Chapter

Amorphous and Crystalline Magnesium Alloys for Biomedical Applications

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Abstract

Amorphous and crystalline magnesium alloys, developed for medical applications – especially implantology – present the characteristics of biocompatible magnesium alloys (Mg-Zn, Mg-Zn-Ca, Mg-Ca etc.). This chapter provides a brief description of the role of magnesium in the human body and the use of Mg in medicine. It presents the concept of using magnesium alloys in medicine (advantages and limitations) and the scope of their potential applications (orthopedic implantology, cardiac surgery etc.). The chapter shows classification of magnesium alloys as potential biomaterials, due to their structure (amorphous, crystalline) and alloying elements (rare earth elements, noble metals etc.). The mechanism and in vitro degradation behavior of magnesium alloys with amorphous and crystalline structures are described. The chapter also discusses the influence of alloying elements (rare earth elements, noble metals) on the in vitro degradation process. It also presents the methods of reducing the degradation rate of magnesium alloys by modifying their surface (application of protective layers).

Keywords: magnesium alloys, metallic glasses, resorbable implants, in vitro degradation behavior, protection coatings

1. Introduction

Magnesium is one of the most common elements in nature. It constitutes 2.7% of the earth's crust and can be found in the form of minerals, such as dolomite, magnesite or kainite [1]. The mechanical properties of pure magnesium are poor, therefore alloying additives are introduced to improve them. Magnesium alloys, in which the major additive is aluminum – typically 6–10% – are the most widely used industrial alloys of magnesium. Zinc or manganese [2, 3] are added to improve corrosion resistance of magnesium alloys. Initially, magnesium alloys were produced mainly for military purposes. Due to the high specific strength and vibration damping capacity, magnesium alloys are mainly used in the automotive industry [3, 4].

Currently, research is carried out mainly on new groups of magnesium alloys, such as Mg-Ca, Mg-Zn and Mg-Zn-Ca, which have not been produced on an industrial scale so far. Studies are carried out on the use of these alloy groups as materials for implants, especially orthopedic ones. Injuries of the osteoarticular system, as well as diseases of the musculoskeletal system, including the continuous increase

in the incidence of bone cancer, are the main and the most common threat to the health of modern society. 2,710,000 cases of orthopedic fractures were noted in Poland in 2010. Due to the aging of the population, it is predicted that, in 2025, their number will reach 3,239,564, and 10 years later – over 4 million. In 2017, 85,488 joint arthroplasties (partial or total) were performed in Poland, including 56,688 of the hip and 27,653 of the knee. Surgical joining of broken bones through their correct connection and immobilization is performed with the use of bone plates, wires, clamps and/or screws. The use of these elements results in bone union and obtaining the correct bone structure, which, in turn, allows the patient to move, and thus return to basic life activity [5–8].

In medical practice, both long-term implants (e.g. joint prostheses) and short-term implants (e.g. plates, bone screws), used to stabilize broken bones, are produced from titanium alloys, cobalt alloys or stainless steel. Implants made of those are classified as neutral, i.e. neutral to the body, as long as protective layers (usually oxide) remain on their surface. Unfortunately, after some time, these layers become corroded and damaged, and implant components – which are usually biologically incompatible (toxic to the body) – pass into the human body, and thus are a threat to health and life. Resorbable biomaterials are an alternative to the metal alloys used so far for short-term orthopedic implants. The resorbable biomaterials used in medical practice so far include oxide glasses (composed of Na, K, Mg, Ca, Si and P oxides), ceramics based on calcium phosphates, e.g. hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$] and polymers, such as polylactide, polyglycolide or copolymers of these materials. Unfortunately, their use in orthopedic implantology is limited. They are mainly used as fillers for bone defects, elements of dentures or coatings for medical implants [9–11]. This is due to poor mechanical properties of resorbable biomaterials. Mechanical strength of the resorbable materials used in medicine is 30–100 MPa [10, 12]. Consequently, mechanical properties of resorbable polymers and ceramics are a barrier to their use as biomaterial for implants, such as short-term orthopedic implants. Accordingly, resorbable metallic biomaterials that can be used for orthopedic implants are necessary. Resorbable metallic biomaterials are an alternative to the metal alloys previously used for short-term orthopedic implants. Magnesium alloys are appropriate materials for resorbable metallic biomaterials.

This chapter presents the role of magnesium in the human body and its use in medicine. It presents the concept and potential applications of magnesium alloys in medicine, as well as classification of magnesium alloys as potential biomaterials due to the structure (amorphous, crystalline) and alloying elements (rare earth elements, noble metals etc.). The chapter also describes mechanisms and degradation behavior (in vitro) of magnesium alloys due to their structure. The impact of alloy additives (rare earth elements, noble metals) and protective coatings on the degradation process of magnesium alloys for biomedical applications in in vitro conditions has also been assessed.

2. The role of magnesium in the human body and its application in medicine

Magnesium is called an element of life, because it participates in many processes of the human body. It is necessary to maintain proper homeostasis, i.e. the proper functioning of the human body. It is estimated that there are approximately 22–26 g of magnesium in the human body [13]. It should be mentioned, that both the value and the range of the concentration of an element in the human body depends on the age, sex, absorption of the elements or even diet. The World Health Organization (WHO) has issued standards defining the daily demand for the element [14, 15].

Similarly, demand for magnesium is different for a certain age. **Table 1** shows the daily magnesium requirement depending on age.

Magnesium is distributed in the body (in the skeletal system: approx. 60%; in skeletal muscles: approx. 20% and other soft tissues: approx. 19%). Magnesium in acidic form, absorbed from food, in about 30%, can be found predominantly in the small intestine. The daily recommended dose of magnesium depends on the age, gender and current condition of the body. It has been proven, that the average dose for an adult human is about 300–400 mg. Approximately 30% of magnesium is absorbed from the gastrointestinal tract. Absorption of this element is influenced, among others, by the amount of consumed protein, fiber and phosphates. The normal blood magnesium level of a healthy person is 0.75–0.95 mmol/dm^3, and its homeostasis is maintained by the kidneys.

Magnesium has a lot of functions in the human body. For example, it:

- regulates the activity of about 300 enzymes involved in metabolic changes,
- is necessary for proper bone mineralization. It has been confirmed that magnesium deficiency disturbs bone mineralization processes, increasing the incidence of postmenopausal osteoporosis [17],
- is involved in nerve conduction and muscle contractility. It is likely that magnesium could be used to treat affective disorders and depression. A positive effect of magnesium on depression symptoms has been demonstrated in patients with low levels of magnesium in erythrocytes [18],
- plays a vital role in most hormonal responses. Magnesium has been shown to influence insulin synthesis, catecholamine storage and parathyroid hormone release,
- participates in the regulation of blood pressure,
- regulates muscle tension,
- regulates the thyroid gland and widens the airways, supporting the treatment of asthma and bronchitis.

Magnesium has been used in treatment of various diseases. **Figure 1** presents the main uses of magnesium for treatment of diseases.

Symptoms of magnesium deficiency influence every system in the human body. The most common symptoms are not very specific – they include fatigue, poor concentration and memory, as well as increased susceptibility to stress. Excessive loss of magnesium can be caused by serious diseases of the gastrointestinal tract (e.g. fistulas, pancreatitis), urinary tract disorders, endocrine disorders (primary

DEMAND FOR MAGNESIUM [mg/24 h]					
Infants	kids < 6 years old	kids 6–9 years old	youth 10–18 years old	adults 19–60 years old	adults < 60 years old
40–60	**80–120**	**170**	**270–400**	**280–350**	**280–350**

Table 1.
Daily recommended dose of magnesium for kids, youth and adults [16].

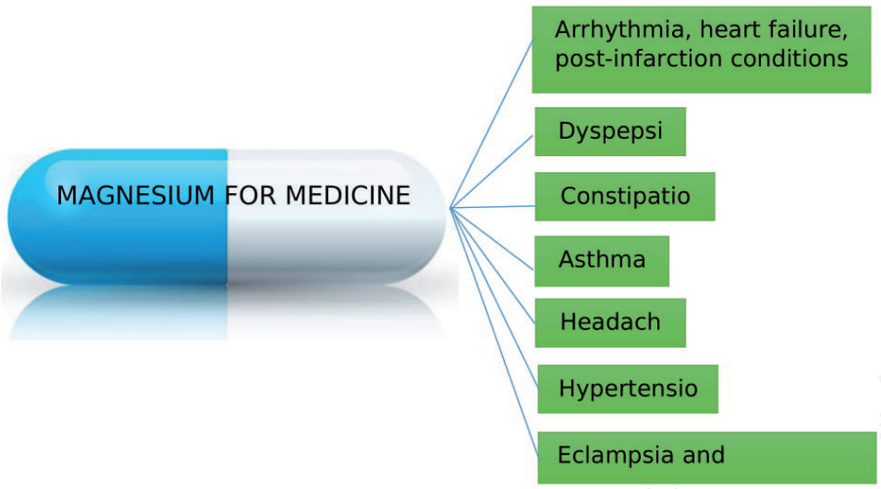

Figure 1.
The most important uses of magnesium in treatment of diseases [19].

hyperparathyroidism, intensive insulin therapy), D3 hypervitaminosis, use of immunosuppressants, increased sympathetic nervous system tension or alcoholism.

