A REVIEW OF METALLIC MATERIALS FOR MEDICAL APPLICATIONS

MÁLEK Jaroslav

CTU in Prague - Faculty of Mechanical Engineering, Department of Materials Science and Engineering, Prague, Czech Republic, EU, jaroslav.malek@fs.cvut.cz

Abstract

Metals and their alloys are used in medicine especially for hard tissue replacements where special properties are required (e.g. biocompatibility, low Young's modulus or corrosion resistance). Another important group is biodegradable materials for fixation devices and stents where the corrosion rate and biocompatibility are essential properties. Stainless steel or Co-Cr-Mo alloys are still used despite their lower biocompatibility and high modulus (~210 GPa). Titanium and its alloys (Ti6Al4V) have good biocompatibility, corrosion resistance and lower modulus (~110 GPa). On the other hand newly developed beta-titanium alloys are promising materials due to their combination of excellent biocompatibility, high strength (> 1000 MPa), very low Young's modulus (~50 GPa) and corrosion resistance. These alloys were developed primarily for bio-applications and they seem to have the best known combination of properties for this purpose. Another important group of metallic biomaterials are biodegradable materials. They are used for short-term applications and eliminate the problems and risks of reoperations. This paper is a short insight of currently used and developed metallic biomaterials.

Keywords: Biomaterials, metals biocompatibility, mechanical properties

1. INTRODUCTION

Metallic materials are one of the most important groups of materials with wide field of applications. They are used as construction materials and during human history they were also used in medicine. Metallic biomaterials are important for surgical and orthopedic instruments as well as hard tissue replacements, augmentations and scaffolds. As a result of increasing life expectancy and quality of life the demand on implants is increasing. It is estimated, that 70 - 80% of implants are made of metallic biomaterials [1].

The first known metallic biomaterial is considered to be a gold plate used by Egyptians and Romans for cranial defect replacements [2]. It was proved that in 1565 the gold plate was used in cleft-palate defect [3]. The requirements on biomaterials significantly increased from that time along with the progress in medicine. The first generation of modern biomaterials was developed between 1940 and 1980 for more sophisticated implants, orthopedic or other devices [4]. In this period ordinary construction metallic materials were used with respect to their corrosion resistance or chemical reactivity. This may have caused problems as these materials may contain elements with potentially adverse effect on living organisms. On the other hand this could be considered as the first approach to the problem of biocompatibility.

The so-called biocompatibility is very important in the field of biomaterials and means the ability of material to be in contact with tissues (or fluids) of the human body without causing significant degree of harm to that body [4]. Its definition is more complicated and evolved during the development of biomaterials. During the late 20th century the demands on biocompatibility spread and other factors were taken into account. Therefore only non-toxic, non-immunogenic, non-carcinogenic, non-thrombogenic or non-irritant materials were considered as biocompatible. It should be pointed out, that the material has to be considered with respect to intended application. So the biocompatibility is depended not only on the material but also on the situation in which the material is used. In some applications specific reaction of the material with tissues is required instead of inert material. Also some applications the material should degrade and not remain in the body for a long time (biodegradable materials). The metals intended for long-term use in human body should consist of elements that cause no harm to human body, despite the fact that this doesn't definitely determine the suitability of the alloy for implantation. Many studies on various elements were performed in order to determine the potential risks. Biesiekierski et al. [5] summarized potential risks of the most common alloying elements used for production of biomaterials. Many elements are alloyed in currently used biomaterials and some of them posses potential inconvenience for use in biomedical applications (e.g. carcinogenic, mutagenic, genotoxic, or cytotoxic) [5]. Some of those elements are listed below and more profoundly discussed in [5] with detailed references. In many cases the metal ions or their oxides are potentially dangerous for human body (e.g. Cr, Ag, Cu). This is also valid for some noble metals or elements widely used as alloying elements in past years [5]. Nickel (Ni) is considered to be genotoxic [6], allergenic and carcinogenic. Unfortunately in some cases the conclusions on biocompatibility of some elements could vary depending on the current study (i.e. experiment conditions and researcher's point of view [7. 8]). Some of the most important elements with respect to some aspects of biocompatibility are listed in **Table 1** based on the work of Biesiekierski et al. [5].

