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Bioorganic Switching of Bioresorbable Magnesium Corrosion in Physiological Media

Robert W. Schurko[1,*]

Chemical Sciences Laboratory, Florida State University, 102 Varsity Way, Tallahassee, FL 32306-4390, USA

*Corresponding author: rschurko@fsu.edu

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Abstract

This study deals not only with the question of influence of the bioorganic molecules on magnesium alloy corrosion, but also with what physical–chemical and transport conditions lead to transformation of the same bioorganic molecule from being a catalyst of Mg corrosion to its inhibitor, from being a protective agent to become delayed corrosion factor. Literature database consisting of 67 entries has been compiled from the papers dealing with degradation of biodegradable Mg, Mg-Ca, AZ31, Mg-Zn-Zr-Y, Mg-Li-Ca, and related magnesium alloys in chlorinated saline, Hanks' solution, simulated body fluid, phosphate buffers, protein media, enzyme media, saccharide media, microbiological immersion system, and bioorganic coating system. Each entry was characterized by the material, molecule or immersion variable, immersion media, corrosion tendency, and interface reaction mechanism. The synthesis shows that bioorganic control depends on four connected switchers: ionic background, alloy surface chemistry, transport/renewal conditions, and reaction time. While Cl-rich saline enhances $Mg(OH)_2$ dissolution, Ca-P rich media are able to transform some organic molecules into mineralization promoters. Glucose accelerates the corrosion due to gluconic acid formation and chloride accumulation in Cl-rich media, however, glucose may contribute to calcium phosphate deposition in Hanks-like solution. While proteins could act as protecting agents due to their adsorption and Ca-P stabilization at quiescent exposure, flowing media could wash out the weakly bound products leading to the opposite effect. Amino acids and vitamins generate the significant alloy-dependent effects since of competition between complexing/adsorbing, Ca-containing surface chemistry, and phosphate agglomeration mechanisms. Coupled glucose-L-cysteine chemistry and glucose-enhanced microbial metabolism reveal that delayed organic reactions may play even a more important role than the initial molecule-by-molecule one. Biologically assisted coatings take advantage of the similar chemistry using glucose, amino acids, ascorbic acid, proteins, peptides, and silk fibroin for mineral, conversion, and composite surface layer formation. Therefore, Mg corrosion testing requires implant-specific medium design rather than the universal simulated fluid approach.

Keywords: biodegradable magnesium; bioorganic corrosion; physiological media; literature classification; glucose; amino acids; protein adsorption; calcium phosphate; corrosion testing.

1. Introduction

Magnesium and its alloys continue to represent one of the most intensively studied families of temporary metallic biomaterials because their density, elastic modulus, and biodegradability are more close to clinical requirements for temporary fixation in comparison with permanent stainless steel, cobalt-chromium, and titanium materials. Early investigations have demonstrated the vast possibilities of using magnesium and its alloys in medicine and biology [1]. Historical and clinical perspectives have revealed why biodegradable magnesium implants could be able to decrease the necessity in surgical reoperation to remove the implant [2]. The analysis focused on corrosion aspects revealed fast degradation and hydrogen evolution as critical limitations [3]. Reviews of magnesium biomaterials linked these limitations with alloy structure and biological performance [4]. Comparative in vitro and in vivo investigations have demonstrated strong dependence of the degradation process on the environment [5]. Broader reviews of biodegradable metals placed magnesium alloys into the general category of temporary metallic materials [6]. The Mg implant can serve as a support for healing tissue and disappear due to its controlled dissolution, which can eliminate the necessity of second surgical procedure for removal of the implant. Attraction of this concept is due to the physiological abundance of Mg^{2+} and the participation of magnesium in enzymatic, bone-remodeling, and metabolic processes. The same property of magnesium, which allows it to dissolve, is the central engineering problem: aqueous corrosion can dissolve load-carrying material, create hydrogen gas, change pH of the local environment, and induce non-uniform penetration before recovery of the tissue.

The traditional corrosion problem of Mg biomaterials was mostly focused on the decrease of average degradation rate of the alloy. This approach is useful, but it does not cover the whole picture. The discussion about the best-practice of testing revealed the significant influence of testing environment on measured degradation [7]. Reviews of biodegradable Mg alloys have underlined the significance of physiological solution chemistry [8]. Comparison of in vitro and in vivo corrosion processes has demonstrated that laboratory media can fail to simulate the biological corrosion process [9]. Further reviews have confirmed the influence of proteins, ions, and flow on surface reaction [10]. Implant surface does not contact only electrolyte;

it contacts the chemically evolved boundary layer containing chloride, phosphate, carbonate, bicarbonate, calcium, sodium, potassium, dissolved oxygen, carbon dioxide, proteins, glucose, amino acids, vitamins, enzymes, secreted compounds of cells, and in some cases microorganisms. These components do not only add minor correction to simple NaCl corrosion rate. They can affect the nature of corrosion-product layer, its compactness, adhesion, porosity, and charge transfer processes. In some cases they reverse the apparent function of organic molecule. Organic molecule, which accelerates degradation in chloride saline, may promote mineral deposition in Ca-P-containing solution; protein, which inhibits attack in static exposure, may be ineffective under flow; and molecule, which is aggressive during immersion, may become useful for construction of the corrosion-protection coating.

More detailed literature background is necessary because two different research directions have been partially isolated in their approaches. One direction investigates corrosion of Mg alloys as the electrochemical and metallurgical problem. Classical works paid much attention to hydroxide instability and peculiar electrochemical behavior of magnesium [11]. Later analysis revealed the role of impurities tolerance, alloying, and hydrogen evolution [12]. Comprehensive reviews linked corrosion with microstructure, cathodic activity, and corrosion product layer stability [13]. Biomedical studies of corrosion processes revealed the influence of pH increase and hydrogen evolution on alloy and medium properties [14]. Another direction investigates Mg alloys as the biodegradable implant materials. Reviews of testing methods paid attention to physiological buffers and limitations of simple immersion protocols [7]. Reviews of biodegradable alloys highlighted the influence of proteins, cells, and mineralization [8]. Comparisons of in vitro and in vivo tests revealed the difficulties of direct translation of laboratory rates into clinical conditions [9]. Recent reviews linked biological medium chemistry with corrosion product formation [10]. Investigations of biofunctional coatings revealed that organic molecules can be used to control corrosion intentionally [15]. Composite coatings revealed the link between corrosion resistance and osteogenic function [16]. Bioorganic corrosion is the point where both traditions meet. It needs the electrochemical accuracy of the first and physiological reality of the second. The analysis of bioorganic corrosion cannot be based on current density or only on medium properties. It should be focused on the key issue: molecular species transform the corrosion product layer while the alloy dissolves beneath it.

The analysis is based on the specific research question: *Which bioorganic constituents act as switchable corrosion regulators of biodegradable Mg alloys, and how can their effects be translated into medium-specific testing and surface design rules for bioresorbable implants?* The difference of this question from conventional review questions consists in the fact that listing of all reported organic additives is not the aim. The aim is identification of variables, which lead to sign changes in corrosion response: acceleration, stabilization, corrosion protection, or conditional behavior. Each visual element in the following scheme is interpreted through corrosion decision, corrosion mechanism, or testing rule, which it supports.

Clinical translation of Mg alloys is difficult partly because degradation is often considered as a single material constant. The literature record suggests that such approach is too limited. The best practice guidelines have shown that the chemistry of immersion should be specified before the comparison of corrosion rates [7]. Methodological investigations have demonstrated that pH control and solution renewals can significantly affect magnesium degradation [17]. Reviews of biodegradable Mg alloys have underlined the influence of buffer composition and physiological ions [8]. Comparisons of in vitro and in vivo tests have revealed that laboratory rankings can be changed under biological exposure [9]. Recent investigations have confirmed the influence of proteins and flow on corrosion product formation [10]. Corrosion rate in static chloride solution is a measure of susceptibility to hydroxide film destruction; corrosion rate in Hanks' solution is a measure of capability of nucleation of Ca–P deposit; corrosion rate in serum-containing flow solution is a measure of stability of corrosion film under adsorption and renewal. The same alloy may generate different rankings in different media because the controlling process is changed. The recognition of such distinction allows to treat the contradictory results as the data and not as the noise.

The second reason of mechanism-based framing consists in the fact that bioorganic molecules are not passive additives. The carboxylate, aldehyde, amine, thiol, aromatic, and heterocyclic groups can participate actively in adsorption, chelation, acid formation, phosphate aggregation, and calcium binding. Such processes occur in boundary layer, which is already enriched with Mg^{2+} and OH^{-} due to anodic dissolution and cathodic hydrogen evolution. Therefore, chemical environment of amino acid or glucose molecule at corroding surface is different from bulk solution described in the experiment. The following analysis treats each bioorganic effect as the interfacial process involving the molecule, the ionic medium, the alloy surface, and corrosion products, which develop with time.

The physiological corrosion environment is shown in Figure 1. The implant surface is represented as the reactive interface and not as the passive metal coupon. Alloy chemistry, processing history, and surface roughness determine the metal side of interface, whereas inorganic ions, organic molecules, pH, oxygen availability, carbon dioxide, flow, tissue location, and microorganisms determine the solution side. Consequently, a useful Mg corrosion test should keep the specific interaction, which occurs in the particular implant environment. Bone screw, vascular scaffold, gastrointestinal device, and implant for diabetic patients do not need the same chemical simplification.

