Fabrication of NO-containing calcium phosphate coatings via direct introduction of argon-nitrogen-mixtures applied in reactive RF-magnetron sputtering

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Abstract. Nitric oxide plays a crucial role in the human body, due to its regulatory effect on vascular tone, cell adhesion, vascular permeability, etc. The introduction of nitric oxide into calcium phosphate coatings can increase the bioactivity significantly. This article proves the possibility of deposition of nitric oxide-containing calcium phosphate coatings on titanium substrates. Therefore, various argon-nitrogen working gas mixtures were used in reactive radiofrequency magnetron sputtering of hydroxyapatite. The amount of nitric oxide increases with the concentration of nitrogen in the working gas mixture. Coatings characterized by a higher deposition rate of nitric oxide are showing also a higher roughness of the surface. Due to the adjustment of these deposition parameters, the morphology of the coating surfaces can be regulated.

1. Introduction

Titanium and its alloys are widely spread in orthopedics and dentistry for production of artificial joints and dental implants. It is necessary to increase biocompatibility of implants for a better restoration of substituted bone tissues and its functions. One of the obvious ways to increase biocompatibility of an implant is to modify its surface by depositing bioactive coatings to support the bone tissue formation process [1]. Hydroxyapatite (HA, Ca_{10}(PO_4)_{6}(OH)_2) is a bio-ceramic material characterized by its chemical composition, which is related to the structure of human bones. Therefore, its highly biocompatible [2]. One of the most used methods of HA deposition on the surface of implants is radiofrequency (RF) magnetron sputtering. This method provides a high adhesion between the surface of an implant and the coating. These HA coatings are close in stoichiometric composition to the composition of the sputtered target. The method allows varying elemental composition of the coating by changing the composition of the target or deposition parameters (discharge power, working gas, etc.).

Currently, composite coatings based on HA and other substances are widely studied. Almost all major systems are involved in the formation of the body's defense mechanisms when a foreign object, like an implant, is introduced into it: cardiovascular, nervous, etc. Therefore, analyzing the body's reactions to implant insertion, it is necessary to pay special attention to one of the most universal regulators of the physiological functions of the body – nitric oxide (NO). The biological role of NO in the human body is very high. All varieties of its biological effects can be represented as a regulation effect on vascular tone, cell adhesion, vascular permeability and so on [3]. It should be noted that, NO performs an important function in the regulation of blood flow, expanding or narrowing the lumen of blood vessels in accordance with the need. However, there is currently no literature on the combined
use of HA and NO in coatings for implants. According to this fact, the research on bioactive calcium phosphate (CaP) coatings doped with NO and deposited on the surface of medical implants should be more in focus in the future.

The aim of this study is to deposit NO-containing CaP coatings formed by sputtering of HA and to investigate some properties.

2. Materials and methods

2.1. Coatings deposition
Deposition of NO-containing CaP coatings formed by sputtering of HA (NO-HA coatings) was carried out in the mixture of argon and nitrogen at different volume concentrations: Ar100 (Ar:N₂ = 100:0), Ar75/N₂:25 (Ar:N₂ = 75:25), Ar50/N₂:50 (Ar:N₂ = 50:50), Ar25/N₂:75 (Ar:N₂ = 25:75) and N₂100 (Ar:N₂ = 0:100). Solid-state HA target with an area 224 cm² was used in the deposition process. Deposition was performed with the use of the universal magnetron sputtering system “Cathode-1M”. Substrates (10 mm in diameter, 1 mm thick) made of VT6 titanium alloy were grinded and polished with the use of Unipol-802 (Zhengzhou TCH Instrument Co., Ltd, Zhengzhou, China) setup. The following parameters were used to form NO-HA coatings: the distance between the target and the sample was 33 mm, the preliminary pressure in the chamber was 3 × 10⁻³ Pa, the working pressure in the chamber was 0.5 Pa, and deposition time was 3 hours at a fixed power density of 6.32 W/cm².

2.2. Research methods
Chemical composition of the plasma was studied during the deposition of coatings by optical spectroscope OCEAN OPTICS HR 2000+ (Ocean Optics, Dunedin, USA). The data were processed using the SpectraSuite software package (Ocean Optics, Dunedin, USA). The thickness of the coatings was measured using the Ellips-1891 SAG (ISP SB RAS, Novosibirsk, Russia) spectral ellipsometric complex. Roughness of the coatings was calculated on the basis of images obtained by atomic force microscope Solver HV (NT-MDT, Zelenograd, Russia). Chemical composition was studied by XPS on an Escalab 250Xi spectrometer (Thermo Fisher Scientific Inc., Waltham, USA). An X-ray tube with AlKα radiation 1486.6 eV was used as a source of ionizing radiation. The energy resolution was 0.5 eV. The decoding of the presented spectra was carried out using the NIST database (National Institute of Science and Technology, USA).

