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Mg-Based Composites for Biomedical Applications

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Abstract

Magnesium (Mg) is a promising material for producing temporary orthopedic implants, since it is a biodegradable and biocompatible metal which density is very similar to that of the bones. Another benefit is the small strength mismatch when compared to other biocompatible metals, what alleviates stress-shielding effects between bone and the implant. To take advantage of the best materials properties, it is possible to combine magnesium with bioactive ceramics and tailor composites for medical applications with improved biocompatibility, controllable degradation rates and the necessary mechanical properties. To properly insert bioactive reinforcement into the metallic matrix, the fabrication of these composites usually involves at least one high temperature step, as casting or sintering. Yet, recent papers report the development of Mg-based composites at room temperature using severe plastic deformation. This chapter goes through the available data over the development of Mg-composites reinforced with bioactive ceramics, presenting the latest findings on the topic. This overview aims to identify the major influence of the processing route on matrix refinement and reinforcement dispersion, which are critical parameters to determine mechanical and corrosion properties of biodegradable Mg-based composites.

Keywords: magnesium, biodegradable composite, bioactive material, temporary implant, severe plastic deformation

1. Introduction

It is known that magnesium is a very low-density metal with great importance for structural applications where low weight is desirable. It is approximately 35% lighter than aluminum, 60% lighter than titanium and 78% lighter than steel. Magnesium and its alloys are also potential materials for structural orthopedic implants, since not only Mg's density (1.738 g/cm^3) but also its tensile strength (80–280 MPa) are similar to that of the bone, with advantages as higher fracture toughness [1]. The similar density and smaller elastic modulus mismatch when compared to other biocompatible metals as stainless steel or titanium alloys alleviates stress-shielding effects between bone and the implant material [2].

For being highly biocompatible and biodegradable, Mg is a potential material for producing temporary implants, dispensing a second surgery to remove the implant after the damage tissue is completely healed. Despite their high biocompatibility and no toxic risk during degradation, the corrosion rate of Mg is still too fast, compromising the structural function of the medical device.

Many studies have been conducted over the topic to overcome these issues, and among the potential solutions, the fabrication of composites show promising results. Some reasons for choosing this approach are the possibility to take advantage of bioactive ceramics' effects as assisting healing or improving the bonding between the tissue and the device, together with the benefits of having a metallic matrix, as good mechanical resistance, better ductility and good energy of impact absorption. Besides, a proper processing technique leads to a more uniform corrosion though the composite, lowering the degradation rate.

This chapter presents an overview having some of the newest studies over Mg-based composites for biological applications and provide a comparison among the processing techniques, effect of reinforcement content in corrosion and mechanical properties.

2. Biocompatible metallic materials

Medical parts as implants, stents, scaffolds and fixation devices are used when a bone is broken, for supportive structural purposes, bearing the body's load until the tissue can properly regenerate. These parts must present the following properties:

- Be biocompatible and have maximum cell viability to avoid any harm as inflammation, infection, or other adverse reactions;
- Not be toxic to the body, and not release toxic elements during degradation,
- Have a morphology that improves healing process and osseointegration [3];
- Have high enough corrosion resistance to assure mechanical integrity until the healing of the tissue;
- Remain stable and integer despite the constant impact of body movement;
- Have suitable mechanical properties as high toughness, tenacity, fatigue strength, stiffness comparable elastic modulus to bone to avoid stress shielding effects [4], and sufficient hardness to increase wear resistance and prevent wear debris.

Biomaterials currently used for this application can be polymers, metals, ceramics or composites. Advantage of metals for load-bearing application is the combination of better mechanical strength compared to polymers and better tenacity when compared to ceramics. The most common metals used are titanium alloys, stainless steel and chromium-cobalt alloy, that are bioinert. These metals have high strength to support body load and can keep a good integrity, staying longer in the body due to their high-corrosion resistance [5]. Iron, magnesium, and zinc are also biocompatible metals, with the advantage of being biodegradable in physiological environment. Other metallic biomaterials include shape memory alloys, tantalum and some precious metals [6].

Table 1 summarizes some mechanical properties, density, pros and cons of the usual biocompatible metals [6, 7]. For comparison, the properties of the cortical bones are: a density around 1.8 g/cm^3 , a modulus of elasticity of the order of 17.0–20.0 GPa in longitudinal direction and 6.0–13.0 GPa in the transversal direction, the tensile strength in the range of 78.8–151.0 MPa in longitudinal direction and 51.0–56.0 MPa in transversal direction, and a fracture toughness in the range of 2–12 $\text{MPa}\cdot\text{m}^{1/2}$ [8].

Material	Stainless steel	Cobalt-base alloys	Ti and alloys	Mg and alloys
Density [g.cm ⁻³]	7.4–8	8–8.5	4.5	1.74–1.81
Young's modulus [GPa]	200	230	106	45
Ultimate tensile strength [MPa]	540–1000	900–1540	900	80–280
Fracture toughness [MPa.m ^{1/2}]	~100	~100	~80	~15
Advantages	Cost, availability, processing	Wear resistance, corrosion resistance, fatigue strength	Biocompatibility, corrosion, low modulus, fatigue strength	Biocompatibility, biodegradable, low modulus, low density
Disadvantages	Long-term behavior, high modulus	High modulus, biocompatibility	Lower wear resistance, low shear strength	High hydrogen evolution during degradation
Primary uses	Temporary devices (fracture plates, screws, hip, nails)	Dentistry casting, prostheses stems	Femoral heads, long-term permanent devices (nails, pacemakers)	Bone screws, plates, pins, stents, nails

Table 1. Characteristics of usual metallic implant materials. Values taken from Ref. [6].

It is possible to notice a considerable mismatch of mechanical properties of these bioinert metals and the cortical bones. When the stress transfer between the implant and the tissue is not homogeneous, stress shielding of the bone may occur. This takes place by differences between Young's moduli of the implant and the bone, what may interfere the regeneration process, cause pain, bone atrophy with resorption of the bone surrounding the implant, loosening of the implant and possibly inducing a new fracturing [9]. Almost 10% from overall operations would undergo for revision surgery for replacing a previously implant, and 79% of all revisions were due to implant loosening [10]. The most common cause of implant loosening is the loss of bone mass due to stress shielding [10].

In the cases which the tissue can regenerate, the implant loses its function after the healing process, and additional surgery may be required to remove it. Besides, an implant which stay in the body for a long period of time can induce some complications, i.e. release toxic elements, permanent physical irritation, a chronic inflammatory response, or infection caused by debris and corrosion products [11, 12].

Biodegradable implants seem to be a clever choice for application where the body can eventually regenerate, since this would dispense the need of a secondary surgery to remove it, diminishing risks of inflammation, pain, surgery risks and costs [2, 12]. So, it is of great interest to develop devices which can be gradually degraded and naturally absorbed by the body while assist tissue healing. Yet, it has been challenging to obtain the combination of a controllable degradation rate, good biocompatibility, and suitable mechanical properties.

