Overview of Biocompatible Materials and Their Use in Medicine

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This survey presents a thorough overview of the main types of biomaterials used for the manufacturing of implants. The use of different materials for the creation and refinement of medical devices aims at optimizing their properties and raising the level of safety for the patients. The purpose of the study is to classify the most common bulk materials used in medicine according to their nature, interaction with the host tissues and their function in the organisms. Some important advantages and disadvantages of the different classes of implant materials are considered. In the last few years there is a strong tendency toward the surface modification of biomedical devices. Various trends in processing of the materials are focused on increasing their corrosion resistance, wear resistance, biocompatibility and microbiological properties.

INTRODUCTION

A large variety of implant devices have improved the quality of life of thousands of people every day. The advancement of technology and the development of modern medicine lead to continuous increase of the diversity of biomaterials. By definition *biomaterial* is any substance (other than a drug) or a combination of substances, natural or synthetic, that can be used for a period of time, independently or as part of a system which treats, augments or replaces any tissue, organ or function of the body. All materials used for fabrication of implants should exhibit a number of properties which do not change after a long periods of contact with the biological environment. This means that the material or its products do not cause cell death, chronic inflammation or damage of the functions of the cells. The requirements to the biomaterials are very strict, due to the fact that in the human body they are exposed to the aggressive effect of body fluids (enzymes, organic acids, etc.) and external factors. It should be noted that human tissue is extremely sensitive to foreign substances and it is possible that they induce symptoms of poisoning and rejection. A number of mechanical properties such as tensile strength, hardness, elasticity, suitable density, wear resistance, etc. are also essential. These parameters correspond to the function that the implant will serve in the organism. For example, a materials used for vessel reconstruction should have high flexibility, whereas, for the making of hip prosthesis the materials should have mechanical strength and high corrosion resistance.

All the above-mentioned considerations show that the creation of biocompatible materials and the construction of implant devices is a difficult task.

CLASSIFICATION OF IMPLANT MATERIALS

According to their function biomaterials can be classified as follows:

Orthopedic (artificial hips, knees, shoulders, wrists, intervertebral disks, fracture fixation, bone grafts), cardiovascular (heart valves, pacemakers, catheters, graft, stents etc.), dental (enamels, fillings,
prosthetics, orthodontics), soft tissues (wound healing, reconstructive and augmentation, intra-ocular lens), surgical materials (staples, sutures, scalpels, surgical tools).

According to their interaction with the host tissue they can be categorized into bioinert, bioactive and bioresorbable materials. The bioactive materials evoke a specific biological response and make connections with the host tissue. The inert material has minimal interaction with the host tissue and stays isolated. The resorbable materials are the ones which resorb gradually into the human body. The mechanism of this process is different and varies from dissolution to hydrolysis or even corrosion. While the implant is resorbing a new bone tissue is forming in its place.

According to their nature biomaterials can be classified as polymers, ceramic materials, metals and composites.

**Polymers**
They are characterized with high molecular weight and long hydrocarbon chains. The technological possibilities in the production of polymers are numerous. This contributes to the creation of various products used for fabrication of implants.

There are two kinds of polymers – synthetic and natural. The natural polymers represent more complex structures. They are not cytotoxic but are often immunogenic. One of the most widely used natural polymers is Collagen I, which can be found in skin, bones and tendons. Synthetic polymers have found their application in orthopedics, dental medicine and as tissue replacements. A big advantage of these materials is the fact that the isotonic physiological solution, which is extremely hostile to medical implants, has little effect on the components of polymer materials. Moreover, there is a slight difference in the elasticity of polymers and bones and this reduces the pressure and bone resorption. A large number of polymers are characterized with high biocompatibility. The main factors, which influence the biocompatibility, are the chemical structure, functional groups and molecular weight. For example, the higher the molecular weight of polyethylene glycol, the lower the protein adsorption. For diethylaminoethyl dextran this increase in the molecular weight leads to a considerable cytotoxic effect. Other properties like wetting ability, hydrophobicity, electrical charge and surface morphology have also great importance.

One disadvantage of these materials is the fact that products which are released in the process of polymers degradation can lead to deterioration of their mechanical qualities and unwanted side effects. Another inconvenience comes from the low solubility, excessive elasticity, the risk of fatigue, etc.

There is a wide diversity of polymers with proven medical applications. For example, resorbable synthetic sutures, bolts and bone plates are made of polycaprolactone. Poly-methyl methacrylate has found its application as a main component is bone cement. Poly dimethyl siloxane is used for producing artificial heart valves. Polymer materials are also used in manufacturing sutures, cements, artificial tendons, teeth implants, spacer in intervertebral implants, liner in acetabular cups for hip replacements, carrier for drug delivery, etc.

