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A Review on Medical Applications of Biodegradable Magnesium Alloy

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ABSTRACT

Biomaterials based on magnesium are potential candidates for use as next-generation biodegradable metals. Magnesium can dissolve in body fluids, which implies the implanted Mg can deteriorate during the healing process. If the deterioration is managed, there won't be any remaining material when the healing process is finished. As a result, the requirement for additional surgeries to remove the implant may be avoided. In addition to being biocompatible, magnesium also shares many of the same mechanical characteristics as human bone. The subject of Mg-based biomaterials has recently had a resurgence in popularity, most likely as a result of technological improvements that have made it possible to better control corrosion. The development of Mg-based biomaterials for orthopedic applications has been limited by difficulties in expecting and controlling the rate of Mg corrosion in an environment, despite its effectiveness in vascular applications.

Keywords: Magnesium, Orthopedic implant, Medical applications

INTRODUCTION

Magnesium (Mg) is a common element found throughout the natural world and is the eighth most common element in the lithosphere and the second most common in the hydrosphere. The Mg is only present in the biosphere in the form of salts or minerals. Mg is the most common intracellular divalent cation and the fourth most abundant element in the human body, therefore it is not surprising that it participates in more than 300 recognized enzymatic activities[1]. Together with many other cellular activities, magnesium contributes to the synthesis of proteins and nucleic acids, mitochondrial function and health, ion channel regulation, stabilization of the plasma membrane, and translational activities. Owing to the significance of the element, prior to exposure, it is necessary to comprehend the harmful implications of changing the magnesium balance on homeostasis[2].

Magnesium Types

Homeostasis

A typical adult human possesses roughly 1 mole of magnesium. Bones hold more than half of this, followed by soft tissue (35–40%) and serum (less than 1%). A healthy diet typically provides enough magnesium, with the digestive system's jejunum and ileum serving as the primary locations for both passive and active absorption. Mg is absorbed, circulated by the body, and then taken up by tissues as required. The movement of magnesium into and out of the intracellular concentration is thus closely regulated to prevent changes that could affect a range of reactions[3]. The high concentration of magnesium in bone, which serves as a reserve of the element for absorbing abrupt variations in serum magnesium levels, is another homeostatic control. Nonetheless, the kidney plays a major role in preserving the homeostasis of Mg. In typical circumstances, only 4 to 7% on the filtered of magnesium expelled in the urine[4]. The amount of Mg expelled can increase to approximately 100% if the renal function is compromised or serum Mg concentrations rise[5].

Hypomagnesemia

Many different factors can contribute to magnesium insufficiency. Main reasons include renal diseases that increase magnesium excretion or intestinal malabsorption of magnesium. Drug-induced renal loss of magnesium, a poor diet, drunkenness, or pathological diseases like diabetes mellitus are examples of secondary causes. There are many more disorders that are also connected to hypomagnesemia, thus this is not a complete list.Cardiovascular dysfunction, including hypertension, arrhythmia, and myocardial infarction, as well as hypocalcaemia, hypokalaemia, neuromuscular hyperexcitability are only a few of the many consequences of magnesium deficiency[6]. Also linked to atherosclerosis, pregnancy, and osteoporosis is long-term Mg shortage. Thankfully, hypomagnesemia is not expected to occur after the implantation of biomaterials based on magnesium. The symptoms of magnesium deprivation do, however, emphasize the ion's significance in a wide variety of processes[7].

Hypermagnesemia

It is much more likely that the usage of Mg-based biomaterials will lead to an excess of Mg being stored and circulated, which may eventually show up clinically as hypermagnesemia. Impaired renal function, which results in a decrease in the quantity of magnesium discharged in the urine, is the most frequent cause of hypermagnesemia. A surplus of Mg can also be released into the circulation and subsequently ineffectively eliminated as a result of rapid muscle breakdown and subsequent renal failure, as is seen with rhabdomyolysis[8]. Reducing magnesium consumption, enhancing kidney function, or utilizing dialysis in cases of renal insufficiency are the main treatments for hypermagnesemia. These treatments might not be completely acceptable if corrosion of an implant made of magnesium results in an excessive release of magnesium. In moderate situations, eating a diet low in magnesium may help any symptoms that do arise; nonetheless, prevention would be the best course of action[9].

The Physical Characteristics and Applications of Magnesium

Magnesium element found by Joseph Black in 1755, it wasn't separated until 1808. Mg was utilized in pyrotechnics, as a reducing agent to create aluminum (Al), and in photography over the course of the following century. The metal itself is thermally conductive, has a good strength to weight ratio, is lightweight (1.74 g/cm3), and is simple to cast. These qualities made magnesium a suitable metal for use in various applications, such as the automotive and aerospace industries. Unfortunately, Mg's tendency to corrode and low elastic modulus made it unsuitable for usage in a variety of applications[10]. But it is these very traits, along with Mg's low relative density, that point to its potential use as a biodegradable metallic biomaterial for orthopedic purposes. This would lessen some of the pathological problems connected to the implantation of permanent metallic components, like the development of inflammatory wear particles and osteopenia, along with implant corrosion. The corrosion of magnesium, however, is the most significant of the above-mentioned characteristics because a biomaterial's ability to perform requires that it maintain proper mechanical stability for a set amount of time. Therefore, it is essential to comprehend the processes involved in the corrosion of magnesium as well as any potential byproducts, especially in a physiological setting[11].

