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Noi functionalizari hibride (anorganic – organic) a suprafetelor biomaterialelor(metale, aliaje) cu molecule bioactive prin tehnici electrochimice.

New hybrid (inorganic-organic) functionalization of biomaterials (metals alloys) surfaces with functional molecules by electrochemical techniques.

Acronim: **HyBioElect**

CONTRACT 10/30-08-2013

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Electrochemically porous oxide layers:

Prepared by controlled oxide growth (anodization) shown schematically in Figure 1. In this figure on the left side (A) it is a schematic electrochemical cell and on the right side it is shown a micrograph of TiO_2 porous oxide layer obtained on a titanium alloy (the photo is part of unpublished results obtained by L. Benea and the research group).

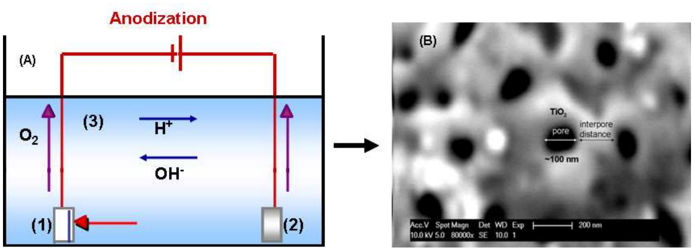

Fig. 1. *Schematic representation of electrochemically preparation of porrous oxide layers: (A) – electrochemical cell with (1) – anode as biomaterial for functionalization; (2) counterelectrode of platinum grid; (3) electrolyte solution for anodization; (B) SEM micrograph of porrous TiO_2 oxide layer [L. Benea and Group, unpublished data]*

Electrochemically deposition of bioactive molecules (BAMs).

After the porous oxide layer is formed on biomaterial surface, the electrodeposition of bioactive molecules (BAMs) such as polyethylene glycol (PEG), hydroxyapatite (HA), chitosan (CH) could be better immobilised on biomaterial surface. The process is shown schematically in Figure 2, where in the left side (A) the electrochemical cell is drawn, in the middle (B) the bonding between porous oxide layer and bioactive molecule like polyethylene glycol (PEG) is much easier step possible by electrodeposition, and on the right side, (C) the biomaterial surface with resulted new hybrid interface layer is shown. Immobilization manner (random or oriented) of BAMs is important for further applications. The interface layer could be reinforced by bio nano dispersed phases as CeO_2 and/or TiO_2.

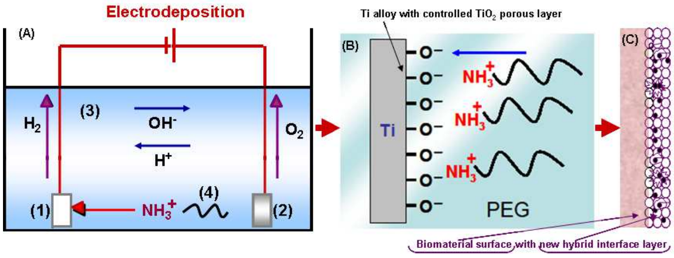

Fig. 2. *Schematic representation of electrochemically deposition of BAMs on porous oxide layer: (A) – Electrochemical cell with (1) – cathode as biomaterial with porous oxide layer; (2) counter electrode of platinum grid (anode); (3) electrolyte solution containing bioactive molecules; (B) Bonding of BAMs like PEG on porous TiO_2 oxide layer and (C) Biomaterial surface with new hybrid interface layer*

Straturile electrochimice de oxid poroase:

Sunt preparate prin creșterea controlată a oxidului (anodizare) prezentată schematic în figura 1. În această figură pe partea stângă (A) este o celulă electrochimică schematică și în partea dreaptă se prezintă o micrografie a unui strat de oxid poros de TiO_2 obținut pe un aliaj de titan (fotografia face parte din rezultatele nepublicate obținute de L. Benea și grupul de cercetare).

