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Biodegradable magnesium alloys for short-term orthopedic implants: properties, surface modification and biological response

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ABSTRACT

Orthopedic diseases pose a significant challenge in the medical field, often requiring innovative solutions to address the unique needs of the patient. Orthopedic implants increasingly demand materials that not only meet mechanical and biological requirements, but also actively participate in the healing process. Magnesium and magnesium-based alloys are lightweight materials that have emerged as promising candidates because of their biodegradability, biocompatibility, and mechanical properties, which closely resemble natural bone. A key advantage of magnesium alloys lies in their ability to slowly degrade in vivo, which translates into their potential for use in temporary, bioabsorbable implants, thus eliminating the need for surgical removal. However, rapid and uncontrolled corrosion remains a critical barrier to their clinical translation. This review provides a focused analysis of current strategies to engineer the controlled biodegradation of magnesium-based orthopedic implants. We critically examine the role of alloying elements, surface modification techniques, and biological interactions in modulating degradation behavior. Particular attention is paid to the interaction between material design and biological response, which is essential for maintaining implant functionality during tissue regeneration. By identifying challenges and highlighting emerging directions, this review aims to support the development of next-generation biodegradable magnesium-based implants tailored for orthopedic applications. We wish to inspire more research and development into magnesium alloys biomaterials for the orthopedic field.

1. Introduction

1.1. Biodegradable implants and the pitfalls of current materials

Every year, the number of bone fractures resulting from accidents or illnesses is increasing. Analyzing global statistics in 2019, there were 178 million (95 % uncertainty interval [UI] 162–196) new fractures and mainly involved injuries such as fractures of the lower leg of the patella, tibia, fibula, or ankle [1]. As the population ages, the number of people suffering from osteoporosis increases, which also greatly contributes to the number of bone fractures that occur. It is estimated that around 200 million people worldwide suffer from osteoporosis, and it is the cause of more than 8.9 million fractures annually worldwide [1,2].

Depending on the location and severity of a fracture, various stabilization methods are used. The most common and cost-effective approach is external stabilization using a traditional plaster cast. However, for more complex fractures, surgical intervention may be necessary, involving internal stabilization with bone plates, screws, or intramedullary nails. For manufacturing such implants, metallic biomaterials are typically used, especially for short-term applications (less than 2 years in the body). Austenitic stainless steel is commonly used for temporary implants, while cobalt-chromium and titanium alloys are favored for long-term applications, which may remain in the body for up to 20 years [3].

Temporary metallic implants usually require surgical removal after a designated period, typically 12–24 months, assuming that no complications occur [4]. This second surgery presents a significant burden, both economically and clinically. Onche et al. [5] reported that the

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removal of orthopedic implants places additional strain on hospital resources and patients, especially in resource-limited settings. The need for repeated anesthesia, risk of infection, prolonged rehabilitation, and psychological stress underscore the drawbacks of nondegradable implants.

In addition to the need for secondary procedures, conventional metallic biomaterials have intrinsic limitations. One major concern is stress shielding, resulting from the significant mismatch in elastic modulus between the implant and natural bone (titanium: ~110 GPa, stainless steel: ~200 GPa vs. cortical bone: ~10–30 GPa) - Table 1 [6]. This mechanical mismatch can reduce the loading stimulus necessary for bone maintenance, leading to bone resorption and eventual implant loosening, reduction in bone thickness, and an increased risk of osteoporosis [7–11]. These materials are also bioinert, failing to promote biological healing or integration without surface treatments. Furthermore, the release of metal ions (for example, nickel, cobalt) from implants may cause adverse tissue reactions or allergies, and the presence of permanent foreign material can increase the risk of chronic inflammation or late infection [12,13].

1.2. *Magnesium and magnesium alloys: promising biodegradable materials*

Unlike the previously described materials, magnesium (Mg) is biodegradable and bioactive, releasing Mg^{2+} ions that are involved in bone metabolism and osteogenesis. In fact, Mg is the fourth most common element in the human body and more than 50 % of its reserves are in the bone [14]. It is an essential nutrient necessary to keep the human body healthy, which can promote bone growth, increase cell adhesion to biomaterials, and support osteoblast differentiation and biomineralization [14]. Mg reacts with physiological fluids in the body to form soluble and non-toxic products that are excreted in urine without posing a health risk [15]. It is easily corroded in physiological environments due to its chemical properties and can degrade.

The dissolution of Mg in an aqueous environment usually proceeds through an electrochemical reaction with water, resulting in the formation of magnesium hydroxide ($Mg(OH)_2$) and hydrogen gas (H_2). This process is described by the following equations:

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

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

$$\text{Product formation: } Mg^{2+} + 2OH^- \rightarrow Mg(OH)_2 \quad (3)$$

However, pure Mg has inadequate mechanical properties and low corrosion resistance. Therefore, various alloying additives are often used to improve strength (Fig. 1). Mg alloys for biomedical applications are characterized by good mechanical properties that are more similar to those of human bone among other metal biomaterials [16,17].

High number of studies have been reported on the development of biomedical Mg alloys with strong commercialization potential (Fig. 2).

These Mg-based systems usually contain alloying additives such as aluminum (Al), calcium (Ca), zinc (Zn), and rare earth elements (REE) [18]. Much attention is paid to the study of finished alloys that have a specific chemical composition, among which we can mention AZ31

Table 1
Mechanical of metal biomaterials [6].

Material	Density	Young's modulus [GPa]	Tensile strength [MPa]	Yield strength [MPa]
Ti alloys	4.4–4.5	110–117	930–1140	758–1117
Co–Cr alloys	8.3–9.2	230	900–1540	450–1000
Stainless steel	7.9–8.1	189–205	480–620	170–310
Magnesium	1.74–2.0	41–45	170–270	65–100
Bone	1.7–2.0	3–20	80–150	130–180

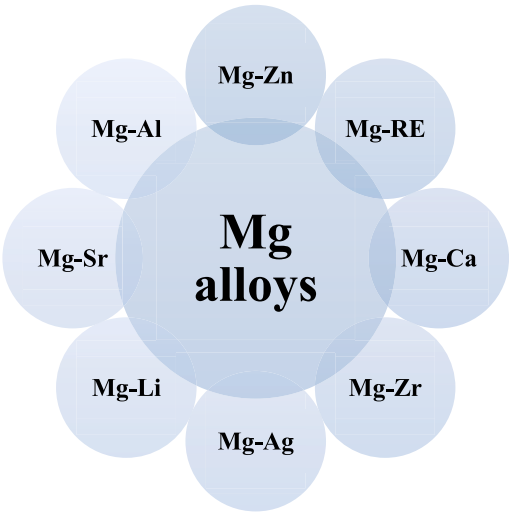

Fig. 1. Magnesium-based alloys for biomedical applications.

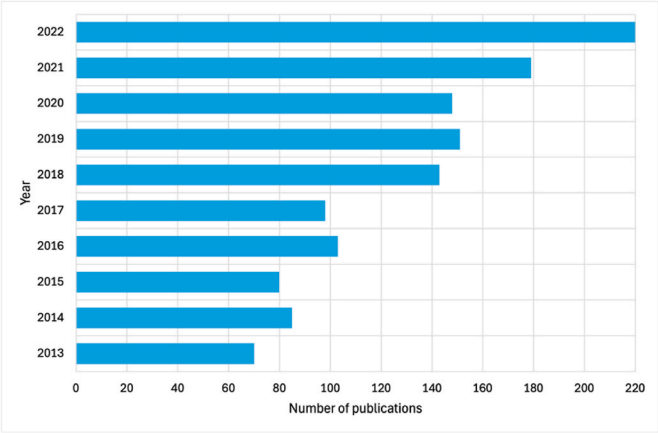

Fig. 2. Number of annual research publications. Based on Y. Zhu et al. "Global trends in the research of biodegradable biomedical magnesium-based materials: a bibliometric analysis" [62].

(Mg–3Al–1Zn), AZ91 (Mg–9Al–1Zn), WE43 (Mg–4Y-3RE-Zr) and ZK60 (Mg-5.5Zn-0.45Zr).

