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Corrosion resistance of PLGA-coated biomaterials

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The aim of the study was to determine the influence of PLGA bioresorbable polymer coating on corrosion resistance of metal biomaterial. Polymer coating deposited by immersion method was applied. Corrosion resistance of metal biomaterials (stainless steel, Ti6Al4V, Ti6Al7Nb) coated with PLGA polymer, after 90 days exposure to Ringer's solution was tested. The amount of metal ions released to the solution was also investigated (inductively coupled plasma–atomic emission spectrometry (ICP-AES) method). The surface of the samples was observed using atomic force microscopy (AFM) and scanning electron microscopy (SEM). Degradation of PLGA was monitored with the use of the ^{1}H NMR spectroscopy and GPC (Gel Permeation Chromatography). The studies were carried out for non-sterilized (NS) and sterilized (S) samples. Application of the polymer coating causes a reduction of release of metal ions to the solution. Depending on metal substrate different course of destruction of polymer layer was observed. After 90 days of incubation in Ringer's solution polymer layer was highly degraded, however, the composition of copolymer (ratio of the comonomeric units in the chain) remained unchanged during the whole process, which suggests even degradation. The polymer layer reduced degradation kinetics of the metal substrate. Moreover, degradation process did not change surface morphology of metal substrate and did not disturb its integrity. The results obtained indicate that the applied polymer layer improves corrosion resistance of the alloys being investigated. Thus, the developed implants with bioresorbable coatings could be advantageous for medical applications.

Key words: *corrosion resistance, titanium alloys, stainless steel, degradation, PLGA, biodegradable coatings*

1. Introduction

Metal implants are the most frequently used in medicine nowadays. These include stainless steel, titanium and its alloys as well as cobalt alloys [15]. The major reason for their extensive use is the low cost. Although many years have been devoted to the study of requirements for their chemical composition, structure and mechanical properties, no satisfactory level of biotolerance has been achieved. Therefore, the crucial current objective is to improve biotolerance of such metal biomaterials through modification of the surface layer [2], [4], [12], [19], [23], [10]. The applied methods of modification of the surface layer aim at improved corrosion resistance and reduced quantity of degradation products. With this purpose in mind, passive layers are formed on implant surface. Unfortunately, exposed to the synergic effect of tissues and body fluids as well as mechanical factors, they degrade. Consequently, such degradation products may irritate the tissues, bring inflammatory response or trigger the allergic and cytotoxic effect [11], [16], [20], [13]. Many attempts are reported in literature to improve bioactivity and biocompatibility of metallic implants by using biodegradable polymeric layers based on aliphatic polyesters [1], [19], [21]. Coating the metal implant surface with a polymer layer pro-

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tects the body against the metal implant degradation products and may also assist the tissue recovery through the controlled release of a drug [8]. Moreover, in the case of slow and prolonged treatment, extending beyond the polymer degradation time, a metal implant ensures the tissue stability throughout the implantation site. One of the most popular aliphatic polyesters is PLGA – poly(lactide-co-glycolide) copolymer, which degrades in the environment of body fluids. PLGA is commercially available and approved by the FDA [19], [21]. However, it should be noted that this commercially available polyester is commonly synthesized using stannous compounds as initiators, mostly $Sn(oct)_2$, which can be relatively toxic [24]. Our goal was to obtain novel metallic implants using self-developed method of surface modification of the metal alloys and additionally coated with biodegradable and bioresorbable layers of poly(lactide-co-glycolide) synthesized with low-toxic $Zr(acac)_4$ initiators. The poly(lactide-co-glycolide) used possessed tailored chain microstructure, resulting from synthesis conditions: temperature and coordination initiator [14]. High biocompatibility of zirconium complexes compared to stannous octanoate $Sn(oct)_2$ has been confirmed [5]. Polymer degradation is a complex process and depends on many factors: molecular weight and geometry of the polymer, additives, size and shape of the sample as well as porosity. The temperature, pH and kind of the degradation medium are also important [22].

Available literature data do not fully explain the influence of biodegradable layer on corrosion resistance of metal substrate.

The study presents the results of tests evaluating the influence of long term submersion in Ringer's solution of metal biomaterials coated with bioresorbable polymer on the polymer degradation, quantity of metal ions released to the solution and corrosion resistance of the metal biomaterials.

