restore function of diseased or damaged bone tissue by combining isolated functional cells and biodegradable scaffolds prepared from engineered bioceramics. Bioceramic materials having better potential to replace the damaged tissues and restore the function of existing tissue. ZrO_2, Al_2O_3 based materials and composites presently used to fabricate implants. Bioceramics including hydroxyapatite, bioglass, and calcium phosphate are using as scaffold, bone filler and coating agent because of their mineral composition similarity with hard tissue. Bioceramic producing a higher tissue response as compared to polymers and metals individually. In this review paper, we highlighted the brief aspects of synthetic bioceramic materials applications in the field of hard tissue engineering.

Keywords: Tissue Engineering, bioceramics, Hydroxyapatite, Calcium phosphate, Bioglass.

INTRODUCTION

Synthetic bioceramics use in tissue engineering to repair, restore, replace, and improve the damaged tissue or organs by applying the ideas and methods of engineering and the life sciences. The human body is an organization holding different organs and tissues with specific functions. Hard tissues are the main component of body that supports the movement and locomotion. An adult human body consists of about 40-50% skeletal muscles. Sometimes skeletal muscles got damaged accidentally, that may be due to contusion, strain, lacerations, trauma and bad surgical procedures [1]. As the human body ages, it experiences different changes prompting to misfortune or harm of tissues or their functionalities. Body tissues have limited self-repair capabilities so that damage related issues could resolve by surgical interventions. The surgical treatment includes local or distant autologous tissue substitution, but limited or deficiency of tissue donor and donor site morbidity. Regeneration of functional tissue *in vitro* may offer a clinically relevant alternative to the auto grafts, where an engineered scaffold uses cells derived from the patient to pre-engineer tissue constructs for implantation [2]. Scaffolds utilized for hard tissue engineering perform outlining of scaffold with suitable structure and mechanical properties that support cell attachment, proliferation, and separation create practical tissue. The properties of implant materials, including mechanical properties, porosity, biocompatibility, bioresorbability, and cytotoxicity need to upgrade for specific applications in hard tissue engineering [3]. In the early years, the focus on anti-infective or antibacterial biomaterials synthesis has been increasing. It helps to prevent scaffolds or implants from undesirable infection and keep sterile. It also reduces the risk rate of infection during special surgery cases [4]. In cases of open fractured joints and bone modification surgeries, the implants can lead to the microbial disease [5]. The microbe's species attached on the surface of materials through different mechanisms. According to early stated mechanism, microbe's adhesion done by passive adsorption through which bacterial cells exposed to a solid surface of biomaterials, which offers surface interactions between materials and bacterial cells [6]. When bacteria try to pass through the biomaterial surface, a biofilm formation started on the surface of biomaterial. In the early phase of adhesion, bacterial colonization start i.e. depends upon the route of contamination. The contamination generated in both dry and wet conditions [4, 7]. This surface contamination can often transfer inside the body tissues by liquid carriers; they may be artificial liquids or physiological fluids. The bacterial adhesion in aqueous solution occurs on biomaterials surface can influenced by different variables (figure 1.).

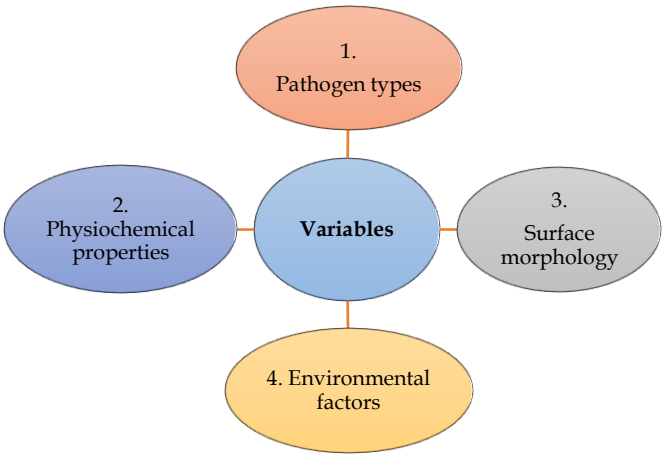

Figure 1. Variables influencing or controlling bacterial adhesion and proliferation