Al is the most used Mg alloying additive [19]. By choosing the right concentration of Al, a biodegradable alloy with improved strength and good corrosion resistance can be obtained. Typically, an Al content of less than 10 wt% is used in Mg–Al systems [20]. The use of a too high Al concentration in the alloy was found to lead to an increased presence of the $Mg_{17}Al_{12}$ phase, which contributes to galvanic corrosion and increased electrochemical activity, accelerating the corrosion process and degradation of the biomaterial [21,22]. In addition, high concentrations of Al are believed to affect the development of dementia and Alzheimer's disease [23–25]. Thus, its use as an alloying element should possibly be limited. The long-term impact of implanting Al-containing materials is unknown, hence special attention should be paid to thoroughly testing these biomaterials *in vitro* before proceeding to clinical trials.

Zn as an alloy additive increases mechanical properties such as hardness, tensile strength, ductility, and deformability of Mg-based alloys, as well as corrosion resistance by increasing the durability of the passivation layer [26]. Hu et al. [27] investigated how the Zn content of an Mg alloy affects its mechanical and corrosion properties. The results showed that the Zn concentration increases together with the corrosion resistance of the alloy, but the mechanical properties decrease. Lei et al.

[28] found out that the corrosion resistance of Mg–Zn alloys improves with increasing Zn content in the range of 1–5 wt%. It is assumed that a concentration of Zn in the alloy up to 6 wt% leads to the most favorable combination of mechanical, corrosion, and biological properties [29–32].

Ca is a key bone building element. On average, the adult body contains approximately 1 kg of Ca, of which more than 99 % is found in bones and teeth [33]. The Mg–Ca alloys show adequate mechanical properties and good biocompatibility. Li et al. [34] examined the effect of Ca content in Mg-*x*Ca systems at concentrations of $x = 1$, 2 or 3 wt% on the mechanical and electrochemical properties, as well as the cytotoxicity of these alloys. It has been proven that as the Ca content increases, the alloy's mechanical properties and corrosion resistance decrease. Therefore, it is generally considered that the concentration of Ca in a Mg alloy should be approximately less than 1 wt% [35].

Zr exhibits low cytotoxicity *in vitro*, excellent biocompatibility in vivo, good corrosion resistance, and osteocompatibility [36]. The corrosion resistance of Zr-containing alloys is relatively satisfactory, although not as good as that of Mg–Al alloys [26]. Alloying Zr can decrease the grain size of Mg alloys, which improves their mechanical properties [37], and an addition of up to about 2 wt% contributes to improved corrosion resistance [38,39].

REEs are often used as alloying additives in biomedical Mg alloys. Among them are yttrium (Y), neodymium (Nd), gadolinium (Gd), dysprosium (Dy), and cerium (Ce) [40–45]. A small addition of REE can significantly affect the microstructure and mechanical properties, as well as the corrosion behavior of Mg alloys. REE, in particular Gd and Y, have been reported to be beneficial for corrosion behavior [6]. Y is a nontoxic Mg alloying element that contributes to slowing the rate of corrosion due to grain fragmentation in the alloy [44,46]. Studies on Mg - Nd alloys have shown that they have good resistance to biocorrosion, and better mechanical properties compared to commercially available Mg alloys [40]. Nd improves the corrosion resistance of Mg by forming stable intermetallic compounds (such as $Mg_{12}Nd$) that are less prone to corrosion. Nd increases the strength of the Mg alloy by refining the grain structure and creating a more homogeneous microstructure. Studies related to the biocompatibility of using Nd in Mg alloys also show that Nd does not exhibit cell toxicity [47].

Table 2 summarizes the influence of the alloying elements described above on the mechanical properties, corrosion behavior, and biocompatibility of the resulting Mg alloys.

Similarly to pure Mg implants [16], Mg alloys could promote bone formation and resorb in vivo [54]. Potential of Mg-based materials in bone healing after fracture trauma is also demonstrated by some in vivo studies. Over the past decades, in fact, clinical trials have been performed in Germany, China, Korea, Singapore, and Austria, where implants made of the Mg alloy MAGNEZIX® (Mg–Y-RE-Zr) or RESOMET™ (Mg–Ca) have been tested to fix cases of bone fractures. Trials were also conducted using Ti alloys for comparison. The results showed that normal healing occurred only when Mg alloys were used, but some minor complications were still evident in both the control and Mg groups. Anyway, secondary surgery was not necessary [55–61]. However, implants based on Mg alloys still suffer from rapid corrosion and hydrogen gas formation, as summarized in Table 3, where a comparison among different metallic biomaterials is reported in terms of advantages and disadvantages.

Rapid degradation issues can be addressed through alloy reformulation and/or surface modification techniques, making Mg alloys promising candidates for next-generation orthopedic implants. Therefore, the last decade has seen a marked increase in the number of published studies and citations related to Mg alloys in biomedical

Table 3
Comparison of materials used for orthopedic implants [17,18].

Material	Advantages	Disadvantages
Ti alloys	● Very good biocompatibility ● Ability to osteointegrate ● Superior corrosion resistance	● Poor tribological properties ● Use of cytotoxic elements in alloys (vanadium) ● Poor shear strength
CoCr alloys	● Long-term corrosion resistance ● Super fatigue and wear resistance ● Biocompatibility	● Difficult to machine and thus expensive to process ● High Young's modulus (stress shielding effect) ● Nickel and chromium as alloying additives causing allergy
Stainless steel	● Good corrosion and fatigue resistance in short-term applications ● Low cost ● Easy to machine	● Tendency to corrode in long-term applications. ● High modulus (stress shielding effect) ● Nickel and chromium as alloying additives causing allergy
Mg alloys	● Excellent physical and mechanical properties compared to other metal or polymer implants ● Very good biocompatibility of Mg and favorable effects on bone strength and growth ● Mg density and Young's modulus are closer to bone than commonly used metal implant materials ● Biodegradability	● Poor corrosion resistance and too rapid degradation ● Release of hydrogen gas ● Increase of local pH around the implant

Table 2
A comprehensive overview of the influence of alloying elements on the mechanical properties, corrosion resistance, and biocompatibility of magnesium alloys.

Alloying Elements	Mechanical Properties	Corrosion Behavior	Biocompatibility	Ref.
Mg–Al–Zn (e.g., AZ91)	Al enhances strength via β-$Mg_{17}Al_{12}$ phase; Zn refines grains and improves ductility	β-$Mg_{17}Al_{12}$ phase can act as a barrier; Zn modifies the phase distribution, enhancing corrosion resistance	Al's potential neurotoxicity is a concern; Zn is biocompatible	[21–25]
Mg–Zn–Ca	Ca addition increases yield strength; excessive Ca leads to brittle Mg_2Ca phases	Ca can form micro-galvanic cells, accelerating corrosion; optimal Ca content improves corrosion resistance	Both Zn and Ca are essential elements with good biocompatibility	[33–35]
Mg–Zr	Zr acts as a grain refiner, improving strength; excessive Zr can lead to unalloyed particles	Zr improves the corrosion resistance; uneven distribution may cause localized corrosion	Zr exhibits good biocompatibility; dosage and valence state are critical	[36–39]
Mg–Zn–Zr	Combination leads to fine-grained structure, enhancing mechanical properties	Zn and Zr synergistically improve corrosion resistance by forming protective films	Zn and Zr are biocompatible, suitable for biomedical applications	[48–50]
Mg–Zn–Ca–REE (e.g., Y, Gd, Nd)	REEs contribute to grain refinement and strength; formation of intermetallic phases like $Mg_{12}RE$	REEs enhance corrosion resistance by forming stable oxide layers; excessive REEs may lead to galvanic corrosion	REEs generally show good biocompatibility; long-term effects require further study	[6,44,46]
Mg–Al–Ca–Y	Al and Ca improve strength; Y refines grains and modifies phase distribution	Y addition reduces $Mg_{17}Al_{12}$ phase continuity, enhancing corrosion resistance	Y is biocompatible; combined additions show promise for implants	[44,46, 51–53]

applications (Fig. 2), highlighting the growing global effort to develop next generation temporary implants [8,9]. This growing body of work reflects not only extensive research effort but also a pressing clinical demand for materials that balance degradation behavior with mechanical support during healing.

2. Magnesium alloys: promises and challenges

Despite their potential as implant materials, Mg alloys still face several unsolved challenges, primarily related to poor corrosion resistance and rapid degradation in biological fluids (Fig. 3). It causes a decrease in the mechanical properties of the implant, which occurs before complete bone fusion. The loss of load-bearing capability compromises the functionality of the implant and negatively impacts the bone healing process.

Therefore, controlling the degradation of Mg alloys is a key issue for their application and, thus, commercialization. Since human bone requires approximately 3–6 months for adequate healing and remodeling, Mg implants should ideally degrade over 12–16 weeks while retaining at least 80 % of their initial mechanical properties to support the healing process (Fig. 4). This is enough time for at least partial bone fusion to occur, and some of the mechanical properties carried by the implant could already be carried by the treated bone.