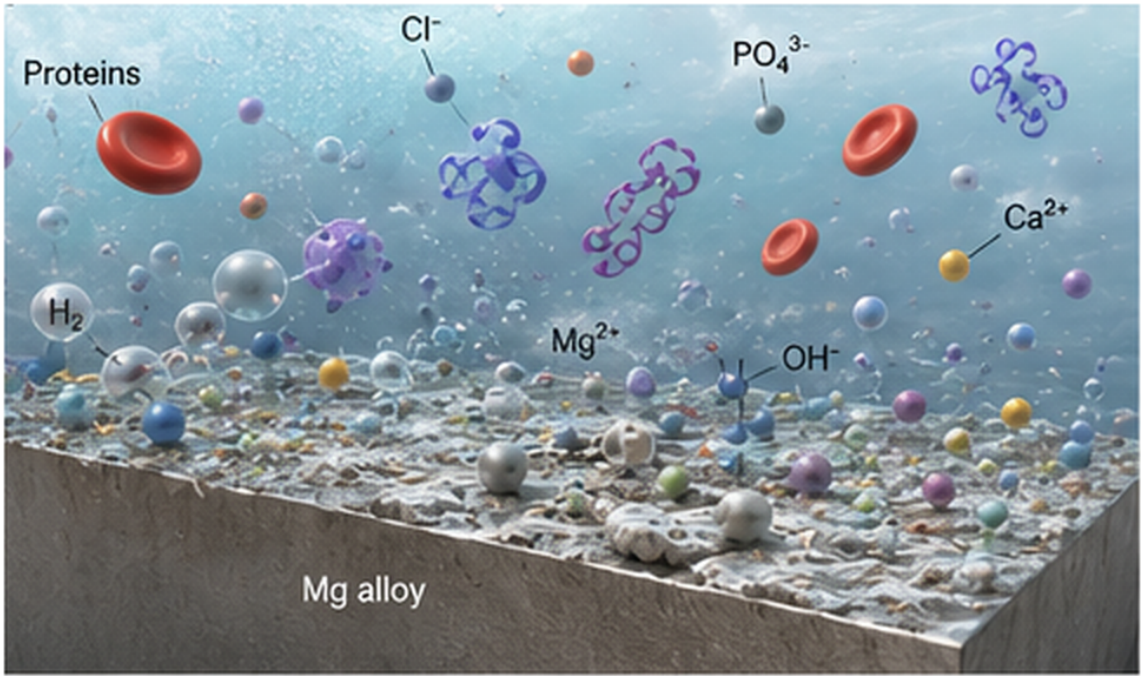

Figure 1: Reactive implant interface.

The environmental map in Figure 1 sets the logic of the following analysis. The principal message is that the electrolyte cannot be simplified only by chloride concentration. Chloride initiates and maintains the process of $Mg(OH)_2$ destruction, but phosphate, calcium, carbonate, and bioorganic molecules determine whether the damaged surface will stay open, will be mineralized, will get the protein layer, or will form the loose and unstable product layer. From the point of view of experimental design it means that corrosion rate in 0.9 wt.% NaCl is not an intrinsic property of material. It is the response of material-medium pair. This distinction is especially important when uncoated alloys are compared with the bioorganic coatings. The same molecule can be in test fluid, in surface film, and in degradation products.

2. Scientific Background

Magnesium corrosion begins with anodic dissolution,

$$\mathrm{Mg} \rightarrow \mathrm{Mg}^{2+} + 2e^{-}. \tag{1}$$

The dominant cathodic route in neutral and alkaline aqueous media is hydrogen evolution,

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

Oxygen reduction can also contribute when dissolved oxygen reaches the surface,

$$2\mathrm{H_2O} + \mathrm{O_2} + 4e^{-} \rightarrow 4\mathrm{OH}^{-}. \tag{3}$$

These reactions generate Mg^{2+} and OH^{-}, which form magnesium hydroxide,

$$\mathrm{Mg}^{2+} + 2\mathrm{OH}^{-} \rightarrow \mathrm{Mg(OH)_2}. \tag{4}$$

The apparent protection associated with $Mg(OH)_2$ is unstable in chloride-containing environments because chloride converts the hydroxide layer into soluble or poorly protective products,

$$\mathrm{Mg(OH)_2} + 2\mathrm{Cl}^{-} \rightarrow \mathrm{MgCl_2} + 2\mathrm{OH}^{-}. \tag{5}$$

Carbon dioxide introduces a buffering pathway through carbonic acid and bicarbonate formation,

$$\mathrm{H_2O} + \mathrm{CO_2} \rightleftharpoons \mathrm{H_2CO_3}, \tag{6}$$

$$\mathrm{H_2CO_3} + \mathrm{OH}^{-} \rightleftharpoons \mathrm{HCO_3^{-}} + \mathrm{H_2O}. \tag{7}$$

It is explicitly stated here that these equations should be interpreted as an interface network rather than as electrochemical facts in isolation. Hydrogen evolution increases pH in the local area and promotes precipitation whereas chloride constantly

reopens the same layer which alkalization tries to stabilize. The combination of carbonate and phosphate allows immobile cation precipitation but the layer is protective only when it is dense enough. Organic molecules enter the interface network through complexation with Mg^{2+}, adsorption at metal/product interface, changes in pH in the area, alteration of Ca–P precipitation or interaction with other organics.

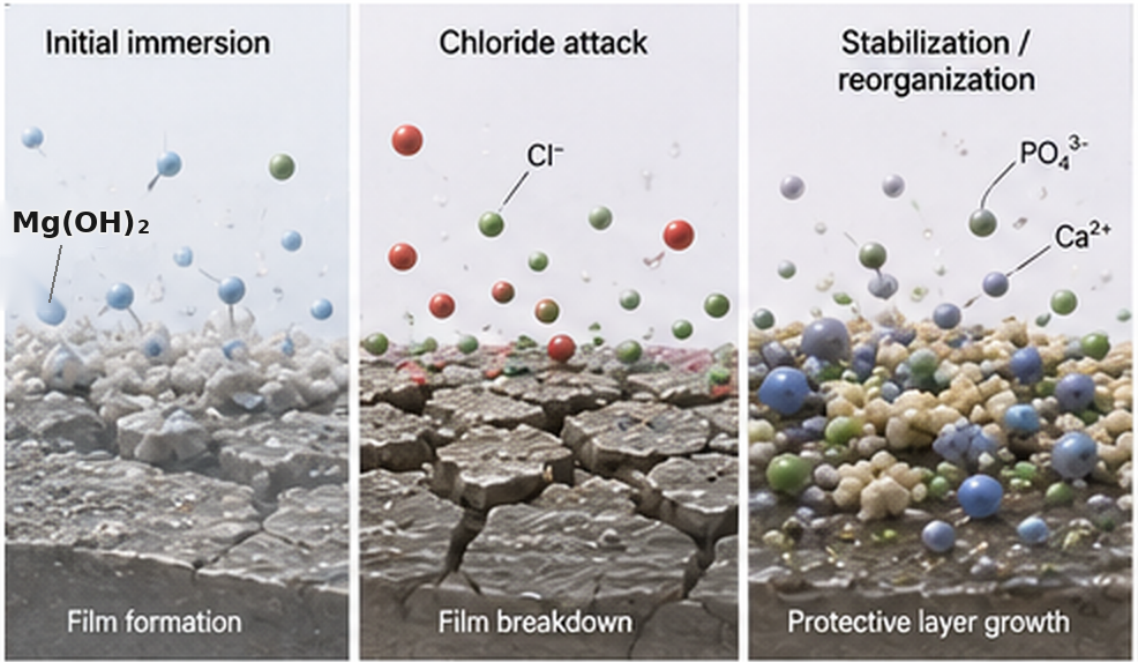

Figure 2: Corrosion-product transitions.

The scheme of the reaction in Figure 2 shows why the molecule cannot be defined accurately unless the medium is specified. Organic acids and carboxylate molecules can dissolve $Mg(OH)_2$ and increase chloride penetration in saline medium. The carboxylate can also precipitate Ca^{2+} in Hanks' solution or simulated body fluid. The interpretation of such reaction requires the knowledge of the entire pathway from the molecule to surface product rather than just the molecule's name. This issue is the basis of the literature-classification approach to use below.

The interpretation of the scheme requires distinguishing the thermodynamic tendency and kinetic persistence of the process. Mg oxidation and cathodic reduction are favorable reactions but the relevant question is whether corrosion products will be stable enough to inhibit transport. First corrosion research has demonstrated the instability of Mg surface films in chloride medium [18]. Electrochemical analysis has revealed a special relationship between magnesium dissolution and hydrogen evolution [11]. Later research has related the effect of alloy chemistry and corrosion products formation as well as the role of impurities [12]. Comprehensive reviews have demonstrated that the product-layer density, crack formation, and local cathodic activity define the persistence [13]. $Mg(OH)_2$ can form a protective layer only temporarily under local alkalization condition. But chloride makes the layer less stable and reopens active areas. Phosphate and carbonate products can be less soluble but their usefulness depends on the nucleation density, adhesion, and resistance to cracks during hydrogen evolution. Organic molecules affect precisely these persistence parameters. They can dissolve Mg^{2+} complexes and thus increase the solubility or enhance the stability of the products by bridging the defects and covering active areas with Ca–P precipitation.

3. Materials and Methods

A literature record of 67 entries was compiled to interpret corrosion observations as material-specific and medium-specific comparisons. It is not a meta-analysis due to the differences in alloy composition, surface finishing, solution volume, immersion time, electrochemical method, temperature, pH regulation, solution renewal, and reporting style of the cited studies. Each corrosion observation was classified as a directional mechanism record. The accompanying file `literature_record.csv` includes 67 records. Each record defines the material class, molecule or exposure variable, medium, corrosion tendency, mechanism class and citation key of the supporting study. The classification is chemical in nature: the comparison is performed between mechanism classes without the forceful integration of different corrosion rates in one numeric scale.

Table 1: Literature-record structure.