**Ceramic Biomaterials**
According to their biological behavior bioceramics follow the standard classification and are divided into three main groups: bioactive (for example: hydroxyapatite, bioglass and glass-ceramics), inert (for example: aluminium oxide, zirconium oxide) and resorbable (for example: calcium phosphates).

From a physicochemical point of view these biomaterials are hard, brittle and insoluble in water. Their advantages are high corrosion resistance, inertness, hardness, low friction, wear resistance, low thermal and electrical conductivity. Furthermore, another very important fact is that they have high biocompatibility. On the whole, the ceramic biomaterials do not cause allergic reactions and do not show signs of cytotoxic effect.

Disadvantages of this type of materials are low impact resistance, difficulties in processing and fabrication. The first ceramic material used in medicine was aluminum trioxide with high density. It is still used for fabrication of maxillofacial implants, bone screws for knee prostheses, blades, and other dental implants. It was experimentally proven that anodic aluminum oxide films with low thickness (10-20 microns) are capable of making technical aluminum alloy biocompatible.

The first experimental research on the use of zirconia as dental implant was published in the 1970’s. Due to its suitable qualities as fracture toughness, increased strength and high biocompatibility, zirconia based ceramics have nowadays extensive use in bone reconstructions. They can be used as an alternative to titanium implants in dentistry. The colour of zirconia is similar to the colour of human teeth and by using
it the blue staining of the gingiva after baring of the titanium implants can be avoided.\textsuperscript{16}

The Ca-P-based ceramics and hydroxyapatite have a composition, physical and chemical properties which are very similar to those of the bone. These ceramic materials promote the formation of new tissues. They are used mainly as coatings for metal implants, which provide osseointegration.

Bioceramic materials are widely used as bone replacements in hip, knee, dental and maxillofacial reconstructions.

**Metals and Metal Alloys**

In the year 1895 W. Lane used metal screws for bone fracture fixation for the first time but later some problems like corrosion and insufficient strength occurred.\textsuperscript{17} Stainless steel was first introduced as biomaterial in the 1920s.\textsuperscript{18} It has the highest level of corrosion resistance of all known materials. The first alloys based on cobalt – CoCrMo and CoCrW were found in 1907 and were first considered to be useful for dental practice due to their resistance in the mouth cavity.\textsuperscript{19} Cobalt-based heart valves were implanted in the 1960s and they function in the organism for about 30 years. At about the same time the biocompatibility of titanium screws in bone tissue was found and later it was proved that these materials become overgrown with tissue and therefore are extremely suitable for orthodontics and maxillofacial surgery.\textsuperscript{20} The first titan-nickel alloys were manufactured in the 1960s. Their mechanical properties were completely different from the ones of the conventional metals – high resistance, low level of ductility and toughness. Stabilized titan-nickel alloy called nitinol was used for clinical purposes in 1972. The first superelastic NiTi – alloys were manufactured in 1978.\textsuperscript{21}

There has been a constant flow of innovative materials and aspirations for improving their qualities. The diversity of metals and alloys with medical application is getting wider and wider with the advancement of technology.

**Stainless steel**

316L stainless steel is a subtype of 316 steel alloy with modified chemical composition. The extra-low carbon content of 316L reduces deleterious carbide precipitation as a result of welding process and the alloy exhibits excellent corrosion resistance around welded areas. Furthermore, this alloy is characterized with inertness, lack of magnetism, toughness and higher ductility compared to titanium due to the hexagonal crystal structure.

Stainless steel has been implanted for many years and this is evidence of its great biocompatibility. Due to the presence of chromium in its composition, a protective oxide film, which sets the corrosion resistance of stainless steel is formed on the surface of the products. This important quality is further developed through the years by adding molybdenum and reducing the amount of carbon. The good ductility of stainless steel makes the producing of orthopedic plates easier.

