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#### Chapter

## Novel Dental Implants with Herbal Composites: A Review

Gopathy Sridevi and Seshadri Srividya

#### **Abstract**

Missing a permanent tooth is a miserable condition faced by a common man. A tooth decay, periodontitis, mechanical trauma, or any systemic complications lead to such a complication. These bone defects when left untreated lead to severe resorption of the alveolar bone. A proper dental filling with an appropriate bone substitute material could prevent such resorption and paves a way for subsequent implant placement. Dental implants are considered as the prime option by dentists to replace a single tooth or prevent bone resorption. A variety of bone substitutes are available differ in origin, consistency, particle size, porosity, and resorption characteristics. Herbal composites in dentistry fabricated using biphospho-calcium phosphate, casein, chitosan, and certain herbal extracts of Cassia occidentalis, Terminalia arjuna bark, Myristica fragans also were reported to possess a higher ossification property, osteogenic property and were able to repair bone defects. C. occidentalis was reported to stimulate mineralization of the bone and osteoblastic differentiation through the activation of the PI3K-Akt/MAPKs pathway in MC3T3-E1 cells of mice. This implant proved better osteoconductivity and bioactivity compared to pure HAP and other BCP ratios. Terminalia Arjuna was also worked in the incorporation in the graft to enhance the osteogenic property of the implant and gave good results. Another implant bone graft was synthesized containing BCP, biocompatible casein, and the extracts of *Myristica fragans* and subjected to *in vitro* investigations and the results revealed the deposition of apatite on the graft after immersing in SBF and also the ALP activity was high when treated with MG-63 cells, NIH-3 T3, and Saos 2 cell lines. This study indicates that the inclusion of plant extract enhances the osteogenic property of the graft. Thus, these novel dental implants incorporated with herbal composites evaluated by researchers revealed an enhanced bone healing, accelerates osseointegration, inhibits osteopenia, and inhibits inflammation. This application of herbal composite inclusion in dentistry and its applications has a greater potential to improve the success rate of dental implants and allows the implications of biotechnology in implant dentistry.

**Keywords:** bone defect, dental filling, implant, hydroxyapatite, osseointegration, herb, osteoconducting

#### 1. Introduction

1

Human teeth are the hardest substance in the human body that enhances the beauty of a person. It is a highly important structure that helps in food chewing to mechanically break down the food by cutting and crushing them in preparation

for swallowing and digesting. It also aids in speech and its articulation of words. Human teeth consist of 20 primary (deciduous, "baby" or "milk") teeth in children and 32 permanent teeth in adults. Teeth are classified as incisors, canines, premolars, and molars. Incisors are primarily used for cutting the food into pieces, canines are used for tearing the tissues of the food, and molars help to grind the food into smaller substances [1].

Teeth are also important for cosmetic purposes as well. Many dental treatments are not purposefully dealt with filling and taking out a tooth, but indeed nowadays people turn out to esthetic dentistry to improve, straighten, lighten, reshape, and repair teeth as well. The field of esthetic dentistry includes the establishment of veneers, crown bridges, implants, tooth-colored filling, and teeth whitening procedures.

#### 1.1 Tooth loss

Tooth exfoliation starts from childhood. A young boy or girl loses the baby teeth, and it gets exfoliated in response to permanent teeth that start developing beneath them. This loss of primary teeth begins around the age of six and continues till 12 years of age. The primary teeth that are vulnerable are the upper and lower lateral incisors that shed at 7–8 years and upper canines are that shed around 10–12 years of age. Only the upper and lower first molars shed at 9–11 years of age and upper and lower second molars shed at 10–12 years of age [2].

#### 1.2 Pathological tooth loss

Tooth loss is a condition that advances with the increase of age. This occurs as a result of mechanical disturbances and abnormal forces that act during the chewing process of hard substances, traumatic injury, etc. Also, a few conditions such as untreated dental caries (tooth decay) and severe periodontal (gum) disease might lead to loss of permanent teeth. Tooth decay is the primary cause of tooth loss. It is caused by the increased plaque retention on the teeth followed by bacterial invasion of the plaque. This ultimately results in dental caries and the formation of cavities. Untreated tooth cavities for a chronic period of time lead to the breakdown of the tooth. This bacterial invasion and retention of plaque deposits also affects the gums and bones attached to the tooth and loses its ability to hold the tooth. Periodontal structures are tissues that support teeth and their attachment to the bone. Diseases of the gums and bones are caused by bacterial invasion of teeth and retention of plaque. It results in diseases of the gums leading to periodontitis and detachment of supporting structures of the teeth and eventually causes tooth loss. So, the ultimate care of oral hygiene is the only preventive measure to prevent tooth loss. Good oral hygiene is the process of maintaining proper brushing of teeth two times a day with fluoridated toothpaste and frequent flossing. Regular dental check-ups every 6 months can be availed to ensure good teeth and prevent tooth loss [3].

