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Mechanical, corrosion and biocompatibility behaviour of Mg-3Zn-HA biodegradable composites for orthopaedic fixture accessories

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A B S T R A C T

Development of biodegradable implants has grown into one of the important areas in medical science. Degradability becomes more important for orthopaedic accessories used to support fractured and damaged bones, in order to avoid second surgery for their removal after healing. Clinically available biodegradable orthopaedic materials are mainly made of polymers or ceramics. These orthopaedic accessories have an unsatisfactory mechanical strength, when used in load-bearing parts. Magnesium and its alloys can be suitable candidate for this purpose, due to their outstanding strength to weight ratio, biodegradability, non-toxicity and mechanical properties, similar to natural bone. The major drawback of magnesium is its low corrosion resistance, which also influences its mechanical and physical characteristics in service condition. An effort has been taken in this research to improve the corrosion resistance, bioactivity and mechanical strength of biodegradable magnesium alloys by synthesizing Mg-3 wt% Zn matrix composite, reinforced with thermally treated hydroxyapatite(HA) [$Ca_{10}(PO_4)_6(OH)_2$], a bioactive and osteogenic ceramic. Addition of 5 wt% HA is found effective in reducing the corrosion rate by 42% and improvement in the compressive yield strength of biodegradable magnesium alloy by 23%. In-vitro evaluation, up to 56 days, reveal improved resistance to degradation with HA reinforcement to Mg. Osteoblast cells show better growth and proliferation on HA reinforced surfaces of the composite. Mg-HA composite structure shows impressive potential to be used in orthopaedic fracture fixing accessories.

1. Introduction

Metallic materials are preferred for orthopaedic implants, due to their unique combination of mechanical strength and fracture toughness, as compared to ceramics and polymer materials (Staiger et al., 2006). Orthopaedic accessories can either be utilized to change a fractured part or to help in healing phenomenon. It can stay in the body permanently or temporarily depending upon the type of utilization, e.g., replacement or healing (Brar et al., 2009). Clinically used biomaterials for orthopaedic application include titanium and its alloys, cobalt-chromium alloys and stainless steel. These materials are non-degradable in physiological environment and remain as a permanent fixture. Thus, these materials being used in bone fixing accessories, necessitates a re-surgery after the healing of the tissue to retract them. It is also unwanted to have the bone tissue grown and integrated with this fixture as that makes the retraction difficult. However, it is often difficult to control bone integration on these fixtures in certain cases, especially when healing process is extended. This process causes economical burden and more importantly patient morbidity (Nayak et al., 2015). In addition to this, the above mentioned metallic materials possess significantly higher elastic modulus and strength, as compared to natural bone. This mismatch of elastic modulus leads to the stress shielding effect (Staiger et al., 2006; Nayak et al., 2015), which reduces stimulation of new bone growth and remodelling to generate required mineral content. As a result, the surrounding bone becomes weak and porous over the time and leads to implant failure.

Magnesium (Mg) has the potential to act as a replacement for orthopaedic implant materials, because of its biodegradability, osteocompatibility and potentials to solve the stress shielding problems (Nayak et al., 2015; Zhang et al., 2017). Mg and its alloys are attracting

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attention of the researchers for use in orthopaedics. This is because of their comparable density (1.78–2.0 g/cm^3) (Guan et al., 2013) to cortical bone (1.8–2.1 g/cm^3) (Zheng and Gu, 2010) and elastic modulus (35–46 GPa), in similar range of natural bone (3–20 GPa) (Nayak et al., 2015). As a result, it avoids the stress shielding effects on the surrounding bone. Additionally, release of Mg ions in living body, during degradation, does not pose any problem related to toxicity. Rather, Mg is required for basic metabolism and one of the necessary elements in bone tissue (Staiger et al., 2006; Saris et al., 2000; Hartwig, 2001). In human body, Mg is the fourth most abundant cation and ~ 1 mol of Mg is stored in the body of normal 70 kg fully grown person (Staiger et al., 2006). Mg acts as a co-factor for numerous enzymes and maintains the configuration of DNA and RNA (Hartwig, 2001).

