

Biocompatibility Study of Silica-Based Magnesium Composites: A Review

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Abstract

Because of their exceptional biodegradability, mechanical strength, and biocompatibility, magnesium-based composites have attracted a lot of interest in the biomedical field. This is especially true in the fields of orthopaedics, tissue engineering, and regenerative medicine. Magnesium has limited utility in load-bearing implants and scaffolds due to its quick corrosion in physiological settings. Magnesium alloys are strengthened with silica (SiO₂), which improves biocompatibility, decreases corrosion rates, and enhances mechanical qualities, so overcoming these constraints. The biocompatibility of silica-based magnesium composites has not been well reviewed, despite the increasing interest in these materials. This study aims to rectify that. By focusing on how these composites interact with cells, tissues, and the immune system, this review hopes to assess their biocompatibility. It delves into the ways in which biocompatibility is affected by variables such silica concentration, surface changes, degradation behaviour, and composite processing processes. Research on cytotoxicity, cell proliferation, osteogenesis, and tissue integration is particularly covered, as are *in vitro* and *in vivo* investigations. The difficulties of improving these composites' mechanical strength, degradation rates, and stability in biological settings are also discussed in the paper. In contrast to previous reviews that have mostly dealt with the mechanical and corrosion characteristics of magnesium alloys, this one focus entirely on the biocompatibility of silica-based magnesium composites, an area that has received very little attention in the literature. The study goes on to talk about how many methods have been used to determine biocompatibility, such as cytotoxicity testing, gene expression analysis, cell viability experiments, and *in vivo* research with animals like rabbits and rats. Research on magnesium composites with silica has shown encouraging findings, suggesting that these materials are more biocompatible than pure magnesium and other magnesium alloys. *In vitro* studies have demonstrated that silica improves bone regeneration, angiogenesis, and osteogenic differentiation of mesenchymal stem cells (MSCs), and *in vivo* studies have shown that silica improves tissue integration, reduces inflammation, and increases bone growth at implant sites. Still, there are obstacles to overcome, most notably regulating the rates of magnesium breakdown, which can have undesirable consequences including gas buildup and the early deterioration of mechanical strength. Surface coatings, alloying, and biodegradable polymer usage are some of the strategies being investigated as potential solutions to these problems. Also, a major obstacle is still making sure silica-magnesium composites are stable over the long run. In spite of these challenges, the encouraging results suggest that magnesium composites based on silica have enormous potential as a material for drug delivery systems, bone tissue engineering, and orthopaedic implants. Researchers, biomedical engineers, and clinicians may benefit greatly from this study since it sheds light on the biocompatibility of these materials and helps direct the creation of safer, more effective biomaterials based on magnesium for use in clinical settings. The results will pave the way for further biological applications of these materials, such as medication delivery and bone healing, and will aid in their successful clinical translation.

Keywords: Biocompatibility, Silica, Magnesium, Composites, Mesenchymal stem cells

Introduction

The biomedical materials community is starting to take notice of magnesium-based composites as a result of its many potential uses, especially in orthopaedics, tissue engineering, and regenerative medicine. In order to improve their overall qualities, these composites include additional reinforcing agents, mainly silica (SiO_2), with the distinct advantages of magnesium (Mg), such as its biodegradability, mechanical strength, and low density. Although biodegradable materials including pure magnesium or magnesium alloys have attracted a lot of attention, their fast corrosion rates in physiological settings have limited their usefulness in therapeutic settings [1-5]. Damage to mechanical integrity, cytotoxicity, and undesirable biological reactions such as gas buildup and tissue irritation may result from corrosion problems. To overcome these drawbacks, magnesium-based composites have silica added to them as a stabilizing agent to reduce corrosion, improve mechanical qualities, and make them more biocompatible [6-11]. Although silica-modified magnesium composites have showed encouraging results in reducing magnesium's negative side effects, our knowledge of these materials' biocompatibility is still quite limited. This study seeks to address this knowledge gap by offering a thorough evaluation of silica-based magnesium composites' biocompatibility [12-16]. It will concentrate on these composites' interactions with biological tissues, cellular reactions, and biomedical application potential. When considering a material's viability for use in healthcare, biocompatibility ranks high among the most important criteria [13-16]. How effectively a material interacts with neighboring tissues, cells, and the immune system without producing negative consequences is determined by its biocompatibility, which is an important property for any material used in biomedical implants or

scaffolds. When it comes to composites made of magnesium, adding silica improves these interactions by encouraging positive biological reactions like adhesion, proliferation, and differentiation while reducing negative ones like inflammation and cytotoxicity [17-21]. Biocompatibility has received less attention in studies of silica-based magnesium composites than its mechanical and corrosion characteristics, despite the

materials' increasing popularity. There has been little investigation into the important biological interactions that impact the performance of magnesium-based materials in medical applications, with most evaluations focusing on either their corrosion behaviour or structural features [22-26]. This feature is addressed in a unique way by this review, which focuses only on biocompatibility of silica-based magnesium composites. It provides a thorough and organized analysis of the current studies and points out where more research is required [27-30]. The intrinsic biodegradability of magnesium makes it an appealing option for use in biological applications. No more need for invasive second procedures to remove implants made of non-biodegradable metals like titanium; magnesium, on the other hand, breaks down naturally over time. But there is a flip side to the coin that is biodegradability [31-35]. The presence of chloride ions in bodily fluids accelerates magnesium's corrosion rate in physiological conditions compared to many other materials. Damage to tissues, discomfort, and swelling may result from the quick corrosion of magnesium, which produces hydrogen gas. In addition, implants made of magnesium may have their mechanical qualities compromised by fast deterioration, which can cause them to fail before enough tissue healing has taken place [36-39]. In response to these issues, scientists have investigated the possibility of creating magnesium-based composites reinforced with a variety of materials, including as ceramics, polymers, and other metals. One of the most encouraging reinforcing agents among them is silica [40-42]. Biomaterials containing silica, also known as silicon dioxide (SiO_2), have found extensive application due to the material's bioactive qualities, which include facilitating osteointegration, improving cell adhesion, and bolstering tissue development [43-45]. Materials based on magnesium that have silica added to them have superior mechanical qualities, a lower corrosion rate, and greater biocompatibility thanks to improved degradation management [46,47]. Because silica slows magnesium's corrosion, the healing process benefits from a more steady and regulated release of magnesium ions. Research on silica-based magnesium composites and their testing for use in biomedicine is extensive. Cell toxicity, osteogenic potential, and *in vivo* behaviour have been the primary areas of investigation in these

materials. Research conducted in a controlled environment has shown that cells, including osteoblasts and mesenchymal stem cells (MSCs), adhere better and multiply more rapidly when silica is added to magnesium composites [48-53]. A bioactive material, silica has the potential to promote bone repair by activating mesenchymal stem cell (MSC) differentiation into osteoblasts. Results from *in vivo* investigations in rabbits and rats have been encouraging, indicating less inflammation, better implant integration with surrounding tissues, and enhanced bone formation [54-58]. The optimization of the biocompatibility of silica-based magnesium composites remains a problem, despite these encouraging results. Reducing the rate of corrosion is one of the main obstacles [59-62]. The breakdown rate of the composite still has to be fine-tuned to coincide with the pace of tissue repair, even if silica aids in magnesium corrosion [63-67]. The mechanical support necessary for tissue regeneration can be compromised if the material breaks down too rapidly. On the other side, if it breaks down too slowly, it could build up degradation products that trigger immune responses or impede tissue development. Research on the relationship between deterioration behaviour, processing techniques used to make the composites, and silica concentration is still continuing strong [68-72]. Despite the fact that silica-based magnesium composites have come a long way, there is a dearth of assessments that concentrate only on biocompatibility [73-75]. The biological interactions of magnesium composites have received less attention in the current literature compared to their mechanical, corrosion, and structural characteristics [76-79]. Researchers studying these composites' biocompatibility seldom provide a cohesive framework for identifying the key aspects that influence their *in vivo* performance, instead presenting results in isolation [80-83]. One big hole in the literature is the lack of research on how these composites affect immune responses and tissue repair over the long term. In addition, there is a lack of consistency in the methods used to assess biocompatibility in the existing research. Magnesium composites based on silica need standardised testing

techniques to reliably evaluate cytotoxicity, cell proliferation, and immunological response. Also, how various silica concentrations, composite manufacturing processes, and surface changes affect these materials' biocompatibility is still a mystery [84-87]. This study seeks to address these gaps by offering a thorough and organized examination of the biocompatibility of magnesium composites based on silica. It will concentrate on the elements that affect their biological performance and their possible therapeutic uses [88-91]. In particular, this study aims to compare and contrast silica-based magnesium composites with other magnesium-based materials in order to provide a comprehensive and current assessment of their biocompatibility [92-95]. This study will analyse the biocompatibility of these composites by looking at their mechanical properties, degradation behaviour, surface features, silica content, and interactions at the cellular and tissue levels [96-98]. The study will also shed light on the obstacles and restrictions that must be overcome in order to maximize the biocompatibility of these composites for use in clinical settings, including drug delivery systems, orthopaedic implants, and bone scaffolds [99-102]. The biocompatibility of magnesium composites based on silica is the only topic of this review, setting it apart from others in the current literature. Few studies have provided a comprehensive examination of the biological interactions between magnesium-based composites and their many other features, including as mechanical strength, corrosion resistance, and structural qualities [103-108]. This review endeavours to provide a thorough grasp of the interactions between these composites and cells, tissues, and the immune system by collecting data from *in vivo* and *in vitro* investigations [109-114]. In addition, the developing technologies and tactics, such hybrid composite materials and sophisticated surface modification techniques, will be examined in the review to improve the biocompatibility of these composites [115-123]. **Figure 1** shows the utility types of diverse magnesium-primarily based totally biomaterials and their corresponding physiological processes.

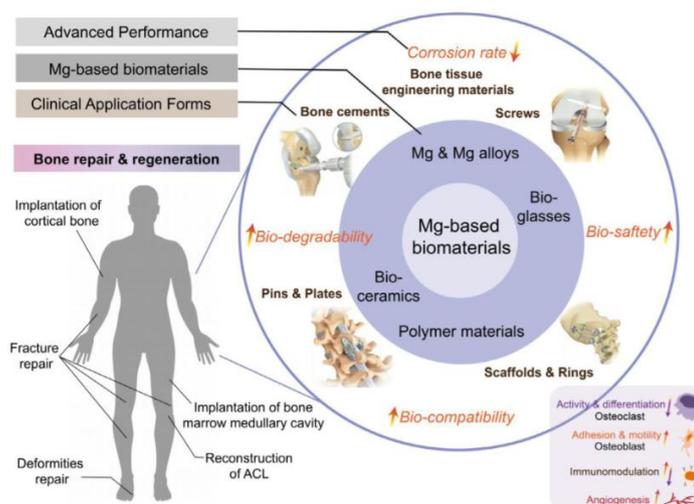


Figure 1 The utility types of diverse magnesium-primarily based totally biomaterials and their corresponding physiological processes [52].

This review covers a wide range of topics relevant to the biocompatibility of silica-based magnesium composites, with a particular emphasis on the following areas [124-126]: (1) Magnesium as a Biodegradable Material: An exploration of magnesium's inherent advantages and challenges in biomedical applications. (2) The Role of Silica in Enhancing Magnesium Composites: A discussion of the properties of silica, the mechanisms through which it improves magnesium composites, and the structural benefits it provides. (3) Types of Biocompatibility Studies: An overview of *in vitro* and *in vivo* testing methods, including cytotoxicity, cell proliferation, and tissue integration studies. (4) Properties of Silica-Based Magnesium Composites: A detailed analysis of the mechanical, corrosion, and surface properties of these composites, along with their biodegradability and bioactive ion release. (5) Mechanisms of Biocompatibility: How silica-based magnesium composites interact with cells, tissues, and the immune system, promoting osteointegration, reducing inflammation, and supporting tissue regeneration. (6) Advanced Surface Modification Techniques: Strategies for improving the biocompatibility of silica-based magnesium composites through coating, functionalization, and nanoparticle incorporation. (7) Challenges and Future Directions: The obstacles facing the development of silica-based magnesium composites, including corrosion control, long-term stability, and standardization of testing protocols.