The Corrosion Performance of Magnesium Alloys

The main obstacle to the use of magnesium and magnesium alloys in a variety of applications where exposure to hostile environments is present has been their quick corrosion. The following reactions show the corrosion mechanisms that take place when magnesium is exposed to an aqueous environment.

$Mg \longrightarrow Mg^{2+} + 2e$

$2H2O + 2e^{-}\ H_2 \longrightarrow + 2OH$

$Mg + 2H2O \longrightarrow Mg\,(OH)_2 + H_2$

The entire process demonstrates how magnesium corrosion results in the production of magnesium hydroxide and hydrogen gas. Modest corrosion occurs as a hydroxide layer forms on the material's surface under typical environmental circumstances[12]. Nevertheless, Mg(OH)2 interacts with chloride ions to generate the extremely soluble compound MgCl2 when exposed to high levels of chloride, like those found in a physiological context. As a result, the Mg substrate dissolves more quickly, producing hydrogen gas and hydroxide ions in the process. Mg and Mg alloys are susceptible to two different types of corrosion in a physiological setting. With single-phase materials, the corrosion is frequently confined, which causes the material's surface to develop pits[13]. Due to there are present many phases serving as a local cathode and anodic causing galvanic corrosion and localized corrosion also occurs. Mg is used as a biomaterial because it doesn't generally corrode, while substantial localized areas of corrosion are likely to cause mechanical failure of an implant at specific locations.

The examination of magnesium materials for surgical applications must take this into account[14]. The use of a magnesium biomaterial that corrodes too quickly could also cause the local pH to rise and hydrogen gas to be produced within the implant environment, both of which could have a substantial impact on the surrounding tissues. These problems are anticipated to make Mg-based materials' corrosion behavior one of the key determinants of their effectiveness as orthopedic biomaterials[15].

Improve Corrosion Rate of Biodegradable Magnesium Alloys

Mg can be purified to significantly lower the rate of corrosion, but because pure Mg has a low yield strength, it cannot be used in orthopedics or other load-bearing applications. On the other hand, some alloying components can be added to pure magnesium to increase its corrosion resistance[16]. The mechanical strength and corrosion resistance of magnesium alloys can be improved by using the right alloying elements, but their cytotoxicity and long-term inflammatory effects are the main causes for worry. As alloying elements may also dissolve in body fluid during degradation, it is important to choose them carefully in order to ensure biocompatibility. Moreover, the inhomogeneous microstructure of the majority of magnesium alloys makes them vulnerable to localized degradation, which could compromise their mechanical integrity while in use[17]. In addition, it is challenging to considerably reduce the deterioration rate just by alloying due to the high electronegative potential of magnesium (-2.4 V). One of the most efficient approaches to increase the surface biocompatibility of Mg and decrease and control the degrading behavior is surface modification. Surface modification is easier and more convenient to apply on Mg alloys to adjust the surface corrosion resistance while maintaining the beneficial bulk properties as opposed to modifying the bulk structure and composition. By creating a resistant barrier against the body environment, Recent research has revealed that altering the surface of implants made of magnesium alloy considerably improves their resistance to corrosion[18]. When compared to alloy design, it is less expensive, easier to create multifunctional surfaces, and doesn't call for the addition of potentially hazardous alloying components[20].

The purpose of surface modification in the case of biodegradable Mg-based implants is merely to regulate their rate of degradation and improve their surface biocompatibility, not to permanently alter the surface properties, which could result in a loss of degradability or toxicity to surrounding tissues. The objective is to achieve a biodegradable dynamic interface that will provide the implants with the desired surface biocompatibility and corrosion resistance while maintaining the mechanical strength of the substrate throughout service. Conversion coatings, sol-gel coatings, chemical deposition, plasma electrolytic oxidation (PEO), hydroxyapatite coatings, and organic coatings are just a few of the surface modification techniques that have been suggested. Recent reviews discuss the specifics of several surface modification techniques and their significance for Mg alloys used in biomedical applications[21].

