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Biodegradable magnesium alloys for medical application

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The microstructure, mechanical properties and dissolution rate of magnesium alloy WE43 at various microstructure parameters in the medium simulating biological fluid have been studied. In order to improve the alloy mechanical properties by ultra-fine grained structure formation, the equal-channel angular pressing was used followed drawing and heat treatment.

Исследованы микроструктура, механические свойства и скорость растворения магниевого сплава WE43, имеющего различные микроструктурные параметры, в среде, имитирующей биологическую жидкость. С целью повышения механических свойств сплава путем создания в нем ультрамелкозернистой структуры использован метод равноканального углового прессования с последующим волочением и термообработкой.

The number of researches intended to improve biological properties of implant materials grew considerably last few years. Among various implant types, the metal materials are of considerable importance. Metals are more suitable for load-bearing applications than ceramics or polymeric materials due to combination of high mechanical strength and fracture toughness [1]. The widely used metallic biomaterials include stainless steels, titanium and its alloys, tantalum, cobalt-chrome and nickel-chrome alloys. Furthermore, new biomaterials based on zirconium are developing. Drawbacks of such metallic biomaterials include the possibility of toxic metal ions and/or corrosion products formation that results in inflammatory responses which reduce biocompatibility and cause tissue damage [1]. Moreover, the elasticity modulus of modern metallic biomaterials is much higher than that of natural bone tissue, that may result in a reduced stimulation of new bone growth and remodeling which decreases implant stability [1]. Modern metallic biomaterials are neutral in vivo, remaining as permanent fixtures, which in the case of plates, screws, and pins used to secure serious fractures, must be removed by a second surgical procedure after the tissue has healed sufficiently [1].

In the course of search for degradable bone implants with high primary stability, a novel type of implant materials on the basis of corroding metals has been found. The degradable metal implants made of magnesium alloys were introduced into orthopedic and trauma surgery in the first half of the last century [2]. Screws and plates made from magnesium alloys provide stable implant materials that degrade in vivo and there is no need for a second operation for implant removal [2]. Good biocompatibility was observed in clinical studies, although large amounts of hydrogen were accumulated as subcutaneous gas bubbles when the magnesium implants degraded too quickly [2]. Thus, for an efficient use of magnesium

alloys as biomaterial, it is necessary to lower, first of all, their dissolution rate in biological environment [3]. Besides, mechanical properties of early magnesium alloys also were not high enough. Recently, a number of novel magnesium alloys with improved corrosion and mechanical properties has been developed. The improved properties of magnesium materials have been provided due to a rational choice of alloying additives, mainly yttrium and rare earth elements, such as neodymium and dysprosium, and also to introduction of small amounts of aluminum and zinc [4]. Those materials include, first of all, WE54 and WE43 type alloys [4, 5]. These magnesium alloys exhibit the tensile yield strength (200 MPa) and modulus of elasticity (45 GPa) exceeding by a factor of 2 and 4, respectively, those of degradable polymeric implant materials currently in use, such as u-HA/PLLA 50/50 (tensile yield strength: 103 MPa, Young's modulus: 12.3 GPa) [2, 4].

It is to note that data on the corrosion rate of these materials in various environments and influence of different alloying elements thereon obtained by various authors are rather inconsistent [2, 3, 6]. Besides, there are no data on influence of the structural factor (in particular, the grain size) on dissolution rate. A further optimization of mechanical properties of alloys is also desirable. The purpose of this is to research the improvement potentiality of mechanical properties of WE43 alloy by ultra-fine-grained structure formation and to study the dissolution rate of the alloy at various structural states in the environment simulating a biological fluid.

