ZnO COATINGS ON Ti6Al4V SUBSTRATE: STRUCTURAL AND ANTIBACTERIAL PROPERTIES IN LITERATURE REVIEW AND RESEARCH

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Abstract:
ZnO, ZnO/Alginate coatings were obtained on the pre-anodized Ti6Al4V substrates by the thermal substrate deposition method (TSD). In the frame of this work, the TSD method was at first applied for obtaining ZnO coating from aqueous alginate-containing and alginate-free solutions on a metal surface. XRD, SEM analyses show that the biopolymer has a significant influence on the formation of the coating, their morphology, texture, structure of ZnO nanoparticles. The average rate of ZnO deposition from alginate containing solution is 30 μm/min, while from alginate-free solutions – 6 μm/min. In the presence of alginate, spherical particles with flower-shaped inclusions are formed, while from the polymer-free solution, single crystals in the form of tetrahedral were obtained. Zone of inhibition test against Gram-positive S. aureus ATCC 25923 and Gram-negative E. coli ATCC 25922 proves the antibacterial activity of the ZnO/Alg coatings.

Key words: thermal substrate deposition, zinc oxide, alginate, coating, antimicrobial activity

INTRODUCTION
Metal materials, mainly titanium and its alloys, are widely used in medicine as implants for replacing solid bone tissue. However, due to the absence or poor bioactivity and osteoconductivity, there is a high probability of rejections; postoperative inflammatory processes and the slow integration of metallic implants into surrounding tissues take place (M. Epple, “Biomaterials and biomineralization,” Wind, p. 165, 2007). Moreover, the aggressive conditions of the body fluids contribute to the biological corrosion of the metal implants. The surface modification of metal implants is one of the promising methods for improving the physicomechanical and biological properties of these materials. It is known that bone mineral contains some substitution like sodium (Na), zinc (Zn), magnesium (Mg), iron (Fe), and carbonate (CO$_3^{2-}$) ions, which influence the dissolution rate of HA, control its crystallinity, lattice structure [8]. HA is flexible and can include different ions in its structure. As well it is known that microbial resistance to antibiotics has been reaching a critical level during the last decades. Given the serious health hazards of bacteria, many inorganic materials have been applied as antibacterial agents to kill bacteria. Among them, there are two-dimensional nanomaterials MoS$_2$ [10], graphene oxide [31], black phosphorus [29], carbon nitride [17] as well as Ag-based materials [12]. Zinc (Zn) is essential in the human body due to its role in many biological functions. Zn$^{2+}$ ions and zinc oxide (ZnO) particles are promising candidates to solve this problem since they possess more excellent durability, lower toxicity, and higher stability and selectivity [21]. Zn possesses antibacterial properties and is a microelement essential for cell proliferation and remodeling of the extracellular matrix [20]. Zn$^{2+}$ is also capable of stimulating epithelial formation during wound healing. ZnO enhances cell viability and osteogenic ability [36], so it is thoroughly investigated as a potential novel antibacterial agent [18].

LITERATURE REVIEW
To date, some different strategies proposed for obtaining those surfaces that are both bioactive and antimicrobial [27]. These strategies are based on different technologies for obtaining both thin (< 1 μm) and thick (> 1 μm) antibacterial, bioactive and biocompatible coatings on various metal surfaces. Of particular note are the technology of electrophoretic deposition [15], micro-arc oxidation [35], plasma electrolytic oxidation (PEO) [23, 24], electrophos-
nent of calcium orthophosphate, in particular hydroxyapatite, and as an antibacterial component – metal ions Zn, Ag, Se or antibiotics [27]. Also, laser cladding was used for composite Ag-ZnO-HA coatings on Ti6Al4V implants with high antibacterial activity (96.5% and 85.8% against E. coli and S. aureus). Synergistic antimicrobial activity (Ag+ and oxygen atom radicals) was investigated in vivo by irradiation of composite GO/Ag/Collagen coatings for 20 min with visible light, 660 nm (96.3% and 99.4% against E. coli and S. aureus, respectively). Bacterial biofilms on bone implants can be destroyed using a coating of red phosphorus (red-phosphorus-IR780-arginine-glycine-aspartic acid-cysteine), which is irradiated with infrared (880 nm) light. The biomedical activity of the Ti surfaces can be improved by pre-treatment, namely the formation of nanotube TiO2 3-D film with subsequent deposition of calcium orthophosphates.

