Volume 8, Issue 6, 2018, 3695 - 3699 ISSN 2069-5837

Biointerface Research in Applied Chemistry

www.BiointerfaceResearch.com

Original Review Article **Open Access Journal**

Received: 01.11.2018 / Revised: 11.12.2018 / Accepted: 14.12.2018/ Published on-line: 15.12.2018

Hydroxyapatite nanofibers as beneficial nanomaterial in dental sciences

Simin Sharifi [1], Masumeh Mokhtarpour [2], Azin Jahangiri [3], Salva Dehghanzadeh [1, 4], Solmaz Maleki-Dizaj[1, 5,*], Shahriar Shahi [1, 4, *]

[1]Dental and Periodontal Research Center, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Department of Physical Chemistry, University of Tabriz, Tabriz, Iran
[3]Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran
[4]Faculty of Dentistry, Tabriz University of Medical Sciences, Tabriz, Iran
[5]Student Research Committee, Tabriz University of Medical Sciences, Tabriz, Iran

*corresponding author e-mail address: ***malekidizaj@tbzmed.ac.ir; sshahriar32@gmail.com***

ABSTRACT

Hydroxyapatite (HA) is recognized as an osteoconductive material with the ability of bone healing acceleration and close adaptation of bony tissue. The exceptional size of nanomaterials makes them attractive carriers for dental applications. Because of structural and compositional similarity of HA to bone, most of the recent researches involve the nanoscale applications of this material. Nanofibers are perfect reinforcing materials compared with other particles and they are now presented with superior potential in the dental field. HA nanofibers have been studied with hopeful results for dental sciences application. In this review, we have focused on the application of HA nanofibers such as tissue regeneration, dental resins, dental implant and treatment of periodontitis in dentistry.

Keywords: *hydroxyapatite; nanofiber; dentistry.*

1. INTRODUCTION

The most ubiquitous family of bioceramics is hydroxyapatites (HA) which they can mimic the porous structure and/or the mineral composition of bone; has high structural and composition similarities to the minerals exist in natural dentin or bones, and form a direct bond with neighboring bone with their capability to stimulate differentiation of mesenchymal cells to osteoblasts [1, 2]. The integration of P or Ca ions into the surface layer and the validity of these results have been proved by several studies. Consequently, it has been extensively adopted as an appropriate biomaterial for bone regeneration making use of its osteoconductivity, bioactivity, biocompatibility, and non-inflammatory properties [3]. HA particles or porous granules have been studied as carriers for several drugs and proteins, for example, antibiotics and growth factors [1].

Currently, the advance in nanotechnology has opened new prospects to produce nanomaterials for several applications [4-11]. The nanostructured form of HA displays a higher surface area and then more reactivity. Nanoform of HA can show outstanding properties in several medicinal fields, especially in dentistry. The dentistry field is very extensive comprising specializations such as orthodontics, endodontics, and periodontics [12-15].

Currently, vast varieties of nanofibers now exist with better potential in the dental field. The nanofibers displayed the ability to improve the mechanical performance of dental composite restoratives. The mechanism of reinforcement effect can be related to preventing cracks propagation particularly with the presence of powerful interfacial binding force between the uniform distribution of the impregnated nanofillers and different phases of the restorative material [16, 17].

HA nanofibers has been studied with hopeful results for regeneration of bone, intervertebral disk, cartilage, meniscus, and ligament. HA nanofiber scaffolds can be applied to resemble the native natural extracellular matrix (ECM), and designed to show high aspect ratio, permeability, surface area, and porosity are distinct which are the advantage of these beneficial scaffolds [18-23]. This paper summarizes the hydroxyapatite nanofibers application in dentistry such as tissue regeneration, dental resins, dental implant and treatment of periodontitis.

