

A novel hybrid approach to develop Bioresorbable Material

Abstract

Damaged/injured tissues within the body are being replaced or reinforced by metallic orthopaedic implants. A bioresorbable implant is able to dissolve within the body, unlike its traditional counterparts. Bulk metallic glasses (BMGs) possess incredible properties, including high biocompatibility by virtue of their amorphous structure and absence of dislocations. However, the fabrication of BMGs is a challenging task because in order to achieve an amorphous structure, fast cooling is a pre-requisite which in the case of casting is very difficult to achieve due to the fact that fast cooling rate and adequate rate of filling of the mold possess a trade-off relationship. Therefore, purpose of this work is to develop a simple novel hybrid approach that is cost effective and attempts to synthesize BMG based on Mg-Ca-Zn constituent. Synthesis of bioresorbable material was attempted by hybridizing a recent friction stir processing (FSP) technique coupled with gas tungsten arc welding (GTAW). Magnesium was employed as base material on which FSP was performed with Calcium granules as reinforcement. After FSP, GTAW process was performed by using Zn as filler material. The added Ca and Zn were found to effectively intermix with the Mg matrix. Especially, a relatively invariable distribution of Ca phases was observed in the stirred microstructure after FSP. The current work is expected to alleviate the physiological issues pertaining to orthopaedic fixations and decrease the need for secondary surgeries in geriatric fractures.

Keywords: bioresorbable, friction stir processing, magnesium, calcium, zinc, gas tungsten arc welding

Introduction

Biomedical Engineering is a recent development which integrates traditionally distinct disciplines i.e., engineering and medical sciences. Synergy between the two disciplines is catalysed through the evolution of compatible biomaterials. Biomaterials such as metals, alloys, ceramics and polymers are engineered substances which can be interfaced with biological systems for medical/dental purpose. These materials have diverse applications in medical field including therapeutic (e.g., treat, augment, repair, or replace a tissue), procedural or diagnostic [1]. Ever since it's active implementation for about half a century this field has experienced a strong growth and transformed the way medical profession is practiced today. Biomaterial science assimilates in itself disciplines of biology, medicine, chemistry, metallurgy, materials technology, tissue engineering and material science. Amalgamation of these disciplines has created urge for development of exotic biomaterials which possess properties close to biological materials and have acceptability in human body environment [2]. Traditionally, stainless steel, titanium and its alloys have been employed in load bearing implants mainly because of their superior corrosion resistance higher strength and toughness [3]. But their stiffness is significantly higher than that of bone and there are other issues of in vivo compatibility, as constituent metals in these alloys are less tolerant in body environment. Particularly, the high Young's modulus of conventional implants (100-200 GPa) "shields" the surrounding tissues from normal stress, leading to problems like adjacent anatomical structures, poor healing, skeleton thickening, implant loosening, etc [4]. Whereas, the relatively lower Young's modulus of Mg alloys (~40 GPa) can effectively prevent such "stress shielding". Issues related to release of wear debris and reactions products at interface (e.g., Hydrogen and other chemicals released due to reaction between implant material and body fluids/tissues) create secondary complications. It is imperative for a good biomaterial to be made from essential body elements having property like bio-restorability [5] such as Ca, Mg, Zn etc, to which the human body is more tolerant [6-7]. The secondary complications often give rise to the need for secondary surgeries to remove the conventional implants. The highest number of bone fractures occur in the elderly people, which are above 65 years of age [8]. Crucially, in the geriatric fractures, performing surgeries again is dangerous to the life of elderly patients due to associated blood loss and tissue damage [9]. This leads to long periods of excruciating inflammations, which can be avoided using bioresorbable materials.

It is becoming common to use biomaterials as whole or part of a living structure (e.g., bone), tissue or devices (biomedical) that performs, enhances or substitute a natural function. These functions may be relatively passive, like existing in heart valve, or may be functionally more bioactive such as hydroxy-apatite coated hip implant etc. Additionally, these materials are also employed in dental applications, instrumentation for surgery and drug delivery. For example, a construct with soaked pharmaceutical products can be placed into the body permitting prolonged release of a drug over an extended period of time. A biomaterial may also be an autograft, allograft or xenograft which is used as a transplant material [10].

There are inherent issues related to release of undesirable reaction products in long term in vivo use of traditional implants (made from Fe/Ti/Co/Cr based materials) [11]. The recent development in synthesizing BMGs entirely from magnesium, zinc and calcium constituents have revolutionized the treatment involving biomaterial implants [6,12-14].

The recent times have witnessed interesting discoveries on a new class of substances known as bio-metallic glasses (BMGs) for biomedical applications [15]. Substances, especially bioactive glasses (such as hydroxyapatite and apatite-wollastonite glass etc.) which contain ions and elements present in physiological environment (Calcium, Potassium, Sodium, Magnesium and Zinc) have demonstrated excellent biocompatibility when clinically used as bone substitutes [16]. The essential biological elements present in BMGs, i.e., calcium, magnesium and zinc, belong to natural constituents (an adult human body comprises about 1000–1500 grams of calcium [17]) and magnesium promotes calcium absorption into bone, thus co-release of magnesium and calcium ions may be beneficial for bone healing [17]; Zinc, on the other hand stimulates bone fracture healing, lowers postmenopausal bone loss, enhances bone mineralization and strength of the skeletal [18-19] and get gradually consumed within the body [20]. From the application perspective, Li et al. [21] incorporated Mg-Ca1.0 alloy into the rabbit femoral shafts and observed its complete absorption in the second month. Apart from bioresorbable nature, the alloying of Mg with Ca also yields better bone-implant contact [22]. The human body is also naturally tolerant to these elements with a daily allowance in an adult’s body being 1000 mg/day for calcium, 420 mg/day for magnesium and 10 mg/day for zinc [11, 23].

