

Modes development of PLGA scaffolds modification by magnetron co-sputtering of Cu and Ti targets

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Abstract. Bioresorbable scaffolds from poly(lactide-co-glycolide) (PLGA) were formed by electrospinning. Then, plasma modification of PLGA scaffolds was carried out by magnetron co-sputtering of copper and titanium targets in Ar. The surface morphology, elemental composition and mechanical properties of the obtained samples were investigated. The modes of plasma modification were selected that could preserve the macrostructure, morphology and mechanical properties of PLGA scaffolds.

1. Introduction

Poly(lactide-co-glycolide) (PLGA) refers to biodegradable synthetic copolymer, that consists of aliphatic polyethers of polylactide (PLA) and polyglycolide (PGA). PLGA is a copolymer with high biocompatibility and controllable degradation rate [1]. PLGA scaffolds are widely used in tissue engineering for soft and bone tissue regeneration [2, 3].

Plasma modification of materials from PLGA allows to increase cell adhesion and proliferation [4, 5]. Compared to treatment in a capacitively coupled plasma or radio-frequency glow discharge plasma, magnetron sputtering can be used to form a uniform, high-purity films of metals and their compound at relatively low temperatures. Despite the advantages of modification by magnetron sputtering, the macrostructure and shape of polymeric scaffold can be damaged [6]. This is due to extremely sensitivity of synthetic biodegradable polymers to elevated temperatures. In example, PLGA scaffold with ratio of lactide to glycolide 85/15 melts at temperatures $\sim 55-60^\circ$. To exclude temperature damage during polymeric scaffolds modification by magnetron sputtering of metallic targets, it's necessary to determine technological modes, which could preserve the macrostructure, morphology and mechanical properties.

There are a number of articles that are dedicated to research of copper-titanium (Cu-Ti) thin films deposition [7–10] on materials of medical application. In example [10], Cu-Ti films have an antibacterial properties and relatively high biocompatibility. So, PLGA scaffolds modification by copper and titanium (Cu-Ti-PLGA) films can add antibacterial properties and preserve high biocompatibility of samples.

The aim of this work is development of modes for PLGA scaffolds modification, by method magnetron co-sputtering, which will preserve the macrostructure, morphology and mechanical properties.

2. Materials and methods

Scaffolds from copolymer poly(lactide-co-glycolide) (PURAC[®], Netherlands) with ratio PLA/PGA – 85/15 were formed by electrospinning method on installation NANON-01A (MECC Co., Ltd., Japan).



To make scaffolds, 4% PLGA solution in dimethylformamide was used (Akros, Russia). Scaffolds were formed under the following technological modes: voltage between collector and needle – 22 kV; the flow rate of polymeric solution – 4 ml/h; cylindrical collector diameter and length – 100 mm, 200 mm, respectively; collector rotation speed – 200 r/min.

PLGA scaffolds modification with linear dimensions $50 \times 50 \text{ mm}^2$ was carried out by co-sputtering of titanium and copper targets on an installation of plasma sputtering [11]. During the modification, the following materials and conditions were used: circular targets from copper (Cu, 99.95%) and titanium (Ti, 99.95%) with diameter $\varnothing 90 \text{ mm}$ and height 8 mm, working gas - argon (Ar, 99.998%), operation pressure - 0.3 Pa. The modes of plasma modification of PLGA scaffolds are shown in table 1.

Table 1. Plasma modification modes of PLGA scaffolds.

Modification modes (samples)	W, W		I, A		t, min
	Cu	Ti	Cu	Ti	
1	300	750	0.6	2.9	12.5
2	130	500	0.3	1.1	29.3
3	600	500	1.1	2.0	10.5
4	200	500	0.5	1.1	19.5

Note: *W* – discharge power; *I* – mean discharge current; *t* – modification time.

In modes 1-4, the copper target sputtering was by using the power supply APEL-M-5PDC (Applied Electronics, Russia) with frequency of 100 kHz and duty cycle of 70%.

In modes 1 and 3, the power supply MPS-3-5-5-1000-PC with frequency of 132 kHz (Intelligent Industrial Systems, Russia) was used to sputter the titanium target. In modes 2 and 4, the electrical supply of magnetron with titanium target was provided by APEL-M-5PDC (Applied Electronics, Russia) with frequency of 100 kHz and duty cycle of 70% was used.