3. The concept and potential applications of magnesium alloys in medicine (advantages and limitations)

The progress of both the medicine and materials engineering results in an intensification of research works on new biomaterials. Nowadays, magnesium alloys are considered potential resorbable metallic biomaterials. Furthermore, it is assumed that a magnesium alloy as a resorbable biomaterial should gradually degrade in the human body until the bone fuses. Degradation products of a resorbable implant would be processed, absorbed or excreted from the patient's tissues and body fluids. The use of implants designed according to this concept does not require re-operation and it allows the foreign object (implant) to stay in the human body. Apart from good mechanical properties and biocompatibility, magnesium has a number of other advantages, such as [20, 21]:

- good strength-to-weight ratio. Pure magnesium has 158 kNm/kg; however, its alloys can reach up to 490 kNm/kg. This is twice as much as the most commonly used titanium alloys (260 kNm/kg), therefore, less material is needed to obtain similar mechanical properties.

- ease of processing magnesium and creating complex shapes, which is extremely important in medical applications, because every person is different and, therefore, it is possible to design a custom-made implant for a specific patient.

- safe degradation – titanium, stainless steel and Co-Cr alloys do not ensure safe degradation. All surgically implanted alloys are subject to electrochemical degradation, as they are in a corrosive environment. Additionally, they are subject to significant wear. Implant particles can be released into the surrounding tissue, causing discomfort and potential health hazards. Magnesium and its alloys can minimize these problems during the degradation process. It is possible that, after a controlled period of time, the implant completely degrades in the human body.

The main problems and research limitations of this concept are as follows:

- production of implants with good mechanical properties, which guarantee the appropriate time (allowing bones to fuse) of the implant's activity in human bodily fluids,

- high degradation of an implant with very intense release of hydrogen, which is harmful to the body. In addition, there is possible exceeding the daily demand for the element (also biocompatible), introducing into the body. Metal alloys used for resorbable biomaterials should only include elements that are already present in the human body in high concentration and are macro- or microelements.

The major problem concerning all metal biomaterials consists in the adjustment of their mechanical properties to those of the reconstructed tissues. The density of steel is approx. 4 times higher than the density of bone tissue. Steel has several times higher yield point and tensile strength, higher elongation and about 10 times higher Young's modulus. The differences in the mechanical properties of materials and those of the tissues they replace result in inappropriate loading of the tissues surrounding the implant, causing pain and discomfort in patients [22].

The density of magnesium alloys is similar to the density of the human bones, therefore, there is no possibility of stress shielding, as in the case of the previously used implant materials, based on stainless steel and titanium. Stress shielding is a process, in which the bone mass and density decrease near the implant, because it transfers the loads. The density of magnesium alloys is three times lower than that of titanium alloys and five times lower than that of stainless steel and Co-Cr alloys. The modulus of elasticity and fracture resistance are much lower than for the biomaterials used so far [23, 24]. In the 19th and 20th centuries, magnesium alloys were used in medicine (**Table 2**). They were used in the form of scaffolds and to improve healing of wounds or organs. In addition, magnesium and its alloys have

Author	Application date	Mg/Mg alloys	Application
Huse	1878	Pure magnesium	Stitches
Payr	1892–1905	Pure magnesium	Nerve's linkers
Hopfner	1903	Pure magnesium	Vessels' linkers
Lambotte	1906–1932	Pure magnesium	Bone screws and plates
Lespinasse	1910	Pure magnesium	Bone plates
Groves	1913	Pure magnesium	Bone pits
Andrews	1917	Mg-Al/Zn	Bone wires
Seelig	1924	Pure magnesium	Bone wires
Verbrugge	1933–1937	Mg-Al6-Zn3-Mn	Bone screws and plates
McBride	1938	Mg-Mn	Bone wires and plates
Maier	1940	Pure magnesium	Stitches
Stone	1951	Mg-Al (2 wt.%)	Bone wires
Wexler	1980	Mg-Al (2 wt.%)	Bone wires
Hussl	1981	Pure magnesium	Vascular wires

Table 2.
Applications of magnesium and its alloys in medicine [25].

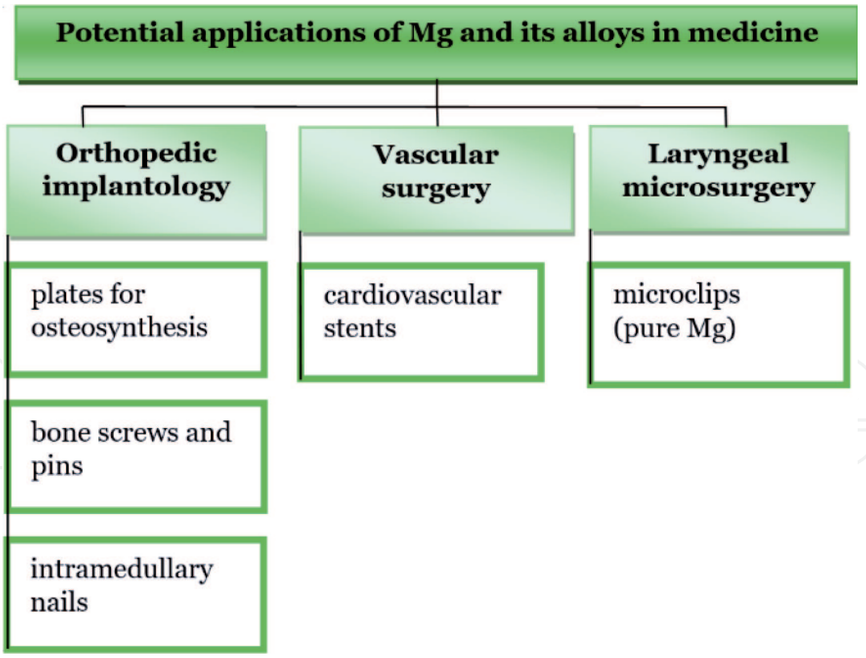

Figure 2.
Potential applications of Mg and its alloys in implantology [17–22].

been used in orthopedic surgery for such elements as screws, plates, fasteners or as stents in the cardiovascular system.

At present, magnesium alloys are mainly considered as potential materials for applications in orthopedic implantology, vascular surgery and laryngeal microsurgery [26–30]. As regards orthopedic implantology, Mg alloys are used as compression screws. MAGNEZIX is the trade name of biodegradable orthopedic screws for human osteosynthesis application [31]. In the literature, there are some reports [32–34] on resorbable stents made of magnesium alloys (their trade name is Lekton Magic, produced by Biotronik company). This material is composed of zirconium (< 5 wt.%), yttrium (< 5 wt.%) and rare earth elements (< 5 wt.%). The stents degrade in a living body with time, but their location can still be identified. Finally, the stent material completely degrades and the space around it is filled with a calcium-apatite complex with an admixture of phosphate elements. The stents were implanted in 20 people and good flow in the implanted blood vessel was achieved after one month. In 2013, Biotronik, a German company, has obtained the CE mark for biodegradable coronary stents made of Mg alloy. It was the leader in development of biodegradable metal coronary stents. The areas of potential applications of magnesium and its alloys in implantology are presented in **Figure 2**.

4. Classification of magnesium alloys considered as potential biomaterials due to their structure (amorphous or crystalline) and alloying elements (rare earth elements, noble metals etc.)

In the context of resorbable orthopedic implants, research was initially carried out on technical magnesium alloys, for example AZ31, AZ91, WE43, LAE442. Unfortunately, magnesium alloys containing aluminum (AZ31) and heavy metals have been excluded as biomaterials because these additives have a toxic effect on the human body. The research was limited to alloys containing biocompatible elements and/or small amounts of rare earth elements, that are tolerated by the human body in appropriate concentrations [15].

As regards magnesium alloys for resorbable implants with a crystalline structure, the following groups of alloys has been examined: Mg-Ca, Mg-Zn, Mg-Zn-Ca, Mg-Mn, Mg-Si, Mg-Zr, Mg-Zn-Zr, Mg-Zn-Y, Mg-Zn-Zr-Y, Mg-Zn-Mn.