One of the disadvantages of this material is the high amount of nickel in it (10-14%), which can cause reactions in tissues and dermatitis.\textsuperscript{22} In some cases its hardness can cause stress fractures and a delay in the healing process.\textsuperscript{23} Stainless steel is used for the making of prosthetic joints, dental implants, cranial implants, load-bearing orthopedic, pacemaker, bone fixation. New types of stainless steel where nickel is replaced with high amount of nitrogen have been developed for decades.\textsuperscript{24} The nitrogen is a stabilizer for austenitic structures, which are not ferromagnetic as contrasted with the ferrite and martensitic ones.\textsuperscript{25} Some experimental tests show that these new materials possess high strength, high elasticity, corrosion resistance and higher biocompatibility than nitinol.\textsuperscript{26}

**Cobalt-chromium alloys**

Co, Cr, Mo, W, Ni and Fe is the composition of these alloys enable the fabrication of extremely hard, non-magnetic, wear resistant, heat resistant implants with high corrosion resistance in body fluids.\textsuperscript{19} The amount of carbon and the microstructure are controlled in the process of producing of the alloys. They are distinguished for their mechanical strength and greater wear resistance in contrast with the titanium implants. On the other hand, they are characterized with lower biocompatibility.\textsuperscript{27}

One of biggest disadvantages of cobalt-based alloys is metal ion release in the surrounding tissues after long-term exposure to body fluids. It was proven that due to interactions with the aggressive surrounding environment orthopedic implants undergo dissolution of the material.\textsuperscript{28} The metal particles are capable of spreading in the organism and they can also be harmful for different organs. According to some authors, CoCr nanoparticles show higher toxicity in comparison with particles with micron size.\textsuperscript{29}

However, according to another research, CoCr nanoparticles are ejected from the organism and there is no solid proof that they cause unwanted reactions in tissues. The effect of these particles
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onto the living organisms has not been examined in detail yet.\textsuperscript{30}

The CoCr-implants are mainly used for the fabrication of orthopedic prostheses and in joint replacement devices. Co-based alloys are also used for cardiovascular pacing leads, styling, catheters and orthopaedic cables. Their biggest disadvantages are the high expenses in manufacture and the difficulties in processing after casting.\textsuperscript{19} One solution to this problem is the electrochemical obtaining of CoCr-alloys from highly effective chromium electrolyte\textsuperscript{31}, which show better results in \textit{in vitro} testing compared to the medical steel \textsuperscript{32}. There are different methods for surface treatment mentioned in literature, aiming at isolating and protecting these materials such as passivation, electropolishing, covering with hydroxyapatite, nitrogen, titanium, etc.

\textit{Titanium and titanium alloys}

The most widely used implant materials in this group are pure titanium, Ti6Al4Vand $\beta$-titanium alloys. Ti6Al4V, Ti6Al4V ELI and Ti6Al7Nb are alloys with improved strength, hardness and inertness.\textsuperscript{33}

In biological environment they show great corrosion resistance, biocompatibility, immunological tolerance, etc., attributed to the protective oxide film, which is formed naturally onto the surface due to the oxygen in the surroundings.\textsuperscript{34} These materials exceed the stainless steel and the CoCr-alloys in experiments with cell cultures.\textsuperscript{35} Another advantage is that they do not cause galvanic corrosion.\textsuperscript{36}

A big disadvantage of titanium materials is their low wear resistance and the difficulties in the mechanical processing of implants due to their hardness. They do not show antibacterial activity and bacteria can easily stick to their surface.\textsuperscript{37} Many previous studies have revealed interesting new approaches in different surface modifications aiming at the creation of antibacterial effect of titanium implants – covering with bio glass, gold, silver, local application of antibiotics or other antibacterial drugs, included in the composition of the coatings, etc. Biochemical approaches such as layer-by-layer deposition of polyelectrolyte films, phage display-selected surface binding peptides and self-assembled DNA monolayer systems are suggested in order to provoke specific cell or tissue response.\textsuperscript{38}

\textit{Nitinol}

This NiTi-alloy, containing 48-52\% nickel is nowadays well-known engineering and medical material. It is characterized with unique qualities – pseudoelasticity and shape memory – which are a result of its specific crystal structure and thermodynamics. They allow the restoration of the shape to its initial shape even after huge deformations and also preservation of the deformed shape to a certain temperature.\textsuperscript{39}

Compared to other metal materials with a wide clinical application (stainless steel 316L and CoCr-alloys), NiTi has lower hardness and higher elasticity.

Nitinol is also used in medical practice because of its great biocompatibility which is a result of the formation of an oxide film from TiO\textsubscript{2} on the surface.\textsuperscript{40} NiTi shows higher corrosion resistance and histological biocompatibility compared with Ti6Al4V. This alloy is considered to be one of the most perspective ones. However, because of its high nickel content and as a result of galvanic corrosion processes there is some evidence of allergic and carcinogenic reactions which are still being examined.\textsuperscript{41}

In modern medicine nitinol is used for producing surgical threads, self-expandable stents in vascular and neurosurgical reconstructions, to avoid pulmonary embolism, etc.\textsuperscript{42} In many cases NiTi stents are often covered with different kind of polymer material to avoid allergic and carcinogenic reactions.

