Type of contribution:
Editorial
Research Paper
Case Study
▶ Review Paper
Scientific Data
Report of Tech. Application

e-issn. 2798-5245

Mechanical Engineering for Society and Industry
Vol. 3, No. 3 (2023) pp 152-165
Special Issue on Technology Update 2023
https://doi.org/10.31603/mesi.10397

Development of magnesium biocomposites with hydroxyapatite or carbonate apatite reinforcement as implant candidates: A review

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This article contributes to:

Highlights:

- Mg-CAp and Mg-HAp biocomposites are promising biodegradable implants.
- The addition of CAp or HAp effectively mitigates Magnesium's high degradation rate.
- Insights into powder metallurgy's potential in synthesizing Mg-CO3Ap composites, along with the efficacy of coating methods in suppressing degradation rates, signify pivotal progress in developing durable implant materials for bone regeneration in medical contexts.

Abstract

Metal materials used as bone implants are not new today. In fact, almost 70% of implant materials are made of metal. Magnesium biocomposites with Carbonate Apatite or Hydroxyapatite reinforcements have promising potential as implants, one of the properties of these composites is biocompatible and bioactive to accelerate bone growth. There have been many studies on the development of Mg-CAp and Mg-HAp as biocomposite implant materials. Various methods of making these biocomposites have been carried out, such as sintering, microwave, coating, casting, and extrusion. From the fabrication process, observations were made regarding mechanical properties and chemical structure. The results show that CAp and HAp can suppress the corrosion rate of Magnesium, which is one of the weak properties that must be improved. Then it can increase the biological activity of Mg composites and has the ability of bone induction and bone conduction. In addition, the mechanical properties have increased in tensile, compression, and microhardness testing. However, so far, the research on Mg-HAp and Mg-CAp has only been limited to animal testing and has not been applied to humans. So, the potential for development and research is still open actually to be implemented in the orthopedic field.

Keywords: Biomaterial, Magnesium, Hydroxyapatite, Carbonate Apatite, Implant

Article info
Submitted: 2023-10-18
Revised: 2023-11-27
Accepted: 2023-11-23

Publisher
Universitas Muhammadiyah Magelang

1. Introduction

The field of biomaterial science has made significant contributions to the rapidly developing surgical and medical technology in recent decades. Biomaterials are processed materials that are biocompatible when implanted into the human body, they can replace and support the functions of bodily tissues and organs effectively [1]–[3]. Biomaterials should possess the ability to support cell attachment, promote subsequent proliferation or differentiation and when implanted into the

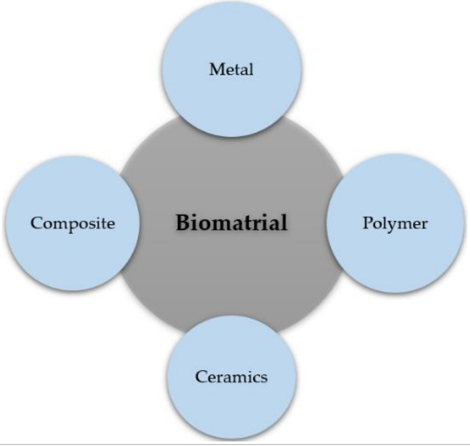

Figure 1. Types of biomatrials

Figure 2. Human bone implants

body be able to program host immune cells. This represents a promising potential for clinical treatments [4]. An implant biomaterial is a prototype attached to the body to replace organ function, which can be composed of one or several constituent biomaterials [5], [6]. The categories of biomaterials as implants are divided into four, namely metal, polymer, ceramic, and composite biomaterials (**Figure 1**). Each type of biomaterial has its advantages and disadvantages according to the needs of the body tissue [7]. The advantages and disadvantages of these biomaterials is presented in **Table 1**.

Metal as a bone implant has long been used as exemplified in **Figure 2** and almost 70% of implant materials are made of metal [11]. Basically, there are two types of implants: non-biodegradable and biodegradable implants. Non-biodegradable implants require post-healing surgery to remove them. For this reason, non-biodegradable implants are no longer being developed today. As a replacement, biomaterial-based implants that can degrade along with organ healing have become the focus of research in the last decade [12].

Metals that are often used as constituents of implants are stainless steel, titanium (Ti), cobalt-chromium alloy (Co-Cr alloy), magnesium (Mg), iron (Fe), and Fe-Mg alloy [13]. Metal biomaterials are widely used in orthopedic and dental applications, because they have better mechanical properties than other materials [14], [15]. Metal materials have advantages compared to other materials, such as tensile strength, modulus of elasticity, resistance to corrosion, easy to form and easy to design, which is why metals are widely used [13], [16], [17]. However, metal materials have several disadvantages such as interference with X-rays or MRI when monitoring patient recovery [[12], [18]. **Table 2** shows the advantages and disadvantages of each metal as an implant.