These substances also found to induce positive biological responses at the tissue interface, but they lack combination of mechanical properties like strength, toughness, hardness and stiffness, consequently their usage is mainly limited to fillers for bony defects. Idea of use of bio-resorbable materials for fixtures and other similar implants, thus, enthralled academics, and researchers and professionals to investigate and promote desirable features and allay adverse ones so that ideal materials can eventually be created. The fact that studies dedicated to increase the corrosion resistance of Mg-Ca implants have been conducted and reported enlightens the practicability of these alloys [24].

In a maiden work Zberg et al. [25] performed in vivo studies on BMG biomaterial of MgZnCa and demonstrated their biocompatibility. They also confirmed that one of the major issues with some elements in BMG i.e., hydrogen production was considerably lessened by zinc and oxygen rich passivating layer. Among major classes of Ca, Mg based BMGs, the glass forming ability (GFA) of magnesium-based Mg-Zn-Ca ternary BMG are limited mainly as the largest critical size diameter (Dc) being limited to 5 mm. In yet another work Wang et al. [10]

fabricated Ca-Mg-Zn (nominal composition represented as Ca65Mg15Zn20 in at. wt.%) BMG by copper mold injection casting process in a controlled Argon inert environment. They used 99.5% pure calcium, 99.99% pure magnesium and 99.99% pure zinc and melted the mix in induction heated quartz tube. The melt was rapidly introduced into a copper mold and cast in rod shaped ingots. Similarly, Cao et al. [23] produced CaMgZn based BMGs in six different molecular composition through casting process. The authors used mixture of pure elements such as magnesium (99.85 wt.%), zinc (99.995 wt.%) and calcium (99.8 wt.%) in Mg–Ca master alloy melted the mix under argon atmosphere in boron nitrate coated graphite crucible. They subjected the melt to cyclic heating; first at 850^{o}C followed by cooling to room temperature, reheating to 700^{o}C then gravity wedge casting and lastly injection casting into copper moulds at 620^{o}C.

Glass is a usual reference for amorphous materials that are prepared by rapidly cooling of molten material. Characteristically, BMGs are frozen to solid state super cooled liquids (SCL) and, hence, their compositions are not limited by thermodynamic/kinetic driven solid solubility theories thereby a broad range of alloy compositions can be synthesized. Heavy molecular and amorphous structure of BMGs inhibits in them superior corrosion resistance and enhanced mechanical properties, and also abilities to be fashioned like thermoplastic polymers i.e., thermo plastic forming [26].

Rapid cooling employed in production of glass reduces the mobility of molecules and stops them from packing into a thermodynamically stable crystalline state. Over half a century it has become known that metals can be cast into glassy state by cooling so quickly (1K/s to 100K/s) that the atoms froze before they could arrange themselves into characteristic lattice. The conditions under which liquid metal can transform into glass make a restriction to produce metallic glasses in forms other than ribbons, foils, spheres, discs or wires, that too with dimension being very small.

Fabrication of orthopaedic implants

The mechanical properties, resistance to wear, resistance to corrosion, biocompatibility and osseointegration are the key parameters which govern the whole area of orthopaedic implants. The contribution of metals in orthopaedic implants is highly significant especially in the permanent prosthetic implants as well as the temporary fixations. The most commonly used metallic alloys in orthopaedic implants are stainless steels, cobalt-based alloys, titanium-based alloys and biodegradable alloys like magnesium-based alloys [27]. It is important to note that the fabrication of implants is not only limited to additive manufacturing, instead subtractive manufacturing like multiple axis machining and automatic coating and cleaning is also being employed wherever the implant geometry is not complex. The current trend pushes towards metal additive manufacturing for fabrication of implants. Electron beam melting and direct metal laser printing are the processes which are being adopted. Electron beam melting gives way for substantial amount of design flexibility as rivalled to the conventional methods of manufacturing [28-29].

Dental implants

The physical, chemical and mechanical properties of a material are not sufficient to govern the biocompatibility characteristics. These characteristics are judged by analysing the direct interactions involving the dental implant and the tissues. The crucial parameters which further govern the design of the dental implants are composition of the biomaterials, implant geometry, biomechanical factors, characteristics of the surface, quality of the bone and surgical technique to be employed. Apart from ceramics, carbons and polymers, metallic materials utilized in fabrication of dental implants are titanium, zirconium, gold and titanium-vanadium alloys [30]. Among these metallic materials, titanium and its alloys are specifically being used in single and multiple tooth restoration implants and as anchorage for fixation devices [31].

