



Original Article

Synthesis of Strontium Substituted Hydroxyapatite Coating on Titanium Via Hydrothermal Method

Le Thi Tam^{1,2}, Vu Dao Kien¹, Ta Quoc Tuan^{1,2}, Le Van Toan^{1,3},
Pham Thi Mai Phuong^{1,2}, Pham Hung Vuong^{1,2,*}

¹*School of Materials Science and Engineering, Hanoi University of Science and Technology (HUST),
01 Dai Co Viet, Hanoi, Vietnam*

²*Laboratory of Biomedical Materials, Hanoi University of Science and Technology (HUST),
01 Dai Co Viet, Hanoi, Vietnam*

³*Le Quy Don Technical University, 236 Hoang Quoc Viet, Hanoi, Vietnam*

Received 02 December 2023

Revised 11 March 2024; Accepted 10 May 2024

Abstract: In this study, strontium substituted hydroxyapatite (SrHA) was successfully deposited onto etched titanium substrates in H₂SO₄ and HCl solution. The deposition was achieved by hydrothermal method by immersing the substrates in a solution containing Ca(NO₃)₂·4H₂O, NH₄H₂PO₄, and 5% Sr(NO₃)₂, followed by heating at 200°C for 12 hours. X-ray diffraction (XRD) analysis confirmed that all SrHA coatings exhibited a crystalline hydroxyapatite structure. Field-emission scanning electron microscopy (FE-SEM) revealed that the microstructure of the SrHA coatings exhibited. Bioactivity and in vitro biocompatibility testing of the SrHA-coated titanium substrates using SBF solution and baby hamster kidney (BHK) cells demonstrated positive results.

Keywords: Hydroxyapatite, Hydrothermal, Strontium substituted hydroxyapatite, Cell attachment, Implant.

1. Introduction

In recent years, advancements in biomaterials have played a pivotal role in the development of biomedical devices, especially in the field of orthopedics and dental implants [1]. Titanium, renowned for its good mechanical properties [2-4], high strength-to-weight ratio [3], good corrosion resistance [5],

* Corresponding author.

E-mail address: vuong.phamhung@hust.edu.vn

<https://doi.org/10.25073/2588-1124/vnumap.4906>

moderate biocompatibility [6]. Titanium (Ti) is a material of choice in biomedical implants because Ti is non-ferromagnetic and magnetic resonance imaging that can be performed on patients with titanium implant without risk [7]. However, challenges persist in optimizing the bioactivity of titanium implants to ensure successful osseointegration and long-term stability within the human body [8] as well as improving the corrosion resistance of the titanium [9, 10]. To address these issues, numerous research studies have been done to improve the bioactivity of the titanium implants with surface modification being a key solution to overcome these problems [11-15].

Among these surface modification techniques with different coating layer, hydroxyapatite (HA), a calcium phosphate compound, has attracted interest due to its biocompatible and bioactive properties, making it an ideal candidate for coating on implant surfaces [16-20]. Hydroxyapatite, with the general formula $\text{Ca}_5(\text{PO}_4)_3\text{OH}$ and unit cell formula $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ [21] belongs to the family of calcium phosphate (CaP) ceramics with Ca/P molar ratio of 1.67, similar to that of natural bone and has favorable surface chemistry supporting bone development [9]. HA also acts as a protective coating for the titanium implants, improving the corrosion behavior of the implants which not only suppresses harmful ions that could be released from the surface of metallic implants but also extends their service life by preventing the failure of the implant that is being protected [22, 23]. Furthermore, the incorporation of strontium into hydroxyapatite introduces an intriguing dimension, as strontium has been reported to exhibit bone-stimulating effects and enhance osteogenic activity, therefore stimulating bone formation, growth, and healing [24-28]. Moreover, it is also reported that the incorporation of strontium increases the adhesion strength of the HA coating to the implants [29, 30].

In the pursuit of optimizing the biocompatibility of titanium implants, various coating methods have been explored to augment their interaction with the biological milieu such as physical vapor deposition [31, 32], sol-gel [33, 34], electrochemical deposition [35, 36], thermal spraying [37, 38] or hydrothermal [39-41]. Among the plethora of available methods, the hydrothermal approach emerges as a compelling choice for the deposition of strontium-substituted hydroxyapatite on titanium surfaces. The rationale behind this selection lies in the unique advantages offered by the hydrothermal method. Unlike other techniques, hydrothermal synthesis occurs under elevated temperatures and pressures in an aqueous environment, allowing for the precise control of particle size and crystallinity [42]. These factors are crucial in tailoring the coating to achieve optimal biological responses, ensuring a harmonious interface between the implant and the host tissue.

The HA coating on etched titanium substrates has been synthesized successfully in our group by previous work [43]. To expand this direction, we report the synthesis of SrHA coating on the etched Ti substrates by the hydrothermal method. Therefore, the aim of this study is to investigate the SrHA films which have been successfully coated on titanium substrates, focusing on their surface morphology and biocompatibility.