Researchers, engineers, and clinicians aiming to maximize the biocompatibility of silica-based magnesium composites for clinical usage will find this review an essential resource since it synthesizes the existing body of research. In the long run, this study hopes to help get magnesium-based biomaterials used more widely by facilitating their safer and more effective design.

Noviyanti *et al.* [127] successfully synthesized an amorphous phase of silica from rice husk using a precipitation method. The extracted silica could be a hydrophobic coating agent. The strongest hydrophobic properties were achieved in sample 10A:5B, with an average contact angle of 105.3°. Other sample compositions showed lower values of the contact angle, which means that the vibration speed of colloid generation affects the quality of the silica coating. Sodium silicate made from the extracted silica could act as a corrosion inhibitor, since it could reduce the corrosion rate and increase the inhibition effect. The highest inhibitory effect was achieved at a sodium silicate concentration of 20 ppm, which was 81.9%.

Magnesium as a biodegradable material

Magnesium as a biodegradable material in biomedical applications

A lightweight and bioresorbable substance, magnesium (Mg) has gained significant interest in several biomedical fields, including regenerative medicine, orthopaedics, and tissue engineering. Medical

implants, especially those meant to restore or build up bone tissues, may benefit greatly from its unusual mix of mechanical strength, low density, and biodegradability [128-133]. When long-term implants aren't an option, as for fixing bone fractures or making stents for the heart, magnesium alloys shine. Unlike more conventional materials like titanium or stainless steel, which need a second procedure to remove the implant after it has served its function, implants made of magnesium gradually dissolve in the body. Magnesium is an appealing option to other metallic implants because of its inherent capacity to promote bone repair via the release of magnesium ions. These ions have been shown to boost osteoblast activity, bone mineralization, and angiogenesis. In addition, the mechanical qualities of magnesium, such its modulus and tensile strength, are similar to those of genuine bone, making it a better material for tissue integration since it mimics the physiological features of bone more precisely [134-136]. The fast deterioration of magnesium-based materials under physiological circumstances poses considerable hurdles, notwithstanding these benefits. Magnesium corrodes in a biological setting when it comes into contact with chloride ions in bodily fluids; this process releases hydrogen gas and hydroxide ions, which raise the pH. The structural integrity of the implant might be compromised before enough tissue regeneration has place due to this fast corrosion, which can lead to implant failure. In addition, localized inflammation, and pain may be caused by hydrogen gas collection at the implant site [137-139]. Furthermore, if the rate of magnesium ion release is higher than the body's ability to digest the ions, it may cause cytotoxicity and hinder cellular activity. Because of these problems, magnesium alloys need a degradation process that is more tightly regulated so that the corrosion rate of the material matches the pace at which tissues repair. Clinical usage of magnesium implants is further complicated by studies showing that excessive ion release may elicit inflammatory reactions and oxidative stress, adding to the complexity of magnesium's cytotoxic effects, especially on immune cells. However, controlling the rate of degradation and the resulting biological consequences is still a major worry when it comes to using magnesium for biomedical applications, even if its biodegradability has its advantages [140-142].

Challenges and strategies to overcome limitations of magnesium

One major obstacle to magnesium alloys' broad use in biomedical applications is the speed with which they corrode in biological settings. The main problem is that magnesium implants deteriorate at uncontrollable rates when exposed to the body's physiological conditions [143-145]. This can cause several undesirable biological responses, including local inflammation, gas formation, tissue irritation, and a premature loss of mechanical strength and stability of the implant. When the implant needs to hold the bone together while the surrounding tissue heals, as it does in load-bearing applications like bone fractures, these issues may become much worse. An imbalance in the release of magnesium ions, brought about by the rapid corrosion of magnesium alloys, may disrupt cellular homeostasis and potentially induce cytotoxicity. This is particularly true in cells that make bone. Inflammatory cytokine production, immune cell activation, and a possible delay in tissue repair are physiological responses to very fast breakdown rates. To overcome these obstacles and achieve the best possible biocompatibility and therapeutic effectiveness with magnesium implants, it is crucial to regulate their corrosion behaviour [146-149]. Various approaches have been considered in an effort to circumvent these restrictions. One way to enhance magnesium's mechanical characteristics and corrosion resistance is to change its alloying elements. Magnesium alloys that include calcium (Ca), zinc (Zn), or rare earth metals have the potential to increase the alloy's mechanical strength, ductility, and resistance to corrosion. Corrosion may be better controlled and hydrogen gas can be released more slowly with the aid of these alloying components. Nevertheless, certain alloying elements might pose additional biocompatibility concerns; for example, they may have cytotoxic effects, which would limit their medicinal usage [150-153]. The creation of protective barriers to delay corrosion by surface coatings or treatments is an additional tactic. To make magnesium implants more resistant to corrosion, scientists have used a variety of coatings, including as organic coatings, ceramic layers (such silica or hydroxyapatite), and polymer films [154-157]. Not only do these coatings keep corrosion to a minimum, but they also modify the release of magnesium ions, which helps

to reduce inflammation and localized tissue damage. In addition, there has been research into the potential of surface modification methods like anodization or plasma electrolytic oxidation (PEO) to produce bioactive surfaces that are both more resistant to degradation and less reactive to biological fluids, thereby improving cell adhesion. Magnesium alloys have the potential to improve their biological performance by inducing cellular responses like angiogenesis and osteogenic differentiation when their surfaces are functionalized with bioactive molecules or growth factors like bone morphogenetic proteins (BMPs). When meticulously planned and executed, these solutions may improve magnesium's biocompatibility for use in tissue engineering and medical implants while simultaneously addressing the problems caused by its fast deterioration [158-161].

Role of silica in enhancing magnesium composites

Biomedical uses of magnesium alloys, which are bioresorbable, have attracted a lot of attention, especially for orthopaedic implants and bone regeneration. Although magnesium-based materials have good mechanical qualities and biodegradability, they have problems such as fast corrosion in biological conditions, which may cause implants to fail before their time [162-164]. A crucial reinforcing component in magnesium composites, silica (SiO_2) has arisen to circumvent these restrictions and improve their performance. Bioactive ceramic silica has great promise as a long-term biomedical application material because of its ability to improve the mechanical and corrosion characteristics of magnesium alloys. Silica's capacity to modify the surface properties of magnesium, its biocompatibility, and its large surface area are key to its success as a reinforcing agent. Incorporating silica into magnesium-based composites provides several benefits, including a slower degradation rate, increased mechanical strength, better biocompatibility, and increased osteoconductive [165-168]. The increased surface area that silica particles provide in comparison to the magnesium matrix, according to their nanoscale size, may interact with the matrix to produce more stable surface layers that can withstand vigorous corrosion under physiological settings. Furthermore, silica's bioactive properties allow it to improve the material's

interaction with biological tissues, which in turn promotes cell adhesion, proliferation, and differentiation, especially in osteoblasts, the cells responsible for bone formation. There are a number of processes at work when silica is added to magnesium alloys, all of which contribute to the composite's improved performance. Regulation of corrosion behaviour is a key mechanism. The strong reactivity of pure magnesium with chloride ions in bodily fluids is the main reason why it corrodes so quickly in biological conditions. When magnesium is mixed with silica, it forms a protective coating on the surface, which slows down the corrosion rate [169-173]. By stabilizing the magnesium surface, this layer decreases the rate of ionic exchange and the amount of hydrogen gas and magnesium ions released into the tissues around it. A persistent oxide layer may be more easily formed on the surface of a magnesium alloy when silica is added, thanks to its passivating action on magnesium. The underlying magnesium is further protected from excessive breakdown and cytotoxic effects are reduced by this oxide layer. A function that silica plays in controlling the concentration of magnesium ions in the surrounding tissue is its capacity to affect the ionic release from magnesium alloys. Inflammation and cell death are 2 of the undesirable biological reactions that may result from an overabundance of magnesium ions, which are cytotoxic. A more regulated and balanced degradation process that better corresponds with the body's healing systems is achieved by using silica, which helps to moderate the release of magnesium ions. The composite's applicability for bone tissue engineering applications is further enhanced by silica's beneficial effects on osteointegration, which include promoting osteoblast activity and enhancing bone mineralization. In terms of structural integrity, mechanical characteristics of silica-enhanced magnesium composites are better than those of pure magnesium [174-178]. Load-bearing applications, such as implants or fixing bone fractures, are not well suited to magnesium because of its brittleness and poor tensile strength, especially when subjected to severe stress [179]. By adding silica nanoparticles or microparticles to the magnesium matrix, the composite material becomes stronger, more mechanically efficient, and more rigid. When added to a material, silica strengthens it by acting as a reinforcing phase. In orthopaedic

applications, where the material has to be able to resist mechanical stresses without breaking too soon, this reinforcing effect is crucial. The addition of silica particles to magnesium alloy microstructure changes the grain size, which in turn improves the composite's strength and ductility. Applications requiring mechanical stability and regulated biodegradability, such as stents, bone fixation devices, and other orthopaedic implants, are better served by silica-magnesium composites due to their superior mechanical qualities. In addition to being strong and mechanically stable, silica-based composites have the added advantage of being more bioactive [180-183]. The production of bioactive ions by silica, including silicon ions, is shown to have important roles in boosting tissue regeneration, cell adhesion, and osteogenesis. In clinical applications, silica-based magnesium composites are even more successful in encouraging bone healing and tissue regeneration due to their bioactivity, which further boosts their osteoconductive. There are a number of approaches to synthesizing silica-based magnesium composites, and each has its own set of benefits when it comes to managing the microstructure and characteristics of the final product [184-188]. The mechanical alloying of silica into magnesium alloys is a popular technique. In this method, magnesium powders are combined with silica nanoparticles or micro-sized particles, and then the mixture is milled using high energy. This causes the silica particles to be distributed throughout the magnesium matrix. This method guarantees that the reinforcing agent is distributed uniformly throughout the material by achieving a homogeneous distribution of silica in the composite. Another technique is sol-gel processing, which involves combining precursors of magnesium alloy with silica sol and then treating the mixture to create a uniform composite [189-192]. By precisely controlling the silica particle size and distribution, the sol-gel process

improves the mechanical and corrosion characteristics of the finished composite. The addition of silica to magnesium alloys is another possible use of casting processes. To achieve the desired microstructural properties in magnesium-silica composites, this method involves adding silica to the molten magnesium during casting. In more recent times, researchers have also investigated the possibility of using 3D printing and electrospinning to create composites of magnesium and silica. The use of these techniques allows for more exact manipulation of the composites' microstructure, porosity, and surface characteristics, which in turn allows for the development of scaffolds that are both mechanically and bio compatibly well-suited to tissue engineering. It is essential to choose the most appropriate synthesis process according to the desired biomedical application since it greatly affects the mechanical strength, corrosion resistance, and bioactivity of the silica-magnesium composite [193-197]. Magnesium alloys that have silica added to them have better biocompatibility, mechanical characteristics, and degradation rate control, making them more suitable for use in biomedical applications. Silica-based magnesium composites have great potential as a material for bone scaffolds, orthopaedic implants, and other tissue engineering applications because to silica's capacity to alter magnesium's corrosion behaviour, reinforce the composite matrix, and encourage osteointegration. The bioactive characteristics of silica, in addition to its reinforcing function, help to make a material that is more dependable, effective, and biocompatible for use in therapeutic settings. New possibilities for the creation of next-generation biomaterials will arise when synthesis methods improve, allowing for the anticipated further improvement of silica-magnesium composites [198-201]. **Figure 2** shows the stress-strain diagrams of Mg and Mg-SiO₂ syntactic foams.