ZnO nanostructures are characterized by the ability to bind the biomolecules in the desired orientation and high biological activity, resulting in enhanced sensing characteristics, that make them a suitable candidate for future small integrated biosensor devices [1]. There are main synthesis methods for oxide metal nanoparticles obtaining: solution-based [9], vapor state [30], and a biological method [6]. Template/surface-mediated synthesis is based on the fabrication of the coating on the substrate surface or the desired nanomaterial within the pores or channels of the nanoporous template [26]. There are methods for coating by ZnO described in the literature: metal-organic chemical vapor deposition and thermal evaporation, the wet chemical method [22], pulsed laser deposition, spray pyrolysis, epitaxial electrodeposition, radiofrequency magnetron sputtering. It was shown that Zn addition to HA does not modify the morphology of the hydroxyapatite coatings, developed by solution precursor plasma spraying using different zinc ion concentrations. But zinc concentration greater than 10 mol% inhibits the formation of HA and favors the formation of calcium zinc phosphate [5]. The ability to modulate the activity of osteoblasts and the antibacterial properties of zinc ions have been revealed in HA + Zn coatings applied by plasma spraying of a solution, which provides ion doping and leads to the deposition of lamellas. The resulting coatings were not cytotoxic to human osteoblasts [26]. Ti-Doped ZnO Nanoparticles Prepared by Modified Oxalate Route exhibit ferromagnetism [19]. In the presence of HA at pH 5 of about 80%, ZnO NPs undergo transformation to scholzite within 4 h. Under neutral or basic conditions, a slow transformation of about 60% ZnO NPs to amorphous inner-sphere Zn adsorption complexes within 30 days occurs. May affect the behavior, fate, and toxic effects of ZnO NPs in the environment. So, HA may affect the behavior, fate, and toxic effects of ZnO NPs in the environment [16]. Addition of ZnO nanoparticles improves mechanical properties and compressive resistance of hydroxyapatite composites [11]. Incorporated into the HA, the Zn2+ improves biocompatibility and corrosion resistance of the coatings, fabricated on pure titanium by the electrolytic deposition [7]. Chemically bonded ceramic coatings have been shown to exhibit exceptional corrosion resistance. Besides, zinc oxide coating has a lower reaction rate and corrosion current density than zinc oxide-free coatings [2].

The choice of synthesis method determines the physico-chemical characteristics of the metal oxide nanoparticle, in particular ZnO, such as the size, dispersity, type of intrinsic and/or characteristic defects, morphology, and crystal structure. In turn, the above-mentioned factors influence on antimicrobial activity of zinc oxide. Thus, it was found that crystallographic orientation and type of surface plane of single-crystal 1-D ZnO nanowire arrays influence the antibacterial properties: the membrane with randomly oriented ZnO nanoarrays exhibited significantly superior antibacterial property. The different morphologies and crystal growth habits affect the antibacterial activity. ZnO nanostructures in the shape of rods and wires can penetrate cell walls of bacteria more easily than spherical ones. Whereas, flower-shaped ZnO nanoparticles have revealed higher biocidal activity against S.aureus and E.coli, than the spherical and rod-shaped nanostructures.

Among the various technologies, the thermal substrate deposition (TSD) technique, introduced by Kuroda [13, 14] and developed by our group [32, 33], was previously used only for the calcium phosphate deposition on titanium substrates.