2. Materials and methods

Materials

In the tests, samples of austenitic stainless steel as well as Ti6Al4V ELI and Ti6Al7Nb titanium alloys were used. Their chemical composition, structure and mechanical properties met the requirements of the ISO 5832-1, ASTM F136-08e1 and ISO 5832-11 standards, respectively. The samples were taken from rods of 6 mm in diameter. Prior to polymer coating the surfaces were ground with grade 600 grinding paper. Titanium alloy samples were additionally subjected to anodic oxidation in phosphoric and sulphuric acid bath at 97 V. Polymer coating based on poly(D,L-lactide-co-glycolide) PLGA(85/15) was synthesized in bulk by the ring opening polymerization of glycolide (Purac) and D,L-lactide (Purac) (first, at 130 °C for 24 hours and next, at 120 °C for 48 hours at argon atmosphere using Zirconium (IV) acetylacetonate ($Zr(acac)_4$) (Aldrich) as a non-toxic initiator.

Polymer coatings on metallic implant

Implants were coated with the PLGA by dip-coating method. Metal rods were immersed into PLGA (10% w/w) solution in dichloromethane for 30 seconds and dried. The part of the samples were sterilized with electron beam (25 kGy).

Polymer coatings characterization and degradation study

Changes of the comonomeric unit composition during degradation were monitored on the basis of ^1H NMR spectroscopy (Bruker-Avance II Ultrashield Plus spectrometer, 600 MHz). The molar mass and molar mass distribution of the polymers were determined by GPC (Physics SP 8800 chromatograph and detector: Shodex SE 61). Degradation was performed in 0.1 dm^3 Ringer's solution for 90 days, at a temperature of 37 ± 1 °C.

Evaluation of corrosion resistance

Resistance to pitting corrosion was tested by the potentiodynamic method, meeting the requirements of PN-EN ISO 10993-15 standard, with the use of PGP201 potentiostat by Radiometer. The reference electrode was the saturated calomel electrode (SCE), while the auxiliary one was a platinum rod. The scan rate was equal to 3 mV/s.

Ion release test

Metal ion concentration in Ringer's solution, following 90-day immersion of samples was measured with JY 2000 spectrometer by Yobin–Yvon, using inductively coupled plasma–atomic emission spectrometry (ICP-AES).

Microscopic investigation

The morphology of the samples before and after corrosion study was analysed using multimode atomic force microscopy (AFM) (MultiMode, di-Veeco, USA, CA), scanning electron microscopy (SEM, Quanta 250 FEG,

FEI Company, Oregon, USA) and stereoscopic microscope Zeiss Stereo Discovery V8 with digital camera MC5s.

3. Results

Surface observations

Observations of the surface of polymer coatings on metal substrate showed that independent of the substrate material PLGA forms continuous layer (Fig. 1a), with few infiltrates (Fig. 1b, c) and bubbles (Fig. 1d). The coatings were transparent which allowed observation of the metal substrate. Independent of the type of metal substrate, scratches which were the effect of the applied mechanical treatment of samples were observed.

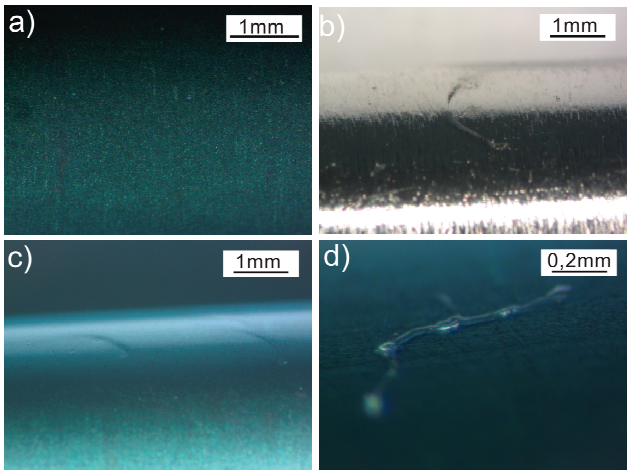

Fig. 1. Exemplary surface of unsterilized samples with PLGA coating, (a) Ti6Al4V alloy, (b) Cr-Ni-Mo steel, (c) and (d) Ti6Al7Nb – stereoscopic microscope

The SEM and AFM (Fig. 2) micrographs of the samples before degradation process show that PLGA was homogenously distributed on the metal samples. The layer thickness measured by means of AFM technique was 8 µm. The surface of the implants was very smooth with roughness parameter of RMS = 2.20 nm and Ra = 0.153 nm.

