Review Article

Dental Implant Bioactive Surface Modifiers: An Update

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Objectives: Main purpose of this review was to present an update on various coating materials utilized in improving the surface chemistry of the dental implants. **Methods:** Literature search was carried out in various on-line databases such as PubMed, Medline, Google scholar, EBSCO, Wiley Science Library, and Saudi Digital Library using appropriate keywords (dental implant surface coatings, dental implant surface modifiers, and dental surface coatings).

Results: Total of 569 studies were retrieved. All the relevant studies among them were reviewed and compiled.

Conclusion: Current implant surface's biomimetic coatings offer many benefits compared to the traditional plasma sprayed coatings. Further incorporation of biomimetic coatings with various material has lead improvement in mechanical and biological properties of implants.

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INTRODUCTION

The replacement of missing teeth with endosseous dental implants is considered as an effective and acceptable treatment method. Moreover, dental implants are standards of care for increasingly aged population with edentulous jaws.^[1,2] Osseointegration refers to the direct association of osseous tissue with an inert alloplastic biomaterial surface.^[3] There is enhanced interest in the planning and advancement of implants to reduce failure and improve longevity.^[4]

The use of micro-rough surface topography has increased the biomechanical properties of the implant–bone interface. Several strategies for improving the biocompatibility and osteogenic capacity of metal implants have been developed ranging from surface modification by inorganic mineral coatings to biocoatings of implant surfaces to control peri-implant tissue responses.^[5]

The real test in implantology today is to join current information in materials science, tissue engineering, and biology to configure metal implant surfaces fit for ideal osseointegration and in the meantime giving epigenetic signs to cells in the peri-implant tissues to induce appropriate natural reactions that

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support bone recuperating and osseointegration over unfavorable impacts and problematic treatment results. Hence, the main aim of this review is to present brief update on the various coating materials utilized to improve the surface chemistry of the dental implants.

MATERIALS AND METHODS

LITERATURE REVIEW STRATEGY

Literature search was carried out in various online databases such as PubMed, Medline, Google scholar, EBSCO, Wiley Science Library, and Saudi Digital Library using appropriate keywords (dental implant surface coatings, dental implant surface modifiers, and dental surface coatings). All the pertinent information related to the dental surface modifiers was reviewed and compiled.

The study proposal was submitted to the research center of Riyadh Elm University and registered (FRP/2018/219).

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< 1

DISCUSSION

The physical, chemical, and mechanical characteristics of the surfaces can be altered by utilizing following methods: (1) addition of a new layer to the surface, (2) changing the surface by applying physical or chemical agents such as plasma or wet chemicals, and (3) subtraction or attrition method to modify the mechanical surfaces.^[6,7]

BIOMIMETIC CA-P COATINGS

Many years of research outcome resulted in mineralized tissues or materials engineered by living organisms in the presence of low-temperature aqueous conditions. These engineered products have excellent mechanical properties and many specific biological functions.^[8]

Biomimetic Ca-P coating on load-bearing dental implants has been developed to take advantage of the superior mechanical properties (titanium and its alloys, alumina and ultra-high-molecular-weight polyethylene) of substrates and excellent biocompatibility of Ca-P materials. The conventional technique for applying a Ca-P coating on metallic implants is plasma spraying. However, plasma spraying has limited only to implants with porous surfaces and polymers.^[9,10] Various techniques can be employed to modify the titanium implant surface to enable the formation of biomimetic Ca-P coatings, but none of them matched plasma spraying.

The biomimetic coating approach is focused on growing a Ca-P thin layer on metals or other implant materials from a physiologically related supersaturated calcifying arrangement at surrounding temperature by mimicking the common bone or tooth mineralization process. Biomimetic approach has many benefits over plasma spraying and considered alternative to plasma spraying in coating of implants.^[2] Recently, it has been demonstrated that the formation of biomimetic Ca-P coatings can be facilitated by fluoride phosphate substitution on the titanium dioxide surface, leading to localized calcium apatite deposition.^[11] Moreover, there is promotion of human stem cell proliferation and differentiation though elevated bone morphogenic protein-2 (BMP-2), RunX-2, and bone sialoprotein expression.^[5]

Recently, Marques *et al.* have shown that the use of higher Ca/P ratios and the addition of silver nanoparticles into the oxide layer presented better surface properties, tribocorrosive behavior, and cell responses of dental implants.^[12]

COATINGS OF THERAPEUTIC AND BIOACTIVE AGENTS

Dental implants play an important role in the substitution of teeth/root frameworks, the repair of large bone deformities, and the bone fracture healing. However, implant loosening, post surgical disease, fracture nonunion, and erratic periodontal regeneration are the issues still concerned with implant coatings. There is a clinical need to apply osteoinductive as well as antimicrobial agents locally to the implant site to help in the reconciliation and recuperating of bone and delicate tissues. Thin coatings of CaPO₄ act to intriguing vehicles for such endeavors. Ca-P materials are thought to be among the most imperative medication on account of their fantastic biocompatibility and wide clinical acknowledgment.^[13]

Presently, incorporation of therapeutic and bioactive agents into Ca-P coating is most preferred. The advancement into the biomimetic coating methods has created a possibility of incorporation of therapeutic agents directly within the Ca-P. The molecules then get dissolved in the calcifying solution to be adsorbed or incorporated into the Ca-P coating during the coating process. This Ca-P coating has been utilized as carriers for proteins and therapeutic agents.^[8]