In our previous work, a thin upper ZnO layer was applied to a calcium phosphate coating [25]. In presenting our work for the first time, the TSD method was used for the deposition of a biologically active ZnO coating on the anodized titanium (Ti6Al4V) substrate surface. The coating structural phases, morphological and antibacterial properties, the influence of the polymer on the formation of ZnO coatings were investigated.

**THE EXPERIMENTAL PART**

The following compounds were used for synthesis: zinc nitrate Zn(NO3)2·6H2O, hydrous ammonia NH4OH, sulfuric acid H2SO4, sodium fluoride NaF, sodium alginate (Alg) (E 401, low viscosity) manufactured by Shanghai Chemical Company Ltd, China. All components were analytically pure and used without further purification.

Two types of coatings were studied and compared in this work, namely the coating of pure ZnO and ZnO obtained in the presence of a polymer – alginate. The coatings were applied to titanium plates pre-anodized in a solution of sulfuric acid and sodium fluoride. Detailed information on the preliminary preparation of substrates and methods of deposition of coatings is given in our work [23].

The ZnO coating medium was prepared as follows: to 200 ml of 0.2 M aqueous solution of Zn(NO3)2·6H2O was added drop by drop under vigorous agitation 30 ml of 25% w/w ammonia to obtain the transparent alkaline solution, containing ZnO nanoparticles. To obtain ZnO/Alg coating medium, an alkaline 3% solution of alginate was added to the above-described ZnO coating medium in a ratio of 1:50, respectively. The titanium plate immersed in the
mother ZnO or ZnO/Alg solutions were heated to a tempera-
ture of 90°C by passing an alternating electric cur-
rent. The precipitation took place within 20 minutes. The
coating is based on the dependence of ZnO solubility on
temperature.

**Instrumental methods.** The X-ray diffraction studies of the
sample crystallographic structure were performed on the
automatized diffractometer DRON3 (LTD «Burevestnik,»
www.burevestnik.ru). The surface morphology of the
samples was examined using a scanning electron micro-
scope (FEI Inspect S50).

**Antibacterial activity of ZnO/Alg coatings.** The modified
disc diffusion method was used to evaluate the antibacte-
rial activity of the ZnO/Alg coating. The method includes a
placing the sample on an inoculated with Gram-negative
bacteria *E. coli* (ATCC 25922) and Gram-positive *S. aureus*
(ATCC 25923) bacteria agar plates, followed by incubation
for 24 hours at 37°C. The microbial inoculum was pre-
pared in a meat-peptone nutrient (MPN) (Makhachkala,
Russia), which was used as a growing medium. The micro-
organisms were cultivated at 37°C and left overnight (late
exponential stage of growth). Bacterial concentration cor-
responded to 0.5 units of optical density according to
McFarland scale was achieved using Densi-La-Meter
(PLIVA-Lachema, Czech Republic, wavelength 540 nm) de-
vice. The overnight bacterial culture spread onto Muller
Hinton agar to obtain the final bacterial concentration
1×10^7 CFU/ml. The antibacterial properties were evalu-
ated by measuring the zone of growth inhibition (ZOI) sur-
rounding the substrate.

**RESULTS**

In this paper, the modified thermal substrate deposition
method from aqueous solutions of precursors was used to
obtain bioactive ZnO and ZnO/Alg coatings on the metal
(Ti6Al4V) substrates. The application of this method for
ZnO coatings is explained by decreasing of the ZnO pow-
der solubility in an aqueous solution with the temperature
increasing. From our testing experiments, we believe that
ZnO manifests the same properties for the coatings, so
the deposition and formation of ZnO nanostructured
coating on the Ti6Al4V substrate occurs approximately at
the same temperatures as that for ZnO powder
(90-100°C). As already noted, the deposition process in-
volves the passage of alternating current through a metal
substrate immersed in an aqueous solution. As a result,
the metal substrate is heated up to a temperature of
100°C due to resistive heating (Joule heating), although
the hydroprocess passes under atmospheric pressure.
The method of obtaining of ZnO coatings are schemat-
ically presented in Figure 1.