The major drawback of Mg and its alloys, particularly in physiological environment, is fast degradation. It has very low corrosion resistance, because of its high reactivity with a standard electrode potential of − 2.37 V, with respect to standard hydrogen electrode (Nayak et al., 2015). In addition to this, Mg has Pilling Bedworth ratio ~ 0.79 (Liu et al., 2010). This indicates the inability of protection by oxide layer formation. As cast pure magnesium shows very high corrosion rate of 2.89 mm year^{-1} in 0.9% NaCl solution and very low mechanical strength (< 30 MPa) (Liu et al., 2010; Chen et al., 2014). However, high corrosion rate of Mg is observed in aqueous physiological environment, which generally contains chloride ions in the order of 150 mmol/L (Kokubo and Takadama, 2006). Chloride ions react with magnesium hydroxide to form highly soluble magnesium chloride and hydrogen gas (Kaesel et al., 2005). Alloying of Mg with other elements and coating on the surface often provides improvement in mechanical and corrosion properties (J. Huan et al., 2010; Z.G. Huan et al., 2010; Waizy et al., 2013; Dey et al., 2013). The first and foremost criterion for the selection of alloying elements for developing Mg alloys for biomedical application is the toxicity of the elements. The corroded products should not contain any toxic element and should be consumed by the surrounding tissues or dissolvable for excretion via the kidneys (Eddy Jai Poinern et al., 2013). Aluminium is one of the well known alloying elements to improve mechanical strength and corrosion resistance of Mg (Lee and Zakiyuddin, 2015). However, high concentration of Al^{3+} ion in body causes neural Alzheimer's disease and it has ability to damage the muscle fibers (Hollósi et al., 1994). Rare earth alloying elements, such as, cerium, praseodymium, yttrium etc., also contribute, individually as well as in combination, in improvement of the mechanical properties and corrosion behaviour of Mg matrix. However, severe hepatotoxicity has been observed after the administration of these elements. Other alloying element, such as, Ca is well known for effective grain refiner, that contribute in enhancing the mechanical properties. The only limitation with Ca is its solubility (< 1.34 wt%) in Mg (Chen et al., 2014). With increase in Ca content, more and coarser phase of $MgCa_2$ form along the grain boundaries, weakening the mechanical and corrosion behaviour of Mg alloy (Li and Zheng, 2013).

Zinc (Zn) acts similar to Al in terms of strengthening the Mg alloys. Zn possesses hexagonal closed packed (HCP) crystal structure, similar to Mg. In addition to this, Zn is one of the nutritionally essential elements in the human body (Li et al., 2015). Mg-Zn alloy generally consists of α-Mg matrix and ϒ- MgZn phase, which helps in improving the mechanical and corrosion behaviour (Zhang et al., 2011). It has also been reported that mixing of Zn up to 3 wt% provides an improvement in strength. However, beyond this composition, the intermetallic phases act as crack initiation sites and reduce ductility (Nayak et al., 2015; cheng Gao et al., 2008). Zn also improves the corrosion resistance of Mg alloys (cheng Gao et al., 2008). In order to further improve the corrosion resistance of the Mg-Zn system, forming a composite with some inert and biocompatible phases as reinforcement could be the better option. Ceramic reinforcement is considered ideal for that purpose as ceramic is inert to corrosion.

