RESEARCH PAPER

Metal-Organic Framework-Based Surface Engineering of Biomedical Magnesium Alloys: Types, Electrochemical Behaviour, Corrosion Protection Mechanisms, Biomedical Applications, and Future Challenges

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Abstract
The biodegradable magnesium (Mg) alloys are found to have some of the most desirable mechanical properties, biodegradability and biological functions, which are beneficial for temporary orthopedic and cardiovascular implants. However, their extremely rapid corrosion rates in physiological environments, hydrogen evolution, localized alkalization, and loss of mechanical integrity early on are great challenges for their clinical translation. Metal-organic frameworks (MOFs) have been the focus of much research in recent years as multifunctional platforms for surface modification to overcome these limitations. The MOF materials offer unique opportunities to enhance their corrosion resistance, bioactivity, antibacterial property, and therapeutic function, because of their highly porous nature, tunable chemical compositions, controlled ion release, and drug loading abilities.
This systematic review provides a detailed review of coating of magnesium alloys using MOFs for biomedical applications with the emphasis on MOF of elements such as Zn, Fe, Co, Cu, Zr, Ti, and Ni. In the review, 180 peer-reviewed publications from 2016 to 2026 were analysed and discussed, which focused on the structural characteristics, preparation methods, electrochemical properties, tribological properties and biomedical applications of MOF-MgAlloys. The Zn-based MOFs are particularly noted for their outstanding corrosion protection properties, osteo-inductive properties, and anti-bacterial activities. The electrochemical mechanisms of corrosion protection are analyzed and discussed, such as: physical barrier effect, pore blocking, controlled ion release, self-healing and hybrid plasma electrolytic oxidation (PEO)-MOF protection. In addition, the review provides a summary of the recent advances of orthopedic implants, cardiovascular stents, drug delivery systems, as well as antibacterial implants and tissue engineering scaffolds.
Although tremendous strides have been made, problems of coating stability over time, lack of delamination, defect formation, cytotoxicity, manufacturing scalability, and insufficient clinical evidence remain. Design of multifunctional MOFs, standardization of electrochemical testing methods, long-term in vivo studies, tribocorrosion testing and artificial intelligence design of MOFs are future research opportunities to be explored. In general, MOF functionalized magnesium alloys could be considered as one of the most rapidly developing and promising classes of next generation biodegradable biomaterials for advanced biomedical applications.
Keywords: Magnesium alloys; Metal-organic frameworks (MOFs); Biodegradable implants; ZIF-8; Zn-MOF; Corrosion protection
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1. Introduction

1.1 Magnesium Alloys as Biodegradable Biomaterials

The alloys of Magnesium (Mg) and their alloys are a unique combination of mechanical compatibility, biodegradability and biological functionality which is the reason for these alloys gaining great research interest as biodegradable metallic biomaterials for orthopedic, cardiovascular and tissue engineering applications [1,2]. The significant difference between conventional implant materials (stainless steel, co-cromium alloys or titanium based alloys) and magnesium implants is that the latter may degrade in the physiological environment over a period of time, avoiding the need for a second surgical removal after healing of tissue [3,4]. The property has given rise to the use of Mg alloys in the design of new generation temporary biomedical implants [5].

The elastic modulus of the magnesium alloys is approximately 41-45 GPa, and is close to natural cortical bone (10-30 GPa) [6,7] which is one of the significant advantages of the magnesium alloys. However, the elastic moduli of conventional metallic implant materials are much higher, thus causing the stress shielding effect and affecting bone remodeling and regeneration [8]. A better mechanical fit of the magnesium alloys allows for better load sharing between the implant and the bone tissue around it which helps to promote natural healing.

Several magnesium alloy systems have been extensively studied and developed and are suitable for biomedical applications. The AZ31 (Mg-Al-Zn) and AZ91 alloys are good mechanical properties and manufacturability, thus many of these alloys are investigated for use as biodegradable implants. Those that are used in biomedical applications and have yttrium and rare earth elements with very good corrosion resistance and mechanical stability are the most widely studied magnesium alloys for the orthopedic or cardiovascular field, such as the alloys WE43. The alloys that are primarily zinc and zirconium are called ZK60 and have high tensile strength, high fatigue resistance and a relatively good biocompatibility [11]. In more recent times, alloys without rare earth elements (REEs), such as Mg-Ca and Mg-Zn-Ca systems have started to gain in increasing interest because the Ca and Zn are naturally occurring elements in the human body and are known to have a positive effect on bone metabolism and regeneration [12,13].

The biodegradability is one of the most peculiar features of magnesium alloys. Upon implantation, the magnesium is gradually dissolved in the body fluids and releases the magnesium ion and corrosion products which are metabolized or excreted in the body [14]. The controlled degradation enables the provision of temporary mechanical support during the healing period, and a progressive load transfer to the newly regenerated tissues [15]. In addition, magnesium ions have been reported to stimulate the proliferation of osteoblasts, to promote bone mineralization and to enhance the osteogenic differentiation in the process of accelerated healing and regeneration of bones and cartilages [16,17].

Although many of these benefits exist, the rapid degradation of magnesium alloys in physiological environments is still the major challenge for their extensive use in clinical applications [18]. Magnesium anodic dissolution and water cathodic reduction produce substantial amounts of hydrogen evolution [19]. However, with an excessive amount of hydrogen production, gas pockets may form around the implant sites which can impact tissue integration and healing [20]. Hydroxyl ions are produced in parallel, which causes the local pH to increase, causing local tissue alkalinization and possible cellular response [21]. The mechanical integrity will also be lost at a faster rate, causing failure of the implant before complete tissue regeneration, because of the rapid corrosion [22]. Although magnesium alloys are highly biodegradable, biocompatible and osteogenic, the uncontrolled corrosion, hydrogen evolution, localized alkalization and early mechanical degradation are still major challenges that hamper the application of magnesium alloys in clinical use [23,24].

1.2 Surface Modification Strategies

To reduce the inherent corrosion susceptibility of magnesium alloys, a tremendous number of surface engineering techniques have been developed to improve the corrosion resistance, bioactivity and performance of implants. One of the most promising approaches that can be employed to create thick ceramic-like oxide layers is plasma electrolytic oxidation (PEO) which can significantly enhance the corrosion and wear protection [25]. A similar process is called micro-arc oxidation (MAO) which generates porous oxide coatings with high substrate adhesion and surface hardness, which is very well suited for biomedical applications [26].

