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Biodegradable Magnesium Alloys: A Review of Material Development and Applications

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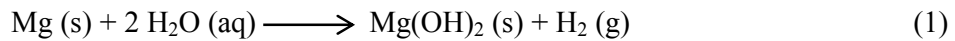
Abstract: Magnesium based alloys possess a natural ability to biodegrade due to corrosion when placed within aqueous substances, which is promising for cardiovascular and orthopedic medical device applications. These materials can serve as a temporary scaffold when placed *in vivo*, which is desirable for treatments when temporary supportive structures are required to assist in the wound healing process. The nature of these materials to degrade is attributed to the high oxidative corrosion rates of magnesium. In this review, a summary is presented for magnesium material development, biocorrosion characteristics, as well as a biological translation for these results.

1. Introduction

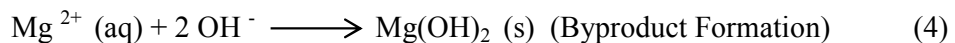
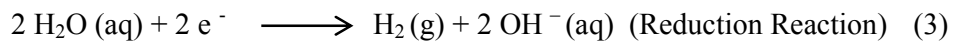
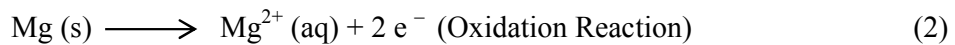
Conventional medical devices require the use of materials which have been experimentally proven to be corrosion resistant when placed within certain fluids. However, with a necessity for next generation biomaterials for medical applications, corrosive materials are being considered for applications where temporary medical device placement is desired. Such cases are commonly found in orthopedic and cardiovascular applications where temporary scaffolds for structural support are required, ultimately enhancing the wound healing and tissue regenerative process. A major line of biodegradable alloys for such purposes are those based upon a magnesium-zinc platform. These alloys have been composed in an array of assortments, and have been tailored for biomedical applications and non-biomedical applications like energy storage [1]. For biomedical applications, selection of elemental compositions for the magnesium alloys should meet the requirements of material science principles for coherent material formation, but more importantly they should yield corrosive by-products that have minimal caustic effects on bodily function during the degradation process. Materials composing of minerals and trace elements already existing within the body are highly advantageous for such purposes. Polymeric materials are highly acclaimed for such biomedical applications due to their biocompatibility, degradation abilities and elastic compliance for cardiovascular applications; however, several mechanical and physical properties such as: loading failure in load bearing devices and post-implantation recoiling for cardiovascular applications are less when compared to that of metallic magnesium alloys [2, 3].

1.1 Magnesium Corrosion: Oxidation-Reduction

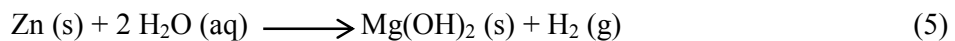
Magnesium alloys corrode/degrade in aqueous materials by several different oxidation-reduction reactions which are influenced by the alloying elements. Generally, the corrosion of magnesium in water will yield magnesium-hydroxide and hydrogen gas evolution. The following net reaction (1) from half-cell reactions are given below:



Contributing Half-cell reactions:



Typically, zinc is used as an alloying element, as it also possess the ability to displace hydrogen ions from solution. If zinc is used as in magnesium-zinc alloys, then the following reactions would occur in addition to those mentioned above:



Magnesium Metal can also remove zinc ions from solution:



As seen from these equations, magnesium reactions with aqueous solutions produce hydrogen gas. This is a problem if the material is used in orthopedic applications where vascularization and transport is minimal, thus resulting in the formation of potentially harmful hydrogen pockets. Experimentation has shown that the addition of Zn has the ability

to significantly decrease the amount of hydrogen gas evolved when measured by electrical corrosion testing [4].

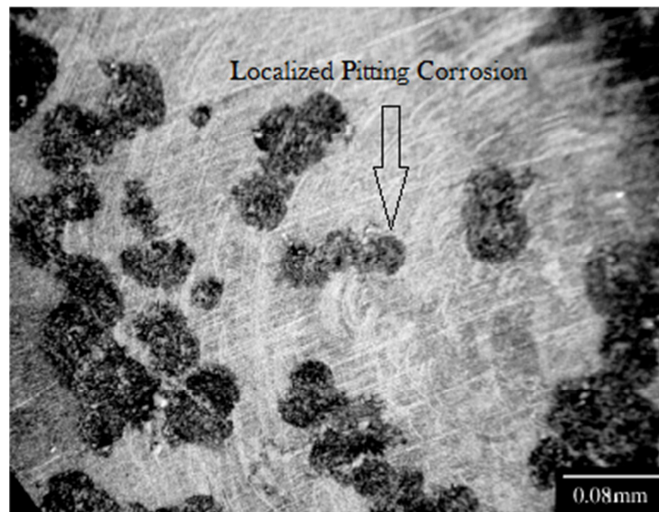


Figure 1. Microphotograph of the magnesium surface after performing polarization analysis in NaCl solution (50x).