\textit{Magnesium alloys}

In recent years, there is a growing interest to these alloys due to their good mechanical properties such as strength, good heat and electric conductivity, biocompatibility, non-toxicity. Magnesium is the lightest of all structural metals and its thickness is close to the one of the cortical bone.\textsuperscript{43}

The research connected to these materials is based on the idea of creating biodegradable implants. Magnesium and its alloys are notable for their low corrosion resistance and it enables the in vivo degradation of the implants. These materials are stronger than polymers, more enduring and ductile than bioceramics and they are also bioactive.\textsuperscript{44}

Magnesium implants can stimulate the forming of new bones which is extremely important in fractures.\textsuperscript{45}

Reactions to the human body like toxicity, allergies, osteointegration are not yet examined in details, but there is evidence of successfully implanted magnesium alloys in fractures without any negative consequences for the patients. There is a growing interest to the modification of the surface of this materials in order to control the pace of biodegradation, their corrosion resistance, biocompatibility and antibacterial activity. In literature are mentioned coatings such as Ca-P, protective oxide...
films, biodegradable polymer coatings, etc.\textsuperscript{46}

**Composite materials**

Composites contain at least two materials, different in their nature, working together and forming the implant design. All of the abovementioned materials possess their own characteristics and combining them can lead to a decrease of their disadvantages - brittleness, ion leaching in surrounding tissues, biocompatibility, bone resorption, etc.

These large group of biomaterials can be classified according to the type of the basic matrix – metal (HA/Ti, HA/Ti6Al4V), ceramic (stainless steel/HA, glass/HA) polymer (carbon/PEEK, HA/HDPE) or according to their behavior in the biomedium – inert (carbon/carbon, carbon/PEEK), bioactive (stainless steel/Bioglass®, HA/HDPE, HA/Ti6Al4V) and resorbable (TCP/PLA, TCP/PHB).\textsuperscript{47}

According to recent literary sources special attention is given to the so-called bioglasses. It is thought that they interact with the tissues at a cell level.\textsuperscript{48}

Bioglasses represent bioactive materials, whose composition includes SiO\textsubscript{2}, Na\textsubscript{2}O, CaO and P\textsubscript{2}O\textsubscript{5}.

The advantages of the composites are connected to their ability to improve cell adhesion and direct bone fixation.\textsuperscript{49}

Composites are widely used in medical practice due to the fact that there is a wide variety of materials in this group of biomaterials. The most common composites used in orthopedics are fibre reinforced polymer composites. Polymer matrix covered with composite materials are among the most preferred for manufacturing of upper and lower limbs prostheses.\textsuperscript{50}

Bioactive composite bone cements are used in dental practice. Composite materials are also used for soft tissues replacements - bulk space fillers, catheters, ureter prostheses, tendons and ligaments, vascular grafts, etc. Due to the lack of magnetism they are also used for production of medical equipment and instruments - surgical clamps, head rest frames, X-ray film cassettes and CT scan couches.

**Conclusion**

This study demonstrates that the developing and modification of the main types of materials used in medical practice is quickly expanding through the years. The aim of the researchers in this scientific field is to optimize the qualities of the biomaterials in order to prevent human health. The requirements to their mechanical, biological and antibacterial properties are extremely high. The surfaces of the used medical devices are in direct contact with the living tissues, therefore, surface modifications are among the most widely used methods for improving their qualities. Some new approaches in this direction are explored with a view to ensure proper functioning, long life and harmlessness of medical devices.

A perfect material which is accessible, easy to work with and biocompatible to the organisms has not been found yet, but the great variety of technological and creative solutions in this direction guarantees the achievement of ever better results.