2. Experiment Procedure

2.1. Preparing Titanium Surface with Etching Solution

The bare Ti plates with dimensions of $10 \times 10 \times 1 \text{ mm}^3$ (Merck, 99.5%). Prior to acid etching, the Ti substrates have been polished by 800 grits of SiC papers. The polished Ti substrates were cleaned in an ultrasonic bath for 10 min and dried in air. Then, the cleaned Ti samples were immersed in a mixed solution of 48% H_2SO_4 (Merck, 98%) and 37% HCl (Merck, 37%) at 60°C for 60 minutes. The etched Ti were then rinsed with distilled water followed by alcohol and dried in air [44].

2.2. Creating Sr-doped HA Coating on the Surface of Etched Titanium

Completely dissolve 4.72 grams of $\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$ (Merck, 99.5%) and 7.45 grams of $\text{Na}_2\text{EDTA} \cdot 2\text{H}_2\text{O}$ (Merck, 99%) in 35 ml of distilled water to obtain solution (a). Completely dissolve 1.4 grams of $\text{NH}_4\text{H}_2\text{PO}_4$ (Merck, 99%) in 35 ml of distilled water to obtain solution (b). Mix solution (b) into solution (a), stirring continuously for about 30 minutes at room temperature. Add 5% mol $\text{Sr}(\text{NO}_3)_2$ (Merck, 99%) denoted as 5SrHA into the above solution, and continue stirring evenly for 30 minutes.

The pH of the solution was adjusted to 9 by gradually adding NH_4OH (Merck, 35%) into the solution, followed by thorough stirring. Etched titanium samples were placed into 100 ml Teflon vessels positioned within stainless steel chamber. Within the Teflon vessels, HA solution supplemented with Sr^{2+} ions was added to facilitate the hydrothermal reaction. The hydrothermal synthesis process was conducted at 200 °C for 12 hours, followed by drying the samples at 60 °C for 1 hour. For comparative analysis, control samples, including non-etched titanium samples, were also synthesized with Sr^{2+} supplemented HA.

2.3. Surface Characterization and Biocompatibility Assessment

The X-ray diffraction (XRD, D8 Advance, Bruker, Germany) was used to characterize the structural phase. Measurements were performed using $\text{Cu-K}\alpha$ radiation $\lambda = 1.54056$ nm. The morphology of 5SrHA was studied using digital optical microscopy (VHX-7000). Field emission scanning electron microscopy (FE-SEM, JEOL JSM-7600F device (Japan) was also used to observe the surface morphology of SrHA. The bioactivity of the 5SrHA was evaluated using simulated body fluid (SBF) model. The 5SrHA was immersed in the SBF solution and then placed in the furnace at a temperature of 37 °C for 7 days. The specimens were then washed three times using ethanol followed by drying at 37 °C for 1 h. The formation of the bone mineral layer on the SrHA was examined using FE-SEM. Period to the in vitro cell tests, the titanium substrate and SrHA coating were sterilized by autoclaving at 121°C for. Baby hamster kidney (*BHK cells*) was maintained in DMEM at 37 °C in humidified air and 5% CO_2 . Cell suspensions density of 2×10^4 cell/ml were then seeded on the Ti and 5SrHA coating. Cell attachment was observed by confocal laser scanning microscopy (FV3000, Olympus, Japan). After culturing for 72 h, the BHK cells on the 5SrHA coating and the Ti were fixed in 4% paraformaldehyde in PBS for 10 min, washed in PBS, permeabilized with 0.1% Triton X-100 in PBS for 5 min, washed in PBS and stained with fluorescent phalloidin for 45 min. The BHK cell nuclei were labelled with DAPI for 5 min. The stained BHK cells attached on the samples were placed on a glass cover slide, and the cell attachment was observed.

3. Results and Discussion

3.1. Surface Characteristics

In Fig. 1, SEM images depict the morphology of HA (Fig.1a) and 5SrHA (Fig.1b). It is observed that in the absence of Sr, the hexagonal rod-like structure of HA is clearly observed on the surface of etched titanium, with the length of rods approximately 110 μm .

In Fig. 2a, the FE-SEM image reveals a hexagonal diameter of approximately 4 μm . Several studies have indicated that as the concentration of Sr^{2+} ions increases in the HA synthesis solution, the size of the HA tubes decreases [24-26, 45]. In Fig.1b, the size of the 5SrHA tubes is not clearly observed, suggesting a structural change in the tubes due to the substitution of Sr^{2+} for Ca^{2+} [45]. The rod-like

structure of the material layer on the 5SrHA sample (Fig. 2b) and the dimensions of the 5SrHA rods is approximately 500 nm, representing a reduction by 21 times compared to the hexagonal rod-like HA (Fig. 1a), with a proportional decrease in the diameter of the 5SrHA rods.