Rare earth elements (REE) are added in order to improve mechanical properties and creep resistance at elevated temperatures [35, 36]. Gadolin (Gd) and yttrium (Y) increase the strength properties during precipitation hardening. Neodymium (Nd) improves tensile strength at ambient and elevated temperatures. Yttrium and strontium (Sr) reduce the texture, and thus anisotropy, in rolled and extruded semi-finished products [35].

Magnesium alloys with the addition of rare earth elements, such as Mg-Y, Mg-Gd [37] and Mg-Nd, have been designed for use as biomaterials. ZW21 and WZ21 alloys (with the addition of Y and Zn) show promising mechanical and corrosion properties. For example, they are ductile (up to 20% elongation) and their tensile strength ≈ 270 MPa. Alloys such as AE21 and WE43 are used for stents [38, 39].

Noble metals as an additive to magnesium and calcium alloys have been studied mainly by the authors of this chapter [12, 40]. There is no information in the literature on the influence of Au and Pt addition on the degradation rate and mechanical properties of magnesium alloys. There are several sources for adding silver to magnesium alloys [41, 42].

The mechanical and corrosion properties of the alloy can be regulated by the structural and chemical composition of the alloy. Compared to their crystalline counterparts, magnesium-based metallic glasses may be more resistant to corrosion, due to their single-phase structure, which may result in a more uniform alloy corrosion. An example confirming the higher corrosion resistance of the amorphous material in physical fluid compared to the crystalline material with the same chemical composition is shown in **Figure 3**.

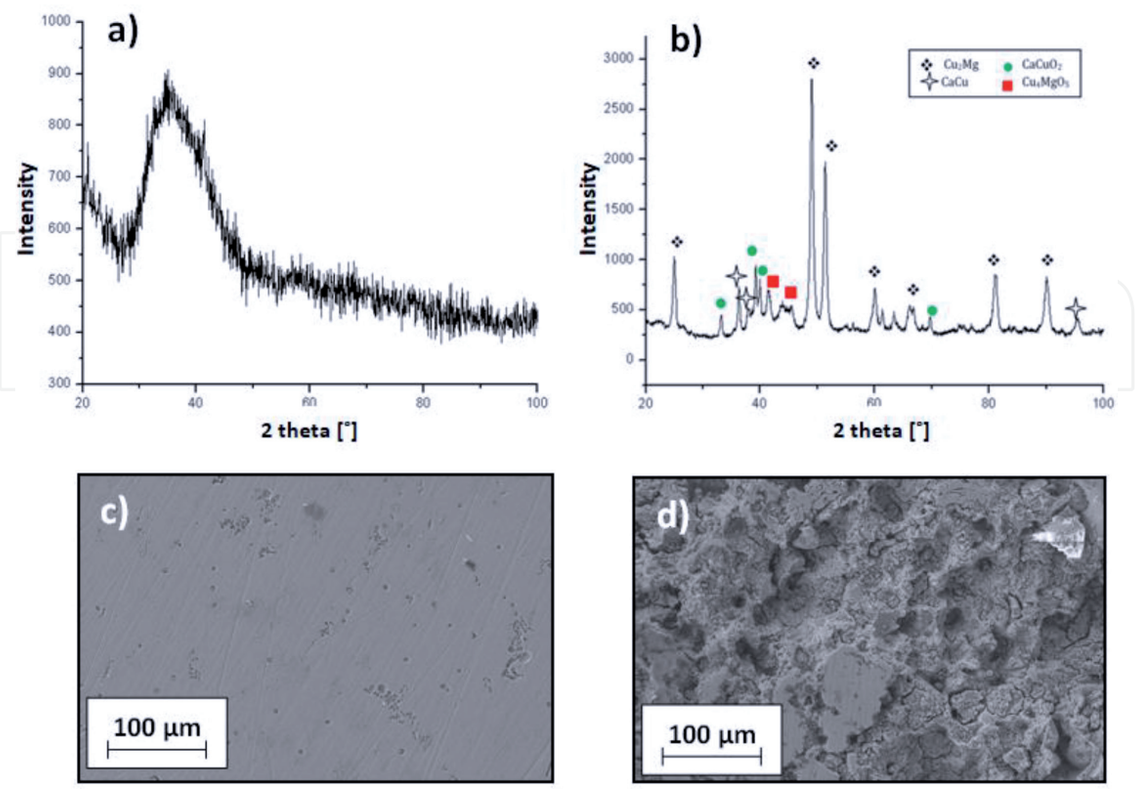

Figure 3.
Results of structural tests of Mg36.6Cu36.2Ca27.2 alloy with amorphous structure (a) and crystalline structure (b) and surface images after 1.5 h of immersion in physiological fluid with amorphous structure (c) and crystalline structure (d) [43].

Magnesium alloys with amorphous structure, such as bulk metallic glasses (e.g. rods, plates) in the following phase systems: Mg-Cu-Y (-Ag, -Pd, -Gd), Mg-Ni-Y (-Nd), Mg-Cu-Gd (-Zn, -Y), Mg-Zn-Ca were obtained. In addition, studies are also carried out on Mg-based metallic glass without rare earth elements. The Laws [44] obtained bulk metallic glasses based on Mg-Cu-Ca, Mg-Ag-Ca, Mg-Cu-Ag-Ca alloy systems. However, for applications in implantology, magnesium alloys should have a biocompatible chemical composition. Therefore, the group of alloys based on the Mg-Zn-Ca phase system is most frequently considered as a new biomaterial for resorbable orthopedic implants [45]. In 2005, Gu et al. were the first to obtain bulk metallic glass in the Mg-Ca-Zn system, which was characterized by good strength properties and high glass transition capacity [46].

In the process of designing new degradable biomaterials, elements with potential toxicological problems should be omitted whenever possible and, if they are absolutely necessary, they should be reduced to the minimum. Calcium and zinc are essential elements in the human body; therefore, these elements should be the first choice for alloying additives in biomedical magnesium alloys. The concentration of calcium should not exceed 2 wt.%, and zinc – 6 wt.%, due to the corrosive properties of these magnesium alloys [47].

The most commonly used chemical elements for magnesium alloys are: Zn, Zr, Ca, Sr., Yb, Al, Li, Mn and rare earth elements (REEs) (Ce, Er, La, Gd, Nd, Y). The following are the additions, the influence of which on the properties of magnesium alloys is described in detail:

- addition of zinc (< 5 wt.%) reduces the harmful influence of iron and nickel impurities, increases corrosion resistance [48],
- addition of zirconium (< 2 wt.%) increases corrosion resistance [48],
- addition of strontium (< 2 wt.%) improves corrosion properties and affects the strength of the alloy, which is similar to the natural bone [48, 49]. Optimal content of Zr and Sr. in Mg-based alloys increases surface energy and the ability to simulate contact osteogenesis. Mg-Zr-Sr alloys (2 wt.% Sr) display the best osseointegration and complete biodegradation [50],
- addition of ytterbium (at the level of 2 wt.%) improves bending plasticity, corrosion properties and biocompatibility [49],
- addition of calcium (> 1 wt.%) in pure Mg reduces corrosion resistance [48]. Calcium in magnesium alloys, without the addition of strontium, reduces surface energy and bone induction [50],
- addition of yttrium (> 2 wt.%) decreases corrosion resistance in Mg-Y alloys [48].

Noble metals, such as gold and silver, were used as alloying additives in pure magnesium to increase its ductility. However, the alloys had low tensile strength [51]. Another source mentions that the addition of silver, as a substitute for calcium, improves the corrosion properties, strength and has an anti-bacterial effect [49].

Figure 4 shows variation in the open-circuit potential with time and polarization curves for pure Mg and $Mg_{65}Zn_{20.1}Ca_{1.7}Yb_{13}Sr_{0.2}$ alloy in Ringer solution at 37°C.

