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Lanthanum-containing hydroxyapatite coating on ultrafine-grained titanium by micro-arc oxidation: A promising strategy to enhance overall performance of titanium

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Titanium is widely used in biomedical materials, particularly in dental implants, because of its excellent biocompatibility and mechanical characteristics. However, titanium implant failures still remain in some cases, varying with implantation sites and patients. Improving its overall performance is a major focus of dental implant research. Equal-channel angular pressing (ECAP) can result in ultrafine-grained titanium with superior mechanical properties and better biocompatibility, which significantly benefits dental implants, and without any harmful alloying elements. Lanthanum (La) can inhibit the acidogenicity of dental plaque and La-containing hydroxyapatite (La-HA) possesses a series of attractive properties, in contrast to La-free HA. Micro-arc oxidation (MAO) is a promising technology that can produce porous and firmly adherent hydroxyapatite (HA) coatings on titanium substrates. Therefore, we hypothesize that porous La-containing hydroxyapatite coatings with different La content (0.89%, 1.3% and 1.79%) can be prepared on ultrafine-grained (~200–400 nm) titanium by ECAP and MAO in electrolytic solution containing 0.2 mol/L calcium acetate, 0.02 mol/L β-glycerol phosphate disodium salt pentahydrate (β-GP), and lanthanum nitrate with different concentrations to further improve the overall performance of titanium, which are expected to have great potential in medical applications as a dental implant.

MeSH Keywords: **Dental Implants • Dentistry • Hydroxyapatites • Titanium**

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Background

Commercial pure titanium and its alloys are widely used as biomedical materials, particularly in dental implants, because of their exceptional biocompatibility, low elastic modulus, excellent corrosion resistance, and high strength-to-density ratio. Within the last decade, the success rate of dental implants made of titanium has been reported to be 90–95% in medically healthy patients [1]. However, titanium implant failures still remain in some cases, varying with implantation sites and patients [2]. With the aging population, the incidence of implant failure will be high in patients with severe alveolar bone absorption and/or poor bone quality [3,4]. Hence, modification in design as well as the surface of implants is essential to improve the biocompatibility of titanium implants, especially with respect to bone cell response, to improve osseointegration of the implants and minimize the risk of implant failures. This may be achieved by surface modification and titanium refinement, which are able to actively interact with the surrounding tissues.

Latest Development of Titanium Refinement and Bioactive Coatings on Titanium Surface

Grain refinement is an effective method to enhance mechanical strength without the need to add a potentially harmful alloying element [5,6]. Ultrafine-grained (UFG) metals processed by equal-channel angular pressing (ECAP) show superior mechanical properties, such as high strength and improved ductility, as well as lower temperature and higher strain rate superplasticity [7,8]. The microstructure of coarse-grained titanium can be significantly refined through the ECAP process, and the resulting strength is enhanced from 463 to 1050 MPa, which is even higher than that of the commercial Ti6Al4V alloys (950 MPa) used for implants [8]. Furthermore, very recent studies reveal that the grain refinement of titanium has superior osteoblast cell compatibility [9] and shows better cell adherence and cell proliferation compared to the coarse-grain grade 2 titanium [10]. Thus, ultrafine-grained pure titanium, with better mechanical properties and extraordinary biocompatibility, seems to be a perfect candidate for use as dental implants.

Grain boundaries may act as fast atomic diffusion channels, and various kinds of non-equilibrium structural defects can accelerate the chemical activity of the UFG materials [11]. Thus, the use of ECAP-treated titanium as a substrate for bioactive coatings may represent an additional advantage over its conventional coarse-grained counterpart.

Rare earth elements (REE) are an important strategic resource widely used in various fields, including industry, agriculture, medicine, and daily life, but eventually accumulated in the human body. In particular, lanthanum (La) is one of the most important REE widely researched in recent years. La is found to have potential value in treatment and prevention of dental root caries [12,13]. La^{3+} promotes the formation of osteoclast-like cells and significantly increases the number and surface area of the resorption pits at the concentration of 1×10^{-8} mol/L, but inhibits bone resorption activity at higher concentrations [14]. Moreover, La has been recognized as a "bone-seeking" element due to the analogy between La^{3+} and Ca^{2+} in ionic radii and coordination tendency [15]. A recent study indicates that the La^{3+} ion can be incorporated into the crystal lattice of hydroxyapatite, resulting in the production of La-containing apatites. La content plays important roles in both the physicochemical properties and biocompatibilities of the La-containing apatites. In contrast to La-free apatite, La-containing apatites possess a series of attractive properties, including higher thermal stability, higher flexural strength, lower dissolution rate, greater alkaline phosphatase activity, preferable osteoblast morphology, and comparable cytotoxicity [16]. Thus, the introduction of La at controlled doses into some biomedical material could become an effective way to improve biomaterial properties. The La-containing apatite possesses application potential in developing a new type of bioactive coating material for dental implants.