There has been also extensive research on protective surface coatings of magnesium alloys using conversion coatings. The coatings obtained by chemical reaction between the substrate and the phosphate, fluoride, rare earth elements or other active species present in the treatment solution, reduce the corrosion rate and improve adherence of the coating to the substrate [27]. Hydroxyapatite (HA) coating is particularly attractive for orthopedic implants because of its good osteointegration and cellular adhesion and proliferation due to its chemical similarity to the mineral phase of the natural bone [28].

To slow down the degradation of magnesium and to encourage biological interactions, barrier layers have been employed, for example, made of polymeric material such as poly(lactic acid) (PLA), polycaprolactone (PCL), chitosan or polyethylene glycol (PEG) [29]. In recent years, nanocomposite coatings with nanoparticles, ceramics, corrosion inhibitors, and therapeutic molecules have been shown to be able to offer good corrosion protection, antibacterial activity and sustained delivery of therapeutic molecules [30].

Although significant improvement has been made in these coating technologies, coating defects, limited capacity to heal, long-term stability and inadequate multifunctionality are still challenges [31]. Therefore, there has been a special focus on new coating materials which possess the corrosion protection and bioactivity/bactericidal and therapeutic functions. Of these new materials, metal-organic frameworks (MOFs) have recently been very interesting as next generation surface modification systems for biodegradable magnesium alloys [32].

1.3 Why MOFs?

Metal-organic frameworks (MOFs) are crystalline porous materials made up of metal ions or metal clusters, called secondary building units (SBUs), linked by organic ligands or linkers, via coordination bonds [33]. The ever-growing variety of metal nodes and organic linkers has given rise to thousands of MOF structures exhibiting highly tunable properties and functionalities, particularly the physicochemical ones [34].

One of the distinguishing features of MOFs is the very high porosity and specific surface area, which can even surpass the ones of traditional porous materials [35]. They have a controllable topology and pore size, surface chemistry and functionality, which can be rationally designed to allow the production of materials for specific applications [36]. This tunability makes MOFs very interesting for biomedical and corrosion applications.

MOFs show a number of unique properties for magnesium alloy implants. Their porous structure may also provide a good physical barrier to the aggressive chloride ions and physiological fluids, thus minimizing substrate corrosion [37]. Furthermore, the MOFs can be loaded with corrosion inhibitors, therapeutic agents, bioactive molecules, etc., which could give them controlled and sustained properties [38]. It has potential for the design of coatings with more than one function like corrosion protection, drug delivery and self healing. One other fascinating property of MOF is that it could be used to liberate biologically active metal ions in a controlled fashion. Zinc-based MOFs also been thought of as potential osteogenic agents and antibacterial agents particularly in orthopedic applications [39]. Iron-based MOFs have shown great biodegradability and drug-loading ability, while cobalt-based MOFs have been shown to have antimicrobial and catalytic properties [40]. Copper MOFs have been reported to be effective in inducing angiogenesis and have a high level of antibacterial activity, but there is some concern with their toxicity [41]. The long-term biomedical applications of the UiO-series MOFs are appealing because of its exceptional chemical stability and corrosion resistance, which is derived from the use of zirconium [42].

The metal nodes of MOFs can be coordinated to a range of organic linkers, such as imidazolates, carboxylates, terephthalates, trimesates and amino-functionalized ligands [43]. The zeolitic imidazolate frameworks (ZIFs), Materials of Institute Lavoisier series (MIL), University of Oslo series (UiO) and Hong Kong University of Science and Technology series (HKUST) are popular MOFs [44]. The ability of these structures to be versatile makes it possible to integrate corrosion protection, anti-bacterial, osteogenic stimulation and therapeutic delivery into one coating platform.

Therefore, MOFs are emerged as a highly attractive type of surface coatings for biodegradable Mg alloys possessing multifunctionality. Such high porosity, tunable chemistry, drug loading, corrosion inhibition, antibacterial properties and bioactive ion release present a huge promise to overcome the current challenges of the coating technology and advance the clinical use of magnesium based biomedical implants.

2. Methodology of Systematic Literature Review

To obtain a thorough understanding of the most up-to-date research related to metal–organic framework (MOF)-based coatings and surface modification of the biomedical magnesium alloys, a systematic literature review was conducted. In particular, the application of Zn-, Fe-, Co-, Cu-, Zr-, Ti-, and Ni-based MOFs in corrosion protection, performance enhancement of electrochemical properties, improvement of tribological properties, antibacterial activity and biomedical functionality fields were specifically focused. The process of selecting studies and extracting data was carried out transparently, repeatably and with methodological rigor, following the guidelines of the Preferred Reporting Items for systematic Reviews and Meta-Analysis (PRISMA 2020). The identification, screening, eligibility and reporting of studies included in systematic reviews are standardized in PRISMA 2020.

2.1 Review Protocol

The review protocol was designed based on the PRISMA 2020. The questions for the review were as follows:

What is the current understanding of MOF functional magnesium alloys for biomedical applications and how does the corrosion resistance, electrochemical behavior, tribological performance and biological functionality change with various metal based MOFs?

The review process consisted of four major stages:

i. Literature identification
ii. Screening and Duplication Removal
iii. Eligibility Assessment: Full text evaluation.
iv. Finalized inclusion of relevant studies

Articles published in journals were included only if they were peer-reviewed articles from January 2016 to March 2026. Conference papers, patents, editorials, book chapters and publications other than English were excluded.

Figure 1. *PRISMA Flow Diagram of Study Selection*

The PRISMA flow diagram provides a description of the systematic selection process and shows the rigorous screening process to obtain the final number of 180 studies.

2.2 Databases

A literature search was conducted in four scientific databases which had a high degree of depth of materials science, corrosion engineering, biomaterials and biomedical engineering research.