Variables: The surface of implants can affected by adhesion of different pathogens, including gram positive and gram-negative bacteria and species. The bacterial shape and strain type also directly influence the pathogen-biomaterial interaction. The physiochemical properties of biomaterials can promote or prevent the bacterial-biomaterials interaction. It includes surface energy, hydrophilicity/super hydrophilicity,

hydrophobicity/super hydrophobicity, hydrophobic functional groups, functional groups presence, and degree of hydration. Surface characteristics including porosity (micro or nano porous), roughness of implant also offers more adhesion with between bacteria. External conditions like presence of electrolytes, pH, temperature, fluid flow rate, viscosity, or shear rate may reduce or enhance the surface activities of materials [8]. These interactions cause the formation of biofilm on the surface of implant that become the reservoir of bacteria and cause chronic infection. When the biofilm formation started, it is difficult to eliminate with antimicrobial treatments. The porous biomaterials like ceramics can used to fabricate antibacterial implants that will resist the biofilm formation. Therefore, the implant should be osteoconductive and anti-infective.

BIOCERAMICS

The bioceramics is a special kind of biomaterials, which are using to treat, augment, repair, or replace the diseased or damaged hard tissue of the body. Other than medical field, ceramics are also using in electronic, optical and energy. The porcelain was the first bioceramic material that was using in the 18th century for the treatment of the crown. After that, plaster of paris was consuming in the 19th century for treatment of dental disorders [9]. Due to technology improvement, the application of bioceramics increased in the 20th century in the medical field [10]. The main reasons behind the application of these materials are biocompatibility, moderate degradation, and high mechanical strength. Additionally ceramics are having properties like low heat conductance, high melting temperatures and difficult to shear plastically. These characteristics make bioceramics body friendly substitute. Special process and parameters are required to fabricate a good porous scaffold [11, 12]. These materials may be polycrystalline (e.g. alumina or hydroxyapatite), bioactive glass or glass ceramics (A/W) and composites (e.g. polyethylene–hydroxyapatite) [13]. Including aluminum oxide (Al_2O_3), Zirconium oxide (ZrO_2), calcium phosphate (CaO) and bio-glass are mostly using in the biomedical field, especially for hard tissue engineering due to their high mechanical properties [14]. The success of these ceramic materials depends on their bio-functionality and biocompatibility. The biocompatibility of a device or material is its ability to achieve that particular response throughout the life of the implant. The success of any implants depends on two factors that are tissue response to the implant and materials behavior after implantation. After implantation, formation of apatite on the surface of bioceramics makes batter bonding between body tissue and implants. The bioceramics mainly classified into three subclasses (shown in fig. 2): nearly bioinert, bioactive and bioresorbable ceramics [15] with different advantages and disadvantages as shown in table 1.

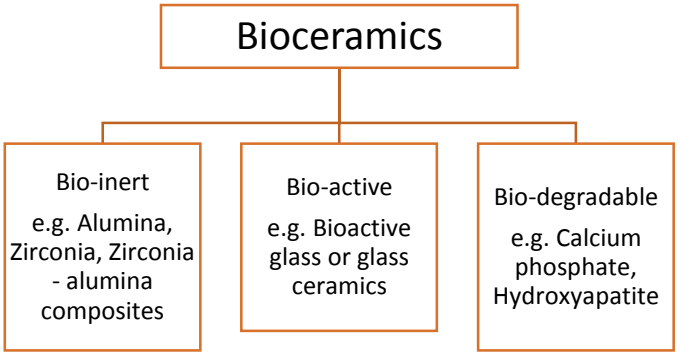

Figure 2. Flow chart for the Classification of Bioceramics:

Table 1. Different properties of bioceramic materials with advantages and disadvantages [11, 16, 17]