3. Magnesium as a biodegradable material

Among the available biodegradable metals, magnesium is very advantageous since it offers necessary stiffness, toughness and tenacity, high damping capacity,

very low density and high biocompatibility. It is the fourth most abundant mineral in the body, being present mostly as surface substituents of the bone's hydroxyapatite, and in skeletal muscle and soft tissue [13]. Also, Mg is involved in more than 300 essential metabolic reactions, being a cofactor for several enzymes that stabilize RNA and DNA structures. It is necessary to assist in cardiac, muscular, nervous, bone and renal function [14]. Its ion (Mg^{2+}) that is released during degradation is used in the regular metabolism having no critical toxic limits or side effects reported [3, 13]. It has great ability to be absorbed and excreted by the body without causing any harm (for example, the corrosion product MgO is totally removed in the urine [11]). During the first half of the 20th century, magnesium was used in surgeries to connect blood vessels and, in some cases, portions of the intestine in animals and in humans. The most advanced clinical applications are biodegradable cardiovascular magnesium stents; however, because it is bioabsorbable, research has been carried out aiming orthopedic applications as non-permanent implants.

The biggest issue that hinders the use of Mg as a biomedical material is its too fast corrosion in body fluid. This characteristic can be related to three main factors: Mg alloys are very reactive, the corrosion products formed in aqueous solutions containing chloride is not protective, and the micro-galvanic interaction between the constituent phases causes the corrosion of the Mg alloys to be significantly greater than that of the Mg of high purity [15].

Besides an early loss their structural function, a fast corrosion releases a big quantity of hydrogen, what may induce some local pH changes, affecting some physiological reactions and leading to an alkaline poisoning effect. Moreover, gas bubbles can accumulate in the implants surrounding surface delay healing and causing necroses due tissue detachments in some cases [3, 16].

3.1 Mg corrosion

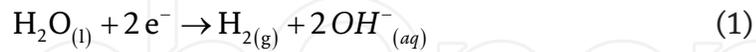
Two types of corrosion occur preferentially in Mg and its alloys, galvanic corrosion and localized corrosion (by pitting or filiform). Galvanic corrosion occurs because magnesium generally behaves anodically in contact with other metals, and it is often used as a sacrificial anode. The standard reduction potential of Mg to form Mg^{2+} is $E^\circ = -2.37$ VSHE and one of its main alloy elements is aluminum (Al), which has a reduction potential $E^\circ = -1.66$ VSHE in the reaction reduction for Al^{3+} . Galvanic pairs are generally formed when the concentration of the alloying element exceeds the maximum solubility limit. The extent of the galvanic effect depends on several factors, such as the crystalline orientation of the magnesium matrix, the type of secondary phases, particles of impurities, the size of the grain and the medium.

The concentration and distribution of the secondary phases are also important. A fine and continuous distribution of the secondary phases normally increases the corrosion resistance of the metal in various media. Alloy elements and other intermetallic phases formed, with electrochemical potential close to that of magnesium, can increase corrosion resistance, reducing galvanic internal corrosion [16].

Magnesium, when immersed in an aqueous solution, presents a double oxide film, an internal layer of MgO, which is adhered to the metal surface and an external and porous layer of $\text{Mg}(\text{OH})_2$ [17]. MgO oxide is a n-type semiconductor, with ΔG formation of -136 kcal/mol at 25°C , has a PB (Pilling Bedworth) ratio of less than 1, and is therefore only partially protective, since the volume of the oxide formed is less than the volume of the reagent metal. The $\text{Mg}(\text{OH})_2$ film has a lamellar structure that facilitates basal cleavage, and has a PB ratio of 1.77, which generates internal compressive stress, leading to cracks in the $\text{Mg}(\text{OH})_2$ film.

In the case of magnesium, unlike aluminum or steel, the oxide layer is crystalline. There is no epitaxy between the oxide layer and the matrix with the compact hexagonal mesh (HCP), leading to a high compressive stress of the layer [18]. One of the ways to reduce discontinuity and have less disorder between the oxide layer and the metal surface is to introduce a large fraction of grain outlines per unit area [19].

Cathodic reactions in neutral or alkaline aqueous media are oxygen reduction to hydrogen evolution, expressed in Eq. 1:



In order to have a complete understanding of the Mg corrosion mechanism, it is necessary to consider a phenomenon called Negative Difference Effect (NDE). This phenomenon is experimentally characterized by an unexpected increase in the hydrogen evolution reaction when the anodic overvoltage is increased. NDE is the main cathodic reaction in the corrosion of Mg and occurs spontaneously in Mg under open circuit conditions. When Mg and its alloys are anodically polarized, hydrogen evolution also occurs, which is normally restricted to the cathodic branch. Anodic polarization causes higher rates of dissolution, and higher rates of NDE are also observed [20]. To explain the corrosion of magnesium and more particularly the NDE phenomenon, several mechanisms have been proposed including the formation of magnesium hydrides, metastable monovalent ions, hydroxides and magnesium oxides [17].

The corrosion rate of magnesium-based biomaterials, when implanted in the human body, depends on the composition of the material and the environmental conditions in which the implant is found, such as temperature, pH and concentration of other ions. A study [21] indicates that, the effects of Mg corrosion products on cellular activity is concentration-dependent, on bone marrow derived stem cells and on osteoclastogenesis *in vitro*. This will vary depending on the state of differentiation of cells and length of exposure. Also, the presence of the corrosion products significantly altered the cells' metabolic and proliferative activities, which further affected cell fusion/differentiation. Maradze and coauthors [21] summarizes the cellular response in the presence of a corroding Mg biomaterial *in vivo* in **Figure 1**.

The corrosion rate of Mg can be reduced by increasing the intensity of the basal planes parallel to the surface [22]. Other strategies to diminishing the degradation rate are grain refinement, alloying, surface modification, conversion coating, and incorporation of other materials to create composites. It is worth noting that, in the case of composites, some of these strategies can be combined. For example, a processing technique that enables a refined microstructure can be selected. Grain refinement has a recognized importance for improving mechanical resistance and also for diminishing the corrosion rate with time due to the development of a more homogeneous protective layer on composites surface [23–25]. Also, the matrix can either be pure Mg or an alloy. Although many Mg-alloys are been developed for improved corrosion resistance and superior mechanical strength [4, 11, 26], care must be taken to choose a composition free of any toxic elements. The insertion of a biocompatible second phase in a magnesium matrix could bring a better mechanical resistance and less pitch corrosion. Furthermore, some bioactive materials that could promote a better bonding between implant and the tissue can be incorporated and accelerate body's healing response in some cases. Also, the addition of a hard phase, combined with mechanical processing, enables a better grain refinement and strengthening. Thus, magnesium matrix composites are potential candidates for structural orthopedic implants.