#### 1.3 Mechanical trauma and tooth loss

There are a few conditions like bruxism otherwise called teeth grinding that occurs during sleep. This condition is very common in people who tend to be awake by profession at night. This tooth grinding increases the wear and tear action on the tooth and causes mechanical injury. The risk of tooth fractures is common in sportspeople, especially in football and goalie. Research reports claim that smoking is another important cause of tooth loss. Reports from countries, such as the United States, Germany, and Japan, show a strong relationship between cigarette smoking and tooth loss. The habit of smoking weakens the body's immune response to

infection and causes immunosuppression. This makes it harder to guard against a gum infection and takes a longer time to heal. Reports reveal that systemic diseases also relate to tooth loss. Conditions, such as cardiovascular diseases, diabetes mellitus, cancer, and osteoporosis, also lead to permanent tooth loss due to their secondary complications. Therefore, tooth loss is not restricted to poor oral hygiene but poor maintenance of overall health [4–6].

#### 1.4 Treatment options for missing tooth

Missing a permanent tooth is a miserable condition. Years after years the treatment options for missing teeth are dental implants, fixed dental bridges, removable partial dentures. Dental implants are considered as the prime option by dentists to replace a single tooth. This procedure involves the surgical mounting of a titanium metal post or frame on the upper or lower jaw along with mounting the replaced missing tooth. This dental implant acts as a permanent base for the replaced tooth. This procedure is highly advantageous because the replaced dental implant resembles a natural tooth and can last for decades. It also acts independently and does not disturb the adjacent normal tooth. The next treatment option is a fixed dental bridge. This procedure provides bridging between the gaps caused by the lost tooth and involves the employment of a dental prosthesis or an artificial tooth. This dental prosthesis would be attached to adjacent teeth and bonded in place with dental cement. A removable partial denture consists of replacement teeth that are attached to a natural-looking pink base. The natural teeth also act to stabilize and hold the removable plastic base in its position place. This pink base is designed in a way that matches the color of the gums and the color of the normal teeth [7].

#### 2. Dental implants

A dental implant is a material placed in or on the oral tissues that help to support the oral prosthesis. An ideal implant material should possess the following characteristics. It should be biocompatible and possess adequate strength, rigidity, good corrosive, and be capable of wear and fracture resistance. The principles of designing a dental implant should be much compatible with the physical properties of the material. Materials that are used for fabricating a dental implant can be considered according to the chemical composition of the implant and their biological responses. Many reports claim that these dental implants may be made from metals, ceramics, or polymers [8].

#### 2.1 Titanium and its alloys

According to the American Society for testing and materials, there are six distinct types of titanium that are widely available as implant biomaterials. They are grade I, II, III, IV Cp Ti, various combinations of titanium, aluminum like alphabeta alloy containing 6% Al and 4% V, alpha-beta titanium alloy containing 6% aluminum and 7% niobium, alpha-beta titanium alloy with non-ferrous metal. The physical and mechanical properties, such as tensile strength and osseointegration, elastic modulus, non-toxic nature, are quite different for the different alloys. The most important property related to the oxygen residuals in the metals and the other two titanium is considered as very low interstitial alloys. Among all the available alloys, the commercially prepared pure titanium alloys are generally considered as pure and mentioned in Grade I, Grade II, Grade III, and Grade IV titanium and has wide applications in implant manufacturing. Some trace elements, such as carbon,

oxygen, nitrogen, and iron, are also considered in this process. Although titanium possesses many strengthening characteristics, literature reports reveal that it evokes a stronger reaction in the host causing hypersensitivity reactions, failed implants with increased concentration of titanium in peri-implanted tissues, regional nodes, and pulmonary tissues based on animal models, allergy to titanium in the form of urticaria, pruritus of the mucosa or skin, atopic dermatitis, poor fracture healing, necrosis and immunosuppression and weakening of orthopedically implanted titanium [9].