2. HYDROXYAPATITE NANOFIBERS IN TISSUE REGENERATION IN DENTAL SCIENCES

Electrospun nanofiber scaffold with its similarity to ECM is celebrated to assist adhesion and proliferation of the cell. Dental pulp stem cells (DPSCs) have the capability to differentiate which is important for the regeneration of tooth. Several investigations have shown that DPSCs is able to attach and proliferate well on electrospun scaffolds [18, 24]. Table. 1 listed application of HA nanofibers in tissue regeneration in dental sciences.

Table 1. Application of HA nanofibers in tissue regeneration in dental sciences.

Structure	Properties	Application	Preparation method	Ref
HA-coated Polycaprolactone (PCL) nanofibrous	Promotion of human PDL fibroblast attachment and improved cell proliferation.	Periodontal tissue regeneration	Electrospinning method	[25]

Structure	Properties	Application	Preparation method	Ref
Modified HA nanofibers with Titanium (Ti)	Promotion of human osteoblasts proliferation, differentiation and increase osseointegration.	Suitable environment for growth and differentiation of cells	Electrospinning method	[26]
Polyvinyl alcohol and HA nanoparticles	Dentin regenerative properties	Future promising applications related to regeneration and replacement of hard tissue such as bone and dentin, not limited to implants coating.	Electrospinning method	[27]
PLGA/HA nanofiber	Characterize the expression pattern of the gene during osteogenic differentiation in several stem cells such as the dental pulp stem cells (DPSCs) on PLGA/HA nanofiber.	Osteogenic differentiation and mineralization of stem cells cultured on the PLGA/HA nanofibers occurred.	Electrospinning method	[28]
Three-dimensional (3D) nanofibrous Poly (ε-caprolactone) (PCL)/Poly lactic acid (PLLA)-HA polymeric	Exhibited higher cell viability, proliferation and differentiation.	Scaffold	Electrospinning method	[29]
Silica glass and HA	The membrane structures would be highly desirable as bone substitutes or tissue engineering templates.	Potential applications in the repair and treatment of bone defects, drug delivery and dental regeneration.	Sol-gel process combined with electrospinning	[30]
Poly(L-lactic acid) (PLLA)/nano- HA hybrid nanofibrous Perfectly PLLA/HA fibrous scaffolds	The growth of DPSCs and PCs is well observed attached to the PLLA/HA fibers	Potential scaffolds for dental tissue engineering.	Electrospinning	[31]
Poly(l-lactic acid) (PLLA)/ Multi-walled carbon nanotubes (MWNTs)/ HA nanofibrous	The biocompatibility of the scaffold has been investigated by DPSCs cell culture on the scaffold.	Potential candidate in dental tissue engineering.	Electrospinning	[32]
Cellulose/nano-HA nanocomposite nanofibers (ECHNN)	Thermostability could be improved with the incorporation of nano-HA. The ECHNN scaffolds were quite biocompatible for human dental follicle cells (HDFCs) attachment and proliferation.	Potentials as scaffold materials in bone tissue engineering.	Electrospinning	[20]
Poly(lactic-*co*-glycolic acid) (PLGA)/ HA (core)-collagen/amoxicillin (shell) nanofiber	The each nanofiber shell is composed of collagen/amoxicillin to improve healing of wound through drug release, and its core is composed of PLGA/HA to inhibit growth of fibroblast into bone defects and improve bone growth.	Guided tissue regeneration (GTR) membranes, which are key materials, utilized to create barriers between bone and soft tissues during repair of bone defect, in orthopedic transplants and dental implants.	Coaxial electrospinning	[33]
Polycaprolactone (PCL)/gelatin/nano-HA nanofiber	Incorporation of nHA in nanofibers indeed enhanced DPSCs differentiation towards an odontoblast-like phenotype in vitro and in vivo.	Support adhesion, proliferation and odontogenic differentiation of dental pulp stem in regeneration.	Electrospinning	[34]