Bioceramics	Artificial Implants	Application	Advantages	Disadvantages
Alumina	Knee, Hip, Shoulder, Elbow, Wrist	Reconstruction of fractured part	High hardness, low friction	Weak in tension
Zirconia	Hip, Tooth	Reconstruction of fractured part	Corrosion resistant, hard, less friction	Friction problems, costly
Bioglass	Spinal fusion	Protect spinal cord		Fragile
Calcium phosphate, Hydroxyapatite	Tooth, bone	Replacement of damaged teeth		Sometime fragile

1. **Bio-inert**: These materials are having stable physiochemical properties and makes good compatibility with the hard tissues. In other words, when the materials, implant into the body there will not be a physiological reaction and immunological rejection by body tissue. They keep their physiochemical and biomechanical properties in the host. They repel corrosion and wear. They have a good strength to resist fracture. Bio-inert materials are applied as a structural-support implant for example, bone plates and bone screw [18, 19]. Still no material is completely bio-inert because all materials produce some kind of reactions after implantation in the body [20]. Alumina and zirconia are traditional bio-inert materials using for dental and orthopedic applications since 1960 [21].

1.1. Alumina (Al_2O_3)

The bio inertness of alumina has proven since 1975. The alumina having great hardness and abrasion resistance. The crystalline nature of alumina makes it insoluble in the regular chemical reagent at room temperature. It is using in many artificial implant fabrications since 1970s, when alumina introduced into artificial femur head [18]. Alumina is highly stable oxide because of ionic and covalent bond present between aluminum and oxygen. These strong bonds, avoid alumina from galvanic reactions or corrosion. Due to the surface energy and surface

smoothness of alumina, it has excellent properties like good corrosion resistance, low wear, and friction coefficient. The aluminum ions have occupied the interstitial sites in the hexagonal structure of Al_2O_3 [22]. The properties like abrasion resistance, strength, and chemically inertness of alumina increase its application in hard tissue engineering. If the alumina implanted in bone marrow, no toxic effect produced in circumferential tissue [23]. The tensile strength can increased by reducing its grain size and by increasing its density. The better substitute to surgical metal alloys can produced by generating pure alumina. Due to the good mechanical behavior, alumina implants leads to long time survival predictions.

1.2. Zirconia (ZrO_2)

Zirconia firstly recognized by Martin Heinrich Klaproth in 1789 and used as a pigment for ceramics for a long time. The zirconia exist in three crystalline form i.e. monoclinic at normal temperature (naturally occurring), cubic and tetragonal at higher temperature. The phase transformation from tetragonal to monoclinic, enhance the toughness because monoclinic is a stable phase at low temperature. The mechanical properties can reduced by doing phase transformation that can lead to cracking. So partially stable zirconia with normal mechanical strength can used in the medical field for implant fabrication [24]. The best example of partially stabilize zirconia is yttria stabilized zirconia. Yttria used to stabilize the phases (tetragonal and cubic) of zirconia and avoid phase transformation. Yttria also used to stabilize zirconia-based implants having better static and fatigue strength [25]. A single water molecule can induce the phase transformation from tetragonal to monoclinic that can lead to surface roughness and micro cracking. Therefore, after several years of implantation, femoral heads start to degrade slowly in the body [26-28]. The nonmetallic compounds such as MgO, CaO, and Y_2O_3 used to improve the stability of zirconia. It has many advantages that create interest over other ceramic materials because of its phase transformation mechanisms that enhance the toughness, which manifested in components made out of them. The good mechanical behavior and wear performance of Zirconia makes it a superior ceramics than alumina [29]. It is a brittle transition metal oxide, which induce the early bone growth and development. It has good mechanical properties with suitable biocompatibility. The specialists on Zirconia as biomaterials began since a quarter century and now Zirconia is in clinical use in complete hip substitution (THR) however, improvements are in advance for application in other medicinal gadgets [30].