In the OCP plot (**Figure 4a**), various levels of recorded curves are visible, which results from differences in chemical compositions. The steady-state for

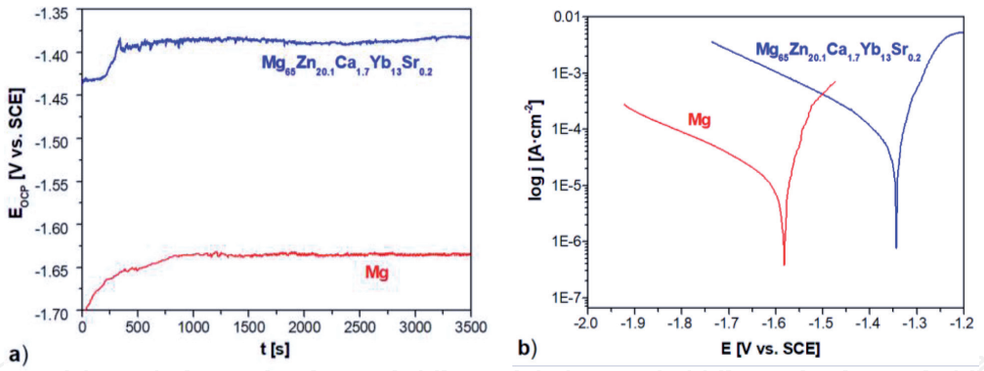

Figure 4.
Variation of the open-circuit potential with time (a) and polarization curves (b) for pure Mg and $Mg_{65}Zn_{20.1}Ca_{1.7}Yb_{13}Sr_{0.2}$ alloy in Ringer solution at 37°C.

pure magnesium is in the range of approx. -1.65 V, while for $Mg_{65}Zn_{20.1}Ca_{1.7}Yb_{13}Sr_{0.2}$ alloy – slightly above −1.4 V. This shift towards positive values indicates favorable behavior of samples with alloy additions. Potentiodynamic measurements (**Figure 4b**) also show the differences between the studied alloys. The values of corrosion current density were slightly higher for magnesium alloy, as compared to pure Mg. However, significant differences in E_{corr} by approx. 0.25 V are observed, which indicates that it is recommended to use alloying elements to improve corrosion resistance. E. Mostaed et al. [52] showed similar results regarding the differences in electrochemical tests between pure magnesium and the ZK60 alloy.

Designing of magnesium alloys as biomedical materials is a great challenge, due to rapid degradation of Mg in the environment of bodily fluids and insufficient implant-bone connection in orthopedic applications [50]. These disadvantages can be limited due to an appropriate selection of alloying additions. The purpose of optimal chemical composition of a new class of Mg-based biodegradable materials is to obtain optimal strength, ductility, resistance to fatigue and corrosion by modifying the structure and phase distribution [50, 53]. Currently, efforts are being made to select alloying additions that would promote osseointegration, understood as the fusion of the implant with the newly formed bone tissue and biodegradation without adverse effects on the functioning of body organs [50].

5. Mechanisms and in vitro degradation behavior of amorphous and crystalline magnesium alloys

In the case of biomedical engineering, corrosion is the main factor determining the usefulness of implant materials. The tendency of biomaterials to corrode in the human body is, in fact, closely connected to their biocompatibility. Before placing in the human body, the material must be examined for the effects on the body and its properties. Ensuring such experimental conditions is difficult, as it is difficult to recreate the environment of the human tissues. Many parameters related to the production of magnesium-based materials and test parameters have an impact on the degradation results (**Figure 5**).

The alloying elements and the processing parameters of Mg have a strong impact on its degradation properties (microstructure of the material described by the grain size, impurity content, type of phases etc.). Calcium as alloying element to Mg alloy is an extremely reactive metal and spontaneously reacts with water generating hydrogen [55].

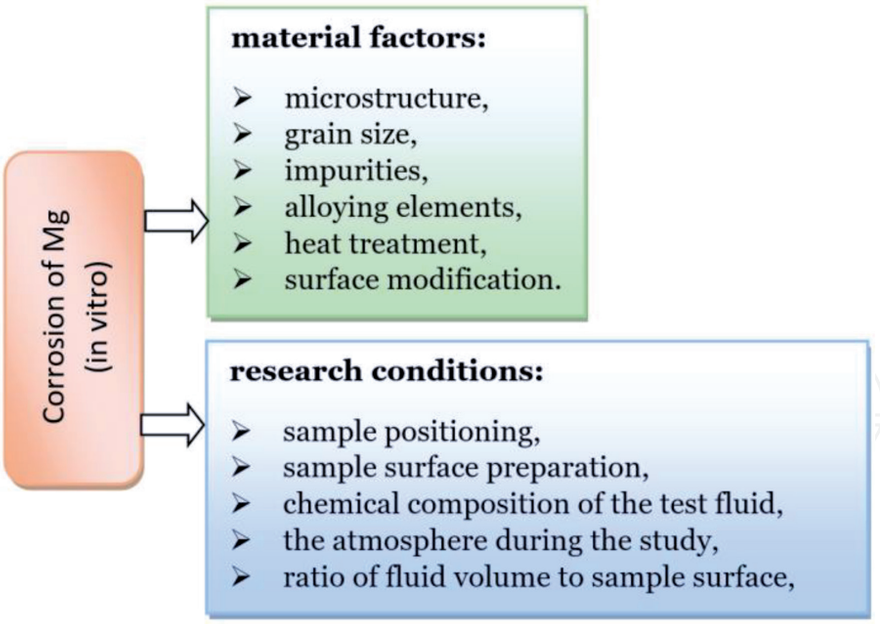

Figure 5.
Parameters influencing the course of magnesium alloy corrosion process (in vitro) divided into subgroups: Research conditions and material factors [54].

Moreover, the research methods and conditions can significantly change the corrosion rate, as well as the formation and composition of the degradation layer, and thus determine the corrosion type [56].

Living microorganisms play an important role in the process of implant degradation. Such metabolic activity may directly or indirectly reduce the quality of the implant due to the corrosion process. Cells can act as an electrolyte on the metal surface, thus changing the corrosion resistance of the implant surface or even its composition [6].

Corrosion of magnesium in an aqueous environment occurs as a result of an electrochemical reaction with water, resulting in the formation of magnesium hydroxide, $Mg(OH)_2$ and hydrogen gas, according to reactions (1–3) [54]:

$$Anodic\ reaction: Mg \rightarrow Mg^{2+} + 2e \quad (1)$$

$$Cathodic\ reaction:: 2H_2O + 2e^- \rightarrow H_2 + 2OH^- \quad (2)$$

$$Overall\ reaction\ (summary\ reaction): Mg + 2H_2O \rightarrow Mg(OH)_2 + H_2 \quad (3)$$

In the initial phase of immersion, the surface of the material is exposed to the electrolyte and the anodic and cathodic reactions begin. Magnesium grains act as an anode and the cathodic reaction takes place in noble regions of alloy, which are grain boundaries, phase separation and precipitation. This leads to the exchange of electrons between the two regions, wherein the magnesium is degraded at the same rate, at which hydrogen is generated as a gas (H_2). The cathodic reaction increases the pH by releasing H_2 gas, while hydrolysis lowers it [54, 57].

When the concentration of Mg^{2+} and the increase of pH reach the solubility limit, magnesium hydroxide $Mg(OH)_2$ is precipitated on the surface of alloy Mg [1]. In an environment, such as body fluids, where the concentration of chloride ions is greater than 30 mmol/dm^3, the hydroxide formed on the surface of the magnesium alloy converts to highly soluble magnesium chloride. This reduces the level

of protection of the surface layer by increasing its activity [58]. The formation of soluble magnesium chloride is described by the reaction (4):

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

This process accelerates the degradation of the material and increases the pH of the environment [6]. The presence of Cl^- ions initiates pitting corrosion.

It should be mentioned that the structure of magnesium alloys mainly affects the course and rate of the degradation process. The analysis of corrosion tests results and studies of degradation products on the surface of the amorphous $Mg_{64}Zn_{32}Ca_4$ alloy allow to distinguish and link the probable stages of the degradation process for the tested alloy in selected micro-areas, which include [59]:

- transformation of the oxide layer into hydroxide,
- penetration of the hydroxide layer by chlorides,
- release of metallic ions and their transfer to solution,
- hydrogen evolution,
- creating a protective layer.

It should be noted, that the specified steps are not consecutive, but may occur simultaneously during the immersion of the amorphous $Mg_{64}Zn_{32}Ca_4$ alloy. Therefore, the degradation of the amorphous $Mg_{64}Zn_{32}Ca_4$ alloy can be considered as a total result of the following processes: the release of alloy components and the formation of protective layers. When the sample is immersed in a chloride solution, degradation occurs directly at the surface, due to the rapid release of active Mg and Ca. On the other hand, this results in enrichment of the sample's surface with less active zinc. With the progress of degradation, zinc is oxidized and accumulates in the vicinity of disturbed chlorides, and therefore protects against further progression of degradation [60, 61]. However, the protective layer is not dense enough to completely prevent degradation. Chlorine ions damage the zinc oxide layer. Damage to the protective layer facilitates the transition to the Ca and Mg ion solution. These mechanisms are repeated until the amorphous magnesium alloy has degraded completely [62].

6. Methods of reducing the degradation rate of magnesium alloys by modifying their surface (application of protective layers)

High corrosion rate of magnesium-based alloys in tissue environment may be limited, in addition to modifying the chemical composition, by surface treatment technologies. The degradation process can be controlled by way of coating the surface or changing its structure [53, 60, 61]. There are two methods of coating: conversion and deposition processes. Conversion coatings are the product of complex interaction of metal dissolution and precipitation, usually during treatment in aqueous solutions, while deposition treatments consist of metallic, inorganic and organic coatings [53, 62, 63]. Modifications in the surface of magnesium alloys by mechanical treatment are also used [62]. The classification of the coating technology for magnesium alloys is shown in **Figure 6**.