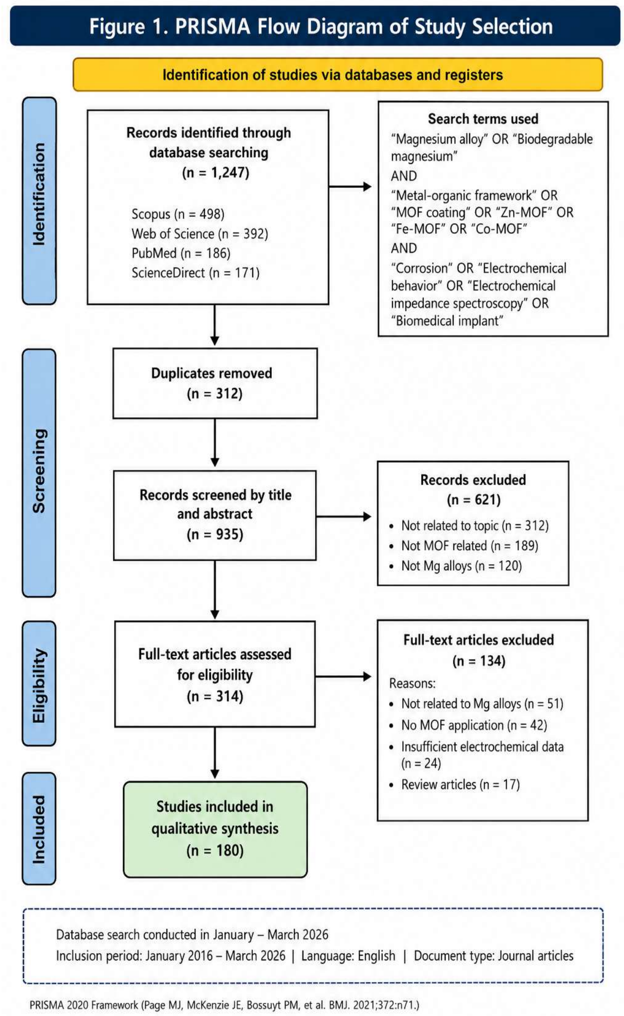


Figure 1. PRISMA Flow Diagram of Study Selection

- **i.** Scopus
- **ii.** Web of Science Core Collection
- **iii.** PubMed
- **iv.** ScienceDirect

The choice of these databases was made because they collectively cover most of the publications on magnesium alloys, corrosion science, metal–organic frameworks, biomaterials, and biomedical surface engineering.

2.3 Search Strategy

A complex search strategy was created based upon combinations of keywords, Boolean logic and database-specific filters. The search was done between January and June, 2026.

The most common search queries were:

"Magnesium alloy"
"Biomedical magnesium alloy"
"Metal-organic framework"
"MOF coating"
"Zn-MOF"
"Fe-MOF"
"Co-MOF"
"ZIF-8"
"Corrosion"
"Electrochemical behavior"
"Electrochemical impedance spectroscopy"
"Biodegradable implant"
"Surface modification"
"Biomedical implant"

A typical search term was:

("Magnesium alloy" OR "Biodegradable magnesium").
AND
("Metal-organic framework" or "MOF coating" or "Zn-MOF" or "Fe-MOF" or "Co-MOF")
AND
("Corrosion" OR "Electrochemical behavior" OR "Biomedical implant")

2.4 Inclusion and Exclusion Criteria

Table 1. *Inclusion and Exclusion Criteria*

Criteria	Inclusion	Exclusion
Publication Year	2016-2026	Before 2016
Language	English	Non-English

Document Type	Peer-reviewed journal articles	Conference papers, editorials, book chapters
Materials	Magnesium alloys with MOF applications	Non-Mg substrates
Study Focus	Corrosion, electrochemistry, biomedical performance, tribology	Unrelated applications
Data Availability	Full-text accessible	Abstract-only studies
MOF Types	Zn, Fe, Co, Cu, Zr, Ti, Ni MOFs	Non-MOF coatings

Based on these criteria a total of 180 studies got selected for final qualitative synthesis.

2.5 Bibliometric Overview

The bibliometric values were analysed to determine the trends in publications, geographical distribution of research, influential researchers, and emerging research themes.

Publication Trend

The selected studies were analysed and it was found that research activity in this area has increased after 2020. The main publications in the period 2016-2019 dealt with traditional corrosion protective coatings of magnesium alloys. Since 2020, however, the emphasis has shifted to MOF-based coatings particularly Zn-MOFs and ZIF derived materials for biomedical applications. In 2024-2025, the surge in interest was evident as the highest number of publications were received in this field.

Geographical Distribution

The top countries in this research area were:

i. China
ii. United States
iii. Germany
iv. Japan
v. South Korea
vi. India

China was the top contributor of publications, as it had extensive research activities in biomaterials, corrosion engineering and MOF synthesis.

Leading Authors

Some researchers emerged as influential in terms of publications and the impact of their work, including:

i. Y. F. Zheng
ii. F. Witte
iii. X. N. Gu
iv. H. C. Zhou
v. O. M. Yaghi
vi. A. Atrens

These authors have made great contributions to biodegradable magnesium alloys, corrosion science and MOF materials.

Table 2. *Bibliometric Summary of Included Studies (n = 180)*

Parameter	**Findings**
Total Studies Included	180
Publication Period	2016-2026
Databases Searched	4
Most Active Country	China
Most Investigated Alloy	WE43
Most Investigated MOF	ZIF-8 (Zn-MOF)
Major Research Theme	Corrosion Protection
Secondary Theme	Biomedical Applications
Emerging Theme	Drug Delivery and Antibacterial Coatings
Common Electrochemical Tests	EIS, PDP, Immersion Tests

Keyword Mapping

From the keyword co-occurrence analysis 5 themes emerged:

i. Degradable Magnesium Alloys.
ii. MOF coatings and corrosion resistance.
iii. Electrochemical characterization
iv. Antibacterial and bioactive coatings.
v. Biomedical implants and tissue engineering.

All of the keywords appeared with high frequencies, with *"Magnesium Alloy", "MOF Coating", "ZIF-8", "Corrosion Resistance", "Electrochemical Impedance Spectroscopy", "Biomedical Implant"* and *" Drug Delivery"* being the most predominant ones, reflecting the main research areas in the study.

The bibliometric results demonstrate the potential of the MOF-functionalized magnesium alloys as a newly emerging interdisciplinary research field of biomaterials, corrosion engineering and electrochemistry and regenerative medicine.

3. Introduction to Metal-Organic Frameworks (MOFs)

Inorganic-organic hybrid materials called metal–organic frameworks (MOFs) are a novel class of porous materials that are built from inorganic nodes containing metals and organic ligands by means of coordination bonds [45,46]. MOFs have also garnered significant interest since their introduction in the late 1990s due to their very high surface area, tunable pore structure, chemically functionalizable surfaces and their diverse applications in gas storage, catalysis, sensing, drug delivery, and corrosion protection [47,48]. Due to its unique modular structure, the MOFs can be designed to control the properties of the structure and its function with great precision, especially for biomedical magnesium alloy surface engineering [49].