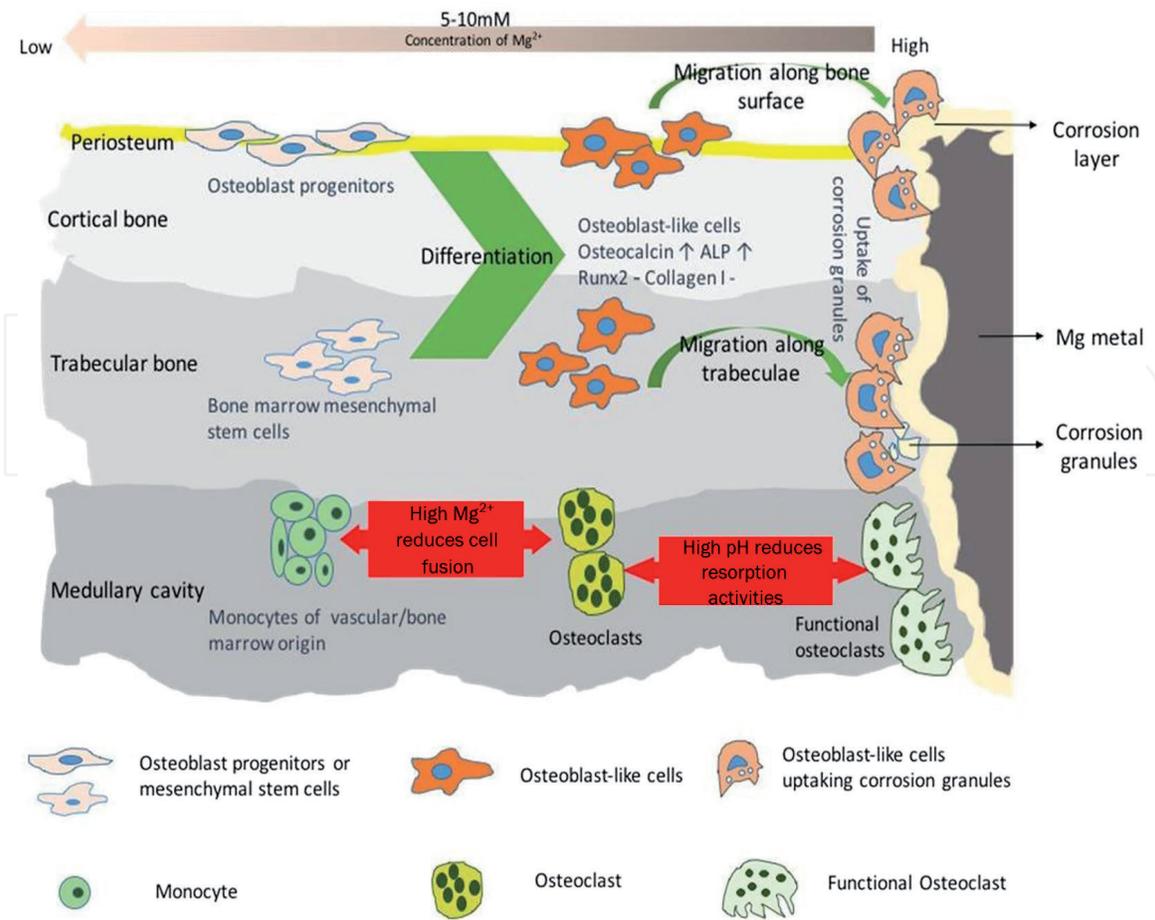


Figure 1. Representation of cellular response in the presence of a corroding Mg biomaterial in vivo [21]. Scientific reports – Open access.

4. Magnesium-based composites for biomedical applications

There are three determinant factors for the biocompatibility, mechanical strength and corrosion behavior of the Mg-composite: grain size, second phase distribution, and materials composition. The first two can be controlled by fabrication and processing technique. The deformation route directly influences the texture of the material, that has a great influence on magnesium corrosion. Also, the reinforcement selection (nature, fraction and morphology) is of great importance for dictating the composite's properties, and it will determine if the device is toxic, inert, or bioactive.

4.1 Selecting the magnesium-matrix

Elements commonly used for Mg alloying are Al, Ca, Cu, Fe, Li, Mn, Ni, Sr., Y, Zn, Zr, and rare earth elements.

Aluminum is the most usual alloying element for Mg. It can enhance the alloy strength by both solid solution and precipitation of intermetallics. Another advantage is the low density of this metal (2.7 g/cm³). Although alloys as AZ91 and ZK60 have been used for biomedical applications, this element should be avoided due to the risk factor of Alzheimer's disease, muscle damage, decrease of activities of osteoclasts, altered functions of the blood-brain-barrier, and increase estrogen-related gene expression in human breast cancer cells when cultured in a laboratory setting [11, 27].

Manganese can improve Mg corrosion resistance by reducing the harmful effects of impurities [27]. Mn is also an essential biological trace mineral that acts in many cellular systems, especially as cofactors for many metalloenzymes as oxidases and dehydrogenases, DNA and RNA polymerases, kinases, decarboxylases and sugar transferases, although excessive amounts could induce neurological disorder [27].

Zinc is another common alloying element in Mg. It is nontoxic, biocompatible and biodegradable, and plays a significant role in human body. Zn is present in metabolic activities, as co-factor for some enzymes and it is essential for immune system. It is readily absorbable by biological functions within the cell [27]. The addition of until 4% wt. Zn increase ultimate tensile strength and elongation of as-cast Mg-Zn alloys.

Calcium is the most abundant mineral in the human body, important for bone function, vascular and heart physiology. Adding in small amounts, it can contribute for mechanical strengthening by solid solution, precipitation and grain boundary pinning. Mg₂Ca is brittle and the addition of >1%Ca deteriorate ductility and mechanical properties. Despite Ca positively influence the cell viability and proliferation rate, the effect of Ca in corrosion resistance is deleterious because it accelerates degradation due to galvanic corrosion.

Kirkland et al. [28] perform a systematic study comparing the degradation of a series of Mg-Ca-Zn alloys. **Figure 2** present average values of the maximum compression strength of their Mg-xCa and Mg-xZn alloys after 1 and 3 weeks of immersion in SBF, in relation to the alloying content. The blue lines indicate the compressive strength of pure Mg, after 3 weeks in SBF (lower line) or without immersion (upper line).

An issue related to the most common alloys is concerned about the biocompatibility and toxicity of alloying elements [29]. The alloying elements might be selected to not only improve corrosion and mechanical properties of the alloy, but also to improve the body response. But mostly, special care must be taken to avoid elements that may release corrosion products that can be toxic to the body. A summary of the influence of metal ions on the variety of processes involved in bone regeneration is depicted in **Figure 3** [30].