3. APPLICATION OF HYDROXYAPATITE NANOFIBERS IN DENTAL RESINS

Hydroxyapatite (HA), tetracalcium phosphate, and dicalcium phosphate anhydrous are biocompatible and typical fillers of calcium phosphates [35-38]. Fillers of calcium phosphates are commonly added at some content for mineral releasing into dental resin composites. Also, several studies have displayed that calcium phosphates are non-toxic [39]. Via introducing inorganic fibers with good stiffness and mechanical properties of dental resin composites can be considerably reinforced. The HA nanofibers reinforcement with huge ratios of slenderness on the targeted dental resins was studied. Compared with other particles, nanofibers are perfect reinforcing materials, since more stress transfer could be displayed by the interaction between the matrix and nanofibers. Meanwhile, the addition of HA nanofibers could be cut down shrinkage of polymerization. Briefly, remarkable stress could be moved from composites matrix to tough HA nanofibers when the composites endure from huge pressure. Therefore, considerable improvement in the mechanical properties of dental composites will be achieved finally. The dental resins composites improvement will decline seriously, but loading of HA nanofibers content outnumbers percolation threshold. Since extremely high loading nanofibers content prone to make reinforcing nanofibers into disadvantages and this will damage dental composites' mechanical performances critically [39, 40].

Chen et al. studied the properties of high aspect-ratio HA nanofibers and the reinforcing effect of such fibers on bisphenol A glycidyl methacrylate (BisGMA)/triethylene glycol dimethacrylate (TEGDMA) dental resins (without silica microparticle filler) and dental composites (with silica microparticle filler) with different mass fractions (loading rates). They exhibited incorporation of the small mass fraction of HA nanofibers with good dispersion can improve the mechanical property of dental composites and dental resins [40].

Shahmirzadi et al. successfully fabricated the novel bisphenol-A glycidyl methacrylate (Bis-GMA)/triethylene glycol dimethacrylate (TEGDMA)/ HA nanofibrous dental resins were and the effect of HA nanofibers with several mass fractions on the mechanical properties of dental resins was studied. The HA nanofibers were prepared by electrospinning method. Integration of lower HA nanofibers loadings into the dental resin improved the flexural strength, flexural modulus, diametral tensile strength, and of compressive strength the dental resins; however, the loading of higher HA decreased the dental resins mechanical properties. Consequently, the lower loading of HA nanofibers can improve the dental resins mechanical properties as novel reinforcing filler [41].

4. DENTAL IMPLANT SURFACE MODIFICATION

The dental implant is often utilized as a more permanent fix to substitute lost tooth. However, osseointegration for the formation of the new bone around the implant is the key factor of the clinical success of the dental implant. The formation of fibrous tissues surround the implant instead of direct contact of bone to the implant surface often is the reason for the implant failure. As the fibrous tissue mechanically is weak, it is unable to provide long-term support for the implant after the process of healing is completed [42-45].

Dental implants with nano-coated HA have been reported to display good futures as implant coating materials. This nanomaterial can stimulate a chemical bond with bone and result in improved osseointegration and biological fixation. Electrospinning method, because of its flexibility in the selection of material and its capability to produce fibers in the nanometer dimension, is perfectly suited in preparing materials for applications in dental science [43, 46].

In vivo investigations have shown faster bony healing surround implants that are coated with HA. There is a direct bonding of HA to bone defined as biointegration. The exact mechanism of this phenomenon isn't clear and requires more clinical and biological studies [47].

To ensure direct implant surface contact to the bone, one method is to encourage mineral deposition on the surface of implant by osteoblast or mesenchymal stem cells. Ravichandran et al. displayed that adhesion of mesenchymal stem cells (MSC) on titanium plate and the alloy is considerably improved with nanofiber coating even with the man-made polymer such as poly (lactic acid)-co-poly (glycolic acid) (PLGA). Combination of the PLGA nanofiber with HA and collagen additional enhances the MSCs adhesion on the surface of implant. Titanium alloy coated with HA nanofibers and PLGA/collagen displayed better proliferation and showed considerably greater mineral secretion and activity of alkaline phosphatase than untreated titanium alloy [48].