Pre-requisites to development of novel biomaterials

Bone plate presented in the 1900s was attached using screws in order to align the healing bone aiding in the healing process, vanadium metal used in this case corroded rapidly and caused opposing healing effects. In the 1930s, the first joint replacement surgery was reported owing to the use of stainless steel and cobalt chromium alloys [32]. Apart from the other classes of materials, novel biomaterials are being fabricated from metals. Choosing metals for the purpose of fabricating biomaterial is because of their exceptional biocompatibility, suitable mechanical properties, adequate corrosion resistance and lower cost [33]. The case with biomaterials is that they cannot be directly judged based on the material properties instead the application in which these biomaterials are being employed plays a crucial role in deciding the material to be chosen. Implants used in cardiovascular and otorhinology applications are fabricated from stainless steel (316L SS), artificial joints necessitate high wear resistance so the best choice of material is Co-Cr-Mo alloys. Moreover, the surface properties of these metallic materials also govern the interactions of cells and tissues with the metal surface [34]. Considering all this information, it is important to realize that a crystal-clear understanding of the environment in which the biomaterial is to be used, the environmental factors, time for which the biomaterial will be functioning, human safety factor are all crucial design parameters which are a pre-requisite to development of novel biomaterials.

Synthesis of BMGs

Amorphous alloys have been processed by “energize and quench” techniques described by Turnbull [35]. Such techniques can be implemented through several processes such as irradiation, plasma processing, ion implantation and ion mixing, laser processing, physical and chemical vapour deposition processes, etc. All these processes usually increase free energy of system comprising of metallic glass elements followed by rapid quenching to either hold the metastable phase or to use it as an intermediate step to achieve the desired microstructure and/or properties. Characteristically, most of these techniques are complex and require sophisticated equipment and instrumentation as well as stringent operating conditions. They are often costly as well.

Typically, indications and deficiencies requiring treatment with bio-implants prevail more in subjects from under-privileged groups. There exists a need to develop novel methods that are simple and cost effective so that implants and other items of biomedical use can become more affordable and benefits can be harnessed for the masses. This paper presents details of a novel work, in brief, on a hybrid approach comprising of a recently developed technology- Friction Stir Process (FSP), coupled with Gas Tungsten Arc Welding (GTAW). The hybrid approach was employed to fabricate Mg based MgCaZn BMG. In fact, the author's tryst with the success in utilising this approach to fabricate metallic foam [36] has encouraged the authors to use this route to fabricate BMGs. As the approach is subject to proprietary issues, exact details and a comprehensive test regime is although restricted. This approach is unique in a way that the processing sequence is simple and it employs a less sophisticated facility.

The primary application of the current study is orthopaedic fixation of bone fracture injuries [4]. This application can be achieved from either the first stage of the present work, i.e., fabricated Mg-Ca system, or via the second stage, i.e., Mg-Zn-Ca system, based upon the requirements and achievement of bioresorbable capacity. Secondly, the usage of relatively less sophisticate equipment to fabricate the Mg-Ca and Mg-Zn-Ca alloys increases their applicability in the patients suffering from orthopaedic maladies by reducing the cost and simplifying the fabrication. Finally, the current study and its feasibility holds tremendous resourcefulness for researchers to employ FSP for designing more complex and physiologically crucial bioresorbable materials of future, which can have numerous associated elements intended for different disorders. Eliminating the need for secondary surgeries in aged patients, who cannot withstand the associated procedures is another important latent application of this work.

Materials and Methods

The FSP is less than two decades old technology [37], in which a non-consumable rotating shouldered tool with a pin is inserted in a rigidly clamped work piece till the shoulder contacts the work piece surface. The interaction of rotating shoulder with a stationary work piece creates sufficient frictional heat to soften the work material under the shoulder. The tool is subsequently made to traverse over the work surface. The pin of rotating and simultaneously traversing tool subjects the softened materials to a stirring action. The stirring action on base metal surface packed with Ca evenly mixes the Ca grains in Mg base metal sheet. The steps involved in FSP are displayed in Fig. 1 [38].

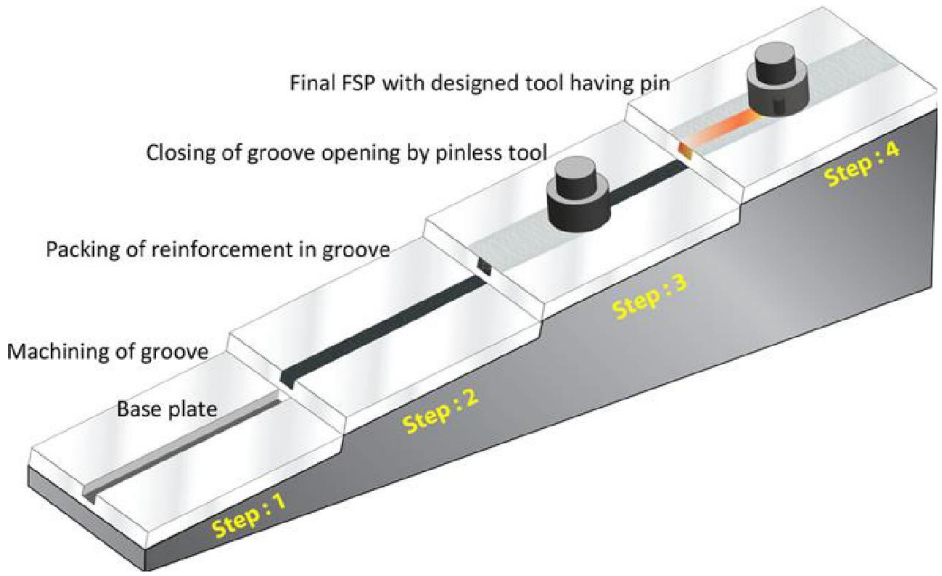

Figure 1: Steps involved in FSP [38].

