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Review

Metallic implants in biomedical applications – a challenge between toxicological risks and benefits

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Abstract. Various alloys formulas are worldwide used in biomedical applications, especially as orthopedic and dental implants. Metal combinations are considered better materials for implants comparing to polymers and ceramics, but the process of corrosion have also to be taken into account when they are chosen. On the other side, when bioactive elements, such as cooper (Cu), silver (Ag), or magnesium (Mg) were alloyed, superior biological functions were reported to be gained. Mg is used in biodegradable alloys implants formulas, but its fast degradation at the implantation site determined its including in various alloys formulas where this disadvantage was tried to be attenuated. Over the time, various titanium (Ti) alloys implants have found their utility mostly in orthopedic area, being preferred for their corrosion resistance and mechanical properties. Here, many combinations were found to be suitable with the assumed aims, but some of them being at the limit of concerns due to included toxic metals into their formula. However, the choice of the most suitable alloy is made in accordance with the purpose of its use, with a careful analysis of both the risks and the benefits. The aim of this paper is to briefly review the most important aspects of various alloys formulas using for biomedical purposes, including here a critical view on their beneficial properties and toxicological risks for the users.

Key Words: alloys, implants, toxic metals, biodegradable

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Introduction

Various alloys formulas are worldwide used in biomedical applications, especially as orthopedic and dental implants. Such materials must have a good biocompatibility, good mechanical properties (e.g., light weight, high strength, superior load-bearing capacity, low elastic modulus), non-magnetic properties, and corrosion resistance (Lee et al., 2020; Liang et al., 2021; Nasker & Sinha 2018). Moreover, suitable combinations have to promote cells` proliferation through their optimal porosity, and cellular absorption and regeneration through their favorable microsurface (Băbțan et al 2020).

Metal combinations are considered better materials for implants comparing to polymers and ceramics, but they were reported with not a proper elasticity developed between the implant material and adjacent bone. This will lead to some disadvantages, such as the carrying of the most external load by the metallic implants and a resulted "stress shielding effect" (Nasker & Sinha 2018). The process of corrosion has also to be taken into account, some ions, such as those of cobalt (Co), chromium (Cr), nickel (Ni), cooper (Cu), aluminium (Al), and vanadium (V), being released into the body and contributing to the cytotoxicity, DNA damage, metal hypersensitivity reactions, pseudotumors, or neurological problems (De Freitas Quadros et al 2019; Konushkin et al 2020; Liang et al 2021; Wang & Xu 2017).

Different attempts to replace potentially toxic metals from various alloys formulas have been made so far. For example, niobium (Nb), tantalum (Ta), and zirconium (Zr) are considered a promising alternative for nickel (Ni) (Konushkin et al 2020). When bioactive elements, such as Cu, silver (Ag), or magnesium (Mg) were alloyed, superior biological functions were gained, for example that of anti-bacterial capacity due to Cu or Ag incorporating, or that of bone growth and regeneration, as a result of Mg (Liang et al 2021).

In fact, Mg is used in biodegradable alloys implants formulas, with improved mechanical properties compared to degradable polymers, but when compared to a non-degradable Ti-6Al-4V alloy, the degradation of the intramedullary pins led to failure at the osteotomy site (Chou et al 2019). The same behavior was reported for the non-toxic CaMgZn bulk metallic glass, which failed in potential skeletal applications due to its too fast completely degradation (after 4h, in vitro and within 4 weeks, in vivo), without an optimal healing in the expected time of at least 12 weeks (Wang et al 2011).

The aim of this paper is to briefly review the most important aspects of various alloys formulas used for biomedical purposes, offering here a critical point of view to aid in the choice of the most suitable alloy in accordance with the purpose of its use.

Materials and methods

Some aspects about various alloys implants formulas and their using were debated here based on the study of 29 scientific papers with relevance in this area. This review is original and is important through the comprehensive presentation of the information.