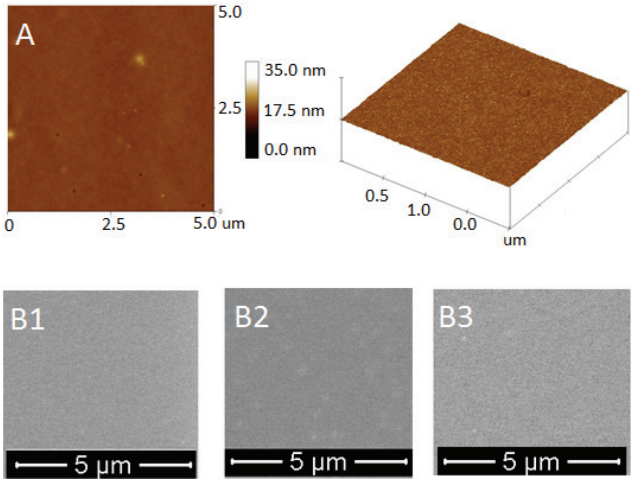

Fig. 2. Sterilized metallic implants with PLGA coatings (before degradation) (A) AFM micrographs of the PLGA coating on Ti6Al4V alloy, (B1) SEM micrographs of the PLGA coating on stainless steel, (B2) SEM micrographs of the PLGA coating on Ti6Al4V alloy, (B3) SEM micrographs of the PLGA coating on Ti6Al6Nb alloy

Ion release

Results of release of metal ions to Ringer's solution after 90 days of incubation were converted into surface mass density and presented in Table 1.

Surface observations after 90 days

After exposure to the corrosive environment visible changes of polymer coating compared to initial state for both unsterilized and sterilized samples were not observed.

Corrosion resistance

Potentiodynamic study showed different curve polarization, dependent on the material surface, Fig. 3. The hysteresis loop observed for the stainless steel proved initiation and progression of pitting corrosion – blue curve. Titanium alloys proved resistance to pitting corrosion in the whole measuring range – red and green curves.

The defined values of corrosion potential E_{cor}, breakdown potential E_b, repassivation potential E_{rep} as well as polarization resistance R_p are presented in Table 2.

Table 1. Results of surface mass density of metal ions, microg/cm^2

	Cr-Ni-Mo + PLGA			Ti6Al4V ELI + PLGA		Ti6Al7Nb + PLGA	
	NS	S		NS	S	NS	S
Fe	0.158(28)	0.196(19)	Ti	0.726(19)	0.540(25)	0.349(99)	0.447(28)
Cr	0.112(28)	0.130(28)	Al	0.400(28)	0.478(19)	0.251(19)	0.200(19)
Ni	0.214(37)	0.191(28)	V	0.345(47)	0.428(25)	–	–
Mo	0.326(37)	0.307(33)	Nb	–	–	0.587(28)	0.317(19)

Table 2. Results of potentiodynamic tests

	Cr-Ni-Mo + PLGA		Ti6Al4V ELI + PLGA		Ti6Al7Nb + PLGA	
	NS	S	NS	S	NS	S
E_{corr}, mV	–456(79)	–249(98)	–418(40)	+124(26)	–393(31)	–313(28)
E_b, mV	+1427(11)	+1451(10)	–	–	–	–
E_{rep}, mV	–62(19)	–18(44)	–	–	–	–
Rp, MΩ cm^2	0.286(97)	0.75(32)	1.96(72)	13.8(40)	4.1(27)	5.3(36)