Although static mechanical properties such as tensile strength and elongation are commonly reported for Mg alloys, these do not fully represent the mechanical demands experienced by orthopedic implants in vivo, where cyclic loading (fatigue) is predominant. Fatigue failure is especially critical in load-bearing bones, where repeated micromotions and stress can lead to premature implant failure before bone consolidation is achieved.

Several studies have demonstrated that Mg alloys exhibit relatively poor fatigue resistance, primarily because of their hexagonal close-packed (HCP) crystal structure and early microcrack initiation caused by corrosion pits. Gu et al. [63] observed a decrease in the corrosion fatigue strength of AZ91 and WE43 biomedical alloys, which they tested in simulated body fluid (SBF) at a load frequency of 10 Hz. Furthermore, dynamic corrosion-fatigue studies reveal that degradation accelerates crack propagation, especially in chloride-rich environments such as SBF. This has led to interest in alloys such as Mg–Zn–Ca, which show improved corrosion fatigue performance compared to AZ31, due to refined microstructure and reduced galvanic coupling. Future implant design and testing should incorporate corrosion fatigue protocols, simulating physiological loads and the environment, to better predict in vivo durability.

Beyond these known issues, important knowledge gaps remain regarding the long-term biocompatibility of Mg implants and the influence of surface modifications on healing outcomes in different bone environments. Although short-term in vivo studies suggest that Mg degradation products can be tolerated, the systemic effects of prolonged exposure, particularly in patients with renal impairment or metabolic disorders, are not yet fully understood [64]. Moreover, most experimental models focus on ideal conditions, overlooking complex clinical variables such as coexisting osteoporosis, impaired vascularization, or altered immune responses [65,66].

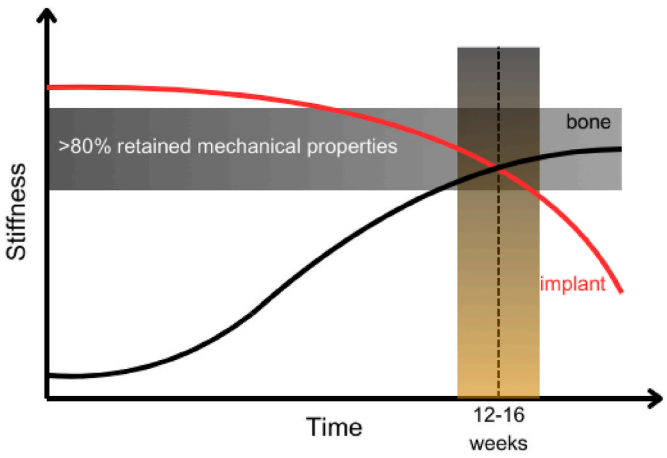

Fig. 4. Schematic representation of the optimal balance between implant degradation and bone healing. For successful fracture repair, magnesium implants should retain over 80 % of their mechanical integrity during the critical healing phase (12–16 weeks). The red curve shows how implant stiffness gradually decreases due to biodegradation, while the black curve illustrates the concurrent increase in bone stiffness during tissue regeneration. The alignment of these two processes ensures mechanical support early on and a smooth transition to full biological function, minimizing the risk of implant failure or delayed healing.

Balancing the rapid degradation of Mg alloys with the mechanical stability required in load-bearing orthopedic implants remains a significant challenge, especially in elderly patients with reduced osteogenic capacity, slower bone regeneration, and compromised vascularization. In such populations, premature loss of implant strength before sufficient bone consolidation can lead to implant failure, nonunion, or refracture [67].

Several approaches have been investigated to address this issue:

i) incorporating REE (Gd, Y) or Ca/Zn elements to refine the alloy microstructure and form stable secondary phases, improving both strength and corrosion resistance [68];
ii) surface modification that delays corrosion-driven weakening of the implant [69];
iii) supplementing surface-treated Mg alloys with slower degradation rates using pharmacologic enhancers (e.g., bisphosphonates or

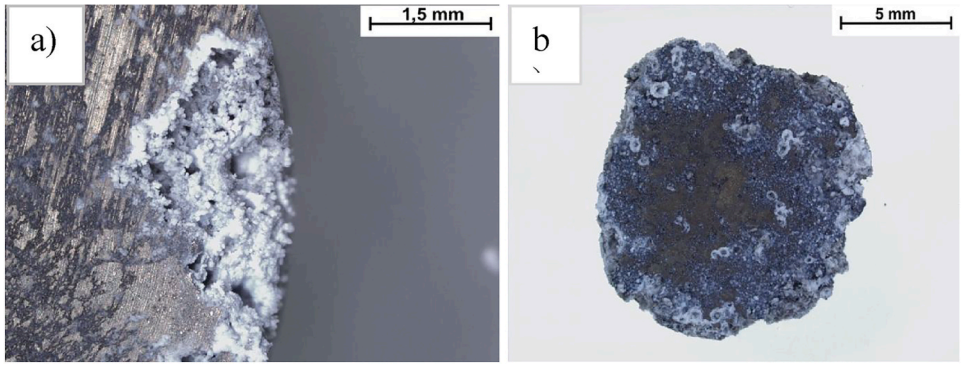

Fig. 3. Optical microscope image of WE43 Mg alloy after degradation in phosphate buffered solution (PBS): a) after 4 weeks, b) after 8 weeks. Original pictures of the authors (digital microscope Leica DVM6).

bone morphogenetic proteins [BMPs]) to promote bone repair [70].

Finally, tailoring degradation rates to individual healing profiles, supported by preclinical degradation studies, mechanical models, and imaging-guided monitoring, will be essential for the safe and effective use of Mg implants in aging populations.

Another critical drawback of Mg alloys is the rapid release of hydrogen gas (H_2) when exposed to the physiological environment. H_2 release during degradation can lead to the formation of gas pockets under the skin that are visible on X-rays. Excess H_2 buildup and high rates of H_2 release can cause blockages of blood flow, tissue necrosis, and delayed healing in the area of adjacent tissues [71,72]. A high number of studies related to H_2 release can be found in the literature, where the highest concentration of H_2 is mentioned in the first days after immersion of samples in solutions that mimic the physiological environment [73,74]. Over time, the level of daily H_2 release stabilizes. Low levels of H_2 release from Mg implants can be tolerated by the body and do not adversely affect the healing process. According to Novian et al. [75] H_2 release of 0.01 (mL/cm^2)/days is safe for the body. In addition, during degradation, there is a local increase in pH 11. Such a local alkalinization results in a reduced cytocompatibility. Thus, excessive hydrogen release during degradation is a significant challenge for researchers. Surface modification techniques have been widely used to slow corrosion and reduce hydrogen evolution [76,77]. Beyond surface treatments, alloying magnesium with elements such as calcium, rare earth metals, and zinc has been shown to improve corrosion resistance by refining the microstructure and stabilizing the passive film, thus decreasing the degradation rate and associated gas formation [78–80].

Fig. 5 summarizes the main problems associated with the use of Mg alloys in implantology.

3. Biocompatibility of magnesium alloys

The primary purpose of implants is to support tissue repair. Implant materials for orthopedic applications are expected to facilitate the adhesion and osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) while promoting osteoblast proliferation and migration. Furthermore, they play a crucial role in regulating the osteo-immune microenvironment, which is essential for callus formation and bone remodeling. To this affordance, the biocompatibility of the material chosen is fundamental [81].

In this regard, several studies have demonstrated that Mg alloys could be a valid candidate for this purpose, increasing the rate of osteogenesis due to release of Mg ions (Mg^{2+}) during the implant degradation [14]. In a normal physiological condition, Mg^{2+} is an essential component of bones. It maintains the regular function of the immune system by regulating proliferation and function of immune cells, promotes metabolism, and protein synthesis. Furthermore, by modulating a wide number of proteins and stabilizing DNA and RNA, Mg^{2+} can influence cellular responses [82,83].

