



## Review

## Review of magnesium-based biomaterials and their applications

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**Abstract**

In biomedical applications, the conventionally used metallic materials, including stainless steel, Co-based alloys and Ti alloys, often times exhibit unsatisfactory results such as stress shielding and metal ion releases. Secondary surgical operation(s) usually become inevitable to prevent long term exposure of body with the toxic implant contents. The metallic biomaterials are being revolutionized with the development of biodegradable materials including several metals, alloys, and metallic glasses. As such, the nature of metallic biomaterials are transformed from the bioinert to bioactive and multi-biofunctional (anti-bacterial, anti-proliferation, anti-cancer, etc.). Magnesium-based biomaterials are candidates to be used as new generation biodegradable metals. Magnesium (Mg) can dissolve in body fluid that means the implanted Mg can degrade during healing process, and if the degradation is controlled it would leave no debris after the completion of healing. Hence, the need for secondary surgical operation(s) for the implant removal could be eliminated. Besides its biocompatibility, the inherent mechanical properties of Mg are very similar to those of human bone. Researchers have been working on synthesis and characterization of Mg-based biomaterials with a variety of composition in order to control the degradation rate of Mg since uncontrolled degradation could result in loss of mechanical integrity, metal contamination in the body and intolerable hydrogen evolution by tissue. It was observed that the applied methods of synthesis and the choice of components affect the characteristics and performance of the Mg-based biomaterials. Researchers have synthesized many Mg-based materials through several synthesis routes and investigated their mechanical properties, biocompatibility and degradation behavior through in vitro, in vivo and in silico studies. This paper is a comprehensive review that compiles, analyses and critically discusses the recent literature on the important aspects of Mg-based biomaterials.

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## 1. Introduction

From materials science point of view, biomaterials can be classified into four different groups as metals, ceramics, polymers and composites. Among these groups, ceramics such as calcium phosphates are widely used as a coating material since they exhibit non-toxicity, good biocompatibility and osteoconductivity [1]. However, they possess poor mechanical properties and high corrosion rate in acidic environment, which restrict their usage as bone implant in load bearing areas [1].

Polymeric biomaterials are widely used for bone tissue engineering applications since they are formable into complex shapes, and their surface properties can be easily modified. Additionally, chemical and mechanical properties of polymers can be altered to certain degrees during sterilization. However, application of polymers is limited due to their unsatisfactory mechanical properties. Moreover, some toxic additives such as plasticizers, antioxidants or stabilizers used in synthesis of polymers can be harmful to the host tissue causing leaching in body fluid [2].

Metal implants are usually preferred to repair bone fracture owing to their outstanding mechanical properties [3]. Stainless steel-, Co- and Ti-based alloys are well-known examples for the commercially available bone implants. Metals are favored for long-term, durable and load bearing implants since they exhibit high strength and outstanding ductility that lead to high resistance to fracture [3]. In addition, metal implants with complex architecture can be produced through various available production methods such as casting, machining and powder metallurgy (PM) [3]. Their biocompatibility and matching mechanical properties to bone are two important factors for implants [3]. Biocompatibility of metallic implants is affected by corrosion and wear. In metallic implants, harmful metal ions arising from corrosion and wear may lead to inflammation, cell apoptosis and other destructive tissue reactions [3,4]. It was reported that release of Cr (Co–Cr alloys), Nb, V and Ni (Ti-based) ions may cause detrimental tissue reaction by exceeding the concentration limit of these elements in tissue or body fluid [3,4]. Ni, as an example, is a highly cytotoxic, genotoxic, carcinogenic and mutagenic element.

Mg and its alloys differ from other biomaterials by presenting compatible mechanical and physical properties to human bone. Their densities and elastic modulus are fairly close to each other which remove elastic mismatches between implants and the bone [5,6]. Moreover, Mg is naturally present in bone composition, and it is one of the required metals for the metabolism [7]. However, the fundamental problem of Mg-based implants is their low corrosion resistance resulting undesirably fast and unexpected degradation within a living system. Research investigations have been aimed to enhance the corrosion resistance and to offer industrially applicable Mg-based biodegradable implants. Furthermore, it is projected that Mg-based biodegradable implant will shift the direction of medical sector in near future as their commercial products start to appear in the market.

Implant material is desired to have very similar mechanical properties with the bone. However, in the current practice, most of the metals used in biomedical applications exhibit significantly higher mechanical properties than the bone. This causes well-known phenomenon of stress shielding, the results of which are bone-matter decomposition and loss of its strength. Stress shielding occurs when the implant carries higher proportion of the applied load, so the adjacent bone is exposed to a reduced load and loses its density in response [8,9]. Among various metal implants, Mg alloys stand out to have Young's modulus most similar to cortical bone (Mg: 40–45 GPa, Cortical bone: 10–27 GPa) whereas the Young's modulus of Ti-based and 316L stainless steel are 110 and 193 GPa, respectively [8,9].

Biodegradable metal implants are new generation of metal implants that exhibit improved corrosion resistance in body fluid during healing process of host tissue [10]. The main duty is to support the host tissue with a slow corrosion rate in the body fluid, and then dissolve completely after healing of the host tissue with no implant debris [10,11]. Among biodegradable metal implants, Mg, Fe and Zn, which are also known as smart implants, have been widely investigated in recent years. The most significant challenge with such biodegradable implants is to maintain their mechanical integrity during healing period of the host tissue [12]. Mg- and Fe-based implants exhibit good mechanical properties as hard tissue implants. However, high corrosion rate of Mg-based materials and very

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