NCJSC Asfendiyarov Kazakh National Medical University

ABSTRACT

on the dissertation of Madi Berikuly Tleshev,
entitled « Preclinical rationale for the application of titanium implants with nanostructured coatings in dentistry»,
submitted for the degree of Doctor of Philosophy (PhD)
in the specialty 8D10103 – Medicine

Scientific advisor:
Doctor of medical sciences,
professor K.D. Altynbekov

Foreign scientific advisor:
Doctor of medical sciences,
professor R.G. Khafizov

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Relevance of the research topic

According to projections by the United Nations, by 2050 the number of individuals aged over 65 will more than double the number of preschool-aged children. Untreated caries of permanent teeth affects approximately 2.2 billion people and remains the most prevalent disease worldwide. The increase in life expectancy and the growing proportion of the elderly population lead to a higher incidence of tooth loss and other dental diseases.

Today, dental implantation occupies a special place in the structure of dental care. Dental implantology is particularly relevant, as this method of prosthetic rehabilitation allows restoration of the dentition in cases of various defects.

The main characteristics of dental implants include the material composition, shape, and surface coating. Titanium implants are most commonly used for tooth restoration due to their high strength and excellent biocompatibility.

Despite the high clinical effectiveness of dental implantation, inflammatory complications remain a leading long-term issue. According to systematic reviews, peri-implantitis is detected in approximately 20% of cases.

One of the key challenges in dental implantology is metal corrosion. Long-term exposure of titanium implants to the aggressive environment of the human body may lead to the release of titanium ions, which can potentially induce toxic reactions. Currently, most implants are manufactured from commercially pure titanium and its alloys. In dental practice, commercially pure titanium grade VT1-0 and titanium aluminum-vanadium alloy Ti-6Al-4V (VT6, international equivalent Grade V) are most widely used.

At present, implants are modified using various approaches. The primary goal is to achieve optimal surface topography, impart specific chemical and physical properties, and introduce nanotechnology-based modifications onto the titanium surface. Common approaches include mechanical, physical, and chemical surface modification methods.

Mechanical surface modification methods, such as sandblasting or machining, create micro-roughness that enhances implant stability and improves osseointegration. Physical methods, including laser treatment and plasma spraying, alter surface properties without changing the chemical composition of the implant, thereby improving biocompatibility and accelerating tissue healing. Chemical methods, such as acid etching or anodization, modify the chemical composition of the surface, enhancing bone attachment and reducing the risk of inflammatory processes. However, techniques such as plasma spraying and anodization also have limitations. According to some data, they may not provide sufficient corrosion resistance, may promote bacterial colonization, and may cause issues related to biological compatibility.

Nanostructured coatings represent a promising direction for improving the properties of titanium implants. They can provide corrosion resistance, antibacterial effects, and enhanced osseointegration due to their unique physicochemical properties. However, their widespread clinical application requires thorough preclinical justification, including the assessment of biocompatibility, corrosion resistance, and antibacterial activity.

Analysis of the literature shows that existing publications are mainly focused on individual characteristics of nanostructured coatings. Comprehensive preclinical studies integrating the evaluation of morphology, elemental composition, corrosion properties, antibacterial activity, and biocompatibility within a single study remain insufficiently represented.

In the context of the need to expand access to dental care, particular importance is given to research aimed at developing domestic technologies for implant surface modification. Kazakhstan possesses a significant raw material base for titanium production, ranking 10th in the world in terms of reserves, which creates real prerequisites for the development of national dental implant systems and improving the accessibility of dental care. This determines the relevance and scientific significance of the present dissertation research.

Aim of the dissertation research

To improve the effectiveness of dental implantation through the preclinical application of nanostructured TiO_2 and TiO_2+Ag coatings on titanium implants.

Research objectives:

1. To develop nanostructured TiO_2 and TiO_2+Ag coatings on titanium implants using an electrochemical method.
2. To investigate the morphological features and elemental composition of the obtained TiO_2 and TiO_2+Ag coatings.
3. To evaluate the corrosion resistance of the coatings by potentiodynamic polarization.
4. To assess the antibacterial activity of the nanostructured TiO_2 and TiO_2+Ag coatings using the disk diffusion test against S. mutans, S. sobrinus, and S. aureus.
5. To investigate the biocompatibility and safety of titanium samples with coatings based on in vitro and in vivo experimental studies.
6. To scientifically substantiate the effectiveness of using implants with nanostructured TiO_2 and TiO_2+Ag coatings based on the results of preclinical studies.