In the present the starting material was in the form of 99.9% pure Mg sheets 200 mm x 70 mm x 3 mm in size used as base metal. Longitudinal grove (3 mm wide and 3 mm deep) was machined on the sheet's surface and commercially Ca was packed in the grove. The surface packed with Ca was subsequently subjected to FSP (details shown in Fig. 2). The FSP was performed using HCHCr tool steel with 18 mm shoulder diameter and 6 mm cylindrical pin. The FPS runs were carried out at 710 rpm spindle rotation, 50 mm/min traversing speed and 1^o tool tilt.

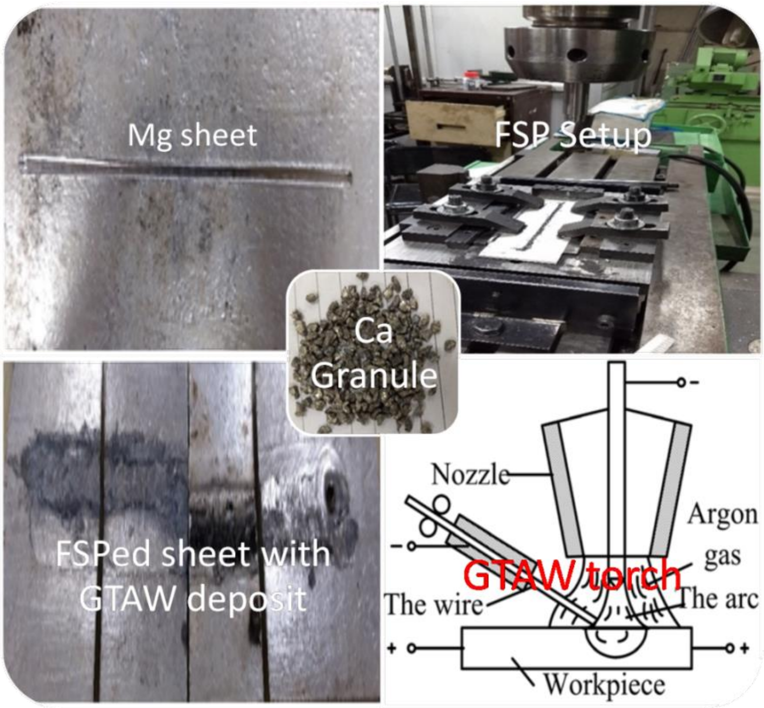

Figure – 2: Pictorials and schematic of details of experimentation

The FSPed region of sheet was deposited with Zn in fused state through GTAW process. The key in present approach is synergy obtained by hybridizing FSP with GTAW process. GTAW is a welding process that uses electric arc produced between a non-consumable Tungsten electrode and work piece. An externally applied filler material can be melted and deposited on the base metal through heat of the arc. The arcing area is protected from atmosphere by inert shielding gases such as argon or helium. A standard GTAW setup comprises of (a) a DC/AC power source which delivers the welding current, (b) a welding torch having a tungsten electrode and gas nozzle (as shown in Fig. 2) [39-40] and (c) inert shielding gas (Ar) supply shields the molten metal pool. The details of the conditions used in GTAW process is shown in Table-1.

Table-1: GTAW process conditions used in hybridization

Process condition	**Details**
Workpiece material	FSPed plate Mg mixed with Ca granules
Filler wire	Commercially pure Zn wire (2mm diameter)
Electric power	3 phase A.C. power
Current	32 A
Electrode	2.4 mm diameter Tungsten electrode
Shielding gas supply	Ar delivered at 7 l/min.

The plates after depositing Zn layer through GTAW need to be subjected to various tests to establish composition of processed region. Tests such as elemental analysis, mechanical property test and electrochemical analyses for biocompatibility can be performed. In the present work microstructural analysis is, however, presented. The microstructural test samples were removed from processed region as shown in Fig. 2 using Wire electric Discharge Machining (WEDM). The samples were then subjected to grinding and polish as per standard microstructural test procedure. Polished samples were subsequently etched (using a reagent comprising of 75ml Ethylene Glycol, 24ml H_2O and 1ml Nitric Acid).