Table 1. Advantages and disadvantages of various implantable biomaterials

Material	Advantage	Disadvantage	Application	Refs.
Metal	Strong and resilient	Non-bioactive	Orthopedic implants, dental implants, artificial joints, heart rings (stents)	[8], [9]
Polymer	Bioactive and inert	Brittle	Orthopedic and dental implants	[10]
Ceramics	Bioactive and aesthetic	Less potent	Implanted artificial joint socket and sutured blood vessel graft	[9]
Composite	Created specifically	It is difficult to make	Orthopedic and dental implants	[10]

Table 2. Advantages and disadvantages of metal implant materials

Material	Advantage	Disadvantage	Refs.
Stainless steel	High wear resistance	High modulus, Low corrosion resistance, Allergic reactions	[14], [20]
Titanium	High biocompatibility, Low Young's modulus, Excellent corrosion resistance, Low density	Toxic due to the presence of aluminum. Highly susceptible to wear and corrosion.	[20]
Cobalt-Cromium	High wear resistance	High modulus Allergic reactions	[14], [20]
Magnesium	Biocompatible, Bio-degradable, Low Young's modulus	Low corrosion resistance	[12], [20]

In its application, metal is in direct contact with body tissues, so it must be biocompatible [19]. In addition, the main requirements for metallic implants are performance and safety in use, including good mechanical and physical properties such as tensile strength, stiffness, and fatigue resistance [21]–[24]. Metal implants are also required to be non-magnetic and have a high mass density [24]. Most implants in use are subjected to both static and dynamic mechanical loads that require an optimal combination of strength and ductility [23]. **Table 3** shows the comparative values of tensile strength, yield strength, and Young's modulus of implant metal materials.

Table 3. Comparison of tensile strength, yield strength and modulus of elasticity of metal implant material

Materials	Tensile strength (MPa)	Yield strength (MPa)	Elastic modulus (GPa)	Refs.
Stainless steel	490–1350	190–690	200–210	[14]
Titanium	690–1100	585–1060	55–110	[14]
Cobalt-Cromium	1180	973	220–234	[25], [26]
Magnesium	160	90	45	[16]

Until recently, the most widely used implant material for medical implants, especially in orthopedics and dentistry, was titanium. Titanium (Ti) has the properties of low density, high strength and corrosion resistance. However, titanium is not able to produce good osseointegration with the bone surface so modifications to the implant surface are needed. Titanium is a bioinert material, so it requires bioactive coatings to trigger osseointegration and reduce the corrosion rate [14].

Meanwhile, magnesium has good potential as an implant candidate, is non-toxic and biocompatible, its properties are needed in the body and helps bone regeneration. While in the body, magnesium undergoes degradation and solubility so that it can be excreted from the body through metabolism without harming the body or biodegradation [16]. However, with its advantages, magnesium is a corrosive metal so it needs to be combined with other materials to resist the rate of corrosion and also has bioactive properties to accelerate bone regeneration. These materials are Hydroxyapatite and Carbonate Apatite, both of which have good bioactive properties and are able to suppress the corrosion rate of magnesium [12], [18]. Therefore, our present article specifically discusses the development of magnesium biocomposites with ceramic reinforcements, both Hydroxyapatite and Carbonate Apatite. Furthermore, the main focus of this study is on the Mg/HAp and Mg/CAp biocomposite fabrication methods and the properties of the resulting biocomposite development materials.

2. Properties of Each Composite Forming Element

2.1. Magnesium (Mg)

Among the various metal materials used as implants, magnesium (Mg) has the potential to be used as a biocomposite because of its good mechanical properties and elastic modulus similar to human cancellous and cortical bone (41 to 45 GPa). In addition, magnesium is also an important element for bone growth and its degradation products are non-toxic to the body with a density value of 1.74-2.0 g/cm^3 [27]. Magnesium even has a high toxicity limit in the body, specifically, at a dosage of 700 mg/day, magnesium serves as an enzyme activator and a regulator of proteins. Additionally, magnesium plays a crucial role in the bone growth and formation process [28], [29].

Magnesium is a macronutrient that is a metabolic product obtained from daily dietary intake. The World Health Organization (WHO) recommends a daily magnesium intake of 280-300 mg/day for adults, 250 mg/day for children, and 80 mg/day for infants. Magnesium plays a pivotal part in vitality digestion system and directs crucial capacities of organs such as the heart, muscles, nerves, bones, and kidneys [30]. Moreover, magnesium plays a key role in preserving bone health and strength. This function is due to the body's requirement for magnesium to form new bone cells and maintain bone density. Numerous studies have shown that meeting the daily magnesium requirement can reduce the risk of osteoporosis, bone fractures, and other bone damage [31], [32].