Homogeneity of the corrosion process is an important aspect that determines the degradation rate and the physical condition of the implant at a specific treatment

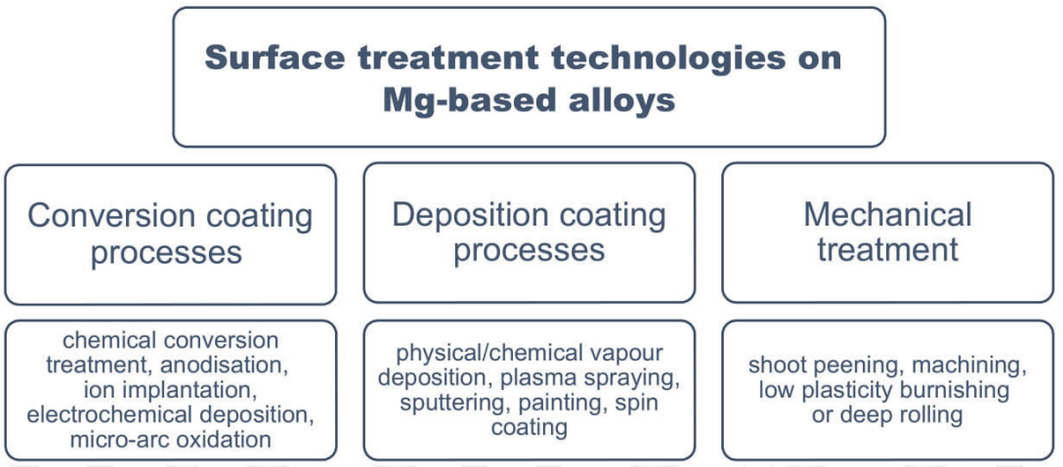

Figure 6.
General classification of surface treatment technologies applied on magnesium alloys [62, 63].

stage [63]. Magnesium alloy coatings often have pores and cracks. Corrosion, which begins in these areas, leads to uneven rate of corrosion, accelerates destruction of the coating and premature degradation of the implant [63, 64]. Therefore, it is important to minimize the porosity of the coating by adjusting the parameters of the application process or the appropriate preparation of the substrate's surface [62, 65]. In addition, protective coatings on biodegradable magnesium alloys should be adapted to specific applications – e.g. vascular stents have different surface requirements than orthopedic implants, where osseointegration with newly formed bone is important [62, 63]. Selected technologies of forming coatings on magnesium alloys are discussed below with regard to their advantages and disadvantages in terms of use, with an aim to reduce the corrosion rate:

- Chemical conversion treatment – coatings based on $Mg(OH)_2$ and fluorine are the most commonly used coatings developed with this technique, increasing corrosion resistance, while remaining non-toxic for the surrounding tissues [63, 66]. Their main advantage is good adhesion [67]. Chemical conversion treatment is still considered an economically viable technique [63, 66].

- Micro-arc oxidation (MAO) – is considered the most cost-effective technology in the production of protective coatings against corrosion on Mg-based alloys. Surface pores and cracks, which accelerate the corrosion rate, are a significant disadvantage of this technology [60, 63].

- Electrochemical deposition (ED) – is one of the most widely used methods. It has the ability to create homogeneous, dense protective layers, preventing further corrosion of the magnesium alloy substrate. Its great advantages, from technological point of view, are reproducibility and low temperatures of deposition [63, 66, 67].

- Anodization – the quality of the coating obtained in this technique is strongly dependent on the parameters of the process: electrolytic composition, applied constant voltage or current, quality of the alloy surface and concentration of the alloying elements. The obtained 5–200 μm thick oxide layer creates functional corrosion protection with excellent adhesion [63, 67]. The main disadvantage of anodization is low wear resistance [67]. The technique makes it possible to obtain nano-tubular porous layers. However, this kind of surface structure is not suitable for some applications, e.g. stents [62, 63].

- Ion Implantation – thin layers, resulting from the process, do not provide the required corrosion resistance. Despite many advantages of this technique, like modification of physical, chemical and electrical properties, ion implantation is expensive and is not suitable for complex geometries of implant components [62, 63, 67].

- Physical/Chemical Vapor Deposition (PVD/CVD) – known, widely used technologies [63]. PVD enables the formation of hard coatings, resistant to tribological wear, but from the perspective of corrosion resistance, the layers are too thin and have pores. CVD is energy-efficient and does not manifest toxicity, but has the disadvantages of complicated layer growth and requires high temperatures [67].

In choice of the coating technology, one should always take into account preservation of the alloy's biocompatibility, due to the potential toxicity of the elements introduced in coating treatments. In addition to coating, an alternative solution is mechanical treatment (shot peening, machining, burnishing, deep rolling), which solves the toxicity problem. The literature also describes hybrid techniques, which combine mechanical treatment with coating, as a promising solution for controlling the corrosion rate and mechanical properties at individual stages of treatment [63]. Biomimetic coatings are also noteworthy, as they are of biological origin and ensure excellent biocompatibility, but further work is required to improve their low adhesion to the substrate alloy [63, 67].

The types of protection coatings used to delay/reduce the degradation rate of magnesium alloys are shown in **Figure 7**. Besides phosphate and fluoride, most of the proposed ceramic coatings are non-resorbable. In the case of resorbable materials, considered polymeric coatings include PLA, PLGA and copolymers. Composite coatings increasing the corrosion resistance of magnesium alloys, tested by several researchers, include the following types of coatings: ceramic-metallic and ceramic-polymer.

As part of the authors' own research, tests of phosphate coatings on magnesium alloys were carried out. In this work [78], the chemical method was used for Ca-P coatings preparation. NaOH and $ZnSO_4$ as accelerators were added to phosphatizing baths, with an aim to form a dense and uniform protective phosphate coating. It

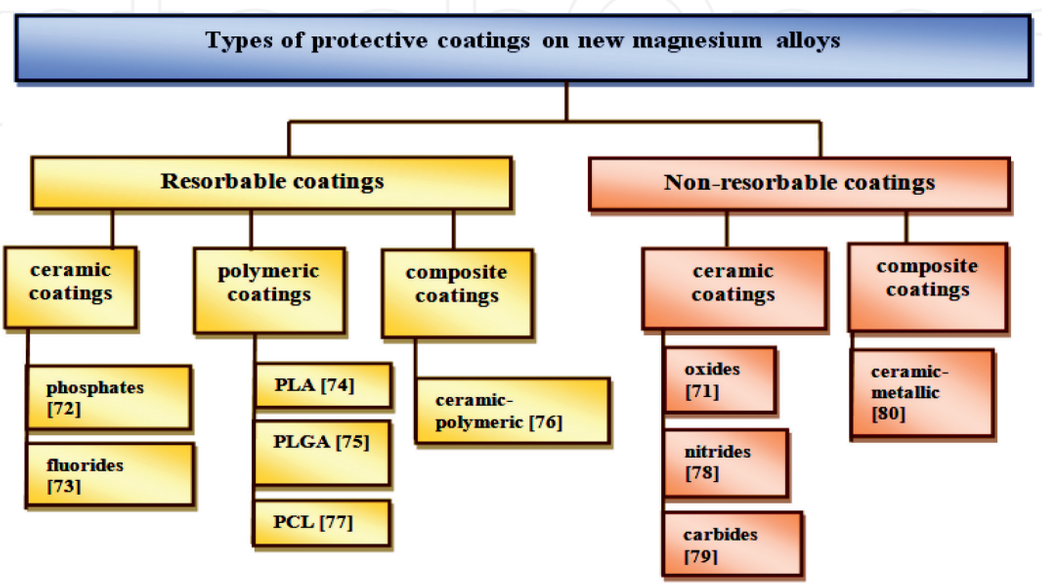

Figure 7.
Types of protective coatings used to delay/reduce the degradation rate of magnesium alloys [68–77].

should be noted, that NaOH and $ZnSO_4$ are used to improve corrosion resistance of Mg alloys. The results of microscopic observations and phase identification of the obtained phosphate coatings (with the use of chemical composition of the phosphating bath) are shown in **Figure 8**.

XRD results indicate that obtained protection layers included dicalcium phosphate dihydrate ($CaHPO_4 \cdot 2H_2O$). Both NaOH and $ZnSO_4$ formed the morphology of the produced layers. The coating obtained by immersion in a phosphatizing bath with $ZnSO_4$ addition (ZnAM50 sample) consisted of petals. The coating obtained by immersion in a bath with NaOH addition (NaAM50 sample) showed plate-like morphology.