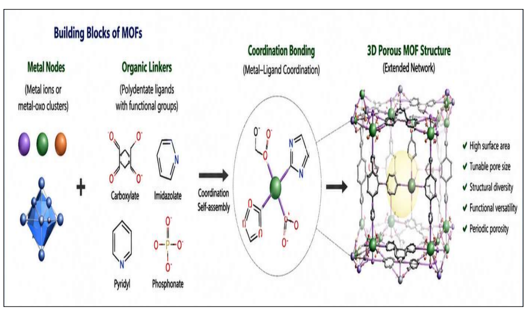
3.1 Structure and Classification

Metal nodes and organic linkers are the basic components of MOFs. Typically, metal nodes are found as single metal ions or metal-oxo clusters, and organic nodes are typically consisted of carboxylate, imidazolate, pyridyl, or phosphonate functional groups [50]. These two components can be synced together to form highly ordered 3-D porous frameworks [51].

MOFs can be divided into a number of categories, depending on the metal center. Many Zn-MOFs have shown a good biocompatibility and antibacterial activity, such as ZIF-8 and MOF-74 [52]. In Fe-MOFs, MIL-53 and MIL-101 are excellent in terms of biodegradability and drug loading properties [53]. Co-MOFs also have catalytic and antimicrobial properties, and Cu-MOFs are widely applied in the field of antioxidant and antibacterial properties and angiogenic properties [54, 55]. It is worth mentioning that Zr-MOFs are extremely corrosion resistant and chemically stable; the UiO-series is outstanding. Newly developed Ti-MOFs and Ni-MOFs have also been proven to be beneficial for biomedical and electrochemical applications [57].

MOFs can also be classified according to their family. These include Zeolitic Imidazolate Frameworks (ZIFs), Materials of Institute Lavoisier (MIL) series, University of Oslo (UiO) series, Hong Kong University of Science and Technology (HKUST) series and Porous Coordination Network (PCN) series [58, 61, 62, 63, 64]. In terms of topology, they are distinct, they are stable, distinct in terms of porosity and biological function.

Figure 2. *General Structure of Metal-Organic*



Frameworks

Table 3. *Major Types of MOFs Relevant to Magnesium Alloy Surface Engineering*

MOF Type	Representative Examples	Major Characteristics	Biomedical Relevance
Zn-MOFs	ZIF-8, MOF-74	Biocompatible, antibacterial	Osteogenesis, corrosion protection
Fe-MOFs	MIL-53, MIL-88, MIL-101	Biodegradable, high drug loading	Drug delivery, bioactivity
Co-MOFs	Co-ZIF, Co-BTC	Catalytic, antimicrobial	Antibacterial coatings
Cu-MOFs	HKUST-1	Strong antibacterial activity	Angiogenesis, infection control
Zr-MOFs	UiO-66, UiO-67	High stability, corrosion resistance	Long-term implant protection
Ti-MOFs	MIL-125(Ti)	Photocatalytic activity	Emerging biomedical applications
Ni-MOFs	Ni-BTC, Ni-MOF-74	Electrochemical functionality	Corrosion and sensing applications

3.2 Synthesis Techniques

Various synthetic methods have been developed for the controlled morphology, crystallinity and porosity of MOFs. The most frequently used process is solvothermal process in which metal salts and the organic ligands react in the presence of an organic solvent at high temperatures and pressures [61]. The more environmentally friendly hydrothermal process is the use of water as a reaction medium [62].

Electrochemical synthesis, in which the metal anode is dissolved, can also be used to obtain MOFs in a fast reaction time [63]; microwave assisted synthesis, in which MOFs are synthesized without compromising the crystallinity, is another option for synthesis [64]; and sonochemical synthesis, which involves ultrasonic irradiation to create the nucleation and crystal growth, is also used [65,66]. Other in-situ growth approaches have also emerged as attractive ways to prepare the MOF coatings on magnesium (Mg) alloy substrates, which have better adhesion to the substrate, corrosion resistance properties, and biomedical application [67–70]. Direct embedding of MOF structure on the implant surface can be achieved by these methods to enhance the stability and multifunctional properties of coatings.

4. Magnesium Alloys with MOFs

The use of metal-organic frameworks (MOFs) has been a promising strategy to overcome the drawbacks of fast degradation, hydrogen evolution and poor biological function of Mg-based implants [71,72]. The highly porous structure, tunable chemistry and multifunction of MOFs make them an ideal candidate to act as a protective barrier and yet provide antibacterial properties, drug delivery, and osteogenic stimulation [73]. In recent years, in-situ growth, hydrothermal deposition, solvothermal synthesis and hybrid coating were studied methods to integrate different metal-based MOFs on the surface of magnesium alloy substrates, for the purpose of improving the corrosion resistance and biomedical performance [74].

4.1 Zn-Based MOFs on Magnesium Alloys

Most studies of MOFs have been conducted on the biomedical magnesium alloys due to the important role of the zinc ions in the human body in bone metabolism and tissue regeneration [75]. The Mg-alloys explored with Zn-MOFs include the zinc-imidazolate based systems, such as Zn-MOF-74, ZIF-8 and Zn-BTC.

The high chemical stability of ZnII containing ZIF-8 is particularly interesting, degradation with pH sensitivity and controlled release of ZnII ions [77]. The corrosion rates of AZ31, WE43 and Mg-Zn-Ca alloys were found to be significantly lower after the coating with ZIF-8, which has been demonstrated in several studies and attributed to the formation of a dense barrier, preventing the penetration of the electrolyte [78]. Furthermore, released zinc ions stimulate the proliferation of osteoblasts, increase alkaline phosphatase activity and stimulate extracellular matrix mineralization, thus stimulating osteogenesis [79].

Furthermore, the ordered porous structure and controlled release of Zn ions from the coatings of Zn-MOF-74 have been reported to be excellent corrosion protection and biocompatibility [80]. Likewise, the antibacterial activity of Zn-BTC and Zn-imidazolate frameworks against both Staphylococcus aureus and Escherichia coli have been demonstrated to be promising, which helps to reduce implant-associated infection risks and still exhibit excellent cytocompatibility [81,82].

The last several studies focused on the hybrid PEO/MOF systems with the growth of the Zn-MOFs on the plasma electrolytic oxidation layers, and multifunctional coatings with increased corrosion resistance, antibacterial and bioactivity were developed [83].