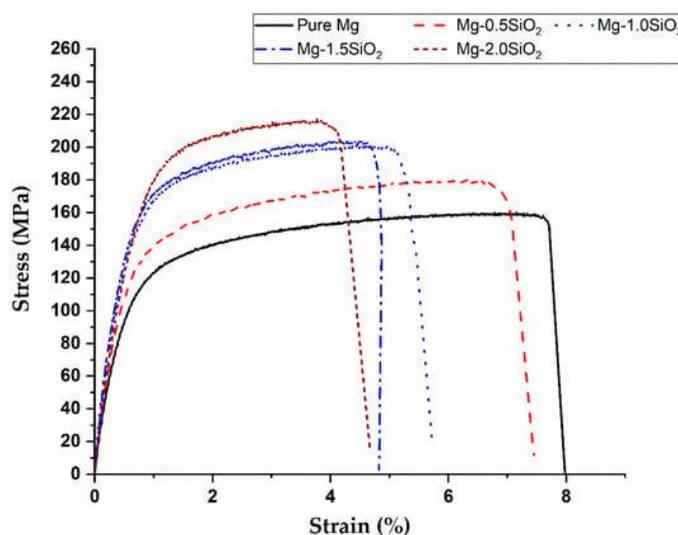


Figure 2 The stress-strain diagrams of Mg and Mg-SiO₂ syntactic foams [53].

Types of biocompatibility studies for silica-based magnesium composites

To determine if silica-based magnesium composites are suitable for use in biomedical applications, such as orthopaedic implants and regenerative medicine, biocompatibility studies are essential. The biodegradability, mechanical characteristics, and bioactivity of these composites made of bioactive silica and magnesium alloys make them a potential replacement for non-biodegradable materials. It is crucial to conduct a thorough examination of their interactions with biological systems to guarantee their safe usage in therapeutic settings. Biocompatibility studies usually include both *in vivo* (on living organisms) and *in vitro* (in a controlled laboratory setting) investigations, along with long-term assessments that take into consideration the materials' continued performance in biological settings. To make sure the composites won't cause any problems when implanted or exposed for a long time, these investigations assist figure out the chances of cytotoxicity, genotoxicity, immunological reactions, and tissue responses [202-204]. To further understand the material's biological interactions, researchers use a wide range of testing procedures, such as cytotoxicity assays, cell viability tests, histology analysis, and animal model studies [57].

Hui Zhu *et al.* [128] Silica-based mesoporous materials, especially mesoporous bioactive glass (MBG), have the potential to be used as drug carriers due to their controllable nanoporous structure as well as

their bioactivity and biocompatibility, allowing for tenable composition. Numerous research papers have reported that MBG can be doped with various therapeutic ions (strontium, copper, magnesium, zinc, lithium, silver, etc.) and loaded with specific biomolecules (therapeutic drugs, antibiotics, growth factors, etc.) allowing for controllable loading and release rates to be achieved. Therefore, the simultaneous delivery of ions and biomolecules using a single MBG carrier is of great interest as it offers synergistic effects towards improved therapeutic outcomes compared to strategies that deliver drugs or ions alone. In this review, we discuss the state of the art in the field of silica-based mesoporous materials used for the simultaneous delivery of ions and therapeutic drugs with osteogenic/semantogenic, angiogenic, antibacterial, and anticancer properties. Literature analysis reveals that specially designed mesoporous nanocarriers can release multiple ions and drugs in therapeutically safe and appropriate amounts to achieve the desired biological effects (*in vivo*, *in vitro*) for specific biomedical applications. This review on the concept of ion/drug codelivery using MBG carriers is expected to demonstrate the advantages of such codelivery systems in clinical use. Areas of future research directions are identified and discussed.

Chen *et al.* [129] Biocompatible mesoporous silica nanoparticles (MSNs) are considered as one of the most promising inorganic drug delivery systems (DDS) to improve the therapeutic efficiency and reduce side effects of anticancer drugs. The complex combination of

multicomponent and MSN molecules endows them with specific functions for cancer treatment and diagnosis, such as targeted drug delivery, intelligent on-demand drug release, synergistic therapy, diagnostic imaging, etc. This report covers the current potential obstacles and future prospects of chemical design/synthesis, *in vitro/in vivo* pharmaceutical evaluation, and potential clinical application of multifunctional mesoporous silica-based nanomaterials for biotechnology and biomedical applications, especially cancer treatment. These topics cover the period from 2001 to 2013. Through comprehensive evaluation of biosafety and pharmaceutical efficacy, the elaborately designed/fabricated mesoporous silica-based composite nanoparticles have shown great potential in clinical applications of efficient diagnostic imaging and chemotherapy of cancer.

Thermos catalytic conversion of biomass is currently a common method to produce activated carbon with excellent textural properties and good adsorption performance [130]. However, activated carbon has the disadvantages of very poor thermal stability and prone to spontaneous combustion. In contrast, silica materials are known for their easy availability, large specific surface area, and good thermal stability. However, their strong hydrophilicity limits their wide range of applications. In light of this, this review summarizes the recent progress of carbon-silica composites, including various preparation methods using various carbon (including biomass resources) and silica precursors, their corresponding structure-function relationships, and their applications in the fields of adsorption, insulation, batteries, sensors, etc. By combining them, the inherent advantages of the individual materials can be maintained while avoiding their shortcomings. Finally, this article discusses some bottlenecks existing in the field of carbon-silica composites from synthesis to applications and proposes corresponding solutions.

Parfenyuk and Dolinina [131] The number of viral infections and viral strains is increasing year by year, necessitating the development of new, more effective antiviral drugs. One of the most cost-effective ways to increase drug efficacy is to develop delivery systems for drugs already known and used in clinical practice, overcoming the challenges that currently limit their efficacy. In this report, we present the current status of silicon-based particles in this field. Silicon-based

materials consist mainly of silicon and its compounds, possibly including other inorganic oxides, and are essentially inorganic. These inorganic properties offer many advantages over organic materials (polymers, lipids, micelles, etc.) that have been widely proposed and are already used for the specified purposes. This report provides information on the structural features and manufacturing processes of silicon-based materials. The paper includes research showing why and how the particles themselves can act as antiviral agents and carriers, overcoming the shortcomings of active drugs and enhancing their antiviral efficacy. The report highlights the great potential of silicon-based inorganic particles (either raw or modified with a variety of inorganic and organic materials) in the fight against widespread viral infections.

Shiv *et al.* [132] Over the past few decades, there has been an increasing demand for the development of polymer nanocomposites due to their superior mechanical, thermal, electrical, tribological properties, etc. Due to their versatility and improved performance, polymer nanocomposites are suitable for a wide range of applications such as automotive, aerospace, electrical, electronics, and construction. The effects of different types of nanofillers are as follows: (A) Metal-based, carbon-based, and silicon-based materials incorporated into polymers have been extensively studied by various researchers. Silicon-based and nanofiller-reinforced polymer nanocomposites have shown promise in recent years in tribological applications such as plastic gears, bushings, and bearings. (B) large number of different studies have demonstrated various excellent properties of silicon-based and hybrid nanofillers in polymer nanocomposites. However, only a few reviews have been published on the effects of silicon-based and hybrid nanofillers on silicon-based and hybrid nanofiller-reinforced polymer nanocomposites. Therefore, the aim of this paper is to review recent progress on the performance of silicon-based nanofillers and hybrid nanofillers incorporated in polymer nanocomposites, with a special emphasis on their tribological properties. This work presents the main results of several studies mainly focusing on the influence of silicon-based nanofillers on tribological properties related to friction, wear resistance and wear mechanisms. The aim of this work is to investigate the influence of silicon-based hybrid nanofillers in polymer nanocomposites on their

tribological properties. Finally, the challenges and future prospects for the tribological properties of polymer nanocomposites reinforced with silicon-based nanofillers are also discussed.

***In vitro* studies: Overview and techniques**

Biocompatibility testing often begins with *in vitro* investigations, which expose cells to substances in a controlled laboratory setting rather than in a live organism. These investigations are crucial for assessing cellular reactions to magnesium composites based on silica before moving on to more involved *in vivo* testing. *In vitro* investigations provide the benefit of being able to evaluate the composites' basic biological characteristics, including their toxicity, cell adhesion, proliferation, and differentiation. Several cell lines may be used for these types of experiments; for example, macrophages, endothelial cells, fibroblasts, and osteoblasts all provide light on the material's behaviour in their own unique ways. As a measure of cell metabolic activity and an indirect indicator of cell viability, the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay is the gold standard for cytotoxicity assessment in *in vitro* investigations. When trying to find out whether a material releases harmful compounds into the culture media that might damage or impede cells, this test comes in handy. In addition, cell proliferation tests like the CCK-8 assay or the BrdU (bromodeoxyuridine) incorporation assay are often used to assess the material's capacity to sustain cell growth over time. The success of the silica-based magnesium composites in integrating into tissues after implantation depends on the results of these experiments [205-207]. The impact of these composites on cellular processes including matrix formation, collagen synthesis, and osteogenesis may be further evaluated with the use of more sophisticated *in vitro* methods such as gene expression studies utilizing quantitative PCR or protein assays. Data on the release of bioactive ions from the composite, including silica and magnesium ions, is also provided by these tests. By measuring macrophage activation or cytokine release, *in vitro* models may also be used to mimic the material's responsiveness to inflammation or immunological responses. Furthermore, a more accurate representation of the *in vivo* tissue responses may be achieved by the use of co-culture methods, which enable the interaction of several

cell types (e.g., endothelial cells and osteoblasts). These *in vitro* experiments allow us to study the fundamental processes by which silica-based magnesium composites either enhance or hinder biological processes such as angiogenesis, osteointegration, wound healing, and cell-material interactions. Findings from these investigations might be a crucial first step before moving on to testing on animals, since they will show if the material is safe to employ in biological applications [208-210].

***In vivo* studies: Animal models and experimental designs**

Research in a controlled laboratory setting is helpful for understanding how cells interact, but studying how silica-based magnesium composites react in a living organism - with all the complicated physiological responses, tissue integration, and systemic effects - is essential. Evaluating the composites' biocompatibility and long-term performance requires *in vivo* testing, which examines their behaviour within a whole biological system. For *in vivo* investigations of silica-based magnesium composites, the majority of the time, little mammals, usually rodents (mice or rats), or bigger animals, such as rabbits or pigs, are used as models. Because of their close anatomical relationship to humans, more complicated models, such as rabbits or pigs, are often required for the development of composite materials for use in bone implants and tissue engineering scaffolds [211-213]. Implanting silica-based magnesium composites into animal tissues such as bone, subcutaneous tissues, or muscle and then periodically evaluating the tissue reaction is the standard procedure for *in vivo* investigations. Imaging methods like X-ray, CT scans, or MRI may provide light on the material's integration and deterioration over time, while histological analysis of tissue sections can disclose the amount to which the material has induced inflammation, fibrosis, or tissue necrosis [59]. In order to evaluate the composite's mechanical performance under physiological loads that are representative of clinical stress situations, these tests are equally important. Evaluating systemic impacts, including changes in blood parameters or organ function, which might suggest toxic or inflammatory reactions, is an additional way to evaluate the biocompatibility of the substance. Overly ion release from the composite may cause gas production, cytotoxicity, or bone resorption, thus it's

carefully regulated. The composite also contains silica and magnesium. In order to prevent mechanical failure or delayed bio resorption, it is important to evaluate the composite degradation rate during *in vivo* testing. This rate should ideally coincide with the pace of tissue healing. Bone mineral density, new bone development surrounding the material, and bone growth at the implant site are some of the parameters examined in animal models to evaluate osteointegration. The activation of bone-forming cells (osteoblasts) may be assessed using immunohistochemistry for particular markers such as osteocalcin and alkaline phosphatase, while micro-CT imaging and histomorphometry analysis can provide comprehensive quantification of bone formation. Examining immune cell infiltration and cytokine production at the site of implantation helps evaluate the inflammatory response, which aims to detect persistent inflammation or responses to foreign bodies. Important information on the safety and effectiveness of silica-based magnesium composites in a live body may be filled in by conducting *in vivo* experiments, which help to bridge the gap between the results of *in vitro* research and their prospective clinical use [60].