Figure 1 presents the current and voltage diagrams of the power supplies for Ti sputtering in modes 3 and 4. There is shown the different shapes of current and voltage for magnetron sputtering of Ti in Ar. The power supply MPS-3-5-5-1000-PC is a current transmitter with double voltage ignition (2x), where the peak current is observed at maximal voltage. So, the sputtered flux from the target to substrate can have a non-uniform energy distribution. Oppositely, near rectangular shapes of voltage and current are observed for the power supply APEL-M-5PDC. This is a source with voltage stabilization, thus the sputtered particles will have uniform energy spectrum. So, the second power supply enables deposition process with lower energy flux onto the substrate.

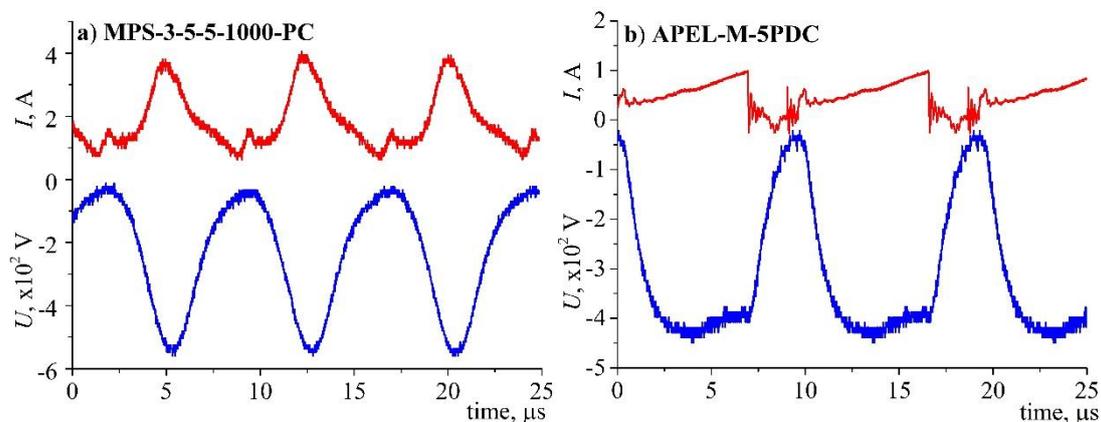


Figure 1. The current and voltage diagrams for Ti sputtering: **a)** modification mode 3; **b)** modification mode 4.

The modification modes were selected for deposition of Cu-Ti films with the thickness of 200 nm onto metallic plates (used as the reference substrate), and elemental ratio of Cu/Ti (in at. %) was equal for

modes 1 and 2 (3 and 4). For deposition of Cu-Ti films with identical thickness, the deposition rates of Cu and Ti were previously determined using a quartz thickness gauge Mikron-5 (Izovak, Belarus). The average deposition rate of Cu film was 0.113 ± 0.010 nm/s (APEL-M-5PDC, power – 300 W). The deposition rates of Ti film were 0.107 ± 0.008 and 0.068 ± 0.004 nm/s for sputtering by MPS-3-5-5-1000-PC (500 W) and APEL-M-5PDC (500 W), respectively. To form coatings with a given ratio of Cu and Ti, proportional values of the discharge power were selected for sputtering Cu and Ti targets.

The surface morphology and elemental composition of the PLGA scaffolds were studied by scanning electron microscopy (SEM) and energy dispersive X-ray spectroscopy (EDS) on a JCM-6000 Plus instrument (Jeol, Japan). To increase the electrical conductivity of PLGA scaffolds surface, a thin layer of gold was deposited on the samples using a SmartCoater device (Jeol, Japan). SEM images were obtained at $1000\times$ magnification. The fiber diameters of the PLGA scaffolds were evaluated using the ImageJ 1.48 program (National Institute of Health, USA) using the plug-in DiameterJ v1.018 (National Institute of Standards and Technology, USA).

