MAGNESIUM, ZINC AND IRON ALLOYS FOR MEDICAL APPLICATIONS IN BIODEGRADABLE IMPLANTS

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Abstract

Biodegradable materials are developed for designing temporary medical implants, like fixation devices for fractured bones or stents. At present, polymeric biomaterials such as poly-lactic acid (PLA) are currently used in these applications. The disadvantage of polymers is a low mechanical strength, hardness and wear resistance that is the main limitation for the use in load-bearing implants. For this reason, extensive research activities are focused on metallic biodegradable materials showing higher strength, hardness, wear resistance and toughness. Among various biodegradable metals, only magnesium, zinc and iron also meet the basic requirement of a good biocompatibility. In the present work, magnesium, zinc and iron based alloys are compared in terms of biocompatibility, mechanical properties and corrosion behavior in the human body environment. Advantages, disadvantages and potential application areas of the three groups of materials are demonstrated.

Keywords: Magnesium, zinc, iron, biomaterial, implant

1. INTRODUCTION

Metallic materials have been used in medicine for joint and bone replacements, fixation devices for fractured bones, dental implants etc. for a long time. Metallic materials possess significantly higher strength, elongation and toughness in comparison with ceramic or polymeric biomaterials. Another advantage of metals is their simple production and processing by using well established technological steps like casting, forging, extrusion, rolling and other. In orthopaedics and traumatology applications, mostly utilized materials are Ti-based alloys (Ti, Ti-6Al-4V, Ti-6Al-4Nb), stainless steels (SUS 316L), Co-based alloys (Co-Cr-Mo). In stents, i.e., tubular implants for restoring damaged blood vessels, oesophagus etc., stainless steels or Nitinol (shape memory Ni-Ti alloys) are currently used. Dental applications employ stainless steels, Nitinol, noble metals and alloys (Au, Pd) and amalgams (Hg-Ag-Cu-Sn alloys). All the above materials have a relatively long tradition in medicine and are generally considered as corrosion resistant in human body fluids due to spontaneous passivation or noble nature [1].

In additon to corrosion resistant biomaterials, biodegradable materials have also attracted a great attention in material engineering and medical community in the past decades. Any biodegradable material for medical use should progressively corrode and degrade in the human body environment to produce non-toxic, non-alergic and non-carcinogenic compounds which can be readily excreted by natural biological processes in the human organism. Biodegradable materials are very suitable for implants with temporary functions like fractured bone fixation screws, plates, nails and stents. When using inert biomaterials for these purposes, a second surgery is often needed to remove them after the healing process has completed. In contrast, a biodegradable material is naturally decomposed and replaced by healing tissue. No surgery for removing it is necessary which reduces patient inconvenience and health cost. Nowadays, biodegradable fixation devices and stents are fabricated from polymeric biodegradable materials, for example, polylactid acid (PLA). But the main drawbacks of polymers are insufficient strength, hardness and wear resistance which limit their use in load-bearing implants. For this reason, extensive research and development activities all over the world are devoted to metallic biodegradable materials possessing higher strength, hardness and wear resistance than polymers and also a good biocompatibility. The most promising candidates for designing biodegradable metallic implants are magnesium, zinc and iron alloys [2-4].

In this study, mechanical properties, corrosion behavior in simulated body fluids and biocompatibility of magnesium-, zinc- and iron-based alloys are characterized and compared. Positive and negative features of these groups of biodegradable alloys are shown. Both results from scientific literature and authors´ own results are used in this comparison.

2. BIOCOMPATIBILITY

Magnesium: Magnesium is an essential element for proper biological functions of human body. It supports a number of enzymatic reactions, positively influences a heart, neurological and digestive functions. It also promote a proper growth of human bones. An average adult body contains approximately 30 g of magnesium concentrated mainly in muscles and bones. The recommended daily allowance for magnesium is about 400 mg and magnesium defficiency may cause heart and vascular problems. Therefore, magnesium is contained in many kinds of medicaments and food supplements. Overdosage with magnesium is rare, because human body can properly regulate the Mg-amount and excess Mg can be successfully excreted by kidneys.

In the past, a number of biocompatibility tests have been carried out with magnesium alloys like Mg-Al-Zn, Mg-Y-Nd, Mg-Zn, Mg-Al-Mn, Mg-Al, Mg-Gd, Mg-Sn, Mg-Zn-Ca etc. Both in vitro tests with cell cultures and in vivo tests with animals show that the biocompatibility od pure magnesium is, in general, very good. In the case of Mg alloys, the biocompatibility depends on alloying elements. Mg alloys containing zinc, manganese, calcium and rare earth metals generally exhibit acceptable biocompatibility. These alloys, after being implanted into human tissues, progressively degrade with no alergic and inflammatory reactions [5, 6]. Magnesium alloys represent the only group of materials which have already been applied in pre-clinical tests with human patients.