Reprinted from *Materials Research*, 10 (1), Wolf Dieter Müller; Maria Lucia Nascimento; Miriam Zeddies; Mariana Córscico; Liliana Mabel Gassa; Mónica Alicia Fernández Lorenzo de Mele, Magnesium and its alloys as degradable biomaterials. Corrosion studies using potentiodynamic and EIS electrochemical techniques, 2007, with permission from Creative Commons Licensing 3.0.

Corrosion is a surface effect, and the medium in which the material is placed greatly influences the parameters and degree to which the corrosion occurs. It has been noted that the corrosion of magnesium in water forms a hydroxide (OH^-) layer on the surface of the material. If the corrosive medium contains any chlorides with concentrations above 30 mmol/L, the hydroxide will be converted to magnesium chloride (MgCl_2) rather than magnesium hydroxide [5]. In the case of biological fluids where chloride concentrations are approximately 150 mmol/L, surface pitting corrosion is observed as seen in Figure 1 [6]. Ultimately, the types of corrosion that are evidenced on the surface of the material are dependent upon the electrolytic medium in which the corrosion of the material is taking place [7, 8].

1.2. General Applications

The ability of magnesium based materials to degrade has led to a multitude of medical applications. With years of research, current studies are now focused on the biological-biomaterial interaction and the cellular mechanisms as to how the materials are biologically influenced by the dissolution of corrosion byproducts from the bulk of the material [2, 9]. Advanced studies are also exploring how polyaprolactone (PCL) and polylactic acid (PLA) polymer coatings influence the corrosion behavior and drug eluting kinetics for biodegradable stent applications [10]. Extensive studies on magnesium stents, including both animal studies and studies on human subjects, as well as exploration by topographic imaging modalities are well underway [9-14]. Orthopedic applications for magnesium materials have been shown to achieve enhanced bone response and excellent interfacial strength when implanted [15]. Magnesium materials have also been used for different types of fixation devices for orthopedic surgery, such as screws, plates, and fasteners [3, 4, 7, and 16]. Recent studies have also shown that the implantation of a magnesium device shows minimal changes to blood composition within a 6 month study post-implantation without causing damage to excretory organs like the liver or the kidneys [17].

2. Magnesium Alloys with Trace Elements

2.1 Material Structure

There are several magnesium compositions which are currently being explored. Some of the alloys are at more developed research stages than others, and each alloy has been tailored for specific applications as previously mentioned. Pure magnesium has been used, as well as other elements including: Zn, Mn, Al, Ca, Li, Zr, Y, and rare earth metals (RE) [1, 4, 6, 18-22]. Including these elements within the Mg matrix creates different mechanical and physical properties for the resulting alloy. If the alloying element can accomplish the metallurgical

principle of forming a Solid-Solution, then solid solution strengthening can be achieved. A Solid-Solution forms when one two or more alloys are completely soluble in one another [23]. When viewing the solid solution formation under a microscope, only a single mixed crystal lattice structure can be visualized rather than two different crystal structures, which would typically occur if the two metals are dissimilar and result in multi-phase formations. Solid Solutions are generally stronger than pure metals, because of the enhanced crystal structure and the introduction of dislocations within the matrix, but are generally less poor electrical conductors when compared to that of pure metal conductivity [24]. This process is known as solid-solution strengthening. The formation of inter-matrix phases improves the strength of the alloy, and is referred to as dispersion strengthening [24]. This is the common practice when forming an alloy. Typically, one metal will have larger atoms relative to other constituents within the material and form a ductile phase called the matrix. The matrix consists of the major volume for the alloy. The second metal added to the alloy consists of smaller atoms that are usually both stronger and harder. When the two metals are mixed together in the formation process, the resulting material is dispersion strengthened. Between the microstructure of two or more phases exist grain boundaries. When dispersion strengthening occurs, micro-scaled precipitates usually form within the grain boundaries, which further strengthen the material as the precipitates prevent slippage of the dislocations or defects within the grain or phase [23]. Such a treatment can be induced by a heat treatment within the manufacturing process, and is referred to as Precipitation hardening [23].