Table 4. *Zn-Based MOFs Investigated on Magnesium Alloys*

Zn MOF Type	Mg Alloy	Preparation Method	Corrosion Improvement	Biological Effect
ZIF-8	AZ31	Hydrothermal	Significant reduction in corrosion current density	Osteogenesis and antibacterial activity
ZIF-8	WE 43	In-situ growth	Enhanced barrier protection	Improved cell proliferation
Zn-MOF-74	Mg-Zn-Ca	Solvothermal	Increased charge transfer resistance	Controlled Zn^{2+} release
Zn-BTC	AZ91	Electrodeposition	Reduced degradation rate	Antibacterial effect
Zn-Imidazolate	WE 43	Hybrid PEO-MOF	Improved corrosion resistance	Enhanced osteointegration

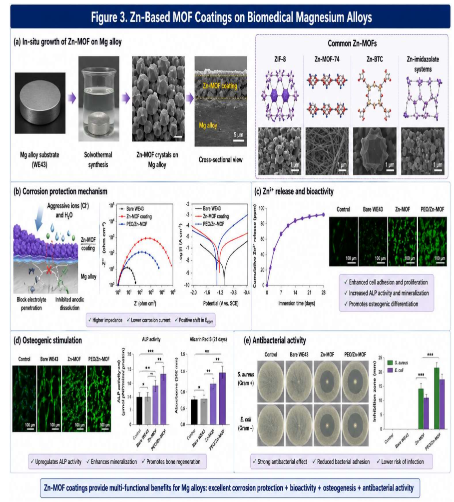


Figure 3. *Zn-Based MOF Coatings on Biomedical Magnesium Alloys*

4.2 Fe-Based MOFs

The MOFs with Fe as building blocks, such as MIL-53(Fe), MIL-88(Fe), and MIL-101(Fe), have been focused on due to their high biodegradability and loading potential for drugs [84]. The gradual liberation of Fe^{3+} ions could assist metabolic processes and tissue regeneration in the cells without inducing excessive accumulation of ions in the cells [85].

MIL-101(Fe) has very high pore volume, which can accommodate various antibiotics, growth factors and anti-inflammatory agents [86]. The MOFs have been explored as a corrosive resistant reservoir with both the corrosion inhibition and local drug delivery. Although there are very few direct deposition studies of magnesium alloys, preliminary studies show that Fe-MOFs-based coatings has a high potential for multifunctional coatings for implants.

4.3 Co-Based MOFs

CO-ZIF and Co-BTC have been shown to have high antibacterial and catalytic activity [89]. They can generate ROS, required for effective bacterial clearance in controlled conditions, without affecting cytocompatibility [90].

Co-MOF coating is a physical barrier which reduces the infiltration of electrolyte and enhances the electrochemical stability for corrosion protection application. They can also be used to achieve controlled degradation and improve the surface functionality [91] due to their catalytic function. However, the release of cobalt ions is of concern and this should be optimised by careful design of the coating and degradation rates.

4.4 Cu-Based MOFs

Copper containing MOFs have been receiving significant attention due to their excellent antibacterial activity, and their ability to facilitate angiogenesis [92]. The controlled release of Cu^{2+} by Cu-MOFs is also a unique property that has been associated with enhanced tissue regeneration and vascularisation, making the Cu-

MOFs attractive for use in orthopedic and wound healing.

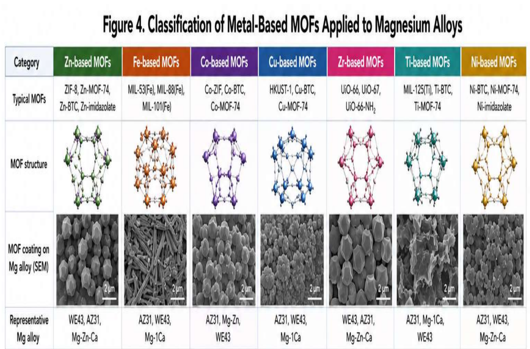
While these are benefits, higher concentrations of copper ions than physiological can lead to cytotoxic effects, oxidative stress and inflammatory responses [93]. It is therefore important to ensure the correct degradation rates and ion release profiles of Cu-MOF coatings to optimise the biological activity and safety of the magnesium alloy.

4.5 Zr-Based MOFs

So far the most chemically stable families of MOFs reported are the zirconium-based MOFs (UiO-66 and UiO-67) [94]. They have a wide range of applications in the biomedical sector due to their good hydrolytic stability, which is necessary for long-term corrosion protection.

The degradation rate for the UiO-series MOFs is slower than for the Zn and Fe MOFs and the structural integrity of the UiO-series MOFs is greater. The properties enable long term corrosion stability and biocompatibility with surface stability [95]. The Zr-MOF materials are therefore becoming more and more attractive as potential materials for long-term protective coatings of biodegradable magnesium implants.

Figure 4. *Classification of Metal-Based MOFs Applied*



to Magnesium Alloys

4.6 Ti-Based and Ni-Based MOFs

Relatively little research has been carried out on magnesium alloy materials for new systems like titanium and nickel MOFs. For future biomedical coating applications, Ti-MOFs have photocatalytic activity, high chemical stability and antibacterial activity, making them very promising agents [95]. Similarly, Ni-MOFs have exhibited interesting electrochemical characteristics as well as corrosion protection properties, but with the concern of Ni toxicity.

No work has been reported on using Ti and Ni based MOFs as biodegradable magnesium implants in the literature. They should be tested for their corrosion resistance, ion release, biological response and long-term in vivo durability to be considered for future research. The capabilities of these MOFs could be integrated into multifunctional hybrid coating systems to open new ways to design next generation electrochemical and biological functional biodegradable implants.

5. Electrochemical Behaviour of Magnesium Alloys Coated with MOFs

The electrochemical properties are crucial factors which determine the applicability of magnesium alloys for biomedical applications. Magnesium is very biodegradable and biocompatible, but has a very negative standard electrode potential and therefore tends to corrode readily in a physiological setting [96,97]. Over degradation leads to loss of mechanical integrity at an earlier age, generation of hydrogen gas and a local alkalization lowers clinical performances [98]. More recently, metal–organic framework (MOF) coatings have been also developed to be effective electrochemical barriers able to control the degradation behavior and to enhance the functionality of the implants [99].

