Acta Biomaterialia 10 (2014) 2919–2934

Contents lists available at ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Review

# Calcium orthophosphate coatings on magnesium and its biodegradable alloys

Sergey V. Dorozhkin *

*Kudrinskaja sq. 1-155, Moscow 123242, Russia*

ARTICLE INFO

*Article history:*
Received 11 December 2013
Received in revised form 7 February 2014
Accepted 12 February 2014
Available online 7 March 2014

*Keywords:*
Hydroxyapatite
Calcium orthophosphates
Magnesium
Biodegradable alloys
Coatings

ABSTRACT

Biodegradable metals have been suggested as revolutionary biomaterials for bone-grafting therapies. Of these metals, magnesium (Mg) and its biodegradable alloys appear to be particularly attractive candidates due to their non-toxicity and as their mechanical properties match those of bones better than other metals do. Being light, biocompatible and biodegradable, Mg-based metallic implants have several advantages over other implantable metals currently in use, such as eliminating both the effects of stress shielding and the requirement of a second surgery for implant removal. Unfortunately, the fast degradation rates of Mg and its biodegradable alloys in the aggressive physiological environment impose limitations on their clinical applications. This necessitates development of implants with controlled degradation rates to match the kinetics of bone healing. Application of protective but biocompatible and biodegradable coatings able to delay the onset of Mg corrosion appears to be a reasonable solution. Since calcium orthophosphates are well tolerated by living organisms, they appear to be the excellent candidates for such coatings. Nevertheless, both the high chemical reactivity and the low melting point of Mg require specific parameters for successful deposition of calcium orthophosphate coatings. This review provides an overview of current coating techniques used for deposition of calcium orthophosphates on Mg and its biodegradable alloys. The literature analysis revealed that in all cases the calcium orthophosphate protective coatings both increased the corrosion resistance of Mg-based metallic biomaterials and improved their surface biocompatibility.



## 1. Introduction

Metals and their alloys play an essential role as biomaterials which can assist in the repair or replacement of load-bearing bones that have become diseased or damaged [1]. Due to their physical nature, the majority of metals have a high strength and a long service life combined with a low elastic modules and low plasticity at body temperature. In view of their chemical properties (corrosion resistance) and biological compatibility (lack of toxicity), the range of applicable implantable metals is restricted to stainless steels, titanium and its alloys (e.g. Ti6Al4V, Ti6Al7Nb and shape memory Ti–Ni alloys), tantalum, cobalt–chromium-based alloys, as well as some noble metals and their alloys (the latter used mainly for dental restoratives). The limitations of these metallic implants involve a possible release of toxic ions and/or particles through corrosion or wear processes. Furthermore, being xenogenic, all metals evoke a physiological response that results in formation of a fibrous capsule, thus isolating the implants from the body [2,3]. In addition, the mechanical properties of these metals and alloys are not well matched with those of bone, resulting in stress-shielding effects that can lead to reduced stimulation of new bone growth and remodeling, which decreases implant stability [4]. Finally, the above-mentioned metals and alloys are essentially neutral in vivo and remain as "permanent" fixtures. Therefore, if plates, screws and pins made of these metals and alloys are used to secure bone fractures, after healing they will have to be removed by a second surgical procedure [5]. Fortunately, there is a small group of biodegradable (also called bioresorbable or bioabsorbable) metals, which are able to degrade relatively safely within the body. The primary metals in this category are magnesium-based and iron-based alloys, although recently zinc has also been investigated [6]. Among them, magnesium (Mg) and its biodegradable alloys (AZ91, WE43, AM50, LAE442, etc.) appear to be the most promising. They can degrade naturally in the physiological environment by corrosion, and thus appear to be suitable candidates for the construction of temporary implants, including stents [7–13]. A few examples of such Mg implants are shown in Fig. 1 [14].

Metallic implants made from biodegradable materials, such as Mg and its alloys, possess some novel biomedical features. After

* Tel.: +7 4992554460.
*E-mail address:* sedorozhkin@yandex.ru

http://dx.doi.org/10.1016/j.actbio.2014.02.026
1742-7061/

being implanted, they will slowly degrade, eliminating the necessity for subsequent surgeries to remove them, thereby accelerating the entire healing process with a simultaneous reduction in health risks, costs and scarring [15]. Nevertheless, to avoid various complications and undesired effects (Fig. 2A,B), a suitable degradation kinetics appears to be critical (Fig. 2C): any biodegradable implant must continue to perform its function(s) until the damaged tissues have been sufficiently recovered or healed [16]. Additionally, the degradation (corrosion) products of such implants must be well tolerated by both the surrounding tissues and the organism as a whole. Fortunately, $Mg^{2+}$ ions are the fourth most abundant cation in the human body and are stored mainly in bones. They are vital to metabolic processes, a cofactor in many enzymes and a key component of the ribosomal machinery that translates the genetic information encoded by mRNA into polypeptide structures [17]. Therefore, contrary to other implantable metals, the wear or corrosion products of which can be potentially toxic or otherwise harmful to patients, those of Mg might be potentially beneficial to patients [18].