Biocompatibility assessment

Any material slated for use in medical applications, particularly those destined for *in vivo* implantation, must undergo rigorous testing to ensure long-term biocompatibility. Biodegradability refers to the gradual breakdown of magnesium-based composites in the body. This includes silica-reinforced composites. Although this helps lessen the frequency of removal procedures, it poses a problem in terms of keeping the material biocompatible and mechanically sound as it degrades. To better understand the long-term effects of these composites on living tissues, researchers conduct long-term experiments that mimic real-life conditions for weeks, months, or even years. Implantation in animal models is a common method for studying this kind of material's mechanical performance, tissue integration, and degradation rates. The resorption of the composite and the potential release of harmful compounds into the surrounding tissues during deterioration are important questions to ask in long-term investigations. An example of an unregulated process that might induce tissue injury, inflammatory reactions, or gas buildup is magnesium breakdown, which can lead to the creation

of hydrogen gas and the release of magnesium ions [214,215]. The development of a fibrous capsule, vascularization, and new tissue growth - all of which contribute to a stable interface between the composite and the surrounding tissue - are also evaluated in long-term research. If we want to know how well implants made of silica-based magnesium composites will hold up over time, particularly in load-bearing uses like bone fixation, we need to do these experiments. In order to evaluate the progress of tissue healing and implant integration over time, sophisticated imaging methods are used. These methods include histological examination, micro-CT scanning, and mechanical testing of the implant site. For the purposes of determining if the material retains its biocompatibility, lacks harmful long-term consequences, and functional qualities as the body heals, these investigations are essential [61].

Genotoxicity, cytotoxicity, and other tests

To ensure biocompatibility, silica-based magnesium composites must undergo cytotoxicity and genotoxicity testing. The term "genotoxicity" describes a substance's ability to harm cells' genetic material, which might result in cancer, mutations, or other hereditary diseases. Inflammation, tissue damage, or implant failure may result from cytotoxicity, which is defined as a material's ability to induce cell death or impede cell activity. Evaluating the safety of silica-based magnesium composites requires both genotoxicity and cytotoxicity experiments. *In vitro* testing involves exposing cell cultures to the substance and then measuring cell survival, metabolic activity, and genetic integrity using a variety of assays. The lactate dehydrogenase (LDH) assay is a popular tool for determining cytotoxicity [216-218]. It detects the amount of LDH, an enzyme released into the culture media in response to cell membrane injury. Another test that may be used to determine genotoxicity is the comet assay, which measures DNA strand breakage in individual cells. On the other hand, genotoxic impact potential and chromosomal damage may be detected using the micronucleus test. These tests are useful for determining if silica-based magnesium composites are safe and whether they may cause cancer or DNA damage. Excessive oxidative stress may lead to cellular damage and inflammation, which further compromises

the biocompatibility of the material. Additional tests, such as the reactive oxygen species (ROS) assay, can be used to assess the oxidative stress that the materials generate. This comprehensive review of biocompatibility studies for silica-based magnesium composites emphasizes the need for a multi-modal testing strategy to evaluate the materials' suitability and performance in biological contexts. To guarantee the safety of silica-enhanced magnesium alloys in clinical settings, these investigations are important. They include *in vitro*, *in vivo*, long-term, and particular cytotoxicity/genotoxicity testing [63].

Properties of silica-based magnesium composites

Bone tissue engineering and orthopaedic implants are 2 areas where silica-based magnesium composites have shown great promise due to their biodegradability, bioactivity, and mechanical qualities. The addition of silica greatly improves the mechanical characteristics of these composites, such as their strength and flexibility. Since pure magnesium alloys have a poor mechanical strength, they are reinforced with silica, a very stable and hard substance. Composites made of magnesium alloys with silica particles or fibres have enhanced tensile strength, hardness, and fatigue resistance, making them ideal for use in load-bearing applications [219]. The composite's adaptability to the body's dynamic forces is made possible by its flexibility, which is equally crucial. Research has shown that silica-based magnesium composites may have their strength-to-weight ratio modified by adjusting the silica concentration and particle size. This adaptability is crucial for a wide range of uses, including scaffolds for tissue regeneration and temporary bone implants. Furthermore, a regulated equilibrium between biodegradability and mechanical strength may be achieved by the interaction of silica and magnesium. Being a biocompatible and biodegradable metal, magnesium breaks down naturally in the body. The presence of silica, a physical barrier that limits excessive corrosion, might affect the pace of breakdown [64,65]. Due to their high corrosion rate in bodily fluids, magnesium alloys pose a threat of gas production and local tissue injury from metal ions. By increasing magnesium's corrosion resistance and decreasing its degradation rate, silica-based composites lessen this

problem, keeping the material's mechanical characteristics intact for tissue regeneration while preventing problems via controlled deterioration. The biological performance of magnesium composites based on silica is significantly affected by surface properties. Acid etching, coating with bioactive polymers, or surface functionalization with bioactive compounds like growth factors are just a few of the surface treatments that may modify surface attributes including porosity, hydrophilicity, and roughness. These changes may enhance the material's interaction with biological tissues by improving cell adhesion, proliferation, and differentiation. Composites made of silica have a rough surface that may help osteoblasts adhere and mineralize, which makes them great for bone healing. The release of bioactive ions is another important feature of these composites. When magnesium alloys break down, they release magnesium ions, which aid in the process of bone repair and osteogenesis. The therapeutic benefits of magnesium ions may be enhanced by including silica, which modulates their release rate. This prevents the negative consequences of excessive ion release. The bioactivity of the composite is further enhanced by the release of silicon ions during silica breakdown, which have been shown to promote collagen synthesis and bone formation. Bone and other tissue repair may be accelerated by the regulated release of bioactive ions, such as silicon and magnesium, which produce an optimal milieu for cellular activity. As a result, biomedical applications such as bone regeneration and orthopaedic devices might benefit from silica-based magnesium composites due to their exceptional mechanical strength, regulated biodegradability, surface bioactivity, and bioactive ion release [66].

Nanoparticles and their role in biocompatibility

Orthopaedic implants, scaffolds for tissue engineering, and devices for bone restoration are just a few of the biomedical uses that have attracted a lot of interest in silica-based magnesium composites due to their biodegradability, bioactivity, and distinctive mechanical characteristics. The addition of silica to the magnesium reinforcing process improves the mechanical characteristics of these composites. While magnesium is biodegradable and biocompatible, its use in load-bearing applications may be restricted due to its comparatively low mechanical strength. Magnesium

alloys are made more stronger, harder, and more fatigue resistant by adding silica, a biocompatible and inflexible substance. Bone implants and other structures that need both structural support and controlled biodegradation might benefit from these materials because of this adjustment, which improves mechanical performance while simultaneously enhancing the materials degradation potential [220,221]. There are many more uses for silica than only mechanical reinforcement. In addition to preventing magnesium from deteriorating too rapidly in the presence of bodily fluids, which may cause problems like gas buildup or uncontrolled ion release, silica is essential for enhancing magnesium's corrosion resistance. Magnesium composites made of silica reduce magnesium's corrosion rate, which means the material may sustain healing while still being strong. To ensure the composite integrates into the biological system gradually and to prevent early material failure, controlled degradation is required. Furthermore, bioactive molecule coating and other surface modifications of silica-based magnesium composites are crucial for increasing tissue integration, osteoblast development, and cellular interactions. The regulated release of bioactive ions, such as silicon and magnesium, from these composites makes them even more osteogenic, creating an ideal setting for the regeneration of bone tissue. Biomedical materials' biocompatibility and performance are greatly impacted by nanoparticles, especially when they are mixed into composites such as silica-based magnesium alloys. The breakdown of biomaterials is an example of a natural process that may introduce nanoparticles into biological systems. Other examples include medical implants, medication delivery systems, and intentionally introduced nanoparticles used in therapeutic applications [68]. Nanoparticles have a wide range of effects on cellular processes, immunological reactions, and tissue integration once they enter the body and begin to interact with biological systems [222,223].

Nanoparticles' chemical make-up, surface charge, size, and shape all have a role in how cells and tissues absorb them, which in turn determines how they interact with biological systems. Toxic consequences or an enhanced intended biological response are 2 possible outcomes of nanoparticle use. Nanoparticles may enhance cell adhesion, proliferation, and differentiation in silica-based magnesium composites, making the material more bioactive. This is particularly true in bone tissue engineering applications. On the other hand, these nanoparticles might cause harm if they cause inflammation or if their breakdown products build up in tissues. Magnesium composite nanoparticles may cause oxidative stress, interfere with cellular function, or set off immunological responses; these are the main toxicological issues linked with these particles. Size and surface characteristics of nanoparticles affect their ability to be taken up by cells and where they end up in the body, 2 aspects that contribute to nanotoxicity. One example is the fact that nanoparticles with a smaller size have a higher potential for cytotoxicity due to their increased ability to cross biological membranes [224,225]. Furthermore, toxic ions or particles may be released during nanoparticle breakdown, which may have negative impacts on living organisms. An essential component of creating safe and effective biomedical materials is finding a balance between the good benefits of nanoparticles and their possible toxicological hazards. Thus, researchers strive to optimize the nanoparticle features to maximize the material's therapeutic qualities while limiting the possibility of detrimental effects [69]. As a result, nanotoxicity becomes a critical factor in the biocompatibility of silica-based magnesium composites. **Figure 3** shows the microhardness measurements of the prepared nanocomposites. The maximum microhardness was achieved at 1.5 vol % Mg-SiO₂ nanocomposite [226-228].

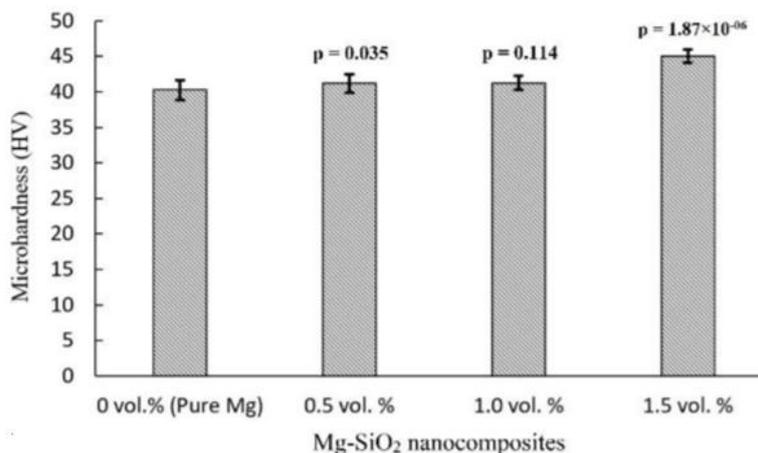


Figure 3 the microhardness measurements of the prepared nanocomposites. The maximum microhardness was achieved at 1.5 vol % Mg-SiO₂ nanocomposite [54].

Mechanisms of biocompatibility in silica-based magnesium composites

Cell-material interaction: Adhesion, proliferation, and differentiation

The biomedical fields of tissue engineering and regenerative medicine stand to benefit greatly from the qualities offered by magnesium composites based on silica. To ensure biocompatibility, it is essential that these composites interact with cells, particularly in ways that encourage cell adhesion, proliferation, and differentiation. The processes are supported by magnesium ions (Mg²⁺) that are produced during biodegradation, and cell-material interactions are improved by silica, which increases the surface area and improves the material's mechanical characteristics. The combination of silica's growth-promoting properties and magnesium ions' ability to induce osteogenesis makes these composites ideal for use in bone healing. By promoting healthy tissue integration and healing, this synergy increases the likelihood of a successful implant outcome over the long run [70].

Immune response and inflammation

Important factors to consider when evaluating biocompatibility include the immunological response and inflammation. The emission of hydrogen gas and ions during magnesium breakdown has the ability to initiate an inflammatory reaction, which in turn may impede the healing process. The addition of silica to the composite, however, reduces the severity of this reaction. In addition to regulating the release of magnesium ions, which helps to reduce immunological activation, silica has anti-inflammatory characteristics. Additionally, it may change the immune response's pro-inflammatory stance to a healing one by influencing macrophage activity. Implants made of magnesium are more likely to remain functional over time because this inflammation-reducing effect improves the material's biocompatibility [71]. **Figure 4** shows Schematic illustration of effects of Mg²⁺ on improvement bone regeneration by inducing desired immune microenvironment.