1.3. Zirconia-Alumina

Zirconia and alumina are having many points of interest on fracture robustness and mechanical properties. Water molecules that leads to cracking and instability of surface grains [31, 32] full filled the presence of oxygen vacancy in zirconia. The issue of surface instability and cracking removed by formulating zirconia-alumina composite [33]. The improved mechanical and morphological properties detected by using zirconia-alumina composites. The doping of alumina helps to stabilize the both phases (monoclinic and tetragonal) of zirconia [34, 35].

2. Bioactive Materials

Bioactive materials having a positive effect on living tissues and having ability to induce a response that helps in the regeneration, repair and reconstruction of body tissues [36]. When bioactive material introduced into the body, it produces a specific biological response that starts to make a chemical bond between the material interface and the tissue. In tissue engineering, bioactive materials are specially used to repair orthopedic, craniofacial (skull and face bones) and dental, chronic osteomyelitis. Examples of bioactive materials are hydroxyapatite, calcium phosphate. Bioglass dental implants got a significant success in the last few years and become a promising material [37]. Bioactive materials generate a hydroxyl apatite layer when immersed in the simulated body fluid (SBF) for some days. The generation of this artificial apatite layer is similar to the inorganic phase of natural human bones. Due to its equivalence, the layer can bond with collagen fibrils and thus to the bone. The surface reaction is dependent on the material composition and small changes can totally suppress the bioactive property [38].

2.1 Bioactive glass and glass ceramic

Larry Hench firstly designed and coined the term bioactive glass1969. The main constituents of glass ceramics are CaO and P_2O_5 [20, 16]. The presence of Ca and P increase the effectiveness of bioglass because these are the main constituents of the mineral phase of bone. Some other precursors (MgO or CaF_2, and Na_2O by K_2O) are also becoming the part of bioactive glass with more or less bioactivity changes. The glass fabrication process altered by addition of small amount Al_2O_3 and B_2O_3 to avoid the inhibition of the bioactivity, they may substitute SiO_2 [39]. The bioglass is a system of SiO_2-CaO-NaO_2-P_2O_5, which is widely used as implants. They have an effect on a living organism, tissue, or cell. Bioglass makes chemically stable bonds and attachments with the skeletal system of the host body. They form apatite layer when come in contact with body fluid. Thus, bioactivity is depending upon the apatite formation that show the compatibility of bioglass with tissues [40]. This apatite leads to the formation of bone like structure that demonstrate the osteoconductivity in bioceramic material. The microstructure of bioglass strengthens the bending strength (215 MPa) and compressive strength (1080 MPa) of whole sections of implant material [41]. Glasses of various compositions (45S5, 58S, 70S30C, S53P4) can obtained and they show very different properties. The silica and apatite are two significant crystal phases of bioglass. Ca and P rich

interface layer generated in between the material and tissues of bone by solid-state reaction. The interface reaction understood as a chemical process, which includes a slight solubility of the glass ceramic [42]. Certain structures of glasses, ceramics, and composites appeared to frame a mechanically strong bond to the bone.

3 Biodegradable Materials

These materials are proficient to react and broken down rapidly when come in contact with body tissue fluid. Biodegradable materials completely degrade into the body tissue fluid because the tissue fluid break down the chemical structure of the materials. These materials do not require secondary surgery for the removal of implants from the body. These are completely absorbed by the body tissues and become the part of hard tissue [43, 44]. The chemicals produced by the ceramic resorption should be able to be treated by the normal metabolic pathways of the body without producing any toxic effect. A number of polymers, ceramics and metals based biodegradable implants were synthesized and studied clinically. The controlled degradation of these materials can be more beneficial for the patients [45, 46].