Results and discussions

If we are started our debate with the subject of biodegradable material implants, it is worth saying that Yang et al (2018) reviewed three main types of them: those based on Mg, which are considered the most popular, Fe-based (potential vascular stents), and Zn-based metal implants (less studied). Various formulas alloys, including Mg-Zn, Mg-Ca, Mg-Sr, Mg-Si, Mg-RE [rare earth (RE) elements], Mg-Mn, Mg-Ag, were developed and investigated (also reviewed by Zhang et al 2014), being characterized by excellent mechanical properties, with a wide range of variation for ultimate tensile strength (86.8-300 MPa) and elongation to failure (3-30%). As previously mentioned, the Mg flaw is represented by its rapid rate of degradation, but it was compensated by other alloying elements adding, improving in this way its degradation behavior, and also per total corrosion resistance and plasticity. On the other side, Fe-based biodegradable alloys are characterized by a higher strength (~1450 MPa) and ~80% elongation, being suitable for stents using. Comparing to Mg-based alloys, their biodegradation rate is very slow, and for improving this, some combinations including Mn, Pd, W, Sn, B, C, S, and Si were considered. Somehow intermediate between Mg-based and Fe-based alloys as a rate of their degradation are Zn-based alloys. And here "alloys" is highlighted, because per se Zn has a very low strength and plasticity. As such example was reviewed to be Zn38Ca32Mg12Yb18, characterized by a higher strength (>600 MPa) than conventional Mg-based alloys (Yang et al 2018).

Testing various Mg-based alloys formulas (MCZ: Mg-Ca-Zn; MS: Mg-Sr; MCZS: Mg-Ca-Zn-Sr), Brooks & Ehrensberger (2017) reported the following order of corrosion resistance: MCZ>MCZS>MS. In fact, MS showed a severe degradation as a result of corrosion, a process which was due to the water reduction reaction and OH- ions generation as byproducts, with a greater environmental alkaline shift in pH. It is worth mentioning here that these Mg-based alloys were designed to reduce the Mg-corrosion (a certainly accomplished purpose), but other reasons included the potential of Zn to increase bone formation and collagen production, of Ca to enhance osteoblast proliferation and differentiation, and of Sr, as a osteogenic factor, to induce differentiation of mesenchymal stem cells towards osteoblastic lineage (Brooks & Ehrensberger 2017). Zhang et al (2014) investigated the effect of Neodymium (Nd) adding in Mg alloys, considering its reviewed limited solubility and significant strengthening effect, without cell toxicity inducing. They prepared four Mg-based alloys, Mg-2.2Nd-xSr-0.3Zr, where x=0; 0.4; 0.7; and 2.0 wt.%. The results on corrosion tests also confirmed that the formula including the highest wt.% Sr was characterized by the fastest corrosion rate, in contrast with that of 0.7 wt.%Sr. When Moreno et al (2019) comparatively studied the degradation (corrosion) behavior of Mg0.6Ca and Mg0.6Ca2Ag alloys with bioactive plasma electrolytic oxidation (PEO) coating enriched in Ca, P, and F, a 2-3 times better improved corrosion resistance was expressed by PEO-coated Mg0.6Ca alloy comparing to the bulk alloy, whereas in the case of Mg0.6Ca2Ag was reported a higher rate of degradation through corrosion for both PEO-coated and non-coated samples. This led the authors of the study not to recommend their application as resorbable implants.

In 2016, Berglung et al investigating the peri-implant tissue response and the biodegradation of a Mg-1.0Ca-0.5Sr alloy in rat tibia, although observed gas bubbles around the degrading implant at early time points (whose lower rate of formation is positively correlated to the biodegradation lower rate), they reported that the bone remained intact with no evidence of microfracture, fact that recommended this alloy as a promising candidate for biodegradable orthopedic implants.