2.1.2 Impurities within Magnesium

Refined magnesium almost always has remnant amounts of other impurity elements. These impurities result from the natural composition of magnesium found within the earth, as well as the casting and refining processes used. The degree of impurities after the refining process is dependent upon the efficiency of the refining process itself. Elements currently

found within the magnesium include: copper (Cu), beryllium (Be), nickel (Ni), and iron (Fe) [25]. Standards for characteristic element inclusion in Magnesium are: 4 ppm Be, 100-300 ppm Cu, 35-50 ppm Fe, and 20-50 ppm Ni (weight percent) [25]. Other elements may be present, and are referred to as general alloying elements [26]. The amount of these impurities should be controlled for any application, especially if pure magnesium is desired. Neglecting to remove the impurities from magnesium can cause detrimental implications once applied to a specific application, especially within the biomedical discipline. An example of such would be a magnesium stent with excessive amounts of nickel, which is known to be harmful to cells; Ni leaching within the body would produce toxic biological effects. Recent studies have further validated Nickel's toxicity on human lung epithelial A594 cells [27].

2.1.3 Impurities and Corrosion Effects

The effect of impurities within the magnesium material for corrosion studies varies. In some instances the impurities may increase corrosion resistance, while in others the corrosion influence may be difficult to determine. Such instances would arise because the corrosion parameters are influenced by the composition of the alloy, the nature of the electrolyte corrosion medium, method of material preparation, whether or not surface treatments were performed, and the degree of imperfections within the material, amongst several other factors [28]. These factors are extremely important when a magnesium based biomaterial is implanted within the body as it will undergo nearly continuous bio-corrosion for its entire lifespan while implanted. Studies have shown that one of the most important factors in determining corrosion of a magnesium implant is dependent on the purity of the material [29]. It has been well noted that Fe, Ni, and Cu are three critical corrosion elements, which when present within magnesium significantly increase the rate of corrosion [30]. These metals are harmful because of their low solid-solubility limits and because they serve as active cathodic sites within the material itself [31]. Cathodic sites are regions within the

material where reduction reactions occur. These regions are essential to the formation of a corrosion cell, and are generally involved with absorbing electrons produced from oxidizing materials (anodic site). At cathodic sites, nearly no material serving as the cathode is lost. The solid-solubility limit of a material is the extent to which an alloying element will dissolve in base materials without forming a different phase [32]. Generally, the higher the solid solubility limit the more likely the alloying element can homogeneously disperse within a material. Whereas, low solid-solubility limits will more readily form separate phases within the material. For example, an alloy of Mg-Cu would more likely be separated into two different phases, a copper phase and a magnesium phase. This can be seen in classical cases of pitting corrosion formation. Biologically, the presence of elements like Fe, Ni and Cu within biomaterials serving as cathodic sites can have very influential results, which may be positive or negative, depending upon the designer's intent for the material. Certainly two phases will more than likely occur, with a preferential dissolution of the anodic material while the mass of the cathodic material will remain. This can pose some problems as the materials will have problems being uptake by enzymatic, metabolic or catabolic reactions if the element can be utilized as a cofactor, or otherwise removed from the body by excretory organs like the kidneys, liver, and spleen [33].

2.1.4 Magnesium and Corrosives

Magnesium materials exposed to atmospheric conditions will develop a thin gray layer on its surface, which is partially protective [5]. Corrosion is promoted when magnesium is put in an environment with free-roaming chlorides or sulfates which may bind to the surface. If such chlorides or sulfates are localized, then pitting corrosion will likely occur [34].

It is proposed that when magnesium is placed in aqueous solutions containing heavy metals like chlorides, copper, nickel, and iron, corrosion is enhanced [5]. The ions from the

aqueous solution plate onto the surface of magnesium (anodic site), forming active cathodic sites, which create a concentration cell between the two surfaces. The interaction between the dissimilar metals, would essentially lead to galvanic corrosion on the surface of magnesium due to the inhomogeneous surface composition and the electrolyte medium which propagates the movement of ions. Ions in general are considered to be corrosive if they have the ability to breakdown the protective layer on the surface of magnesium, such as chlorides and oxidizing salts. Passivating elements like chromates, vanadates, and phosphates have been used to retard corrosion because of their ability to form a passive surface film [35-37].