Magnesium stands as a vital mineral that aids various physiological functions within the human body. It contributes to stabilizing the structure of proteins, nucleic acids, and cell membranes, while also promoting specific catalytic or structural activities among proteins, enzymes, or ribozymes. Additionally, magnesium boasts non-toxic and non-irritating properties. Its presence within cells and bones supports osteoinductivity. Consequently, owing to these attributes, magnesium naturally aligns with the body's biocompatibility [33]. Despite these benefits, magnesium also presents certain limitations, including rapid degradation, limited strength, and toughness, displaying a yield strength of 30 MPa, an ultimate tensile strength of 100 MPa, and a strain ε of 7% [34]. Changes are required for Mg to be created as a fabric for implantable biocomposites.

Corrosion affects all metals, with its rate influenced by environmental acidity, ion concentration and type, protein absorption capacity, and the biochemical activity within the neighboring tissue. The magnesium erosion handle is defined by Eqs. (1) to (3) [30].

$$M \rightarrow M^{n+} + ne^- \qquad \text{Anodic reaction} \qquad (1)$$

$$2H_2O + 2e^- \rightarrow H_2 + 2OH^- \qquad \text{Cathodic reaction} \qquad (2)$$

$$M^{n+} + nOH^- \rightarrow M(OH)_n \qquad \text{Final reaction} \qquad (3)$$

The oxide layer acts as a barrier to prevent migration of ions to the metal surface. However, chloride ions from the human tissue environment can break down, corrode and dissolve metals, as formulated in Eq. (4) [30].

$$Mg(OH)_2 + 2Cl^- \rightarrow MgCl_2 + 2OH^- \qquad (4)$$

2.2. Hydroxyapatit (HAp)

Hydroxyapatite (HAp) is a ceramic that has wide applications in bone tissue engineering and bone regeneration. HAp is a material whose structure is similar to human hard tissue. HAp material can be used as a bone replacement implant material or as an artificial bone replacement material [35], [36]. The use of HAp as a synthetic bone implantation material has been widely used. One application is as a metal coating material that will be implanted into the body as a contact material for artificial components of human tissue. It has been proven that biocomposites with the addition of HA have good material properties and are not harmful to the body [37], [38].

Some of the specific properties that HAp possesses include being non-toxic and biocompatible which can be used with bone tissue. HAp is not only a biocompatible, osteoconductive, non-toxic, and nonimmunogenic agent but also bioactive or can form direct chemical bonds with living tissues. HAp fiber materials, which consist entirely of HAp fibers, have demonstrated their ability to support the proliferation and differentiation of osteogenic cells making them effective scaffolds for bone regeneration [39], [40].

Research on biocomposites with the addition of HAp in metals shows an increase in modulus and compressive strength compared to pure metals, as well as improved cytocompatibility. The addition of HA with magnesium can also improve their mechanical properties, including density, hardness, elastic modulus, reduction of corrosion rate, and thermal stability. Later, biocomposites composed of HAp showed phase stability, mechanical strength, and biocompatibility [41]–[44]. Linsheng et al. [45] conducted research on the manufacture of Mg-HAp biocomposites using the electrophoretic deposition method, from the study showed that magnesium matrix HAp biological composite materials can improve calcium deposition and induce the formation of bone-like apatite without cytotoxicity, good biocompatibility and bioactivity.

2.3. Carbonate Apatite (CAp)

Bone apatite is not Hydroxyapatite but Carbonate Apatite (CAp), which contains 6-9% by weight of carbonate in the apatite structure. Carbonate Apatite has bone-like properties compared to Hydroxyapatite. Pure chemical mimicry of bones made from CAp was recently achieved through a precipitation dissolution reaction in a solution [46]. CAp powder can be easily prepared by mixing Ca^{2+}, $PO_4{}^{3-}$, dan $CO_3{}^{2-}$ in an aqueous solution. However, all powders, including CAp powder and HAp powder, are recognized as foreign substances. These elements correspond to those found in bones, as shown in **Table 4**.

Carbonate Apatite (CO_3Ap, CAp) is a type of bioceramic material based on calcium phosphate, like Hydroxyapatite (HAp). In addition, CAp has similar properties to HAp, such as biocompatibility, bioactivity, and bioresorption. However, CAp is considered more potential for bone healing as it is more easily absorbed (osteoconductivity) [47]. The studies that have been conducted show that in

Table 4. Components of the adult human hard tissue network [46]

Elemen	Enamel	Dentine	Bone
Ca^{2+}	36.5	35.1	34.8
PO_4 as P	17.7	16.9	15.2
$CO_3\ 2^-$	3.5	5.6	7.4
Na^+	0.5	0.6	0.9
Mg^{2+}	0.44	1.23	0.72
Cl^-	0.30	0.01	0.13
$P_2O_7^{4-}$	0.022	0.10	0.07
K^+	0.08	0.05	0.03
F^-	0.01	0.06	0.03
Total Inorganic	97	70	65
Absorbed H_2O	1.5	10	10

the formation of new bone tissue with CAp, there is no formation of fibrotic tissue. In addition, CAp material can be absorbed and completely replaced by new bone tissue within 1-1.5 years [48].