Albumin

Bovine serum albumin was used as a model protein to examine the possibility of protein incorporation into and release from a biomimetic Ca-P coating. It is inferred from studies that once a protein has been incorporated into a biomimetic Ca-P coating, its long-term sustained release can be achieved along with the degradation of Ca-P coating during the implantation. Bovine serum albumin is combined with calcium phosphate coating on implants by applying biomimetic techniques resulting in a remarkable change in crystal morphology and composition. This is suggestive of co-precipitation, a novel method of combining osteoinductive agents into calcium phosphate coatings, there by creating a coating that is both osteoconductive as well as osteoinductive in nature.^[14]

Bone morphogenic proteins

Study conducted in orthotropic animal models with fibrous nonunion fractures BMP-2 and BMP-7 has been found to be innocuous and effective in improving and speeding up bone healing process. Moreover, BMP-6 utilized to produce a biomimetic microenvironment to encourage osteogenic activity under physiological conditions with least paracrine signalization.^[15] Moreover, BMP2-coprecipitated calcium phosphate granules in animal models suggesting a potential osteoinducer to enhance the therapeutic effects of the graft materials.^[16] Hence, carrier should be selected carefully for the effective use of osteoinductive agents. The combination of biomimetic Ca-P coatings and osteoinductive agents can enhance inductive capacity.^[5]

Bisphosphonates

Bisphosphonates are the current therapeutic agents of choice for patients with osteoporosis. Through osteoclast inhibition, the systematic use of bisphosphonates, including etidronate, alendronate, pamidronate, and risedronate, can lead to reduced bone turnover, increased bone mass, and improved mineralization. Studies have shown similar promising results for the local use of bisphosphonates at implantation sites. Beneficial effects were obvious when implant sites received irrigation of aminobisphosphonate solution indicating higher efficacy in increasing bone formation.^[17] Animal model studies have suggested that the local delivery of bisphosphonate compounds around implants.^[18]

However, recent meta-analysis failed to establish the actual effect of bisphosphonates on the osseointegration and survival of dental implants due to the lack of proper studies.^[19]

Antibiotics

One of the advantages of Ca-P coatings is the ability to serve as carrier of antimicrobial agents. Sufficient concentration of antibiotics can be impregnated into the coating to have a sustained release of the drug. Coprecipitation with biomimetic Ca-P coating can provide an opportunity to load higher amount of antibiotics, thus preventing postsurgical infection at high-risk site of implants for infection.[20] The calcium phosphate coatings with fluoride and zinc ions have shown bactericidal and potential bioactive properties for dental implants.^[21] Further, utilization of ceramic biocomposites to deliver antibiotics along with other materials such as basic major proteins, bisphosphonates, and growth factors is underway.^[20] Moreover. nanostructured titanium-based biomaterials developed to enhance osteointegration and prevent from bacterial infection.^[22,23]

AMELOGENIN

Amelogenin proteins, the important components of the developing dental enamel extracellular matrix have been found to facilitate growth of apatite crystals during the formation of enamel. The use of normally occurring matrix proteins that control mineral crystal development has potential to biologically regulate bone formation on dental implant surfaces. Therefore, enamel extracellular proteins are considered as possible material for bioactive implant coatings. Enamel matrix protein deposition precedes hard-tissue development in the jaw bones. Therefore, pretreated implant surface with enamel matrix could start cell interaction leading regeneration of bone. ^[24] *In vitro* studies conducted among rats have shown that the initial adhesion and induction of hard-tissue

differentiation were improved by amelogenin coating. In addition, new bone formation was obvious surrounding implanted material.^[25]

SURFACE TEXTURE

Osseointegration was the term first coined by Brånemark in 1952, that implies to an anchorage mechanism, whereby artificial components can be reliably and predictably incorporated into living bone.^[26] This anchorage can persist under all normal loading conditions. Six factors are prerequisites for establishing reliable osseointegration: implant material, implant design, surface quality, status of the bone, surgical technique, and implant loading conditions. The role of material properties for achieving a successful long-term clinical performance is related to the type of local tissue conditions and clinical needs. Inertness of a material is the preferred characteristic for most of the long term implants placed inside the bone.^[27]

The surface properties of materials are regarded as critical for the tissue response with materials. Micro- and nano-textured surfaces have influence on cell behavior in many ways. Surface topographical features range from the nanometer to the millimeter are significant for cellular responses as well as the integrated tissue response around the implants. The claim of a roughened oral implant surface is based on an improved micromechanical interlock. It is generally agreed that an increase of surface roughness promotes the incorporation of implants in bone.^[28]

MODIFICATION OF THE SURFACE OXIDE

The surface oxide layer of titanium implants can be manipulated chemically and there has been speculation whether the biological properties of the oxide surface may then be changed and even improved. The surface oxide may be modified using different techniques such as heat treatment, sol-gel-derived oxidation, and electrochemical oxidation. The sol-gel technique is another interesting method for the modification of oral implant surfaces. Hydrophilic, roughened, and partly porous sol-gel-processed titanium alloy surfaces reveal higher osteoblast-like cell adhesion and mineralization *in vitro*.^[28]

FLUORIDE

Manipulation of the titanium dioxide is possible by use of hydrogen fluoride at low concentrations without affecting surface micro-texture significantly. Little amount of fluoride is incorporated within the titanium dioxide. This ion implantation within superficial layer will alter the biological response of the material. Bone density and calcification of the bone have improved if fluoride is available during remodeling process of the bone.

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Fluoride is considered as enhancer of bone cells growth and needs appropriate growth factors for induction of calcification.^[28]

CONCLUSION

Today's implant surface biomimetic coatings have lot of benefits compared to the traditional plasma sprayed coatings. Biomimetic Ca-P coating of implants is a perfect carrier for the osteoinductive proteins, growth factors, and antibiotics. Incorporation of biomimetic coatings with amelogenin has lead enhanced mechanical and biological properties. Manipulation of implant surface topographies permits site-directed successful bone regeneration therapies.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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