The degradation tests of magnesium alloys with Ca-P layers were also performed (**Figure 9a** and **b**) in Ringer's solution at 37°C. The results of electrochemical tests indicated that coated samples have more positive value of E_{corr} than non-coated AM50 sample (**Figure 9a**). In addition, the cathodic part of potentiodynamic curve

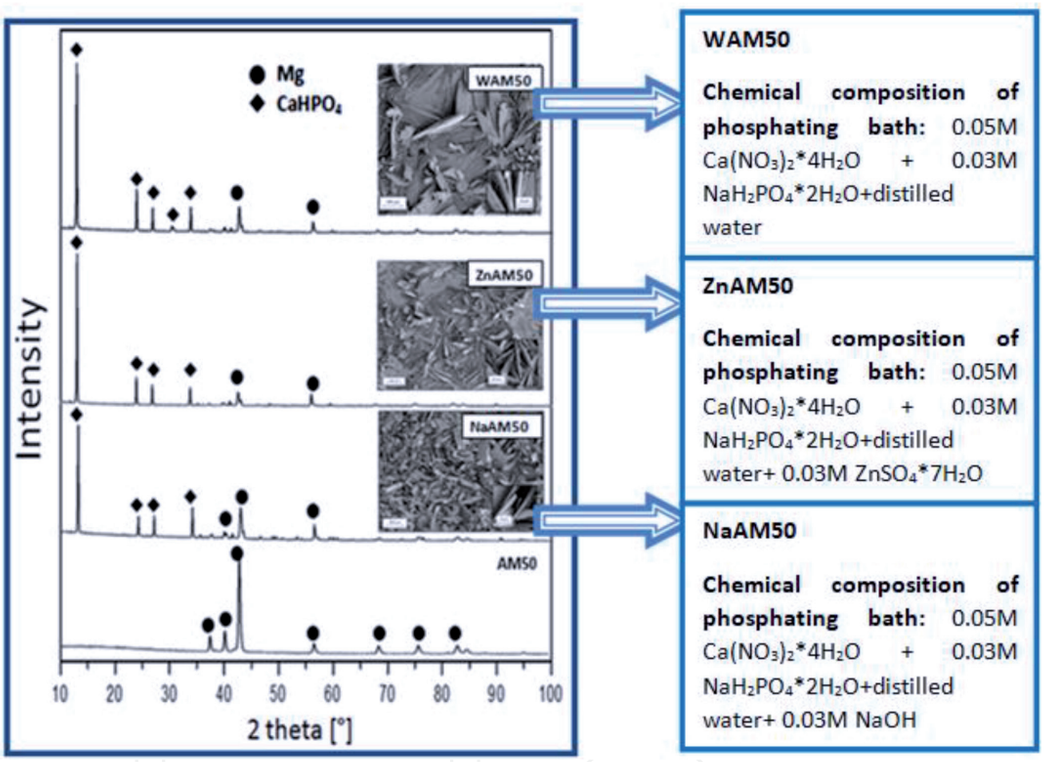

Figure 8.
X-ray diffraction patterns and SEM images of Ca-P coatings on Mg alloy [78].

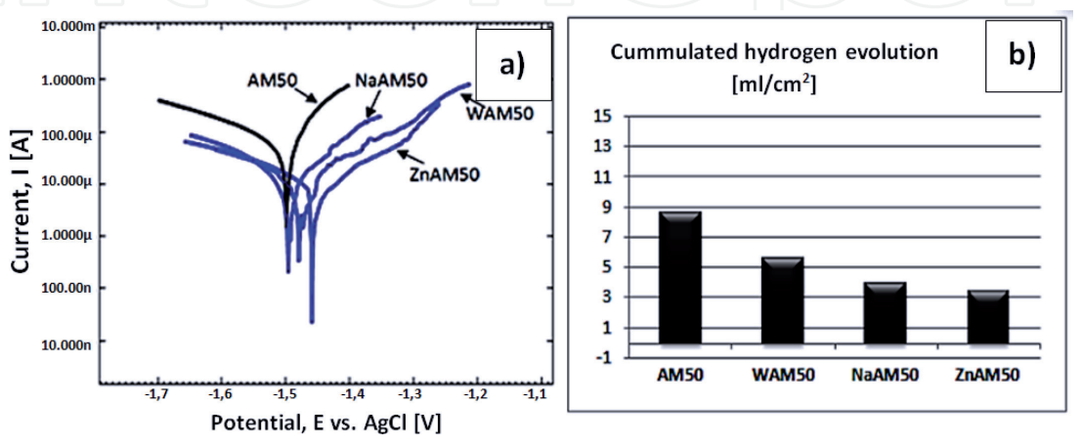

Figure 9.
Results of degradation tests of Mg alloys with calcium phosphate coatings in Ringer's solution at 37°C: (a) polarization curves, (b) hydrogen evolution [78].

determined for the coated samples is located in a low current range, which indicated a low cathodic activity. It corresponds with the immersion tests results (**Figure 9b**). The volume of evolved hydrogen (hydrogen is a result of cathodic reactions) in an uncoated sample was higher than its level in coated samples.

The degradation rate of ceramic material determines the occurrence of defects, cracks and flaws in technology. Defected ceramics can be destroyed in contact with water. Inclusions of other phases are equally disadvantageous to ceramic materials, that lead to their degradation. In contact with water, these inclusions accelerate aging and increase volume. These processes also have a direct impact on deterioration of the mechanical properties of ceramic materials [79].

7. Conclusions

Magnesium is a very important macroelement for the human body and serves a lot of functions. Its deficiency can cause many disorders and health ailments. Accordingly, magnesium is widely used in therapy, primarily for the treatment of heart disease, cardiovascular system or respiratory system. This became a premise for the use of magnesium and its alloys in medicine as a potential biomaterial for medical implants. The concept of using magnesium alloys as resorbable medical implants assumes that it will be non-toxic to the human body. The alloy components will also be elements present in the human body. The resorbable biomaterial of a magnesium alloy would be an alternative to the previously used implants, mainly orthopedic ones. Unfortunately, the high degradation rate of the magnesium alloy and the release of hydrogen gas in the environment of physiological fluids limit the use of these alloys as a biomaterial. Therefore, the research community continues to test different types of surface treatment for magnesium alloys, to protect it from rapid degradation. Taking into account the results of the global research and the authors' own research, this seems to be the right way to obtain a resorbable biomaterial of magnesium alloy.

Conflict of interest

The authors declare no conflict of interest.

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References

[1] Braszczyńska-Malik KN. Magnesium alloys and composites based on their matrix. Czestochowa: Czestochowa University of Technology; 2017. 136 p.

[2] Skrzypek SJ, Przybyłowicz K. Engineering of metals and their alloys. Krakow: AGH Publishing House; 2012. 656 p.

[3] Dobrzański LA, Tański T, Dobrzańska-Danikiewicz AD, Król M, Malara S, Domagała-Dubiel J. Structure and properties of Mg-Al-Zn alloys. Open Access Library. International OCSCO World Press; 2012.

[4] Dziubińska A. Forming of flat parts with ribs from magnesium alloy (Ph.D. thesis). Lublin: Lublin University of Technology; 2015.

[5] Marciniak J. Biomaterials engineering. Selected issues. Gliwice: Jacek Skalmierski's Computer Laboratory Publishing House; 2009.

[6] Marciniak J. Biomaterials. Gliwice: Silesian University of Technology; 2013.

[7] Osteoporosis - silent epidemic in Poland [Internet]. 2015. Available from: http://www.osteoporoza.pl/attachments/1907_Raport_System_OP_Minist-7_2015.02.10.pdf [Accessed: 2020-09-14]

[8] 85488 endoprosthesis in 2017 [Internet]. 2017. Available from: https://www.mp.pl/pacjent/ortopedia/aktualnosci/188266,85-488-endoprotezoplastyk-stawowych-w-2017-r?fbclid=IwAR1PRpkyh4u-bYeE4EX4yJfIcsW83RrwWaOMFk8p8A-leOgltgL5I_3AhW8 [Accessed: 2020-09-14]

[9] Pamuła E. Biomaterials for tissue engineering. Research on the structure and biological properties of aliphatic polyesters. Krakow: Polish Society for Biomaterials; 2008.

[10] Błażewicz S, Stoch L. Biomaterials. Vol 4. Warsaw: Exit Academic Publishing House; 2003.

[11] Greenberg AM, Prein J. Craniomaxillofacial Reconstructive and Corrective Bone Surgery. Principles of Internal Fixation Using the AO/ASIF Technique. Switzerland: Springer-Verlag; 2002.