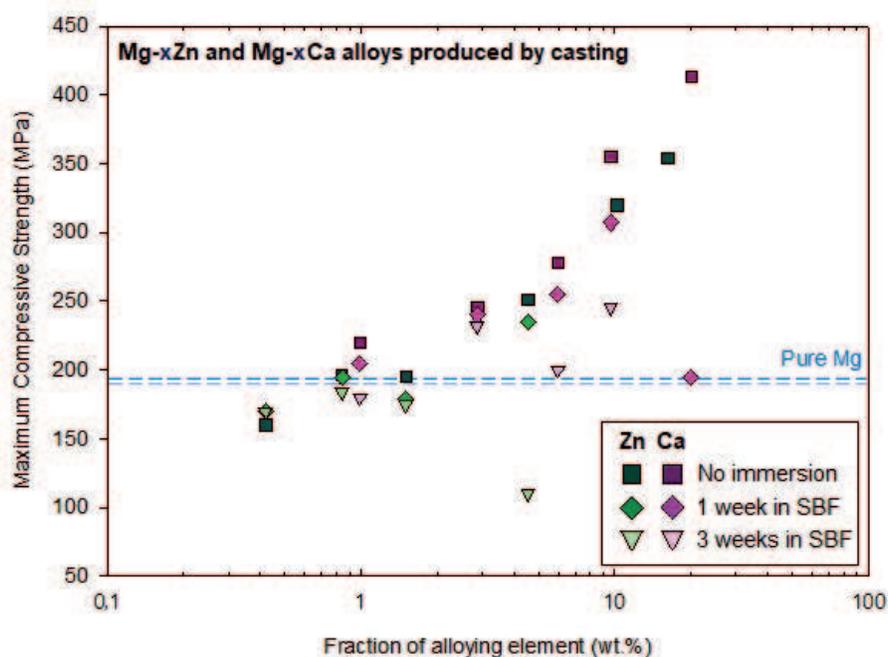


Figure 2. Effect of alloying content in the compression strength of Mg-xCa and Mg-xZn alloys after 1 and 3 weeks immersed in SBF. Based on Ref. [28].

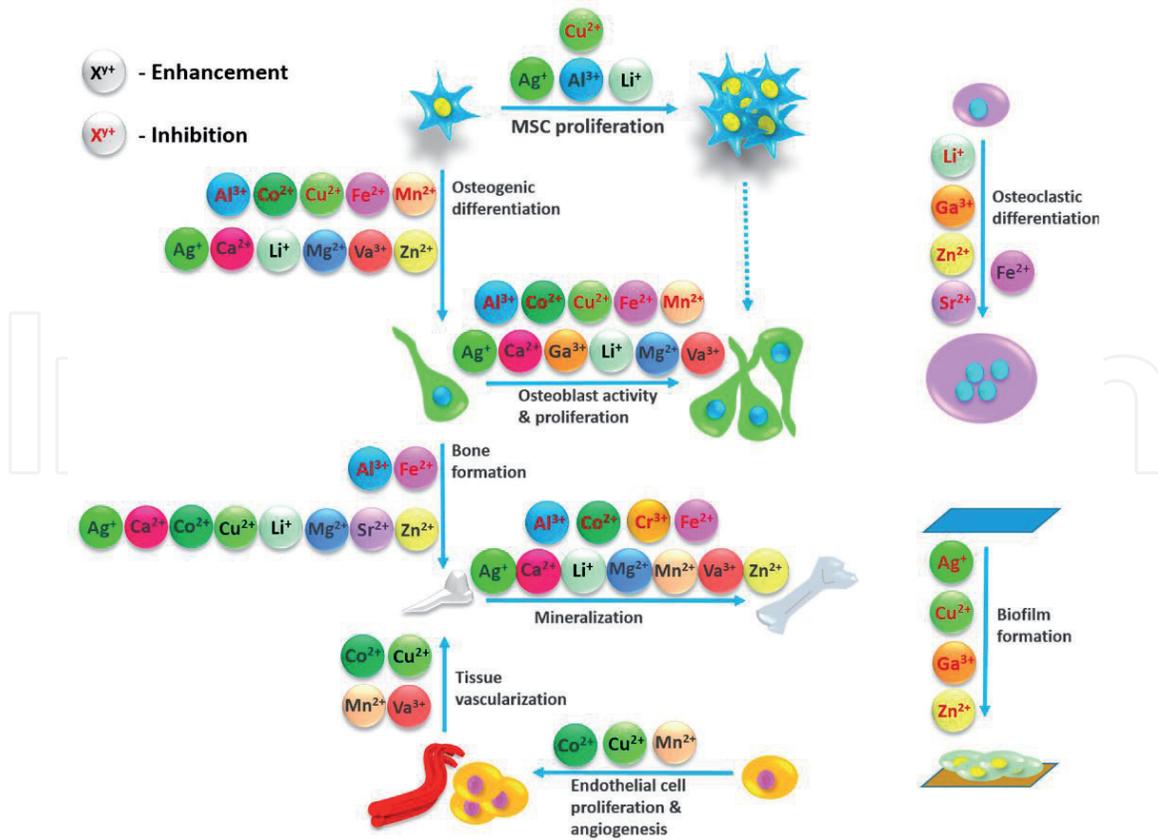


Figure 3. Summary of the influence of metal ions on processes involved in bone regeneration [30]. MDPI-open access.

4.2 Selecting the reinforcement

The reinforcement selection (nature, fraction and morphology) is of great importance for dictating the composite's properties. Primarily, it should be highly compatible and safely absorbable by the body without any harm to the organism. It should also achieve a good interfacial bonding with the matrix, since a discontinuous matrix can lead to stress concentration, facilitating crack evolution and increasing localized corrosion.

The most common materials used to reinforce Mg-based composites aiming biomedical applications are silica-based or phosphate-based ceramics [4]. Bioactive glasses (BG) is an important silica-based material that can make a strong bonding to the bone. It is intrinsically brittle. They display significant bioactivity, improves hemocompatibility, and the ionic dissolution products of bioactive glasses stimulate osteoblast proliferation [31]. They are used in dental implants and for artificial bone. Some papers have reported that addition of BG to Mg matrix can improve the biocompatibility of pure Mg [32]. Yet, calcium phosphates such as hydroxyapatite (HA) and tricalcium phosphate (TCP) are the most popular choice to fabricate Mg-matrix composites aiming biomedical application. B-TCP has a great importance for being bioresorbable, bioactive and osteoconductive material. It is used for bone tissue regeneration. HA can form strong chemical bonds with the osseous tissue and it is one of the main components affecting the mechanical strength to bone, providing it stiffness [1]. It is commonly used as orthopaedical implants, dental implants and coating metallic implants, tissue engineering scaffolds. Yet, bone grafts made exclusively of HA present a low fracture toughness ($0.7 \text{ MPa}\cdot\text{m}^{1/2}$, [16]).