Table 1 Some biocompatibility factors of most common elements [5]. Other means not listed factor (e.g. neurological effect, hemolysis)

Element	Biocompatible	Carcinogenic	Genotoxic	Mutagenic	Cytotoxicity	Allergenic	Other
Ti	Yes	No	No	No	Medium	No	No
V	No	Yes	Yes	Yes	High	Disputed	No
Cr	No	Disputed	Yes	Yes	High	Yes	No
Fe	No	No	Yes	Disputed	Medium	No	No
Co	No	Yes	Yes	Yes	High	Yes	Yes
Ni	No	Yes	Yes	Yes	High	Yes	Yes
Zr	Yes	No	No	No	Low	No	No
Nb	Yes	No	No	No	Low	No	No
Mo	No	Disputed	Yes	Yes	Low	Yes	Yes
Ag	No	No	No	No	High	Yes	Yes
Hf	Unknown	Unknown	Unknown	Unknown	Medium	No	Unknown
Ta	Yes	No	No	No	Low	No	No
Pt	No	Yes	Yes	Yes	High	Yes	No
Au	Yes	No	No	No	High	No	No
Al	No	No	Yes	No	Low	No	Yes
Sn	Yes	No	No	No	Low	No	Yes

The biocompatibility is also attached with other properties (e.g. wear debris or corrosion resistance of the alloy). The desired corrosion resistance varies with respect to the term of use in human body and is different for long-term implants and short-term implants. For short-term use biodegradable materials are desired in order to avoid reoperation. On the other hand the biomechanical compatibility is important for long-term implants. This means that the material should have suitable mechanical properties to fulfill the desired function for a long time. The implant should have similar mechanical properties to those of replaced tissue. The Young's modulus of cortical bone was reported to be between 10 and 40 GPA [9]. Most metallic materials for implants have significantly higher modulus (110 - 230 GPa). In the case when the material of the implant has significantly higher Young's modulus than the surrounding bone a stress shielding effect may occur [10. 11]. In this case most of the load is taken by the implant and the bone lacks of loading. This can lead to bone resorption, fracture and implant loosening.

2. BIOMATERIALS FOR LONG TERM USE

There are several groups of metallic materials that are used for long-term biomedical applications. The main demand is corrosion resistance, biocompatibility and sufficient strength for intended application.

2.1. Stainless steel

The most common from this group of materials is AISI 316L stainless steel. It has high strength and fatigue limit and also good corrosion resistance. On the other hand the presence of problematic Cr and Ni elements could be a problem as well as higher modulus (~193 GPa). Several attempts to develop Ni-free stainless steel were made by replacing Ni with other austenite stabilizers N or Mn [12]. On the other hand some problems caused by limited workability due to high N content occurred [13, 14]. Nevertheless AISI 316L is still used in huge amounts due to its relatively cheap price.

2.2. Cobalt alloys

The most common from this group of materials is Co-Cr-Mo (~28 wt.% Cr and ~5.9 wt.% Mo) alloy and its modifications as low Ni or low C modifications [14]. These alloys are used for dental implants and especially for parts of implants subjected to wear debris. They have excellent corrosion resistance and wear resistance. However relatively high Young's modulus (~240 GPa), high density and also limited biocompatibility, despite the high corrosion resistance, could be problematic [5, 15].

2.3. Titanium alloys

Titanium alloys show excellent corrosion resistance, small density and high strength. Pure titanium (grade 2) is known to have excellent corrosion resistance and biocompatibility. On the other hand its lower strength predicts this material only for implants that does not bear significant load [16]. The most common alloy is Ti6Al4V (or Ti6Al4V ELI) developed in 1950's for aerospace industry [14, 17]. It is used also for implants. Due to its better corrosion resistance and high strength this alloy replaced in some applications the AISI 316L stainless steel. The fact that this alloy was not originally developed for bioapplications has several disadvantages. It contains Al and V (not fully biocompatible elements). Although it has significantly lower elastic modulus (110 GPa) than steel or Co-Cr alloys it is much more than that of human bone. The Ti6Al4V alloy has been later modified with respect to its biocompatibility. The amounts of V and Al were reduced and replaced with other elements with lower cytotoxicity (e.g. Nb). This lead to new alloys suitable for implants - Ti-6Al-7Nb or Ti-5Al-2.5Fe [14]. Later the Al and V free titanium alloys have been developed (e.g. Ti-15Sn-4Nb-2Ta-0.2Pd). These alloys consist mainly of elements with superior biocompatibility, but they have in general still Young's modulus close to 110 GPa. This is caused by their microstructure of α+β-Ti phases and therefore they are known as α+β alloys [14]. From the 1990's new generation of titanium alloys for bioapplications was developed. These are β-titanium alloys. Biocompatible elements (e.g. Nb, Ta) are added in these alloys. They decrease the α-β transition temperature and therefore stabilize the β-Ti phase. The advantage of β-titanium alloys is their combination of low Young's modulus with excellent biocompatibility. Very low modulus (as low as ~50 GPa) can be achieved which is close to that of bone. These alloys have lower strength than α+β titanium alloys after annealing, but significant increase in strength can achieved after cold introducing cold deformation. During cold deformation no increase (or even slight decrease) in modulus is observed [18]. The ability of cold working with high degree of deformation (up to 99%) is also significant advantage of β-titanium alloys. The tensile strength may exceed 1000 MPa. The most promising alloys are based on Ti-Nb-Ta-Zr alloying system (e.g. Ti-35Nb-7Zr-5Ta; Ti-29Nb-13Ta-4.6Zr).