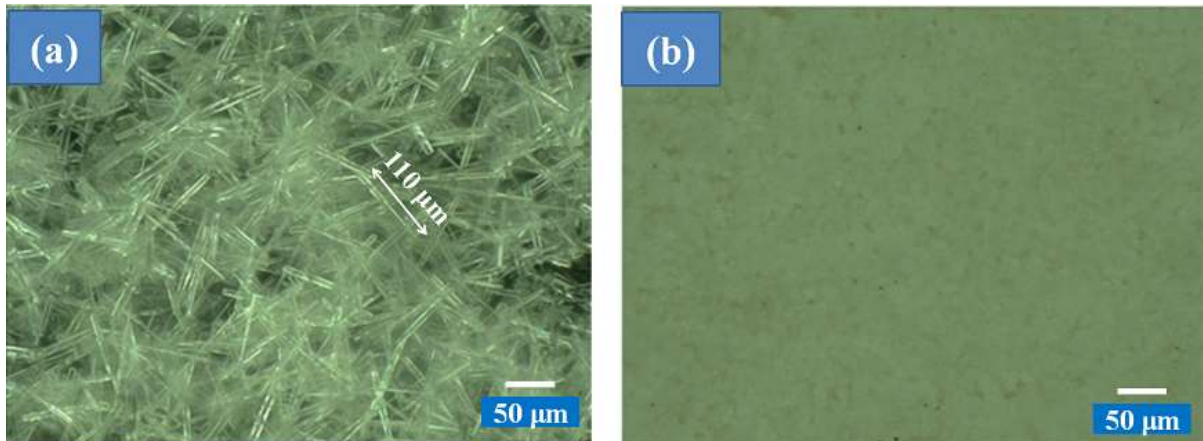


Figure 1. Digital optical image of the (a) HA coating and (b) 5SrHA on the etched titanium substrate.

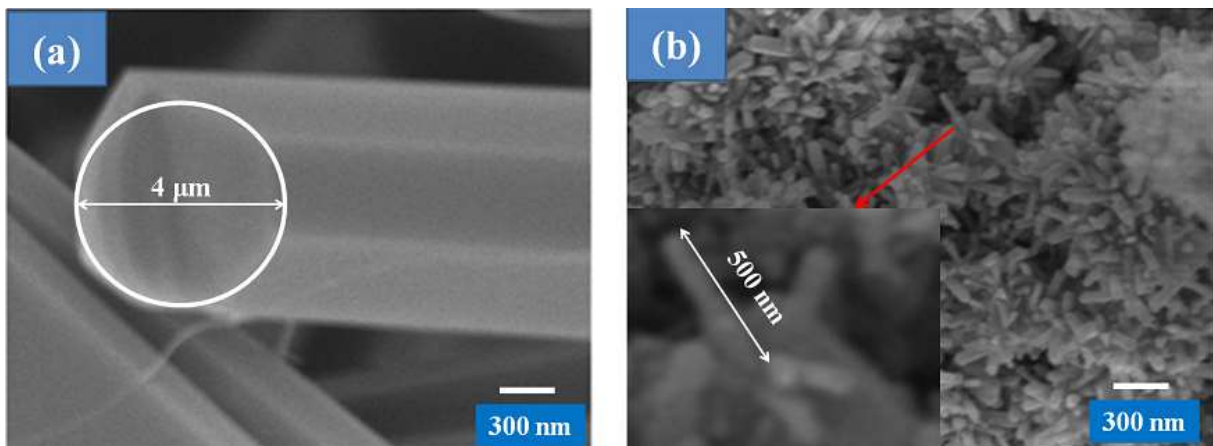


Figure 2. FE-SEM images of (a) HA and (b) 5SrHA coating on etched Ti substrate.

3.2 Chemical Composition Analysis

Fig. 3 illustrates the X-ray diffraction patterns of two types of coatings: HA (Fig. 3a) and 5SrHA (Fig. 3b) on etched titanium plates. Interestingly, there is no noticeable difference in the peak positions between Fig. 3a and Fig. 3b. This can be explained by the nature of pure HA, which is known to exist as the compound $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ according to the standard reference JCPDS 09-0432. When Sr^{2+} replaces Ca^{2+} in this compound, it forms $\text{Ca}_{10-x}\text{Sr}_x(\text{PO}_4)_6(\text{OH})_2$, where x ranges from 0 to 10. This new compound maintains a hexagonal structure similar to $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$. Additionally, since the ionic radii of Sr^{2+} and Ca^{2+} ions are very similar, there is no significant peak shifting observed in Fig.3. Consequently, there is no need to mark the positions of each compound in the X-ray diffraction patterns of the HA and 5SrHA samples.

Fig. 4 clearly shows the EDS image of the 5SrHA sample regarding its chemical composition and the content of elements on the surface of the 5SrHA sample. The Sr content in the 5SrHA sample is relatively high at 16.3% by weight, resulting in a Sr/(Sr+Ca) ratio of 0.38. This explains the relatively high substitution of Sr^{2+} for Ca^{2+} .

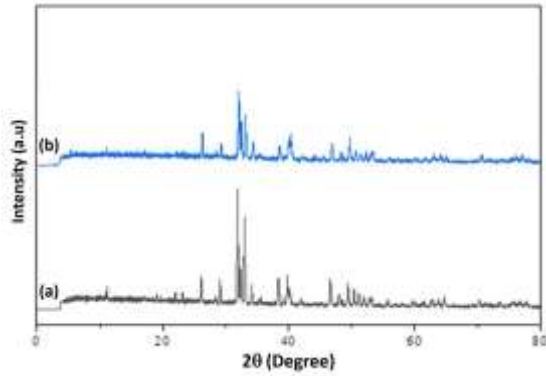


Figure 3. XRD pattern (a) HA and (b) 5SrHA coating on the etched titanium.