Results and Discussion

The micrographs of transverse sectioned FSPed plates, taken from a metallurgical optical microscope, are shown in Fig. 3. Micrographs reveal that the processing has resulted in effective intermixing of Calcium granules, seen as dark phase, in the Mg base material. Rad et al. [41] depicted the micrographs of Mg with increasing content of Ca, i.e., at 0.5 %, 1.25 %, 2.5 %, and 5 % Ca. The mixture of phases formed using FSP in the current study (Fig. 3) has high morphological similarity with the Mg-5Ca alloy in their analysis. Further, $MgCa_{4.5}$ alloy studied by Sakiewicz et al. [42] is again strikingly similar to Fig. 3, wherein the bright phase is investigated to be α-Mg and the dark phase is found to be a eutectic of α-Mg and Mg_2Ca using scanning electron microscopy, energy dispersive spectroscopy and x-ray diffraction. The Mg_2Ca intermetallic is known to be common for the Mg-xCa alloy system [43]. Therefore, although FSP process can be claimed to produce heterogenous metal matrix composites, the Ca content in the current study apparently remains around 4-5 %, indicating considerable compositional invariability. Further, hydroxyapatite (HA) and β-tricalcium phosphate (β-TCP), which are bio-ceramics having the compositions of human bones can be used to reinforce the Mg-Ca alloys to improve their biocompatibility [44]. Although the Mg_2Ca intermetallic is known to increase the corrosion rate [21], the formation of Mg-Ca system using FSP is likely to enhance the corrosion resistance. The stirring action subject the process zone to severe plastic deformation this causes the Ca grains to finely divided and mixed with the Mg base metal. Plastic deformation at the processed zone owing to the stirring action of the rotating tool resulted in the grain refinement of the plate surface [45].

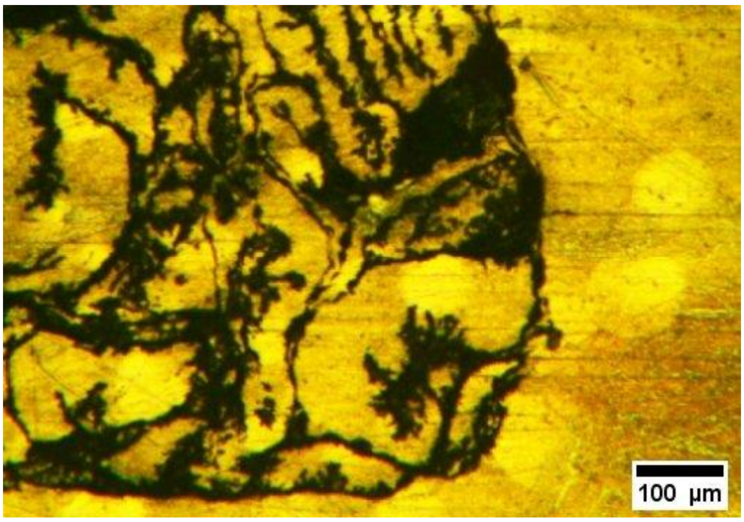

Figure 3: Micrograph from processed zone at 100x (Mg is seen as bright phase and Ca as dark phase)

Deposit of liquid Zn over processed zone by GTAW (As shown in Fig. 2) and mixing of Mg and Ca under high heat of the arc resulted in formation of a wide bead which solidified in a mixed dendritic and columnar cast structure as shown in Fig. 4. Intense heat of the arc has a peak temperature of the order of 7000^{o}C. Intense temperature coupled with high arc force results in mixing of the three elements in molten metal pool, subsequent solidification and cooling cause formation of bulky intermetallic formation. Spectroscopy of the dendrites suggested formation of heavy compound similar to Mg-Ca-Zn based BMGs. Importantly, the β-tricalcium phosphate (β-TCP) bio-ceramic can also be used to further enhance the mechanical and corrosion resistance of Mg-Zn-Ca alloys [46]. The efficient addition of Zn to Mg containing matrix is also enhances the corrosion resistance [47], thus potentially improving the biocompatibility, in addition to the corrosion resistance provided by FSP.

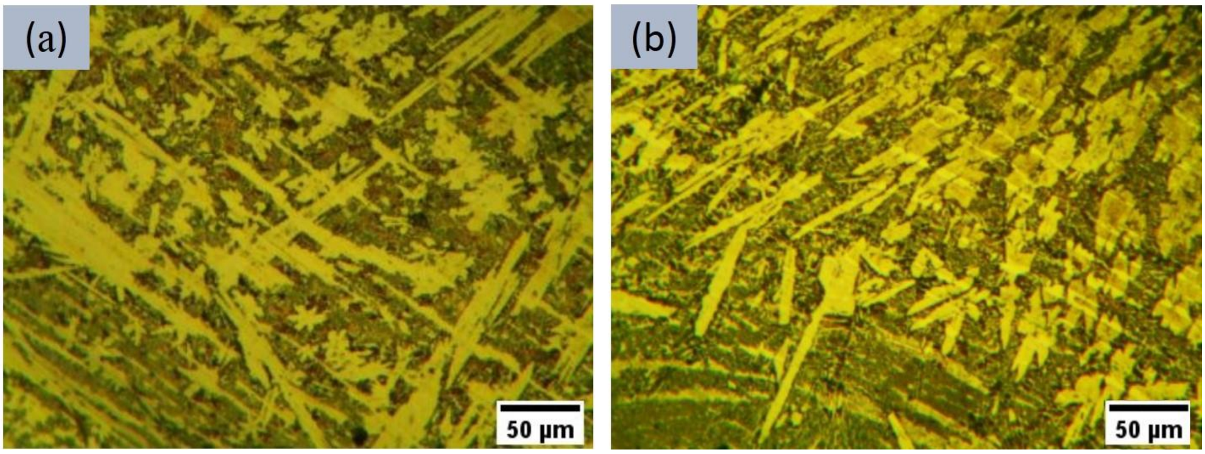

Fig. 4 Cast structure of GTAW bead taken at 200X revealing formation of large dendrites and spectral scanning suggest the phase comprising of Mg, Ca and Zn.