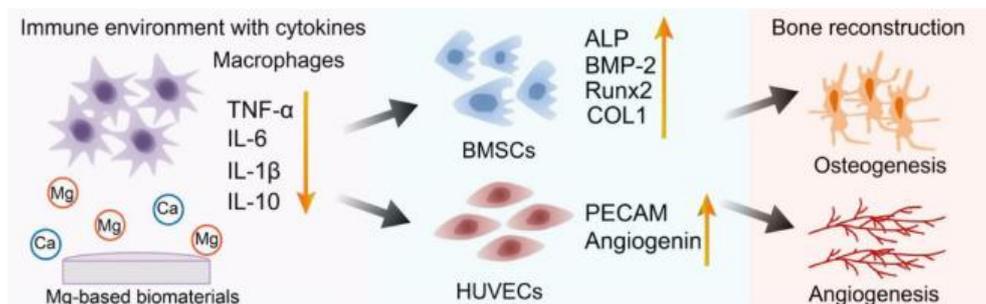


Figure 4 Schematic instance of results of Mg^{2+} on development bone regeneration through inducing fevered immune microenvironment [52].

Osteointegration and bone regeneration

Another important part of biocompatibility for silica-based magnesium composites is osteointegration, which is the process by which implants connect with bone tissue. Osteoblast proliferation and differentiation are essential for bone formation, and these materials produce bioactive ions that enhance these processes. While silica promotes collagen production and osteoblast activity, the breakdown process releases magnesium ions in a regulated manner that activates osteogenic pathways. Research has shown that these composites greatly improve bone regeneration and help the implant integrate better with the surrounding bone, which keeps the implant in place and prevents problems caused by non-biodegradable materials [72].

Biodegradation and its impact on local tissues

Magnesium alloys are known for their biodegradability, which is an important property of these composites. To avoid harmful tissue responses or premature mechanical strength loss, the rate of breakdown of magnesium must be regulated as it slowly dissolves in the body, releasing bioactive ions. Incorporating silica slows the deterioration rate, which in turn prevents excessive corrosion and neutralizes pH fluctuations, both of which may be harmful to nearby tissues. By stimulating cell proliferation, angiogenesis, and osteogenesis, this regulated degradation improves tissue repair. An ideal biodegradable implant material would be a combination of magnesium and silica, as it would allow for both safe disintegration and successful tissue regeneration [73].

Cellular response to silica-based magnesium composites

Mesenchymal stem cells (MSCs) and osteogenesis

Magnesium composites based on silica hold great promise for improving cellular responses essential to tissue regeneration, especially in vascular and bone repair. As these composites break down, magnesium ions are released into the environment. Magnesium ions are essential for the promotion of mesenchymal stem cell (MSC) development into osteoblasts, the cells that build bone. Research shows that signalling pathways - including MAPK and Wnt/ β -catenin - are activated by magnesium ions [229-231]. These pathways are crucial for the development of osteoblasts and the mineralization of bones. In addition, silica particles enhance collagen production and osteoblast proliferation, which speeds up bone healing, adding to the composite's bioactivity. In situations where the integration of tissue is of the utmost importance, such as in bone scaffolds and implants, silica-magnesium composites are an excellent choice because they enhance osteogenic differentiation and bone formation, as shown in both *in vitro* and *in vivo* studies [74,75].

Endothelial cells and angiogenesis (promotion of angiogenesis)

The creation of new blood vessels, or angiogenesis, is greatly aided by silica-based magnesium composites, which also aid in osteogenesis. Magnesium ions, released during magnesium breakdown, promote angiogenesis by increasing endothelial cell proliferation, migration, and tube formation. The addition of silica improves the composite's surface properties, making them an ideal environment for endothelial cell adhesion and

proliferation. These composites enhance the production of angiogenic factors, which have a role in the recruitment of endothelial cells and the development of new blood vessels. These factors include vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). When it comes to repairing complicated tissues that rely on vascularization for their survival, the composite's capacity to regenerate bone and vascular tissue is enhanced by the combined action of silica and magnesium [76].

Macrophages and inflammatory responses

One of the most important factors influencing the biocompatibility of magnesium composites based on silica is the inflammatory response that is caused by breakdown of magnesium alloys. Inflammation and macrophage activation may result from the breakdown of magnesium, which produces hydrogen gas and magnesium ions. The inflammatory reaction may be modulated, however, by adding silica to the composite. To promote tissue repair and regeneration, silica affects macrophage activity by changing their phenotype from pro-inflammatory (M1) to anti-inflammatory (M2). Research has shown that silica may increase the production of IL-10 and TGF- β , 2 anti-inflammatory cytokines, and decrease the secretion of TNF- α and IL-1 β , 2 pro-inflammatory cytokines. Since excessive inflammation may impede tissue repair and implant integration, this immune response control is crucial for enhancing the overall biocompatibility of magnesium-based composites [77].

Cytotoxicity testing in silica-magnesium composites and biocompatibility

Before using silica-based magnesium composites in biomedical devices like implants or scaffolds, it is crucial to assess their biocompatibility via cytotoxicity testing. The breakdown of these composites, especially the discharge of magnesium ions, shouldn't harm the tissues in the area. Cell cultures such as endothelial cells, fibroblasts, and osteoblasts are used in *in vitro* cytotoxicity assays to evaluate the effects of degradation products on cell viability, proliferation, and death. Since the magnesium ions are released at a regulated pace that does not overwhelm the cells, research has shown that silica-based magnesium composites display minimal cytotoxicity. In addition, silica may improve the

material's surface properties, which increases cell adhesion and decreases inflammatory reactions, and modulate the pace of degradation, all of which contribute to a decrease in cytotoxicity. As a whole, silica-magnesium composites are biocompatible, meaning they help cells survive and operate while reducing any potential harmful effects on cells that might restrict tissue regeneration [78].

Examples of successful biocompatibility studies

***In vitro* studies: Cell culture models**

To fully comprehend the cellular level of biocompatibility of silica-based magnesium composites, *in vitro* research using cell culture models are crucial. To evaluate the effects on cell viability, proliferation, differentiation, and gene expression, these studies usually expose different cell types to the degradation products of magnesium-based composites. These cell types include osteoblasts, endothelial cells, fibroblasts, and mesenchymal stem cells (MSCs). An important component in bone regeneration, researchers have shown that magnesium ion release from these composites improves osteogenesis in MSCs. This, in turn, promotes osteoblast differentiation and stimulates collagen formation. The inclusion of silica particles in the composite enhances its surface properties, which in turn promotes improved cell adhesion and proliferation. Silica improves the adhesion and development of endothelial cells on the composite surface, whereas magnesium ions encourage cell migration and proliferation, which are crucial for angiogenesis. Promising prospects for future *in vivo* testing and clinical applications, *in vitro* cytotoxicity experiments shown that regulated ion release from silica-magnesium composites did not significantly harm the cells, but rather supported their survival and function [79].

***In vivo* studies: Animal models (e.g., rats and rabbits)**

It comprised of better understand the biological reactions of silica-based magnesium composites in a more complicated living system, *in vivo* investigations using animal models, including rabbits and rats, are very beneficial. In order to determine whether magnesium-based composites effectively promote bone regeneration and osteointegration, they are often implanted into critical-sized bone lesions in animal investigations.

Research on rats has shown that the breakdown of magnesium alloys in composites aids in bone repair. Magnesium ions, in their role as signalling molecules, enhance mineralization of the bone by stimulating osteoblast activity. Similarly, silica promotes osteoblast proliferation and collagen synthesis, 2 processes that are essential for the formation of new bone tissue [232-234]. By enhancing the quality of bone repair and increasing the development of new blood vessels - a vital aspect for tissue regeneration - silica-magnesium composites have shown encouraging results in rabbit models, which are often used to examine bigger implants and their long-term implications. Additionally, animal studies evaluate the immunological response and inflammation caused by these composites. The findings show that the addition of silica helps control macrophage activation, which in turn decreases the pro-inflammatory response and improves tissue integration [80].

Clinical trials and translational research

Clinical studies and translational research are necessary to connect laboratory results with practical uses of silica-based magnesium composites, but preclinical animal models do provide important data. Orthopaedic implant use of biodegradable magnesium alloys has been the subject of many clinical investigations, with some investigations now looking at the possibility of silica incorporation into these composites to improve their performance. Studies on bone grafts, stents, and scaffolds have shown that silica and magnesium work together to improve biocompatibility and aid in bone repair by increasing osteoblast activity and collagen production. Magnesium alloys have shown promise in early clinical studies as a healing aid without the typical long-term problems associated with non-biodegradable materials, such as persistent inflammation or implant failure. In order to make sure that silica-magnesium composites are safe and beneficial for patients to use, researchers are trying to improve their mechanical characteristics, degradation rates, and bioactivity. Their main goals are to promote tissue regeneration and have regulated ion release. The practicality of these materials, especially for use in the cardiovascular and orthopaedic systems, can only be shown via these clinical trials [81].

Key findings from published studies

Published investigations have shown that silica-based magnesium composites have considerable promise in a variety of biological applications. Studies conducted *in vitro* have shown time and time again that MSCs are perfect for bone regeneration because magnesium ions boost osteogenesis and encourage osteoblast differentiation. Incorporating silica into magnesium alloys increases bioactivity by facilitating angiogenesis, strengthening collagen production, and boosting cell attachment. Consistent with these observations, *in vivo* investigations in animal models have shown that silica-magnesium composites promote angiogenesis by improving endothelial cell function, and also increase bone repair and osteointegration in deficits of crucial magnitude. Additionally, silica helps reduce the likelihood of unfavourable immunological responses by mitigating the inflammatory response and changing macrophage polarization from pro-inflammatory to anti-inflammatory. Research into the function of silica is anticipated to enhance the material's performance by optimizing its degradation rates and enhancing its interaction with surrounding tissues. Clinical trials involving magnesium-based implants have demonstrated positive short-term outcomes regarding tissue healing and biocompatibility. Taken as a whole, these results lend credence to the idea that silica-based magnesium composites might be an excellent and adaptable material for use in many different biomedical fields, including vascular tissue engineering, tissue scaffolding, and bone regeneration [82].

Applications of silica-based magnesium composites in health

Orthopaedic applications: Bone repair and implants

In the field of orthopaedics, silica-based magnesium composites have shown remarkable potential, especially for use in implant production and bone healing. There will be less need for further procedures to remove magnesium implants since the material is bioresorbable, meaning it dissolves naturally in the body. One important component of effective bone healing is the release of magnesium ions during the breakdown of magnesium alloys. These ions are known to promote osteoblast differentiation and bone

formation. Because silica improves osteointegration by increasing collagen production and cell attachment, these composites acquire extra bioactivity when silica is added to them. By acting as a scaffold for new tissue formation, this combination does double duty: it strengthens the bone's mechanical stability and speeds up the healing process. Research using animal models has shown that silica-magnesium composites may aid in the regeneration of bone in critical-sized defects by stimulating the production of new blood vessels and bone (osteogenesis) and by facilitating the creation of new bone (angiogenesis). In addition, the mechanical strength is maintained until the bone has healed enough to reabsorb the composite, which leaves no foreign material behind, thanks to the slow decay of magnesium alloys in the material [83].

Cardiovascular applications: Stents and vascular grafts

The creation of biodegradable stents and vascular grafts is an area where silica-based magnesium composites shine in cardiovascular applications. Stainless steel or cobalt alloy stents, the conventional

kind, are permanent implants that need further surgery to remove; magnesium's inherent biodegradability is a major advantage in this regard. One option is stents made of silica-magnesium composites, which may maintain the artery walls and blood flow while the body heals. After some time, the stents will gradually break down and be absorbed. In order to reestablish a healthy vascular network and avoid restenosis, the magnesium component promotes angiogenesis and endothelial cell proliferation. A stent's mechanical qualities are enhanced by the addition of silica to these composites, guaranteeing that it will retain its structural integrity during the early stages of healing. In addition, silica has the potential to dampen inflammation, alter the immunological response, and foster an optimal healing environment. These composites also have comparable benefits when used as vascular grafts; they may support the repaired circulatory system structurally and then dissolve away, leaving behind the regenerated tissue [84]. **Figure 5** shows Schematic illustration of bifunctional PLLA/mSiNP nanocomposite coating on the Mg stent surface [55].