2.1.5 Magnesium and Humidity

Magnesium is a metal that readily corrodes in the presence of water, as shown in equation (1). Atmospheric conditions contain certain levels of water content in the form of humidity, and the corrosion of magnesium alloys increases with relative humidity [5]. The corrosion of magnesium increases significantly when exposed to pure water [38]. Studies have shown that at after 18 months of study, neither pure magnesium nor any of its alloys exhibit evidence of surface corrosion at 9.5% relative humidity (RH) . Whereas, minimal corrosion occurs at 30% RH. At 80% RH, substantial surface corrosion occurs [38]. Therefore, when conducting corrosion experiments on magnesium and any of its alloys, atmospheric humidity must be strictly controlled. This is especially true to evaluate the corrosion behavior of implantable medical devices manufactured from magnesium based materials.

2.2 Alloying Elements

There have been several different types of alloying elements used in magnesium based materials in an attempt to control their corrosion properties and feasibility for biomaterial implant. Elements like Mn, Cu, Al, Ca, Zr, Gd, and Zn have all been explored [39].

2.2.1 Manganese

Manganese is primarily added to magnesium alloys to improve their corrosion resistance. This is achieved by reducing the harmful effects of impurities [40]. It has been shown that when Mn is added to Mg, the corrosion contribution from the impurity of Fe is rendered inactive because Mn atoms surround the Fe atoms and act as local cathodes [41]. Manganese is also an essential biological trace mineral which serves in many roles within cellular systems, particularly as different cofactors for many metalloenzymes such as: oxidases and dehydrogenases, DNA and RNA polymerases, kinases, decarboxylases and sugar transferases [42, 43]. In humans, excessive amounts of Mn have been shown to induce “Manganism” which is a neurological disorder similar to Parkinson’s disease [44].

2.2.2 Copper

The addition of copper has been shown to increase the strength of magnesium casts, but also accelerate magnesium alloy corrosion rate in a NaCl electrolyte medium [30]. In galvanic corrosion processes when two or more dissimilar metals are in contact, the more noble metal in the galvanic series will be preserved. For example, an Mg/ Fe alloy, Mg is less noble (more negative voltage potential) than Fe, and so it can be considered a sacrificial anode that will corrode more readily than Fe. Copper has been shown to have many deleterious biological effects and in particular cellular cytotoxicity; however, it is an essential trace element in all living things [45]. Excessive copper amounts in the body have been linked to neurodegenerative diseases like Alzheimer’s, Menkes, and Wilson disease [46]. A cohort study of 4035 men of age 30-60 years old, were used for a baseline study to assess the association between Magnesium, Zinc, and Copper serum concentrations and all-cause, cancer, and cardiovascular disease mortality. Results revealed that serum levels with a) High

Copper, low magnesium, and b) concomitance of low zinc, with high copper or low magnesium increase the mortality risk for middle-aged men [47].

2.2.3 Aluminum

Alloys containing aluminum generally possess a high quality combination of mechanical properties, corrosion resistance, and die-castability [39]. It has been noted that aluminum tends to rapidly diffuse from the material matrix which contributes to creep deformation [39]. The poor creep resistance is substantial at temperatures above 125°C [48]. The normal operational temperature under biological conditions is $37 \pm 0.7^{\circ}\text{C}$ [49]. It is highly unlikely that substantial creep deformation is of immediate concern if Aluminum-Magnesium based alloys are used as biomedical implants. However, the tendency for aluminum to readily diffuse from the material matrix is of concern. Aluminum has a low density and is a passivating element, which lends to its corrosion resistance properties. Biologically, aluminum toxicity in the body has been shown to be detrimental to the body. In high doses, aluminum has been shown to cause neurotoxicity, with altered functions of the blood-brain-barrier [50]. Additionally, aluminum has been shown to increase estrogen-related gene expression in human breast cancer cells when cultured in a laboratory setting [51]. Aluminum has also been linked to Alzheimer's disease; however its implications as a causal factor are still ongoing [52]. Pathological results have shown that amyloid fibers or brain plaques in elderly patients contain enhanced amounts of aluminum [53].

2.2.4 Zinc

Zinc is commonly used as an alloying element for magnesium alloys, and the yield strength of magnesium alloys increase with its zinc content [54]. Magnesium alloys are especially important for orthopedic applications as it contains a Young's modulus with a

value of 3-20 GPa, which is very similar to the Young's modulus for bone 20 GPa [55]. One of the main challenges with using magnesium for orthopedic applications is that as magnesium corrodes/degrades in aqueous or liquid environments, hydrogen gas evolution occurs, as shown in equation (1). This is of major concern for orthopedic applications where the hydrogen gas accumulates and forms hydrogen gas pockets [56]. This is due to bone being poorly vascularized, with insufficient mechanisms to remove the excess hydrogen gas. Hydrogen gas evolution would be less of a concern in applications such as cardiovascular stents where the hydrogen gas could be removed from the implant site by convective transport phenomena.