Summary of the main research results

According to scanning electron microscopy, uniform nanostructured TiO_2-based coatings with granular agglomerates were formed on the surface of titanium samples. The elemental composition was predominantly represented by titanium and oxygen (Ti 60%, O 39%).

Potentiodynamic studies conducted in a NaCl medium demonstrated an increase in corrosion resistance following coating deposition: the dissolution onset potential shifted from 2.25 V (uncoated titanium) to 2.75 V (TiO_2 coating).

Comprehensive biocompatibility assessment confirmed the absence of acute and subacute toxicity, skin irritation, sensitizing effects, and cytotoxicity in fibroblast cultures, as well as no implant rejection in in vivo experiments. The TiO_2+Ag coating provided the most favorable tissue response: wound healing occurred by day 8, compared to 9–10 days for TiO_2 and 10–11 days for uncoated titanium.

According to the disk diffusion test, no diffusion-based antibacterial effect of the TiO_2+Ag coating was observed.

Scientific novelty

1. An electrochemical method for the formation of a nanostructured titanium dioxide (TiO_2) coating on the titanium surface was developed and patented (Utility Model Patent No. 7907 dated March 31, 2023; Baeshov A.B., Altynbekov K.D., Baeshova A.K., Khalmuratova Zh.K., Tleshev M.B.).
2. The effectiveness of using nanostructured TiO_2 and TiO_2+Ag coatings for dental implantation was scientifically substantiated and confirmed by preclinical studies.

Main provisions submitted for defense

1. The application of the developed nanostructured TiO_2 and TiO_2+Ag coatings on titanium implants is a preclinically substantiated method for improving the effectiveness of dental implantation by enhancing corrosion resistance and ensuring high biocompatibility.
2. Within the framework of the preclinical study, the use of nanostructured TiO_2 and TiO_2+Ag coatings formed by an electrochemical method has been scientifically substantiated for application in practical dentistry.

Practical significance of the research results

It has been established that TiO_2 and TiO_2+Ag nanostructured coatings formed on titanium by an electrochemical method improve the corrosion resistance of the material. These findings can be applied to justify the selection of titanium dental implant surfaces for use under conditions of increased corrosive load.

A comprehensive preclinical evaluation framework for titanium implant coatings has been developed and validated. This framework includes control of coating structure and composition, electrochemical testing, and assessment of biological safety (in vitro and in vivo) with histological verification of local tissue response. This may be applied as a practical protocol for testing new variants of implant surface modifications.

As a result of the study, a utility model patent No. 7907 dated March 31, 2023 (Baeshov A.B., Altynbekov K.D., Baeshova A.K., Khalmuratova Zh.K., Tleshev M.B.) was obtained for an electrochemical method of forming a nanostructured titanium dioxide coating on titanium surfaces.

Practical recommendations have been developed for the application of TiO_2 and TiO_2+Ag coatings in the manufacturing of titanium dental implants. These include requirements for coating reproducibility and a set of mandatory preclinical tests prior to transition to the clinical stage.

Personal contribution of the doctoral candidate

With the participation of the doctoral candidate, Utility Model Patent No. 7907 was obtained.

The doctoral candidate participated in the preparation of titanium samples and the formation of nanostructured coatings using an electrochemical method. The doctoral candidate investigated the surface morphology and elemental composition of the coatings and conducted corrosion and antibacterial tests.

The doctoral candidate coordinated the in vitro and in vivo studies, performed analysis and interpretation of the obtained results, statistical data processing, and comparison with literature data, and prepared the dissertation text, conclusions, and practical recommendations.

Conclusions

1. Nanostructured TiO_2 and TiO_2+Ag coatings on titanium implants were obtained using an electrochemical method.
2. Scanning electron microscopy revealed a uniform structure of the TiO_2 and TiO_2+Ag coatings, and their elemental composition was confirmed: Ti 60% and O 39%.
3. Nanostructured TiO_2 and TiO_2+Ag coatings improve the corrosion resistance of titanium implants in NaCl solution; the dissolution onset potential was found to shift from 2.25 V to 2.75 V.
4. In the disk diffusion test, the TiO_2+Ag coating did not demonstrate diffusion-mediated antibacterial activity against S. mutans, S. sobrinus, and S. aureus; the inhibition zones were 0 mm. This indicates the need to apply contact-based assessment methods in further studies.
5. TiO_2 and TiO_2+Ag coatings are biologically safe. No pathological changes were detected in studies of acute and subacute toxicity, irritating, sensitizing, or cytotoxic effects.
6. Based on the results of preclinical studies, the effectiveness of using nanostructured TiO_2 and TiO_2+Ag coatings in dental implantology has been scientifically substantiated.