Also, in order to prevent some shortcomings of Mg-implants, such as those already mentioned of quickly corrosion at the physiological pH range of 7.4-7.6, and H2 gas releasing around the implant area (also reviewed by Staiger et al 2006), Mushahary et al (2013) developed four Mg-Zr alloys formula, such as: Mg-5Zr; Mg-5Zr-Ca; Mg-2Zr-5Sr; Mg-Zr-2Sr. The authors hypothesized that the inclusion of Sr, Zr, and Ca can influence alloys degradability and biocompatibility; moreover, the adding of Sr was supposed to influence the Mg alloys surface properties and to control the interactions of these alloys with osteoblast cells. However, their results are interesting, some of them even supporting the favorable effect of Sr in such alloys. For example, their tested alloys showed a range of the compressive strength between 209.7 and 255.7 MPa, as minimum and maximum values for Mg-2Zr-5Sr and Mg-5Zr-Ca alloys, respectively. The recorded values were reported to fit into the range of compressive strength of normal cortical bone (164-240 MPa), excepting this maximum value of Mg-5Zr-Ca alloy, the addition of Ca being considered the reason of its stiffer and more inflexible character comparing to the other three alloys. Measuring the hydrophobicity of the investigated alloys, the authors reported the following order for this indicator, based on the surface energy: Mg-5Zr-Ca>Mg-5Zr>Mg-2Zr-5Sr>Mg-Zr-2Sr. In fact, the higher is the surface energy, the higher is the hydrophilicity of the investigated alloy. Thus, for the reviewed study, Mg-Zr-2Sr alloy showed the least surface energy, being considered the most hydrophobic, while Mg-5Zr-Ca showed the most surface energy, being considered the most hydrophilic. Based on histological investigations of the implant-induced bone properties at 12 weeks after implantation, Mg-2Zr-5Sr and Mg-Zr-2Sr implants were reported to show firm adhesion of the new tissue to the implant surface and a uniform osteoblast-rich bone tissue. In contrast to this "contact osteogenesis", Mg-5Zr and Mg-5Zr-Ca implants were reported to induce a "distance osteogenesis". In fact, Mg-2Zr-5Sr and Mg-Zr-2Sr implants showed a complete degradation, which was hypothesized to be responsible for the activation of osteoclasts. This was in contrast with poor degradation reported for Mg-5Zr and Mg-5Zr-Ca implants, even after 12 weeks, fact which is related to a weaker activation of osteoclasts. However, Sr-containing alloys were characterized by a more optimized evolution of H2 gas releasing and biodegradation behavior if compared to Sr-non-containing alloys. A possible limited toxic effect on kidneys` function was supposed based on elevates values for urea in rabbit blood samples at 3 months post-implantations, excepting Mg-Zr-2Sr alloy. The liver function was not affected and although the implantation of Mg-5Zr and Mg-2Zr-5Sr translated into a slightly increasing in lymphocytes, hematocrit, mean corpuscular volume, and mean cell hematocrit concentration, and of Mg-Zr-2Sr, into a platelet count increasing, not any kind of blood indicators disturbance was considered (Mushahary et al 2013).

The same sustaining of Sr including in Mg-based alloys was found in the investigations of Jiang et al (2018) on the degradation properties (rate and mode) and the behavior via direct culture with bone marrow-derived mesenchymal stem cells

(BMSCs) of each 4 alloys formula for Mg-xSr (x=0.2; 0.5; 1; 2 wt%) and Mg-1Ca-xSr (x=0.2; 0.5; 1; 2 wt%). The authors reported Mg-1Sr and Mg-2Sr to have the lowest degradation rate among all studied MgSr and MgCaSr alloys; MgCaSr alloys were reported for an improved adhesion of MBSCs on their surface as compared to MgSr alloys, except for Mg-1Ca-0.2Sr. In conclusions, authors recommended Mg-1Sr, Mg-1Ca-0.5Sr, and Mg-1Ca-1Sr for further in vivo studies.

He et al (2007) reported an obvious decreasing in elongation to fracture of a Mg-based alloy [Mg-(9-10)Gd-3Y-0.4Zr] after 0.4-0.6 wt.% Ca additions, but a remarkable corrosion resistance increasing and a creep resistance slightly improvement. A low corrosion rate and a good biocompatibility were supposed for Ca addition less than 1% wt.% in MgCa alloys.

The yttrium (Y) addition in Mg-1Ca-1Y formula did not meet the expectations in corrosion resistance improving comparing to Mg-1Ca alloy formula (Li et al 2010). However, investigating the potential of migration and of accumulation of Y from Mg-based implants, Turyanskaya et al (2016) launched a series of concerns about the Y migration into the bone and its remaining in the tissue even after the complete degradation of the implant, considering that the potential health impact of this rare element it is not enough estimated to be assumed.

In 2014, Walker et al reviewed a potential risk of Mg implants related to the hypermagnesemia. Various symptoms of the stored and circulating Mg excess, which may result after its mobilization from the implant, were well-documented, including here a gradual evolution from a fall in blood pressure, nausea, and mental impairment, to neuromuscular system impairment, with progressive muscle weakness and a potential respiratory failure, and in worst cases, hypotension, bradycardia, and cardiac arrest. To avoid these, the authors documented the possibility of Mg-based alloys using as materials for vascular implants, which seems to be more successful comparing to orthopedic applications, in the view of their reviewed authors. However, Wang et al. (2016) experimented with rats and confirmed that Mg implants did not induce any extra damage in their kidneys, liver, and hearth tissue, even in the case of renal failure.