Recent advances in the development of Mg alloys for orthopedic implants have highlighted not only their favorable mechanical properties and biodegradability, but also their complex interactions with the host immune system and the local biological environment. Their immunomodulatory effects extend beyond macrophage polarization as demonstrated by emerging research. For example, Mg^{2+} released during degradation has been shown to modulate neutrophil activity by suppressing excessive neutrophil extracellular trap (NET) formation and reducing infiltration density via altered CXCL8/IL-8 signaling. The latter may contribute to a more controlled inflammatory response and improved tissue integration [84–86]. Furthermore, Mg^{2+} ions can influence dendritic cell function by inhibiting their maturation and shifting cytokine profiles toward anti-inflammatory phenotypes. This is evidenced by increased IL-10 and reduced IL-12p70, ultimately dampening adaptive immune activation and T cell priming [87]. These effects are complemented by observations of increased regulatory T cell populations and enhanced proliferation of hematopoietic stem cells in the bone marrow niche [87–89]. It suggests that Mg alloys may promote long-term immune tolerance and tissue regeneration. Notably, sex-specific and age-related differences in immune response to Mg-based implants have also been reported, indicating the need for personalized approaches in clinical applications [90,91].

However, fast implant degradation due to a corrosion process in body fluids, which occurs in Mg-based materials, becomes a serious concern. In fact, the corrosion process of Mg involves the oxidation of the metal and the reduction of water and oxygen, giving rise to OH^- ions, H_2 gas, and reactive intermediate species (RIS). These products alter the metal surface local microenvironment and affect immune cells (i.e. macrophage polarization). RIS and free radicals interact with lipids and proteins, with consequent reduction of disulfide bonds or functional groups such as carboxyl, carbonyl and thiol groups, or even changing the oxidation state of metal ions [92,93]. An increased pH can cause hemolysis [94], while the accumulation of H_2 gas can damage the surrounding tissues around the implant [95]. Therefore, with different biological responses due to an increase in the corrosion rate, the transition from a biocompatibility condition to cytotoxicity is fast (Fig. 5).

In this context, subsequent inflammatory reactions due to the recruitment of inflammatory cells at the localized corrosion site are also occurring. Inflammatory cells can generate new inflammatory species such as H_2O_2 and HClO, which can drive the corrosion of implant alloys [96]. In the implant local environment, electrochemical interaction processes and mass transport can take place, promoting faster implant corrosion [97–99].

Another critical issue is the development of infections at the implant-tissue interface due to the adhesion of bacteria to the surface of the

Fig. 5. This figure highlights the critical points associated with the use of Mg alloys in implantology. Solutions to ensure controlled degradation kinetics, improved implant stability, and biocompatibility in clinical applications are the current challenges.

implant. Infections further stimulate inflammatory processes, amplifying corrosion. This gives rise to a complex and dynamic phenomenon based on solution chemistry, influenced by biochemical and biological factors in a feedback loop. The degradation of the implant affects the biological response, and the biological environment affects the way the implant corrodes (Fig. 6). The local increase of pH and the release of Mg^{2+} ions during corrosion create an environment that inhibits adhesion and biofilm formation. Some studies demonstrate significant reductions in colonization of Gram positives and negatives compared to conventional materials [100–102]. In this regard, standardized protocols for evaluating both immunological and antibacterial outcomes over clinically relevant time frames should be developed.

4. Surface modification strategies for controlling degradation

Problems associated with too rapid degradation and the inability to maintain adequate mechanical properties of Mg alloys prevent their wide use as temporary orthopedic implants. Therefore, researchers are studying how to improve their properties [101,103–106]. One solution is to modify the surface of Mg alloys with layers or coatings designed to ensure controlled degradation of the implant while maintaining its functionality [107,108].

4.1. Plasma electrolytic oxidation

The most used method for surface modification of Mg alloys is plasma electrolytic oxidation (PEO), also known as microarc oxidation (MAO). This treatment method involves the formation of a protective layer by plasma discharge in an alkaline electrolyte in the presence of the workpiece, which is the anode. Consequently, the plasma generated causes a brief and partial melting of the material's surface and the formation of a magnesium oxide (MgO) coating [109]. Fig. 7 shows SEM images of the WE43 alloy surface after PEO modification with different electrolytes.

Table 4 summarizes the parameters of the PEO process and their effects on the quality of fabricated coatings, which will be widely discussed in the following.

The applied voltage as well as current density in PEO processing are crucial in producing a good quality coating. Literature reporting on the effect of applied current parameters on the PEO process [110,111] shows that the thickness and the pore size of the coatings increased together with the applied voltage. Zhuang et al. [112] studied the effect of current density in the range of 5–20 A/dm^2 on the properties of AZ31 alloy using a phosphate-based electrolyte. They observed an increase in thickness and pore size and a decrease in the number of pores when raising the current density. In addition, they found that the applied current density has a strong effect on the corrosion resistance of the produced coatings. The best properties are shown by the coating

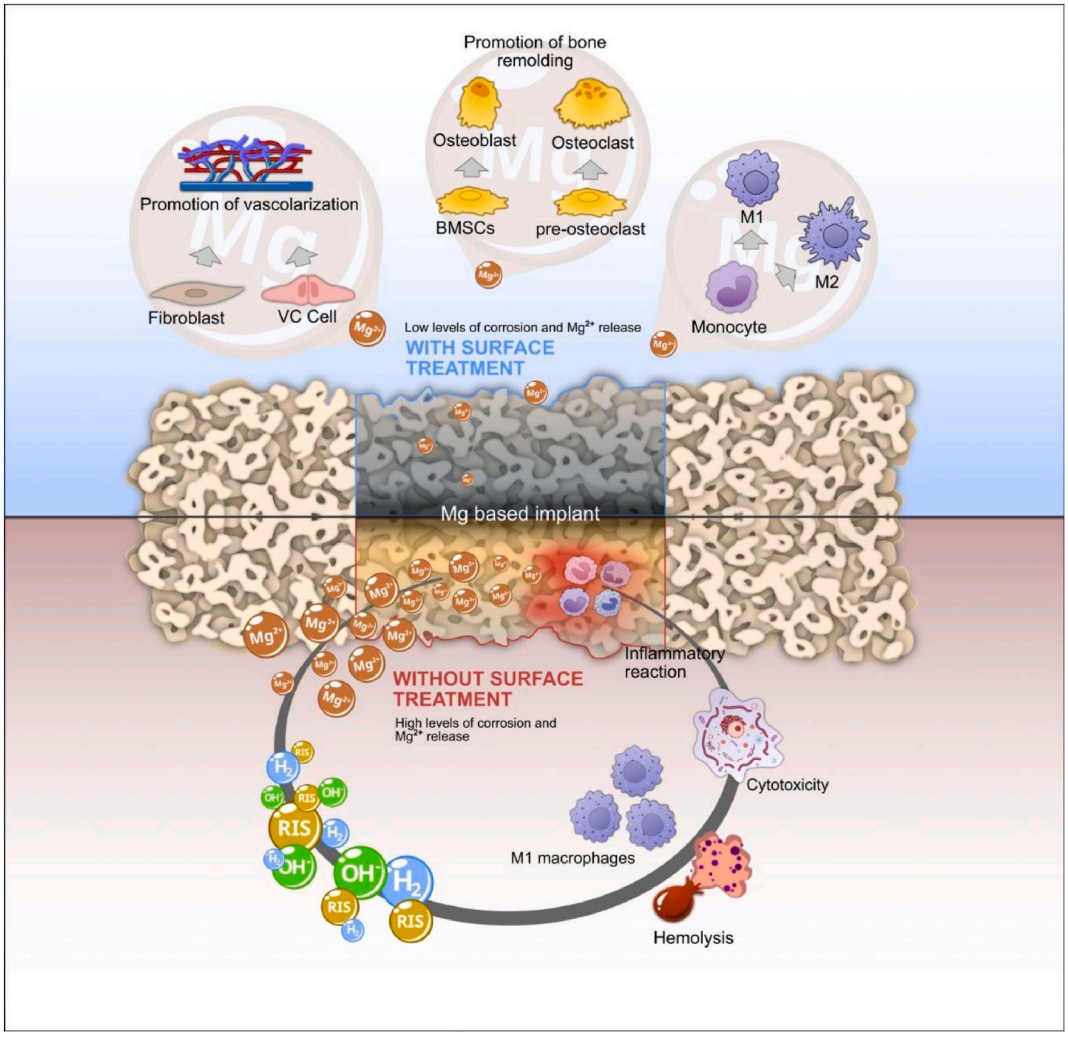

Fig. 6. Interaction of Mg-based implants with the biological environment in a low-level corrosion condition (upper part) and a high-level corrosion condition (down part). Implant degradation affects the biological response, and the biological environment affects the way the implant corrodes.