Carbonate Apatite can bind bone structures effectively and stimulate the formation of hard tissue. Research conducted by Tjahajawati et al.[49] demonstrates that CAp implanted in the skulls of rats almost completely transformed into new bone after 24 weeks. This provides evidence that CAp has good bioactive properties. CAp can be absorbed by osteoclasts and promote osteoblast differentiation. In a study conducted by Ishikawa & Hayashi, CAp demonstrated significantly higher osteoconductivity compared to HAp. Subsequently, granular CAp has been approved for clinical use in Japan in 2017 [46], [50]. However, CAp begins to lose its CO_3 content at around 400 °C and decomposes at sintering temperatures. In the 1970s, powder HAp, which has a composition similar to bone apatite but lacks carbonate, was discovered in Japan. The discovered HAp exhibits osteoconductivity, a property necessary for direct bone bonding when implanted as an implant [50].

3. Mg-HAp and Mg-CAp Biocomposites

Because of the extensive research done on magnesium as a potential biodegradable metal implant, Hydroxyapatite or Carbonate Apatite shows promising properties as a bone substitute. Therefore, Magnesium-Hydroxiapatite or Carbonate Apatite alloys are potentially promising orthopedic implant candidates. In natural bone apatite, there exists a natural blend of magnesium and carbonate, comprising approximately 4-7.5% by weight carbonate and 0.5-0.6% by weight magnesium within its crystal structure, characterized by a plate-like morphology [30]. However, combining the two materials is not easy.

There are many ways to fabricate a biocomposite with a metal reinforcement matrix. The fabrication method can affect the structure of the composition and consolidation between the particles that are composed. Some fabrication methods in the studies that have been done are cystitis, coating, sintering, combustion, microwave, and extrusion. Shows some of the studies that have been conducted on Mg-HAp and Mg-CAp biocomposites with various fabrication methods and the resulting material properties.

Agha [51] conducted research on the effect of adding calcium phosphate to magnesium to observe the degradation rate and osteoblasts of the composites formed. The study used the composition of pure Mg material by Magnesium Innovation Center with the addition of calcium phosphate. The fabrication method by casting. Initially, pure Mg was melted and then maintained at 720 °C. Preheated calcium phosphate was introduced while stirring continuously for 15 minutes. This molten mixture was poured into a preheated permanent steel mold (550 °C) using boron nitride (BN) as a mold release agent. Subsequent observations showed that, based on our findings, bicarbonate plays an important role in the formation of magnesium carbonate, and that osteoblasts contribute to changes in chemical composition by promoting apatite precipitation. The addition of calcium phosphate inhibits the Mg degradation or corrosion rate.

Iafisco et al. [52] examined the potential of magnesium-carbonate Apatite as an embed. In this ponder, the bioactivity of apatite synthesized in vitro illustrated its potential utilization to create biomedical gadgets with anti-osteoporosis usefulness and appeared the quickest corruption energy. The amalgam utilized was biomimetic nanocrystalline apatite substituted with Mg, CO_3 and the characterizations performed were assessment of chemical-physical properties, morphology, degradation rate, and in vitro bioactivities. The method of making the samples was by synthesizing with 0%-12% CAp. In this study, the focus was on creating nanocrystalline apatite co-substituted with Mg CO_3. The findings suggested that including 12 wt% CAp represented the stability threshold for the Mg-CO_3 apatite structure. This composition exhibited outstanding bioactive properties and effectively curbed the degradation rate of magnesium.

Rahyussalim et al. [53] conducted perceptions related to the potential of Carbonate Apatite as an elective fabric for bone substitutes. The audit article highlights Carbonate Apatite's defenselessness to corruption in a powerless acidic environment and osteoclast resorption. It's famous for being osteoconductive, cultivating bone tissue arrangement without fibrotic tissue. Carbonate Apatite offers a comparable carbon substance to human bone, is profoundly absorbable, and can be substituted by bone tissue inciting an osteoblast reaction. Subsequently, it's considered an elective to manufactured bone joins, although its clinical trials have advanced as it were to creature testing stages. Carbonate Apatite, when in powder shape, leads to precious stone arrangement due to provocative responses, requiring its handling into pieces through high-temperature sintering. Past inquiries about demonstrates that carbonate examples containing 12% carbonate substance can be sintered at lower temperatures extending from 600°C to 750°C.