3.1 Calcium Phosphate Ceramics (CPC)

Calcium phosphate based materials are using in biomedical field since 20 years. It is an inorganic phase of bone minerals and helps in the calcification and the resorption process of bone with improved biological affinity and activity. From last three decades calcium phosphate based materials used as substitutes for bone tissues. These used in implants fabrication, coatings, and clinical settings [47-49]. The scaffold of calcium phosphate should well designed with controlled porosity and structure. Natural bone contains 25% water, 60% inorganic mineral, and 15 % organic mineral phases. Bone consists of 70% inorganic mineral phase that can replaced by calcium phosphate. The 3D plotting helps more in the scaffold fabrication. The 3D designed scaffolds express better porosity and mechanical properties that enhance cell attachment and proliferation. The morphology and microstructures of composites and scaffolds characterized by electron microscopy [50, 51]. Bone mineral gems are extremely small and have an expansive surface territory. Despite what might expected, calcium phosphate biomaterials display an insignificant surface area and have solid precious crystal bonds. Hydroxyapatite and β-tricalcium phosphate has shown very good stability, biocompatibility, and osteoconductivity that increases the scope of these materials in tissue regeneration. The porous calcium phosphate and composites are using as a carrier for drugs, ions, biological agents, suitable for the tissue engineering. Amorphous calcium phosphate and poly (L-lactic acid) nano fibrous composites well applied for sustained release of ions because of its well porosity and biological characteristics [52].

3.2 Hydroxyapatite

Synthetic hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) is similar to a natural mineral form of the apatite in bones and widely used for bone repairs. It is a hexagonal alloplastic material. It is a biocompatible and crystalline. Henceforth, its structural composition is same as to natural bone [53]. It has nominal stoichiometric Ca/P atomic ratio of 1:67. The hydroxyapatite makes similar chemistry with the mineralized phase of bone [54, 55]. It produces an osteoconductive effect with high biocompatibility that form bone bonding between material and tissue. Although hydroxyapatite has, high, constituent similarity to bone but mechanical properties is very low as compared to natural bone. At nanoscale, hydroxyapatite power has become the main attraction to improve biological and mechanical properties. To get nano range hydroxyapatite particles, many methods are investigated e.g. hydrothermal [56], micro emulsion [57], sol gel [29, 58], co precipitation [32], and mechanochemical [59]. Hydroxyapatite is an excellent carrier of growth factors and osteogenic cell, which significantly enhances their efficacy as a carrier in the future [60]**.** HA is brittle in nature with lower young modulus and fracture toughness [61]. Differences in composition of apatite in natural bones and tooth enamels revealed in table 2.

Table 2. Composition of Apatites and hydroxyapatite

Constituents	Apatite In enamel (wt %) in bone (wt %)		Hydroxyapatite
Ca	36	24.50	39.60
P	17.10	11.50	18.50
Na	0.50	0.70	
K	0.08	0.03	
Mg	0.44	0.55	
F	0.01	0.02	
Cl	0.30	0.10	
CO_3^{2-}	3.20	5.80	
Trace Elements			
Ca:P (Molar ratio)	1.62	1.65	1.67

The use of HA as an implant material should be, in the first place, recognized for its good biocompatibility. The biocompatibility of HA was widely examined and stated by many authors [62-67]. It has been studied that the presence of HA did not disturb the normal process of bone tissue maintenance and bone - HA interface [63]. Contamination free HA fabricated by freeze-drying confirmed by XRD analysis. *Lee and co-workers* fabricated crack free six types of HA scaffolds, these scaffolds did not affect the crystallinity of HA. The porosity of scaffolds varies by changing HA concentration [68].

Properties of bioceramic materials

1 Mechanical Properties

All the bioceramic materials are having different properties (Table 3.) so they have different biomedical applications. The applications of materials depend upon their anticorrosive and biological behavior. The glass ceramics are risk-free and easily make bonding with the bone without producing toxicity. Therefore, the composites are more useful due to their inert and bioactive properties. These composites may consist improved biological and mechanical properties.