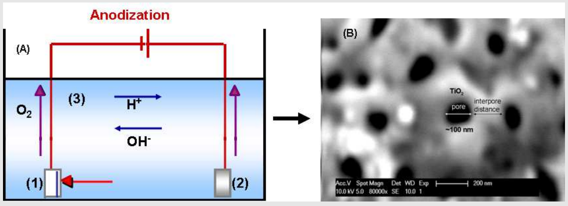

Fig. 1. *Reprezentarea schematică a preparării straturilor de oxid poroase (A) – celula electrochimică cu (1) – anod ca și biomaterial pentru functionalizare; (2) contra-electrod din rețea de platină; (3) soluția de electrolit pentru anodizare; (B) micrografie SEM a stratului de oxid poros de TiO_2 [L. Benea și grupul, date nepubilcate].*

Depunerea electrochimică a moleculelor bioactive (BAM-uri):

După ce stratul de oxid poros este format pe suprafața biomaterialului, electrodepunerea moleculelor bioactive (BAM-uri), cum ar fi polietilen glicol (PEG), hidroxiapatita (HA), chitosan (CH) pot fi mai bine imobilizate pe suprafața biomaterialului. Procesul este prezentat schematic în figura 2, unde în partea stângă (A) este desenată celula electrochimică, în mijloc (B) legătura dintre stratul de oxid poros și molecula bioactivă ca polietilen glicol (PEG) este un pas mult mai ușor posibil prin electrodepunere, iar în partea dreaptă, (C) este arătată suprafața biomaterialului cu noul strat de interfață hibrid rezultat. Modul de imobilizare (aleatoriu sau orientat) al BAM-urilor este important pentru aplicațiile ulterioare. Stratul de interfață ar putea fi consolidat prin faze bio nano dispersate precum CeO_2 şi/sau TiO_2.

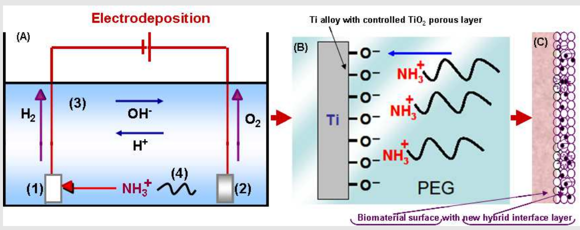

Fig. 2. *Reprezentarea schematică a depunerii electrochimice a BAM-urilor pe stratul de oxid poros: (A) – Celula electrochimică cu (1) – catod drept biomaterialul cu stratul de oxid; (2) contra-electrodul rețea de platină (anod); (3) soluția de electrolit conținând molecule bioactive; (B) Legarea BAM-urilor precum PEG pe stratul de oxid poros de TiO_2 și (C) Suprafața biomaterialului cu noul strat de interfață hibrid*

Surface modifications by electrodeposition of chitosan

Electrodeposition of chitosan films

The electrodeposition of chitosan hydrogel onto conductive surfaces normally could be achieved from aqueous solution under ambient condition. A broad spectrum of applications ranging from the fabrication of composite films, and surface layer coatings to biosensors has been demonstrated based on this technique.

The electrical input induces a sol–gel transition of this stimuli-responsive polymer, there are still open questions and complications about the chitosan microstructure and deposition mechanism.

General scheme of chitosan electrodeposition is presented in Fig. 3, where it can be seen the elecrochemical cell, the electrodes and the structural changes of chitosan from soluble to insoluble one.

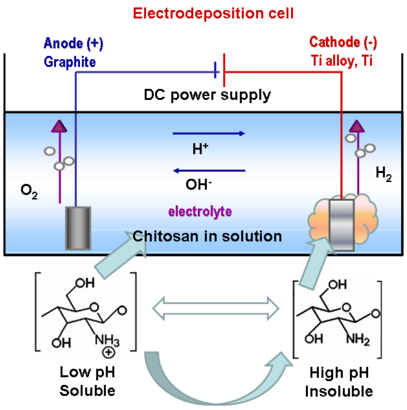

Fig. 3. Schematic illustration of the chitosan electrodeposition

When an anode and cathode are immersed in a chitosan solution and a voltage is applied, electrochemical reactions lead to a locally high pH adjacent to the cathode surface, Fig. 4.

Fig. 4. Sol-Gel interface formed at cathode during chitosan electrodeposition.

[L. Benea & Group-unpublished data]

A sol–gel interface was observed, which separates the transparent polyelectrolyte and the ordered textured hydro gel region. Such an interface was proportionally with the deposition time. This is consistent with another study that shows that the interface is actually a pH gradient caused by the electrolysis of water, separating the gel neutralized (pH = 10) and the deposition acid solution (pH = 5.3).

Chitosan solution stability function of pH is presented in Fig. 5.

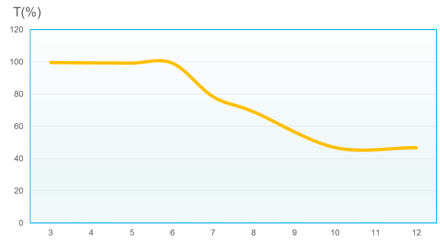

Fig. 5. Evaluation of stability according to pH by measuring the transmitance at 600 nm [L. Benea & Group-unpublished data]

From the literature it is known that chitosan provides mild conditions for the immobilization of proteins and enzymes for the applications in biomedical devices.