Rahyussalim et al. [54] investigated the blend, auxiliary qualities, debasement inclinations, and biocompatibility of the Magnesium-Carbonate Apatite (Mg-CO3Ap) Composite, considering its potential as a base fabric for biodegradable orthopedic inserts. The ponder utilized the powder metallurgy strategy, including the dry mixing of Mg powder and CO3Ap powder. Different composite examples were made, counting unadulterated Mg, Mg-5CA, Mg-10CA, and Mg-15CA. The blending preparation happened at 200 RPM employing a planetary ball process. Vacuum drying at 200°C for 12 hours was conducted to play down water substance and anticipate the oxidation response. In this way, the powders were compressed at 265 MPa and 350°C utilizing water-powered stamping inside a suppress heater to create miniplate's for biomechanical tests and barrel squares for biocompatibility and erosion evaluations. The discoveries demonstrated that the inclusion of the CAp rate drove a lessening within the composite's erosion rate. For occasion, the erosion rate for Mg-15% CAp was measured at 5.7608 mm per year, whereas Mg-5% CAp showed the next rate at 20.3071 mm per year. Furthermore, Mg with a 10% CAp substance illustrated favorable biocompatibility, even though its biomechanical properties and debasement rate fell underneath the required guidelines.

Sader et al. [55] explored how the inclusion of magnesium and carbonate within the apatite lattice affects the physico-chemical characteristics of biomaterials. It evaluated the properties and dissolution tendencies of unsintered magnesium and carbonate-substituted apatite (MCAp) with consistent Mg/Ca molar ratios (0.03) and varying C/P ratios [A (3Mg/0C); B (3Mg/1C); C (3Mg/3C); and D (3Mg/5C)] synthesized using a water deposition method. The (Ca+Mg)/P molar ratio increased with carbonate incorporation, while magnesium content did not contribute to this ratio. The integration of magnesium into the apatite lattice directly correlated with the Mg/Ca ratio. Even a limited inclusion of magnesium disrupted the apatite lattice, reducing its crystallinity and subsequently elevating its dissolution rate. The study highlighted that heightened carbonate content within the sample resulted in smaller crystallite size and increased calcium release into the medium. In an acidic buffer, the MCAp with higher CO2 content exhibited greater calcium release over the same duration. This occurrence was attributed to carbonate substitution within the apatite structure, creating a more soluble biomaterial that hastened degradation within the body.

Hiromoto et al. [56] focused on carbonate apatite coatings for biodegradable magnesium alloys. Rods, measuring 16 mm in diameter and 1-2 mm thick, were produced via rod extrusion using Magnesium Electron, UK. The material compositions examined included HAp-WE43, (CAp0.4M, CAp1.1M, and CAp1.9M) WE43. Coating was achieved using (NaHCO3). The findings indicated that as the carbonate content increased in the samples, there was a reduction in crystallite size and an elevation in calcium release into the surrounding medium. The developed CAp coating displayed significant promise as a bioabsorbable coating and a means of controlling corrosion.

Setyadi et al. [57] examined the creation of magnesium-carbonate Apatite for orthopedic implants using traditional sintering and spark plasma sintering techniques. They used commercial Mg powder and local CA powder (size ±74 µm) as the raw materials. Mixing with a planetary ball mill for 5 hours at 200 rpm resulted in four different compositions of Mg-nCA, where n = 0, 5, 10, and 15% wt CA. For the conventional sintering process, warm compaction (WC) involved heating the powder in a mold cavity (10 mm diameter) to 330 °C (heating rate 10 °C per min), pressing it at 350 MPa using a punching tool. Within the Start Plasma Sintering (SPS) preparation, the Mg-nCA powder was set in a graphite shape depth (20 mm distance across, 11 mm tallness) and warmed up to 350 °C, at that point raised to 400 °C (sintered temperature) for 15 minutes at a punch weight of 12.5 kN. Comes appears that the SPS preparation essentially progressed Mg-CA characteristics compared to CS. Relative thickness expanded by around 0.7-2.4%, hardness by around 2-13%, and erosion rate diminished by roughly 32-49% after the SPS handle compared to the beginning state sometime recently sintering. Also, the SPS structure showed a lower basic oxygen substance compared to the CS structure. In general, the SPS strategy demonstrated more effectiveness in creating Mg-CA powder-based composites than the CS handle.

Adzila et al. [58] explored the impact of sintering conditions on Magnesium-Hydroxyapatite (MgHA) synthesized via a mechanochemical method, specifically analyzing temperatures ranging from 1000°C to 1300°C. The varying alloys included Mg-free HA, 1%, 3%, 5%, 7%, and 9% MgHA. Observations revealed that increasing the temperature from 1200°C to 1250°C augmented the density of HA. Moreover, there was a consistent rise in the average hardness of HA when sintered between 1000 °C and 1300 °C. The highest hardness recorded was with 3% MgHA, reaching 5.42 GPa when sintered at 1200^{o}C. However, the incorporation of 9% MgHA led to a deterioration in the HA properties, manifesting as a hardness lower than 2.00 GPa. The findings strongly indicated that introducing magnesium (Mg) into Hydroxyapatite (HA) powder significantly influenced its properties, impacting factors like phase stability, bulk density, and hardness.