The application of hydroxyapatite (HA) coatings on dental implant devices offers the advantage of a combination of mechanical properties of the metal and the favorable bioactivity of the ceramics. To coat HA on the surface of titanium implants, many surface treatment techniques, including plasma spraying, immersion in physiological fluid, sol-gel method, cathodic deposition, ion-beam techniques, and plasma nitriding have been used [17–22]. However, there are many concerns and controversy as to their long-term effectiveness and performance. MAO is a promising technology that can produce porous, rough, and firmly adherent inorganic lanthanum-containing hydroxyapatite (La-HA) coatings on titanium substrates. It has large-scale fabrication capability, and the amount of lanthanum incorporated into the coatings can be optimized by altering the electrolyte composition [23–25].

Hypothesis and Evaluation of the Hypothesis

Fabrication of ECAP-treated Ti specimen

On the basis of the above analyses, we propose the hypothesis that ultrafine-grained commercially pure titanium sample, which has various advantages over its conventional coarse-grained counterpart, prepared by ECAP, can be used as a substrate for bioactive coatings. Pure Ti billets, 20 mm in diameter and 100 mm in length, will be processed by ECAP for 8 passes at a rate of 6 mm s^{-1} at 450 [6]. These processing parameters are optimized for the best combination of ductility and efficiency in grain refinement. The deformed microstructures, mechanical properties, and biocompatibility of pure titanium that are influenced by varied technological parameter will be investigated. Then the UFG (~200–400 nm) titanium samples will be coated by porous lanthanum-contained hydroxyapatite layer via the MAO process.

Synthesis of La-HA coatings by MAO

A 2 kW alternating current MAO device will be used to fabricate La-HA coatings. A mixed aqueous solution containing 0.2 mol/L calcium acetate, 0.02 mol/L β-glycerol phosphate disodium salt pentahydrate (β-GP), and lanthanum nitrate with different concentrations (0, 0.3 g/L, 0.7 g/L, and 1.0 g/L) will be used as the electrolyte system.

Because no upper limit has been defined for the amount of lanthanum that should be incorporated into the hydroxyapatite coatings, it has to be optimized to provide enough to favor bone formation without having deleterious effects on bone mineralization. In addition, the optimal dosage of La depends on a complicated environment, not only crystal itself, but also the adjacent tissue fluid *in vivo*. Therefore, in this study, a series of La-HA coatings are produced on UFG titanium samples using MAO, with the different substitution degrees.

In previous studies, the oxide coating included Ca- and P-containing phases such as $CaTiO_3$, α-$Ca_3(PO_4)_2$, β-Ca_2PO_7, $CaCO_3$, CaO, or amorphous apatite [26–29]. Further work is needed on hydrothermal treatment, heat treatment, or a simulated body fluid (SBF) incubation treatment of the coatings [26,27,30,31] to improve its bioactivity [32]. Now we can create lanthanum-containing hydroxyapatite coatings directly through the MAO process by controlling the parameters of MAO and adding La element in the electrolytic solutions, getting rid of the additional treatment of titanium coatings, and thus improving efficiency and affordability.

Coating characterization and bioactivity evaluation

The surface topography, thickness, phase, composition morphology, surface roughness, and adhesion strength of the coatings will be characterized by field emission scanning electron microscope (FESEM), scanning electron microscope (SEM), X-ray diffraction (XRD), electron probe microanalysis (EPMA), scanning electron microscopy (SEM) with energy dispersive X-ray spectrometer (EDS), atomic force microscope (AFM), and nano-indentation testing system.

Then, based on the above preliminary analyses of coating, *in vitro* biological responses at the bone-implant interface and *in vivo* osteoblast/osteoclast responses to the La-HA coating will be investigated and the optimal La content to substitute in hydroxyapatites (HA) coatings can be clarified as well. Especially, studies will be performed to answer the question "What will happen to the structure and properties of La-containing hydroxyapatite coatings after La is incorporated into its crystal lattice via MAO process?"

It will be found that the thickness of La-HA coatings decreases and the contents of La on the coatings and the adhesion strength of coatings increase as the concentrations of La in electrolyte increasing. The XRD and EDS results will show that the porous coating is made of La-containing HA film and La content in La-containing hydroxyapatite coating are 0.89%, 1.3% and 1.79%, respectively.

Conclusions

Based on the thorough understanding of the latest developments in titanium refinement and surface modification, porous La-containing hydroxyapatite coatings with different La content (0.89%, 1.3%, and 1.79%) can be prepared on ultrafine-grained titanium by MAO. This strategy could possess application potential in developing an easy to perform surface modification method with low production costs and a new type of bioactive coating material for titanium implants with an optimized combination of mechanical properties and effective osseointegration function.

Conflicts of interest statement

None declared.

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