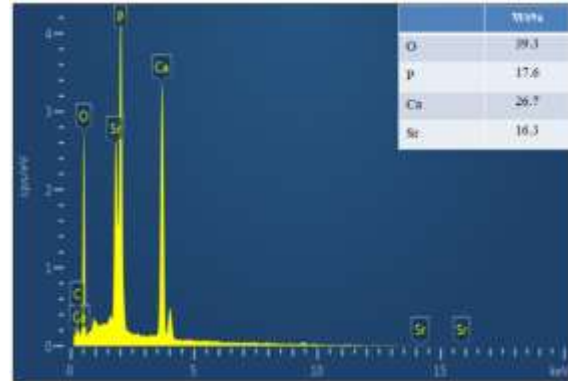


Figure 4. EDS of 5SrHA coating on the etched titanium.

3.3. Bioactivity of 5SrHA Coating on Titanium

Fig. 5 illustrates FE-SEM images of apatite minerals formed outside the 5SrHA crystals by immersing the 5SrHA sample in SBF solution at 37 °C for 7 days. These new bone minerals cover the surface of the rod-like HA crystals, altering their morphology. This demonstrates that the 5SrHA coating on titanium subjected to etching exhibits relatively good biological activity, facilitating the exchange of materials with the living environment, and resulting in the formation of a bonded bone mineral layer.

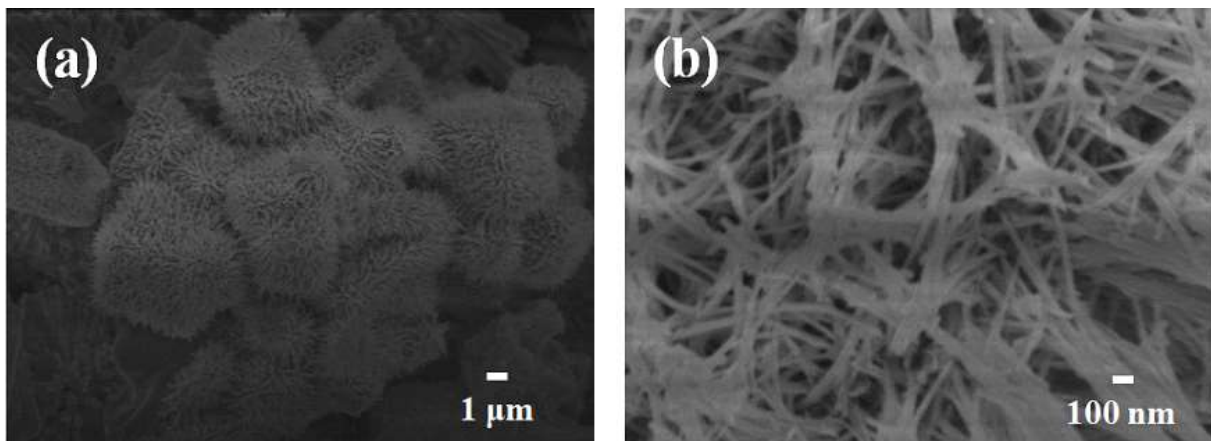


Figure 5. FE-SEM images showing the bioactivity of 5SrHA coating on etched titanium immersion in SBF for 7 days with (a) 3k and (b) 40k magnification.

3.4 Biological Compatibility Testing

Fig. 6 depicts confocal laser scanning microscope (CLSM) images of BHK cell attachment on both Ti and 5SrHA coatings after 72 hours of culturing. As described in Figure 6, cells on Ti and SrHA exhibit normal fibroblastic cell morphology, with clear nuclei and cell membranes. However, the cell density on SrHA is significantly higher than that on Ti. This indicates that the SrHA coating on etched titanium is a biocompatible coating layer after hydrothermal processing, with potential for further investigation in implant materials.