Results of the hybrid processing approach presented in this paper comprising of FSP of Mg plate with Ca granule as reinforcement resulted in fine mixing of Ca with Mg as evident from

Fig 3. A bead of Zn deposit was overlaid on the Mg+Ca regions by GTAW and the resultant bead after solidification and mixing of molten metal as shown in Fig. 4 reveals formation of heavy molecular formation of intermetallic similar to BMGs.

Conclusions

The aim of this work is to develop processing route for promising biomaterial class of BMGs that is unsophisticated as well as cost effective both. This is done in order to harness the potential of such exotic biomaterials for the benefit of masses. The processing sequence in FSP coupled with GTAW hybrid route to performed synthesize MgCaZn based BMG like composition demonstrated that this approach of synthesis is not only unsophisticated but cost effective as well. This hybrid approach is unlike other routes suitable for bulk manufacturing as well. Although further processing such as phase homogenization, thermoplastic forming etc. can be performed to augment the synthesized substance structurally and in consistency. Also tests such mechanical properties, elemental analysis and biocompatibility must be performed to characterize the parameters necessary to prescribe the bio-suitability of the synthesized material.

This paper pushes the understanding of biomaterials from the view point of material, medical and bio engineers taking into account the conventional methods of characterization of materials, application of biomaterials in the medical domain and the response of human body. The potential use of bioresorbable material, bulk metallic glasses and how a deep understanding of material science plays a crucial role in improving the available literature for these bio materials is highlighted. The traditional and present use of biomaterials is highlighted in this work keeping the manufacturing point of view in place. The issues faced during the application of biomaterials and the way ahead as well as how the scope of biomaterials can be widened is discussed. Orthopaedic implants and their uses from the viewpoint of material chosen is discussed. Fabrication, manufacturing techniques and processes employed in orthopaedic implants is debated. A brief note about dental implants is also given in this work. Further, the pre-requisite knowledge for development of novel biomaterials along with the materials and method are talked about in this work.

Acknowledgements

Authors thank Mr Harsh Kaushik, Mr Tushar Sardana and Mr Vipin Goyal for their support. Thanks, are also to Mr Noor Zaman Khan and Dr Zahid A Khan.

Conflict of Interest

None

Funding/Sponsorship

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sector.

Authors contribution

Nabeel Ali: Writing- Original draft preparation, Visualization **Nadeem Fayaz Lone:** Writing- Original draft preparation, Visualization **Arshad Noor Siddiquee:** Conceptualization, Methodology, Visualization, Supervision **Iffat Imran:** Resources, Data Curation **Julfikar Haider:** Supervision, Writing- Reviewing and Editing **Vipin Goyal:** Investigation **Vrishin Puri**: Investigation **Tushar Sardana:** Investigation

References

[1] Sidra A, Farzan Athar H, Iffat I. Recent progress in development and applications of biomaterials. *Materials Today: Proceedings.* 2022;62:385-391. https://doi.org/10.1016/j.matpr.2022.04.233

[2] Brian L. Biomaterials: A Systems Approach to Engineering Concepts. London: Elsevier; 2017.

[3] Xiao M, Chen Y M, Biao M N, Zhang X D, Yang B C. Bio-functionalization of biomedical metals. *Materials Science and Engineering: C.* 2017;70:1057-1070. https://doi.org/10.1016/j.msec.2016.06.067

[4] Salahshoor M, Guo Y. Biodegradable orthopedic magnesium-calcium (MgCa) alloys, processing, and corrosion performance. *Materials (Basel)*. 2012; 5:135-55. https://doi.org/10.3390%2Fma5010135

[5] Daniel Wee Yee T, Jaryl Chen Koon N, Yingying H, Phillip En Hou W, Hwa Linag L, Subbu S V et al. Bioresorbable metals in cardiovascular stents: material insights and progress. *Materialia.* 2020;12:100727. https://doi.org/10.1016/j.mtla.2020.100727

[6] Sung Youn C, Soo-Won C, Kui Won C, Hyun Kwang S, Yu Chan K, Jae Young J et al. Biocompatibility and strength retention of biodegradable Mg-Ca-Zn. *Journal of biomedical materials research part b applied biomaterials.* 2012;101:201-212. https://doi.org/10.1002/jbm.b.32813

[7] Donghui Z, Irsalan C, Yingchao S, Zhaoxiang Z, Jiayin F, Kee-Won L et al. Mechanical strength, Biodegradation, and in Vitro and in Vivo Biocompatibility of Zn biomaterials. *ACS Applied Materials & Interfaces.* 2019;11:6809-6819. https://doi.org/10.1021/acsami.8b20634

[8] Bergen GS, Chen LH, Warner M. Injury in the United States; 2007 chartbook. Hyattsville, MD: National Center for Health Statistics: 2008.