Chitosan/hydroxyapatite composite films

Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ is the major inorganic component of natural bones. Synthetic hydroxyapatite has been commonly used as a coating material for metallic implants due to its biocompatibility and ability to form strong bonds with bones. The possibility to prevent the implant caused infections using the antimicrobial properties of Ag has generated an interest in the development of hydroxyapatite composites containing Ag.

Preparation of Ag colloidal particles

The colloidal silver particles were prepared starting from silver nitrate solution and ascorbic acid. The study to establish optimum concentrations of both solutions was conducted by measuring in time the UV-VIS spectrum of prepared colloidal solutions.

A UV-VIS spectrum of colloidal silver particles is presented in Fig. 6.

After stabilization of colloidal the silver particles they were added to chitosan solution before elecrodeposition.

The interest in electrochemical deposition of chitosan with hydroxyapatite and silver particles for biomedical applications stems from the high purity of the deposited material and the possibility to form uniform deposits on substrates of complex shape. The coating technique enables a good control over the thickness, morphology, crystallinity, and stoichiometry of the deposits.

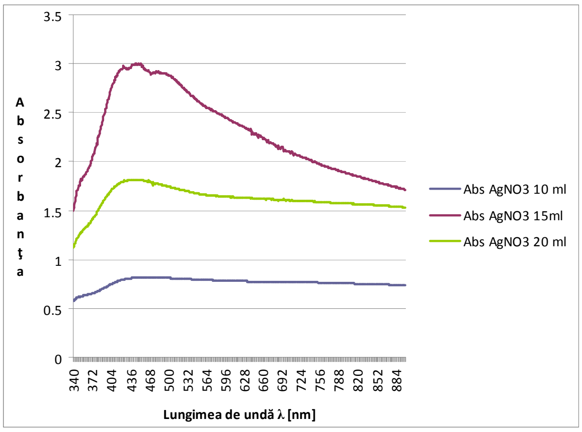

Fig. 6. Evaluation of stability of colloidal silver particles by measuring the absorbance [L. Benea & Group-unpublished data]

The use of chitosan enables the room temperature processing of the coatings, eliminating the problems related to the sintering of hydroxyapatite. The room temperature processing offers a possibility of co-deposition of other functional materials and fabrication of advanced nanocomposite coatings for biomedical applications.

Electrodeposition of chitosan into porous oxides

The simplest fabrication method of chitosan films consists of coating the surface with chitosan solution and evaporating the solvent. This leaves behind a solid chitosan film with a thickness dependent on the solution concentration. The coating procedure can be performed on flat surfaces or on different electrode geometry.

One promising stratrgy is to deposit the chitosan or modified chitosan into nanoporous oxyde layers formed annodically on biomaterials surface like titanium alloy. Such a nanoporous oxide layer was obytained on Ti-6Al-4V by electrochemical treatment and demonstrated already an improvement of corrosion resistance of this alloy in physiological solution [1 ,2]. In Fig. 7 a schematically electrodeposited film of chitosan into nanoporous TiO_2 layer is shown.

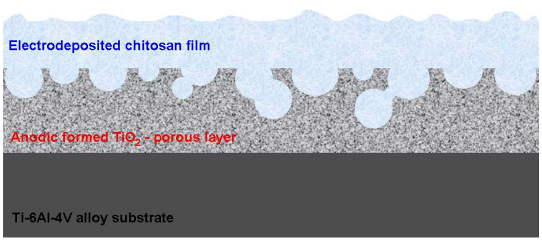

Fig. 4. Schematic presentation of chitosan electrodeposited film into nanoporous TiO_2 layer of titanium alloy.

[L. Benea & Group-unpublished data]

The chitosan deposition can be performed by electrodeposition or codeposition using a variety of solutions and dispersed phases. Therefore, a large variety of chitosan films can be formed by choosing a different modifying substance, modification method, and deposition method.

Due to its porous structure and dense amine groups, chitosan is well-suited for further attachment of biomolecules and therefore a suitable method for surface modification of biomaterials.

The work is in progress.

[1] E. Mardare, L. BENEA, J-P. Celis. Dig J Nanomater Bios. **3**, 933 (2012).
[2] L. Benea, E. Mardare-Danaila, M. Mardare, J.-P. Celis, Corros. Sci. **80**, 331 (2014).

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