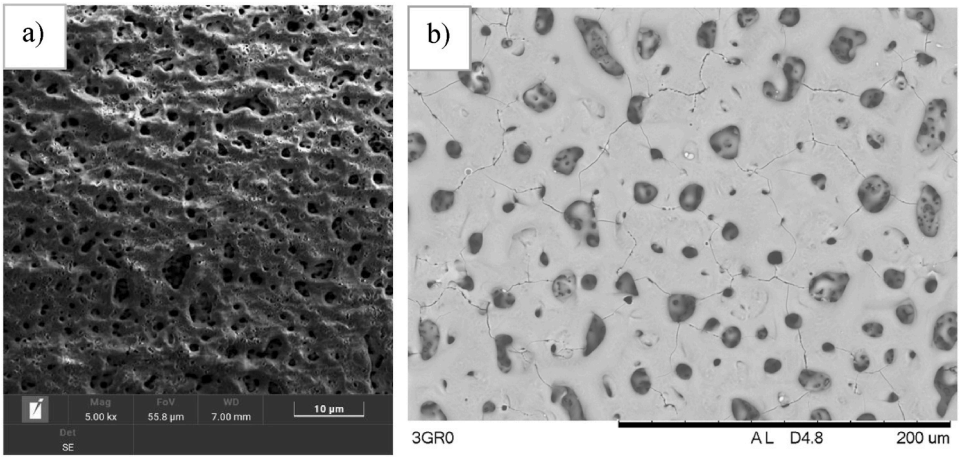

Fig. 7. SEM micrographs showing the morphology of the Mg alloy (WE43) surface after plasma electrolytic oxidation (PEO) treatment in various electrolytes: a) Phosphate-silicate electrolyte - the surface exhibits a dense porous structure with uniformly distributed micropores of different sizes; b) Phosphate electrolyte - the surface shows a smaller number of larger pores embedded in a relatively smooth matrix, with visible cracks. These morphological differences reflect the significant influence of the electrolyte composition on the surface properties of the PEO-treated Mg alloy. Original photos from the authors (scanning electron microscope TESCAN VEGA).

produced at 10 A/dm^2.

The concentration and composition of the electrolytes used, as well as the process parameters, such as voltage or current density, frequency, and duty cycle, have a significant effect on the surface morphology, thickness, porosity, and corrosion resistance of PEO coatings. Silicate or phosphate solutions are mostly used as electrolytes in PEO coating processes for Mg alloys. Oxide coatings using phosphate electrolytes are characterized by a higher thickness and contain more micropores than those obtained with a silicate electrolyte. The layer formed in silicate electrolytes is more compact and uniform and consists primarily of MgO and forsterite (Mg_2SiO_4), while the coatings formed in phosphate-based systems are mainly composed of MgO and $Mg_3(PO_4)_2$ phases [113]. The literature reports on the effect of the electrolytes used on the quality of the coatings produced by the PEO technique, suggesting that the phosphate-based coatings show weaker corrosion resistance compared to those produced using the silicate-based electrolytes [114–116].

Beyond these commonly used systems, aluminate-based electrolytes have also been explored in PEO treatments for Mg alloys [117,118]. These electrolytes typically lead to the formation of alumina-rich layers that offer excellent hardness and chemical stability. However, their biological performance is limited, and they often require additional surface modifications to enhance bioactivity.

Each type of electrolyte contributes specific characteristics to the resulting oxide coating. Phosphate-based systems are advantageous in biomedical applications due to the incorporation of phosphorus and calcium elements, which are known to enhance bioactivity and support osteointegration [119,120]. On the other hand, silicate-based electrolytes produce denser coatings with better corrosion and wear resistance, although with comparatively lower bioactivity [121,122]. Aluminate-based systems offer mechanical robustness [118], but lack inherent biofunctionality. To address these trade-offs, recent studies have investigated the use of mixed electrolytes. Of particular interest are those that combine silicate and phosphate components [122,123], to synergistically improve both corrosion resistance and biological performance. Thus, careful tailoring of the electrolyte composition remains crucial for optimizing PEO coatings on Mg alloys intended for biodegradable orthopedic implants.

An increasingly explored strategy for tailoring the properties of PEO coatings on Mg-based biomaterials is the incorporation of suspended particles into the electrolyte solution. The addition of bioactive or functional particles, such as hydroxyapatite (HA), zinc oxide (ZnO), titanium dioxide (TiO_2), or graphene oxide (GO), can significantly influence the composition, microstructure, and performance of the resulting oxide layer [124]. These particles may be incorporated into the coating during plasma discharges, becoming embedded within the growing oxide matrix and modifying its physicochemical properties. In the context of orthopedic applications, HA particles are of particular interest due to their chemical similarity to natural bone, which enhances bioactivity and supports osseointegration. Similarly, ZnO or silver (Ag) nanoparticles confer antibacterial properties [125,126], while GO may improve corrosion resistance and mechanical integrity [127]. Particle size, concentration, and dispersion stability within the electrolyte play a critical role in determining the uniformity and effectiveness of their incorporation. Furthermore, electrolytes containing particles can alter the discharge behavior during PEO, potentially leading to more refined surface morphologies or enhanced porosity control [128]. The inclusion of functional particles in the PEO electrolyte represents a promising route to engineer multifunctional coatings that simultaneously address biodegradability, biocompatibility, and local tissue interaction in Mg-based implants.

4.2. Polymer coatings

Surface modification using biodegradable polymer coatings is a potential method to slow down the degradation of Mg alloys. Compared to other techniques, biodegradable polymer coatings are attractive for medical applications, as several of them are available on the market and are biocompatible. Among the most studied are coatings made from polylactic acid (PLA), poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL), chitosan, and collagen.

PLA is an interesting material to consider for implant coating [129,130], due to its low hydrolytic degradation by a bulk erosion process, which involves the ester backbone randomly breaking. Lactic acid obtained is a by-product of human metabolism that consequently degrades into carbon dioxide and water through the citric acid cycle [130]. One of his optically active enantiomers, poly(l-lactic acid) (PLLA), is also of interest in the orthopedic field [131].

PLGA is a biocompatible synthetic copolymer approved for use in human clinical trials. It can simply hydrolyze to lactic and glycolic acid during normal metabolism. Moreover, PLGA is easily processed by simply changing the ratio of the two starting co-monomers and has controllable degradation properties as well [132]. However, bone tissue regeneration can be affected by the acidic environment developed in local tissues during PLGA degradation [133].

PCL is one of the most widely used polymers in tissue engineering [134]. Food and Drug Administration (FDA)-approved [135,136], PCL is

Table 4
Parameters of the PEO process and their effects on the final coatings.

Parameters		Effect on coating
Electrolyte composition		Determines the phase structure, thickness, porosity, and compactness of the coating.
	• *Silicate-based*	Forms $MgSiO_3$-rich porous layers. Improves corrosion resistance. Produces hard and compact coatings. Shows lower biological activity
	• *Phosphate-based*	Forms thicker, microporous layers with magnesium phosphates. Enhances bioactivity and supports cell adhesion and osteointegration.
	• *Aluminate-based*	Forms dense $MgAl_2O_4$-rich coatings. Increases mechanical strength and corrosion resistance. May reduce biocompatibility
Electrolyte pH		Controls chemical reactivity. pH between 9 and 13 supports MgO formation. Too high pH increases porosity and risk of cracking
Additives		Modify corrosion resistance and hardness. Improve coating structure and help seal pores. Some additives enhance bioactivity.
Voltage		Moderate voltage promotes formation of dense oxide layers. Excessive voltage increases porosity and reduces corrosion resistance.
Current density		Moderate current density produces well-sealed coatings. High current density may cause cracks and internal stresses.
Power supply mode		The choice of mode affects coating structure and quality.
	• *Direct current (DC)*	Leads to faster oxide growth but less control over porosity.
	• *Pulsed DC*	Improves coating uniformity, reduces thermal stress, and enhances corrosion resistance.
	• *Alternating current (AC)*	May result in more porous and less uniform coatings but it is easier to scale up for industrial use
Pulse frequency		Lower frequency leads to longer pulses, which improve crystallinity and coating density. Too low frequency may cause local defects.
Process time		Longer treatment time results in thicker coatings and better corrosion protection. Excessive time can lead to cracks and localized corrosion.

a biocompatible polymer with a low degradation rate, biodegradability, and high strain failure rate. Furthermore, it is processable through a variety of technologies due to its glass transition temperature, low melting point, and solubility in several different organic solvents [137]. Despite the above-mentioned benefits, only a few papers reported on the use of PCL coatings to decrease the corrosion rates of Mg alloys [138–140].