5. HYDROXYAPATITE NANOFIBERS FOR THE TREATMENT OF PERIODONTITIS

Periodontitis is a common human microbial infection that causes inflammation and destruction of the gums and supporting structures of the teeth. Study of Deepak et al. provides a holistic method for the periodontitis treatment involving localized delivery of nanometric HA as a reinforcing filler and silver–metronidazole as antiseptic of periodontal pocket adjunct to recent periodontal treatment due to its broad-spectrum antimicrobial action and low systematic toxicity. Electrospinning method was utilized to prepare medicated nanofiber supplemented with layers of antibacterial-HA for dental application. Their observations showed that the above formulation is beneficial in the periodontitis treatment [49].

6. CONCLUSION AND FUTURE DIRECTIONS

Nanomaterials play an critical role in the design of ideal material for dental sciences application. In dental sciences, HA nanofibers utilize in tissue regeneration, dental resins, dental implant and treatment of periodontitis. Electrospun nanofiber scaffold with its similarity to natural ECM is celebrated to assist adhesion and proliferation of dental stem cells. The HA nanofibers reinforcement with huge ratios of slenderness on the targeted dental resins was studied and compared with other nanoparticles, nanofibers are perfect reinforcing materials. Dental implants with nanofiber HA have been reported to show good futures as implant coating materials. They can induce a chemical bond with bone and result in improved osseointegration and biological fixation. Antiseptic formulations with nanofiber HA are beneficial in the periodontitis treatment. HA nanofiber is great nanomaterial in the mentioned application so more investigations need to found other beneficial methods for more applications in dentistry.

7. REFERENCES

[1] X. Shi, Y. Wang, L. Ren, Y. Gong, D.-A. Wang, Enhancing alendronate release from a novel PLGA/hydroxyapatite microspheric system for bone repairing applications, *Pharmaceutical research*, 26 (2009) 422-430.

[2] M. Nakashima, G.T.J. Huang, Pulp and dentin regeneration, *Stem cells in craniofacial development and regeneration*, DOI (2013).

[3] L.-H. Li, Y.-M. Kong, H.-W. Kim, Y.-W. Kim, H.-E. Kim, S.-J. Heo, J.-Y. Koak, Improved biological performance of Ti implants due to surface modification by micro-arc oxidation, *Biomaterials*, 25 (2004) 2867-2875.

[4] A. Hamidi, S. Sharifi, S. Davaran, S. Ghasemi, Y. Omidi, M.-R. Rashidi, Novel aldehyde-terminated dendrimers; synthesis and cytotoxicity assay, *BioImpacts: BI*, 2 (2012) 97.

[5] S.M. Dizaj, M. Barzegar-Jalali, M.H. Zarrintan, K. Adibkia, F. Lotfipour, Calcium carbonate nanoparticles; potential in bone and tooth disorders, *Pharmaceutical Sciences*, 20 (2015) 175.