The opportunity to match the superior compressive strength and biological performance of bioactive ceramics, with the toughness and resilience of Mg and production of biodegradable and bioactive composites is of great research interest.

There are many researches over the fabrication of a magnesium-based composite with biocompatible ceramic reinforcements dispersed into the metallic matrix. Many review papers about Mg-based composites for biomedical applications have also been published, covering since fabrication methods, mechanical properties improvement, corrosion behavior and also biocompatibility *in vitro* and *in vivo* [4, 7, 33–35].

4.3 Selecting the fabrication technique

The fabrication methods used to produce Mg-based composites for biomedical purposes are listed below. The processes techniques can be divided in either liquid state (casting) or solid-state processing route (powder metallurgy). Routes that involves casting promotes the insertion of the hard phase in a liquid bath of the matrix-metal, while solid-state routes achieve dense consolidated composites without melting the materials. In this case, the particles consolidation should be induced by high-temperature diffusion and/or plastic deformation. To ensure a full densification of the composite, great majority of the solid-state techniques takes place at high temperatures, but below materials' melting point. All processing techniques should enable an efficient matrix-reinforcement bonding and a homogeneous dispersion of the hard phase, since agglomeration and internal cracks are deleterious to corrosion and mechanical properties [36, 37].

4.3.1 Casting

Many metallic composites are synthesized by casting techniques. They can be fabricated by pumping the melted metal at high pressure into a die which can contain the reinforcement dispersed or as a preform. Alternatively, the hard phase can be added to the matrix by stirring it into the melted metallic bath.

Khanra et al. used stir casting to fabricated Mg-HA and ZM61-HA composites having different amounts of HA (0, 5, 10 and 15 wt%), then performed hot extrusion at 320°C on the billets [38, 39]. The addition of HA induced grain refinement, an increase in compressive strength but a decrease in tensile strength. Since the alloy have superior strength than the pure metal, (ultimate tensile strength – UTS of the Mg-0 HA is 187.9 while UTS of ZM61-0HA is 301 MPa) the ZM61-HA composites presented higher mechanical properties than Mg-HA ones (UTS of Mg-15HA is 136.7 MPa, against 225.5 MPa from the ZM61-15HA).

Melting and hot extrusion were also applied to synthesize Mg-Zn-Zr matrix composites with 0, 0.5, 1 and 1.5 wt% HA as reinforcement [40, 41]. Common results were the improved of mechanical properties with HA addition, and reduction in corrosion rate for composites having 1 wt% HA.

Kumar et al. [42] synthesized HA-MgO composites using 0, 0.25, 0.5, 1 and 2% MgO by melting infiltration. The mass loss, after 21 days in SBF, of pure HA is 0.43 ± 0.08 mg, which is significantly higher than the HA-1.0 MgO composite (0.21 ± 0.03 mg). As increasing the amounts of MgO, a remarkable increase in the mechanical properties of the composite was achieved.

4.3.2 Powder metallurgy processing

Powder metallurgy (PM) techniques involves a methodology composed of powders mixture, compaction and sintering of the materials, usually in an inert atmosphere. The mixture is commonly performed by ball milling especially when a better interaction between matrix and reinforcement is expected. Uniaxial pressing at room temperature is generally applied to create the green compacts before

the sintering steps. Other processes as isostatic pressure, hot pressing [43, 44] and double-step sintering [45] have also been used to assure a better densification of Mg-HA composites. Conventional sintering strongly relies on diffusional processes, that are favored by longer times and higher temperatures, and this can lead to a significant grain growth during the process.

Setyadi et al. [46] fabricated Mg-CA composites having 5, 10, 15 wt% of carbonate apatite (CA) by powder metallurgy. The higher milling times and higher content of CA lead to an increase in hardness of until ~20% when compared to pure magnesium (hardness whet from 37.3 HV in pure consolidated Mg to 44.8 HV for 7 h of milling and 15% CA). The optimal composition was obtained for the composite with 10 wt% of CA. Salleh et al. [47] produce Mg6.5Zn matrix composites with 0 and 10 wt% of HA by mechanical milling and PM. The progressive effect of HA followed by the Zn addition, decelerate the degradation rate of Mg. The composite exhibited the highest corrosion resistance in Hank's Balanced Salt solution (HBSS). The compressive strength for the alloy and the composite, after 7 days of immersion, are considerably higher compared to the cortical bone.

Double step sintering PM (450°-550°) was applied by Jaiswal et al. [45] to fabricate Mg-3Zn matrix composite reinforced with 0, 2, 5 and 10 wt% of HA. It was reported that the addition of 5 wt% HA is found effective in reducing the corrosion rate by 42% in SBF. Mg-Zn with 5% HA showed improvement in the compressive yield strength of biodegradable magnesium alloy by 23%.

Ball milling and hot extrusion at 270°C were used by Stüpp et al. [43] to produce ZK60-HA composite with 0, 10, 20 wt% HA. A slight improvement in the corrosion resistance was observed for the composites in DMEM + FBS. Samples showed a slight increase in the compressive yield strength with the addition of HA.

Spark plasma sintering (SPS) apply high-pressure to enable a better densification of the sample using considerably less time and lower temperatures than in conventional sintering, and thus achieves finer grain sizes. Sunil et al. [48] used ball milling and SPS at 450° to produced Mg-HA composites having 0, 8, 10 and 15 wt% of HA. Fracture toughness and Young's modulus decreased with the increase of HA content, but were improved in relation to the as cast Mg. The Mg-10%HA composite present the better corrosion resistance among the samples.

Microwave-assisted processing is another sintering technique which a uniform heat is induced with an accurate energy balance by electromagnetic waves in a high-frequency electric field. It promotes a rapid sintering of the Mg to a sample which density is near the theoretical value, using relatively low energy consumption. This approach was used by Wan et al. [32] to produce Mg-BG composites with 5, 10 and 15% of BG. The materials were ball milled and sintered in a microwave furnace at 500°C. It was reported that the addition of bioactive glass can considerable reduce hydrogen evolution, avoid significant pH change and improve biocompatibility when compared to pure Mg. The best mechanical and biological behavior was presented by the Mg-10%BG composite. The improvements in compressive strength and modulus are 34.0 and 18.7%, respectively, compared to pure Mg. Xiong et al. [49] also used the same procedure to prepare Mg-HA composites having 5, 10 and 15 wt% of HA, and observed that mechanical properties and corrosion resistance of Mg-HA composites were better than the ones of pure Mg. The HA was well dispersed in all samples, but the optimum composition was found to be 10% of HA. This reinforcement addition not only presented the lower corrosion current density (1×10^{-4} A/cm²) but also increased the compressive strength and modulus by about 67.5 and 42.8%, respectively.