Recently, Mg based MMCs are gaining great interest due to their adjustable corrosion resistance and mechanical behaviour (Ratna Sunil et al., 2014; Witte et al., 2007a). It has been observed that shape, size and dispersion of reinforcement particles greatly influence the mechanical as well as corrosion properties of MMCs (Ratna Sunil et al., 2014; Witte et al., 2007a). Considering their biocompatibility, bio glass, inert alumina and hydroxyapatite (HA) are found suitable as reinforcement in Mg based MMCs (Ratna Sunil et al., 2014; Witte et al., 2007a; Z.G. Huan et al., 2010; J. Huan et al., 2010; Mantripragada et al., 2013; Khanra et al., 2010; Campo et al., 2014; Zhao et al., 2011). HA has same chemical and crystal structure to the mineral part of bone (Ratna Sunil et al., 2014; Lahiri et al., 2012). HA reinforcement in magnesium matrix is a suitable addition as it has ability to support the epitaxial precipitation of Ca/P compound (apatite) layers onto the exposed area of composites in physiological environment. This white precipitated compound layers protect the surface from corrosion and retains mechanical strength (Ratna Sunil et al., 2014; Witte et al., 2007a; Zhao et al., 2011; Muthupandi et al., 2013a). Being bioactive in nature HA has potential to integrate in bone configuration and help bone in-growth in the structure. The presence of nano HA in the Mg based composite increased pronounced bio mineralization by immersing the samples in supersaturated simulated body fluid (Sunil et al., 2014). In addition to this, it has also been reported that composite formed by the addition of 20 wt% HA reinforcement in AZ91D (Mg-9 wt% Al-1 wt% Zn) matrix, fabricated by powder metallurgy route, could decrease the corrosion rate of Mg-MMCs by approximately 37% (Witte et al., 2007a). However, this system is not suitable for orthopaedic application, owing to its high Al content. In another study, HA was incorporated in Mg-3Zn alloy through selective laser melting and result showed that degradation rate slowed down due to the decrease of the grain size and formation of apatite layer on the surface (Shuai et al., 2017). Researchers have explored the potential of Mg-3Zn-0.5Zr matrix with different composition of HA (0.5, 1 and 1.5 wt%) as reinforcement to tailor the corrosion and mechanical properties of composite. HA reinforcement of 1.5 wt% is found to improve the ultimate tensile strength, yield strength and elongation by 10%, 16% and 46%, respectively (Ye et al., 2010). The strength of Mg-3Zn-0.5Zr-1.5HA composite is 302 MPa, which is higher than the natural bone (124 MPa) (Pal, 2014). It possesses the risk of developing stress shielding effect. Further, biocompatibility of Zr alloys is also not yet proven beyond question. Ratna et al. Ratna Sunil et al. (2014) have also synthesized Mg matrix composites with varying HA content (0, 8, 10 and 15 wt%), using high energy ball milling, followed by spark plasma sintering. Significant improvement in corrosion resistance was observed for all Mg-HA composite and ~ 3.7% improvement in fracture toughness was noted with 8 wt% HA addition. Another study on Mg-HA composite, fabricated through powder processing, reports ~ 65% improvement in corrosion resistance for Mg-15 wt% of HA composite, when immersed in PBS solution for 100 h. However, the compressive yield strength was decreased by ~ 5% with the addition of 15 wt% HA to Mg. On other hand, Khanra et al. (2010) have fabricated Mg-15HA composite through casting route and found 15% improvement in compressive yield strength as compared to bare Mg alloy. Hence, it is observed that the processing method greatly influences the mechanical properties of composites. Still there is a lack of literature on compression studies of these composites with different processing route.

It can be concluded from the available literature that, there is lack of systematic study on mechanical properties and biocompatibility in HA reinforced biocompatible Mg based composites. In addition to that, longer duration in-vitro degradation studies are also essential, because these composites would remain in the body over 8–16 weeks before being fully replaced by natural tissue (Staiger et al., 2006; Witte et al., 2005). Thus, it is important to investigate the integrity of such composites for long exposure in simulated body environment, which is not reported yet. Further, biocompatibility of Mg-HA composites is also barely studied. These results are essential for designing the Mg based composite for temporary internal fracture fixing accessories.

In consideration to the present context, the main goal of this