[6] S.M. Dizaj, F. Lotfipour, M. Barzegar-Jalali, M.-H. Zarrintan, K. Adibkia, Physicochemical characterization and antimicrobial evaluation of gentamicin-loaded CaCO3 nanoparticles prepared via microemulsion method, *Journal of Drug Delivery Science and Technology*, 35 (2016) 16-23.
[7] S. Maleki Dizaj, F. Lotfipour, M. Barzegar-Jalali, M.-H. Zarrintan, K. Adibkia, Ciprofloxacin HCl-loaded calcium carbonate nanoparticles: preparation, solid state characterization, and evaluation of antimicrobial effect against Staphylococcus aureus, *Artificial cells, nanomedicine, and biotechnology*, 45 (2017) 535-543.
[8] A. Eftekhari, E. Ahmadian, V. Panahi-Azar, H. Hosseini, M. Tabibiazar, S. Maleki Dizaj, Hepatoprotective and free radical scavenging actions of quercetin nanoparticles on aflatoxin B1-induced liver damage: in vitro/in vivo studies, *Artificial cells, nanomedicine, and biotechnology*, 46 (2018) 411-420.
[9] S. Zununi Vahed, N. Fathi, M. Samiei, S. Maleki Dizaj, S. Sharifi, Targeted cancer drug delivery with aptamer-functionalized polymeric nanoparticles, *Journal of drug targeting*, DOI (2018) 1-22.
[10] E. Hamidi-Asl, J.-B. Raoof, N. Naghizadeh, S. Sharifi, M.S. Hejazi, A bimetallic nanocomposite electrode for direct and rapid biosensing of p53 DNA plasmid, *Journal of Chemical Sciences*, 127 (2015) 1607-1617.
[11] S. Jafari, N. Maleki-Dizaji, J. Barar, M. Barzegar-Jalali, M. Rameshrad, K. Adibkia, Methylprednisolone acetate-loaded hydroxyapatite nanoparticles as a potential drug delivery system for treatment of rheumatoid arthritis: In vitro and in vivo evaluations, *European Journal of Pharmaceutical Sciences*, 91 (2016) 225-235.
[12] Z. Khurshid, M. Zafar, S. Qasim, S. Shahab, M. Naseem, A. AbuReqaiba, Advances in nanotechnology for restorative dentistry, *Materials*, 8 (2015) 717-731.
[13] S.T. Ozak, P. Ozkan, Nanotechnology and dentistry, *European journal of dentistry*, 7 (2013) 145.
[14] S. Maleki Dizaj, F. Lotfipour, M. Barzegar-Jalali, M.-H. Zarrintan, K. Adibkia, Application of Box–Behnken design to prepare gentamicin-loaded calcium carbonate nanoparticles, *Artificial cells, nanomedicine, and biotechnology*, 44 (2016) 1475-1481.
[15] M. Virlan, D. Miricescu, R. Radulescu, C. Sabliov, A. Totan, B. Calenic, M. Greabu, Organic nanomaterials and their applications in the treatment of oral diseases, *Molecules*, 21 (2016) 207.
[16] D. Elkassas, A. Arafa, The innovative applications of therapeutic nanostructures in dentistry, *Nanomedicine: Nanotechnology, Biology and Medicine*, 13 (2017) 1543-1562.
[17] S.A. Saunders, Current practicality of nanotechnology in dentistry. Part 1: Focus on nanocomposite restoratives and biomimetics, *Clinical, cosmetic and investigational dentistry*, 1 (2009) 47.
[18] H. Yoshimoto, Y. Shin, H. Terai, J. Vacanti, A biodegradable nanofiber scaffold by electrospinning and its potential for bone tissue engineering, *Biomaterials*, 24 (2003) 2077-2082.
[19] H.W. Kim, J.H. Song, H.E. Kim, Nanofiber generation of gelatin–hydroxyapatite biomimetics for guided tissue regeneration, *Advanced functional materials*, 15 (2005) 1988-1994.
[20] C. Ao, Y. Niu, X. Zhang, X. He, W. Zhang, C. Lu, Fabrication and characterization of electrospun cellulose/nano-hydroxyapatite nanofibers for bone tissue engineering, *International journal of biological macromolecules*, 97 (2017) 568-573.
[21] A. Pangon, S. Saesoo, N. Saengkrit, U. Ruktanonchai, V. Intasanta, Hydroxyapatite-hybridized chitosan/chitin whisker bionanocomposite fibers for bone tissue engineering applications, *Carbohydrate polymers*, 144 (2016) 419-427.
[22] K. Yamaguchi, M. Prabakaran, M. Ke, X. Gang, I.M. Chung, I.C. Um, M. Gopiraman, I.S. Kim, Highly dispersed nanoscale hydroxyapatite on cellulose nanofibers for bone regeneration, *Materials Letters*, 168 (2016) 56-61.
[23] X. Gao, J. Song, P. Ji, X. Zhang, X. Li, X. Xu, M. Wang, S. Zhang, Y. Deng, F. Deng, Polydopamine-templated hydroxyapatite reinforced polycaprolactone composite nanofibers with enhanced cytocompatibility and osteogenesis for bone tissue engineering, *ACS applied materials & interfaces*, 8 (2016) 3499-3515.