One of the most successful methods to overcome the problem of hydrogen gas evolution from magnesium alloys is to alloy the material with zinc. Hydrogen evolution and Electrochemical Impedance Spectroscopy tests (EIS) reveals that in alloys with less content of Zn result in strong H₂ gas evolution during degradation in simulated body fluids, whereas Zn-rich alloys hardly form any hydrogen gas [57]. It is believed that the presence of Zinc in a Magnesium alloy achieves such a process in two ways. The first is that the Zinc ions in solution immediately around the bulk material are removed from solution, as shown in equation (7). The zinc ions that are in solution further compete with the Mg⁺² ions in solution for binding with free OH⁻ anions forming Zn(OH)₂, which ultimately reduce the amounts of free H₂ gas.

Zinc is also an essential trace mineral to plants, animals, humans, and microorganisms [58, 59, and 60]. It is essential to hundreds of biological enzymes, and transcription factors which are often coordinated with amino acids [61, 62]. If Zn is used as an alloying element in a biomedical implant, its dissolution from the bulk material due to corrosion when placed *in vivo* would be less detrimental than other elements like Mn, and Al, because Zn is readily absorbable by biological functions within the cell. Excessive amounts of Zn have the

potential to be corrosive in nature if ingested [63]. When zinc (Zn^{+2}) ions react with hydrochloric acid (HCl), Zn-Cl products are formed which has been shown to damage parietal cells lining the stomach.

3. Magnesium and its alloys- Corrosion Studies using Potentiodynamic and Electrical Impedance Spectroscopy

The corrosive nature of biomaterials is very important to understand. It provides insight into how the material will behave once *in situ*, and it can estimate a materials biomimetic nature and at what rate a material will take to corrode/degrade. In order to simulate the biological environment a biomaterial will encounter once placed within a recipient, accelerated corrosion techniques using different simulated body fluids are used [64]. Corrosion studies using electrolyte media containing organic constituents is challenging. What is of interest is how the material corrodes in the presence of the organic containing medium, but more importantly how the organic medium interacts with the surface of the material during corrosion. There are two methods to evaluate the corrosion reactance of the material: Weight by Loss Methodology or Accelerated Electrochemical Processes [65].

3.1 Negative Difference Effect

Predicting the corrosion behavior of Magnesium is very challenging, because it does not follow the normal corrosion behavior as other materials. Typically, anodic and cathodic reactions model the behavior of all electrochemical corrosion processes. The anodic and cathodic reactions are usually inversely related. As the applied potential (E_{app}) or current density increases, the anodic reaction rate increases and the cathodic reaction rate decreases. An anodic increase of the applied potential causes an increase in the anodic dissolution rate, while the cathodic site decreases in hydrogen evolution [8].

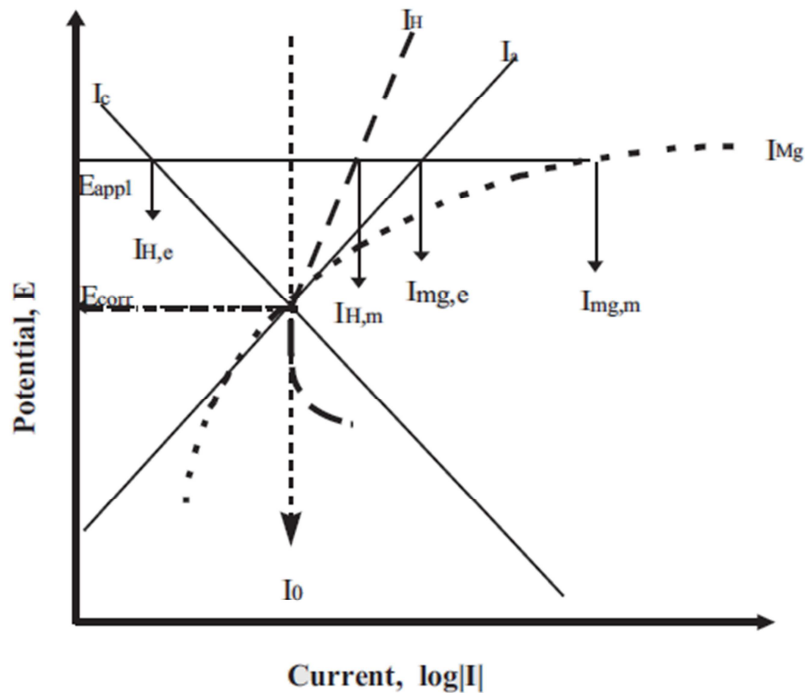


Figure 2. Tafel Kinetic Plot showing the Negative Difference Effect (NDE) compared to normal predictive behavior expected for metals by Tafel theory [66].