Zinc: Like magnesium, zinc is a very important element for proper functions of human body. In trace amounts it supports immune system, synthesis of enzymes, proteins etc. Zinc is generally considered as a relatively non-toxic element despite the recommended daily allowance of zinc is 40 mg, i.e., lower than that of magnesium. Short-term overdoses of 150 mg per day do not cause significant problems. However, available biocompatibiity data of Zn alloys is very limited. The first in vivo tests were carried out recently [7] in which Zn wire was implanted into aorta of experimental rats. No negative or inflammatory reactions were detected indicating a good biocompatibility of zinc. However, these tests should be taken as preliminary and much more in vitro and in vivo experiments are necessary to verify biological behavior of zinc.

Iron: Iron is considered as relatively non-toxic metal. In human body it is essential for proper tranfer of oxygen towards tissues. The recommended daily allowance of iron is about 10 mg. The available reports on the in vitro and in vivo biocompatibility tests with iron alloys imply that the biocompatibility of iron is relatively good [8]. But, as in the previous case, additional experiments are needed for verification of these findings.

3. MECHANICAL PROPERTIES

Densities and basical mechanical properties of magnesium, zinc and iron alloys are summarized in **Table 1**. Intervals of mechanical propertes are shown for each group of materials because mechanical properties strongly depend on the alloy´s chemical composition and state (as-cast, as-wrought, as-heat-treated etc.). In addition, mechanical properties of biodegradable polymeric material (PLA), inert metallic biomaterials and bone tissue are given. The most important observation is that all the three groups of biodegradable metallic materials possess significantly higher strength than the biodegradable PLA. It means that these materials can be used for highly mechanically loaded implants applied to fix fractured or fragmented bones (screws, plates etc.).

Table 1 Densities and mechanical properties of various kinds of biomaterials [3, 6, 9 - 11]

Material/tissue	Density (g/cm^3)	Tensile strength (MPa)	Young modulus of elasticity (GPa)
Ti-based alloys	~4.5	600-1200	110
Stainless steels	~8	600-1000	200
Polylactid acid (PLA)	~1	~30	~2
Bone tissue	~2	30-280	5-20
Mg-based alloys	~2	100-400	50
Zn-based alloys	~7	100-400	90
Fe-based alloys	~8	200-1400	200

Magnesium: The positive feature of magnesium based alloys is also a low density and low modulus of elasticity which is closer to that of the human bone tissue in comparison with other metallic biomaterials. Low modulus of elasticity supports a proper transfer of mechanical loading between bone tissue and implant and, therefore, a good healing process of the bone. In case of an implant with a high modulus, the mechanical loading would be carried more by implant than by bone which would result in slowed down growth of the new bone tissue.

Zinc: Zinc alloys show a strength similar to magnesium alloys, but their density and modulus of elasticity are slightly higher which may negatively influence the healing process due to non-uniform transfer of loading between implant and growing bone.

Iron: Iron alloys possess the highest strength among the three groups of materials and are thus very suitable for designing implants exposed to high mechanical loading like screws for fixation of plantar bones. But iron alloys have a significantly higher modulus in comparison with hard bone tissue which may cause problems in the healing process indicated before.

4. CORROSION PROPERTIES

Table 2 summarizes the corrosion rates of magnesium, zinc and iron based alloys in simulated body fluids (SBF). In the scientific literature, a number of solutions simulating body fluids have been proposed ranging from simple solutions with only NaCl to very complex compositions with inorganic salts, proteins, glucose etc. For this reason, corrosion rate intervals are given in **Table 2**, because the corrosion rate is strongly influenced by the structural state and chemical composition of the alloy and by the chemical composition of a testing SBF.

In general, biodegradable metals corrode more rapidly in simple SBFs containing only chlorides, for example, in the simulated physiological solution (SPS). Chlorides are known to destroy the compactness of protective surface layers of corrosion products. On the contrary, corrosion experiments in more complex SBFs containing hydrogenphosphates, dihydrogenphosphates, hydrogencarbonates, organic compounds and other substances provide slower corrosion rates due to the formation of insoluble surface phosphate and carbonate layers.