Over the time, various titanium (Ti) alloys implants have found their utility mostly in orthopedic area, for fixations of fractures, especially of long bones, of spine, various arthritic joint replacements and maxillofacial applications (Bayrak et al 2020). The bio-inert nature of Ti alloys often leads to insufficient and/or delayed osteointegration (Liang et al 2021), but they are preferred due to their highly reported biocompatibility, corrosion resistance, and mechanical properties (Ji et al 2020; Spataru et al 2021).

Their manufacturing and the finding of an optimal formula is a great scientific challenge. Systems containing multiple elements instead of a single one are named High-Entropy Alloys (HEAs) (Li et al 2013), their combined formula adding combined advantages of their components.

When an alloy formula is considered for biomedical applications, two important aspects have to be considered: the passivation film forming on the alloy surface, and the corrosion resistance. The passivation film represents an indicator of such materials biocompatibility, since is related to physicochemical and biological processes that occur at the interface between implant and tissue (Ji et al 2020). The corrosion behavior of the implant is important both in estimating its cytotoxic effect by various ions releasing to the body fluid and in estimating its own period of life (Matsuno et al 2001; Nasker & Sinha 2018). Excellent corrosion resistance was reported for refractory metals such as Co-Cr alloys, Ta, Nb, and Ti (Matsuno et al 2001); Nb was reviewed to enhance the stability of the passivation film, being head of a pure metals biocompatibility comparison: Nb>Ta>Ti>Zr>Al>Mo (Ji et al 2020).

In fact, Ti is one of the most used metal in biomedical devices and tissue engineering applications since its alloys began to replace stainless steel and Co-Cr alloys in biomedical applications. There are well-known two structural types of Ti, one of α-phase, which has a hexagonal compact (hcp) crystalline structure below 8820C, being initially developed for military and aircraft applications due to its good mechanical resistance, and a second type, the β-phase, which above the aforementioned temperature it has a body-centered cubic (bcc) crystalline structure, fact which relates it to a low elastic modulus and high resistance to corrosion and wear (De Freitas Quadros et al 2019). Since the 1960s, α+β type alloys gradually replaced hcp-Ti in biomedical uses, but some concerns of toxic metals (Al, V) mobilization from Ti-6Al-4V determined, in the 1980s, the development of V-free Ti alloys, with similar properties to those of Ti-6Al-4V. However, nowadays the β-type titanium is widely used in biomedical alloys which include into their structure various metallic elements, such as Fe, Ta, Nb, Mo, Ni, Cr, Cu etc., as β-phase stabilizers (Eisenbarth et al 2004). Tantalum, for example, despite its highly production costs, is characterized by a good biocompatibility, good corrosion resistance, and high mechanical strength; it is effectively assisted in its actions by Zr, an element which belongs to the same family of Ti on the periodic table (De Freitas Quadros et al 2019). One of the first Ti-based alloys developed for biomedical uses were those containing Ti-Nb-Ta-Zr in different proportions (Ti-15Zr-4Nb-4Ta; Ti-29Nb-13Ta-4Zr; Ti-15Zr-4Nb-4Ta; Ti-23Nb-0.7Ta-2Zr). All of them were characterized by a good biocompatibility, the best corrosion resistance being associated with Ti-20Nb-13Ta-5Zr formula (as reviewed by Konushkin et al 2020).

In 2001, Matsuno et al tested the biocompatibility of various metals in implant wires used in Wistar rats. All the tested elements were of high purity (99.9% Ti; 97% Hf - hafnium; 99.9% Nb; 99.95% Ta; 99.97% Re-rhenium), two little known metals being investigated in this research, Hf from group 4A and Re from group 7A. The authors reported no inflammatory response to alloyed metals either in soft or hard tissue, a sufficient biocompatibility, a good corrosion resistance, with a healing around implants` position of insertion over the 4-week period of experiment.

Testing the biocompatibility of pure elements used in β-Ti alloys, Eisenbarth et al (2004) found a reduced corrosion resistance of molybdenum (Mo), Zr, and Al. The cell proliferation was somehow increased on Nb, and slightly reduced on Al and Zr, with a distinct reduction ascertained on Mo. The highest mitochondrial activity of cells cultures was observed in the case of Nb; a slightly decrease was reported for Zr, while Al and Mo led to a reduced mitochondrial activity and a subsequent cutback of cell viability. The osteoblast-like cells showed a great variation in their morphology on Mo, while on Nb, Ta, and Zr did not significantly differ.