Record field	Question answered	Example entry	Use in interpretation
Material	Which substrate was tested?	CP Mg, Mg–0.8Ca, AZ31, Mg–Li–Ca	Separates organic effects from alloy-specific surface chemistry
Organic constituent or exposure	What variable was changed?	Glucose, BSA, L-cysteine, dynamic flow	Identifies the active organic or transport condition
Medium	Where did the reaction occur?	NaCl, Hanks, SBF, phosphate buffer	Prevents false generalization across fluids
Direction	What tendency was reported?	Accelerating, protective, stabilizing, mixed	Captures sign changes and reversals
Mechanism category	Why did the effect occur?	$Mg(OH)_2$ damage, Ca–P deposition, adsorption, chelation	Links response direction to a surface process
Citation key	Which reference supports it?	`Mei2019`, `Hou2020`	Links each entry to its supporting publication

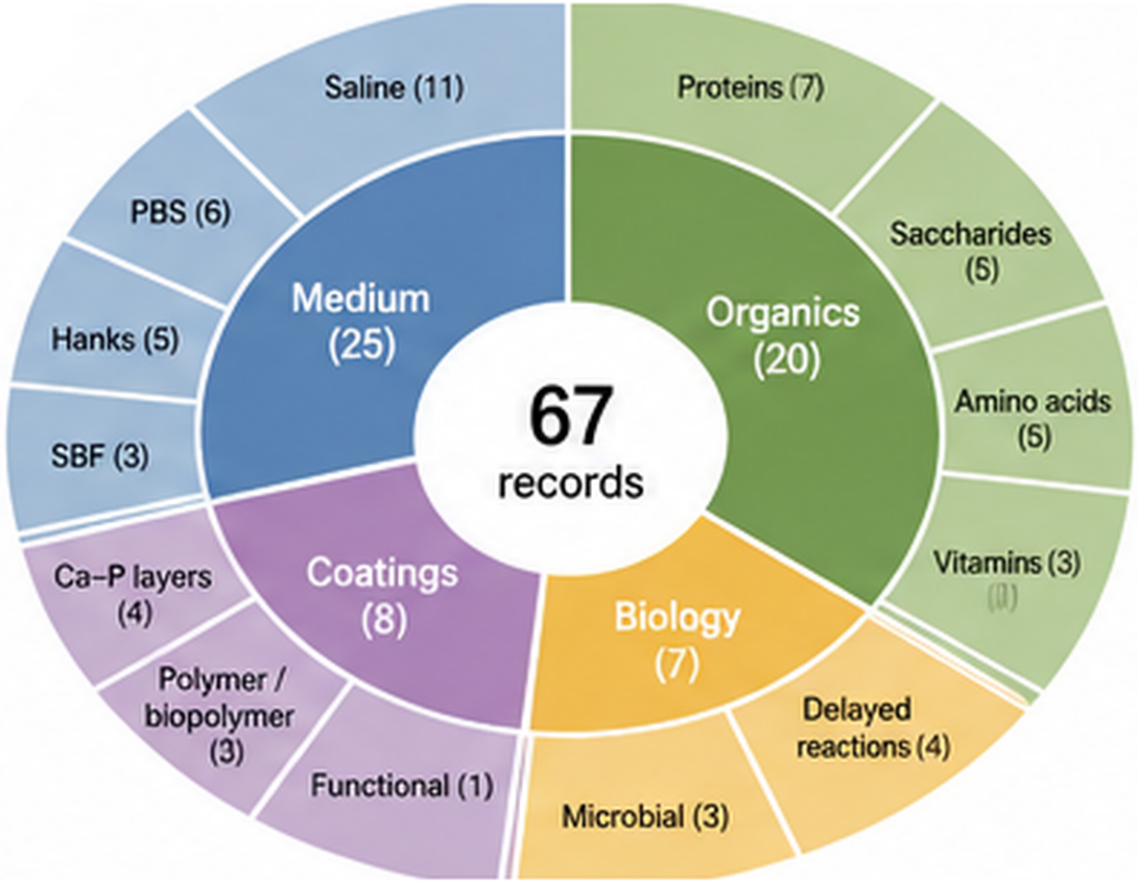

Figure 3: Classified evidence distribution.

The distribution chart in Figure 3 brings organization to the literature record prior to the discussion of mechanism-specific topics. The central count of record defines the evidence base, while the surrounding divisions distinguish medium chemistry, dissolved organics, biological drift, and coating data. This organization is crucial because the following discussion does not treat all records as equivalent measurements. Each record is interpreted as a material-medium-response measurement, which tells the reason behind molecular acceleration of corrosion in one medium and stabilization of the surface in another.

This record organization makes clear the use of the literature evidence. The intention is not to say that all rows are equal measurements. Electrochemical test record, immersion mass loss record, and surface morphology record differ in evidentiary value but can be compared as mechanism-direction statements when the material and medium are preserved. The 67-entry record answers the research question by revealing the repetitions: glucose reverses sign between NaCl and Hanks-type media, protein reverses sign between static and dynamic exposures, and amino acids reverse sign between CP Mg and Mg–Ca alloys.

The classification follows three controls: citation traceability, medium specificity, and separation of solution chemistry from coating chemistry. Only relative to the control condition used in the cited paper a corrosion response is recorded, only in a specific medium a molecule is marked as inhibitor or accelerator, and a coating protection method is separated from the same molecule dissolved in solution. These controls are critical because bioorganic effect is often exaggerated once molecules

are separated from the experimental conditions.

These literature records are further classified in mechanism families. Dissolution and complexation records reveal cases of prevention of stable precipitation or increase in soluble Mg-containing species. Adsorption records reveal cases of reduction of access to reactive sites via proteins, amino acids, and peptides. Mineralization records reveal Ca–P, hydroxyapatite, or conversion-film pathways. Transport and biological-drift records reveal flow-mediated removal, enzyme-specific disruption of product or microbial acidification. The classification differentiates the analysis from a review due to the identification of switching rules.

The same literature record defines the strength of each claim. Statements are not generalized to broad claims unless the record contains the material, medium, and response direction. If a study provided only qualitative morphological change in surface, the record was used for formulation of a mechanistic statement rather than ranking of performance. If a study compared concentrations, the trends were preserved in the table like in saccharide and amino-acid tables. Such approach helps to keep the analysis grounded on the original evidence without the false precision in combination of current density, mass loss, hydrogen evolution, and microscopy measurements.

This procedure puts the particular emphasis on the reversals. Conventional review could consider opposite reports as disagreements produced by experimental variations. Classification approach asks about presence of the controlling variable among the opposite responses. Among the recorded literature, most of the reversals correspond to the change in ionic background, substrate composition, flow, concentration, and exposure duration. The recorded comparisons thus transform potential inconsistencies into a diagnostic pattern: a molecule becomes switchable when it has enough chemical functionality for participation in competing interfacial pathways.

4. Results

4.1 Medium chemistry and surface-product stability

The first result from the literature map is that inorganic medium chemistry defines the boundary condition of all organic phenomena. The susceptibility of biodegradable Mg alloys to chlorides was linked with breakdown of $Mg(OH)_2$ and localized dissolution [19]. Subsequent work confirmed the sensitivity of magnesium degradation to aggressive physiological ions [20]. Phosphate buffers and SBF-like solutions create further channels through the Mg phosphate, Ca phosphate, carbonate, and mixed corrosion-product generation. Hanks' solution, Earle's solution, and culture media introduce bicarbonate, glucose, amino acids, and sometimes proteins, turning the surface into a mineral-organic interface instead of just a hydroxide/chloride interface. Reviews of biodegradable Mg testing emphasize the necessity of reproducing physiological temperature and pH [8]. Guidance on best practices also highlights the importance of buffer chemistry and fluid renewal [7]. Later reviews emphasize the roles of proteins and other organic factors [10]. Comparisons of in vitro–in vivo conditions make the necessity of physiological relevance clear before making any biomedical conclusions [9].

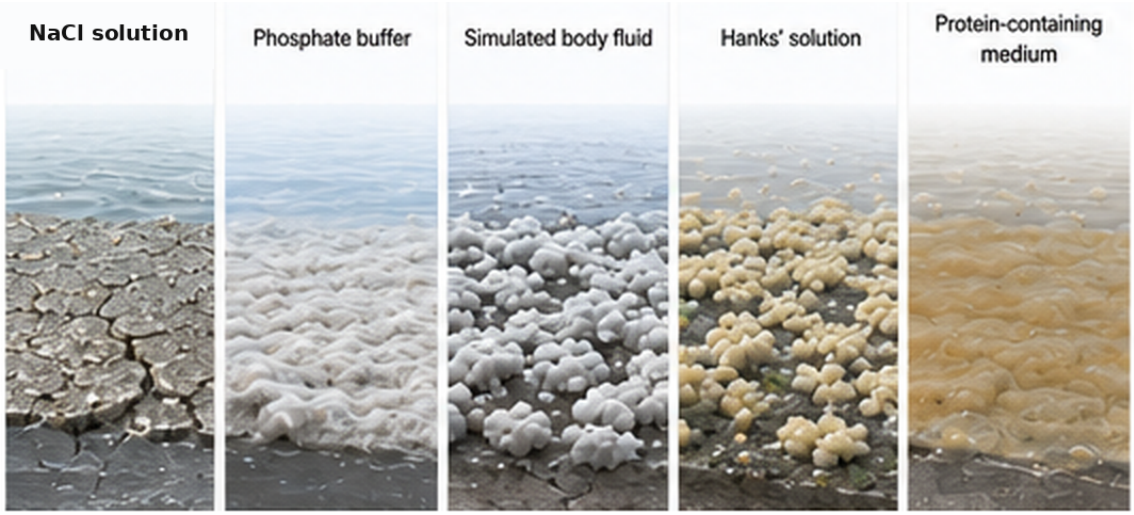

Figure 4: Medium-dependent surface states.

As can be seen from Figure 4, corrosion rankings in one medium cannot simply be extrapolated to another because of medium-specific chemical pathways. Exposure to saline mostly tests the breakdown of hydroxide films and localized chloride attack. A medium containing calcium and phosphate checks whether the dissolved products can reform into a mineral layer. A medium with proteins or cells adds adsorption and complexation. The consequence of the described sequence is that

the test target changes: from resistance to chloride attack to formation of mineralized precipitates to maintenance of an organic-mineral layer under biological chemistry. Thus, the same alloy can look unacceptable in one test and promising in another without any result being wrong.

For the design of corrosion experiments, the above-described result provides a practical rule. Saline is still important as an aggressive medium to test material's resistance to corrosion, but it should be understood as a stress test, not a full-spectrum physiological simulation. Solutions like SBF or Hanks-like solutions are more appropriate if the mineralization of the surface is expected to define orthopedic corrosion rate. Fluids with proteins are required when the medical device is exposed to flowing blood or interstitial fluid. Glucose and sterile conditions are required when the diabetic or nutrient-rich conditions are relevant. So, the record of 67 media supports the following rule for media selection: pick the simplest medium that simulates dominant physiological interaction, not the medium that enables obtaining convenient corrosion number.