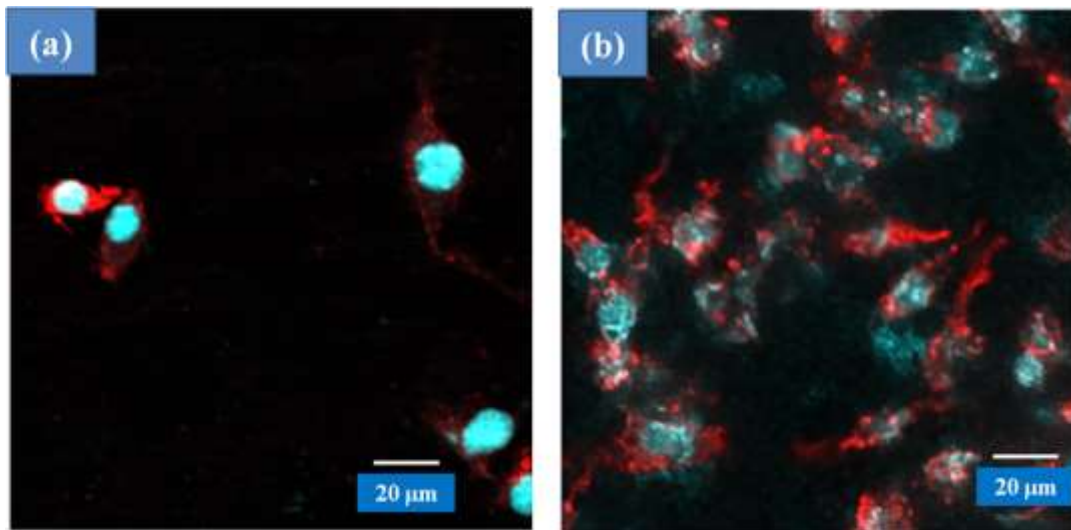


Figure 6. CLSM image showing the biocompatibility of samples coating on etched titanium (a) Ti; (b) 5SrHA

4. Conclusion

In this study, 5SrHA samples were successfully deposited onto etched Ti substrates by hydrothermal method. The HA coating exhibited a rod-like hexagonal morphology. Substituting Ca^{2+} with Sr^{2+} from $\text{Sr}(\text{NO}_3)_2$ solution in the HA crystal structure significantly reduced the dimensions of the SrHA structure, with a relatively high Sr content, and the $\text{Sr}/(\text{Sr}+\text{Ca})$ ratio was 0.38. The 5SrHA coating was evaluated for its interaction with simulated body fluid (SBF) after 7 days, demonstrating good biological compatibility as evidenced by BHK cell attachment after 72 hours.

Acknowledgments

This research was funded by the Ministry of Education and Training (MOET) under grant number CT2022.03.BKA.04.

References

- [1] S. Prasad, M. Ehrensberger, M. P. Gibson, H. Kim, E. A. Monaco, Biomaterial Properties of Titanium in Dentistry, *Journal of Oral Biosciences*, Vol. 57, No. 4, 2015, pp. 192-199, <https://doi.org/10.1016/j.job.2015.08.001>.