Ratna Sunil et al. [59] focused on exploring the processing and mechanical behavior of degradable structured magnesium-Hydroxyapatite (Mg-HA) implants. Various composite compositions of 8%, 10%, and 15% by weight of Mg-HA were utilized. These powders underwent milling, consolidation, and sintering in a graphite mold under a uniaxial pressure of 50 MPa for 10 minutes in a vacuum at 450°C, using a spark plasma sintering (SPS) system. Notably, the ball milling process revealed that HA particles became coated after approximately 20 hours of stirring. X-ray diffraction (XRD) analysis of the powder phases confirmed the presence of HA, MgO, and Mg after sintering. Corrosion analysis indicated that the 10% HA alloy exhibited the highest corrosion resistance along with the maximum Vickers hardness. Moreover, the Mg-8%HA composition demonstrated favorable Young's modulus and crack resistance. Conclusively, the study suggested that the Mg-8%HA and Mg-10%HA compositions displayed promise for degradable orthopedic implant applications. These compositions showcased improved corrosion resistance and superior mechanical properties, making them potential candidates for such biomedical applications.

Gupta et al. [60] investigated characterizing a biodegradable composite metal lattice of Mg AZ31/HA employing a quick microwave sintering strategy. They utilized magnesium combination (AZ31) and Hydroxyapatite powder in shifting compositions of 0, 10, 15, and 20% by weight. The think about pointed to evaluate the physical, microstructural, mechanical, and biodegradation properties of the created composites. The AZ31 powder from Nextgen Steel & Amalgams, India, with molecule size of 40 µm, in conjunction with Hydroxyapatite from Aldrich Chemical Company Inc., USA, were utilized. The powder blend experienced compaction into green pellets (Ø13 mm x 3 mm) through inactive pressure driven weight set at 450 MPa. XRD examination demonstrated that the incorporation of HA powder particles driven to decreased thickness and expanded microhardness within the composite materials. Among the compositions, AZ31-15HA displayed predominant erosion resistance and negligible relative weight misfortune amid a 24-hour inundation test. Taking after this test, XRD investigation of the AZ31-15HA sintered tests uncovered the nearness of unused phases such as Mg(OH)2 and Ca(OH)2. These recently shaped stages were credited to the improvement of erosion resistance within the fabric.

Kaygili et al. [61] investigated the characterization of Magnesium-Hydroxyapatite combinations synthesized by the combustion strategy. In his investigation, Kaygili utilized HAp tests with distinctive sums of Mg 1.2% and 2.4% with a blend temperature of 600oC. Whereas the diminish of gem estimate, crystallinity, stretch, and anisotropic vitality thickness values were watched. The ponder gives data that the stage composition is impacted by the Mg substance, i.e. the number of HAp stages diminishes with expanding sums of Mg. Meanwhile, Xiong et al. [62] studied characterizing biomedical Hydroxyapatite /magnesium (HAp/Mg) composites produced via powder metallurgy involving microwave processing. Mg powder and HAp powder underwent a 4-hour ball milling process. The HAp substance within the blend was set at 5%, 10%, and 15% by weight, separately. The blend was cold squeezed in a steel barrel from beneath a weight of 50 MPa. The coming about green compact was cemented by sintering at 500°C for 10 minutes in an argon environment employing an NJZ4-2 microwave heater, taken after by cooling to room temperature inside the heater. The discoveries show that the HAp/Mg composites showed improved mechanical properties, and counting made strides in flexural quality and compressive quality compared to unadulterated Mg. Particularly, the flexural quality of Mg-10HA was measured at 191.4 MPa, whereas unadulterated Mg displayed 132.7 MPa. Additionally, the compressive quality of Mg-10HA comes to 200 MPa, outperforming the 117 MPa displayed by unadulterated Mg. In addition, the HAp/Mg composites illustrated predominant cytocompatibility and bioactivity in comparison to unadulterated Mg, highlighting their potential for biomedical applications.