The medium-dependent result also helps to understand why translation of in vitro results into in vivo situation for degradable Mg is challenging. In vivo surface is constantly affected by buffering action of tissue, protein renewal, cellular uptake, carbonate exchange, and mechanical disturbance. Static medium in vitro can simulate selected chemical factors but tends to overestimate local supersaturation, amplify the pH increase, and keep corrosion products that would be removed or remodeled in tissues. That is why medium should be chosen depending on the research question: NaCl for chloride sensitivity, phosphate buffer for precipitation chemistry, Hanks-like media for mineralized tissue fluid, serum-containing media for proteins, and dynamic systems for transport-limited interfaces.

The presented data also explain why chemically similar media give different results. Chloride and buffered chloride solutions both contain aggressive ions, but the buffered solution modifies alkalization and precipitation processes. Hanks' solution and SBF both contain mineral-forming ions, but their ionic composition, bicarbonate presence, and renewal conditions shift the surface state from loose deposits to more coherent Ca-P layers. Culture media include amino acids, vitamins, glucose, and proteins that could either stabilize corrosion products or complex them and make them more soluble. The consequence of such sequence is not a smooth range of "more physiological" media but a set of chemical tests with different interfacial mechanisms emphasis.

The interpretative power of the above-presented result is maximal in case of using media contradicting each other. A chloride-only test checks whether the corrosion product can resist aggressive ions. A mineral-forming test checks whether dissolution products can be reorganized into the barrier. Serum-containing test checks whether an organic layer can stick while continuing to produce alkalinity and hydrogen. They are not competing definitions of physiological correctness but different experimental questions. Therefore, a rigorous corrosion study should define the question, which is being answered by the medium before presenting corrosion response.

4.2 Protein adsorption and fluid transport

Protein adsorption is the fast biological event after implantation of a material in vivo. Albumin, fibrinogen, serum proteins and other components of plasma can form adsorption layers and influence electrochemical reactions, cells' behavior, bacterial adhesion and corrosion products growth. Albumin was found to inhibit corrosion of Mg-Ca alloys and filament corrosion caused by chlorides [21]. Medium containing serum proteins was found to alter the magnesium corrosion and product formation [22]. A more recent study also demonstrated the role of serum in Ca-P deposition and organic-mineral adhesion [23]. This effect explains the reasons why protein-free experiments may overestimate corrosion in some stagnant exposure cases.

The effects of proteins, however, are not always protective. Depending on transport conditions proteins can provide protection or stimulate corrosion. Under the static immersion proteins can cover active areas, hinder electrolyte access and favor the deposition of products rich in Ca-P. Dynamic flow can lead to opposite effects due to removing the weak adsorption layer, corrosion products and local saturation of protective ions. Dynamic flow also reduces pH increase near the surface needed for the stability of $Mg(OH)_2$ and other mineralized products. Thus, the dynamic effects are essential for vascular scaffolds and blood-contacting devices when static immersion is not an adequate substitute of service conditions.

The dynamic protein flow sequence in Figure 5 allows distinguishing two phenomena, which are often confused. Protein adsorption can be protective on the molecular scale, but adhesion under dynamic flow is needed for protection of devices. If the renewal rate exceeds the protein/mineral layer formation rate, the inhibitor becomes an element of the unstable interfacial cycle. It also means that the measurement of only the protein concentration cannot describe its effects on magnesium corrosion. The adequate reporting protocol should include shear or flow condition, renewal rate, pH control, calcium and phosphate concentration, and exposure time. The absence of these parameters makes protein-containing tests uncomparable between laboratories.

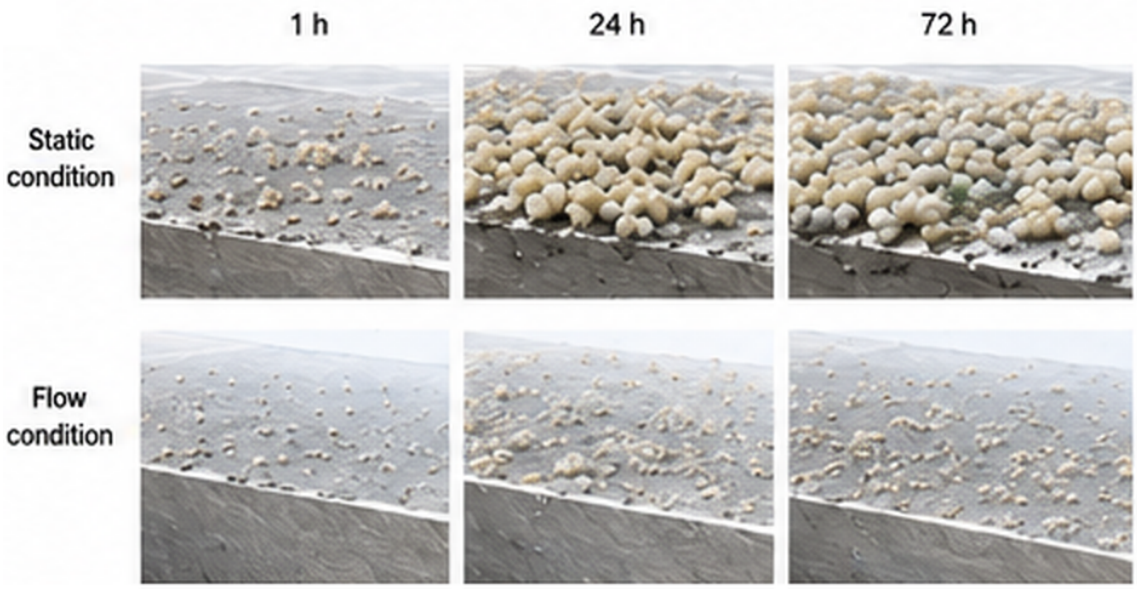

Figure 5: Protein retention under transport.

One more consequence is that protein adsorption has to be considered as the competitive phenomenon, rather than the protective film. Protein can block reactive areas, but it also can chelate metal ions, influence the wetting properties, local transport and adhesion of mineral products. Surface alloy composition is an additional factor because the second phases and alloying elements can have different preference for protein fragments. The observations that calcium and cerium-containing areas can enhance fibrinogen fragment adsorption and other elements have different preferences indicate that biological layer can be heterogeneous according to the microstructure. If the protein layer is unevenly distributed, then it can protect from corrosion some areas and leave other galvanically active parts unprotected.

In this context, the results about proteins suggest the need to include flow and surface chemistry in the reporting standards. The albumin adsorption can reduce the direct access of chloride under suitable conditions [21]. The observations related to serum show that the retention of Ca-P and adhesion of the film depends on the medium [23]. The concentration of albumin or serum cannot explain whether the layer is attached, what kind of mineral products are retained and whether the local chloride access is limited. For the vascular devices the static serum test can be useful for describing the adsorption but not service adhesion, while for bone-contacting implants the weaker flow can be sufficient for adsorption-assisted mineralization.

Enzymes are an example, which is similar to the protein case, but is even more specific. The pepsin-containing simulated gastric fluid was shown to change the corrosion product layer and decrease the local attack of Mg wire [22]. On the contrary, pancreatin-containing simulated intestinal fluid can accelerate corrosion due to the disturbing $MgHPO_4$-rich products [24]. The point here is not only the fact that the enzymes are proteins, but the fact that the catalytic properties and organ-specific chemistry of the medium determine the product-layer evolution pathway. The gastrointestinal magnesium devices, therefore, have to be tested in the specific media mimicking each organ.

4.3 Biochemistry of saccharides and glucose-based response switching

Among other examples of bioorganic sign switching, glucose stands out because of its physiological relevance in biological fluids and even higher importance in the case of diabetes. It was shown in glucose-based corrosion studies that the substance can promote Mg corrosion in chloride-containing solutions [25]. Other works related this effect with glucose oxidation, acidification, and formation of soluble magnesium carboxylates [26]. Other studies related to bioorganic reactions demonstrated that the same substance can act differently in phosphate- and calcium-containing solutions [24]. Finally, more recent researches established the connection between glucose-based species and Ca–P deposition along with the change in surface protection [27]. Under chloride-containing saline, glucose can be oxidized to carboxyl-containing products, such as gluconic acid. This products react with $Mg(OH)_2$, reduce pH locally, form soluble magnesium carboxylates, and help retain Cl^- ions on defective surfaces, resulting in weak surface, prone to crack growth and new corrosion. Under Hanks solution, the presence of Ca^{2+} and phosphate will change the reaction path; glucose or glucose-based species can contribute to Ca–P deposition on the surface, making it more protected.

The simple reaction pathway is:

$$CH_2OH(CHOH)_4CHO \xrightarrow[37^\circ C]{O_2} RCOOH, \tag{8}$$

$$2\mathrm{RCOOH} + \mathrm{Mg(OH)_2} \rightarrow (\mathrm{RCOO})_2\mathrm{Mg} + 2\mathrm{H_2O}. \quad (9)$$

These formulas explain the saline case, but they are not sufficient to predict the Hanks case, where competitive precipitation comes into play. Presence of calcium and phosphate allows carboxyl-containing compounds to influence calcium deposition and phosphate nucleation, moving the interphase away from hydroxide dissolution.

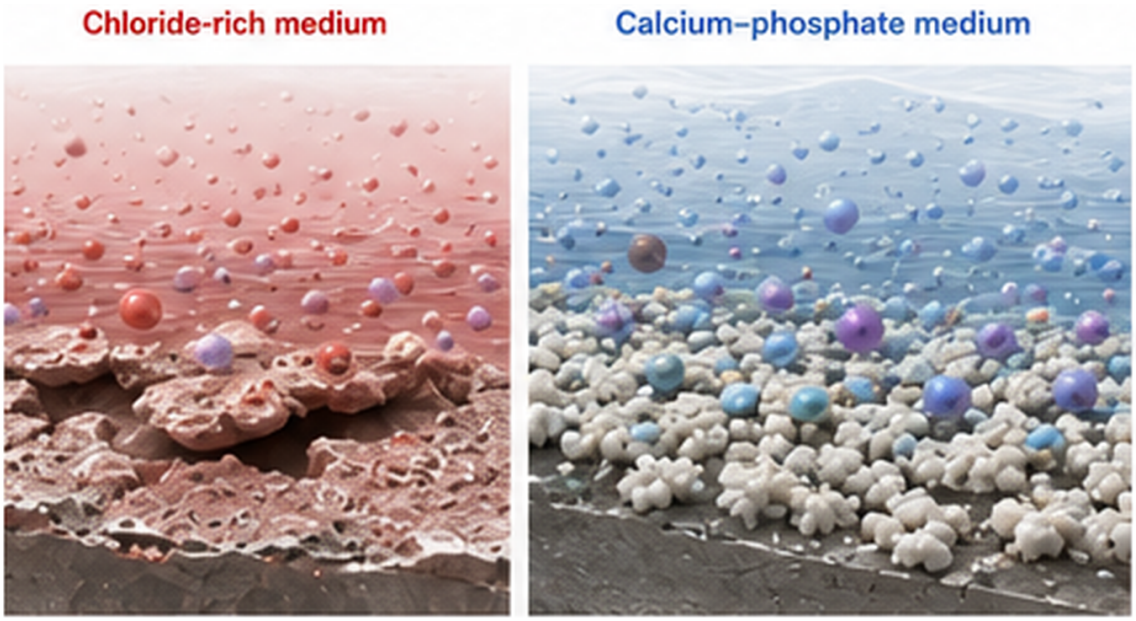

Figure 6: Glucose-dependent surface contrast.