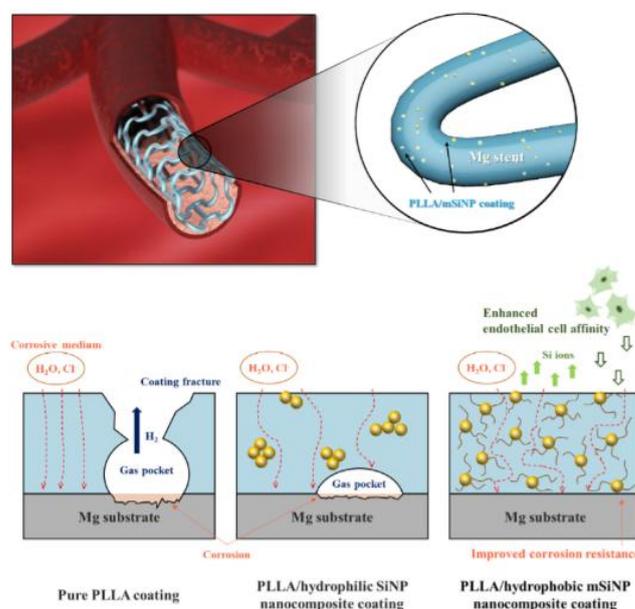


Figure 5 Schematic illustration of bifunctional PLLA/mSiNP nanocomposite coating on the Mg stent surface [55].

Drug delivery systems: Biodegradable carriers

One area of research into magnesium-silica composites is their potential use as biodegradable controlled-release medication carriers in medication administration systems. Using magnesium for

medication administration has many benefits, one of the most important being that it breaks down over time, allowing the loaded substance to be released gradually without invasive surgery. Composites with silica added increase the material's surface area, which in turn makes

it easier to regulate the dosage release. Sustained and localized medication release may enhance therapeutic benefits while limiting systemic toxicity; this is especially helpful in applications like chemotherapy. Degradation also releases magnesium ions, which may improve the drug's efficacy by acting on cellular activities. Research has shown that magnesium composites based on silica may be used to transport various medicinal substances, such as antibiotics, anti-inflammatory medicines, and anticancer agents, all while exhibiting regulated breakdown and release patterns [235-237]. This renders them very suitable for use in targeted medication administration, particularly in cases when the drug's presence must be maintained for an extended period to facilitate tissue repair or tumor suppression [85,86].

Tissue engineering: Scaffolds for regeneration

Scaffolds for tissue regeneration, particularly in soft tissues, bone, and cartilage, are well regarded in tissue engineering when made of silica-based magnesium composites. The capacity to promote the formation of new tissues relies on the unique mix of biodegradability, mechanical strength, and bioactivity offered by these composites. The scaffold acts as a mechanical support system during the early stages of recovery, but it degrades over time due to magnesium's biodegradability, enabling full resorption without removal. Crucial to these composites is silica, which improves cell adhesion, increases scaffold surface characteristics, and encourages stem cell differentiation into specific tissue types (e.g., osteoblasts for bone repair). Bioactive ions that stimulate cell proliferation, angiogenesis, and tissue remodelling may be more easily released over a surface as large as silica's. The composite scaffold offers structural support and a favourable environment for cellular processes, such as the migration, proliferation, and differentiation of stem cells; studies have shown that silica-magnesium scaffolds have the ability to regenerate bone and cartilage. With their potential for use in tissue engineering, these composites pave the way for novel regenerative medicine techniques that may be fine-tuned for particular uses, such as skin regeneration, nerve tissue mending, and orthopaedic repairs [87-89].

Industrial applications of silica-based magnesium composites

Manufacturing processes for medical devices

Because of its exceptional biodegradability, mechanical strength, and biocompatibility, silica-based magnesium composites have attracted a lot of interest from medical device manufacturers. When employed in high-performance applications like scaffolds and implants, the production procedures for these composites need accuracy. A crucial process for making silica-magnesium composites is powder metallurgy, which involves combining silica particles with magnesium alloy powders, compressing the combination under high pressure, and then sintering it. In medical applications, where controlled degradation rates and customized mechanical strength are crucial, this technique enables fine control over the porosity, microstructure, and mechanical characteristics of the composite. Also, casting and forging methods are used, too, when the situation calls for them. Implants, scaffolds, and stents all need certain geometries, and these are often achieved by processing magnesium alloys with silica inclusion into thin-walled, complicated forms. Since the silica content affects the mechanical characteristics and degrading behaviour of the material, it is important that the production process be optimized to provide a homogeneous silica content in the magnesium matrix. For these products to pass the rigorous medical industry tests for biocompatibility, mechanical performance, and *in vivo* lifespan, quality control procedures must be implemented [90-92].

Integration with 3D printing technologies

The use of 3D printing technology in conjunction with silica-based magnesium composites has completely altered the process of creating customized medical implants and devices for individual patients. Using additive manufacturing, especially 3D printing, makes it feasible to create intricate, personalized geometries that would be very challenging, if not impossible, to do with more conventional manufacturing methods. The ability to precisely manage the porosity, surface texture, and overall form of medical devices such as stents and bone scaffolds via 3D printing is crucial for facilitating tissue development and guaranteeing successful implant integration. Printable filament or ink-like solutions made of magnesium alloys and silica nanoparticles may

be extruded or deposited layer by layer. Thanks to this, scaffolds with large surface areas can be made, which helps cells connect and migrate more easily. To further simulate the heterogeneity of real bone or tissue, 3D printing also allows for the construction of scaffolds with varied mechanical characteristics throughout various implant locations. Along with these benefits, 3D printing shortens the time it takes to create prototypes and final products, which in turn lowers production costs and increases manufacturing efficiency for medical devices. Medical implants may now be improved in both functionality and performance with the use of 3D printing technologies, which allow for the exact and customized fabrication of silica-based magnesium composites [93,94].

Cost-effectiveness in medical manufacturing

When it comes to medical manufacturing, using silica-based magnesium composites may significantly save costs. This is especially true when you include in the long-term savings from fewer secondary operations and implant removals. When mixed with silica, magnesium alloys provide a viable alternative to more costly metals for making biodegradable implants, such as titanium and stainless steel. Reduced healthcare expenditures are a direct result of magnesium composites' biodegradability, which does away with the necessity for removal surgery [238-240]. In addition, there is a rising need for affordable materials that nevertheless provide good performance, and these composites find a home in the medical manufacturing sector. Due to its abundance and cheap cost, magnesium helps keep raw material prices down. Silica, on the other hand, increases the variety of possible uses by improving mechanical qualities and making it more biocompatible, all without drastically raising manufacturing costs. There is less material waste and more efficient, on-demand fabrication of patient-specific implants thanks to the integration of 3D printing technology. Various biomedical uses, including as drug delivery systems and orthopaedic implants, may benefit from silica-based magnesium composites due to their cost-effective production options. For underdeveloped nations without easy access to high-tech medical equipment, these composites may be a good alternative due to their biodegradable composition and affordable manufacturing processes [95-97].

Biocompatibility considerations for industrial use

For industrially manufactured silica-based magnesium composites, biocompatibility is still an important factor to address, especially for medical devices that touch living tissues. It is crucial to evaluate how the composite materials will interact with the body's tissues, immune cells, and fluids to make sure they won't trigger negative reactions or immunological responses. Degradation rates, ion release, and the possibility of inflammation must be carefully considered when working with silica-based magnesium composites, despite their generally outstanding biocompatibility. For example, the local tissue environment may be affected by variables such as pH, temperature, and the presence of other ions in the body, all of which can impact the rate of magnesium breakdown. By regulating the breakdown rate, silica allows for a more regulated release of magnesium ions, which in turn lessens the likelihood of local toxicity and inflammatory reactions. Enhancing biocompatibility and promoting beneficial biological interactions may be achieved by surface modifications of silica-magnesium composites, such as coating with bioactive compounds or adding functional groups. Ensuring these materials fulfil the regulatory criteria for medical devices requires a comprehensive knowledge of their behaviour *in vivo*. To guarantee the product is safe for clinical use, biocompatibility tests comprising cytotoxicity, genotoxicity, and immune response assessments must be carried out at every stage of development [98-100].

Agricultural applications of silica-based magnesium composites

Agricultural tools and implements

Composites made of silica and magnesium are becoming more popular in the farming industry, especially for use in the creation of tools and equipment for the field. These composites are ideal for uses requiring materials that can endure severe climatic conditions because the addition of silica to magnesium alloys improves their mechanical qualities, such as strength and endurance. The silica-magnesium composites provide protection against corrosion for agricultural equipment including Plows, hoes, and irrigation systems that are subjected to soil abrasion, moisture, and corrosion. Composites made of

magnesium alloys, which are already strong and lightweight, become much more resistant to wear and deterioration when silica is added. This is especially helpful for agricultural equipment that has to last a long time. In addition, these composites are great for uses where sustainability is a top priority since they are biodegradable. The use of biodegradable materials in soil-contact instruments might help alleviate a growing problem in contemporary agriculture: The buildup of non-biodegradable trash. Thus, magnesium composites based on silica may aid in the preservation of agricultural machinery for a longer period of time and reduce their impact on the environment [101,102].

Role in soil health and fertility enhancement

Magnesium composites based on silica also show potential in agriculture for boosting fertility and soil health. Photosynthesis and enzyme activation are 2 processes that rely on magnesium, a mineral vital to plant development. Soil mineral content and nutritional balance may be enhanced by adding magnesium compounds. To maximize this impact and improve soil structure, silica might be added to the composite. Soil aeration, water retention, and drainage are all enhanced by silica, which benefits root development and microbe activity. Magnesium ions are released when magnesium alloys break down in soil. Plants absorb these ions and become healthier as a result. This method of slow-release fertilization reduces the frequency of fertilization by supplying plants with magnesium gradually. And since silica is a buffer that may help neutralize acidic or alkaline soils, its presence in the composite could lead to improved soil pH management. Soil quality, nutrient availability, and long-term soil fertility can all be improved using silica-based magnesium composites, which mean they can help with sustainable agriculture [103].

Biodegradable fertilizers and pesticides

The creation of biodegradable fertilizers and insecticides is another significant use of silica-based magnesium composites in agriculture. Soil toxicity, water pollution, and biodiversity loss are some of the environmental problems that might be associated with traditional pesticides and fertilizers, notwithstanding their effectiveness. A more environmentally friendly option would be biodegradable insecticides and

fertilizers manufactured from silica-magnesium composites, which release their active components into the soil slowly and under regulated circumstances. A natural fertilizer, the magnesium ions generated by these composites may increase plant growth and harvest yields. At the same time, silica may improve nutrient stability and distribution, which means plants can absorb them more efficiently. Additionally, a more environmentally friendly method of pest management may be achieved by including biodegradable insecticides into the silica-magnesium composite matrix. There is less chance of over-application and less environmental damage since nutrients and pesticide chemicals are released gradually as the composite degrades. In line with the increasing focus on sustainable agriculture practices, silica-based composites in herbicides and fertilizers provide a safer and more ecologically conscious way to safeguard crops and regulate nutrients [104].

Impact on plant growth and crop yields

Research has shown that plant development and crop yields are positively affected by the use of silica-based magnesium composites in agriculture. Plants rely on magnesium for several essential functions, including photosynthesis, enzyme activation, chlorophyll formation, and more. Soils that are magnesium deficient may benefit from the gradual release of magnesium ions from biodegradable composites, which may improve plant development overall. Additionally, silica, a crucial micronutrient, may help plants grow stronger and healthier by increasing the production of secondary metabolites and strengthening the cell walls of plants. Root growth, nutrient absorption, and tolerance to environmental challenges like drought and disease may all be improved by silica-based composites, according to studies [241-243]. Because of these advantages, agricultural yields are increased, which is especially true for high-value commodities like maize, vegetables, and rice. These advantages, which boost agricultural output over the long run, are guaranteed by the slow degradation of silica-magnesium composites. Another way these composites help with sustainable farming is by cutting down on the usage of synthetic herbicides and fertilizers. Therefore, magnesium composites based on silica provide a potential way to enhance plant

development and agricultural production with less negative effects on the environment [105,106].

