

## An Outlook on Magnesium-Based Biodegradable Implants

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In this ageing population, the use of implants for repair of bone fractures is increasing rapidly. Mini-implants such as plates and screws are often used for bone fracture healing. Currently non-degradable implants made of metallic materials such as stainless steel, titanium alloys or chromium-cobalt alloys are commonly used [1]. However, the long-term exposure of these non-degradable implants greatly increases the risk of complications such as foreign body reactions and inflammation due to the release of metal ions or particles as a result of corrosion/wear [2]. This necessitates a secondary surgical process to remove the implant after healing of the tissues. In fact, repeat surgery is a risk and also increases the costs to both the patient and the health care system.

The problems associated with non-degradable implants have led to a growing interest in biodegradable materials. The idea is that the implant remains in the body i.e., serving its purpose during the healing process, and then naturally degrades in the body fluid and excretes without any complication. Biocompatible and biodegradable polymers e.g. polylactide, polyglycolide and their copolymers are commercially available, but the mechanical strength of these polymers is too low to be used in orthopaedic load-bearing applications [3].

Magnesium, a light weight metallic materials, is a potential material for biodegradable implant applications, since magnesium degrades in body fluid and the degradation product is non-toxic and soluble in body fluid [3]. Importantly, magnesium has similar mechanical properties to natural bone, especially the compressive yield strength of magnesium is closer to that of natural bone than that of the commonly used metallic biomaterials [4]. This attractive property could also avoid the risk of stress shielding effect which generally delays the bone healing process [3]. It has to be noted that magnesium is basically essential to human metabolism and moreover research work has shown that magnesium contributes to bone strength [5]. Magnesium is also a co-factor for many enzymes, and stabilizes the structures of DNA and RNA [6]. Although it is reported that high level of magnesium ( $> 1.05$  mmol/L) in the human body could lead to complications, hyper-magnesium is rare due to efficient excretion of magnesium products in urine [7].

Due to the high degradation rate of pure magnesium in near neutral pH and high chloride concentration of body fluid, magnesium cannot be used as an implant in its purest form. The high electronegative potential of magnesium and the non-protective degradation product (oxide/hydroxide) contribute to its high degradation rate. The extremely high degradation rate of magnesium in body fluid not only dissolves the implant before the tissues sufficiently heal, but it also creates hydrogen (a cathodic reaction) gas pockets which potentially affect the healing process [3]. The other consequent problem as a result of the high degradation rate of magnesium is the potential loss of mechanical integrity during service. Although temporary implants are expected to degrade at a slow rate, they need to possess the desired strength in the initial period of healing process. Generally, implant materials are subjected to various modes of loading and as a result can cause failure of implants [8]. Importantly, stress when assisted with degradation can cause catastrophic failure in certain metallic materials. The process is commonly known as Environment-Assisted Cracking (EAC). This phenomenon is particularly relevant for biodegradable

biomaterials and is critical to note that magnesium undergo EAC in chloride-containing environments [9].

Alloying is one of the widely used methods to decrease the degradation rate of metallic materials. In the last five years, a number of magnesium alloys have been tested under in-vitro conditions to understand their degradation behaviour and mechanisms [10-14]. AZ (aluminium, zinc) series magnesium alloys are the most highly researched material due to their commercial availability [11,13]. Magnesium-calcium alloys and rare-earths containing magnesium alloys e.g. ZE41, WE43, WE54 and LAE442 (containing rare-earth mixtures such as cerium, lanthanum, ytterbium, neodymium and praseodymium) have also been tested [12,14,15]. However, the enhancement in the degradation resistance of magnesium due to alloying has not been encouraging. Due to the high electronegative potential of magnesium ( $-2.4$  V with respect to hydrogen electrode) and its poor passivating tendency, alloying alone may not provide the required protection. Moreover, the inhomogeneous microstructures in these alloys can cause localized degradation [12,16]. It is critical to minimize the localized degradation of magnesium-based biodegradable biomaterials, at least during the initial stage of service, for better mechanical integrity.

Surface coating is a potential method to minimize the initial localized degradation resistance of magnesium alloys. Importantly, the coating should be biocompatible and biodegradable with degradation rate lower than that of magnesium alloys. Recent studies on calcium phosphate and polymer coatings on magnesium alloys have shown significant improvement in the general and localized degradation resistance [17-19]. Hence, the outlook for magnesium-based biodegradable implants seems promising.

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