The glucose contrast in Figure 6 solves one half of the research problem. Glucose is neither a corrosion accelerant nor inhibitor, as an isolated variable. It amplifies whatever reaction network is predominant in the medium. In saline, that network consists of hydroxide film disruption and chloride retention, so glucose-induced acid chemistry is destructive. In Hanks solution, there is a Ca–P precipitation reaction network, so glucose can provide a more persistent protective layer. This result has implications for diabetic implant evaluation: adding glucose to the saline does not mimic mineralized tissue fluid, as it will emphasize corrosive chemistry while lacking Ca–P buffering.

The table with saccharide responses in Table 2 demonstrates that the sign of the response is joint function of sugar type, alloy composition, and medium. Pure Mg and Mg–0.8Ca do not exhibit identical responses to galactose, fructose, and mixed saccharides. The alloy with calcium is more vulnerable to organic disruption in saline, but can utilize SBF chemistry to form protective Ca–P phase. From the experimental design perspective, it means that saccharides should be recorded along with concentration and ionic background of the medium. Glucose concentration alone, without information about the medium, is not a transferable corrosion variable.

Concentration values in the saccharide table reveal why careful diabetic simulation experiments are required. High glucose concentration in NaCl isolates aggressive acid and chloride-retention chemistry, while high glucose concentration in a Ca–P-containing medium tests whether mineralization is able to overcome this aggressive pathway. The difference is crucial because clinical hyperglycemia is never observed in a medium stripped of calcium, phosphate, proteins, bicarbonate, and cellular buffering capacity. Thus, a magnesium alloy diabetes simulation experiment should keep glucose concentration and physiological ions competing with glucose-derived corrosion products. Such an experiment will either confirm or deny the presence of a corrosive hazard in the mineralized tissue environment, but the latter cannot be exaggerated.

Saccharide records also demonstrate that glucose is not an adequate representative of carbohydrates in terms of their corrosion effects. Comparative glucose studies already demonstrated dependence on medium composition and alloy state [25]. Bioorganic corrosion studies proved that different saccharides affect pure Mg and Mg–Ca alloys differently [24]. Further research confirmed that glucose-derived chemistry can interact with Ca-containing phases and precipitated products [27]. This explains why galactose, fructose, glucosamine, and mixed saccharides show different signs on pure Mg and Mg–0.8Ca. Glucosamine can accelerate corrosion even in saline and SBF, while fructose can promote phosphate-rich deposits in simulated body fluid.

Table 2: Saccharide response map.

Material	Saccharide	Concentration	Medium / additive	Observed tendency
Pure Mg	Glucose	0, 2.5, 5.0 wt.%	0.9 wt.% NaCl	Increasing corrosion with concentration
Pure Mg	Glucose	1, 2, 3 g L^{-1}	Hanks solution	Lower corrosion at 3 g L^{-1}
Mg–1.35Ca	Glucose	0, 25, 50 g L^{-1}	0.9 wt.% NaCl	Increasing corrosion with glucose
AZ31	Glucose	0–3 g L^{-1}	NaCl + Tris	Higher glucose accelerates corrosion
Mg–Zn–Zr–Y	Glucose	1 and 3 g L^{-1}	Hanks solution	3 g L^{-1} gives lower corrosion
AZ31	D-fructose	1 g L^{-1}	Simulated body fluid	Decreases corrosion by phosphate deposition
Pure Mg	Glucose	5.83×10^{-3} M	0.9 wt.% NaCl	Accelerated
Mg–0.8Ca	Glucose	5.83×10^{-3} M	0.9 wt.% NaCl	Accelerated
Pure Mg	Galactose	1.11×10^{-3} M	0.9 wt.% NaCl	Decelerated
Mg–0.8Ca	Galactose	1.11×10^{-3} M	0.9 wt.% NaCl	Accelerated
Pure Mg	Glucosamine	4.97×10^{-3} M	0.9 wt.% NaCl	Accelerated
Mg–0.8Ca	Glucosamine	4.97×10^{-3} M	0.9 wt.% NaCl	Accelerated
Pure Mg	Fructose	4.44×10^{-4} M	0.9 wt.% NaCl	Decelerated
Mg–0.8Ca	Fructose	4.44×10^{-4} M	0.9 wt.% NaCl	Accelerated
Pure Mg	Mixed saccharides	Physiological mixture	0.9 wt.% NaCl	Decelerated
Mg–0.8Ca	Mixed saccharides	Physiological mixture	0.9 wt.% NaCl	Accelerated
Pure Mg	Mixed saccharides	Physiological mixture	SBF	Accelerated
Mg–0.8Ca	Mixed saccharides	Physiological mixture	SBF	Decelerated

4.4 Amino Acids, Vitamins, and Metal Alloy Specific Response

Amino acids control magnesium corrosion via multiple pathways at the same time including adsorption via amine, carboxyl, thiol, aromatic or heterocyclic functionalities, Mg^{2+} chelation, phosphate association and surface product alteration. Alanine, glutamic acid and lysine can help form phosphate containing product in phosphate buffer solution, while L-cysteine can adsorb onto pure magnesium via deprotonated carboxylate and sulfide functionality under basic condition. The inhibition process can be depicted as:

$$\mathrm{Mg(OH)_2 + 2RCHNH_2COOH \rightarrow (RCHNH_2COO)_2Mg + 2H_2O}, \tag{10}$$

$$\mathrm{Mg^{2+} + RCHNH_2COO^- + H_yPO_4^{(3-y)-} \rightarrow Mg(RCHNH_2COO)_xH_yPO_4}. \tag{11}$$

The same coordination chemistry may be dangerous when soluble complexes block the precipitation of an insoluble protective film. Medium studies of organic constituents in protein- and amino acid-containing media showed the inhibiting or accelerating effect of these compounds on Mg degradation [22]. Studies of glucose and amino acid interactions confirmed that combined organic compounds affect local corrosion chemistry [25]. Studies of amino acids in particular demonstrated the connection between side-chain chemistry, adsorption, complexation, and product-layer formation [28]. More extensive bioorganic studies proved that effects of amino acids depend on the alloy and medium type [24]. This dual nature is the reason for greater variability of amino acid effects than the effects of inorganic ions.

The chart in Figure 7 presents the strongest reversals in the history of effects of organic compounds on Mg. Rows with opposite colors in CP Mg and Mg–0.8Ca show that side-chain chemistry alone cannot determine the role of an amino acid or a vitamin. Cysteine, aromatic amino acids, and selected vitamins become interesting due to their different directions depending on the alloy chemistry. Therefore, the visual presentation justifies the table that follows: adsorption, coordination, and mineralization processes should be considered along with alloy composition, pH, concentration, and immersion time.

The table of amino acids shows the strongest alloy dependence in the 67-entry record. The inhibition effect of glycine in Hanks solution may evolve into the corrosion acceleration due to the evolution of surface layer chemistry [29]. General comparisons of effects of amino acids on Mg and Mg–Ca alloys proved strong alloy-dependent reversals [24]. Many amino acids accelerate corrosion of Mg–0.8Ca in NaCl medium while slowing down the corrosion of CP Mg. This reversal indicates that Ca content in alloy affects the interaction of amino acids with corrosion products. The response of organic molecules is not determined by the polar character and size of molecules but by the ability of organic compounds to stabilize or destroy the alloy-dependent surface layer.

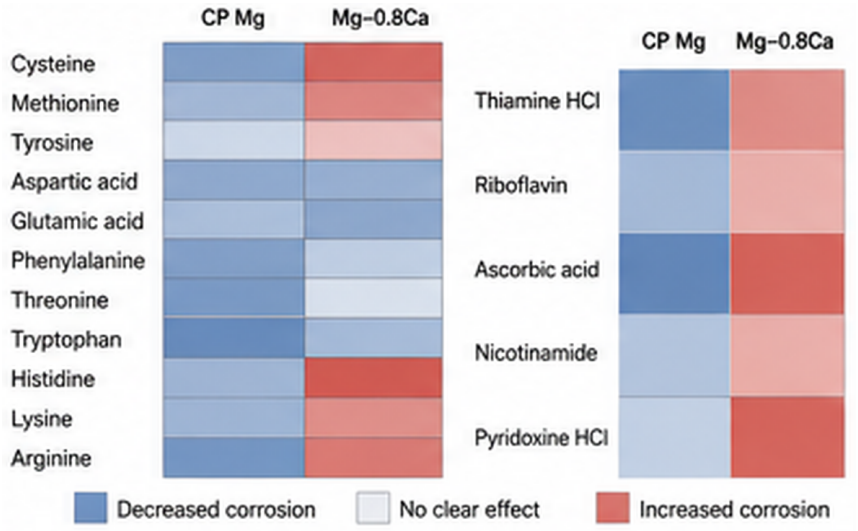

Figure 7: Compound response by alloy.

This table also illustrates the danger of the interpretation of electrochemical measurements performed at a single time point. An organic molecule can decrease the current density during short immersions due to the blockage of active sites while creating soluble complexes, which are then damaging during prolonged immersion. Another organic molecule can initially look like an inert compound but start promoting deposition of phosphate-rich corrosion products during long-term immersion. This fact means that amino acid studies should combine electrochemical measurements (polarization/impedance) with surface chemistry, pH, and long-term immersion results.