- [2] M. Prakasam, J. Locs, K. S. Ancane, D. Loca, A. Largeteau, L. B. Cimdina, Biodegradable Materials and Metallic Implants-A Review, *Journal of Functional Biomaterials*, Vol. 8, No. 4, 2017, pp. 44-59, <https://doi.org/10.3390/jfb8040044>.
- [3] M. Esposito, Y. Ardebili, W. Hv, Interventions for Replacing Missing Teeth: Different Types of Dental Implants, *The Cochrane Library*, 2003, pp. 1-117, <https://doi.org/10.1002/14651858.CD003815.pub4>.
- [4] I. Lundstrgm, Physico-chemical Considerations of Titanium as a Biomaterial, *Clinical Materials*, Vol. 9, No. 2, 1992, pp. 115-134, [https://doi.org/10.1016/0267-6605\(92\)90056-y](https://doi.org/10.1016/0267-6605(92)90056-y).
- [5] R. R. Wang, A. Fenton, Titanium for Prosthodontic Applications: A Review of the Literature, *Quintessence International*, Vol. 27, No. 6, 1996, pp. 401-408, <https://doi.org/10.1016/j.heliyon.2022.e11300>.
- [6] X. Liu, P. K. Chu, C. Ding, Surface Modification of Titanium, Titanium Alloys, and Related Materials fFor Biomedical Applications, *Materials Science and Engineering R: Reports*, Vol. 47, 2004, pp. 49-121, <https://doi.org/10.1016/j.mser.2004.11.001>.
- [7] J. Tormanen, O. Tervonen, A. Koivula, J. Junila, L. Suramo, Image Technique Optimization in MR Imaging of a Titanium Alloy Joint Prosthesis, *JMRI*, Vol. 5, No. 5, 1996, pp. 805-811, <https://doi.org/10.1002/jmri.1880060515>.
- [8] N. L. Valverde, J. F. Fraile, J. M. Ramírez, B. M. D. Sousa, S. H. Hernández, A. L. Valverde, Bioactive Surfaces Vs. Conventional Surfaces in Titanium Dental Implants: A Comparative Systematic Review, *Journal of Clinical Medicine*, Vol. 9, No. 7, 2020, pp. 1-28, <https://doi.org/10.3390/jcm9072047>.
- [9] M. S. Safavi, F. C. Walsh, M. A. Surmeneva, R. A. Surmenev, J. K. Allafi, Electrodeposited Hydroxyapatite-Based Biocoatings: Recent Progress and Future Challenges, *Coatings*, Vol. 11, No 1, 2021, pp. 1-62, <https://doi.org/10.3390/coatings11010110>.
- [10] M. Geetha, A. K. Singh, R Asokamani, A. K . Gogia, Ti Based Biomaterials, the Ultimate Choice for Orthopaedic Implants - A Review, in *Progress in Materials Science*, Vol. 54, No. 3, 2009, pp. 397-425, <https://doi.org/10.1016/j.pmatsci.2008.06.004>.
- [11] N. Kittur, R. Oak, D. Dekate, S. Jadhav, P. Dhattrak, Dental Implant Stabilitya Its Measurements to Improve Osseointegration at the Bone-Implant Interface: A Review, *Materials Today: Proceedings*, Vol. 43, 2020, pp. 1064-1070, <https://doi.org/10.1016/j.matpr.2020.08.243>.
- [12] S. O. R. Sheykhleslami, J. K. Allafi, L. Fathyunes, Preparation, Characterization, and Corrosion Behavior of Calcium Phosphate Coating Electrodeposited on the Modified Nanoporous Surface of NiTi Alloy for Biomedical Applications, *Metallurgical and Materials Transactions A: Physical Metallurgy and Materials Science*, Vol. 49, No. 11, pp. 20185878-5887, <https://doi.org/10.1007/s11661-018-4847-1>.
- [13] D. L. Cochran, R. K. Schenk, A Lussi, F. L. Higginbottom, D. Buser, Bone Response to Unloaded and Loaded Titanium Implants with A Sandblasted And Acid-Etched Surface: A Histometric Study in the Canine Mandible. *J Biomed Mater Res*, Vol. 40, 1998, pp. 1-11, [https://doi.org/10.1002/\(sici\)1097-4636\(199804\)40:1%3C1::aid-jbm1%3E3.0.co;2-q](https://doi.org/10.1002/(sici)1097-4636(199804)40:1%3C1::aid-jbm1%3E3.0.co;2-q).
- [14] A. Palmquist, O. M. Omar, M. Esposito, J. Lausmaa, P. Thomsen, Titanium Oral Implants: Surface Characteristics, Interface Biology and Clinical Outcome, *Journal of the Royal Society Interface*, Vol. 7, No. 5, 2010, pp. S515-S527, <https://doi.org/10.1098/rsif.2010.0118.focus>.
- [15] P. Amaravathy, S. Sathyanarayanan, S. Sowndarya, N. Rajendran, 2014, Bioactive HA/TiO₂ Coating on Magnesium Alloy for Biomedical Applications, *Ceramics International*, Vo. 40, No. 5, pp. 6617-6630, <https://doi.org/10.1016/j.ceramint.2013.11.119>.
- [16] M. Yoshinari, Y. Oda, T. Inoue, K. Matsuzaka, M. Shimono, Bone Response to Calcium Phosphate-Coated and Bisphosphonate-Immobilized Titanium Implants, *Biomaterials*, Vol. 23, 2002, [https://doi.org/10.1016/s0142-9612\(01\)00415-x](https://doi.org/10.1016/s0142-9612(01)00415-x).
- [17] S. Kimiyasu, Mechanism of Hydroxyapatite Mineralization in Biological Systems, *Journal of the Ceramic Society of Japan*, Vol. 115, No. 1338, 2007, pp. 124-130, <https://doi.org/10.2109/jcersj.115.124>.
- [18] M. Aminzare, A. Eskandari, M. H. Baroonian, A. Berenov, Z. R. Hesabi, M. Taheri, S. K. Sadrnezhaad, Hydroxyapatite Nanocomposites: Synthesis, Sintering and Mechanical Properties, *Ceramics International*, Vol. 39, No. 3, 2013, pp. 2197-2206, <https://doi.org/10.1016/j.ceramint.2012.09.023>.
- [19] G. L. Darimont, R. Cloots, E. Heinen, L. Seidel, R. Legrand, In Vivo Behaviour of Hydroxyapatite Coatings on Titanium Implants: A Quantitative Study in the Rabbit, *Biomaterials*, Vol. 23, 2002, [https://doi.org/10.1016/s0142-9612\(01\)00392-1](https://doi.org/10.1016/s0142-9612(01)00392-1).