Table 3. Comparative mechanical properties of biomaterials [69, 70, 17]

Biomaterials	Density (g/cm^3)	Bond Strength (GPa)	Compressive strength (MPa)	Young Modulus (GPa)
Alumina	3.3-3.9	300-400	2000-5000	260-410
Zirconia	6.0	200-500	2000	150-200
Bioglass	2.5	50	600	75
Hydroxyapatite	3.1	120	500-1000	73-117
Glass Ceramic	2.8	215	1080	118
Bone	3.88	60-160	130-180	3-30

2 Biological Properties

a) Similarity with bone

The some properties like composition, porosity and mechanical properties tries to make similarity between bone and ceramic materials. The macro porous (100-500 μm) structure of bioceramics allows tissue ingrowth as well as microstructure (1-10 μm) allows ingrowth of blood vessels during hard tissue formation [71]. The hydroxyapatite derived from natural resources showing similar interconnecting pore structure as bone. However, in case of synthetic bioceramic materials, pores created by using progenitors with different methods. In some synthetic bioceramics, pores and crystal size influenced by final sintering temperature. These bioceramics show degradation in cell mediated acidic conditions. *In-vitro* and *in-vivo* degradation of natural origin and synthetic origin bioceramics depends upon specific surface area, porosity, crystallinity, and structural composition. The bioceramic scaffold with the property of osteoconductivity and inductivity helps to form new bone by allowing cell proliferation, attachment and migration of bone cells [72]. The scaffolds derived from bioceramics are having relevant mechanical properties to the natural bones as shown in table 3. The success of scaffolds depends upon composition and particle size that may interfere with hard tissue formation [73].

b) Bioactivity

Every material has distinct bioactivity or the ability to make bonding with body tissues. The immune response of the body would be different for different bioactive materials. The bioactivity of any material depending upon various factors, including physiochemical and morphological characteristics of materials. Bioceramic is an inorganic material that have a biological or synthetic origin. The bioactive ceramics including bioglass and different types of calcium phosphate provide the best substitutes to autografts and allografts. The fabrication methods and composition of bioceramics affect the bioactivity of materials [74]. Bioceramic materials also release calcium and phosphate ions that makes a Ca-P layer. When the material start to dissolve other ions including Mg^{2+}, K^+, CO_3^{2-} and Cl^- are also assimilated and form crystal of calcium phosphate that enhance bone deposition. SEM with EDX confirm the generation of Ca/P layer that enhance the cell adhesion on the surface of material [75]. The bioceramics show four type mechanism of tissue attachment including; (1) fully inert and dense surface that allows easy cell attachment and tissue on growth, (2) porosity allows to tissue ingrowth, (3) the dense phase allow for surface attachment by chemical bond formation and (4) easily break down and integrate with surrounding tissue. The outer porosity of material enhances the interlocking and make connectivity with the surrounding tissue. While inner dense part of a material performs as a load-bearing region. The assimilation of biological agents with biomaterials can enhance the biological activity and clinical potential [69, 76]. These biological agents change the surface chemistry of ceramic materials. Due to phase similarity between bioceramic and inorganic bone part, biological agents helps to attach bone cell to the surface of the material and allow for the strong bond formation between the two interfaces. According to Hench and Andersson, the strength of bonds between bone and the material vary from 15 to 25 MPa that is better than inert glass (0.5 MPa) and smooth titanium (2 MPa) [77]. The material starts to dissolve and releasing ions in the tissue fluids that directly affect the function of bone cell [78, 79]. The adhesion of cells on the surface of the scaffold can simply examined by using confocal laser scanning microscopy (CLSM). The CLSM shown pre-osteoblast cells attachment on HA scaffold i.e. similar to bone like structures. The stretched filopodia and spread cytoplasm proved the good biocompatibility of HA scaffolds [69].