Wang & Xu (2017) reviewed that CoCrMo alloys (e.g. Co28Cr6Mo) are more wear-resistant comparing with Ti-alloys (e.g. Ti-6Al-4V), but the problem of Co and Cr mobilization into blood stream remains still concerning. They also reviewed some of HEAs, such as Nb-Mo-Ta-W; V-Nb-Mo-Ta-W; Ta-Nb-Hf-Zr-Ti; Hf-Nb-Ti-Zr; Hf-Mo-Ta-Ti-Zr; Hf-Mo-Nb-Ta-Ti-Zr, all of them exhibiting high yield strength (σy=900-1600 MPa) at ambient temperature, and a good biocompatibility for the vast majority of included elements, excepting the toxic vanadium. Furthermore, it seems that released metal ions of Zr, Nb, and Ta (belonging of Ti-type ion) do not express toxicity due to their not always combining with biomolecules but rather with a water molecule or an anion near the ion to form an oxid, hydroxide, or an inorganic salt. The aforementioned authors tested an alloy containing Ti20-Zr20-Nb20-Ta20-Mo20, with Hf excluded due to its less resistance to tribocorrosion in simulated body fluid but Mo included due to its high elastic modulus (E=324 GPa) and its expected wear resistance role. Their obtained results revealed a room-temperature compressive yield strength of σy=1390±75 MPa, excellent corrosion resistance comparable to Ti-6Al-4V alloy, and pitting resistance remarkably superior to CoCrMo alloy.

In 2019, De Freitas Quadros et al prepared and characterized a Ti-alloy for biomedical applications, containing β-stabilizers elements such as Ta, but also Zr, a neutral element, both for a better corrosion resistance. When their formula (Ti-25Ta-10Zr) was characterized, three crystalline structures were observed, one hexagonal (α-phase), a second one orthorhombic (α``- phase), both dissolved in a third one, cubic body-centered. The results of its indirect cytotoxicity showed not any kind of indirect cytotoxic effect for primary cultures of osteogenic cells, with a proper maintain of cells` morphology and their division. The aforementioned authors also reviewed two Ti-based alloys, Ti-20Nb-20Ta-20Zr-20Mo and Ti-29Nb-13Ta-4.6Zr, both with excellent properties, the first one with a high biocompatibility when compared to commercially pure Ti, and superior hardness and yield stresses to Ti-6Al-4V alloy, and the second one, with an unsatisfactory mechanical durability to be used as biomedical implant.

In 2020, Konushkin et al developed and tested a new homogeneous alloy containing 62%Ti, 20%Nb, 13%Ta, 5%Zr (Ti-20Nb-13Ta-5Zr), whose surface was depleted in terms of Ti content (~20%), Nb (5%), but enriched in terms of Ta content (~25%), with a large amount of oxides (~50%). It was shown that the yield strength of the alloy was of 680 MPa and the tensile strength of about 745 MPa. Regarding its effect on reactive oxygen species generation (hydroxyl radicals and hydrogen peroxide) and on long-lived reactive protein species (LRPS), it was shown that the generation of reactive oxygen species was more active with temperature increasing; when compared to a medical nitinol alloy (NiTi), an increase in rate formation of hydrogen peroxide, by almost 3 times, and hydroxyl radical, by almost 7 times, was observed in the case of nitinol, and only a 1.5-2 fold increase in the rate of formation of hydrogen peroxide and hydroxyl radical was observed in the case of Ti or Ti-20Nb-13Ta-5Zr alloy. Nitinol led to an increase in LRPS generation rate by about 55%, while the Ti-20Nb-13Ta-5Zr alloy increased this rate only by 30%. When Ti-20Nb-13Ta-5Zr alloy was added, a high mitotic index and low content of non-viable cells on growing cell cultures was also reported.

Lee et al (2020) reviewed that, despite similar surface morphologies and porous network, Ti-6Al-4V alloy is more effective in bone regeneration than CoCr. When they tested Ti-6Al-4V screws with a micro-rough surface structure in comparison to conventionally machined Ti-6Al-4V ELI screws (smooth surface structure), a higher bone-to-implant contact was demonstrated for the first type of implants, with a higher osseointegration rate through a more significant local damage in the rabbit tibiae and a well-developed new bone along their micro-rough surface.