[24] S. Kumbar, R. James, S. Nukavarapu, C. Laurencin, Electrospun nanofiber scaffolds: engineering soft tissues, *Biomedical materials*, 3 (2008) 034002.
[25] S.-H. Park, T.-I. Kim, Y. Ku, C.-P. Chung, S.-B. Han, J.-H. Yu, S.-P. Lee, H.-W. Kim, H.-H. Lee, Effect of hydroxyapatite-coated nanofibrous membrane on the responses of human periodontal ligament fibroblast, *Journal of the Ceramic Society of Japan*, 116 (2008) 31-35.
[26] M.P. Bajgai, D.C. Parajuli, S.J. Park, K.H. Chu, H.S. Kang, H.Y. Kim, In vitro bioactivity of sol-gel-derived hydroxyapatite particulate nanofiber modified titanium, *Journal of Materials Science: Materials in Medicine*, 21 (2010) 685-694.
[27] G.-M. Kim, A.S. Asran, G.H. Michler, P. Simon, J.-S. Kim, Electrospun PVA/HAp nanocomposite nanofibers: biomimetics of mineralized hard tissues at a lower level of complexity, *Bioinspiration & biomimetics*, 3 (2008) 046003.
[28] Y.P. Yun, S.E. Kim, J.B. Lee, D.N. Heo, M.S. Bae, D.R. Shin, S.B. Lim, K.K. Choi, S.J. Park, I.K. Kwon, Original Paper: Comparison of Osteogenic Differentiation from Adipose-Derived Stem Cells, Mesenchymal Stem Cells, and Pulp Cells on PLGA/Hydroxyapatite Nanofiber, *Tissue Engineering and Regenerative Medicine*, 6 (2009) 336-345.
[29] M. Samiei, M. Aghazadeh, E. Alizadeh, N. Aslaminabadi, S. Davaran, S. Shirazi, F. Ashrafi, R. Salehi, Osteogenic/odontogenic bioengineering with co-administration of simvastatin and hydroxyapatite on poly caprolactone based nanofibrous scaffold, *Advanced pharmaceutical bulletin*, 6 (2016) 353.
[30] J.A. Garibay-Alvarado, L.F. Espinosa-Cristóbal, S. Yobanny, Fibrous silica-hydroxyapatite composite by electrospinning, *International Journal of Research- Granthaalayah*, 5 (2017) 39-47.
[31] M. Xu, F. Mei, D. Li, X.P. Yang, G. Sui, X.L. Deng, X. Hu, Electrospun poly (L-lacticacid)/nano-hydroxyapatite hybrid nanofibers and their potential in dental tissue engineering, Key Engineering Materials, *Trans Tech Publication*, 2007, pp. 377-380.
[32] X.L. Deng, M. Xu, D. Li, G. Sui, X. Hu, X.P. Yang, Electrospun PLLA/MWNTs/HA hybrid nanofiber scaffolds and their potential in dental tissue engineering, Key Engineering Materials, *Trans Tech Publication*, 2007, pp. 393-396.
[33] Y. Tang, L. Chen, K. Zhao, Z. Wu, Y. Wang, Q. Tan, Fabrication of PLGA/HA (core)-collagen/amoxicillin (shell) nanofiber membranes through coaxial electrospinning for guided tissue regeneration, *Composites Science and Technology*, 125 (2016) 100-107.
[34] X. Yang, F. Yang, X.F. Walboomers, Z. Bian, M. Fan, J.A. Jansen, The performance of dental pulp stem cells on nanofibrous PCL/gelatin/nHA scaffolds, *Journal of Biomedical Materials Research Part A: An Official Journal of The Society for Biomaterials, The Japanese Society for Biomaterials, and The Australian Society for Biomaterials and the Korean Society for Biomaterials*, 93 (2010) 247-257.
[35] R.W. Arcís, A. López-Macipe, M. Toledano, E. Osorio, R. Rodríguez-Clemente, J. Murtra, M.A. Fanovich, C.D. Pascual, Mechanical properties of visible light-cured resins reinforced with hydroxyapatite for dental restoration, *Dental Materials*, 18 (2002) 49-57.
[36] C. Domingo, R. Arcís, E. Osorio, R. Osorio, M.A. Fanovich, R. Rodríguez-Clemente, M. Toledano, Hydrolytic stability of experimental hydroxyapatite-filled dental composite materials, *Dental Materials*, 19 (2003) 478-486.
[37] M. Uo, F. Watari, Investigation on the mechanism of the osteoinduction for calcium phosphate, Program and Abstracts of International Conference on Osteoporosis and Bone Research 2008, 2008.
[38] K. de Groot, Bioceramics Calcium Phosphate: 0, *CRC* press2018.
[39] X. Li, W. Liu, L. Sun, K.E. Aifantis, B. Yu, Y. Fan, Q. Feng, F. Cui, F. Watari, Resin composites reinforced by nanoscaled fibers or tubes for dental regeneration, *BioMed research international*, 2014 (2014).
[40] L. Chen, Q. Yu, Y. Wang, H. Li, BisGMA/TEGDMA dental composite containing high aspect-ratio hydroxyapatite nanofibers, *Dental Materials*, 27 (2011) 1187-1195.
[41] N.J. Shahmirzadi, S.H. Inanloo, Effect of hapnanofibers prepared by electrospinning process on the mechanical properties of dental resins, *Biomedical and Pharmacology Journal*, 8 (2015) 283-289.