Environmental and socioeconomic impact of silica-based magnesium composites

The biodegradability and eco-friendliness of silica-based magnesium composites make them a sustainable alternative to traditional materials in many agricultural and industrial uses, which has important social and economic implications. These composites are perfect for use in medical implants, agricultural tools, and even biodegradable fertilizers and pesticides because the biodegradability of magnesium alloys is enhanced by silica, allowing them to gradually degrade in natural environments without leaving harmful residues. The use of non-biodegradable materials in industries such as agriculture and manufacturing may result in the buildup of harmful waste over time, and this degrading process helps to alleviate that problem. Furthermore, silica is an abundant and eco-friendly ingredient that adds to the composite's sustainability and helps keep environmental impact to a minimum. Despite the obvious benefits of these composites, it is important to think about the hazards and ensure the safety of everyone involved [107]. This is especially true when thinking about how quickly magnesium degrades and how it might affect ecosystems and human health. Too fast of a degradation rate can cause magnesium ions to be released into the environment, which might change the pH and hurt plants, soil, or human tissues in medical settings. It is important to carefully analyse the material qualities in diverse applications, since the addition of silica might impact the composite's long-term durability. Both consumers and businesses rely on public opinion to determine whether or not these materials are safe to employ on a large scale and effective. People may be sceptical about novel composite materials, especially in industries like agriculture and medicine where the effects on the long run are crucial [244]. To address these issues, it is crucial to have open communication, conduct thorough testing, and educate the public about the safety and advantages of magnesium composites made of silica. Finally, a cost-benefit analysis is essential from a socioeconomic standpoint for determining if these materials can be used on a big scale. Reduced environmental impact, lower disposal costs, and the potential for improved crop yields or medical

outcomes could make the long-term benefits of silica-based magnesium composites more valuable than the initial investment, which may be higher owing to specialized production techniques and material costs. As manufacturing processes improve and expand, the price of these materials might fall, allowing for their wider usage in sectors as diverse as healthcare and agriculture. Hence, silica-based magnesium composites seem to have a very positive environmental and socioeconomic impact, encouraging sustainability and providing long-term benefits across a variety of sectors. However, there are still concerns about degradation rates, safety, and public perception that need to be addressed [108].

Challenges in biocompatibility of silica-based magnesium composites

Biocompatibility of silica-based magnesium composites is an important issue in the biomedical field, and there are still many unanswered questions about this material. Some of these questions include how to control corrosion and degradation, how it will interact with other biomaterials, how long it will remain compatible in human systems, and how to standardize testing procedures. When subjected to physiological circumstances, magnesium alloys corrode quickly, which is a major problem since it may cause the uncontrolled release of hydrogen gas and magnesium ions. Although biodegradable implants and other uses benefit from magnesium's degradation, the process must be tightly regulated to prevent the material from losing mechanical strength while healing and to prevent the degradation products from harming neighboring tissues [109]. It is necessary to create sophisticated coatings and surface treatments to control the pace of corrosion since several elements, such as the alloy's composition, the presence of silica, and the local pH conditions, may affect this rate. Another major obstacle is ensuring that magnesium composites based on silica can be biocompatible with the human body over the long term. Over time, the material's disintegration might alter the local microenvironment, which in turn can create an inflammatory response or hinder normal tissue repair due to the buildup of degradation products. To make sure these composites don't harm healing or generate chronic side effects in the long run, we need to know how they behave over time, especially how they affect immune response and tissue regeneration. In addition, it is

important to consider how silica-based magnesium composites interact with other biomaterials that are often used in medical implants, including titanium alloys, ceramics, and synthetic polymers. Because problems like galvanic corrosion and impaired mechanical integrity might arise from material qualities that aren't well-matched, these interactions can affect the composite's biocompatibility and overall performance. Because of the complexity of many medical applications requiring multi-material systems, it is essential to thoroughly investigate the synergy between various materials to guarantee predictable composite behaviour in these contexts [245-248]. The last obstacle to the development and practical use of silica-based magnesium composites is the absence of established testing methodologies to determine their biocompatibility. There has to be a standardization of procedures for biocompatibility testing so that studies may consistently and reliably evaluate factors including cytotoxicity, genotoxicity, immunological response, and long-term tissue integration, among many others. Different interpretations of material performance due to inconsistent testing methods might delay regulatory clearance and the translational process for these composites [110]. To fully utilize silica-based magnesium composites in clinical settings, it is essential to overcome these obstacles by creating more effective degradation control methods, conducting long-term biocompatibility studies, evaluating material compatibility, and standardizing testing procedures.

Advanced surface modification techniques for biocompatibility

Coating techniques for silica-based magnesium composites

In order to make silica-based magnesium composites more biocompatible, surface coating is essential. Coatings limit corrosion rates and improve mechanical qualities. Despite its biodegradability, magnesium breaks down quickly in living organisms, leading to the buildup of hydrogen gas and an elevation in local pH that may have harmful effects on tissues. Anodization, plasma spraying, and sol-gel coating are among the coating methods investigated for this problem. Magnesium alloys are protected from corrosion and have their mechanical qualities enhanced by anodization, which generates an oxide coating on

their surface. One method is plasma spraying, which deposits a layer of ceramic or polymer onto the composite. Another intriguing option is sol-gel coatings, which may be functionalized with bioactive molecules and produce thin, adherent films. Coatings derived from silica, in example, may improve the material's durability and provide a good surface for cells to cling to and grow on. To further enhance biocompatibility and facilitate tissue repair, these coatings may be engineered to permit the regulated release of magnesium ions [111].

Functionalization with bioactive molecules

One potential way to improve the interaction between silica-based magnesium composites and biological systems is to functionalize them with bioactive compounds. Incorporating bioactive compounds into the composite surface allows for the stimulation of certain cellular responses that are essential for tissue regeneration. These molecules may be growth factors, peptides, or proteins. The composite surface may be modified to enhance osteogenesis and angiogenesis by adding bone morphogenetic proteins (BMPs) or vascular endothelial growth factors (VEGFs). These processes are essential for bone repair and tissue regeneration [249,250]. Chemical functionalization techniques allow for the covalent bonding of bioactive compounds to composite surfaces, guaranteeing a stable attachment and regulated release over time. The material's bioactivity is enhanced and its features are tailored to particular therapeutic demands via this method. For example, it may be used to stimulate endothelial cell proliferation to regenerate blood vessels or to facilitate osteointegration in bone healing. Adding bioactive compounds to the composite may make it more biocompatible by lowering inflammation and encouraging the body's macrophages to switch from an inflammatory to an anti-inflammatory response, which aids in healing [112].

Surface roughness and porosity optimization

Magnesium composites based on silica have different biocompatibilities and biological responses depending on surface porosity and roughness. The adhesion, proliferation, and differentiation of cells - essential for tissue integration and regeneration - can be greatly influenced by the surface microstructure. For example, cell attachment may be enhanced by a rough

surface, while nutrient and waste product transfer can be facilitated by porosity. If you want your composite to work better as a scaffold, you need to optimize these qualities. Composites may have their surface roughness and porosity modified using techniques including etching, electrochemical deposition, and laser treatment. Pores made of micro- or nanoscale material on magnesium composites, for instance, may improve osteoblast adhesion and stem cell development into bone-forming cells. Additionally, the material's porosity enables it to imitate the structure of real bone, which enhances tissue integration. To improve biocompatibility without compromising the structural integrity of the material, it is necessary to strike a delicate balance between increasing porosity and smoothness without compromising the mechanical strength of the composite [113].

Polymer blending and hybrid composites

One further cutting-edge method for making materials more biocompatible is to mix polymers and make hybrid composites using magnesium compounds derived from silica. When silica-magnesium composites are combined with polymers like poly (lactic acid) (PLA), polycaprolactone (PCL), or polyvinyl alcohol (PVA), a hybrid material is formed that combines the best features of the 2. Silica and magnesium provide bioactivity and biodegradability to the composite, while polymers enhance mechanical flexibility, processability, and degradation control. To further improve the composite's capacity to encourage tissue regeneration, the polymers may also serve as carriers for the regulated release of growth factors or medications. Furthermore, by combining different types of polymers, the composite's surface qualities may be improved, leading to better cell adhesion and proliferation. To further enhance the composite's biocompatibility and osteoinductive characteristics, natural polymers like chitosan or collagen may be used. Tissue engineering scaffolds made of hybrid composites are ideal for applications where the mechanical and bioactive characteristics of the material need to be fine-tuned to suit the requirements of certain tissues, such as vascular, bone, or cartilage. In regenerative medicine, hybrid composites that combine inorganic (magnesium and silica) and organic (polymers) components may improve

the material's overall performance via a synergistic impact [114].

Advanced technologies in biocompatibility studies

Nanotechnology and smart materials

Biocompatible materials have come a long way thanks to nanotechnology, especially silica-based magnesium composites. Improved biological responses, including enhanced cell adhesion, proliferation, and differentiation, may be achieved by employing nanoparticles to increase the surface characteristics and bioactivity of these materials. Composites with improved mechanical strength and surface reactivity may be made, for instance, by adding nanoparticles of silica to magnesium alloys. A better regulated degradation process and reduced potential cytotoxicity may be achieved via the effect of silica's nanoscale characteristics on the release kinetics of magnesium ions. Adding nanoparticles to a material may also enhance its interaction capabilities with biological tissues, which can be useful in bone healing applications where it can promote osteointegration. The idea of "smart materials," which react to environmental factors like temperature, pH, or mechanical stress, is another fascinating advancement in nanotechnology. This may include adding responsive components to silica-based magnesium composites so that they adapt their behaviour to environmental changes, such as changing the rate of disintegration or releasing bioactive compounds as required. By responding dynamically, the composite's biocompatibility may be greatly improved, making it more suitable for use in tissue repair [115].

Computational modelling of biocompatibility

Predicting and assessing the biocompatibility of silica-based magnesium composites prior to *in vivo* testing is becoming more dependent on computational modelling. These models provide light on the possible interactions between materials and cells and tissues by using sophisticated algorithms and simulations to forecast the materials' behaviour in biological systems. As an example, CFD can model the biodegradation of magnesium alloys, allowing one to foretell when magnesium ions will be released and how this would affect local pH and tissue reaction. In a similar vein, researchers may learn about a material's ability to affect cellular processes using molecular dynamics (MD)

simulations, which represent the molecular level interactions between bioactive compounds or ions and cell membranes. By finding optimal compositions, surface treatments, and degradation profiles, computational models that integrate with experimental data may speed up the creation of biocompatible materials. Before doing comprehensive laboratory testing, these models may assist in optimizing the material's qualities for particular uses, including medication delivery systems or implants. They do this by projecting the expected cellular responses, immunological reactions, and overall efficacy [116].

High-throughput screening methods

One important methodology for quickly determining if silica-based magnesium composites are biocompatible is high-throughput screening (HTS). The goal of high-throughput screening (HTS) is to expedite the evaluation of biological characteristics by testing a large number of material samples or formulations in parallel using automated procedures. Many parameters, including cell survival, proliferation, differentiation, and bioactive molecule or ion release rates, may be assessed using HTS in the setting of silica-magnesium composites. HTS systems may evaluate the composites' ability to sustain biological function in a variety of environments by using a variety of cell culture models, including simple 2D monolayers and more involved 3D cell cultures [251,252]. To find out which formulations or surface treatments result in the best biocompatibility, HTS may also be used to assess the material's interaction with different cell types such as macrophages, endothelial cells, and osteoblasts. Testing several possible composites quickly and efficiently is possible with HTS because of its scalability, which speeds up the process of developing safer and more effective materials for use in biomedicine. Researchers may learn more about how biocompatibility works, including changes in gene expression, protein release, or inflammatory reactions, by combining HTS with molecular tests [117].