In 2020, Nasakina et al reported the use of a Ti-28Nb-5Zr alloy for wires with a diameter of 1200 μm, the results obtained in their investigation confirming a β-phase composition with super-elasticity and shape memory effect, corrosion resistance and biocompatibility; the tensile strength was measured at 840 MPa and no toxicity was detected.

In a review of Băbțan et al (2020), Selective Laser Melting (SLM) – manufactured titanium scaffolds were found with a significant value for bone reconstructions in the oral and maxillofacial surgery field. The SLM technique offers an exceptional control over the structure of the base, since the higher the power of laser intensity and the lower scanning speed are, a lower surfaces porosity is obtained, but with increased material texture and its mechanical properties anisotropy. In fact, cellular adhesion is related to the porosity degree of Ti-scaffold surface, improved adhesion of fibronectin, mesenchymal stem cells, or collagen fibers being observed on rough scaffolds, with positive surface charge and molecular hydrophilicity. SLM-generated Ti-scaffolds were reported with no cytotoxicity, a proper tissue integration being assured by the following features: 400 to 600 μm pre dimensions, 75-88% porosity, and a coat of hydroxyapatite or SiO2-TiO2. When Ti-6Al-4V alloy surfaces were treated with anodic oxidation and plasma oxidation, layers with high hardness were obtained, with an increase of 118% by plasma oxidation, and of 35%, by anodic oxidation process, when compared to as-received condition. As a result of plasma oxidation, the surface roughness was slightly greater than that of the as-received condition (~220 nm vs ~200 nm), while anodic oxidation process decreased the surface roughness to ~130 nm. Regarding the corrosion resistance, that of as-received sample was lower than those of oxidized surfaces, while anodically oxidized sample presented the highest corrosion resistance. The anodized surfaces showed a higher cell viability (fibroblast, osteoblast) than those obtained by plasma oxidation.

When Ji et al (2020) studied the effect of Nb addition on the biological corrosion behavior and passivation film characteristics of Ti-Zr alloys, they found that with Nb content increasing, the corrosion resistance first decreased and then started to increase when the amount of added Nb was 20 wt.%. The best reported corrosion combination was Ti-Zr-Nb each 33.335%, other investigated combinations having 20%, 10%, 5%, and no Nb added. The addition of Nb also changed the alloy passivation film characteristics, the content of Ti2O3 being reduced, while the presence of Nb oxides (NbO, NbO2, Nb2O5) being reported. Whatever, among alloys tested formula, authors concluded that the aforementioned was the best one due to its low corrosion current density, high total impedance, high passivation film stability, and good biocompatibility.

Ti-Mg composite materials are less used due to limited solubility of Mg in Ti, and decreased final mechanical properties when Mg content increased to 1.25 wt.%. Moreover, high content of Mg (2.5 wt.%) in Ti-Mg composite could lead to significant cytotoxicity, while 0.312~0.625 Mg wt.% could promote cell attachment, proliferation, and differentiation. A composite formula including Ti-0.625 Mg was reported to have an enhanced regenerative potential and osteointegration when compared to pure Ti implant in the femurs of rats (Liang et al 2021).

When Mo was added to a Ti-based alloy (Ti-20Mo-xSi, where x=0.05; 0.75; 1.0 wt.%), its β-phase was constructed while the modulus of elasticity decreased with the amount of Si but the mechanical properties improved with Si addition. Neither of the investigated materials affected cell growth and morphology, all of them presenting a good biocompatibility (Spataru et al 2021).

Conclusions

Finding a suitable formula for alloys with biomedical applications is often a challenge for specialists in the field. Each alloy is a unique structure and its choice as an implant material it must be matched with the proposed aim. Apparently, the use of Mg is advantageous due to its lower toxicity, but its premature degradation at the incorporation site leads to a rethinking of its use as such. It appears that Sr added to Mg alloys is associated with a higher rate of corrosion degradation, as is the addition of Ag, although this has not always been proven. The addition of Ca increases the inflexibility of Mg alloy, making it stiffer, but a better strength and biocompatibility have also been reported, depending essentially on its share in the final formula. Ti based alloys are considered among the most suitable for biomedical applications in the orthopedic sector, being resistant to corrosion and with good mechanical properties. Other combinations, such as CoCrMo, for example, may be even better in terms of strength, but in many cases the risk of toxic metals mobilization into the blood must be taken seriously.

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