Chitosan is a natural polymer with a three-dimensional network structure, exhibiting very interesting properties for orthopedic applications due to its biocompatibility, biodegradability, and osteoconduction capability [141–143]. Furthermore, chitosan boasts several other biological properties, such as blood coagulation, immune regulation, antibacterial and antitumor activity [144]. Chitosan-based coatings show low degradation and, depending on the biological context, also the possibility to swell or dehydrate. They promote cell growth, spread, and proliferation together with good mechanical strength, high compression strength (7.68 MPa), and well-matched bone elastic modulus (0.46 GPa) [145,146].

Collagen is a fundamental fibrous protein in the human body, found primarily in skin, bones, cartilage, tendons, and ligaments. It is essential for the structure, strength, and elasticity of these tissues. It plays an important role in cell attachment, mechanical support, and apatite nucleation. Therefore, collagen is a good candidate for coating Mg alloys over conferring corrosion protection and extra-surface bioactivity due to its high osteoconductivity, bioresorbability, and fibril-forming property [147–150].

Dip coating is the most commonly used technique for applying polymer coatings to Mg alloys, involving the immersion of the alloy into a polymer solution, withdrawn from the solution at controlled speed, and then dried to form a thin layer. Other methods include spray coating [151] and ultrasonic spraying [153]. In spray coating, the polymer is sprayed onto the surface, enabling precise control of the coating thickness. In ultrasonic spraying, fine droplets are sprayed onto the surface of the material to obtain continuous, homogeneous coatings characterized by good adhesion to the substrate, with properties that can be controlled by changing the process parameters [152].

Polymer coatings on Mg alloys used in orthopedic implants play a crucial role in enhancing the biocompatibility and corrosion resistance of these materials. Biodegradable polymers [153] form protective barriers that significantly slow down the corrosion of Mg alloys in biological environments. This is important because of the rapid release of hydrogen gas, which can cause subcutaneous gas pockets and complicate the healing process. Because of its hydrophobic nature and flexibility, polymer coating reduces direct contact between the implant and body fluids. This limits the degradation rate of the metal and extends the functional lifespan of the implant [154]. Additionally, these polymers exhibit high biocompatibility, minimizing inflammatory responses, and promoting better tissue integration [155].

Table 5 summarizes the surface layer modification methods using biodegradable polymer coatings and their effects on the performance properties of various Mg alloys.

Table 5
Surface modification of Mg alloys using polymer coatings.

Alloy	Coating	Effects	Ref.
Pure Mg	PLLA and PCL	• Increased cytocompatibility compared to uncoated Mg, • suppression of pH increases during Mg degradation, • reduction in alloy degradation rate.	[156]
AZ31 and Mg4Y	PLGA	• Short-term (3 days) corrosion protection, • reduced degradation rate, • Increased biocompatibility.	[157]
AZ91	PLA	• Significantly increased alloy resistance to degradation (up to 48 h), • Increased degradation resistance but poor adhesion when PLA coating thickness increases.	[158]
Mg–1Ca and Mg–6Zn–10$Ca_3(PO_4)_2$	chitosan	• Corrosion resistance of the Mg–Ca alloy increased after coating, • Lower corrosion rate and metal ions release, • reduction of hydrogen evolution, • improved biocompatibility.	[159, 160]
AZ31	collagen	• Reduced corrosion rate, • improved biocompatibility.	[161]
Mg/HA composite	PCL and PCL/HA	• reduction of degradation rate, • improvement of mechanical integrity preservation, • lower hydrogen release and corrosion rate.	[162]
Pure Mg	PCL + MXene	• Up to 28 days of effective protection • no cytotoxic effect • significantly better corrosion resistance compared to the substrate	[163]

Although it is evident in the literature that polymer coatings have enhanced the performance of Mg alloys, no coated system is yet ready for real applications. Some important factors, such as coating adhesion, permeability, and degradation, must be considered for effective use in real implants. In particular, the adhesion strength between the coating and the substrate during H_2 production is not as strong as expected. A common issue is delamination, which is caused by differences in thermal expansion or mechanical stresses [164,165]. This exposes the underlying material to accelerated corrosion, which can lead to premature implant failure. Therefore, ongoing research, aimed at optimizing the structure and properties of polymer coatings, is essential to improve their durability and performance in orthopedic applications. A promising alternative is the combination of ceramics and polymers, which shows good results in slowing down the degradation of Mg-based implants [166]. Moreover, composite coatings also endow the alloys with potential bioactivity in long-term tests.

4.3. Sol-gel coatings

Another method of surface modification of Mg alloys that is of particular interest is the development of coatings using sol-gel technology. Sol-gel is a wet chemical process that involves hydrolysis and condensation reactions of hydrolysable precursors to form small colloidal nanoparticles suspended in a liquid also known as sol (Fig. 8). The sol particles are then polycondensed to lead to an extended gel network associated with a change from a linear structure to a cross-linked one. The gel obtained consists of a solid network along with a liquid phase and can be applied to the desired surfaces. The final stage of the coating process is drying under ambient conditions or applying heat treatment, which leads to the formation of xerogel after the elimination of the solvent phase. This leads to the formation of a dense hard layer that ensures proper adhesion to the substrate [167–169]. Sol-gel coatings can be applied to metal substrates using various techniques (Fig. 9), the most common of which are dip coating and spin coating methods [167]. The use of the sol-gel method to modify the surface of biomaterials allows for the obtaining of coatings that increase the biocompatibility of the coated material, increase corrosion protection, or improve antibacterial properties using a drug-releasing system [170–172].

Coatings produced by the sol-gel technique have been widely studied in terms of their application to improve corrosion resistance, and thus the biocompatibility of Mg alloys. In fact, coating the alloys with sol-gel allows isolation of the substrate from the aggressive medium, which reduces its reactivity, affecting the rate of degradation and providing better functionality of the biomaterial. The most commonly used protective coatings are based on titania (TiO_2), silica (SiO_2), hydroxyapatite, or silanes, among others [169,173–176].

Wan et al. used the sol-gel method to produce a TiO_2 coating on the AZ91 alloy [177]. The results showed that the hydrogen evolution rate in the immersion test for TiO_2-coated samples was lower compared to the substrate. The applied surface modification successfully improved the corrosion resistance of the Mg alloy. In another study by Hu et al., a layer of nano TiO_2 was applied to the magnesium alloy AZ31, which reduced the corrosion rate and influenced the reduction of the corrosion current density by almost 3 orders of magnitude compared to uncoated samples [175]. The improvement in corrosion resistance is also confirmed by the results of Kania et al., which applied the TiO_2 spin-coating technique to the $MgCa_4ZnGd$ alloy [178]. Furthermore, the coating applied by the sol-gel method was found to decrease the release of H_2 compared to the uncoated sample.

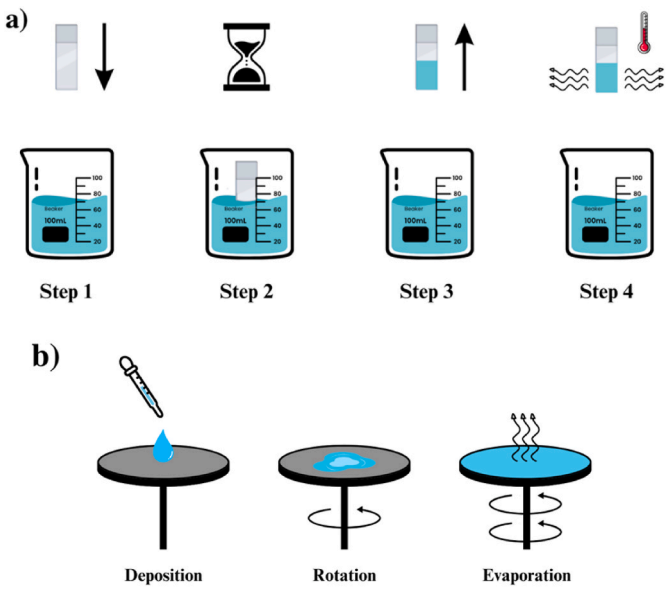

Fig. 9. Sol-gel deposition techniques: a) dip coating, b) spin coating.