In the available review papers, it is possible to notice that all methods described to produce the biodegradable composites involve at least one steep of high temperature processing. Yet, it was recently reported that different bioactive

composites were fabricated by high-pressure torsion (HPT) at room temperature, combining Mg and alloys with bioactive reinforcement as hydroxyapatite or bioactive glass [50].

4.3.3 Severe plastic deformation

Severe plastic deformation (SPD) are processes techniques where high hydrostatic pressures are applied while the materials goes through an intensive shear, but without significant change in sample's dimensions. This enables multiple consecutive process steps and then accumulation a great amount of deformation. As a result, the processed materials go through extensive grain refinement, homogenization of second phases' distribution and alteration of the texture, which can contribute to the reduction of corrosion [24, 25, 37, 51]. Yet, it is observed that corrosion analysis of magnesium alloys with ultrafine grains is particularly complex, as it may involve factors such as texture, formation of unstable passive film and of heterogeneous structures resulted from dynamic recrystallization.

Equal channel angular pressing (ECAP) and high-pressure torsion (HPT) are well-known SPD techniques that can not only process bulk samples but also consolidate metal particles and produce metal-matrix composites with a refined microstructure. The mechanism of powder consolidation SPD processes differs from conventional sintering routes because the bonding between particles is caused by deformation of the particles, rather than the atomic diffusion. Thus, shorter times and lower temperatures are needed to consolidate the particles into a fully dense sample.

Silva et al. [25] reported the beneficial effects in SPD Mg in compared to as cast or hot rolled samples. As is showed in **Table 2**, the SPD processed samples present smaller grain sizes, thus better mechanical properties and better corrosion properties. Besides the formation of a protective film composed of corrosion products - that reduced the loss of mass after long intervals immersion – Mg biocompatibility was not affected by this treatment.

It is difficult to standardize and control the texture of the alloys during SPD processing. However, it is known that HPT processing leads to a preferential orientation of the grains, of the magnesium alloy, in (0002) or basal plane. Since the basal plane is more stable than other non-oriented planes or grains, thus the increase in oriented grains (0002) increases corrosion resistance [18].

High-pressure torsion was also used to fabricate Mg-based bioactive composites, but at room temperature [50, 52]. The matrix where composed by commercially pure Mg or the AZ91 alloy, and the selected reinforcement were bioactive glass or hydroxyapatite. SEM images of the materials are depicted in **Figure 4**.

Processing	Grain size (μm)	Yield stress (MPa)	Corrosion potential (V)	Corrosion current (A/cm^2)	Corrosion rate ($\text{g}/\text{cm}^2/\text{h}$)
As cast	480	34	-1.48	7	54
Hot-rolled	16	110	-1.61	350	—
Hot-rolled + ECAP	3.2	140	-1.51	40	25
HPT	0.56	80	-1.49	8	19

*Corrosion rate calculated from the H_2 evolution after 48 h of exposure in 3.5% NaCl solution.

Table 2.
 Properties of pure Mg processed by different techniques [25].

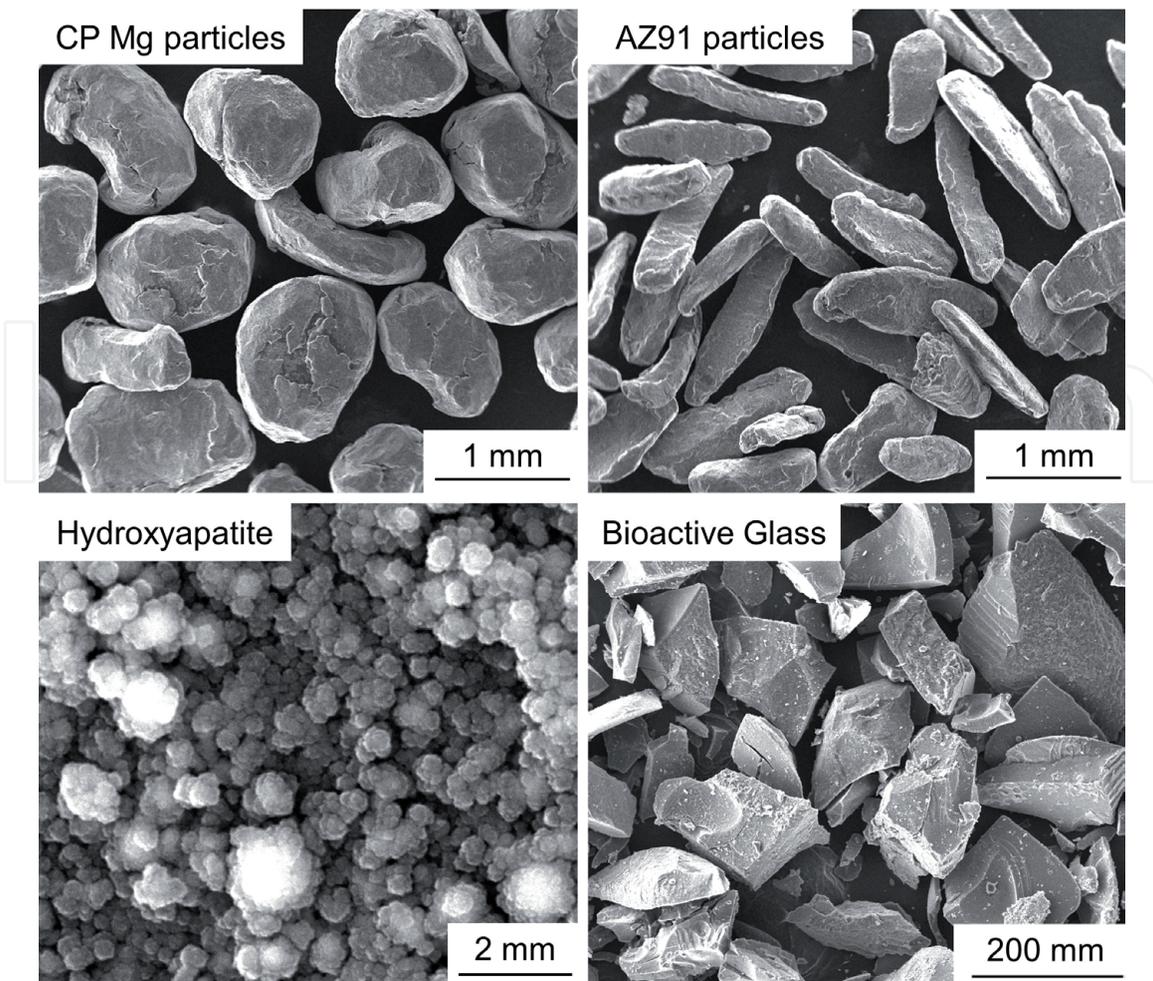


Figure 4. Particles used as starting materials to produce Mg-based composites at room temperature using high-pressure torsion [50]. [50] MDPI-open access.