Reprinted from *Corrosion Science*, 39 (5), G. Song, A. Atrens, D. Stjohn, J. Nairn, Y. Li, The electrochemical corrosion of pure magnesium in 1 N NaCl, 21, Copyright 1997, with permission from Elsevier.

As shown in Figure 2, for metals like Zinc, Copper, Iron, and Steel, normal anodic (I_a) and cathodic (I_c) partial reactions are marked, which are consistent with Tafel theory. According to such theory, the rates of these two partial reactions are equal at the corrosion potential (E_{corr}). Normally, positively increasing the applied potential (E_{appl}), would cause a shift in anodic potential (I_a) to $I_{Mg,e}$ while the cathodic potential would decrease along the curve I_c to $I_{H,e}$. However, this is certainly not the case for Magnesium based alloys. For magnesium alloys, a positive increase in the applied potential (E_{appl}) causes an increase in both the anodic partial potential and the cathodic partial reaction, represented by dashed lines I_H and I_{Mg} , respectively. This is the most important feature of the Negative Difference Effect (NDE) which Magnesium alloys experience.

3.1.1 Magnesium Corrosion Mechanisms

The corrosion behavior of magnesium involves different processes attributed to the NDE. Several different theories have been proposed to explain the entire corrosion system magnesium experiences. However, most models proposed do not universally explain all of the corrosion behaviors experienced and observed. Figure 3.a.I and 3.a.II, represent a model explaining the formation of a Partially Protective Surface Film. Naturally, thin passivating films form on the surface of magnesium which protect it from further corrosion [5].

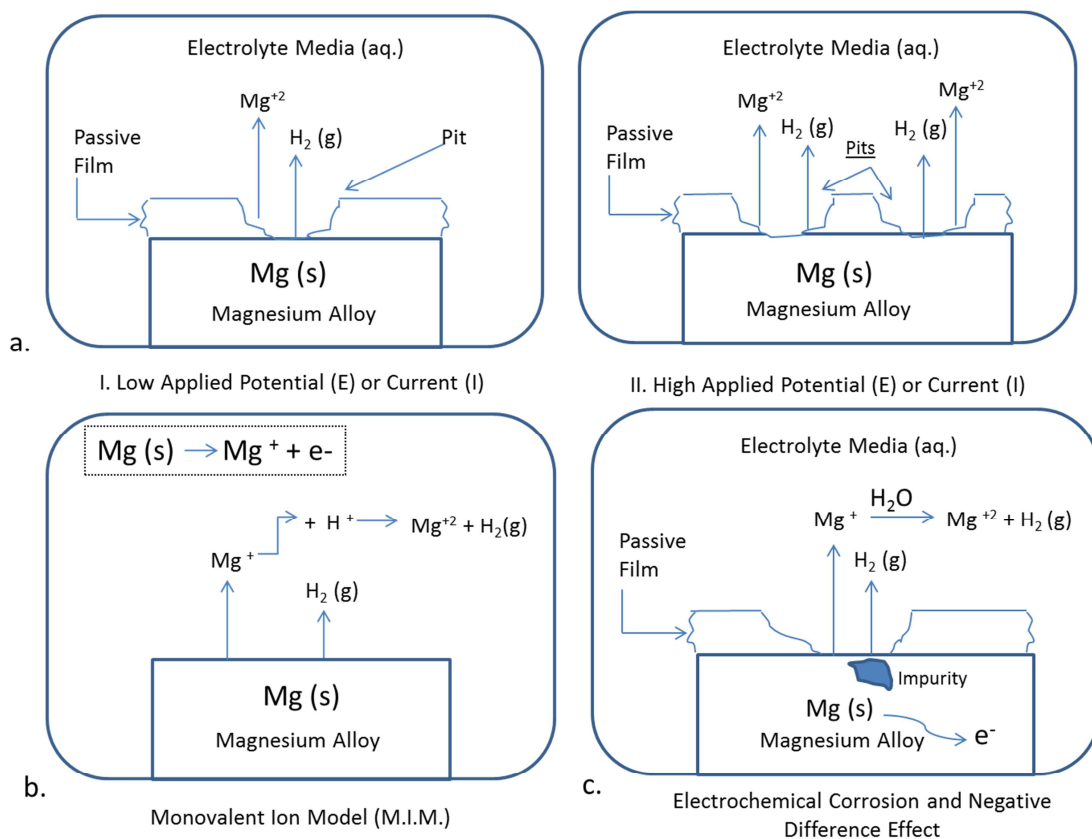


Figure 3. Schematic illustrating different corrosion mechanisms for Magnesium. a (I) - Mg^{+2} and $H_2(g)$ evolution under low E or I. a(II) - Mg^{+2} and $H_2(g)$ evolution at high E or I, with multiple pit formation. b. Monovalent Ion Model. c. Negative Difference Effect (NDE) and Mg^{+2} and $H_2(g)$ evolution during accelerated electrochemical corrosion testing.