Approbation of the dissertation results

The main provisions of the dissertation were presented at the following conferences and forums:

1. I International Forum “Asfen.Forum – New Generation 2023” (June 5–6, 2023, Almaty, Asfendiyarov Kazakh National Medical University).
2. Young Scientists Medical Forum “SOVMIN FORUM-94: Pulse of Time” (November 3, 2023, Central Clinical Hospital JSC, Almaty).
3. IX Arctic Dental Forum with international participation (November 23, 2023, Arkhangelsk, Russia).
4. Congress “Dentistry of the 21st Century: Traditions, Achievements, and Prospects”, dedicated to the 65th anniversary of the Faculty of Dentistry (May 24, 2024).
5. All-Russian Scientific and Practical Conference with international participation “Mirgazizov Readings. Innovative Technologies in Dentistry: Responses to Modern Challenges and Development Prospects” within the Forum “Dentistry of Tatarstan–2024” (May 24, 2024, Kazan, Russia).
6. XIII International Scientific and Practical Conference “Priorities of Pharmacy and Dentistry: From Theory to Practice”, dedicated to the 135th anniversary of Sanzhar Asfendiyarov (November 15, 2024).
7. International Forum “ANaMed Forum – New Generation 2025” (June 4–5, 2025).

8. III Republican Scientific Conference of Young Specialists “SOVMIN FORUM 2025” (December 3, 2025).

Publications

1. Tleshev M.B., Altynbekov K.D., Nysanova B.Zh., Shayakhmetova M.K. Materials used in dental implantation (literature review). Pharmacy of Kazakhstan. 2022; 4(243): 110–114.
2. Tleshev M.B., Kulmanbetov R.I., Nysanova B.Zh., Altynbekov K.D. Features of corrosion resistance of titanium implants with nanostructured coatings. Phthisiopulmonology. 2024; (3). National Scientific Center of Phthisiopulmonology of the Republic of Kazakhstan.
3. Tleshev M.B., Nysanova B.Zh., Kulmanbetov R.I., Altynbekov K.D. Features of antibacterial properties of titanium implants with nanostructured coatings. Phthisiopulmonology. 2024; (3). National Scientific Center of Phthisiopulmonology of the Republic of Kazakhstan.
4. Nysanova B.Zh., Kulmanbetov R.I., Ruzuddinov T.B., Tleshev M.B., Shokhanova Zh.N., Zhaishieva Sh.A., et al. Application of nanocomposite materials in modern dentistry: a literature review. Phthisiopulmonology. 2025; 1(47).
5. Tleshev M., Nysanova B., Onaibekova N., Kulmanbetov R., Altynbekov K. Surface modification of dental implants in dentistry. Fluoride. 2024: e293.
6. Tleshev M.B., Altynbekov K.D., Nysanova B.Zh. Preclinical substantiation of the use of titanium implants with nanostructured coatings in dentistry. In: Proceedings of the 1st International Forum “Asfen Forum”, June 5–6, 2023, Almaty; 2023: 538.
7. Altynbekov K.D., Nysanova B.Zh. Investigation of properties of titanium implants with modified coatings. In: Proceedings of the 2nd International Forum “Asfen.Forum – New Generation 2024”. Almaty: Asfendiyarov Kazakh National Medical University; 2024. p. 818.
8. Baeshov A., Altynbekov K., Baeshova A.K., Khalmuratova Zh., Tleshev M.B., Sarybayev B.A. Electrochemical method for producing titanium dioxide: Utility model patent No. 7907 of the Republic of Kazakhstan. Filed January 29, 2023; published March 31, 2023.

Structure and scope of the dissertation

The dissertation consists of an introduction, four chapters, a conclusion, final conclusions, a list of references, and appendices. The research work is presented in 137 pages of typed text, including 69 figures, 19 tables, and 3 appendices. The reference list comprises 202 sources in English and Russian.