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ABSTRACT

Biodegradable materials are being widely investigated for internal fracture fixation devices to avoid second surgery and long-term complications associated with permanent implants. In recent years, iron (Fe) based alloys have been largely explored as degradable biomaterial because of their good mechanical properties and biocompatibility. However, their degradation rate is a concern. Bacterial infection is another clinical challenge associated with degradable implants.

In this research work, Fe-Mn-Cu (up to 10 wt.% Cu) alloys are initially prepared as a proof-of-concept by powder metallurgy route to understand the metallurgical and biological effect of Cu addition in Fe-Mn alloy. Nearly 6 times increase in degradation rate for 10wt.% Cu alloy was observed compared to the base alloy due to Cu precipitation and local galvanic cell formation. Increased bactericidal activity with higher Cu addition in Fe-Mn alloy was observed in broth micro-dilution test, while *in vitro* cytocompatibility study showed more than 70% cell viability for all alloys.

Fe-Mn-Cu alloys, prepared through powder metallurgy route, showed high corrosion rate and significant bactericidal properties; but presence of high amount of porosity (19%-22%) adversely effected its mechanical properties. Thus, for better metallurgical processes and property evaluation, Fe-Mn-xCu (x= 0, 5 and 10 wt.%) alloys were prepared through melting-casting route. XRD analysis confirmed austenite phase stabilization, which give MRI compatibility. Following the Thermo-Calc prediction, Cu rich phase formed along the austenite grain boundaries, which are expected to increase the degradation rate by formation of local galvanic cells. Degradation behaviour were investigated through static immersion and electrochemical polarization, where enhanced degradation is found for higher Cu added alloys. When challenged against *E.Coli* bacteria, the Fe-Mn-Cu alloy extract showed significant bactericidal effect compare to the base alloy. High degradation rate is beneficial for bactericidal properties because of high Cu concentration, but it also raises concern regarding biocompatibility. However, continuous MG63 and MC3T3-E1 cell proliferation was observed in *in vitro* cytocompatibility studies for all the alloys. Moreover, the newly developed alloys did not show any kind of tissue necrosis around the implants in *in vivo* rabbit femur model. Rather, better osteogenesis and higher new bone formation were observed with Fe-Mn-10Cu alloy as evident from micro-CT and fluorochrome labelling analysis.

Addition of high Cu content (10wt.%) in Fe-Mn alloy increased the degradation rate significantly (0.072 mmpy) compare to base alloy (0.058 mmpy), but it deteriorated mechanical properties (strength and ductility) of the system. Therefore, in another study, a low Cu alloy (Fe-Mn-3Cu) was thermo-mechanically processed through cold rolling, annealing and age treatment, so that degradation rate and bactericidal properties are improved without compromising the mechanical properties. The main strategy here is to precipitate Cu nano-particle, restrict the grain growth and rather refine the grain size during age treatment. Nano Cu rich precipitate formation, their composition and distribution were evaluated using STEM and atom probe tomography analysis. Significant enhancement of degradation behaviour (0.091mmpy), due to grain refinement and Cu precipitation, was observed after 12

hours of age treatment, which was even higher than Fe-Mn-10wt.%Cu alloy. Electrochemical impedance spectroscopy and Mott Schottky were also performed for better corrosion property analysis, which showed lower polarization resistance, impedance, phase angle and higher defect density of the age treated alloy. Although higher degradation of these alloys raises concern regarding its biocompatibility, *in vitro* and *in vivo* biocompatibility studies did not show any toxicity. Therefore, thermo-mechanically treated Fe-Mn-3Cu alloy has high potential to be used for internal fracture fixation devices, specifically for load bearing applications like bone plate and screw.

Fe-25Mn-10Cu alloy showed excellent bactericidal and degradation properties, but compromises with the tensile properties. Therefore, Fe-25Mn-10Cu alloy was projected as scaffold material for non-load bearing small scale bone defects, where compressive properties are more important. Scaffolds with multiscale porosity and interconnectivity, were developed through powder metallurgy route using naphthalene as spacer material. Porosity in the scaffolds ranged from 42-76%, where majority of the macro-pores ($\geq$20μm) form interconnected channel network. XRD analysis confirmed the presence of MRI compatible antiferromagnetic austenite as major phase in all the scaffolds. Developed scaffolds in this study had minimum ultimate compressive strength of 7.21 MPa (for 30 Naph), which lies within the range of human cancellous bone UCS (2–12 MPa). Degradation rates of the scaffolds were determined from static immersion test, where scaffold with highest porosity (76%) showed highest degradation rate of 2.71 mmpy. Increased degradation rate of the scaffolds did not lead to cytotoxicity on MG63 cells as studied by alamar blue assay and live/dead imaging. When implanted in rabbit femur, scaffold with higher porosity showed enhanced osteogenesis, as evident through micro-CT and histological analysis. It is hypothesized that presence of multiscale porosity with high degree of interconnectivity facilitated the better bone regeneration within and around the Fe-Mn-Cu scaffolds.

Finding a balance among degradation rate, mechanical properties, bactericidal properties and biocompatibility is a critical challenge in Fe based biomaterials. This present research work provides some insights on processing routes, optimization of compositions as well as post processing methods to address those critical issues towards development of load-bearing implants and non-load-bearing scaffolds.