This model shows that the NDE is responsible for the breakdown of the thin protective film when current is flowing through the interfacial electrical double layer formed between the magnesium surface and the electrolytic medium. This leads to divalent ions being released from the magnesium surface through oxidation, further releasing it into the corroding medium. At low applied voltages or current density, less localized corrosion pitting is evident (Figure 3.a.I), as compared to higher voltages or current density values, where more pit formation occurs (Figure 3.a.II). The hydrolysis of magnesium will lower the pH and increase the parasitic corrosion rate [67]. This model was questioned as to the protective nature of the film formation, however, recent research investigating the corrosion behavior of AZ91 magnesium alloy, shows that corrosion products $Mg_5(CO_3)_4(OH)_2 \cdot 8 H_2O$ and MgO form a passive film on the surface of the material retarding further corrosion [68].

Another model proposing the NDE on the corrosion behavior of magnesium is the monovalent ion model (Figure 3.b). This model proposes that a transient Mg^+ monovalent ion is evolved by the reaction:



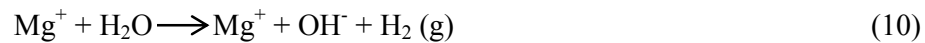
The Mg^+ would then chemically react with two protons to yield hydrogen gas via:



Song and Atrens notably identify that this monovalent ion model (M.I.M.) falls short of explaining how the magnesium dissolution rate can drop down to near zero at a potential approximately 1000 mV higher than Mg^+/Mg_{eqm} potentials [66].

3.1.2 Electrochemical Corrosion Model

One of the most coherent magnesium corrosion models is proposed by Song et al., as shown in Figure 3c. This model combines the M.I.M. with the protective film model as discussed above, to provide a model that addresses the shortcomings of other models, while accounting for the NDE and the electrochemical processes [69]. This model introduces the idea that with an increasing applied potential or current density, more area on the surface of the material becomes film free. In the film-free areas, magnesium corrosion produces the monovalent Mg^+ ion (8), which can still react with water to produce hydrogen gas:



This model proposes that with an applied potential or current density that is negative, the surface film should be intact [69]. Because the entire surface is covered with a film, the oxidation of magnesium is very low. This addresses the protective nature of the film formation. This model still permits cathodic hydrogen evolution to occur at a negative potential, which would decrease with increasing potential until a pitting potential is reached [69]. Such pitting or localized corrosion would break down the protective layer, allowing for more hydrogen evolution and magnesium ions to be released into solution from the now film-free region. As the potential or current density continues to increase, more hydrogen evolution would occur which is supported by the M.I.M., and fulfills the first condition of the NDE. The anodic dissolution of magnesium (8) shows that only one electron is involved in the reaction. Meaning, if the current density were to be held constant, more magnesium would be dissolved into aqueous solution. This is the second condition expressed by the NDE. Hence, this is one of the few complete models accounting for the NDE, while logically piecing together the other chemical and electrochemical tendencies.

3.2 Non-Electrochemical Testing Methodology

When evaluating corrosion characterization using organic media, weight by loss methodology is the safest technique as there is no applied electrical voltage to accelerate the corrosion process; however, a significant amount of experimental time is required to evaluate and characterize corrosion reactions and rates [70]. Alternative methods include accelerated corrosion methods using a potentiostat that primarily serves to maintain a constant potential difference between the working electrode (specimen) and the reference electrode [71].