3. Results and discussion
The optical spectrum of the RF-magnetron discharge plasma obtained by sputtering of the HA target in an atmosphere of argon and nitrogen with different concentrations is shown in figure 1.
In the optical spectrum of plasma, the maximum optical intensity is observed in the spectral wavelength range of 300-440 nm. The obtained spectra are characterized by a number of spectral lines associated with both elements of the sputtered calcium phosphate target and particles of the working and reactive gases. In the studied spectral range, Ca was identified at wavelengths 353.9 nm and 391.8 nm; Ca$_2$ was identified at wavelengths 423.3 nm; CaO and CaO$_2$ were identified at wavelengths 391.8 nm and 423.3 nm, respectively [4, 5]. In addition, PO bonds were present at 337.5 nm and 400.2 nm. The above elements and bonds correspond to the sputtered HA target. Argon atoms were also present at wavelengths of 404.7 nm, 416.5 nm, 419.2 nm, 420.6 nm, 428.4 nm, 430.3 nm and 433.7 nm, as well as its ions at a wavelength 426.6 nm [6]. Nitrogen molecules were identified at wavelengths of 329.2 nm, 371.2 nm and 406.2 nm [7]. It is worth to note, that the highest intensity of reflections attributed to the elements of the sputtered target is characteristic for a mixture of gases or pure nitrogen, rather than for pure argon. This is due to the fact, that by using a mixture of gases, the Penning effect takes place, which increases the efficiency of the processes of ionization [8]. Lines in the range from 308-318 nm correspond to OH groups.

Table 1 shows the thickness of the obtained coatings and their roughness.

| Gas ratio          | Ar100 | Ar 75/N$_2$25 | Ar 50/N$_2$50 | Ar 25/N$_2$75 | N$_2$100 |
|--------------------|-------|---------------|---------------|---------------|-----------|
| Coating thickness, nm | 499 ± 10 | 370 ± 16 | 632 ± 11 | 480 ± 42 | 598 ± 55 |
| Roughness, nm     | 16.368 | 11.121 | 32.867 | 19.820 | 28.471 |

The smallest values of roughness and deposition rate are observed for the coating of the Ar75/N$_2$25 group. However, the roughness of coatings increases with the deposition rate growth. At a low flux of sputtered atoms on the substrate, there is a high probability of their immobilization on the deepening of the titanium substrate remaining after its polishing. Filling the unevenness of the substrate with deposited particles reduces the surface roughness. As the deposition rate and, accordingly, the flow of particles on the substrate increase, the probability of collision of deposited particles with the subsequent formation of clusters of atoms, preceding the formation of nuclei and islands, increases. Thus, at high deposition rates, the coalescence of islands into a single coating occurs before the irregularities of the substrate are filled. Accordingly, the maximum roughness is observed for coatings that are formed at the highest rate. A similar pattern and its explanation are described in [9].

Figure 2 shows the O 1s, P 2p, N 1s and Ca 2p XPS spectra of the resulting coatings.

Figure 2. XPS spectra of samples: a – 1s spectrum of nitrogen, b – 1s spectrum of oxygen, c – Ca2p spectrum of calcium compounds, d – 2p spectrum of phosphorus compounds.

Various bonds depending on the ratio of inert and reactive gases are represented in 1s spectrum of nitrogen (figure 2a). Thus, coatings obtained in argon and with a 25% addition of nitrogen are characterized by the presence of the C-CN bond with a binding energy of 399.3 eV [9]. Its presence in
the coating indicates slight contamination of the samples. A further increase in the percentage of nitrogen in the gas mixture makes it possible to obtain the NO bond, which corresponds to a binding energy of ~ 397.5 eV. This concentration increases with the percentage of nitrogen in the gas mixture and reaches a maximum with the plasma of pure nitrogen. Formation of NO is also proved by the 1s spectrum of oxygen (figure 2b). The presence of the NO bond, as well as an increase in its concentration, is observed with an increase in the percentage of nitrogen in the gas mixture. This bond is absent in the coating obtained in pure argon. In addition, the deconvolution of the presented peaks makes it possible to identify the presence of bonds characteristic of the sputtered target, namely Ca$_3$PO$_4$ at a binding energy of 530.6 eV and Ca(H$_2$PO$_4$)$_2$ with a binding energy of 532.4 eV.

The 2p spectrum of calcium compounds is shown in (Figure 2c). In all the spectra presented, the contributions of Ca2p$_{3/2}$ and Ca2p$_{1/2}$ can be distinguished. The spin-orbit splitting is of the order of ~ 1 eV for coatings obtained in different deposition modes. Thus, for the Ca2p$_{3/2}$ peak, three most intense regions corresponding to different bonds can be identified. Ca$_3$PO$_4$ bonds correspond to a bond energy of 347 eV, for Ca(HCOO)$_2$ bonds the most typical bond energy is 347.2 eV, and Ca(H$_2$PO$_4$)$_2$ bonds correspond to a binding energy of about 347.5 eV [10].

Presence of calcium compound bonds with phosphorus, as well as oxygen, is consistent with the 2p spectrum of phosphorus (Figure 2d). Deconvolution of the presented spectra makes it possible to establish the presence of two phosphate bonds with different binding energies. For the Ca(H$_2$PO$_4$)$_2$ bond, the characteristic binding energy is about 132.6 eV, and for Ca$_3$PO$_4$ it is about 133.6 eV [10].

4. Conclusion
In this work, NO-containing CaP coatings were deposited on the Ti substrates via reactive RF-magnetron sputtering. The content of NO in the coatings increases with the higher quantity of nitrogen in the chamber. This result allows the manufacturing of implants with CaP coatings providing gradual release of NO molecules due to the gradual dissolution process of coatings. However, biological studies of the coatings are needed to determine the optimal NO concentration in the coatings and the working gases ratio in the chamber. This approach is successful way to release NO over the coating. This method can therefore also used as an alternative way to immersion of the implant into drug-containing solution or manufacturing of implants with a polymer layer doped with drugs.

Acknowledgements
The reported study was funded by RFBR and National Science Foundation of Bulgaria (NSFB), project number 20-53-18003/20.

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