Silica sol-gel coatings slow down the degradation and corrosion of Mg alloys, as confirmed by the results of Castro et al. [179]. However, recent research has focused on the development of new silane-based coatings [168,169]. Studies on the application of silane coatings have shown that silane can effectively protect metal substrates from corrosion in the absence of topcoats. In addition, silanes can also be used to pretreat metal surfaces before the next coating layer: thin layers of silane (~100 nm), obtained from a 2 % solution, effectively act as an adhesion promoter and corrosion retarder under various top coatings (polyesters, polyurethanes, acrylics) [169].

Hydroxyapatite (HAp) coatings produced by the sol-gel method have also found applications to modify the surface layer of Mg alloys. Because of the unique properties of HAp coatings, such as improved bone bonding ability, enhanced corrosion resistance of metallic biomaterials, and excellent biocompatibility, they are potentially the best solution to achieve the desired properties of Mg alloys for orthopedic applications. Singh et al. evaluated the HAp coating applied to the Mg–3Zn alloy by the sol-gel method [180,181]. The results showed that the coated substrates had better mechanical properties, similar to those of natural bone, thus avoiding the stress shielding effect. In addition, the use of the HAp coating allowed a 40-fold increase in corrosion resistance and improved biocompatibility through better bone cell proliferation. In a study by Tang et al. [182] the HAp coating was able to slow down the rate of hydrogen release daily, while Rojaee et al. [183] have produced a nanostructured HAp coating that can stabilize the behavior of local alkalization around a degrading Mg alloy. The results clearly indicate that HAp coatings have the potential to eliminate many of the problems associated with the use of Mg alloys as orthopedic implants.

Despite their chemical versatility and excellent corrosion protection, sol–gel coatings on Mg alloys often face critical challenges in adhesion strength and long-term mechanical stability. This is particularly evident under physiological conditions involving dynamic loading. The

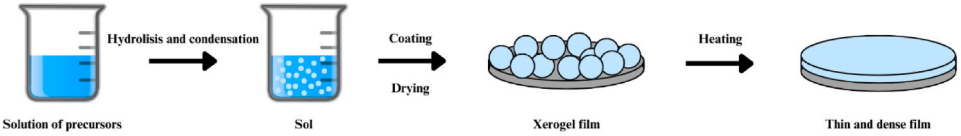

Fig. 8. Scheme of coating preparation by the sol-gel method.

inherently brittle nature of sol–gel-derived oxide layers, combined with the potential mismatch in thermal expansion coefficients between the coating and the substrate, can lead to delamination or microcracking under stress or during degradation [184]. Moreover, the porous and fragile interface formed during hydrolysis and condensation reactions may compromise adhesion, particularly in wet environments mimicking body fluids.

Studies have shown that without additional surface pretreatments (e.g. acid etching or silane functionalization), the coating-substrate bond strength may be insufficient for implants subjected to repetitive mechanical loads such as walking or joint movement. To overcome this, recent research has focused on hybrid sol–gel systems, incorporating organic–inorganic binders to improve flexibility, toughness, and adhesion [185,186]. Nonetheless, more systematic evaluations under simulated mechanical fatigue and immersion conditions are needed to validate sol–gel coatings for clinical-grade orthopedic applications.

4.4. Duplex coatings

PEO treatment and the use of polymer or ceramic coatings, despite their many undoubted advantages, often prove to be an insufficient type of long-term surface modification of Mg alloys [112,151]. Therefore, researchers are increasingly developing a combination of these techniques using duplex coatings. Much attention is paid to the surface modification of Mg alloys using PEO treatment first, followed by the application of polymer layers or coatings produced by the sol-gel technique [187].

Lu et al. [188] in their study used PLLA to seal the MAO coating produced on the WE42 alloy for possible use in the bloodstream. The results showed that after a 4-week immersion test, the MAO coating deteriorated significantly, while the MAO/PLLA coatings underwent little change. The results also showed a significant reduction in the concentration of ions released into the environment, so it was concluded that using an additional PLLA coating effectively improved corrosion resistance. Furthermore, the results of the hemolysis test showed a two-fold reduction in hemolysis rate after applying the PLLA coating to the MAO-treated sample. PLA polylactide and PCL polylactone, respectively, were applied to Mg alloys after MAO treatment [189]. The results showed that the applied polymer coatings significantly increased the corrosion resistance of Mg alloys and provided effective protection in the environment of simulated body fluids.

Zheng et al. have developed a duplex HA/MAO coating on the Mg alloy AZ31B [190]. The application of the coating produced by the sol-gel technique significantly increases the corrosion resistance of the Mg alloy with respect to MAO treatment alone, resulting in a reduction in the primary degradation of the AZ31B alloy. The use of a combination of MAO and, consequently, TiO_2 coating by sol-gel technology was also investigated [191,192]. A better stability of MAO/TiO_2-coated samples was achieved in immersion tests together with a significant improvement in corrosion resistance by slowing down the degradation time of the substrates. Thus, it can be concluded that the combined strategies are effective and increase the potential for a wider application of biomedical Mg alloys.

A summary of the modification methods used and their impact on the properties of Mg alloys is presented in Table 6.

A combined strategy involving alloy composition optimization, surface engineering, and microstructural refinement is essential to address hydrogen evolution in Mg-based orthopedic implants. Further in vivo studies are necessary to validate these approaches for safe clinical application.

A multidisciplinary approach involving corrosion science, orthopedics, immunology, and biomechanics is essential to address these gaps and facilitate the safe clinical translation of Mg-based implants. To advance clinical translation, future research should prioritize multisite implantation models and patient-specific factors such as age, bone density, and comorbidities. The development of multifunctional coatings that combine corrosion control with therapeutic functionalities (e.g., antimicrobial or osteoinductive agents) may also help address current limitations.

Table 6
An overview of the impact of methods used to modify the surface of Mg alloys.

Technique	Corrosion protection mechanisms	Mechanical integrity	Biological outcomes	Surface Properties	Fabrication and technological notes	Limitations
PEO	High corrosion resistance; reduction in corrosion current density; significant slowdown in degradation rate; localised corrosion possible in pores if unsealed	It can increase surface hardness, but introduces brittleness and potential local stresses	Excellent osteointegration; facilitates bone cell adhesion; promotes osteoconduction; limited possibility of drug delivery	Rough surface; hydrophilic and porous structure	Moderate cost; requires high-voltage setup and control of multiple parameters; easy scale-up for simple shapes	Brittleness, poor adhesion on some alloys, needs sealing.
Polymer coatings	Good corrosion resistance, depending on the thickness and integrity of the coating; acts as a barrier to the environment, limiting contact with the electrolyte; degradation can be controlled by a suitably designed polymer	They do not significantly change the properties of the substrate, but can improve elasticity and resistance to cracking	They can be biocompatible or bioactive; they enable the release of drugs	Smooth (Ra <0.5 μm), hydrophobic unless functionalized	Low temperature, easy processing (dip-coating, spray)	Sensitive to hydrolysis; low adhesion on metallic Mg without pretreatment
Sol–gel	High corrosion resistance; production of thin, homogeneous oxide layers; reduction of ion diffusion and passivating effect; dense amorphous films; cracking risk if too thick	Minimal mechanical impact due to low thickness; can improve adhesion of subsequent layers; negligible fatigue impact	The biological response depends on the composition and chemical modification potential of the layer; customisable bioactivity (e.g. silanol, CaP); some cytotoxicity if residues are not removed	Smooth; can be functionalized; low porosity	Low cost; simple equipment; can coat complex shapes; low thermal budget	Fragile; poor adhesion without interlayer or heat treatment
Duplex	Best long-term protection and stability; combines the corrosion properties of ceramic layers and the barrier properties of polymer coatings; increased chemical stability	Adhesion improved; combines surface hardness with outer layer flexibility; reduces crack initiation	Enhanced bioactivity; drug delivery feasible; lower inflammation markers	Tunable roughness; hybrid surfaces; can combine hydrophilic/ hydrophobic domains	More complex proces; needs optimization for layer compatibility	Process complexity; risk of delamination if mismatched materials

5. Integrative approaches beyond surface treatments

Surface treatments of Mg alloys seem to offer a valid solution to their fast corrosion rate in working conditions. Techniques such as PEO, polymer coatings, sol-gel, or a combination of them, have demonstrated success in enhancing corrosion resistance and osteointegration. However, this is still not enough. Before the first products could be clinically available, studies focused on the degradation process under physiological conditions should be conducted. In fact, having the environment a considerable influence on the implant degradation behavior, a mechanistic understanding of a physiological context is mandatory [193]. This should include biological entities such as proteins and cells, among others. Although in the last decade the study of Mg and Mg alloys degradation has made a great step forward with respect to the prediction of the in vivo degradation rate [193], the scientific community is still far from fully understanding the complex mechanism behind. Dynamics and evolution of the environment itself, including corrosion products, should be considered. Assessing the above-mentioned aspects involves the combination of *in vitro* and in vivo testing that often show discrepancies. The difference arises because in vivo degradation is influenced by a combination of factors including the specific tissue environment, the presence of biological entities, and interference of the immunitary system, which are difficult to replicate *in vitro*. Different solutions simulating physiological conditions were proposed in several studies, moving from NaCl to Hanks balanced salt solution (HBSS), or simulated body fluid (SBF), or even cell culture medium [193]. Different simulated solutions resulted in different degradation rates [194] and degradation products [195,196], suggesting different degradation pathways and mechanisms [193–196]. This makes clear that choosing a suitable physiological solution is of utmost importance.