3.2.1 Electrochemical Testing Methodology

Two important electrochemical corrosion techniques for the analysis of magnesium are: Cyclic Potentiodynamic Polarization and Electrical Impedance Spectroscopy. Cyclic polarization theory is based upon the concept that the material's steady state corrosion rate can be changed by varying the applied voltage and observing a change in current density. The corrosion behavior of a material is commonly characterized based upon a cyclic polarization curve of potential versus logarithmic current density [72]. Analysis of such cyclic polarization curves can provide information pertinent for biological implants such as pitting potential (E_P), Breaking potential (E_B), hysteresis and terminating current density (i_T). In generating cyclic polarization curves, measurements begin at the E_{corr} value, and forward scans in a positive direction past the breaking potential (E_B) until the potential reaches the preset (i_T). At this point, the scan reverses to some endpoint, which is either the original E_{corr} value or a value below E_{corr} . If a hysteresis loop forms from the downward scan from point E_B to the endpoint, the material is susceptible to localized corrosion; the larger the loop, the more susceptible the material to localized corrosion [73]. If no hysteresis loop is generated, then the material is not susceptible to localized corrosion and it is quite possible that a uniform passive film could be protecting the surface which could be removed from corrosion,

thus resulting in uniform or localized corrosion. Similar information can be obtained by analyzing Tafel Kinetics plots which plot current density vs. voltage. These plots reveal the passive and corrosion currents (i_p , i_{corr}), and the breakdown and corrosion potentials (E_{bd} , E_{corr}). Mueller et al., has successfully shown that the presence of organic contents in the electrolyte medium used for corrosion significantly influences these parameters as shown in Figure. 4.

Electrical Impedance Spectroscopy is also an important technique requiring a more complex interpretation from the results, but also avails important information about the degradation/corrosion rate of a material which is governed by kinetics and thermodynamics [74]. Researchers in Germany have successfully demonstrated that electrochemical corrosion techniques using EIS and Cyclic Polarization can be used to evaluate the corrosion behavior of material in organic electrolyte media with protein albumin which significantly contributes to differences in corrosion behavior [75]. Albumin is a major protein found within blood plasma with cations: Ca^{+2} , Na^+ , K^+ . Evaluating corrosion behavior with protein Albumin is biologically relevant because most of the clotting factors found within whole blood are found within plasma [76]. When an implant comes into contact with blood, most of these proteins adsorb onto its surface leading to clinical complications like thrombosis.

3.2.2 Cyclic Polarization and Electrical Impedance Spectroscopy Experiments in Organic Electrolyte Media

In a study by Mueller et. al, corrosion studies were conducted on a test sample of AZ31 (Mg-Zn) alloy in different NaCl concentrations (.1% and 1%) and a Phosphate Buffer Saline (PBS) medium with protein Albumin [75]. Based upon the current density (mA) vs. potential curves, it is evident that there are regions of passive formations at voltages around -1.7 V for all alloy samples regardless of the electrolytic medium.

Current Density vs. Potential (V) curves reveal that the passivation region continues until the breakdown potential (E_{bd}) at about -1.1 V [75]. Scanning Electron Microscope images of the surface reveal that localized pitting corrosion is characteristic which was also documented to begin at E_{bd} [75]. It has also been shown that “cracks” developed on the surface of the alloy, which can be attributed to hydrogen evolution. A mechanism by which this occurs is that hydrogen adsorbs onto the surface at points of defects within the material, where surface stress is high [77]. Once a crack is generated, hydrogen will be initiated within the cracked region at the site of high stress and the electrolytic solutions then comes into contact with the inside of the crack [78]. This can further the corrosion process. Another very important surface attribute which could accelerate corrosion is surface roughness. Surface roughness for biomaterials is particularly important when considering applications where the material serves in flow systems, as it significantly contributes to corrosion behavior [79]. Flow accelerated corrosion typically increases surface roughness, and as a result of increased surface roughness, corrosion rate increases with time [80]. It has also been characterized that the presence of protein Albumin in PBS reduces Passive (i_p) and Corrosion (i_{corr}) currents when compared to values where corrosion experiments were conducted in PBS alone [75]. This phenomenon can most likely be attributed to protein adsorption [81, 82]. Electrical Impedance Spectroscopy results further support that chloride ions favor the metal dissolution, while the presence of phosphate ions and protein in electrolytic media reduces the corrosion attack [75].

4. Conclusion and Suggested Research

In this review investigation the current progress of research for magnesium alloys has been presented and discussed. The biological implication of alloying elements included in magnesium bulk material as well as corrosion by-product formation has been proposed. Research efforts have positively charted both mechanical and material properties; however clinical needs and material-cellular/protein studies are needed. Magnesium based alloys show a tendency for biocompatibility, and materials for specific medical applications should be developed, especially for cardiovascular applications where hydrogen evolution is less problematic as compared to orthopedic applications. Corrosion behavior characterization with more *in situ* experimental parameters is particularly desirable. Biomedical research expertise is required to translate the wealth of biomedical research data into an understanding of how these materials will behave within test subjects.

Acknowledgements:

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