The WE43 alloy (ELEKTRON WE43 CASTINGS, Magnesium Elektron, Manchester, England) belonging to the most corrosion-resistant magnesium-based alloys was studied. The composition of WE43 determined by laser mass spectrometry is presented in Table. There were two kinds of samples: plates ($10.3\times10.3\times2$ mm^3) and wires (22 mm length and 1.2 mm in diameter). The plate-shaped samples were cut out by spark cutting from a semi-finished product and ground and polished prior to tests. To form the ultra-fine-grained structure by an intensive plastic deformation, the equal-channel angular pressing was chosen [7]. A blank of 20 mm diameter were subjected to 12 straining cycles in an equal-channel angular press mold. The deformation temperature was varied in the range 320–370°C. To provide homogeneous deformation, the extrusion was realized under changing the extrusion direction each time and rotating the blank by 90 degrees. Then the blank was extruded into a 5 mm diameter rod and drawn down to 1.2 mm. Finally, the wire was heat treated at 320°C for 1 h. The alloy microstructure was examined using an optical microscope (MIM-4) and scanning electron microscope (REMMA-202) on samples prepared by standard metallographic methods. The ultimate tensile strength σ_{UTS}, yield strength σ_{YS} and elongation δ were measured using an 1231U-10 testing machine.

Table. Elemental composition of WE43 alloy (wt.%)

Alloy	Mg	Y	Nd	Zr	La
WE43	Bal.	4.18	2.14	0.47	0.27

The corrosion tests of samples were realized in a 1 % solution of NaCl in the dynamic mode. A testing setup to work with different numbers of samples (from 1 to 3) simultaneously has been developed. The testing setup comprised a vessel of 3 dm^3 capacity; a pump; connecting tubes of 9 mm diameter and chambers for 200 mm long samples. The fluid flow rate was 2 dm^3/min. The samples for corrosion tests were prepared as follows. After a preliminary buffing, the samples were chemically polished using etching agent HNO_3:H_2O (3:2) during 2–3 s. The chemically etched samples were washed in distilled water. The prepared and weighed samples were chambered. The flow speed of 1 % NaCl solution above the sample surface was sufficient to entrain the hydrogen bubbles arising at the surface. The pump was switched off after a specified time, the samples washed in distilled water and dried. The surface changes were examined in the optical microscope at different magnifications. The samples were weighed using an analytical balance with accuracy $\pm5\cdot10^{-5}$ g. Then the sample mass loss and corrosion rate were calculated.

The microstructure of industrial alloy and alloy after intensive plastic deformation and heat treatment are shown in Fig. 1, 2. The research has shown that the industrial alloy WE43 (Fig. 1) have a grain size about 10 μm (there are areas with the minimal grain size about 3 μm and separate grains of 17 μm size). A two-phase structure is observed with equiaxial and homogeneous grains. The second phase amounts ap-

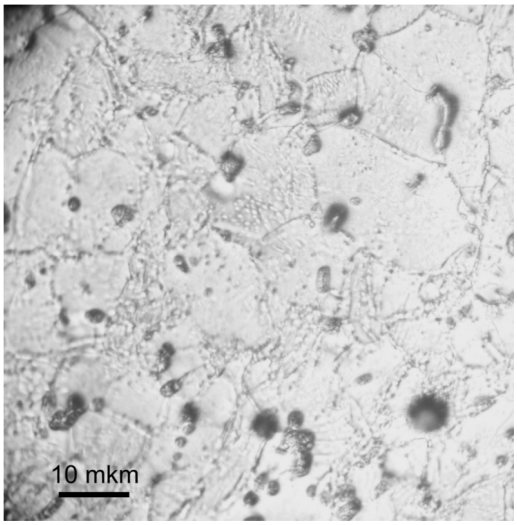

Fig. 1. The microstructure of industrial alloy WE43 (immersion).