Bao et al. [63] explored the deposition of magnesium-substituted Hydroxyapatite coatings onto magnesium alloy surfaces intended for biomedical use. Sol-gel and dip-coating technologies were employed in this investigation. A Ca-Mg mixture was stirred for 2 hours at 60 °C until a homogenous and transparent mixture was achieved. Coating procedures involved immersing magnesium substrates into the prepared sol, followed by drying at 150 °C for 10 minutes. This pre-coating and drying sequence was repeated four times. Subsequently, the dried coatings underwent calcination for 2 hours in a conventional furnace at 500 °C. The discoveries highlighted that the consolidation of magnesium-substituted Hydroxyapatite coatings outstandingly improved erosion resistance. Magnesium, being one of the foremost electrochemically dynamic metals, is inclined to erosion. The Hydroxyapatite coating acted as a protective layer, effectively preventing corrosion of the magnesium alloys. Furthermore, the introduction of magnesium within the Hydroxyapatite coating led to improved in vitro bioactivity. This enhancement promoted the formation of new apatite layers on the coating surface when exposed to simulated body fluids. Additionally, the study noted that the coatings exhibited a solid nature, further affirming their durability and stability.

Hariowibowo et al. [64] examined the impact of microwave irradiation's intensity and duration on synthesizing MgHA crystals. To make the MgHA powder, diammonium hydrogen phosphate, magnesium hydroxide, and calcium hydroxide were utilized as sources for phosphate, magnesium, and calcium, separately. The blend included continuously including 0.6 M watery phosphate arrangement and 0.2 M fluid magnesium arrangement into a 1 M watery calcium arrangement while continuously releasing and mixing to make a MgHA arrangement. This solution underwent microwave irradiation at varying power levels (450 and 720 W) and for different durations (ranging from 2 to 10 minutes). Following irradiation, filtration paper was used to filter the solution, and the resulting samples were oven-dried to a consistent mass. The dried samples were finely ground for further analysis and characterization. The MgHA powder generated through microwave irradiation exhibited rod-shaped particles measuring between 72 and 97 nm. X-ray diffraction (XRD) analysis unveiled that elevating the irradiation power and duration correlated with a reduction in lattice parameters, crystal size, and crystallinity index. Observations via scanning electron microscope (SEM) revealed that the presence of Mg2+ in HA led to particle agglomeration due to the small crystallite size and the amorphous phase of MgHA. **Table 5** recapitulation of the methods employed in previous studies.

Concurring with the ponders that have been conducted, the manufacture of Mg-HAp and Mg-CAp biocomposites is still for the most part by coating, blending, sintering, and combustion strategies. These methods are often used because of the ease of the research process, but methods such as extrusion have not been widely practiced because of the more complicated fabrication process. According to Setyadi et al. [34] the extrusion method can increase the consolidation between alloy particles, the goal is for the alloy to have a much better hardness value and reduce its degradation rate as a biodegradable implant material. The availability of equipment and much more complex methods such as hot extrusion is still a constraining factor. The hot extrusion method requires more complex equipment. It is necessary for the powder metallurgy fabrication process, intending to increase the bond between materials by strengthening deformation which is believed to be able to increase mechanical strength and suppress the rate of magnesium degradation. However, so far the coating, sintering, and casting fabrication methods have shown that Mg-CAp and Mg-HAp biocomposites can meet the implant characteristics required today.

The production cost of a biocomposite implant predominantly differs depending on the various types, and fabrication methods, as the equipment to be used is different. The raw materials used are also a determining factor. However, this time we ignore the production equipment, because the research was carried out in existing laboratories and the studies that have been carried out do not explain the fabrication costs. The various studies conducted, almost all used Magnesium products that have been commercialized. Several studies used Mg Merck with a price range of 245-264 USD /kg. Then the Carbonate Apatite or Hydroxiapatit reinforcement is capable of self-production with existing raw materials and even with waste or natural resources, such as marine biota, animal bones, limestone, and so on containing calcium carbonate (CaCO3) with a synthesis process. Details of production costs cannot yet be calculated with certainty, but related raw material costs can be determined by several references that mention the name of the Magnesium product and the HAp or CAp production process used in the study.