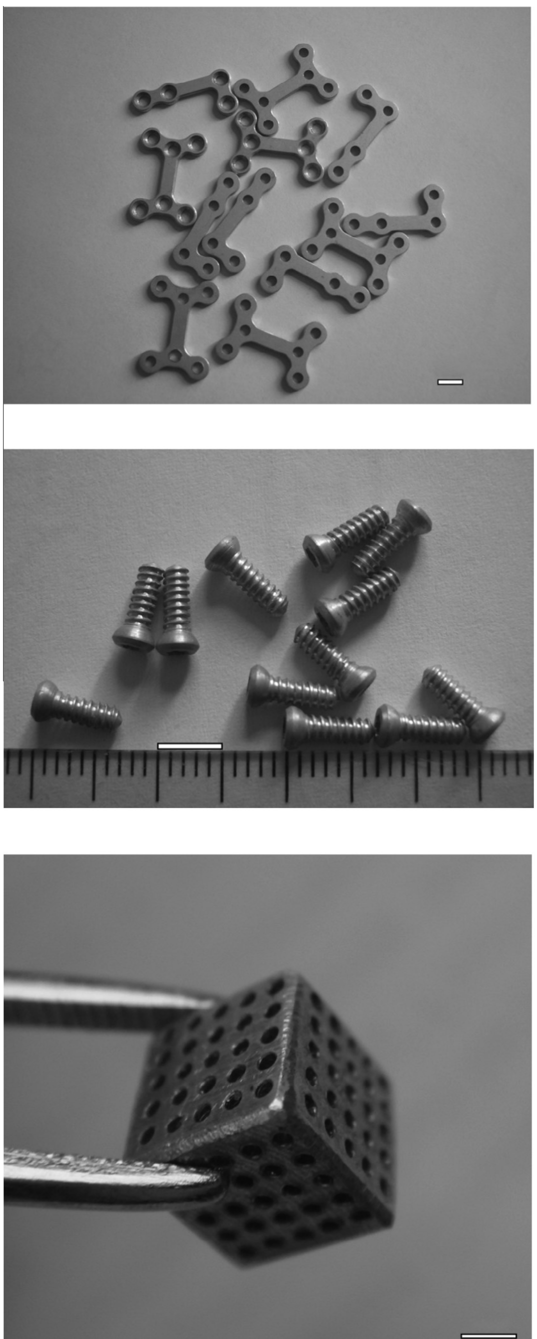

**Fig. 1.** Biodegradable orthopedic devices prepared from Mg and its alloys: (top) bone plates; (middle) screws for orthopedic fixation; (bottom) a porous scaffold for bone void filling. Scale bar = 10 mm. Reprinted from Ref. [14] with permission.

As can seen from the above, Mg, its biodegradable alloys and their corrosion products are well tolerated by the human body. However, in the vast majority of the cases, the in vivo corrosion kinetics of Mg and its alloys exceeds that of bone healing (Fig. 2A,B); therefore, it must be slowed down for implant applications. Numerous investigations have shown that both the properties and functional activity of any implantable biomaterial can be influenced by surface modifications, such as polishing, oxidation, passivation, coating deposition, ion-implantation, etc. [19,20]. Of these techniques, the application of synthetic calcium orthophosphate coatings appears to be the most effective way of achieving surface modification, and moreover improves the biocompatibility and osteointegration of metallic implants.

## 2. A brief description of the two major constituents

### 2.1. Magnesium and its alloys

Mg is the eighth most abundant element on the surface of our planet, making up ~1.93% by mass of the earth's crust and ~0.13% by mass of the oceans. Mg is an alkaline earth element, which are located in the second group of the periodic table. All alkaline earth elements possess a very high chemical reactivity and form compounds with an oxidation number of +2. Therefore, they are not found free in nature. The first isolation of elemental Mg was performed by Sir Humphry Davy in 1808 [21,22]. In 1852, Robert Bunsen achieved viable commercial production of Mg by electrolysis, and Mg then began to be produced in small quantities in America and Europe, initially for pyrotechnical use and as igniting bands or wires for flashlights of the nascent photographic industry [23].

Mg and its biodegradable alloys are light in weight and low in density (1.738 g $cm^{-3}$ for pure Mg and 1.7–2.0 g $cm^{-3}$ for the alloys—values that are similar to the density of bones: 1.8–2.1 g $cm^{-3}$). Due to its relatively low melting point (650 °C), Mg is considered a fusible metals. The elastic modulus of Mg is ~45 GPa [24], which is much closer to that of bone (trabecular/cancellous bones: 3–14.8 GPa, cortical bones: 18.6–27 GPa [25,26]) compared to compared to the moduli of other implantable metals: Ti alloys, 110–117 GPa; stainless steels, 189–205 GPa; Co–Cr alloys, ~230 GPa. In addition, the numerical values of the compressive yield strength of bones and Mg are 130–180 and 65–100 MPa, respectively, while those of fracture toughness are 3–6 and 15–40 MPa $m^{-2}$, respectively. Hence, by using Mg and its alloys for bone grafting the stress-shielding effect can be mitigated [7,10]. In addition, some antibacterial properties of Mg have been reported [27].

From the chemical point of view, its high reactivity (the standard electrode potential of $Mg^{2+}_{(aq)} + 2e^- \leftrightarrow Mg_{(s)}$ is −2.37 V, that of $Mg^{+}_{(aq)} + e^- \leftrightarrow Mg_{(s)}$ is −2.70 V and that of $Mg(OH)_{2(s)} + 2e^- \leftrightarrow Mg_{(s)} + 2OH^-$ is −2.69 V [28]) makes Mg readily soluble in body fluids, which is the primary reason of its in vivo biodegradability. Therefore, when Mg is exposed to aqueous solutions, the following oxidation reaction takes place on its surface [29,30]:

$$Mg + 2H_2O = Mg(OH)_2 \downarrow + H_2 \uparrow$$

This provides a possibility to measure the corrosion kinetics of Mg and its biodegradable alloys by the release kinetics of hydrogen (Fig. 3) [31]. Unfortunately, the oxidized surface layers consisting