[9] Chen WC, Yu SW, Tseng IC, Su JY, Tu YK, Chen WJ. Treatment of undisplaced femoral neck fractures in the elderly. Journal of Trauma and Acute Care Surgery. *J Trauma*. 2005;58(5):1035-9. https://doi.org/10.1097/01.ta.0000169292.83048.17

[10] Wang Y B, Xie X H, Li H F, Wang X L, Zhao M Z, Bai Y J et al. Biodegradable CaMgZn bulk metallic glass for potential skeletal application. *Acta Biomaterialia.* 2011;7:3196-3208. https://doi.org/10.1016/j.actbio.2011.04.027

[11] Donatella G, Gabriela C, Susanna S, Lucia S, Federica F, Alessandra S et al. Cytokine release in mononuclear cells of patients with Co–Cr hip prosthesis. *Biomaterials.* 1999;20:1079-1086. https://doi.org/10.1016/S0142-9612(99)00004-6

[12] Gu X, Shifleta GJ, Guo FQ, Poon SJ. Mg–Ca–Zn bulk metallic glasses with high strength and significant ductility. *Journal of Material Research.* 2005;20:1935-1938. https://doi.org/10.1557/JMR.2005.0245

[13] Senkov ON, Scott JM. Glass forming ability and thermal stability of ternary Ca–Mg–Zn bulk metallic glasses. *Journal of Non-Crystalline Solids.* 2005;351:3087-3094. https://doi.org/10.1016/j.jnoncrysol.2005.07.022

[14] Park ES, Kim DH. Formation of Ca–Mg–Zn bulk glassy alloy by casting into cone-shaped copper mold. *Journal of Materials Research.* 2004;19:685-688. https://doi.org/10.1557/jmr.2004.19.3.685

[15] Schroers J, Kumar G, Hodges TM, Chen S, Kyriakides TR. Bulk metallic glasses for biomedical applications. *Biomedical Materials and Devices.* 2009;61:21-29. https://doi.org/10.1007/s11837-009-0128-1

[16] Cai. S, Zhang WJ, Xu GH, Li JY, Wang DM, Jiang W. Microstructural characteristics and crystallization of CaO–P_2O_5–Na_2O–ZnO glass ceramics prepared by sol–gel method. *Journal of Non-Crystalline Solids.* 2009;355:273-279. https://doi.org/10.1016/j.jnoncrysol.2008.11.008

[17] Ilich JZ, Kerstetter JE. Nutrition in Bone Health Revisited: A Story Beyond Calciu. *Journal of the American College of Nutrition.* 2000;19:715-737. https://doi.org/10.1080/07315724.2000.10718070

[18] Humayun K, Khurram M, Cuie W, Yuncang L. Recent research and progress of biodegradable zinc alloys and composites for biomedical applications: Biomechanical and biocorrosion perspectives. *Bioactive Materials.* 2021;6:836-879. https://doi.org/10.1016/j.bioactmat.2020.09.013

[19] Masayoshi Y. Role of zinc in bone formation and bone resorption. *The Journal of Trace Elements in Experimental Medicine.* 1998:119-135. https://doi.org/10.1002/(SICI)1520-670X(1998)11:2/3%3C119::AID-JTRA5%3E3.0.CO;2-3

[20] Yingchao S, Irsalan C, Yadong W, YI-Xian Q, Linggian C, Yufeng Z et al. Zinc-Based Biomaterials for Regeneration and Therapy. *Trends in Biotechnology.* 2019;37:428-441. https://doi.org/10.1016%2Fj.tibtech.2018.10.009

[21] Li Z, Gu X, Lou S, Zheng Y. The development of binary Mg–Ca alloys for use as biodegradable materials within bone. Biomaterials. *Biomaterials*. 2008;29(10):1329-1344. https://doi.org/10.1016/j.biomaterials.2007.12.021

[22] Thomann M, Krause C, Bormann D, Von der Höh N, Windhagen H, Meyer- Lindenberg A. Comparison of the resorbable magnesium. alloys LAE442 und MgCa0. 8 concerning their mechanical properties, their progress of degradation and the bone- implant- contact after 12 months implantation duration in a rabbit model. *Materialwissenschaft Und Werkstofftechnik: Entwicklung, Fertigung, Prüfung, Eigenschaften Und Anwendungen Technischer Werkstoffe.* 2009;40(1- 2):82-87. https://doi.org/10.1002/mawe.200800412

[23] Cao JD, Kirkland NT, Laws KJ, Birbilis N, Ferry M. Ca–Mg–Zn bulk metallic glasses as bioresorbable metals. *Acta Biomaterialia.* 2012;8:2375-2383. https://doi.org/10.1016/j.actbio.2012.03.009

[24] Denkena B, Lucas A. Biocompatible magnesium alloys as absorbable implant materials–adjusted surface and subsurface properties by machining processes. *CIRP annals*. 2007;56(1):113-116. https://doi.org/10.1016/j.cirp.2007.05.029

[25] Bruno Z, Peter JU, Jörg FL. MgZnCa glasses without clinically observable hydrogen evolution for biodegradable implants. *Nature Materials.* 2009;8:887-891. https://doi.org/10.1038/nmat2542

[26] Möncke D, Topper B, Clare AG. Glass as a State of Matter—The “newer” Glass Families from Organic, Metallic, Ionic to Non-silicate Oxide and Non-oxide Glasses. *Reviews in Mineralogy and Geochemistry.* 2022;87:1039-1088. https://doi.org/10.2138/rmg.2022.87.23

[27] Weihong J, Paul KC. Orthopedic Implants. *Encyclopedia of Biomedical Engineering.* Chapel Hill, NC, US: Elsevier. 2019:225-239