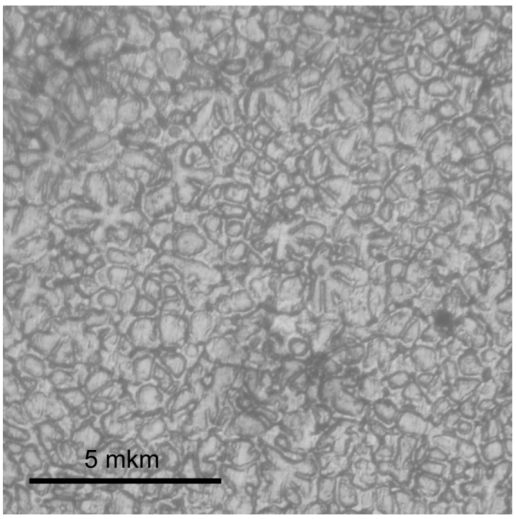

Fig. 2. The microstructure of ultra-fine-grained alloy WE43.

proximately 2 %, its inclusions are very small, located both at the grain boundaries and within the grain volume, the inclusion size being about 3–6 μm. As a result of the mechanical and heat treatment, there is grain refinement down to 0.5–1 μm (Fig. 2), while the second phase inclusions become unobservable at the current magnification. The results of tensile tests are shown in Fig. 3, 4, where the ultimate tensile strength σ_{UTS}, yield strength σ_{YS} and elongation δ values are compared for the industrial WE43 alloy and ultra-fine-grained samples. It is obvious that mechanical properties of the alloy depend heavily on the structural factor. The samples of ultra-fine-grained alloy exceed the industrial one by 30 % in yield strength, by 13 % in ultimate tensile strength and 40 % in elongation.

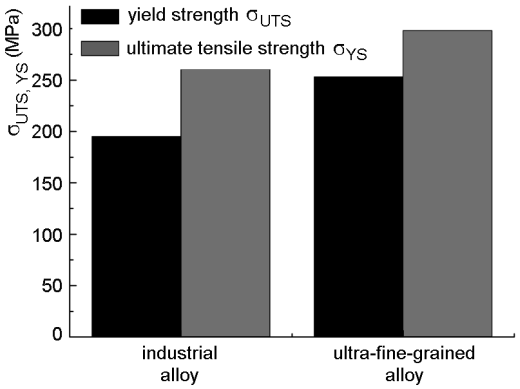

Fig. 3. Diagram of ultimate tensile strength σ_{UTS} and yield strength σ_{YS} comparison for the specimens of industrial and ultra-fine-grained alloy WE43.

At the first stage of the corrosion test, the dissolution of industrial WE43 alloy was studied. The sample exposure time was 10 days. During that time, the samples were removed in the Day 1, 2, 3, 4, 7, 8, 9 and 10 to determine the mass loss as a function of exposure duration and to calculate the corrosion rate V_{CORR} (mg/cm^2 per day). During the first few hours of the fluid circulation, a reddish tint occurrence was visually marked on the sample surface. The film became grey gradually. The maximal mass loss was observed at the first day. Then the protective film thickness increased, its color became brighter, and the mass loss was slowed down. At this stage, spotted inclusions and unidirectional chains (areas with the increased content of rare earth elements) were observed under a microscope against a light matte background. The inclusions had in an initial stage a shiny black-silvery surface. Mechanical damaging of the inclusion has activated occurrence of a white spot. After 4 h of exposure in NaCl solution, the surface became homogeneous (effect of alignment of the broken layer). A white oxide film on the areas enriched in rare earth elements was formed later (after 7–8 days).

The second stage of experiment was the dissolution study of ultra-fine-grained WE43 alloy. The exposure time was 7 day. During these 7 days, the samples were removed after each 24 h to determine the mass loss as a function of the exposure duration time and to calculate the corrosion rate V_{CORR} (mg/cm^2·per day). After the corrosion tests, the diagrams of corrosion rate in

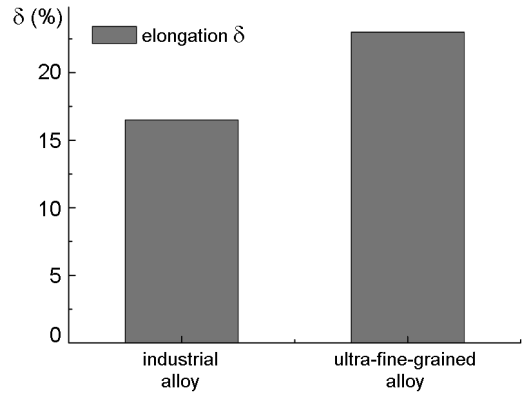

Fig. 4. Diagram of elongation δ comparison for the specimens of industrial and ultra-fine-grained alloy WE43.