Corrosion rates determined by in vitro experiments in SBFs can be used only for a rough estimation of the in vivo degradation rates. Any biodegradable implant should possess 100 % of the initial strength for at least 6 weeks after implantation. In addition, the total degradation time of biodegradable implant should not be shorter than 6-12 months in dependence on the implant type and location.

Table 2 Corrosion rates of magnesium, zinc and iron based alloys in simulated body fluids [3, 12-18]

Material	Corrosion rates in SBFs (in mm per year)
Mg-based alloys	0.3 - 20
Zn-based alloys	0.1 - 0.5
Fe-based alloys	0.1 - 0.9

The data in **Table 2** demonstrates that magnesium alloys corrode at the highest rates from all the three groups of materials. It is connected with a low nobility of magnesium in comparison with zinc and iron. The standard potentials of Mg, Zn and Fe are -2.4 V, -0.8 V a -0.4 V (versus SHE), respectively. Zinc and iron alloys show significantly lower corrosion rates in comparison with magnesium.

Magnesium: Corrosion process of magnesium involves anodic and cathodic reactions:

Anodic reaction: $Mg \rightarrow Mg^{2+} + 2e^-$ (1)

Cathodic reaction: $2H_2O + 2e^- \rightarrow H_2 + 2OH^-$ (2)

One can see that gaseous hydrogen evolves and a local increase of pH near to implant occurs during the corrosion process. Both these corrosion products are harmful for proper healing and growth of the surrounding tissue. Therefore, the in vivo corrosion rate of magnesium alloy should be as low as possible which facilitates absorption and outward diffusion of undesirable hydrogen and OH^- ions by body tissues and fluids. This requirement represents the basic limitation for widespread utilization of Mg implants in medical practice. Unfortunately, the majority of biodegradable Mg alloys show too high corrosion rates during in vitro and in vivo experiments. But the most recent studies indicate that some magnesium alloys containing rare earth metals might fulfil the above demand.

Zinc: The mechanism of zinc corrosion is following:

Anodic reaction: $Zn \rightarrow Zn^{2+} + 2e^-$ (3)

Cathodic reaction: $O_2 + 2H_2O + 4e^- \rightarrow 4OH^-$ (4)

The positive feature of zinc corrosion is that it does not produce gaseous hydrogen due to a high hydrogen overpotential of Zn. Corrosion of zinc in SBFs is much slower than that of magnesium and insoluble corrosion products on the zinc´s surface contribute to a relatively good corrosion resistance of zinc [3, 7].

Iron: The mechanism of iron corrosion resembles that of zinc:

Anodic reaction: $Fe \rightarrow Fe^{2+} + 2e^-$ (5)

Cathodic reaction: $O_2 + 2H_2O + 4e^- \rightarrow 4OH^-$ (6)

Like zinc, the corrosion process of iron does not produce hydrogen gas and occurs at a significantly lower rate in comparison with magnesium. Protective layers of insoluble corrosion products form on the surface of iron implants exposed in vivo [7]. The main problems associated with iron alloys arise from their too low corrosion rates when exposed in vivo. Therefore, ways how to accelerate the corrosion process of iron in vivo are extensively searched for. The influence of additions of various alloying elements like Mn, P, Pd, Si and other has been studied.

CONCLUSIONS

Table 3 summarizes positive and negative features of the three groups of biodegradable materials. It can be concluded from this Table that there is no biodegradable material which can be considered as entirely optimal. Although the polymeric material (PLA) possesses a suitable combination of modulus of elasticity, corrosion rate in vivo and biocompatibility, its drawback is a low strength and other mechanical characteristics. Magnesium based alloys have a higher strength than polymer but still suffer from too high in vivo corrosion rates. Advantages of zinc alloys are a higher strength than polymers and a lower corrosion rate than magnesium. Iron exhibits a high strength, low corrosion rate, but too high modulus of elasticity. Regarding biocompatibility of Zn and Fe, many questions remain unanswered and much more in vitro and in vivo tests are needed to solve them.

Table 3 Summary of advantages and disadvantages of biodegradable materials (the mark + means that a material is advantageous, the mark - suggests a less advantageous material and the mark - indicates that a material´s characteristic is disadvantageous). PLA = polylactid acid, i.e., the commercial biodegradable material utilized for bone fixations

Material	Strength	Modulus of elasticity	Corrosion rate	Biocompatibility
PLA	- -	+	+	+
Mg-based alloys	-	+	-	+
Zn-based alloys	-	-	+	+?
Fe-based alloys	+	- -	+	+?

ACKNOWLEDGEMENTS

The basic research on biodegradable materials is financially supported by the Czech Science Foundation under the project no. P108/12/G043.

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