![Fig. 1 Scheme for the deposition of the ZnO coating on an ano-
dized Ti6Al4V substrate using TSD method](image)

One of the methods for modifying the surface of a tita-
nium implant is the formation of oxide films (TiO2) on it by
anodizing, which improves implant anticorrosion re-
sistance. Oxide film also is characterized by high adsorp-
tion properties. In the presented paper, ZnO and ZnO/Alg
coatings were deposited on an anodized titanium surface.

As mentioned above, zinc oxide coatings on a titanium
substrate were deposited from the polymer-containing
solution (ZnO/Alg) and polymer-free solution (ZnO). Fig-
ure 2 shows the surface morphology of these coatings.

![Fig. 2 Surface morphology of the coatings obtained by the TSD
method on the titanium substrate:
(A), (B) - ZnO at different magnifications; (C), (D) - ZnO/Alg at
different magnifications](image)

It is evident that the presence of a polymeric component
sodium alginate in the mother solution significantly af-
fects the formation of coatings, which differ in morphol-
ogy. In the presence of alginate, spherical particles with
flower-shaped inclusions are formed, while from the pol-

eymer-free solution, single tetrahedra-shaped crystals
were obtained. The thickness of the ZnO coating depo-
sited for 20 minutes on titanium substrate is 180 μm, while
the thickness of the ZnO/Alg coating, deposited under
similar conditions is 600 μm. The average rate of deposi-
tion from alginate containing solution is 30 μm/min, while
from alginate-free solutions – 9 μm/min.

The X-ray diffraction patterns of the samples are present
in Figure 3. The major peaks of TiO2 and ZnO phases on
the corresponding diffractograms are marked with Miller
indexes. The Ti6Al4V anodized substrate diffractogram
shows peaks belonging to TiO2 (JCPDS Card No 76-0322
Rutile). Some peaks of rutile are also present on diffracto-
grams of samples with ZnO and ZnO/Alg coatings, but the
intensity of these peaks is minimal compared to that of
ZnO peaks. XRD indicates the formation of an additional
minor phase of Titanium Oxide TiOx (JCPDS Card No 01-
072-2101) after staying titanium substrate in alkaline con-
ditions by the ZnO deposition. The primary phase of the
coating is ZnO (JCPDS 03-0891). For both ZnO and ZnO/Alg
c Coatings, the XRD analysis also shows the presence of the
single phase of ZnO (JCPDS 03-0891) without any additional peaks. The highest intensity peaks at (002) show that the growth direction of ZnO nanoparticles is along the c-axis for both coatings. But other peaks characteristic of the ZnO phase such as (100), (101), (102) is more intensive in the XRD pattern for ZnO/Alg compared with ZnO coating, which proves the formation of particles of different shape under the influence of polymer molecules.

The texture is present for ZnO coatings. The Harris method (Harris texture index, HTI) was used for its quantitative estimation. The crystallite sizes by Scherrer (L) were evaluated for all major peaks of the ZnO phase, as well as its unit cell parameters (a and c, nm) using (1 0 3) and (0 0 2) peaks respectively. The excellent resolution of (0 0 2) and (0 0 4) peak allowed to separate the contributions from small sizes of coherent scattering regions (LWH) and the presence of microstrains (ε) into the peaks broadening. The separation of these contributions was performed with the Williamson–Hall method.

These results are present in Table 1.