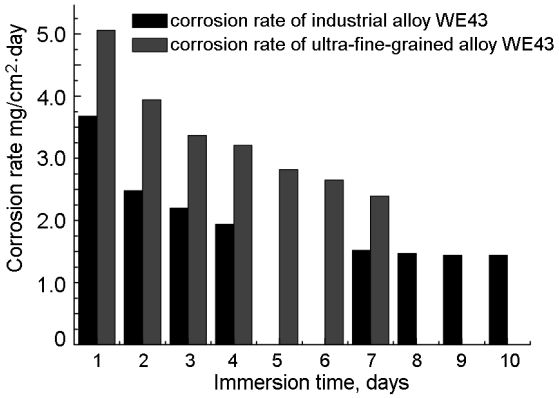

Fig. 5. Diagram of corrosion rate comparison of industrial and ultra-fine-grained alloy WE43 in 1 % NaCl solution.

1 % NaCl solution were plotted for industrial and ultra-fine-grained alloy (Fig. 5). It was revealed that the mass loss of the industrial alloy amounted 13.4 % for 10 days, while for the ultra-fine-grained alloy it was 33 % for 7 days. Thus, the corrosion tests have shown that the ultra-fine-grained alloy is more susceptible to corrosion than the industrial WE43 alloy. This fact may be due to a larger area of the grain and interphase boundaries in the ultra-fine-grained material.

The corrosion of magnesium depends essentially on the environment composition. Unprotected magnesium exposed to open air will develop a gray oxide film of magnesium hydroxide $Mg(OH)_2$ which slows the corrosion [1]. These $Mg(OH)_2$ films are slightly soluble in water; however, a severe corrosion occurs in aqueous physiological environments where chloride ions are present at levels on the order of 150 mmol/L, because $Mg(OH)_2$ reacts with Cl^- to form highly soluble magnesium chloride and hydrogen gas. Pitting of magnesium is observed at Cl^- concentrations exceeding 30 mmol/L [1]. Also, it is well known that, during magnesium alloy corrosion, a protective layer of oxide and hydroxide is formed on the metal surface, whose properties depend on the electrolyte type [5]: an extreme protective behavior is induced by strongly passivating anions, such as chromates or fluorides, while negative effects are produced by pitting agents, such as chlorides [5].

The doping is an essential way to improve mechanical properties and corrosion resistance of magnesium [1]. It follows from results of this work that not only elemental composition of the alloy, but also its structure parameters are of a considerable importance in dissolution.It has been found [3] that the corrosion rate of magnesium alloys in biological tissues (in vivo) is considerably lower than in physiological solution (in vitro). It is believed [1] that the full dissolution time of a bone implant in a body should make 12–18 weeks. So, not only variations in the alloy composition can be used for dissolution time optimization, but also variations in structural state.

Thus, using the method of equal-channel angular pressing in combination with a programmed heat treatment, it is possible to obtain samples of WE43 magnesium alloy with grain size about 1 μm. The alloy with such a microstructure provides essential advantages in mechanical and plastic properties in comparison with industrial analog (grain size about 10 μm). The corrosion rate of alloys with various microstructures in a physiological solution have been defined. It is shown that the alloy with a fine-grained microstructure is dissolved faster than the coarse-grained material.

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Біорозчинні сплави магнію для медичного застосування

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Досліджено мікроструктуру, механічні властивості і швидкість розчинення магнієвого сплаву WE43, що має різні мікроструктурні параметри, у середовищі, що імітує біологічну рідину. З метою підвищення механічних властивостей сплаву шляхом створення у ньому ультрадрібнозернистої структури використано метод рівноканального кутового пресування з наступним волочінням і термообробкою.