Moreover the metastable β-titanium alloys exhibit interesting properties as superelasticity or shape memory effect. This is caused by the reversible stress-induced martensitic transformation (SIM) [19]. The shape memory alloys are used for stents and some orthopaedic devices. The most frequently used alloy is Nitinol (50 at.%Ti-50 at.% Ni), which has also very low Young's modulus. The presence of allergenic Ni may cause problems and therefore new Ni-free alloys with shape memory effects are being developed. Among these the highest values of recoverable strain were achieved at Ti-Nb based system, although the values are slightly lower than that of Nitinol [19-22]. Also other shape memory alloys based on Ti-Mo; Ti-Ta or Ti-Cr alloying systems were studied [1].

3. BIODEGRADABLE MATERIALS

The biodegradability means that the material degrades in the human body due to corrosion processes. The degradation (corrosion) products have to be non allergenic, non-toxic or carcinogenic and are excreted by the human body. Biodegradable materials are therefore used mainly for fixation devices (screws, nails etc.) of fractured bones and also for stents [23] The main benefit of biodegradable materials is the elimination of operation for removing the implant. Biodegradable metallic implants are not currently commercially available, but intensive development in this field is going on. There are 3 main groups of metallic biodegradable materials:

3.1. Mg based alloys

Magnesium and its alloys were proposed and even tested for biodegradable implants (wire ligatures) at the end of 19th century by Erwin Payr [24]. Primarily pure Mg was used, but the tensile strength of pure Mg is low and its corrosion rate is too high. The corrosion rate of Mg alloys differs considerably depending on chemical composition. Suitable value of corrosion rate for biodegradable materials should be around 0.5 mm/year. Moreover hydrogen evolution during Mg corrosion has been reported, which may cause serious problems (i.e. embolism) [24, 25]. The tensile strength of bone is approximately 100 MPa [1]. Most of the newly developed magnesium alloys have similar or higher tensile strength. The commercially available AZ31, WE43, AZ91 or LAE442 alloys are investigated for utilization as a biodegradable material. The development of new Mg-based alloys was introduced by various authors and two main groups are currently investigated. The first group is Mg alloys with rare earth metals and the second group is Mg-Zn-(Al) based alloys [26]. Some of the developed alloys are Mg-Gd-Y or Mg-Nd-Y [23], Mg-Zn [27] or Mg-Zn-Ca [24, 28]. These alloys reach the tensile strength typically 100-350 MPa which is sufficient for most of intended applications [23]. The Mg based alloys seem to be the most promising group among the biodegradable materials.

3.2. Zn based alloys

Zn alloys are also investigated as biodegradable materials. In general they have lower corrosion rate in comparison with Mg alloys. Zn-Mg system has been studied [23] or Zn-Ca system [29]. The tensile strength is comparable with Mg based alloys, but in general the Young’s modulus is higher (~ 90 GPa).

3.3. Fe based alloys

These alloys were developed for stents where the mechanical properties of Mg alloys could not be satisfactory. Pure Fe was investigated in vivo and showed no cytotoxicity [30]. On the other hand the corrosion rate of pure Fe is much lower than that of Mg and Zn based alloys. The degradation rate of such implant is to slow. Due to that reason new Fe-Mn based alloys were developed in order to increase both the degradation rate and strength [31, 32].

4. POROUS MATERIALS

Porous materials are used for specific applications (i.e. scaffolds or augmentations). The implant is used for bearing the load in a place of defect and the surrounding bone gradually grow through the pores in implant. The porosity characteristics (i.e. size, shape or volume fraction) are essential for good osseointegration. In fact all of the above mentioned materials can be used as porous materials [33, 34]. Porous materials have lower density and Young’s modulus, but also lower strength and significantly lower fatigue limit than the same bulk materials. Porosity may have also adverse effect on corrosion resistance. Naturally porous biocompatible materials (Ti-Si based alloys) were also developed [35].

5. CONCLUSION

Metallic materials are often used in medicine in a wide field of applications. Formerly construction materials designed for other applications were used, but in last decades new generation of biomaterials designed primarily for medicine was developed. The choice of specific material is strongly depended on intended application and especially the period of intended use. Biodegradable materials, especially Mg based alloys, are developed for s short term use. The most promising group in long-term used materials seem to be the β-titanium alloys as they exhibit excellent combination of high strength, low Young's modulus, excellent biocompatibility and corrosion resistance.

ACKNOWLEDGEMENTS

This work was supported by Ministry of Education, Youth and Sport of the Czech Republic, program NPU1, project No LO1207.

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