[12] Babilas R, Bajorek A, Włodarczyk P, Łoński W, Babilas D. Effect of Au addition on the corrosion activity of Ca-Mg-Zn bulk metallic glasses in Ringer's solution. Materials Chemistry and Physics. 2019;226:51-58. DOI: doi.org/10.1016/j.matchemphys.2018.12.088

[13] Karmańska A, Stańczak A, Karwowski B. Magnesium - the actual state of knowledge. Bromatology and Toxicological Chemistry. 2015;4:677-689.

[14] Kabata-Pendias A, Pendias H. Biogeochemistry of trace elements. Warsaw: PWN Publishing House; 1999.

[15] Zhang BP, Wang Y, Geng L. Biomaterials - Physics and Chemistry, Croatia: InTech; 2011.

[16] Vitamin and mineral requirements in human nutrition [Internet]. 1998. Available from: https://apps.who.int/iris/bitstream/handle/10665/42716/9241546123.pdf [Accessed: 2020-09-14]

[17] Reginster JY, Strause L, Deroisy R, Lecart MP, Saltman P, Franchimont P. Preliminary report of decreased serum magnesium in postmenopausal osteoporosis. Magnesium. 1989;8:106-109.

[18] Nechifor M. Magnesium in major depression. Magnesium Research. 2009;22:163S–166S

[19] Guerrera MP, Volpe SL, Mao JJ. Therapeutic uses of magnesium. American Family Physician. 2009;80:157-162

[20] Seal CK, Vince K, Hodgson MA. Biodegradable surgical implants based on magnesium alloys - a review of current research. Materials Science Engineering. 2009;4:012011. DOI: 10.1088/1757-899X/4/1/012011

[21] Chakraborty Banerjee P, Al-Saadi S, Choudhary L, Eslami Harandi S, Singh R. Magnesium implants: prospects and challenges. Materials. 2019;12/1:136. DOI: 10.3390/ma12010136

[22] Agarwal S, Curtin J, Duffy B, Jaiswal S. Biodegradable magnesium alloys for orthopaedic applications: A review on corrosion, biocompatibility and surface modifications. Materials Science and Engineering C. 2016;68:948-963. DOI: 10.1016/j.msec.2016.06.020

[23] Staiger MP, Pietak AM, Huadmai J, Dias G. Magnesium and its alloys as orthopedic biomaterials: a review. Biomaterials. 2006;27/9:1728-1734. DOI: 10.1016/j.biomaterials.2005.10.003

[24] Witte F, Hort N, Vogt C, Cohen S, Kainer KU, Willumeit R, Feyerabend F. Degradable biomaterials based on magnesium corrosion. Current Opinion Solid State Materials Science. 2008;12/5-6:63-72. DOI: 10.1016/j.cossms.2009.04.001

[25] Zheng Y. Magnesium alloys as degradable biomaterials. Boca Raton: CRC Press; 2015.

[26] Ali M, Hussein MA, Al-Aqeeli N. Magnesium-based composites and alloys for medical applications: A review of mechanical and corrosion properties. Journal of Alloys and Compounds. 2019;792:1162-1190. DOI: 10.1016/j.jallcom.2019.04.080

[27] Hong K, Park H, Kim Y, Knapek M, Minarik P, Mathis K, Yamamoto A, Choe H. Mechanical and biocorrosive properties of magnesium-aluminum alloy scaffold for biomedical applications. Journal of Mechanical Behavior and Biomedical Materials. 2019;98:213-224. DOI: 10.1016/j.jmbbm.2019.06.022

[28] Bommala VK, Krishna MG, Rao CT. Magnesium matrix composites for biomedical applications: A review, Journal of Magnesium Alloys. 2019;7(1):72-79. DOI: 10.1016/j.jma.2018.11.001

[29] Echeverry-Rendon M, Allain JP, Robledo SM, Echeverria F, Harmsen MC. Coatings for biodegradable magnesium-based supports for therapy of vascular disease: A general view. Materials Science and Engineering C. 2019;102:150-163. DOI: 10.1016/j.msec.2019.04.032

[30] Chen J, Tan L, Yu X, Etim IP, Ibrahim M, Yang K. Mechanical properties of magnesium alloys for medical application: A review. Journal of the Mechanical Behavior of Biomedical Materials. 2018;87:68-79. DOI: 10.1016/j.jmbbm.2018.07.022

[31] Seitz JM, Lucas A, Kirschner M. Magnesium-based compression screws: a novelty in the clinical use of implants. The Journal of The Minerals, Metals & Materials Society. 2016;68:1177-1182. DOI: 10.1007/s11837-015-1773-1

[32] Ilnicka M, Wawrzyńska M, Biały D. Biodegradable coronary stents – overview. Acta BioOptica et Informatica Medica. 2009;15;369-372. DOI: polona.pl/item/37787964

[33] Lobodzinski SS. Bioabsorbable coronary stents. Folia Cardiologica Excerpta. 2009;4:247-250

[34] Barlis P, Tanigawa J, Di Mario C. Coronary bioabsorbable magnesium

stent: 15-month intravascular ultrasound and optical coherence tomography findings. European Heart Journal. 2007;28:2319-2325. DOI: 10.1093/eurheartj/ehm119

[35] Pekguleryuz M, Kainer K, Kaya A. Fundamentals of magnesium alloy metallurgy. Cambridge: Woodhead Publishing Limited; 2013.

[36] Rokhlin LL, Nikitina NI. Recovery after ageing of Mg-Y and Mg-Gd alloys. Journal of Alloys and Compounds. 1998;279/2:166-170. DOI: 10.1016/S0925-8388(98)00655-0

[37] Kania A, Nowosielski R, Gawlas-Mucha A, Babilas R. Mechanical and corrosion properties of Mg-based alloys with Gd addition. Materials. 2019;12/11:1775. DOI: 10.3390/ma12111775

[38] Hanzi AC, Gerber I, Schinhammer M, Loffler JF, Uggowitzer PJ. On the in vitro and in vivo degradation performance and biological response of new biodegradable Mg-Y-Zn alloys. Acta Biomaterialia. 2010;6/5:1824-1833. DOI: 10.1016/j.actbio.2009.10.008

[39] Heublein B, Rohde R, Kaese V, Niemeyer M, Hartung W, Haverich A. Biocorrosion of magnesium alloys: a new principle in cardiovascular implant technology? Heart. 2003;89/6:651-656. DOI: 10.1136/heart.89.6.651

[40] Cesarz-Andraczke K, Nowosielski R, Babilas R. Corrosion properties of Mg-Zn-Ca-(Cu,Au) metallic glasses in artificial physiological fluid. Archives of Civil and Mechanical Engineering. 2019;19/3:716-723. DOI: 10.1016/j.acme.2019.02.008

[41] Wang L, Qin G, Sun S, Ren Y, Li S. Effect of solid solution treatment on in vitro degradation rate of as-extruded Mg-Zn-Ag alloys. Transactions of Nonferrous Metals Society of China. 2017;27/12:2607-2612. DOI: 10.1016/S1003-6326(17)60288-7

[42] Feng Y, Zhu S, Wang L, Chang L, Guan S. Fabrication and characterization of biodegradable Mg-Zn-Y-Nd-Ag alloy: Microstructure, mechanical properties, corrosion behavior and antibacterial activities. Bioactive Materials. 2018;3/3:225-235. DOI: 10.1016/j.bioactmat.2018.02.002

[43] Nowosielski R, Cesarz K, Nawrat G, Maciej A, Babilas R. Corrosion tests of amorphous and crystalline Mg36.6Cu36.2Ca27.2 alloy in physiological fluid. Corrosion Protection. 2013;4:144-151

[44] Laws K, Shamlaye K, Wong K, Gun B, Ferry M. Prediction of glass-forming compositions in metallic systems: Copper-based bulk metallic glasses in the Cu-Mg-Ca system. Metallurgical and Materials Transactions. 2010;41A:1699-1705. DOI: 10.1007/s11661-010-0274-7

[45] Gu X, Zheng Y, Zhong S, Xi T, Wang J. Wang W. Corrosion of, and cellular responses to Mg-Zn-Ca bulk metallic glasses. Biomaterials. 2010;31:1093-1104. DOI: 10.1016/j.biomaterials.2009.11.015

[46] Li Q, Weng H, Suo Z, Ren Y, Yuan X, Qiu K. Microstructure and mechanical properties of bulk Mg-Zn-Ca amorphous alloys and amorphous matrix composites. Materials Science and Engineering A. 2008;487:301-308. DOI: 10.1016/j.msea.2007.10.027

[47] Park JB, Bronzino JD. Biomaterials: principles and applications. Florida: CRC Press; 2003.