Table 3: Amino-acid response map.

Amino acid	Concentration (M)	Mg–0.8Ca	CP Mg
Alanine	8.53×10^{-4}	Accelerated	Accelerated
Serine	1.90×10^{-4}	Accelerated	Decelerated
Aspartic acid	9.01×10^{-5}	Decelerated	Decelerated
Proline	4.95×10^{-4}	Accelerated	Accelerated
Glutamic acid	1.90×10^{-4}	Accelerated	Accelerated
Cysteine	4.13×10^{-4}	Accelerated	Decelerated
Glycine	7.19×10^{-4}	Accelerated	Decelerated
Asparagine	1.00×10^{-4}	Accelerated	Decelerated
Leucine	3.96×10^{-4}	Accelerated	Decelerated
Isoleucine	3.20×10^{-4}	Accelerated	Decelerated
Methionine	1.01×10^{-4}	Accelerated	Decelerated
Arginine	2.07×10^{-4}	Accelerated	Accelerated
Histidine	2.45×10^{-4}	Accelerated	Decelerated
Valine	3.59×10^{-4}	Accelerated	Accelerated
Tryptophan	1.47×10^{-4}	Accelerated	Accelerated
Threonine	2.69×10^{-4}	Accelerated	Accelerated
Phenylalanine	2.42×10^{-4}	Accelerated	Decelerated
Glutamine	7.25×10^{-4}	Accelerated	Accelerated
Lysine	3.97×10^{-4}	Accelerated	Accelerated
Tyrosine	1.38×10^{-4}	Accelerated	Decelerated
Ornithine	1.06×10^{-4}	Accelerated	Accelerated
α-Aminobutyric acid	1.94×10^{-5}	Accelerated	Decelerated
Taurine	1.68×10^{-4}	Accelerated	Accelerated
Cystine	9.90×10^{-5}	Accelerated	Decelerated
All listed amino acids	Mixed	Accelerated in NaCl; decelerated in SBF	Decelerated in NaCl and SBF

The chart additionally differentiates two interpretations which are usually combined in literature. Previous protein- and amino-acid investigations have shown that the single organic classification is not able to predict the similar response for all types of magnesium [22]. Special side-chain investigation revealed that amino acids containing sulfur and aromatic ones can influence the process of adsorption and complexation [28]. Comparative researches have proved that the final result depends on both alloy chemistry and medium chemistry [24]. Therefore, a particular side-chain classification can help understand the general trend in one material, but it does not automatically imply the same behavior in other materials. For example, amino acid containing sulfur cysteine inhibits corrosion of commercial pure Mg but accelerates Mg–0.8Ca in the corresponding NaCl entries. Aromatic phenylalanine and tyrosine inhibit corrosion of pure Mg but accelerate corrosion of Mg–0.8Ca. These examples demonstrate that second-phase chemistry of alloy and derived Ca can affect adsorption or

complexation. Therefore, the surface is not an inert receptor for the amino acid. The surface itself acts as a co-reactant, defining whether the organic species becomes the member of protective cluster or soluble degradation mechanism.

The vitamins also demonstrate this phenomenon at the lower concentrations. The effect of vitamins is not very strong, but its direction differs for Mg–0.8Ca and CP Mg. Ascorbic acid, folic acid, riboflavin, and pyridoxine-HCl can accelerate Mg–0.8Ca in NaCl and decelerate CP Mg. Thiamine-HCl can decelerate both alloys. The mixture of vitamins can decelerate both alloys in SBF due to formation of the minerals changing the reaction balance [24].

Table 4: Vitamin response map.

Vitamin	Concentration (M)	Mg–0.8Ca	CP Mg
Ascorbic acid (VC)	1.14×10^{-4}	Accelerated	Decelerated
Folic acid (VB9)	2.27×10^{-6}	Accelerated	Decelerated
Inositol (VB8)	3.89×10^{-5}	Accelerated	Accelerated
Riboflavin (VB2)	2.66×10^{-7}	Accelerated	Decelerated
Pyridoxine-HCl (VB6)	4.82×10^{-6}	Accelerated	Decelerated
Thiamine-HCl (VB1)	2.96×10^{-6}	Decelerated	Decelerated
Nicotinamide (VB3)	8.19×10^{-6}	Accelerated	Accelerated
Choline chloride (VB4)	7.16×10^{-6}	Decelerated	Accelerated
Calcium pantothenate (VB5)	2.10×10^{-6}	Accelerated	Accelerated
All listed vitamins in NaCl	Mixed	Accelerated	Decelerated
All listed vitamins in SBF	Mixed	Decelerated	Decelerated

The vitamin data supports a guarded inference. It has been established that ascorbic acid treatment can contribute to formation of carbon-containing and hydroxide rich film on magnesium [30]. Similarly, conversion coating experiments show that ascorbic acid can contribute to the formation of Ce-based protective films [31]. This is not a negligible information since the physiological levels of such compounds are low. The primary implication of the observations is that the minor organic compounds play an indirect role of probes of Mg surface chemical stability since these organic molecules can make the difference between stable and unstable corrosion products in case when alloy chemistry and medium composition are close to a transition.

The vitamin map also clarifies a threshold concept for Mg biomaterials. Not all the molecules can affect corrosion through their mass concentration, but these molecules can change the interfacial chemistry in case when the surface is unstable. This applies to biodegradable Mg since the corrosion front produces a highly pH, Mg^{2+}-rich boundary layer, which is significantly different from bulk solution chemistry. Therefore, small organic species can have a disproportionate effect if they are accumulated within the corrosion product or can participate in conversion film chemistry. The future works must include the information about the location of these molecules in the process (whether the compound is in the solution, adsorbed at the surface, or incorporated into the corrosion product).

The comparison between amino acids and vitamins refines the way of thinking about minor organic constituents. The amino acid is significant due to its higher concentration or obvious adsorption site, while a vitamin is secondary since its concentration is low. However, the evidence points to a different view. Vitamins of lower concentration serve as probes of surface instability: if the Mg–Ca surface changes its direction with the addition of some organic compound, the corrosion product is already close to stability threshold. That is why the vitamin data is not a side information; rather, the data demonstrates the ability of the Mg corrosion in physiological fluids to be redirected due to subtle effects when chloride breakdown, Ca–P precipitation and complexation are balanced.

4.5 Delayed organic reactions and microbial corrosion drift

The physiological solutions are characterized by the simultaneous presence of multiple organic molecules. The map of the literature shows that the combined effects cannot be estimated by summation of the responses of individual molecules. The key example of coupled effects is the glucose and L-cysteine. L-cysteine alone can inhibit corrosion of the pure magnesium in certain alkaline saline solutions, while glucose and L-cysteine together accelerate the corrosion rate. The amino and aldehyde groups of these molecules can react through condensation to form Schiff-base-related species,

$$\mathrm{RNH_2} + \mathrm{R'CHO} \rightarrow \mathrm{RN{=}CHR'} + \mathrm{H_2O}. \tag{12}$$

Acidification of the solution by glucose at an early immersion stage is conducive to magnesium dissolution [25]. Joint effect of glucose and L-cysteine revealed that the formation of Schiff base derivatives and complexes prevents $Mg(OH)_2$ precipitation [26]. Thus, due to the alkalinization of the solution by corrosion, the interaction of chlorides and organics becomes even more effective.

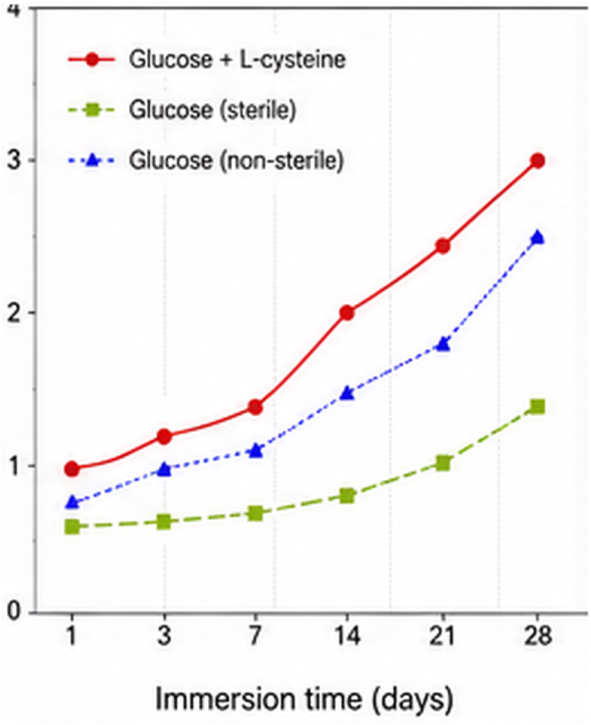

Figure 8: Delayed bioorganic corrosion trends.

The delayed-corrosion feature in Fig. 8 underlines the temporal aspect of bioorganic corrosion. Adsorption or inhibition at the beginning does not guarantee protection because organic compounds can be utilized, modified, or integrated into soluble complexes. Delayed chemical reactions explain why short electrochemical studies may underestimate later acceleration. It is also seen why only the initial composition of the solution should be provided. Post-immersion pH, concentration of dissolved Mg^{2+}, organic compounds utilization, and surface products should be studied if coupled systems of organic substances are considered.

The above mentioned coupled systems make it clear why corrosion monitoring should go beyond the initial electrochemical responses. A short polarization curve can reveal adsorption or a temporary change of charge transfer, but it may miss the organic compounds consumption such as glucose, amino acids, and proteins. The interface can pass through various stages: an early stage of acidification, hydroxide deposition, chemical interaction of the organic compound, complex formation, product cracking, and its stabilization or a new attack. So, a single endpoint could provide a correct but incomplete answer. The most informative test is a combination of electrochemistry with immersion morphology, pH changes, and surface properties after immersion. This approach is especially needed for glucose–amino acid mixture because the aggressive species can be created by their reaction.

The next factor which makes Mg corrosion complex is the presence of microorganisms. Long-term research demonstrated that glucose can help to support bacteria and accelerate degradation of Mg–Li–Ca alloys [32]. Surface treatment and antibacterial control confirmed that renewal and bacteria suppression can stabilize degradation [31]. Glucose can be a nutrient source in the long immersion tests. Bacteria can decrease the pH of Hanks solution to the acidic region, accelerate degradation, and weaken mechanical retention. It means that this is not a criterion for classifying all glucose-containing experiments as microbiological tests, but it means that nutrient-rich exposure should be considered as susceptible to microbiological drift without the documentation of sterilization and renewal.