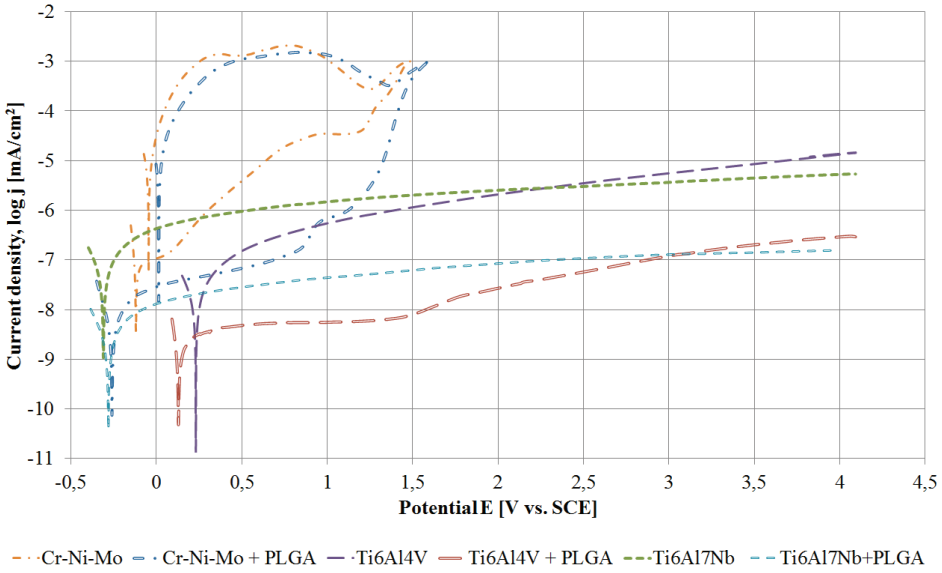

Fig. 3. Typical polarization curves for: Cr-Ni-Mo, Cr-Ni-Mo+PLGA, Ti6Al4V, Ti6Al4V ELI+PLGA, Ti6Al7Nb and Ti6Al7Nb+PLGA

Surface observations after potentiodynamic tests

After the potentiodynamic tests of the PLGA coated stainless steel samples, the presence of a few discontinuities was observed (Fig. 4). These discontinuities were accompanied by corrosion damage characteristic of pitting corrosion. However, in most cases, surface damage of metal substrate was not accompanied by rapture of layer continuity. Similar character of the damage was noticed either for non-sterilized and sterilized samples. The polymer coating on titanium alloys substrate was continuous. However, increase in the number of bubbles was observed. Bubbles probably were located on the border of the polymer–metal substrate (Fig. 4a), so that in a few cases breaking the continuity of coating was observed (Fig. 4b).

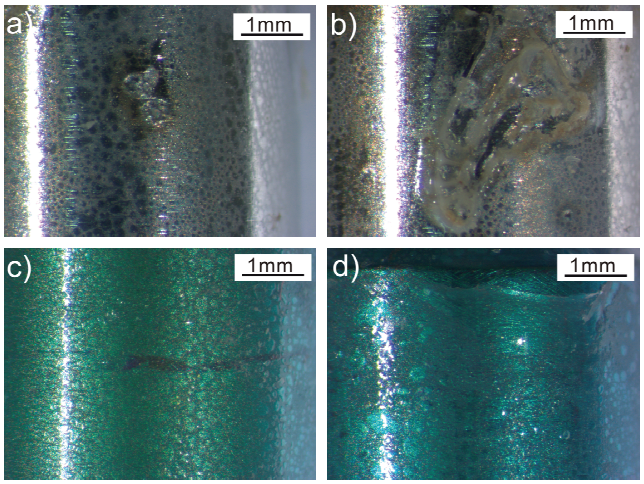

Fig. 4. Exemplary PLGA coating damage after potentiodynamic tests: (a) and (b) stainless Cr-Ni-Mo + PLGA, (c) Ti6Al4V + PLGA, (d) Ti6Al7Nb + PLGA – stereoscopic microscope

Degradation study of poly(D,L-lactide-co-glycolide) layers

NMR analysis revealed a slight decrease of glycolidyl units content in the polymeric chain during 90 days, which suggests even way of degradation. In the NMR spectra of PLGA we observed signals assigned to main polymeric chain but also signals corresponding to the short chains of oligomers. The presence of oligomers was also confirmed by GPC, because apart from significant decrease of molecular weight of PLGA (from 50 kDa to 3–5 kDa after 90 days), also the dispersity (M_w/M_n) of the samples increased to around 5. Although PLGA was highly

degraded after 90 days, the content of the comonomeric units remained unchanged.

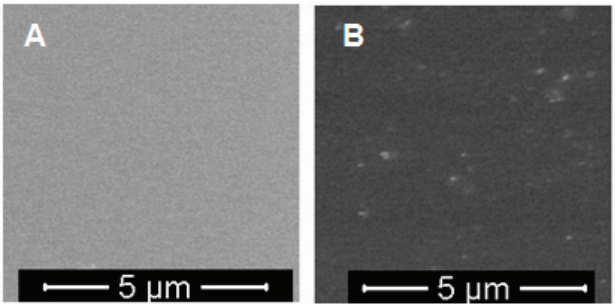

Fig. 5. SEM micrographs of the PLGA/metal implant (stainless steel): (A) before degradation, right: after 90 days of degradation, (B) visible particles on the right figure come from the remaining salt crystals of the incubation medium

SEM micrographs of the samples before degradation process show that PLGA was homogenously distributed on the metal samples. After 90 days of degradation the coating maintains its continuity, PLGA is still homogenously distributed on the metal samples, its surface is smooth, Fig. 5.