- [20] N. Eliaz, N. Metoki, Calcium Phosphate Bioceramics: A Review of Their History, Structure, Properties, Coating Technologies And Biomedical Applications, *Materials*, Vol. 10, No. 4, 2017, pp. 334, <https://doi.org/10.3390/ma10040334>.
- [21] A. Haider, S. Haider, S. S. Han, I. K. Kang, Recent Advances in the Synthesis, Functionalization and Biomedical Applications of Hydroxyapatite: A Review, *RSC Advances*, Vol. 7, No. 13, 2017, pp. 7442-7458, <https://doi.org/10.1039/c6ra26124h>.
- [22] T. S. Zaporozhets, A. V. Puz', S. L. Sinebryukhov, S. V. Gnedenkov, T. P. Molina, N. N. Besednova, Biocompatibility of Modified Osteoinductive Calcium-Phosphate Coatings of Metal Implants, *Bulletin of Experimental Biology and Medicine*, Vol. 162, No. 3, 2017, pp. 366-369, <https://doi.org/10.1007/s10517-017-3617-1>.
- [23] Y. Guo, Y. Su, R. Gu, Z. Zhang, G. Li, J. Lian, L. Ren, Enhanced Corrosion Resistance and Biocompatibility of Biodegradable Magnesium Alloy Modified by Calcium Phosphate/Collagen Coating, *Surface and Coatings Technology*, Vol. 401, 2020, pp. 126318, <https://doi.org/10.1016/j.surfcoat.2020.126318>.
- [24] D. Gopi, A. Karthika, S. Nithiya, L. Kavitha, In Vitro Biological Performance of Minerals Substituted Hydroxyapatite Coating by Pulsed Electrodeposition Method, *Materials Chemistry and Physics*, Vol. 144, No. (1–2), 2014, pp. 75-85, <https://doi.org/10.1016/j.matchemphys.2013.12.017>.
- [25] D. Gopi, A. Karthika, D. Rajeswari, L. Kavitha, R. Pramod, J. Dwivedi, Investigation on Corrosion Protection and Mechanical Performance of Minerals Substituted Hydroxyapatite Coating on HELCDEB-Treated Titanium Using Pulsed Electrodeposition Method, *RSC Advances*, Vol. 4, No. 66, 2014, pp. 34751-34759, <https://doi.org/10.1039/c4ra04484c>.
- [26] Y. Huang, Q. Ding, X. Pang, S. Han, Y. Yan, Corrosion Behavior and Biocompatibility of Strontium and Fluorine Co-Doped Electrodeposited Hydroxyapatite Coatings, *Applied Surface Science*, Vol. 282, 2013, pp. 456-462, <https://doi.org/10.1016/j.apsusc.2013.05.152>.
- [27] Z. Y. Li, W. M. Lam, C. Yang, B. Xu, G. X. Ni, S. A. Abbah, K. M. C. Cheung, K. D. K. Luk, W. W. Lu, Chemical Composition, Crystal Size and Lattice Structural Changes After Incorporation of Strontium Into Biomimeticapatite, *Biomaterials*, Vol. 28, No. 7, 2007, pp. 1452-1460, <https://doi.org/10.1016/j.biomaterials.2006.11.001>.
- [28] A. L. Oliveira, R. L. Reis, P. Li, Strontium-substituted Apatite Coating Grown on Ti6Al4V Substrate Through Biomimetic Synthesis, *Journal of Biomedical Materials Research - Part B Applied Biomaterials*, Vol. 83, No. 1, 2007, pp. 258-265, <https://doi.org/10.1002/jbm.b.30791>.
- [29] Y. Huang, M. Hao, X. Nian, H. Qiao, X. Zhang, X. Zhang, G. Song, J. Guo, X. Pang, H. Zhang, Strontium and Copper Co-Substituted Hydroxyapatite-Based Coatings with Improved Antibacterial Activity and Cytocompatibility Fabricated by Electrodeposition, *Ceramics International*, Vol. 42, No. 10, 2016, pp. 11876-11888, <https://doi.org/10.1016/j.ceramint.2016.04.110>.
- [30] Y. Huang, H. Qiao, X. Nian, X. Zhang, X. Zhang, G. Song, Z. Xu, H. Zhang, S. Han, Improving the Bioactivity and Corrosion Resistance Properties of Electrodeposited Hydroxyapatite Coating by Dual Doping of Bivalent Strontium and Manganese Ion, *Surface and Coatings Technology*, Vol. 291, 2016, pp. 205-215, <https://doi.org/10.1016/j.surfcoat.2016.02.042>.
- [31] V. F. Pichugin, R. A. Surmenev, E. V. Shesterikov, M. A. Ryabtseva, E. V. Eshenko, S. I. Tverdokhlebov, O. Prymak, M. Epple, The Preparation of Calcium Phosphate Coatings on Titanium And Nickel-Titanium by Rf-Magnetron-Sputtered Deposition: Composition, Structure and Micromechanical Properties, *Surface and Coatings Technology*, Vol. 202, No. 16, 2008, pp. 3913-3920, <https://doi.org/10.1016/j.surfcoat.2008.01.038>.
- [32] M. A. Surmeneva, M. V. Chaikina, V. I. Zaikovskiy, V. F. Pichugin, V. Buck, O. Prymak, M. Epple, R. A. Surmenev, The Structure of An Rf-Magnetron Sputter-Deposited Silicate-Containinghydroxyapatite-Based Coating Investigated by High-Resolution Techniques, *Surface and Coatings Technology*, Vol. 218, No. 1, 2013, pp. 39-46, <https://doi.org/10.1016/j.surfcoat.2012.12.023>.
- [33] G. Choi, A. H. Choi, L. A. Evans, S. Akyol, B. B. Nissan, A Review: Recent Advances in Sol-Gel-Derived Hydroxyapatite Nanocoatings for Clinical Applications, *Journal of the American Ceramic Society*, Vol. 103, No. 10, 2020, pp. 5442-5453, <https://doi.org/10.1111/jace.17118>.
- [34] A. Ç. Kılınc, S. Köktaş, A. A. Gökteş, Characterization of Eggshell-Derived Hydroxyapatite on Ti6Al4V Metal Substrate Coated By Sol-Gel Method, *Journal of the Australian Ceramic Society*, Vol. 57, No. 1, 2021, pp. 47-53, <https://doi.org/10.1007/s41779-020-00511-y>.