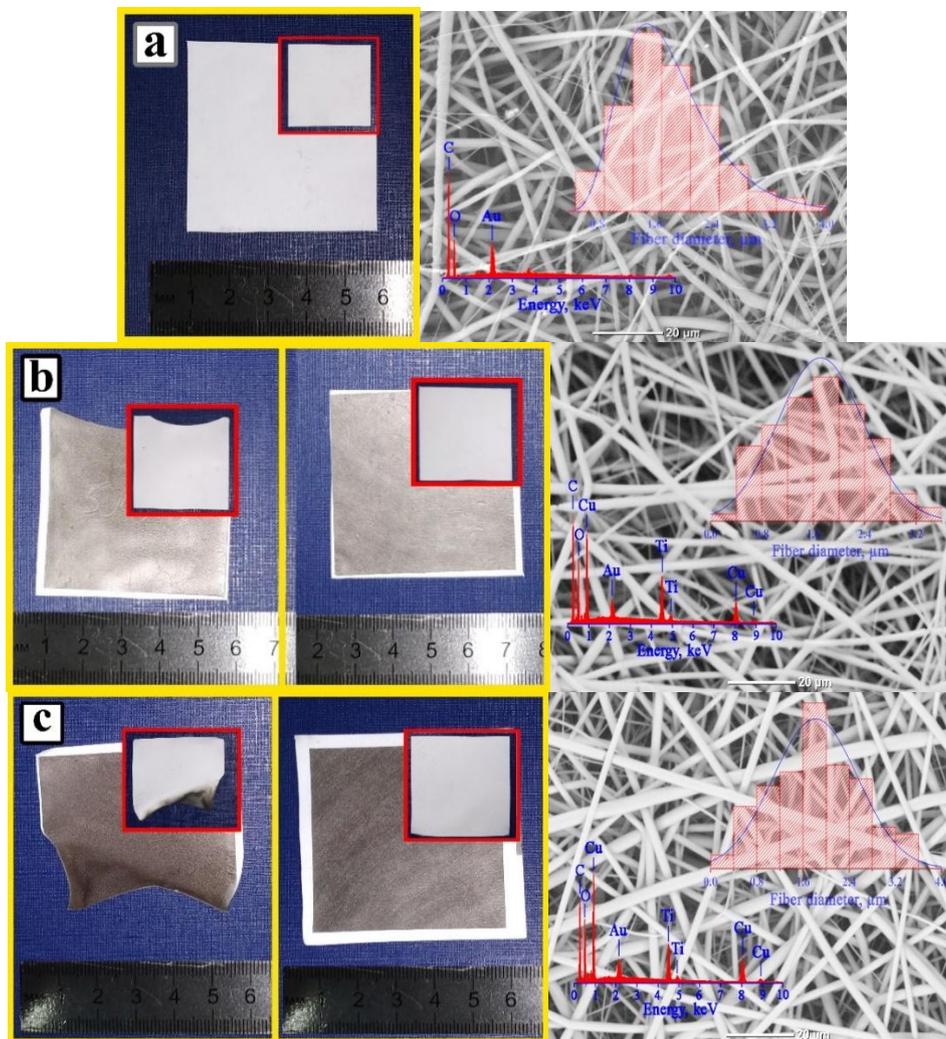


Figure 2. The outer view of the PLGA scaffolds (left and center) and its microstructure, histograms of fiber diameter distribution and EDS spectra (right): **a)** non-treated PLGA scaffold; **b)** from left to right: sample 1, sample 2, SEM image of sample 2; **c)** from left to right: sample 3, sample 4, SEM image of sample 4.

The mechanical properties of the PLGA scaffolds with the size of $30 \times 10 \text{ mm}^2$ were evaluated on an Instron 3343 instrument (Illinois Tool Works, USA) under an uniform tension. The device was equipped with an Instron 2519-102 sensor (Illinois Tool Works, USA). The crosshead speed was chosen 10 mm/min, the distance between the clamps was 20 mm.

Statistical data processing was performed using the OriginPro[®] 2019 program (OriginLab, USA). The thickness of the PLGA scaffolds and Cu-Ti films was estimated using one-way analysis of variance. Differences in fiber diameters, elongation, tensile strength and Young's modulus were evaluated using the Mann-Whitney U test. The differences were calculated with statistically significant of $p < 0.05$.

3. Results and discussion

Figure 2 shows the outer view of the PLGA scaffolds and their microstructure. The histograms of fiber diameter distribution and EDS spectra are also added.

Non-treated PLGA scaffold has a white color in both sides (figure 2a). All modified scaffolds have a metallic luster. The samples 1 (figure 2b, left) and 3 (figure 2c, left) have noticeable defects: the scaffold 1 has a burn through in the form of an arc, the scaffold 3 has a large area damaged by high temperature. The samples 2 (figure 2b, center) and 4 (figure 2c, center) do not have any visible defects, as evidenced by their SEM images: for the sample 2 – figure 2b, right, for 4 – figure 2c, right, respectively. Sand-gray color is observed on the modified surface of the PLGA scaffolds 1 and 2, brown color at the samples 3 and 4. The absence of color differences between-modes 1 and 2 (3 and 4) can indicate the same ratio of Cu/Ti on their surfaces. The back side of the samples retains white color.