Computational modeling could be a feasible option to overcome the important gap between *in vitro* and in vivo studies. Several different models have recently been proposed, based on physical [193], analytical [197], and phenomenological [196] description of Mg degradation, as well as machine learning models, to better predict the lifespan of implants. A very recent pioneering study focused on assessing the very complex tissue-material interaction [198]. In this work, the existing suitable mathematical models of bone growth and Mg-based implant degradation were expanded and refined, showing a high predictive power of the model in the relative bone volume fraction modeling. This study represents an important achievement and, at the same time, the starting point for further simulating the bone ultrastructure to biodegradable implants response. More studies should be conducted in this direction to assess the short-, medium-, and long-term stability of the implants, avoiding the large number of experiments that are currently required.

Variations in pH and temperature, as well as the induction of mechanical stress in the local environment of the implant, represent critical challenges, and their measurement is far from straightforward. Patient-friendly, non-destructive, and non-invasive monitoring of implants remains complex and resource-demanding. Recently, some research groups have shared possible solutions in this regard. Rich et al. [199] developed an implantable sensor array to measure pH, temperature, and stress placed 1–2 mm from magnesium and titanium implants in a sheep osteotomy model. They showed that the pH around the Mg implants was significantly higher (7.4 ± 0.8) than around the titanium implants (6.6 ± 0.4), which directly proves the alkalization of the local environment during degradation.

Zhao et al. [200] employed an electrochemical H_2 microsensor to measure H_2 concentrations at three anatomical locations in a rabbit ulna fracture model. The highest levels were found in the bone marrow one week after implantation, reaching 1460 ± 320 μM-significantly higher than in the subcutaneous tissue (550 ± 210 μM) and the skin surface (120 ± 50 μM), indicating gas accumulation within the low permeability marrow compartment. Similarly, An et al. [201] used highly sensitive microsensors with tip diameters of 50–100 μm to measure H_2 concentrations in the periosteum, callus, and bone marrow of rats implanted with magnesium intramedullary nails. They observed localized H_2 release peaking at 400 μmol/L in the bone marrow and 40 μmol/L in the callus, with the highest values detected on day 9 after fracture. In contrast, Noviana et al. [202] assessed H_2 evolution by observing radiographically the formation of the gas cavity and by direct measurement of the cavity size in rats implanted with porous Mg disks. Although no direct concentration was reported, the study estimated approximately 1L of H_2 produced per gram of Mg and noted that excessive accumulation contributed to increased mortality, highlighting the importance of controlled degradation rates.

Mathew et al. [203] studied a biodegradable implant made of WE43 Mg alloy in rats using a non-invasive NIR optical sensor, employing spectroscopic analyses at time points of 0, 3, 7, and 14 days. They observed a change in the spectral signal over time, indicating dynamic tissue reactions around the implant, which confirmed the usefulness of the method for monitoring the resorption process. The method could collect information on oxygen saturation, hemoglobin concentration [204,205], and water content, providing indirect feedback on physiological healing processes. Near-infrared (NIR)/IR spectroscopy provides non-destructive, non-invasive and patient-friendly technology. These results open the way for the future development and fabrication of predictive models based on specific physical patterns, in turn correlated to implant performance and its interaction with the biological environment. With in situ real-time monitoring, abnormal healing processes could be detected early, while unnecessary medical interventions could be avoided for patients showing regular monitoring results.

6. Conclusions and future perspectives

Mg and its alloys are valid materials for the fabrication of temporary implants. Their high biocompatibility, very good mechanical properties, and close resemblance to natural bone in terms of density and elastic modulus make them excellent alternatives to currently used metal-based biomaterials. Important progress has already been made in the development of Mg alloys. However, their poor corrosion resistance is still a drawback being directly related to pH changes in the surrounding area, and H_2 gas released as well. This certainly limits their use in real applications. Currently, Mg-based materials are in fact used only as screws, pins, and fixation plates. On the alloy side, while rare earth elements (REEs) such as Gd, Y, and Nd have shown promise, their cost and regulatory status may limit clinical use. Therefore, exploring Zn–Ca–Sr-based Mg alloys offers an exciting direction because of their natural occurrence in bone tissue, low cytotoxicity, and potential to support both biodegradability and mechanical performance. Recent works also suggest investigating Mg–Li–Zn systems for their enhanced ductility, as well as Zr-containing alloys for grain refinement without compromising corrosion resistance. Combining low-REE or REE-free compositions with targeted surface engineering could lead to next-generation resorbable implants optimized for clinical translation. In addition, new alloying elements must be searched for increased biocompatibility of the alloys. On the surface treatment side, several options are available, such as PEO treatment and polymeric or sol-gel coatings, to be applied alone or in combination. Hybrid sol-gel coatings showed high potential in delaying the degradation of the alloys and improving osteogenesis and osseointegration at the same time. Future research should focus on synergistic combinations of surface modification techniques to enhance both the corrosion resistance and biofunctionality of Mg implants. For instance, duplex coatings combining PEO with polymeric layers (e.g., PCL, PLA, or chitosan) can seal pores, prolong degradation time, and improve bioactivity. Another promising approach is integrating PEO with sol-gel sealing or with layered double hydroxides (LDHs) loaded with anti-inflammatory or osteogenic agents. Furthermore, micro/nano-structured PEO surfaces followed by biomolecule grafting (e.g., BMP-2, VEGF) could significantly promote osteointegration. The lack of understanding how surface treatments influence healing in various bone

types is equally significant. Despite the successful results in improving corrosion resistance and osteointegration, their site-specific efficacy remains inconsistent. It would be worthwhile to pursue research into the differences in the application of modified Mg alloys to various types of bone tissue (cortical, cancellous) to examine their degradation behavior and treatment effectiveness. Another possibility that also remains unexplored is to compare the effect of Mg implants on bone tissue affected by osteoporosis. This is particularly important in the context of the possibility of using this type of implant in elderly and ill patients.

Further studies should also consider the lack of standardization in in *vitro* static and in vivo dynamic biodegradation testing including geometric and mechanical changes (i.e. implant shape, mechanical strength, and elastic modulus variations) as well as various biological interactions, which have been barely reported in the literature until now. In the case of degradable materials, this is even more important when considering that a continuously changing interface between material and cells is developing over time. Biological clues such as cellular communication and material-protein interactions must be analysed, as they additionally will have an impact on the material degradation.

Now, we cannot conclude that a universally accepted Mg alloy for any orthopedic application exists. Anyway, when clinical needs are better correlated with each Mg-based alloy biofunctional properties, new designs and production for orthopedic implants will be possible soon.

Author biography

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Dr. Alessandra Scano, graduated with a Master of Science in Pharmaceutical Chemistry and Technology (2005) and in Cellular and Molecular Biology (2019) at the University of Cagliari, Italy. In 2009, she received her PhD in Chemical Science. She spent one year (2009) as Postdoc at Materials and Surface Science Institute (MSSI), University of Limerick (Ireland). From 2010 to 2013, she worked as researcher at the Asociacion de la Industria Navarra (AIN), Spain. Since 2014, she is back to University of Cagliari where she is Assistant Professor and part of the Chemistry of Micro- and Nanostructured Materials Research Group. Her research includes synthesis by Top-Down (Mechanochemistry) and Bottom-Up (Sonochemistry, Microemulsions, Sol-gel) approaches, and morphological, structural, textural, and thermal characterization of nanocomposites, nanocrystalline and nanoporous materials for various applications. She is author/co-author of several papers published in international journals, one special issue, one book and one patent.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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