4. Discussion

Prolonged exposure of metal implant in human body may cause development of corrosion processes. Corrosion processes are most often a result of synergistic interaction of mechanical factors and tissue environment. Depending on implantation time of metal implant into human body, development of corrosion processes can occur locally or systemically. The consequence of prolonged exposure of implant in the body is release of its corrosion products not only into tissues surrounding the implant, but also to detoxification organs [7], [18]. However, a primary factor affecting a course of body's defence response is a material's corrosion resistance, and, in particular, its corrosion products. This will require modification of a surface layer of metal implants. Most often passive layers reduce the amount of metal ions released from metal substrate to tissue environment. The polymer layer applied by dip coating forms a uniform layer, however some discontinuities in the form of bubbles were observed. There was no influence of radiation sterilization on topography of the polymer coating. Exposure of the polymer coating to Ringer's solution caused damage of the surface which resulted in releasing degradation products to the solution. Some insignificant influence of sterilization upon degradation of the base metal materials was observed, Table 1. The sterilized stainless steel samples showed increased mass density of Fr and Cr ions, as compared to unsterilized ones, while for Ni and Mo some decreased values were observed. Also titanium alloys showed no explicit effect of sterilization upon the quantity of

Table 3. Results of degradation study of the polymer coating: 0 – before degradation, 90 – after 90 days of degradation

		Cr-Ni-Mo + PLGA		Ti6Al4V + PLGA		Ti6Al7Nb + PLGA	
		NS	S	NS	S	NS	S
M_n, kDa	0	51	42	48	40	50	42
	90	5.5	3.0	6.6	3.0	3.0	2.0
GG/LL content, %	0	15.5/84.5	16/84	15.5/84.5	16/84	15.5/84.5	16/84
	90	14/86	15/85	15/85	15/85	15/85	15/85

metal ions being released to the solution. Mass density of metal ions from the samples of metal biomaterials coated with PLGA is remarkably lower than that on the surface of uncoated biomaterials [2], [17]. Hitherto, no studies have been performed on metal ions releasing from substrate coated with a bioresorbable polymer.

In studies, the tests performed showed a favourable influence of polymer coating on pitting corrosion resistance of metal biomaterials. The recorded potentiodynamic curves depended on the type of material substrate. Titanium alloys were characterized by high corrosion resistance in the whole measuring range (+4000 mV). For the stainless steel a hysteresis loop indicating pitting corrosion was identified. This was confirmed by microscopic observation of the samples after corrosion tests (Fig. 4). For titanium alloys a significant increase in the number of bubbles, located on the border of metal substrate–polymer coating were observed.

Regardless of the applied material substrate beneficial effect of radiation sterilization on parameters describing corrosion resistance (E_{corr} and R_p) was observed, Table 2. The observed courses of polarization curves for the sterilized and unsterilized samples with PLGA coatings correspond to

those observed for the samples without polymer coating [6], [9]. Steam sterilization caused an increase of corrosion resistance compared to the unsterilized samples and those without the polymer coating [3]. Until now, researchers have not analysed a radiation sterilization on corrosion resistance of metal biomaterials coated with bioresorbable polymer.

Degradation of biodegradable PLGA layer proceeded evenly, which is very advantageous for medical implants. Moreover, there was no influence of the type of metal material on the polymer degradation. Even way of polymer degradation during 90 days resulted from tailored copolymer chain microstructure. It should be emphasized that degradation process did not change surface morphology and did not cause formation of pores that could disturb its integrity. Polymer coating can enhance biocompatibility of implants through improved corrosion resistance and reduction of the quantity of metal ions being released from the metal substrate.

Based on the results of this work it can be concluded that the obtained polymer coating protects the metal base effectively against the corrosive environment.

5. Conclusions

Proposed in this research the method of modifying surface layer of metal biomaterials by applying the coating of PLGA bioresorbable polymer has beneficial effect on corrosion resistance. Based on the studies performed, reduction of kinetics of metal ions released from metal substrate to corrosive environment was observed. This shows good barrier properties of the polymer coating. In the case of the stainless steel, for which in potentiodynamic tests pitting corrosion was observed, the applied polymer coating prevented releasing of corrosion products to tissue environment.

The process of PLGA degradation during 90 days was proceeded intensively but evenly due to tailored copolymer chain microstructure, which resulted from synthesis condition, especially from using Zr(acac)4 as initiator. The surface morphology did not change during degradation, which ensures its integrity.

It needs to be highlighted that bioresorbable polymer coatings applied to metal substrate could be used as carriers for drugs. Application of the bioresorbable PLGA coating on metal biomaterial substrates increases corrosion resistance.

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