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**References**

1. Bergmann CP, Stumpf A. Biomaterials BT. - Dental Ceramics: Microstructure, Properties and Degradation. In: Bergmann C, Stumpf A, editors. Berlin, Heidelberg: Springer Berlin Heidelberg; 2013:9-13.
2. Jones JR, Hench LL. Biomedical materials for new millennium: perspective on the future. Mater Sci Technol 2001;17(8):891-900.
3. Hench LL. Biomaterials: A forecast for the future. Biomaterials 1998;19(16):1419-23.
4. Hermawan H, Mantovani D. Degradable metallic biomaterials: the concept, current developments and future directions. Minerva Biotecnol 2009;21(4):207-16.
5. Bohner M. Resorbable biomaterials as bone graft substitutes. Materials Today 2010;13(1):24-30.
6. Nagaoka S, Mori Y, Takiuchi H, et al. Interaction between blood components and hydrogels with poly(oxyethylene) chains. In: Shalaby SW, Hoffman AS, Ratner BD, Horbett TA, eds. Polymers as Biomaterials. Boston, MA: Springer US; 1984:361-74.
7. Fischer D, Li Y, Ahlemeyer B, et al. In vitro cytotoxicity testing of polycations: influence of polymer structure on cell viability and hemolysis. Biomaterials 2003;24(7):1121-31.
8. Wang Y, Robertson JL, Spillman WB, et al. Effects of the chemical structure and the surface properties of polymeric biomaterials on their biocompatibility. TL - 21. Pharm Res 2004;21(8):1362-73.
9. Silver FH. Scope and markets for medical implants. In: Biomaterials, Medical Devices and Tissue Engineering: An Integrated Approach. Dordrecht: Springer Netherlands; 1994:1-45.
10. Yamada S, Heymann D, Bouler J-M, et al. Osteoclastic resorption of calcium phosphate ceramics with different hydroxyapatite/β-tricalcium phosphate ratios. Biomaterials 1997;18(15):1037-41.
11. Vandrovcová M, Áková LBAČ. Adhesion, growth and differentiation of osteoblasts on surface-modified materials developed for bone implants. Physiol Res 2011;8408:403-17.
12. Aldini NN, Fini M, Giavaresi G, et al. Improvement in zirconia osseointegration by means of a biological glass coating: An in vitro and in vivo investigation. J Biomed Mater Res 2002;61(2):282-9.
13. Sáenz A, Rivera-Muñoz E, Brostow W, et al. Ceramic Biomaterials: an Introductory Overview. J Mater Educ 1999;21(5-6):297-306.
14. Kiradzhiyska DD, Feodorova YN, Draganov MM, et al. Influence of surface treatment on the biocompatibility of aluminum substrates promising for medical application. AIP Conf Proc 2016;1722:1-5.
15. Cranin AN, Schnitman PA, Rabkin M, et al. Alumina and zirconia coated vitallium oral endosteal implants in beagles. J Biomed Mater Res 1975;9(4):257-62.
16. Depprich R, Zipprich H, Ommerborn M, et al. Osseointegration of zirconia implants compared with titanium: an in vivo study. Head Face Med 2008;4(1):30.
17. Lee CK, Karl M, Kelly JR. Evaluation of test protocol variables for dental implant fatigue research. Dent Mater 2009;25(11):1419-25.
18. Hendra Hermawan, Dadan Ramdan JRPD. Metals for Biomedical Applications. In: Fazel PR, editor. Biomedical Engineering - From Theory to Applications. IntTech; 2011:411-31.
19. Marti A. Cobalt-base alloys used in bone surgery. Injury 2000;31 Suppl 4:18-21.
20. Roberts WE, Smith RK, Zilberman Y, et al. Osseous adaptation to continuous loading of rigid endosseous implants. Am J Orthod 1984;86(2):95-111.
21. Gravina M, Canavarro C, Elias CN, et al. Mechanics of bone-fracture fixation by stiffness-graded plates in comparison with stainless-steel plates. Biomed Eng Online 2005;4:46.
22. Yang K, Ren Y, Wan P. High nitrogen nickel-free austenitic stainless steel: A promising coronary stent material. Contact Dermatitis 2001;44(2):103-4.
23. Ganesh VK, Ramakrishna K, Ghista DN. Biomechanics of bone-fraction fixation by stiffness-graded plates in comparison with stainless-steel plates. Biomed Eng Online 2005;4:46.
24. Yang K, Ren Y, Wan P. High nitrogen nickel-free austenitic stainless steel: A promising coronary stent material. Sci China Technol Sci 2012;55(2):329-40.
25. Talha M, Behera CK, Sinha OP. A review on nickel-free nitrogen containing austenitic stainless steels for biomedical applications. Mater Sci Eng C Mater Biol Appl 2013;33(7):3563-75.