The delayed-corrosion curve in Fig. 8 demonstrates also the existence of the microbial drift as a hidden variable in Mg corrosion test. This test can change from chemical degradation to accelerated biologically-assisted acidification without changing the composition of the nominal solution. It is important for the simulation of diabetic patients because glucose influences chemical corrosion and microbial ecology. Thus, sterilization, frequency and duration of renewal, and antibacterial additives should be considered as corrosion parameters.

4.6 Bioorganic-assisted protective surface layers

The same bioorganic chemistry that causes ambiguities in the solution can be also used for surface protection. Glucose-assisted hydrothermal treatment is capable of forming Ca-P/$Mg(OH)_2$ coating on pure Mg [33]. Studies of amino acid-assisted Ca-P coating revealed that L-cysteine and its analogs can influence the coating thickness and corrosion resistance [34]. Antimicrobial peptide hydroxyapatite coating proved that organic functionality can be used together with the bacterial suppression [15]. Silk fibroin and Ca/Sr/P composite film also connect the problem of corrosion protection with the problem of cytocompatibility and osteogenicity [16].

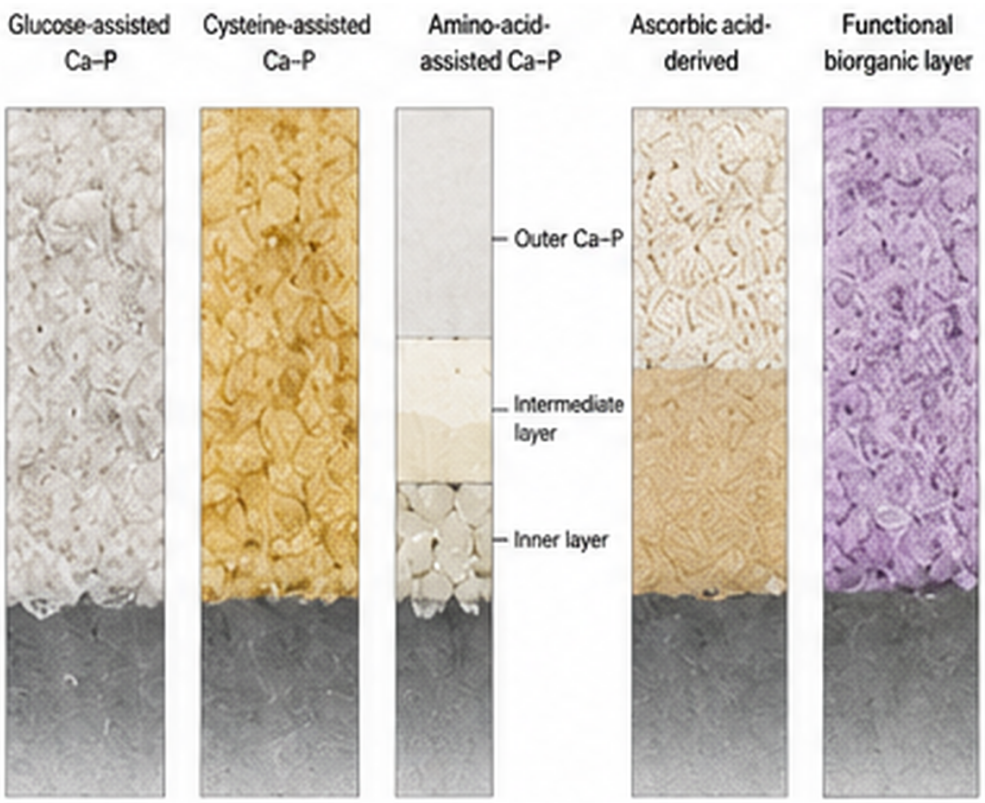

Figure 9: Bioorganic protective layers.

The coating-layer plate in Fig. 9 represents the shift of perspective from passive exposure to active interface engineering. A molecule which destabilizes $Mg(OH)_2$ during immersion could yet be helpful if it promotes an active formation of mineral or hybrid films prior to implantation. The performance criteria are also different. An additive to the solution has to be helpful during exposure, while the additive to the process – has to ensure formation of a stable coating that will withstand following exposure. This distinction helps explain the seeming contradiction in reported effects of glucose, L-cysteine, amino acids, and ascorbic acid.

The coating table indicates that bioorganic-mediated protection is efficient in case the molecular function goes together with the inorganic mineralization. Glucose and amino acids work if they promote Ca–P formation; ascorbic acid works if it contributes to the chemistry of compact conversion films; peptides and silk fibroin work if they mediate coating corrosion and antimicrobial or osteogenic functionality. A general principle here is that bioorganic coatings cannot be judged solely based on the corrosion current. Their clinical importance depends also on adhesion, cracking resistance, biological activity, and stability under flowing/renewal conditions.

The coating data need extra attention because they show the positive aspects of the same chemistry which causes complexity in immersions. Glucose-mediated hydrothermal processing results in a Ca–P/$Mg(OH)_2$ coating with a sandwich-like structure [33]. The studies on amino acid-mediated coatings demonstrated that carboxyl and mercapto functional groups can coordinate with Ca^{2+} and increase thickness of deposited coating [34]. Glucose products destabilizing $Mg(OH)_2$ in solution can assist in coating formation in the process of alkaline hydrothermal processing. L-cysteine molecules reacting with glucose become hazardous in solution but their functional groups contribute to mineralization of coating formation. The reported thicknesses in the Ca–P series coated with amino acids change from 3.470 ± 0.47 µm for conventional Ca–P to 6.06 ± 0.77 µm for Ca–P_{Phe}, 7.63 ± 0.70 µm for Ca–P_{Met}, and 8.231 ± 1.37 µm for Ca–P_{Asn}. It becomes clear that the organic molecule does not play just the labeling role but also influences the coating architecture and, therefore, pathways for chloride and water.

Table 5: Coating strategy map.

Bioorganic component	Surface system	Protection mechanism
Glucose	Ca–P/$Mg(OH)_2$ coating on pure Mg	Induces calcium phosphate deposition and forms a crystalline mineral-hydroxide layer
L-cysteine	Ca–P coating on AZ31 at 60 °C	Carboxyl and mercapto groups complex with Ca^{2+} and increase coating thickness
Phenylalanine	Ca–P_{Phe} coating on AZ31	Produces a thicker amino-acid-assisted mineral layer than conventional Ca–P
Methionine	Ca–P_{Met} coating on AZ31	Increases coating thickness and changes mineral growth
Asparagine	Ca–P_{Asn} coating on AZ31	Produces the strongest resistance among the listed amino-acid-assisted Ca–P coatings
Amino acids in sol–gel coatings	TEOS/MTES or TEOS/TEVS hybrid layers	Improve compactness and provide green inhibiting functionality
Ascorbic acid	$Mg(OH)_2$/C film on AZ31	Supports a carbon-containing hydrothermal film with improved resistance
Ascorbic acid	Ce-based conversion coating on AZ91D	Promotes uniform adhesion and stronger resistance than Ce film without ascorbate
Antimicrobial peptides	AMP-loaded hydroxyapatite coating	Reduces degradation while inhibiting *Staphylococcus aureus* growth
Silk fibroin and Ca/Sr/P species	Composite film on fluoride-treated Mg–1Ca	Improves corrosion resistance, cytocompatibility, and osteogenic response

An interpretation of the coating table thus needs to consider the relationship between corrosion resistance and biological function. Antimicrobial-peptide-coated hydroxyapatite offers control of degradation with inhibition of *Staphylococcus aureus* [15]. Silk-fibroin and Ca/Sr/P composite films applied to fluoride-modified Mg–1Ca offer control of degradation with cytocompatibility and osteogenesis [16]. Neither of these coating systems should be interpreted solely in terms of a barrier action during early stages of exposure. A more relevant question regarding a degradable implant coating is whether the coating moderates early corrosion attack, prevents deep local damage, and allows a regulated transition from coated metal to corrosion products integrated within the tissue.

The strategy table also distinguishes two contrasting philosophies of design. The first approach attempts to isolate Mg from the environment with a dense barrier, whereas the second one accepts controlled exposure and utilizes bioorganic chemistry to steer the corrosion products toward a more favorable mineral, polymer-mineral, or bioactive layer. The latter philosophy appears more realistic for degradable implants because complete and long-lasting isolation is neither achievable nor desirable. Instead, the target is synchronous degradation: the surface slows down early attack, prevents deep local penetration, facilitates tissue integration, and allows gradual corrosion product formation.

The same rationale governs the interpretation of surface treatments. A coating that retards corrosion in NaCl proves barrier action in aggressive chloride medium, while a coating that functions in Hanks' solution or SBF proves compatibility with mineral precipitation. If a coating is supposed to incorporate peptides, proteins, or silk fibroin, a biologically relevant medium is an integral part of the material testing process and not an additional biological assay. An integrated view is crucial for degradable metals because corrosion resistance, ion release, and biological response occur simultaneously.

The pair of L-phenylalanine and $Zn(NO_3)_2$ can be regarded as an example of the solution-inhibitor system close in mechanism to the coating design. Such a system has been shown to produce high efficiency of inhibition of AZ31B in dilute chloride medium and act as a mixed inhibitor with predominant anodic inhibition mechanism. This finding is valuable since it shows that the combination of organic and inorganic inhibitors can be more effective than individual components. However, when considering these systems for biomedical applications, cytocompatibility, dose, release, and interaction with Ca–P deposition must be determined [35].

5. Discussion

Results obtained in classified literature can be summarized to provide testing and design guidelines without distilling the system into a rigid checklist. Medium selection should match the intended implant environment and not just laboratory convenience. The orthopedic implants require calcium-phosphate-containing and pH-buffered medium to allow mineral deposition. Vascular implants require protein-containing flow and renewal. The gastrointestinal implants require enzyme-specific fluids. Diabetic implants require glucose control and sterilization monitoring. The organic molecules should be considered according to their mechanism pairs: glucose with Ca–P availability, protein with flow conditions, amino acid with alloy surface chemistry, and microbial nutrient with renewal schedule.