Table 5.
List of fabrication methods for Mg-HAp and Mg-CAp

Materials	Methods	Variations	Results	Refs.
Mg-HAp	Electrophoretic Deposition Experiment (Coating)	Mg-HAp	1) The composite material had no inflammatory reaction, or cytotoxicity but excellent biocompatibility. 2) Composite material could promote deposition of calcium, and induce bone-like apatite with excellent bioactivity	[45]
Mg, Ag dan Gd	Coating	Mg, Mg-2Ag and Mg-10Gd	Bicarbonate plays an important role in the formation of magnesium carbonate, and the osteoblasts contribute to the alteration of the chemical composition by enforcing apatite precipitations.	[51]
Mg-CO3-Sr	Synthesis	MCAp, MSCAp1, MSCAp2 and MSCAp3	Incorporation of 12 wt.% of CAp destabilized the crystal structure of Mg-CO3-apatite and all apatites exhibited in vitro bioactivity	[52]
Mg-CAp	Synthesis	100 : 0 (pure Mg), 95 : 5 (Mg-5CA), 90 : 10 (Mg-10CA), and 85 : 15 (Mg-15CA).	Mg-CO3Ap composite is a potential biodegradable implant material. But, interparticle consolidation needs improvement for better properties.	[53]
Mg-CAp	Synthesis by Aqueous Precipitation	(3Mg/0C/1P); (3Mg/1C/1P); (3Mg/3C/1P) and (3Mg/5C/1P)	The carbonate content in the samples resulted in a decrease in crystallite size and an increase in the release of calcium to the medium.	[55]
Mg-HAp-CAp	Coating	WE43 alloy diameter of 16 mm and a thickness of 1–2 mm.	The carbonate content in the samples resulted in a decrease in crystallite size and an increase in the release of calcium to the medium	[56]
Mg-CA	Spark Plasma Sintering	Mg-0CA Mg-5CA Mg-10CA Mg-15CA	1) The SPS structure has a lower oxygen content compared to the CS structure. 2) The sintering process with SPS is considered effective.	[57]
Mg-HA	Synthesized by Mechanochemical	Mg free HA, 1%MgHA 3% Mg HA, 5%MgHA, 7%MgHA and 9%MgHA	The incorporation of magnesium (Mg) into Hydroxyapatite (HA) powder influenced its properties, such as phase stability, bulk density, and hardness.	[58]
Mg-HA	Spark Plasma Sintering	M-Mg, Mg-8HA, Mg-10HA and Mg-15HA	The Mg-8%Ha and Mg-10%Ha compositions hold promise for use in degradable orthopedic implant applications due to their superior corrosion resistance and mechanical properties.	[59]
Mg-HA	Rapid Microwive Sintering	AZ31-0HA, AZ31-10HA, AZ31-15HA and AZ31-20HA	1) Adding HA powder particles decreases density and enhances microhardness. 2) AZ31-15HA demonstrates the highest corrosion resistance and a relatively low relative weight loss in the immersion test for 24 hours.	[60]
Mg-HA	Combusion	1.2MgHAp and 2.4MgHAp	The phase composition is affected by the Mg content. Specifically, the amount of HAp phase decreases with an increasing amount of Mg.	[61]
Mg-HAp	Microwive Sintering	Mg, HAp-5/Mg, HAp-10/Mg, and HAp-15/Mg	1) The HAp/Mg composite exhibits superior mechanical properties (flexural and compressive strength) compared to pure Mg. 2) The HAp/Mg composite exhibits superior cytocompatibility and bioactivity as compared to pure Mg.	[62]
Mg-HA	Coating by Sol Gel	0,5 and 1,5 HA coating on Mg	1) Magnesium-substituted Hydroxyapatite coatings improve corrosion resistance. 2) Incorporation of magnesium in the Hydroxyapatite coating results in better in vitro bioactivity	[63]
Mg-HA	Synthesis via Microwave	Mg-HA	Substitution of Mg causes the particles to agglomerate, which is more pronounced with higher irradiation power and longer irradiation time.	[64]

4. Conclusion

The references studied in our current article highlight several significant findings regarding the potency and potency of Mg-CAp and Mg-HAp biocomposites as viable biodegradable implants. These materials exhibit commendable biocompatible, bioabsorbable, and biodegradable properties, thus positioning them as promising candidates for medical implant applications. Additionally, the addition of CAp or HAp effectively mitigates the very high degradation rate of Magnesium, thereby presenting a viable solution to improve its stability. The synthesis of Mg-CO3Ap composite via powder metallurgy demonstrated its potential as a biodegradable orthopedic implant material, although it requires improvements in particle consolidation to optimize its properties. In particular, the duration of ball milling significantly influenced the resulting composite, with the 5 hours process showing the least toxic content and the most homogeneous mixture without agglomeration. Although conventional sintering methods fail to produce high mechanical property values for biocomposites, powder metallurgy is emerging as a promising technique to improve particle bonding. In addition, the coating method, which is widely used in Mg-HAp and Mg-CAp research, effectively suppresses the degradation rate and increases the microhardness, thereby demonstrating its efficacy in improving the durability of the material. Meanwhile, the casting method demonstrated the ability to produce Mg-CAp or Mg-HAp with commendable mechanical properties, thereby providing another opportunity for potential implant materials. It is important to note that although these advances have progressed to animal experiments, their direct application to the human body remains unexplored. Nevertheless, this comprehensive review provides important insights for the development of biomaterials, especially in bone regeneration in medical applications, marking a valuable contribution in this field.

Authors' Declaration

Authors' contributions and responsibilities - The authors made substantial contributions to the conception and design of the study.

Funding – No information about funding from the authors.

Availability of data and materials - All data are available from the authors.

Competing interests - The authors declare no competing interest.

Additional information – No additional information from the authors.

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