[28] Mohd J, Abid H. Current status and challenges of Additive manufacturing in orthopaedics: An overview. *Journal of Clinical Orthopaedics and Trauma.* 2019;10:380-386. https://doi.org/10.1016/j.jcot.2018.05.008

[29] Orthopedic Design and Technology. Technology Revision: Changes in Implant Manufacturing. Accessed 23 May 2019. https://www.odtmag.com/issues/2019-05-24/view_features/technology-revision-changes-in-implant-manufacturing/

[30] Laura G, John Paul S, Teja G, Joo LO. Current trends in dental implants. *Journal of the Korean Association of Oral and Maxillofacial Surgeons. 2014;*40:50-60. https://doi.org/10.5125%2Fjkaoms.2014.40.2.50

[31] Ferracane JL, Giannobile WV. Novel Biomaterials and Technologies for the Dental, Oral, and Craniofacial Structures. *Journal of dental research. 2014;*93:1185-1186. https://doi.org/10.1177%2F0022034514556537

[32] Parida P, Mishra SC. UGC sponsored national workshop on innovative experiments in physics. *Biomater Med*. 2012;*9*(10).

[33] Mitsuo N. Recent metallic materials for biomedical applications. *Metallurgical and Materials Transactions A. 2002;33:477-486.* https://doi.org/10.1007/s11661-002-0109-2

[34] Raghavendra GM, Varaprasad K, Jayaramudu T. Biomaterials: Design, Development and Biomedical Applications. *Nanotechnology Applications for Tissue Engineering*. William Andrew. 2015:21-44. https://doi.org/10.1016/C2014-0-00006-8

[35] David T. Metastable structures in metallurgy. *Metallurgical Transactions B. 1981;12:*217–230. https://doi.org/10.1007/BF02654454

[36] Shandley R, Maheshwari S, Siddiquee AN, Mohammed SM, Chen D. Foaming of friction stir processed Al/MgCO3 precursor via flame heating. *Materials Research Express*. 2020;7(2):026515. https://doi.org/10.1088/2053-1591/ab6ef0

[37] Mishra RS, Mahoney MW, McFadden SX, Mara NA, Mukherjee AK. High strain rate superplasticity in a friction stir processed 7075 Al alloy. *Scripta Materialia.* 1999;42:163-168. https://doi.org/10.1016/S1359-6462(99)00329-2

[38] Sandeep R, Sachin M, Arshad Noor S, Manu S..Distribution of reinforcement particles in surface composite fabrication via friction stir processing: Suitable strategy. *Materials and Manufacturing Processes.* 2018;33:262-269. https://doi.org/10.1080/10426914.2017.1303147

[39] Ghasem Azimi R, Sajjad GY, Rahmatollah E, Mohsen S, Saeid L. Remanufacturing the AA5052 GTAW Welds Using Friction Stir Processing. *Metals.* 2021;11:749-761. https://doi.org/10.3390/met11050749

[40] Haichao W, Shengsun H, Zhijang W, Qifeng X. Arc characteristics and metal transfer modes in arcing-wire gas tungsten arc welding. *The International Journal of Advanced Manufacturing Technology. 2016;86:*925-933. https://doi.org/10.1007/s00170-015-8228-2

[41] Rad HR, Idris MH, Kadir MR, Farahany S. Microstructure analysis and corrosion behavior of biodegradable Mg–Ca implant alloys. *Materials & Design*. 2012;33:88-97. https://doi.org/10.1016/j.matdes.2011.06.057

[42] Sakiewicz P, Piotrowski K, Bajorek A, Młynarek K, Babilas R, Simka W. Surface modification of biomedical MgCa4. 5 and MgCa4. 5Gd0. 5 alloys by micro-arc oxidation. *Materials*. 2021;14(6):1360. https://doi.org/10.3390/ma14061360

[43] Makkar P, Sarkar SK, Padalhin AR, Moon BG, Lee YS, Lee BT. In vitro and in vivo assessment of biomedical Mg–Ca alloys for bone implant applications. *Journal of applied biomaterials & functional materials*. 2018;16(3):126-136. https://doi.org/10.1177%2F2280800017750359

[44] Wang X, Dong LH, Li JT, Li XL, Ma XL, Zheng YF. Microstructure, mechanical property and corrosion behavior of interpenetrating (HA+ β-TCP)/MgCa composite fabricated by suction casting. *Materials Science and Engineering: C*. 2013;33(7):4266-4273. https://doi.org/10.1016/j.msec.2013.06.018

[45] Cavaliere P, DE Marco PP. Friction stir processing of AM60B magnesium alloy sheets. *Materials Science and Engineering A. 2007;462:*393-397. https://doi.org/10.1016/j.msea.2006.04.150

[46] Liu DB, Huang Y, Prangnell PB. Microstructure and performance of a biodegradable Mg–1Ca–2Zn–1TCP composite fabricated by combined solidification and deformation processing. *Materials Letters*. 2012;82:7-9. https://doi.org/10.1016/j.matlet.2012.05.035

[47] Prosek T, Nazarov A, Bexell U, Thierry D, Serak J. Corrosion mechanism of model zinc–magnesium alloys in atmospheric conditions. *Corrosion Science*. 2008;50(8):2216-2231. https://doi.org/10.1016/j.corsci.2008.06.008