5.1 Corrosion Mechanism of Bare Mg Alloys

The corrosion of magnesium alloys in aqueous physiological environments takes place by simultaneous anodic dissolution and cathodic hydrogen evolution reaction [100].

Anodic Reaction

$$Mg \rightarrow Mg^{2+} + 2e^{-}$$

Cathodic Reaction

$$2H_2O + 2e^{-} \rightarrow H_2 + 2OH^{-}$$

The magnesium ions that are formed react with the hydroxyl ions to form magnesium hydroxide:

$$Mg^{2+} + 2OH^{-} \rightarrow Mg(OH)_2$$

The physiological fluids however do have more chloride ions levels which are able to cause the protective layer of $Mg(OH)_2$ to become depleted and allow corrosion through pitting or local degradation processes [101]. In general, the corrosion current density and corrosion rate of the bare magnesium alloys are high.

5.3 Electrochemical Protection Mechanisms of MOFs

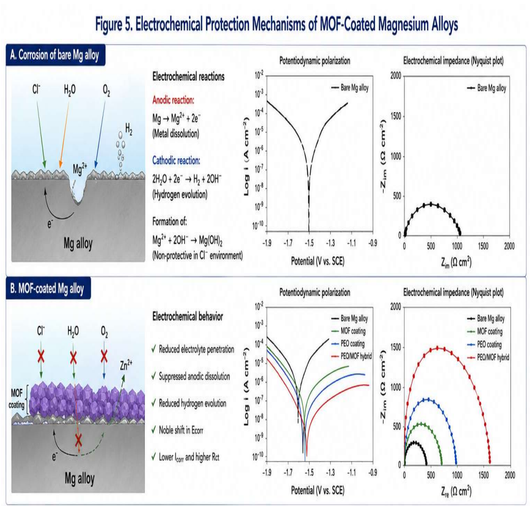
The MOF coatings provide several synergistic effects to provide additional corrosion protection. Firstly, the highly ordered framework is a physical barrier to minimize the direct contact between the electrolyte and the magnesium substrate [102]. Secondly, the pores in the MOF are also possible to increase the blockage of pores and prevent the penetration of chloride ions, which will delay the onset of corrosion [103].

Some MOFs are able to exhibit a self-healing property in the form of gradual delivery of corrosion inhibitors and/or bioactive ions which can regenerate the protective surface layers upon damage of the surface coating [104]. In addition, the ions emitted from the controlled release rate can also have corrosion inhibition activity, such as Zr4+ ions, Fe3+ ions and Zn2+ ions [105].

One of the most promising approaches is to combine plasma electrolytic oxidation (PEO) and MOF coatings. MOF growth on a porous PEO layer can lead to the creation of a hierarchically structured protective structure with high electrochemical stability, in these systems [106]. It has been recently proven that PEO-

MOF hybrid coatings offer a substantial decrease in corrosion current density and increase the charge transfer resistance as compared to either PEO or MOF only [107].

Figure 5. *Electrochemical Protection Mechanisms of MOF-Coated Magnesium Alloys*



MOF-Coated Magnesium Alloys

5.3 Electrochemical Characterization

Potentiodynamic polarization (PDP) and electrochemical impedance spectroscopy (EIS) are common methods used for the electrochemical evaluation of a device [108].

The two most important parameters during the PDP testing are:

- **i.** Corrosion potential (Ecorr): thermodynamic corrosion tendency indicator.
- **ii.** Corrosion current density (Icorr): a measure of the rate of corrosion.

The lower the Icorr, the better the corrosion resistance.

Data from EIS analysis includes the information on the integrity of the coating, and data about the charge transfer processes. Important parameters include:

- **i.** Charge transfer resistance (Rct): the higher the value the better the corrosion resistance.
- **ii.** Constant phase element (CPE): surface heterogeneity and coating capacitance.
- **iii.** Nyquist plots: semicircle diameter is related to corrosion protection.

There are other tests used to assess degradation, such as hydrogen evolution tests, in which the degradation rate is measured directly, and immersion tests, in which the long term behaviour of corrosion under physiological conditions and mimicking the environment is determined [109].

5.4 Comparative Electrochemical Performance

Table 5. *Comparative Electrochemical Performance of MOF-Coated Magnesium Alloys*

MOF Type	Ecorr (V vs SCE)	Icorr (μA/cm²)	Rct (Ω·cm²)	Degradation Rate
Bare WE43	-1.62	85-120	250-500	Very High
ZIF-8	-1.48	5-15	5,000-12,000	Low
Zn-MOF-74	-1.45	3-10	8,000-15,000	Low
MIL-101(Fe)	-1.43	8-18	4,500-10,000	Moderate-Low
Co-ZIF	-1.46	6-20	4,000-9,500	Moderate
HKUST-1 (Cu-MOF)	-1.44	5-16	5,500-11,000	Moderate-Low
UiO-66	-1.39	2-8	10,000-20,000	Very Low
PEO/ZIF-8 Hybrid	-1.35	1-5	20,000-45,000	Very Low

The UiO-series MOFs (Zr-based), and hybrid PEO/Zn-MOF coatings exhibit the highest electrochemical performance and have high charge transfer resistance, low corrosion current density and provide excellent long term stability among the different MOFs investigated [110].

6. Tribological Behaviour of MOF-coated Magnesium Alloys

The tribological characteristics of biodegradable magnesium alloys should be considered in the field of biomedical applications in which they are subjected to repeated loading and mechanical interaction. Magnesium alloys have excellent biocompatibility and biodegradability, but generally low hardness and wear resistance, and are easily degraded in service. Damage may lead to the corrosion processes being accelerated, the generation of more debris and the reduced stability of the implant, especially in orthopedic implants where cyclic mechanical stresses are present [112].

6.1 Wear Problems of Mg Alloys

The low hardness of magnesium alloys is mainly explained by the hexagonal closed packed (hcp) crystal structure of the alloys which allows few slip systems to be activated during the deformation process [113]. Therefore, during the physiological loading, magnesium alloys are extremely susceptible to abrasive, adhesive and surface plastic deformation wear [114]. Protective layers of corrosion also come in contact with fresh surfaces of the metal when interactions with the surface cause rupture of the corrosion layers which can leave the metal degraded [115]. Moreover, biodegradable magnesium implants are a challenge due to the effect of tribocorrosion, which is the combined effect of mechanical wear and electrochemical corrosion [116].