[42] J. Yazdani, E. Ahmadian, S. Sharifi, S. Shahi, S.M. Dizaj, A short view on nanohydroxyapatite as coating of dental implants, *Biomedicine & Pharmacotherapy*, 105 (2018) 553-557.
[43] L. Gaviria, J.P. Salcido, T. Guda, J.L. Ong, Current trends in dental implants, *Journal of the Korean Association of Oral and Maxillofacial Surgeons*, 40 (2014) 50-60.
[44] R. Smeets, B. Stadlinger, F. Schwarz, B. Beck-Broichsitter, O. Jung, C. Precht, F. Kloss, A. Gröbe, M. Heiland, T. Ebker, Impact of dental implant surface modifications on osseointegration, *BioMed Research International*, 2016 (2016).
[45] B. Chrcanovic, J. Kisch, T. Albrektsson, A. Wennerberg, Factors influencing early dental implant failures, *Journal of dental research*, 95 (2016) 995-1002.
[46] R. Asri, W. Harun, M.-A. Hassan, S. Ghani, Z. Buyong, A review of hydroxyapatite-based coating techniques: Sol–gel and electrochemical depositions on biocompatible metals, *Journal of the mechanical behavior of biomedical materials*, 57 (2016) 95-108.
[47] A.B. Novaes Jr, S.L.S.d. Souza, R.R.M.d. Barros, K.K.Y. Pereira, G. Iezzi, A. Piattelli, Influence of implant surfaces on osseointegration, *Brazilian dental journal*, 21 (2010) 471-481.
[48] R. Ravichandran, Biomimetic surface modification of dental implant for enhanced osseointegration, 2009.
[49] A. Deepak, A.K. Goyal, G. Rath, Development and Characterization of Novel Medicated Nanofiber for the Treatment of Periodontitis, *The American Association of Pharmaceutical Scientists PharmSciTech*, DOI (2018) 1-11.