The AZ91–5%BG and Mg–5%BG composites [50] exhibited small impedance arcs and fast corrosion in HBSS due to the presence of cracks developed inside BG particles during processing. Adding the bioactive ceramic improved hardness of all composites, and this gain was more expressive for the ones with CP-Mg matrix (77% higher than the monolithic HPT-processed Mg). It was reported that a good dispersion of HA and an efficient consolidation of the matrix were achieved for the Mg–5HA (**Figure 5**). The tensile strength and the hardness of this composite was improved in relation to the pure metal. As Mg is soft and the particles are relatively big, it can easily deform around the ceramic particles, either HA or BG. On the other hand, AZ91 has a better strength than the pure metal (**Figure 6a**), so it is harder to consolidate. Besides, bioactive glass particles are sharp and fragile, so they can fracture during processing and induce localized corrosion in discontinuities surrounding.

This corroborates with the poor corrosion resistance of the BG reinforced composites, especially the AZ91–5BG, as shown in **Figure 6b**. The size and nature of the reinforcement are indeed determinant for slower corrosion rate due to the tendency to develop cracks during processing. This fact was also observed in Mg-quasicrystals composites [53] which fractured along the coarse quasicrystalline particles and on the matrix-reinforcement interface after tensile test.

In the Mg–5%HA composite [52] the addition of HA enhanced the corrosion resistance after 10 hours of immersion in HBSS, the impedance increases and the mass loss rate decreases in the composite. The composite exhibited enhanced hardness and ultimate tensile strength in comparison to pure Mg process by HPT. The corrosion evolution behavior of the Mg–5%HA reported by Lopes et al. [52] seems to be slower

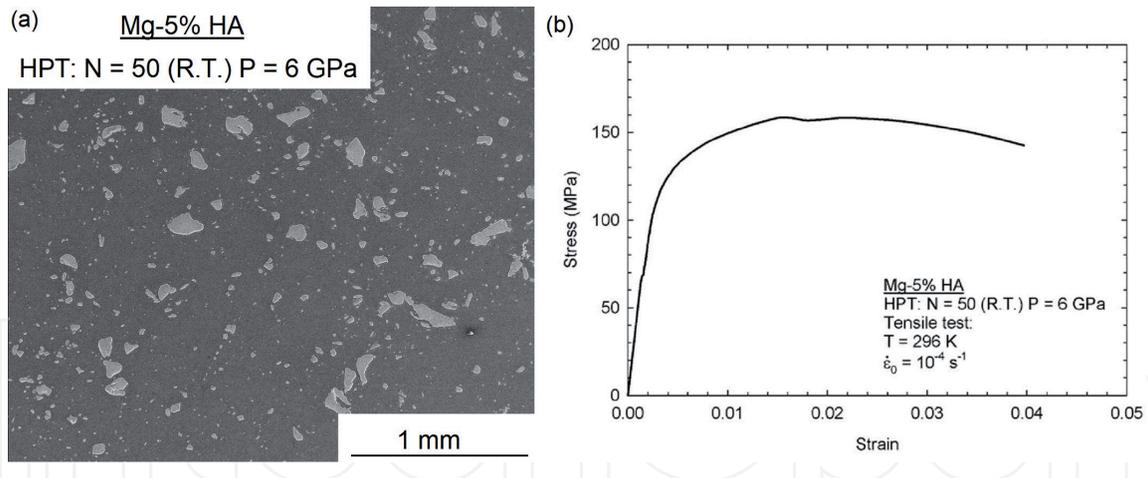


Figure 5. (a) SEM backscattered electron image of the mid-radius area of the Mg-HA composite, and (b) its respective stress vs. strain curve [50]. MDPI-open access.

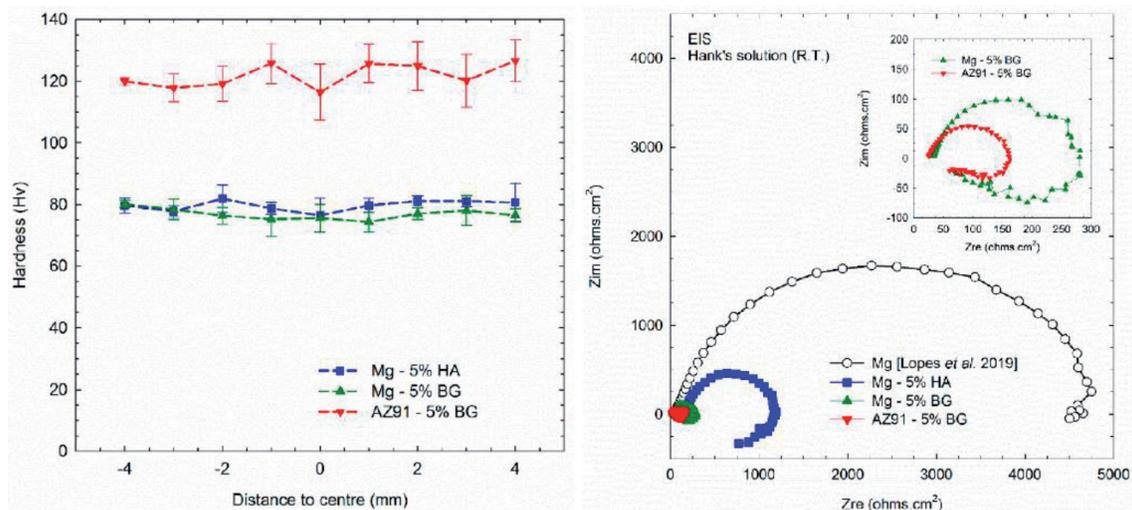


Figure 6. (a) Microhardness distribution along the disc diameter in the different Mg composites, and (b) electrochemical impedance spectroscopy tests in Hank's solution for the different composites [50]. MDPI-open access.

than for the Mg-5%BG reported by Castro et al. [50] due to the smaller size and morphology of HA particles, what facilitates a better continuity of the matrix and less stress concentration on the Mg-5%HA composite. In relation to pure Mg, immersion tests of the Mg-5%HA composite leads to a resulting superficial layer that appears to be thicker and the corrosion seems to be more generalized, what contributes for the diminishing of the corrosion rate after longer immersion times (**Figure 7**).