Due to decrease in the power supplied to a magnetron with copper target, and the power supply replacement for magnetron with a titanium target, a decrease of the Cu-Ti coatings deposition rate and the energy flux entering the surface of the modified samples occurred. In this case, the substrate temperature usually decreases. Therefore, the modification modes 2 and 4 were able to maintain the PLGA scaffold appearance and shape.

Further measurements were carried out with the samples without defects: samples 2 and 4, non-treated PLGA scaffold. The modified samples have a non-woven structure, which is observed for the materials made by electrospinning. Three peaks are observed in the EDS spectrum of non-treated PLGA scaffold, which indicates on the presence of carbon, oxygen, and gold (figure 2a, right). The peaks of copper, titanium, carbon, oxygen and gold are observed in the EDS spectra of the modified samples.

Table 2 shows the mean fiber diameter, elemental composition and the elements ratio of PLGA scaffolds.

Table 2. Mean fiber diameter, elemental composition and elemental ratio of the samples.

Sample	Mean fiber diameter, μm	Elements atomic concentration, %				Elemental ratio	
		C	O	Cu	Ti	C/O	Cu/Ti
Non-treated PLGA scaffold	1.80±0.62	59.9	40.1	-	-	1.5	-
2	1.69±0.67	57.2	37.1	3.7	2.0	1.5	1.9
4	1.82±0.73	56.1	37.2	4.9	1.8	1.5	2.7

Mean fiber diameter of studied PLGA scaffolds ranges from 1.02 to 2.55 microns. During plasma modification of PLGA scaffolds in modes 2 and 4, the average fiber diameter authentically does not change.

The ratio of C/O is 1.5 for the original PLGA scaffold, after plasma modification does not change. The Cu/Ti ratios for modified PLGA scaffolds 2 and 4 are equal to 1.9 and 2.7, respectively.

Table 3 shows the mechanical properties of the PLGA scaffolds in non-treated state and after modification by copper and titanium.

Table 3. Mechanical properties of the PLGA scaffolds.

Sample	Tensile strength, MPa	Relative elongation, %	Young's modulus, MPa
Non-treated PLGA scaffold	3.4±0.2	250±30	85±6
2	3.3±0.1	240±20	86±5
4	3.6±0.1	230±30	89±5

Values of the PLGA scaffolds tensile strength varies between 3.2-3.7 MPa, elongation are 210-280%, Young's modulus are 79-95 MPa. Plasma modification in the modes 2 and 4 authentically does not change the mechanical characteristics of the PLGA scaffold. It could be related with the preservation of the PLGA scaffolds macrostructure and morphology after plasma modification.

4. Conclusions

Plasma modification in modes 1 and 3 does not save the macrostructure and shape of the PLGA scaffold. The modes 2 and 4 allow to maintain the form, outer view, morphology and mechanical properties of PLGA scaffold.

The modes–1 and 3 are not recommended for PLGA scaffolds modification, as they lead to destruction and deformation of the samples, while the modification modes 2 and 4 allow to save their properties.

The preservation of shape and macrostructure of the PLGA scaffolds after plasma modification in the modes 2 and 4 is associated with the decrease of total power of the magnetrons during plasma modification and lower energy flux to the scaffolds, when Ti target was sputtered using the power supply APEL-M -5PDC.

References

- [1] Gentile P, Chiono V, Carmagnola I and Hatton P 2014 *International Journal Molecular Science* **15** 3640–59
- [2] Pattison M A, Wurster S, Webster T J and Haberstroh K M 2005 *Biomaterials* **26** 2491–500
- [3] Doğan A et al. 2014 *Material Science Engineering* **44** 246–53
- [4] Park K et al. 2007 *Journal of Biomaterials Science* **18** 369–82
- [5] Roh H S, Jung S C, Kook M S and Kim B H 2016 *Applied Surface Science* **388** 321–30
- [6] Bolbasov E N et al. 2017 *Applied Surface Science* **398** 63–72
- [7] Wojcieszak D et al. 2015 *Materials Science and Engineering: C* **56** 48–56
- [8] He X et al. 2017 *Ceramics International* **43** 16185–95
- [9] Sreedhar M et al. 2015 *Applied Physics A* **120** 765–73
- [10] Finke B et al. 2012 *Advanced Engineering Materials* **14** B224–30
- [11] Sidelev D V et al. 2017 *Vacuum* **143** 479–85