- [35] J. Wang, Y. Chao, Q. Wan, Z. Zhu, H. Yu, Fluoridated Hydroxyapatite Coatings on Titanium Obtained by Electrochemical Deposition, *Acta Biomaterialia*, Vol. 5, No. 5, 2009, pp. 1798-1807, <https://doi.org/10.1016/j.actbio.2009.01.005>.
- [36] N. Eliaz, S. Shmueli, I. Shur, D. Benayahu, D. Aronov, G. Rosenman, The Effect of Surface Treatment on the Surface Texture and Contact Angle of Electrochemically Deposited Hydroxyapatite Coating and on Its Interaction with Bone-Forming Cells, *Acta Biomaterialia*, Vol. 5, No. 8, 2009, pp. 3178-3191, <https://doi.org/10.1016/j.actbio.2009.04.005>.
- [37] M. F. Morks, Fabrication and Characterization of Plasma-Sprayed HA/SiO₂ Coatings for Biomedical Application, *Journal of the Mechanical Behavior of Biomedical Materials*, Vol. 1, No. 1, 2008, pp. 105-111, <https://doi.org/10.1016/j.jmbbm.2007.04.003>.
- [38] P. Fauchais, A. Vardelle, Innovative and Emerging Processes in Plasma Spraying: from Micro-To Nano-Structured Coatings, *Journal of Physics D: Applied Physics*, Vol. 44, No. 19, 2011, pp. 194011-194026, <https://doi.org/10.1088/0022-3727/44/19/194011>.
- [39] Y. Z. Huang, S. K. He, Z. J. Guo, J. K. Pi, L. Deng, L. Dong, Y. Zhang, B. Su, L. C. Da, L. Zhang, Z. Xiang, W. Ding, M. Gong, H. Q. Xie, Nanostructured Titanium Surfaces Fabricated by Hydrothermal Method: Influence of Alkali Conditions on the Osteogenic Performance of Implants, *Materials Science and Engineering C*, Vol. 94, 2019, pp. 1-10, <https://doi.org/10.1016/j.msec.2018.08.069>.
- [40] D. He, X. Zhang, P. Liu, X. Liu, X. Chen, F. Ma, W. Li, K. Zhang, H. Zhou, Effect of Hydrothermal Treatment Temperature on the Hydroxyapatite Coatings Deposited by Electrochemical Method, *Surface and Coatings Technology*, Vol. 406, 2021, pp. 126656-126683, <https://doi.org/10.1016/j.surfcoat.2020.126656>.
- [41] D. Liu, K. Savino, M. Z. Yates, Coating of Hydroxyapatite Films on Metal Substrates by Seeded Hydrothermal Deposition, *Surface and Coatings Technology*, Vol. 205, No. 16, 2011, pp. 3975-3986, <https://doi.org/10.1016/j.surfcoat.2011.02.008>.
- [42] W. L. Suchanek, R. E. Riman, Hydrothermal Synthesis of Advanced Ceramic Powders, *Advances in Science and Technology* Vol. 45, 2006, pp. 184-193, <https://doi.org/10.4028/www.scientific.net/ast.45.184>.
- [43] N. H. Thong, B. T. Hue, L. Q. Duong, L. V. Toan, H. N. Van, D. T. Tung, C. X. Thang, N. V. Tung, N. T. Lan, H. V. Vuong, L. T. Hung, P. H. Vuong, Synthesis of Hydroxyapatite Coatings with Hexagonal Crystal Structure on Etched Titanium by Hydrothermal Method, *VNU Journal of Science: Mathematics – Physics*, Vol. 38, No. 4, 2022, pp. 85-92, <https://doi.org/10.25073/2588-1124/vnumap.4740>.
- [44] X. Hu, H. Shen, Y. Cheng, X. Xiong, S. Wang, J. Fang, S. Wei, One-step Modification of Nano-Hydroxyapatite Coating on Titanium Surface By Hydrothermal Method, *Surface and Coatings Technology*, Vol. 205, No. 7, 2010, pp. 2000-2006, <https://doi.org/10.1016/j.surfcoat.2010.08.088>.
- [45] L. Stipniece, S. Wilson, J. M. Curran, R. Chen, K. S. Ancane, P. K. Sharma, B. J. Meenan, A. R. Boyd, Strontium Substituted Hydroxyapatite Promotes Direct Primary Human Osteoblast Maturation, *Ceram. Int.*, Vol. 47, 2021, pp. 3368-3379, <https://doi.org/10.1016/j.ceramint.2020.09.182>.
- [46] H. E. Boujaady, M. Mourabet, A. E. Rhilassi, M. B. Ziatni, R. E. Hamri, A. Taitai, Adsorption of A Textile Dye on Synthesized Calcium Deficient Hydroxyapatite (Cdhap): Kinetic and Thermodynamic Studies, *J. Mater. Environ. Sci.*, Vol. 7, 2016, pp. 4049-4063, <https://www.researchgate.net/publication/309107468>.
- [47] S. Agrawal, M. Kelkar, A. De, A. R. Kulkarni, M. N. Gandhi, Newly Emerging Mesoporous Strontium Hydroxyapatite Nanorods: Microwave Synthesis and Relevance As Doxorubicin Nanocarrier, *J Nanopart Res*, Vol. 20, 2018, pp. 230-241, <https://link.springer.com/article/10.1007/s11051-018-4335-y>.