[48] Ding Y, Wen C, Hodgson P, Li Y. Effects of alloying elements on the corrosion behavior and biocompatibility of biodegradable magnesium alloys: A review. Journal of Materials

Chemistry B. 2014;2:1912-1933. DOI: 10.1039/c3tb21746a

[49] Meagher P, O'Cearbhaill ED, Byrne JH, Browne DJ. Bulk metallic glasses for implantable medical devices and surgical tools. Advanced Materials. 2016;28:5755-5762. DOI: 10.1002/adma.201505347

[50] Mushahary D, Sravanthi R, Li Y, Kumar MJ, Harishankar N, Hodgson PD, Wen C, Pande G. Zirconium, calcium, and strontium contents in magnesium based biodegradable alloys modulate the efficiency of implant-induced osseointegration. International Journal of Nanomedicine. 2013;8:2887-2902. DOI: 10.2147/IJN.S47378

[51] Pogorielov M, Husak E, Solodivnik A, Zhdanov S. Magnesium-based biodegradable alloys: Degradation, application, and alloying elements. Interventional Medicine and Applied Science. 2017;9:27-38. DOI: 10.1556/1646.9.2017.1.04

[52] Mostaed E, Vedani M, Hashempour M, Bestetti M. Influence of ECAP process on mechanical and corrosion properties of pure Mg and ZK60 magnesium alloy for biodegradable stent applications. Biomatter. 2014;4:e28283. DOI: 10.4161/biom.28283

[53] Liu C, Ren Z, Xu Y, Pang S, Zhao X, Zhao Y. Biodegradable magnesium alloys developed as bone repair materials: A review. Scanning. 2018;2018. DOI: 10.1155/2018/9216314

[54] Degradation testing of magnesium and its alloys aiming at biodegradable implant applications [Internet]. 2016. Available from: https://lirias.kuleuven.be/bitstream/123456789/552754/1/PhD+thesis+manuscript+-+I%C3%B1igo+Marco.pdf [Accessed: 2020-09-14]

[55] Babilas, R.Ł., Cesarz-Andraczke, K., Babilas, D., Simka, W. Structure and Corrosion Resistance of $Ca_{50}Mg_{20}Cu_{30}$ Bulk Metallic Glasses. Journal of Materials Engineering and Performance, 2015; 24/1: 167-174. DOI: 10.1007/s11665-014-1308-x

[56] Schweitzer PA. Fundamentals of metallic corrosion. Atmospheric and media corrosion of metals. New York: CRC Press; 2007.

[57] Rad B, Idris MH, Kadir MRA, Farahany S, Fereidouni A, Yahya MY. Characterization and corrosion behavior of biodegradable Mg-Ca and Mg-Ca-Zn implant alloys. Applied Mechanics and Materials. 2012;121-126:568-572. DOI: 10.4028/www.scientific.net/AMM.121-126.568

[58] Haynes WM. Handbook of Chemistry and Physics. 97th ed. CRC Press; 2016. 2670 p.

[59] Cesarz-Andraczke K. Resorbable Mg-based bulk metallic glasses [Ph.D. thesis]. Gliwice: Silesian University of Technology; 2016.

[60] Wu W, Wang Z, Zang S, Yu X, Yang H, Chang S. Research progress on surface treatments of biodegradable Mg Alloys: A Review. ACS Omega. 2020;5:941-947. DOI: 10.1021/acsomega.9b03423

[61] Li Y, Zhao S, Li S, Ge Y, Wang R, Zheng L, Xu J, Sun M, Jiang Q, Zhang Y, Wei H. Surface engineering of biodegradable magnesium alloys for enhanced orthopedic implants. Nano Micro Small. 2019;15:1-10. DOI: 10.1002/smll.201904486

[62] Hornberger H, Virtanen S, Boccaccini AR. Biomedical coatings on magnesium alloys - A review. Acta Biomaterialia. 2012;8:2442-2455. DOI: 10.1016/j.actbio.2012.04.012

[63] Uddin MS, Hall C, Murphy P. Surface treatments for controlling corrosion rate of biodegradable

Mg and Mg-based alloy implants. Science and Technology of Advanced Materials. 2015;16:53501. DOI: 10.1088/1468-6996/16/5/053501

[64] Zeng RC, Yin ZZ, Chen XB, Xu DK. Corrosion types of magnesium alloys. In: Magnesium Alloys - Selected Issue [Internet]. 2018. Available from: https://www.intechopen.com/books/magnesium-alloys-selected-issue/corrosion-types-of-magnesium-alloys [Accessed: 2020-09-14]

[65] Zhang P, Zuo Y. Relationship between porosity, pore parameters and properties of microarc oxidation film on AZ91D magnesium alloy. Results in Physics. 2019;12:2044-2054. DOI: 10.1016/j.rinp.2019.01.095

[66] Zheng YF, Gu XN, Witte F. Biodegradable metals. Materials Science and Engineering: R: Reports. 2014;77:1-34. DOI: 10.1016/j.mser.2014.01.001

[67] Echeverry-Rendon M, Allain JP, Robledo SM, Echeverria F, Harmsen MC. Coatings for biodegradable magnesium-based supports for therapy of vascular disease: A general view, Materials Science and Engineering C. 2019;102:150-163. DOI: 10.1016/j.msec.2019.04.032

[68] Gao Y, Jie M, Liu Y. Mechanical properties of Al_2O_3 ceramic coatings prepared by plasma spraying on magnesium alloy. Surface and Coatings Technology. 2017;315:214-219. DOI: 10.1016/j.surfcoat.2017.02.026

[69] Jiang S, Cai S, Lin Y, Bao X, Xu G. Effect of alkali/acid pretreatment on the topography and corrosion resistance of as-deposited CaP coating on magnesium alloys. Journal of Alloys and Compounds. 2019;793:202-211. DOI: 10.1016/j.jallcom.2019.04.198

[70] Feng Y, Zhu S, Wang L, Chang L, Yan B, Song X, Guan S. Characterization and corrosion property of nano-rod-like HA on fluoride coating supported on Mg-Zn-Ca alloy. Bioactive Materials. 2017;2:63-70. DOI: 10.1016/j.bioactmat.2017.05.001

[71] Shi P, Niu B, Shanshan E, Chen Y, Li Q. Preparation and characterization of PLA coating and PLA/MAO composite coatings on AZ31 magnesium alloy for improvement of corrosion resistance. Surface and Coatings Technology. 2015;262:26-32. DOI: 10.1016/j.surfcoat.2014.11.069

[72] Manna S, Donnell AM, Kaval N, Marwan F. Improved design and characterization of PLGA/PLA-coated Chitosan based micro-implants for controlled release of hydrophilic drugs. International Journal of Pharmaceutics. 2018;547/1-2:122-132. DOI: 10.1016/j.ijpharm.2018.05.066

[73] Reza H, Rad B, Fauzi Ismail A, Aziz M, Hadisi Z, Chen X. Antibacterial activity and corrosion resistance of Ta_2O_5 thin film and electrospun PCL/MgO-Ag nanofiber coatings on biodegradable Mg alloy. Ceramics International. 2019;45/9:11883-11892. DOI: 10.1016/j.ceramint.2019.03.071

[74] Ling L, Cui L, Zeng R, Li S, Chen X, Zheng Y, Kannan MB. Advances in functionalized polymer coatings on biodegradable magnesium alloys - A review. Acta Biomaterialia. 2018;79:23-36. DOI: 10.1016/j.actbio.2018.08.030

[75] Mashtalyar DV, Sinebryukhov SL, Imshinetskiy IM, Gnedenkov AS, Nadaraia KV, Ustinov AY, Gnedenkov SV. Hard wearproof PEO-coatings formed on Mg alloy using TiN nanoparticles. Applied Surface Science. 2020;503:1-12. DOI: 10.1016/j.apsusc.2019.144062

[76] Wang S, Si N, Xia Y, Liu L. Influence of nano-SiC on microstructure and property of MAO coating formed on AZ91D magnesium alloy. Transactions of Nonferrous Metals Society of China.

2015;25:1926-1934. DOI: 10.1016/S1003-6326(15)63800-6

[77] Singh B, Singh G, Sidhu BS, Bhatia N. In-vitro assessment of HA-Nb coating on Mg alloy ZK60 for biomedical applications. Materials Chemistry and Physics. 2019;231/1:138-149. DOI: 10.1016/j.matchemphys.2019.04.037

[78] Cesarz-Andraczke K, Nowosielski R, Basiaga M, Babilas R. Study of the morphology and properties of biocompatible Ca-P coatings on Mg alloy. Materials. 2020;13/2:1-13. DOI: 10.3390/ma13010002

[79] Sobczak-Kupiec A, Wzorek Z. Physicochemical properties of calcium orthophosphates important for medicine. Chemistry. 2007;10:309-322.