6.2 MOF-Assisted Wear Protection

Recently MOF coatings have been found to be promising tribological surface modifiers that are effective in enhancing wear resistance and corrosion protection [117]. The lubricating effect of porous MOF structures that help prevent direct contact between metal surfaces during sliding interactions is one important mechanism [118]. Furthermore, by helping load distribution in the coated surface and avoiding the stress concentration, the MOFs will help avoid the surface deformations [119].

Another significant contribution is provided by surface hardening in the case of application of MOFs in combination with ceramic oxide layers – specifically plasma electrolytic oxidation (PEO) coating [120]. When added together PEO-MOF can be considered as a hybrid system that may improve hardness and adhesion between coating and base material and decrease wear rate of the system compared to uncoated magnesium alloys [121]. Also, the multifunctional tribological performance and continuous protection are possible in the physiological environment when incorporating the agents for lubrication or bioactive molecules within some MOFs [122].

6.3 Friction Coefficient Reduction

A number of studies have shown that the friction coefficients after deposition of MOF layer on magnesium alloy substrates were significantly decreased [123]. The wear resistance of Zn-based MOFs, especially ZIF-8, has exhibited excellent performance, which can be attributed to the strong adhesion with the substrate and compact crystalline morphology [124]. In the same way, the UiO-series Zr-MOFs have been seen to possess great mechanical stability and low friction properties [125].

Table 6. *Tribological Performance of MOF-Coated Magnesium Alloys*

MOF Type	Wear Rate	Friction Coefficient	Improvement
Bare Mg Alloy	High	0.55-0.70	Reference
ZIF-8	Low	0.25-0.35	Significant wear reduction
Zn-MOF-74	Low	0.28-0.38	Improved lubrication
MIL-101(Fe)	Moderate	0.30-0.42	Enhanced load distribution
Co-ZIF	Moderate	0.32-0.45	Improved wear resistance
HKUST-1	Moderate	0.30-0.40	Antibacterial tribological coating
UiO-66	Very Low	0.20-0.30	Excellent wear protection
PEO/ZIF-8 Hybrid	Very Low	0.15-0.25	Maximum tribological improvement

7. Biomedical Applications

Such developments are MOF coating on biodegradable magnesium alloy, which bring new opportunities in the field of multifunctional biomedical implants. In addition to corrosion resistance, the properties mentioned above are also valid for controlled ion release, antibiotic properties, drug loading and osteogenic properties, which makes MOFs very promising for the development of future implant systems [126,127]. The synergistic effect between the magnesium alloys and MOFs offers a platform that can simultaneously fulfill degradation control and biological performance requirements [128].

7.1 Orthopedic Implants

So far, the most intensively studied use of MOF coated magnesium alloys is in the medical field, specifically for orthopedic implants. Several types of magnesium alloy implants are available that have been found to fail after fracture healing without the need for implant removal surgery, including bone screws, fixation plates, pins and intramedullary devices [129]. The activity of osteoblasts, which is essential for bone regeneration, production of alkaline phosphatase, and extracellular matrix mineralization has been shown to be stimulated by Zn-MOF coatings, thus improving bone regeneration [130]. In addition, Fe-MOF and Zr-MOF coatings have been demonstrated to have positive effects on the stability and long-term corrosion resistance of implants during the healing process [131].

7.2 Cardiovascular Stents

Biodegradable magnesium stents are good alternatives to permanent metallic stents as they offer temporary support to the vessel and resorb after the remodeling. [132] Another benefit of MOF coatings is their ability to provide controlled degradation and inhibit surface degradation which may be associated with high corrosion rates and negatively affect the mechanical properties [133]. The electrochemical stability and biocompatibility of Zr based MOFs and Zn based ZIF coatings have been found to be outstanding, and therefore they are promising for use in cardiovascular applications [134].

7.3 Drug Delivery Systems

Due to the extremely high surface area and pore volume of MOFs, they are a useful choice for drug encapsulation and delivery [135]. MOF can be used in conjunction with magnesium implants to deliver antibiotics, anti-inflammatory agents, growth factors and anti-cancer drugs locally into the targeted tissues [136]. The MOFs based on Fe have the distinct advantage of large pore structures and high loading capacity, especially for Fe-based MOFs, such as MIL-101(Fe) [137].

7.4 Antibacterial Implants

Infections involving implants are still a significant problem in orthopedic and cardiovascular surgery. A few of the metal-organic frameworks, such as the Zn-MOFs, Cu-MOFs, and Co-MOFs, are also found to have good antibacterial property, due to the controlled release of metal ions and production of reactive oxygen species (ROS) [138]. Zn-MOF coating has been found to be efficient against two strains namely Staphylococcus aureus and Escherichia coli and it is also good cytocompatibility [139]. Cu-MOFs are highly effective antimicrobial and angiogenic agents and Co-MOFs have additional catalytic and antimicrobial capabilities [140,141].

7.5 Tissue Engineering

Another area of potential use of magnesium alloys coated with MOFs is tissue engineering. The slow degradation of the magnesium affords mechanical support during regeneration of tissues and the bioactive ions released by MOF promote the response of cells and

the formation of the extracellular matrix [142]. The Zn ions of Zn-MOFs were reported to show pro-osteogenic effects [143] and the Fe ions were reported to participate in cellular metabolism and tissue healing.
Recently, it was demonstrated that magnesium scaffolds functionalized with MOF can stimulate the adhesion, proliferation and differentiation of stem cells and control degradation [144]. Additionally, in the case of Cu-MOFs, the angiogenic properties which are crucial for a tissue regeneration process can be obtained [145]. Because of this, the use of MOF-coated magnesium alloys is increasing as scaffolds for bone tissue engineering and regenerative medicine applications is becoming more popular [146-150].

Table 7. *Biomedical Applications of MOF-Coated Magnesium Alloys*

Application	Representative MOFs	Major Benefits
Orthopedic Implants	ZIF-8, Zn-MOF-74, UiO-66	Osteogenesis, corrosion control
Bone Screws and Plates	Zn-MOFs, Fe-MOFs	Improved healing and biodegradation
Cardiovascular Stents	ZIF-8, UiO-67	Controlled degradation, biocompatibility
Drug Delivery Systems	MIL-101(Fe), UiO-66	High drug loading and sustained release
Antibacterial Implants	Zn-MOFs, Cu-MOFs, Co-MOFs	Infection prevention
Tissue Engineering Scaffolds	Zn-MOFs, Fe-MOFs, Cu-MOFs	Bone regeneration and angiogenesis
Regenerative Medicine	Hybrid PEO-MOF coatings	Multifunctional therapeutic platform

8. Limitations of MOF Coatings on Magnesium Alloys

While MOF coatings on biodegradable magnesium alloys have a tremendous potential, there remain numerous scientific and technological questions to be tackled before MOF coatings can be used in large scale clinical and industrial applications. It is crucial to understand these negative aspects and take them into account when designing future research and when the transfer to biomedical applications is successfully made [151,152].