c) Biodegradation

The cell-mediated degradation supports acidic conditions that consisting phagocytic cells and osteoclasts, referred as *in-vivo* degradation [80]. The dissolution of material can influence by material related parameters like structure, composition, porosity, surface area, crystallinity [81, 69, 82]. It also depends upon properties of physiological solution including pH, concentration of ions, temperature, and protein concentration and buffer capacity. The degradation of ceramic material and development of apatite layer on the materials surface studied by using simulated body fluid (SBF). Because SBF is tris-buffer that consisting similar ionic concentration and pH to the blood plasma. For *in-vitro* testing SBF is become a good substitute to blood plasma. The material is required to place in the physiological solution for some time that give the information about material surface, chemical reactivity and composition of the solution [83]. The resultant hydroxyapatite layer formation in SBF confirms the chemical reactivity and functional ability of materials, i.e. bond formation between

material and host tissue cells. However, serum proteins (albumin and globulin groups) can resist the hydroxyapatite layer formation [75]. The generation of surface apatite or Ca/P layer depends upon dissolution-precipitation reactions that can analyzed by FTIR and SEM with EDX. These dissolution-precipitation reactions modify the surface charge chemistry of biomaterials when immersed in SBF that can analyzed by zeta potential measurements. After formation of calcium-phosphate layer, the surface charge of material move from negative to positive. By modification, chemical reactivity, degradation rate, and strength of the materials can be enhanced [84].

d) Bio toxicity

The development of new generation advance bioceramics increases the risk of toxicity in the human body. Before bioceramics clinical applications, the performance and biocompatibility should tested at the cellular level. The detailed biological, mechanical, physiochemical and morphological testing analysis is required before material implantation. It ensures the long life of the implants without local or systematic toxicity. Sometime nanosized wear particulates of bioceramics behave in a different way that produce toxicity. Thus, these small wear particulates produce chronic effects like inflammation and osteolysis. Therefore, toxicity evaluation of bioceramic materials is becoming major criteria before clinical trials [85]. The best option for toxicity evaluation is to take trial of material on the human body but is not easy because of legal and ethical considerations. The long time direct contact of bioceramic implant with the body tissue, enhance the risk that becomes a critical issue [86]. Cytotoxicity, histotoxicity, and genotoxicity evaluation is mandatory in case of permanent replacement of tissue because it directly affects the surrounding tissues. The ISO and FDA (Food and Drug Administration) have given various procedures, standards, protocols and guidelines to estimate the biocompatibility of newly formed advance materials [87]. The three phases of clinical testing as recommended by ISO (International Organization for Standardization) need to follow to check the biocompatibility of bioceramics [88]. The first phase of ISO provides the test procedures and methods for biological characteristics evaluation. It including the important aspects like positive, negative control materials, choice of cell lines and media and extraction conditions. The second phase gives information about animal welfare requirements, third phase of ISO provides the guidelines for test procedures, and test related issues [85]. The guidelines of FDA for materials testing is also similar in some areas, but the requirements and procedures for test are slightly different. The non-clinical testing, including in-vitro and in-vivo trials of biomaterials performed with GLP (Good Laboratory Practice) regulations. Thus, biocompatibility validation of a material need to follow GLP regulations that prevent biocompatibility related issues [89].

Conclusion

This review article has given the brief explanation of traditional and current synthetic bioceramic materials used for the hard tissue engineering. These materials enhance the compatibility, suitability, and life of the implants. These materials need further research for the improvement of quality and stability of implants for the patients. Still, some materials, including, hydroxyapatite, and bioactive glass ceramics need more research for the improvement of mechanical properties. Bioglass and bioglass based materials are highly biocompatible and rapidly degrade in the body. However, mechanical property of bioglass based materials is still a major problem. So metal-bioglass composites can used to get desired mechanical properties in some cases. The main benefit of bioglass is that it produces apatite layer when it encounter body fluid. That apatite layer induce the bone regeneration. Other materials as if Alumina is also producing good mechanical properties, but the use of zirconia with alumina enhance the mechanical as well as biological characteristics. Hydroxyapatite is naturally similar with the bone hydroxyapatite therefore it is used for orthopedic as well as dental applications. These synthetic materials are having some advantages as well as disadvantages. Therefore, bioceramics are more favorable material than other materials. The nano structure based bioceramic materials can be more suitable for the future applications.

Compliance with ethical standards

In this research work, all the authors announce that there is no conflict of interest. This research work does not contain any studies with human participants or animals performed by any of the authors.

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