26. Li M, Yin T, Wang Y, et al. Study of biocompatibility of medical grade high nitrogen nickel-free austenitic stainless steel in vitro. Mater Sci Eng C 2014;43:641-8.
27. Peterson CD, Hillberry BM, Heck DA. Component wear of total knee prostheses using Ti-6Al-4V, titanium nitride coated Ti-6Al-4V, and cobalt-chromium-molybdenum femoral components. J Biomed Mater Res 1988;22(10):887-903.
28. Oztürk O, Türkun U, Ergözlu AE. Metal ion release from nitrogen ion implanted CoCrMo orthopedic implant material. Surf Coatings Technol 2006;200(20):5687-97.
29. Behl B, Papageorgiou I, Brown C, et al. Biological effects of cobalt-chromium nanoparticles and ions on dural fibroblasts and dural epithelial cells. Biomaterials 2013;34(14):3547-58.
30. Madl AK, Kovochich M, Liong M, et al. Toxicology of wear particles of cobalt-chromium alloy metal-on-metal hip implants Part II: Importance of physicochemical properties and dose in animal and in vitro studies as a basis for risk assessment. Nanomedicine 2015;11(5):1285-98.
31. Kiradzhiyska D, Mamtcheva R, Mileva D, et al. On the influence of some factors on the functional properties of electrogalvanic coatings promising for medical applications. Bulg Chem Commun 2015;47:480-6.
32. Kiradzhiyska DD, Mamtcheva RD, Mileva DL, et al. Investigation of chromium-cobalt coated scaffolds on cell cultures in vitro. Folia Med (Plovdiv) 2014;56(4):275-81.
33. Guillemot F. Recent advances in the design of titanium alloys for orthopedic applications. Expert Rev Med Devices 2005;2(6):741-8.
34. Pohler OE. Unalloyed titanium for implants in bone surgery. Injury 2000;31 Suppl 4:7-13.
35. Hendrich C, Noth U, Stahl U, et al. Testing of skeletal implant surfaces with human fetal osteoblasts. Clin Orthop Relat Res 2002;(394):278-89.
36. Disegi JA, Eschbach L. Stainless steel in bone surgery. Injury 2000;31 Suppl 4:2-6.
37. Ren L, Yang K. Antibacterial design for metal implants. Metallic Foam Bone: Processing, Modification and Characterization and Properties. Elsevier Ltd; 2016:203-216.
38. Panayotov IV, Vladimirov BS, Dutilleul PYC, et al. Strategies for immobilization of bioactive organic molecules on titanium implant surfaces - a review. Folia Med (Plovdiv) 2015;57(1):11-8.
39. Otsuka K, Ren X. Physical metallurgy of Ti-Ni-based shape memory alloys. Prog Mater Sci 2005;50(5):511-678.
40. Shabalovskaya S, Anderegg J, Van Humbeeck J. Critical overview of Nitinol surfaces and their modifications for medical applications. Acta Biomater 2008;4(3):447-67.
41. Lukina E, Kollerov M, Meswania J, et al. Fretting corrosion behavior of nitinol spinal rods in conjunction with titanium pedicle screws. Mater Sci Eng C 2017;72:601-10.
42. Duerig TW, Tolomeo DE, Wholey M. An overview of superelastic stent design. Minim Invasive Ther Allied Technol 2000;9(3-4):235-46.
43. Kirkland NT. Magnesium biomaterials: past, present and future. Corros Eng Sci Technol 2012;47(5):322-8.
44. Yazdimamaghani M, Razavi M, Vashaee D, et al. Porous magnesium-based scaffolds for tissue engineering. Mater Sci Eng C 2017;71:1253-66.
45. Staiger MP, Pietak AM, Huadmai J, et al. Magnesium and its alloys as orthopedic biomaterials: A review. Biomaterials 2006;27(9):1728-34.
46. Zhao D, Witte F, Lu F, et al. Current status on clinical applications of magnesium-based orthopaedic implants: A review from clinical translational perspective. Biomaterials 2017;112:287-302.
47. Wang M. Developing bioactive composite materials for tissue replacement. Biomaterials 2003;24(13):2133-51.
48. Porter AE, Taak P, Hobbs LW, et al. Bone bonding to hydroxyapatite and titanium surfaces on femoral stems retrieved from human subjects at autopsy. Biomaterials 2004;25(21):5199-208.
49. Pishbin F, Simchi A, Ryan MP, et al. Electrophoretic deposition of chitosan/45S5 Bioglass® composite coatings for orthopaedic applications. Surf Coatings Technol 2011;205(23):5260-8.
50. Scholz M-S, Blanchfield JP, Bloom LD, et al. The use of composite materials in modern orthopaedic medicine and prosthetic devices: A review. Compos Sci Technol 2011;71(16):1791-803.