Table 1

| Sample | Value (nm) | LWH (nm) | a (nm) | c (nm) |
|--------|------------|----------|--------|--------|
| ZnO    | 27.3       | 39.3     | 26.3   | 18.0   | 106.0  | 0.325 |
| HTI    | 0.177      | 3.389    | 0.096  | 0.078  | 2.862  | 0.521 |
| ZnO/Alg| 12.0       | 50.8     | 15.7   | 10.3   | 69.6   | 0.322 |
| HTI    | 0.036      | 2.455    | 0.036  | 0.047  | 1.591  | 0.518 |

On the first look, the crystallinity of the ZnO phase in the ZnO coating is higher than of the ZnO/Alg, but the intensity of most peaks is higher in the case of the sample ZnO/Alg. This fact could be explained by the presence of a higher amount of microstrains in the case of the ZnO sample, which is confirmed by their values in (0 0 1) direction. Both samples have a significant texture. HTI shows its decrease for the ZnO/Alg as compared to the ZnO. Changes in the structure are due to the influence of sodium alginate. Alginate macromolecules in the presence of divalent metal (Zn²⁺) tend to adopt an ordered confirmation through dimerization, so they create controlled conditions for the growth of ZnO nanoparticles.

The antibacterial activity of the ZnO/Alg coating was investigated against the Gram-negative *E. coli* and Gram-positive *S. aureus* bacteria. The zone of inhibition test determined the antibacterial properties. Bacterial growth was visualized after overnight incubation of the substrates at 37°C. The diameter of the inhibition zone against the test strains was measured around the ZnO/Alg coated substrates, placed on the inoculated medium. The results of antimicrobial activity are representing in Table 2 and Figure 4. The growth inhibition zone (in mm) around coated substrates reflects the antimicrobial susceptibility of the coating. Larger the zone of inhibition, higher is the antimicrobial activity.

Table 2

| Microorganism test - strains | Growth inhibition zone (mm) by modifying the agar diffusion method |
|-----------------------------|-------------------------------------------------------------|
| *S. aureus* ATCC 25923 | 16.0±1.33 |
| *E. coli* ATCC 25922 | 20.0±0.66 |
| Note: p≤ 0.05 |

Fig. 4 Antimicrobial activity of ZnO coating against (A) *E. coli* ATCC 25922; (B) *S. aureus* ATCC 25923

Thus, it may be pointed out that ZnO nanoparticles deposited in the presence of alginate in on Ti6Al4V substrate by the TSD method demonstrated a pronounced inhibitory activity against both *S. aureus* and *E.coli* bacteria. This fact confirms the literature data that ZnO nanoparticles are characterized by increased antimicrobial activity. Although the exact antibacterial mechanism of metal nanoparticles is still incomplete, some distinctive points have been proposed, which include a formation of reactive oxygen species (ROS) on the surface of metal oxide nanoparticles, metal ion release and ion invasion into the bacterial cell wall, direct mechanical destruction of the membrane that can induce bacterial cell death.
The modern development in the field of metal implants is aimed at increasing their biocompatibility, antibacterial activity, lack of toxicity, modulation of inflammation, and fast osseointegration, which is closely related to the modern clinical demand. The results of this work are a step in this direction, namely - the creation of multifunctional implant surfaces.

CONCLUSIONS
At first, the ZnO, ZnO/Alg coatings were obtained on the pre-anodized Ti6Al4V substrates by the TSD method. It has been experimentally proved that this method can be effectively applied to obtain a zinc oxide coating on a metal surface. ZnO coatings were obtained from alginate-containing and alginate-free solutions. Natural biopolymer alginate has a significant influence on the formation of the coating, morphology, texture, structure of ZnO nanoparticles. The average rate of the ZnO deposition from alginate containing solution is 30 μm/min, while from alginate-free solutions, 6 μm/min. The thickness of the ZnO coating deposited for 20 minutes is 180 μm, while the thickness of the ZnO/Alg coating, deposited under similar conditions, is 600 μm. For this coating, an increase in the ZnO crystallites size and microstrains along the (0 0 1) direction are characteristic. The ZnO coating demonstrates growth inhibition zones around coated substrates about 16 mm for the S. aureus and 20 mm for the E. coli. The obtained coatings are promising for medical implants, based on titanium and its alloys, due to their antibacterial properties.

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