Advanced imaging techniques for tissue interaction studies

The research of material-tissue interactions has been greatly enhanced by advanced imaging methods, which enable high-resolution, real-time viewing of the interactions between biological systems and silica-based

magnesium composites. Advanced imaging techniques allow for cellular and subcellular level analysis of composite surface morphology and degradation behaviour. These techniques include confocal laser scanning microscopy (CLSM), scanning electron microscopy (SEM), and transmission electron microscopy (TEM). The processes of cell attachment, migration, and differentiation on composite materials, as well as the degradation of the material and the corresponding tissue response, may be better understood with the use of these imaging methods. To better understand the long-term effects of the surface characteristics of magnesium-silica composites on cellular activity, CLSM can follow fluorescently tagged cells as they interact with these materials. In addition, imaging methods such as positron emission tomography (PET) and *in vivo* bioluminescence are used to investigate the materials' breakdown, tissue integration, and possible harmful consequences over extended periods of time in live beings. Important information on the safety and effectiveness of silica-based magnesium composites for medical uses may be gleaned from these imaging techniques, which enable the viewing of real-time tissue responses like inflammation or angiogenesis. When testing the biocompatibility of novel biomaterials over the long term, sophisticated imaging methods are vital because they reveal the exact spatial relationships between the materials and the human body [118].

Future directions in biocompatibility research

Research into the biocompatibility of silica-based magnesium composites has great promise for the future, because to developments in personalized medicine and continuous improvements in composite materials. Composite material innovations are aiming to improve the bioactivity, degradation rates, and mechanical strength of magnesium alloys for use in many biomedical applications. These applications include drug delivery systems, cardiovascular implants, and bone healing. Hybrid composites, bioactive ceramics, and nanoparticles are some of the innovative reinforcements being investigated by researchers as potential ways to improve the mechanical properties, degradation profiles, and biological behaviours of materials. On top of that, personalized medicine is gaining popularity, which means that materials' biocompatibility will be customized for each patient

according to their specific genetic makeup, environmental circumstances, and clinical conditions. Improving the success rates of implants and regenerative treatments might be achieved by tailoring the surface characteristics, degradation rates, and ion release profiles of silica-magnesium composites to each patient's specific tissue healing requirements. Biocompatibility is an ongoing process that has to be studied over many years to evaluate the performance of these sophisticated materials in real-world clinical settings, therefore long-term investigations are also crucial for clinical validation. To ensure the successful implementation of silica-based magnesium composites into clinical practice, researchers need a better understanding of their long-term interactions with human tissues, including the rates of degradation, immune responses, and tissue integration [119]. This can only be achieved through long-term *in vivo* studies. Since silica-based composites may provide a scaffolding for stem cells to repair injured tissues, its incorporation into regenerative medicine and stem cell treatment is an encouraging step in the right direction. It is feasible to create sophisticated biomaterials that promote tissue regeneration and increase the body's capacity for self-healing by merging stem cell treatment with the biological characteristics of silica-magnesium composites. These composites might be seeded with stem cells, including mesenchymal stem cells, to encourage angiogenesis in vascular tissue engineering or osteogenesis in bone repair. Thus, regenerative medicine, long-term clinical validation, personalized medicine, and material science are going to be the main points of future biocompatibility studies. This bodes well for the creation of better, more individualized biomedical solutions [120].

Socio-environmental concerns

Ecological impact of magnesium-based composites

Because of their biodegradability, magnesium-based composites, especially those that include silica, are gaining popularity as environmentally benign materials. Degradation of these materials often results in the release of non-toxic byproducts such as magnesium ions (Mg^{2+}). This quality provides a major ecological benefit over conventional, non-biodegradable materials, particularly in fields like medicine and industry where

disposal into the environment over the long term is an issue. Nevertheless, if not handled with caution, the hydrogen gas released during the breakdown of magnesium alloys might have an impact on nearby ecosystems. The fast deterioration of aquatic habitats' chemistry due to corrosion poses a threat to marine life. Minimizing possible environmental concerns requires knowing and managing the breakdown rate of these composites [121].

Sustainability of silica as a reinforcing agent

If you're looking for a sustainable reinforcing ingredient for magnesium composites, silica is a great choice. Sand and quartz are 2 of the most common and readily accessible natural sources of silica. In comparison to more conventional reinforcements made of metal or polymer, silica for composites usually requires less energy during manufacture, making it a greener option. Still, habitat destruction and energy use are 2 examples of the localized environmental consequences that might result from its mining and processing. Improving processing methods to reduce energy consumption and waste is the key to making silica-based composites more environmentally friendly, which is the biggest obstacle to their widespread usage in the future [122].

End-of-life management and disposal

Before silica-based magnesium composites are widely used, especially in industrial and medical settings, it is crucial to think about how to handle their end-of-life. Reducing the need for significant disposal methods, these composites are intended to biodegrade either inside the body or in natural habitats. The successful recycling of these composites is essential for their long-term disposal in industrial applications, such as equipment and agricultural implements. Composites containing magnesium and silica make direct recycling more difficult, despite the fact that both materials are typically recyclable. Minimizing environmental effect at the end of life requires more study into efficient recycling and disposal technologies [123].

Environmental regulations and compliance

Environmental requirements must be followed as the usage of silica-based magnesium composites grows in many sectors, especially in the biomedical field. New

materials are subjected to thorough safety and environmental impact assessments prior to market approval under regulatory frameworks for biomedical devices. These frameworks include the REACH (Registration, Evaluation, Authorization and Restriction of Chemicals) in the European Union and the guidelines on medical device biocompatibility issued by the U.S. Food and Drug Administration. Concerns including toxicity, environmental degradation, and recycling procedures are addressed by these rules, which establish criteria for the creation and use of eco-friendly products. In addition to meeting safety requirements, silica-based magnesium composites that comply with these rules will help create a more sustainable and environmentally friendly future [123].

Comparative analysis of silica-based magnesium composites with other biocompatible materials

Magnesium vs. titanium alloys in biocompatibility

While alloys made of magnesium and titanium are both quite biocompatible, their mechanical characteristics and biodegradability couldn't be more different. The biodegradability of magnesium alloys makes them useful in situations where the material has to disintegrate over time, such as in bone restoration. It may be challenging to manage the corrosion rate of magnesium, which can lead to the emission of hydrogen gas and an inflammatory reaction. Titanium alloys, on the other hand, are perfect for long-term implants but will need to be removed at some point due to their stability, resistance to corrosion, and lack of biodegradability. Composites made of magnesium and silica provide a potential alternative to surgically removed implants for short-term use, while titanium provides greater mechanical strength and long-term endurance [122].

Silica-based composites vs. polymer-based biomaterials

Magnesium composites made of silica have better bioactivity and mechanical characteristics than biomaterials made of polymers. The structural integrity needed for load-bearing applications, such as bone healing, is usually lacking in polymers, despite their flexibility and lack of toxicity. Silica, on the other hand, makes magnesium composites stronger and more

bioactive, which makes them better for bone tissue creation. Due of their slower breakdown rates, polymer-based materials may not integrate well with tissues over time. Composites made of silica have an advantage in uses that call for bone healing due to its ion release and regulated breakdown, which aid in tissue regeneration and osteointegration [123].

Performance and durability comparison

When looking at lifetime and mechanical strength, titanium alloys beat out polymers and silica-based magnesium composites. Having said that, when it comes to biodegradability, magnesium composites are the way to go for temporary implants. The controlled deterioration of magnesium is a difficulty since, in the early stages post-implantation, its mechanical stability might be compromised by its quick corrosion. This problem is solved by using silica-modified magnesium composites, which increase mechanical characteristics and decrease corrosion resistance [124].

Advantages and disadvantages in different medical applications

When it comes to temporary, biodegradable materials, magnesium-based composites, particularly those reinforced with silica, are a great choice for medical uses including drug delivery systems and bone scaffolds. The biggest drawback is that it's not easy to manage how fast they corrode, which might cause problems. Titanium alloys, on the other hand, are great for joint replacements and other uses that need structural stability and longevity. Although polymer-based biomaterials have their utility in soft tissue, they do not possess the necessary mechanical strength for load-bearing applications. When deciding on a material, it is important to consider the biodegradability, strength, and long-term stability of the medical application as a whole [125].

Case studies and clinical trials of silica-based magnesium composites

Bone repair applications

Biodegradable bone scaffolds and implants made of silica-based magnesium composites are among the many potential uses for these materials in bone healing. Their efficacy in facilitating osteointegration, in which the secretion of magnesium ions promotes osteoblast

development and enhances bone repair, has been shown in clinical experiments. As an example, research on animal models of bone repair scaffolds made of magnesium-silica composites revealed encouraging outcomes, such as lower inflammatory responses and increased bone mineralization compared to traditional magnesium implants. In these studies, the scaffold was able to sustain structural integrity throughout bone formation thanks to the controlled degradation of the composites; as the bone tissue grew, it dissolved gradually. The use of silica-based magnesium composites in temporary bone implants may prove to be a more effective alternative to conventional, non-biodegradable materials such as titanium, according to these findings [126].

Vascular implants and stent technology

Potential stent technologies based on silica-based magnesium composites are being investigated in the vascular implant sector. Because they break down naturally when the artery recovers, magnesium-based stents are a great alternative to surgical removal. Research has shown that composites made of magnesium and silica may reduce the likelihood of restenosis (re-narrowing of the blood vessel) and yet provide sufficient mechanical support for the healing process. One research found that silica-modified magnesium alloy stents improved vascularization by increasing endothelial cell migration and proliferation. Nevertheless, there are still important questions that need answering, such as how to regulate the degradation rate to prevent premature failure or an overreaction of the immune system [115].

Orthopaedic trauma and joint replacement

Because of their biodegradability, magnesium-silica composites are being investigated for use as temporary fixatives to aid in bone healing in orthopaedic trauma and joint replacement applications. Research has shown that composites made of magnesium, particularly when mixed with silica, offer many advantages over conventional metal alloys, including faster healing, less inflammation, and better tissue integration. Because they are resorbed when the bone heals, these composites might be a better option than permanent implants for fracture repair from a patient's perspective [119].

Drug delivery and controlled release

Composites made of silica and magnesium provide controlled release mechanisms for drug delivery systems, which have the potential to completely alter current methods of treatment. Their one-of-a-kind characteristics make it possible for the medication and magnesium ions to be released gradually, enabling targeted, prolonged distribution. Clinical experiments have shown that these composites may enhance the bioavailability and effectiveness of certain medicinal agents, including anti-inflammatory medicines and antibiotics, when used as drug carriers. These composites are perfect for treating localized infections or chronic illnesses since the controlled release reduces systemic negative effects and guarantees that the medicine reaches the target region properly [120].

Conclusions

Among the many promising biomedical uses for silica-based magnesium composites are drug delivery devices, vascular implants, and bone healing. Composites made of magnesium alloys with added silica are perfect for use as biodegradable bone scaffolds because they improve the material's mechanical qualities, increase cell adhesion, and induce osteogenesis. In addition, silica is essential for regulating magnesium's degradation rate, which keeps these composites stable for the right amount of time before they may safely break down in the body. Composites like this not only aid in osteointegration but also stimulate angiogenesis, a critical step in tissue regeneration, by increasing the number of endothelial cells. The development of magnesium composites based on silica still faces a number of obstacles, notwithstanding their potential. The need to regulate the *in vivo* corrosion rate of magnesium alloys is an important consideration as unchecked deterioration could cause excessive inflammation or early implant failure. Additional study is necessary to determine the optimal degradation rates for certain medicinal uses, however silica may slow things down. To further assure the safety and longevity of these composites, more research is needed to completely understand their long-term biocompatibility, especially in human systems. In terms of their prospective use in biomedicine, silica-based magnesium composites continue to hold great promise. New developments in surface modification

methods, better degradation control, and bioactivity tailoring will increase their use in clinical settings, especially in personalised medicine and regenerative medicine. These materials have the ability to revolutionize treatment tactics in several medical fields via their use in stem cell treatments, tissue engineering, medication delivery, and more flexible solutions for tissue regeneration. Problems with degradation control, long-term safety, and biocompatibility testing standards must be resolved before silica-based magnesium composites may realize their full therapeutic potential. To get past these obstacles, new approaches to material production and testing are needed. By delivering safer, more effective, and more versatile medical solutions, these composites have the potential to greatly enhance patient care if they are successfully integrated into clinical practice.

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Declaration of Generative AI in Scientific Writing

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