Modern Applications of Magnesium As a Biomaterial

The suggested contemporary usage of magnesium-based biomaterials are not too dissimilar from those of the past. Vascular uses, as well as the field of magnesium alloy development concerned with choosing suitable magnesium-based materials for orthopedic applications are the two main areas of research. The most effective of them has been the use of magnesium alloys as vascular implant materials[22]. After thorough research and with successful use in large animal studies, a Mg alloy stent was effectively used to treat an occlusion of the left pulmonary artery in a premature newborn, allowing reperfusion of the lung. Mg alloy stents have continued to be successfully used in further clinical tests in both infants and adults, revealing complete corrosion of the implants within four months. The advancement of Mg-based orthopedic materials is somewhat behind schedule. With a lot of work being done in vitro on a range of materials and some basic in vivo study being done, the current research is still in an early stage. The investigation of Mg materials as clinically relevant implants, either in an in vitro or in vivo setting, is, nevertheless, very uncommon. The bulk of the handful who have looked into Mg for such purposes have inserted screws into rabbits' long bones, while one study inserted screws into a sheep's pelvis. In one instance, the mechanical performance of the implant under consideration was quite extensively evaluated. Yet, assessments of implant behavior and tissue response have often been somewhat simplistic. Moreover, there was no surgical stress delivered to the bones prior to the insertion of these implants, hence their functionality was not evaluated[23].This scant exploration of therapeutically applicable Mg-based implants is most likely the result of ongoing problems with unpredictable implant material corrosion. Before the implant can be morally used in a therapeutically appropriate context, such as fracture fixation. In particular, corrosion will harm the implant's mechanical integrity. But, once this knowledge is attained, it may be possible to use magnesium materials for scaffolds, plates, and wires in addition to screws, in operations where bone transplants have traditionally been used. The latter is particularly significant because using auto grafts is currently the norm for replacing damaged or removed bone. They, however, need a second surgical site, and the morbidity at the extraction site is frequently rather high. Allografts are alternatives that can cause immune responses and pathogen translocation[24]. Hence, the creation of a structured, biodegradable, porous device with suitable mechanical qualities would be a great substitute. Mg is a candidate material that meets many of the desired criteria, and preliminary study examining the production methods and early corrosion rates suggests that such materials have excellent promise. Figure 1 shows many applications of magnesium as biodegradation materials[25].

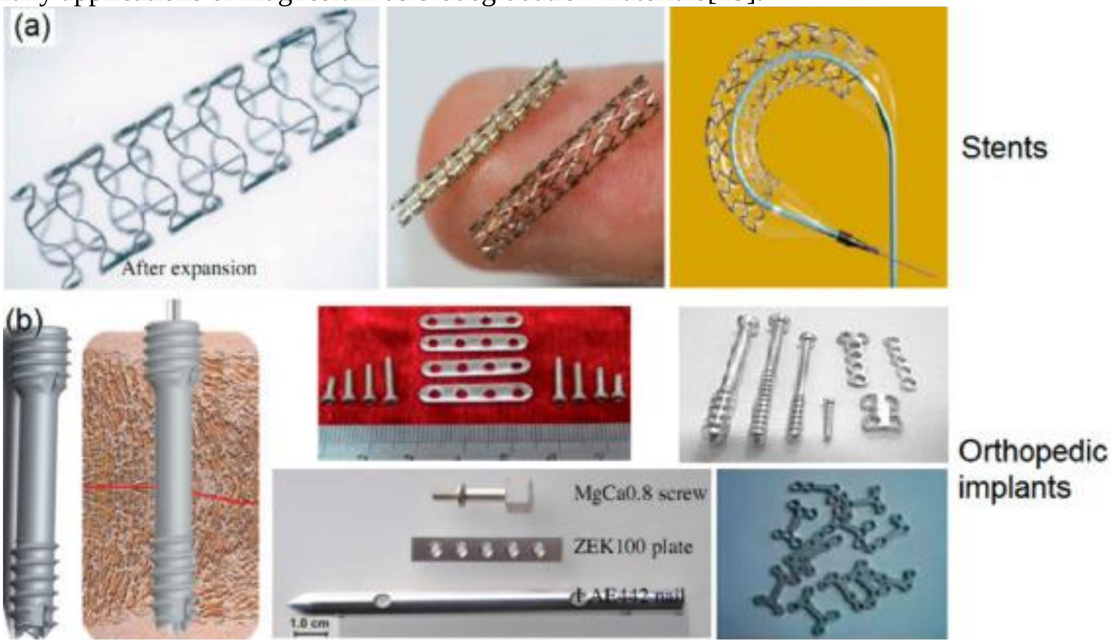

Figure (1): many applications of magnesium as biodegradation materials a) at stents b) at orthopedic implants [25].

CONCLUSION

Finding Mg alloys that may be used as orthopedic implants has a lot of potential in the realm of biomaterials. The advantage of a moderately strong material for which corrosion might be customized for the particular use is obvious. Also, the recent success of Mg alloys as vascular stents has already established the clinical precedence for the usage of such materials. To monitor and evaluate Mg-based biomaterials' resistance to corrosion and biocompatibility in orthopedic applications, respectively, is difficult, which is a problem for the area. Two elements are crucially important for success. This would greatly improve the amount of comparable data and avoid performing experiments too frequently. Second, it is critical that the field promote greater clinician engagement, enabling the design and development of the materials for specific therapeutic usage from the very beginning.

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