8.1 Poor Long-Term Stability

One of the drawbacks of MOF coatings is that they are not very stable in physiological conditions in the long term. Aqueous solutions, especially acidic or chloride rich conditions, cause a slow degradation of many MOFs [153]. Although the Zr-MOFs of the UiO-series are very stable, in extended implantation, few of the Zn-, Fe- and Co-based MOFs can undergo framework collapse.

8.2 Delamination Problems

The adhesion of coating to the magnesium alloys, however, remains a great challenge for MOF functionalized magnesium alloys. A mechanical stress during implant loading may cause the coating to delaminate or if corrosion occurs the volume changes may cause coating delamination and loss of coating.Mechanical stress during implant loading can cause delamination of the coating, and volume changes during corrosion can lead to delamination of the coating and loss of the coating [155]. In many cases, however, after the defects in the coating the poor bond strength between magnesium substrate and MOF layer will cause localized corrosion [156].

8.3 Defect Formation

There are microcracks, pores, grain boundaries and structural defects that are often present on the surface of MOF coatings due to the synthesis process or because of post-synthesis.In MOF coatings, microcracks, pores, grain boundaries and structural defects may be formed during the synthesis process and/or after synthesis. These defects can also allow electrolyte to penetrate the coating and reduce the corrosion protection resulting in local corrosion [158]. Furthermore, it is difficult to get defect-free MOF coatings onto complex implant geometries.

8.4 Cytotoxicity Concerns

Many MOFs are highly biocompatible, but there are concerns about the effect of high release levels of metal ions. Furthermore, Cu-MOFs can produce high levels of Cu^{2+} which can lead to oxidative stress and inflammation [159]. Similarly, Ni-MOFs can also have toxic properties since Ni^{2+} can be an allergen and toxic to cells at high concentrations [160]. Thus, kinetic optimization of the release of the ions needs to be carefully developed to guarantee biological safety.

8.5 Scale-Up Challenges

Almost all MOF coating technology is still in the laboratory stage of synthesis. However, process reproducibility, coating uniformity, cost effectiveness and quality control are issues in the industrial-scale manufacturing [161,162]. Scalable and standardized fabrication routes need to be developed before commercial use becomes possible.

8.6 Lack of Clinical Studies

A key limitation could be the absence of clinical data. Most investigations are limited to in vitro and small animal models and there are only a handful of studies using large animal models or human studies [163]. More studies should be performed to investigate the long-term safety of the implants, degradation in vivo and in vitro, immune reaction and performance of implants in clinical use [164–170]. Thus, large amounts of preclinical and clinical studies will be needed before magnesium implants with MOF coatings can be routinely used in clinical practice.

9. Research Gaps and Future Directions

Despite all these advances in MOF-coated magnesium alloys, there are still a number of key fundamental issues to be addressed. A solution to these challenges will be critical to realize laboratory-based innovations to clinically viable implant technologies [171].

i. The first one is that actually, there is not much direct comparison between different MOF systems. Most of the research on-going is on the individual MOFs based on Zn, Fe, Co, Cu and/or Zr, which is not very helpful in assessing what MOF would deliver the best corrosion protection or biological activity under the same conditions, [172]. It is an emergency to carry out comparative investigations with the same magnesium alloy substrate, test environment and evaluation method.
ii. Another drawback is the absence of tribocorrosion tests. The majority of the studies only focus on electrochemical corrosion properties, and very little is known about the relation between electrochemical corrosion and wear properties in orthopedic implants [173]. Likewise, a lack of long-term in vivo studies with humans exist, with the majority of studies been limited to short-term animal studies [174].
iii. Another difficulty is that there is no standardized electrochemical testing protocol. There is a wide range of different electrolytes, immersion times, scan rates and EIS parameters used in the literature, which makes it hard to draw a proper comparison between different studies [175].
iv. Further research is desired for the synthesis of multifunctional MOFs that can simultaneously perform as corrosion protection agent, antibacterial agent, drug carrier and osteogenic stimulator [176]. In this context, ZIF-8 and Zn-MOF-74 are particularly interesting because of their good corrosion resistance as well as their high bioactivity, owing to the release of bioactive Zn ions [177].
v. Last but not least, the use of artificial intelligence (AI) to guide the design of MOFs is barely explored. Machine learning techniques can be applied to identify the best MOF structures for specific biomedical applications, to predict the degradation pathways, and to identify the most suitable MOF structures to fulfill the desired objective [178–180].

10. Conclusions

One of the most promising surface engineering approaches to enhance the performance of biodegradable magnesium alloys for biomedical applications is metal–organic framework (MOF) coatings. MOFs are extremely porous, controllable materials which provide excellent corrosion protection as well as the potential of releasing bioactive ions, anti-bacterial properties, drug delivery and the promotion of tissue regeneration.

The Zn-based MOFs have proven to have remarkable properties such as corrosion resistance, osteogenic activity, and antibacterial activity, which are likely to have great potential for biomedical applications. The Zr-series MOFs are highly chemically stable and with good protection capacities, Fe-series MOFs (MIL) have excellent drug-loading capacities and biological functionality.

Electrochemical measurements always indicate that the coating of MOF can substantially decrease the corrosion current density, increase charge transfer resistance and prevent hydrogen evolution of uncoated magnesium alloys. In addition, hybrid systems of PEO-MOFs are also a very promising approach to combining the advantages of high corrosion and tribological properties. While all these are improved, there remain various issues that need to be resolved; long-term stability, coating defects, some metal ions are toxic, scalability in production, and comprehensive clinical trials are not yet available. There are suggestively marked needs for further studies to create multifunctional MOF systems, create standardized testing protocols, test in vivo over a longer period of time, design MOF materials using AI. The further development of the MOF-based magnesium alloys should have an impact on the next generation of biodegradable implants in the field of orthopedic, cardiovascular and regenerative medicine.

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