In another recent work, a combined method of cyclic extrusion compression (CEC), equal channel angular pressing (ECAP) and conventional extrusion were employed to fabricate Mg-HA composites with 2, 5 and 10 wt% HA at 400°C [54]. Among all samples, the Mg-5HA composite presented the finest grains and exhibited the highest hardness and strength. Hydrogen evolution tests and potentiodynamic polarization tests showed that among all samples, this composite has the lowest values of evolved hydrogen, weight loss and corrosion current density. Its corrosion resistance is also better than in cast and extruded pure Mg. The CECAP-FE process proved to be able to achieve a good and homogenous reinforcement dispersion until 5 wt% of HA. Adding more reinforcement deteriorate mechanical properties and corrosion resistance, what is directly related to the development of the inhomogeneous microstructure and HA agglomerations.

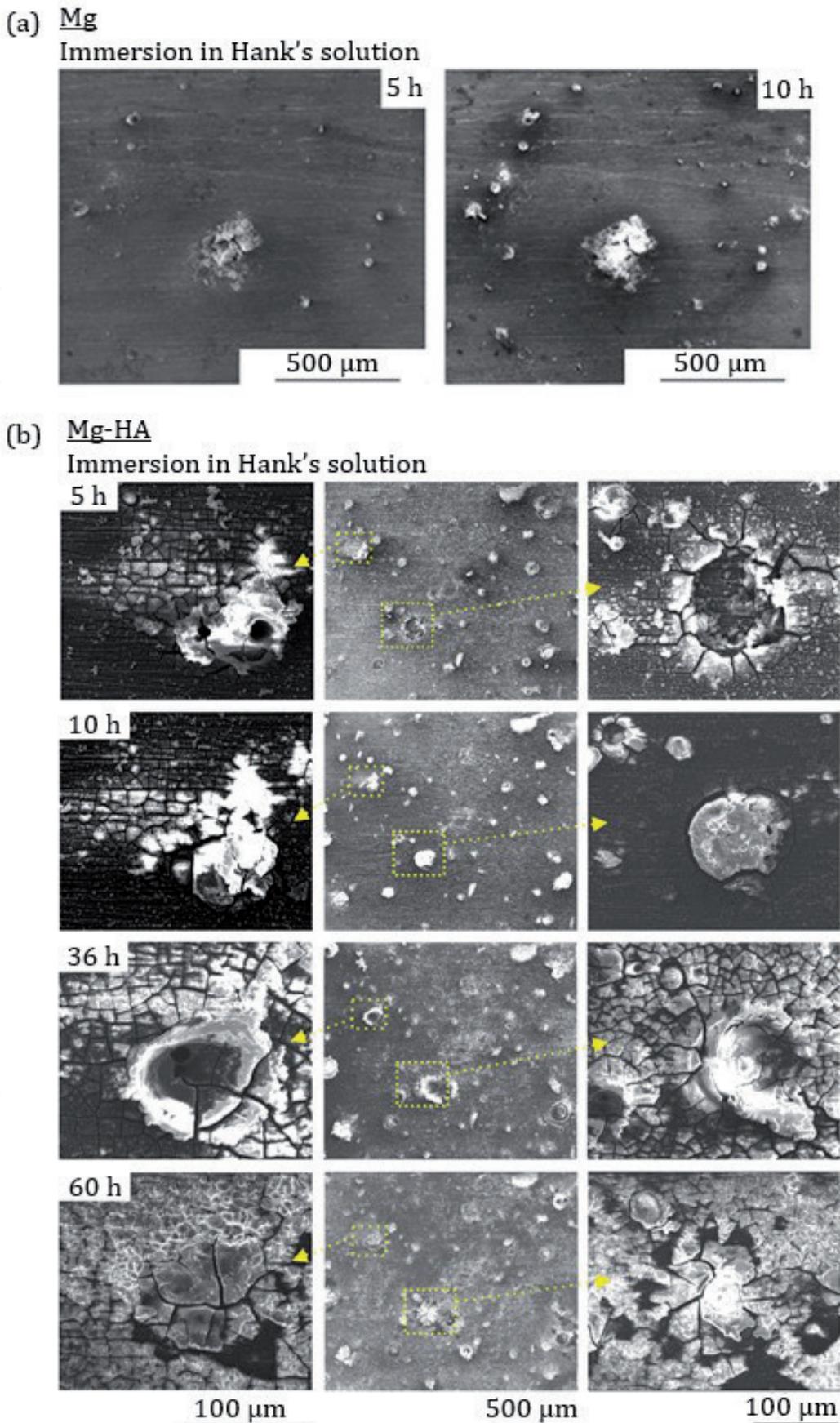


Figure 7. (a) Mg and (b) Mg-HA surfaces after immersion in Hank's solution. (reproduced with permission [52]. Copyright 2020, AEM/license number: 4924491163715).

The thin surface layer of magnesium oxides and hydroxides formed when these materials are exposed to neutral or alkaline solutions have time-dependent stability and, in many studies conducted on magnesium alloys with ultra-fine grains, the results

for the evolution of this stability over time are inconsistent [55]. For example, in the research works of Minárik et. al [56] and Zhang et. al [57], there was an increase in the stability of Mg oxides and hydroxides over time, while Song et. al. [58] observed a decrease in this stability. There are also studies in which growth and decreased stability were reported during the analysis period [59]. This factor is relevant, and as the results of polarization tests or hydrogen evolution - which involve immersion - may be affected by the protective oxide instability [55]. The contradictory conclusions of corrosion studies in pure magnesium and magnesium alloys may be due to these microstructural heterogeneities resulting from the recrystallization dynamics [55, 58–61].

5. Concluding remarks

Magnesium-based composites are recognized as promising materials for biomedical applications due to the combination of good mechanical properties, low density, and possibility to achieve a slower corrosion rate and enhance healing by the presence of bioactive materials.

Several studies conducted by many research groups all around the world leads to the conclusion that a more controllable corrosion rate relies on a homogeneous second phase distribution, and refined matrix absent of cracks or stress concentrators.

The use of fabrication methods based on the plastic deformation of metallic particles requires less time and lower temperatures to produce whole dense materials in comparison to techniques primarily relied on diffusional processes. These processes enable the achievement of smaller grain sizes and thus better mechanical properties and slower corrosion rates. Besides, the use of SPD for processing Mg-based materials does not compromise biocompatibility.

The possibility to create composites without using high-temperature steps is interesting not only due to the operational and energetical advantages (it is less energy and time consuming, generates no fumes, and avoid grain growth), but also due to the potential of creating controlled drug delivery system with medicines that are temperature sensitive and could deteriorate during conventional processing.

It appears that combining materials and techniques could be more efficient than a singular approach to overcome the current issues to produce an ideal biodegradable implant. Yet finding the best materials combination, adjusting their proportion, and selecting the most suitable fabrication route with optimized parameters is still challenging.

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Conflict of interest

The authors declare no conflict of interest.

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