The rule table translates the literature review findings into experimental guidelines. The key point is that test realism cannot be achieved by putting every physiologic molecule in every medium. Test realism is achieved by maintaining the

controlling interaction for the device. A highly complex medium, which is poorly controlled, can be less informative than a simpler medium chosen for the specific mechanism. The 67-item record also indicates that future studies should report negative and reversal results more explicitly. Such results are not contradictions; they are the evidence of switching behavior.

The rule table also provides instructions on how to report data. A corrosion study should report the history of alloy processing, surface preparation, electrolyte composition, buffer system, gas composition, protein or glucose content, renewal schedule, and medium sterilization. Then, the electrochemical data should be correlated with the mass loss, hydrogen evolution, pH change, and post-exposure surface chemistry. In case of a coating, these data should be complemented with the information on film thickness, adhesion, crack density, degradation during immersion, and biological function.

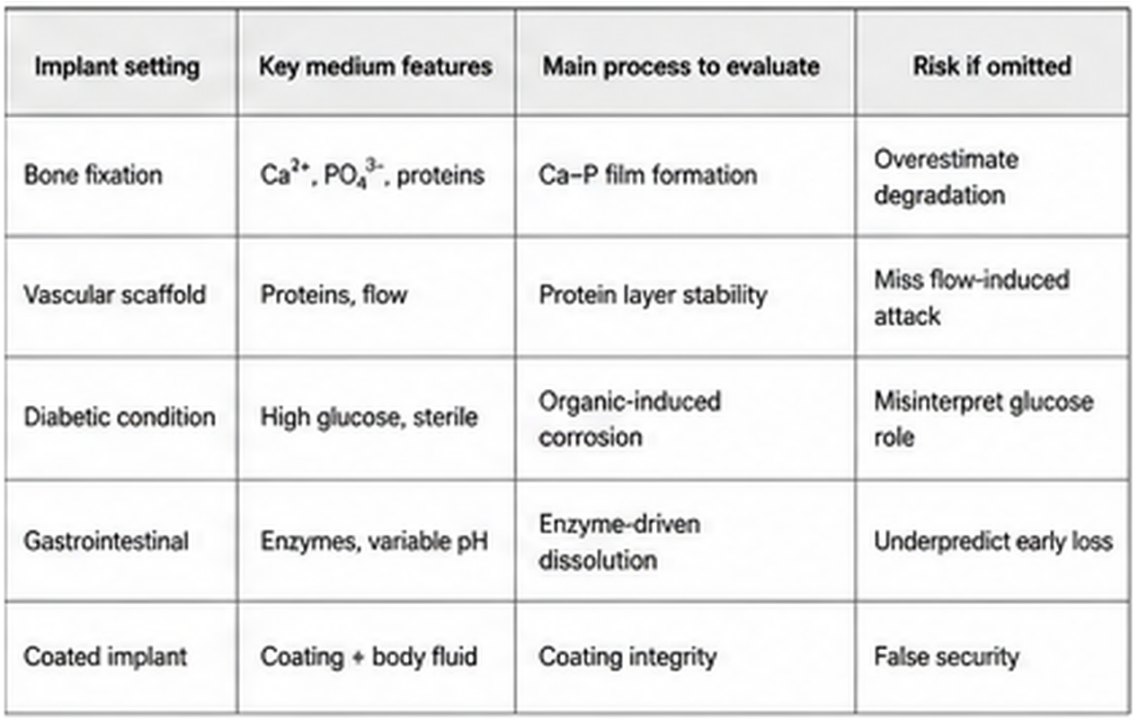

Figure 10: Implant-specific test selection.

The test selection plate in Figure 10 represents the translation of the evidence record to implant-specific corrosion practice. Bone anchoring, vascular scaffolding, diabetes exposure, gastrointestinal location, and coated implant investigation are represented as distinct test problem sets because each of these environments modifies the surface process that needs to be measured. The accompanying text table retains the same format, maintaining the necessary medium attribute, the risk of its omission, and the recommended target of interpretation.

Table 6: Implant-specific testing rules.

Implant setting	Required medium feature	Main risk if omitted	Preferred interpretation target
Bone fixation	Ca^{2+}, phosphate, bicarbonate, pH control	Underestimation of mineral deposition and surface stabilization	Balance between chloride damage and Ca–P barrier formation
Vascular scaffold	Serum proteins, flow, renewal, oxygen control	False protection from static protein adsorption	Adhesion of protein/mineral layers under transport
Diabetic exposure	Defined glucose, Ca–P background, sterile renewal	Confusion between chemical glucose effects and microbial acidification	Glucose as chemical switch and microbial nutrient
Gastrointestinal exposure	Pepsin or pancreatin in organ-specific fluid	Missing enzyme-dependent product-layer changes	Enzyme-specific stability of phosphate and hydroxide products
Bioorganic coating	Coated surface plus clinically relevant fluid	Overvaluing coating made for a single aggressive electrolyte	Film adhesion, cracking, barrier stability, and biological function

Surface engineering should follow the same logic. The goal should not be just to limit Mg dissolution through an initial electrochemical measurement. An effective surface should control the degradation morphology and kinetics. Dense Ca-P, hydroxyapatite, conversion, mineral-polymer, and peptide-based coatings should be tested on their capacity to maintain

adherence as the substrate alkalizes and releases Mg^{2+} and hydrogen. Bioorganic surfaces that perform well in static but not in dynamic conditions could still be suitable for bone contacting implants, but not for blood contacting implants. On the other hand, surfaces that allow controlled degradation could be superior to those that prevent corrosion only temporarily.

The synthesis is bounded by a clear set of parameters as well. This literature record captures directions and mechanisms reported by researchers, but does not impose a universal numerical ranking because the protocols of exposing devices to biological media are still too diverse. One study gives information about the current density, another study reports mass loss, hydrogen evolution, surface morphology, or biological response. These outcomes cannot be aggregated without losing information about the mechanism. Hence, the significance of this literature record lies in diagnostics – identifying the parameter that must be held constant before quantitative comparisons become possible. And this limitation is also an advice for future research: standard biological medium should be used along with medium modified for particular implants.

The research question may be answered now at the mechanistic level. Bioorganic compounds act as switchable regulators if their functional groups participate in multiple interfacial interactions. Carboxyl and aldehyde groups could destroy $Mg(OH)_2$ layer or promote Ca–P deposition. Amino, thiol, aromatic, and heterocyclic groups could adsorb protectively or form soluble complexes. Proteins could form a barrier on the surface or become unstable during exposure to flow. Glucose could influence the chemistry of the surface and microbial communities indirectly. The key factors here are medium composition, alloy chemistry, transport, and time.

And the reporting implication is no less important for science. A study on the corrosion behavior of biodegradable Mg should not leave the reader to guess if a new portion of the solution was introduced, if glucose was sterilized, if proteins were exposed to flow, and if the final pH was significantly different from the initial pH. All these details are important since they determine the mechanism. Similarly, figures and tables should contain information about the studied mechanism. Useful figures reveal what mechanism has been tested, and useful tables retain the variables necessary for explaining reversals. The literature record used here follows this logic by putting material, molecule, medium, direction, and mechanism all together, not separating them into unrelated observations.

The design implication is that every study should distinguish screening tests from mechanism tests. Best-practice guidance recommends the use of clearly defined media for screening and comparison [7]. Reviews on biological-media composition emphasize the need to add proteins and flow to the list when translation is the objective [10]. Studies on coatings show that Ca–P mineralization and organic-assisted surface modification are best studied in dedicated mechanism tests [34]. Screening tests may include exposure to the NaCl solution to reveal the corrosion sensitivity to chloride ions, but this cannot be considered the biological prediction. Mechanism tests should reveal the process that is studied, such as Ca–P precipitation, protein adsorption in the flow regime, acid chemistry caused by glucose, or destruction of the surface by enzymes. Translation-oriented tests, in turn, should combine the mechanism that dominates the corrosion process with the conditions of the clinical setting of an implant. The tiered interpretation allows aggressive and realistic tests to exist alongside each other without mixing them up. And it also explains why a coating performing well in saline solution may require a separate evaluation in the Ca–P containing or protein containing media.

6. Conclusions

For this study, the question posed was what bioorganic compounds serve as regulators of biodegradable magnesium alloys and how this should influence the testing protocols and coating designs. The answer is that bioorganic regulation is neither molecule-specific in the sense of inhibitor/accelerator nor molecule/constituent-specific. It depends on the environment conditions. The same molecule is capable of switching direction depending on changes in the ionic composition, alloy surface state, transport condition, or the exposure period.

As seen from the classified literature review, this switching logic is persistent. High chloride saline stimulates $Mg(OH)_2$ dissolution, so glucose-based acidification and organic complexing often become the source of corrosion acceleration. On the other hand, Ca–P containing media can transform glucose, fructose, amino acids, and related organics into mineralization assistors making them protective or stabilizing in the cases when precipitation prevails. Protein effects should be interpreted differently since their adsorption can lead to decreased corrosion under static conditions, while under the flow condition the weakly attached protein/mineral aggregates can be washed away.

Consequently, one can conclude that there is no way to conduct a reliable evaluation of corrosion rate in magnesium implants without consideration of the specific environment and interface mechanisms in place. Biocompatible magnesium alloy should be assessed in Ca–P containing media with appropriate buffer; vascular devices need protein-containing fluid with the flow; diabetic implants should be tested in glucose environment with strict sterilization and fluid renewing; gastrointestinal environment requires enzyme-specific solution; and the effectiveness of bioorganic coating depends on the fluid chemistry that is to be regulated. Bioorganic molecules thus should be considered as conditional interface regulators

whose role is not in their universality, but ability to direct corrosion-product chemistry in specific environments.

In other words, this classification allows answering the question specifically rather than summarizing the literature in general terms. Bioorganic molecules are not mere constituents of the environment to be used after choosing an alloy; they are active regulators of the interface. Only combination of the medium, material type, transport condition and exposure period makes the effect predictable. Thus, the conclusion is formulated in such a way that it transforms the observed inconsistency of the literature into useful guidance for future research.

Declarations

Conflict of interest

The author declares no conflict of interest.

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