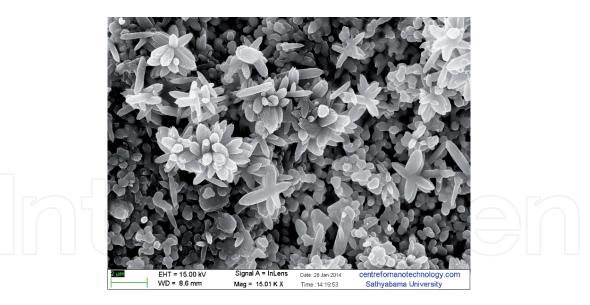
#### 2.2 Ceramics

Ceramics has been widely used as a dental implant coating and it was the first introduced material in the field of implant dentistry. Hydroxyapatite is one of the most known biocompatible materials commonly used as a coating for metal implants. These hydroxyapatite coatings create a good interfacial strength between bone and implant. It provides greater implant stability and improves bone healing that lies adjacent to implants. The use of hydroxyapatite improves the capacity of osseointegration and increases the rate of rehabilitation of patients. This method of implanting decreases the time from implant insertion to final reconstruction of the implant [10]. There are various methods to coat hydroxyapatite on implants, they include sol–gel coating, electrophoretic deposition, plasma spraying, sputter-deposition, and biomimetic precipitation. Ceramic materials that are used for dental implanting and coatings. The materials used are hydroxylapatite (HA), tricalcium phosphate, fluorapatite (FA), tetracalcium phosphate, calcium pyrophosphate, brushite, bioglasses, aluminum oxide, zirconium oxide, etc. (Figure 1).

#### 2.3 Metals as dental implants

In the field of dental implanting, metals are widely selected based on factors that involve properties belong to its biomechanical characteristics, machining characteristics, and surface finishing characteristics as well. In the present day, metals, such as Co-Cr, stainless steel, and gold are quite outdated in the dental implant industry and the currently available dental metals are alloys of titanium and zirconium as well. Certain components of dental implants such as the abutment screws and some attachments of the implants are also made of alloys of gold, stainless steel, and Co-Cr. Titanium is mostly considered as an effective material by most of the dentists for its wide intraosseous applications. It has enormous and typical properties, such as lesser readily affected or corroded by the environment, high resistance to chemical dosing, and capability to repair on its own. The resistance to being deformed elastically—modulus of elasticity was very compatible with that of bone and titanium oxide [11, 12]. Although titanium is a typical material suitable for dental implanting, it faces a lot of shortfalls. These drawbacks and detrimental properties of titanium ultimately resulted in prompting the scientists to look and research the new implant from other biomaterials [13].

The next innovation to overcome the said shortfalls led to the development of ceramic implants [14]. And as a result of this zirconia is used as another material for dental inserts. This in turn contrasted with metallic components zirconia demonstrated the least particle discharge and they are thought to be dormant in the body [15]. Zirconia acts as a tooth-like shading and possesses great mechanical properties and has great biocompatibility. In such a way, it is by all accounts an appropriate dental material [16]. The utilization of zirconia implants keeps a strategic distance from the inconvenience and acquiesces to the demand of numerous patients without metal inserts. The material additionally gives high quality, crack sturdiness,



**Figure 1.** *SEM-image of hydroxyapatite.* 

and biocompatibility [17]. There are various materials used for fabricating endosseous dental implants like titanium, titanium alloy, stainless steel, alumina, carbon, bioglass, polyurethane, etc. [18–20].

A novel implant, the ceria-stabilized zirconia-alumina-aluminate composite was developed and was established for its significant effect that it is not prone to aging. This implant represents a probable alternative to the yttrium-stabilized zirconia that is used for ceramic oral implants. This implant was evaluated for its long-term stability due to its make with Ce-TZP-comp and it proved a significant lowest fracture load after combined loading/aging [21].

#### 2.4 Polymers

A variety of polymers have been utilized as dental implant materials [22]. A portion of the polymer materials is polymethylmethacrylate, polytetrafluoroethylene, polyethylene, polyurethane, and polysulfone, etc. When polymer acts as a coating layer, inferior mechanical properties, lack of adhesion to living tissues, and adverse immunologic reactions are eliminated [23–26]. In the present day, polymeric materials are constrained to assemble the shock retaining segments joined into the superstructures bolstered by inserts [26]. A wide variety of biomaterials have found profound applications in the form of inserts. This type of insert in implantology requires a suitable biomaterial of choice. The presently available biomaterials, such as bioceramics and other composite biomaterials, are under higher consideration and the precise examination of such biomaterial definitely have a promising future in the field of dental applications.

#### 3. Herbal composites in dentistry

Herbal medicine is an indigenous system of traditional Hindu medicine and is native to the Indian subcontinent. Contemporary practices derived from ayurvedic traditions are also a type of alternative medicine. Ayurveda recommends some daily use therapeutic procedures for the prevention of and maintenance of oral health. It involves Dant Dhavani (brushing), Jivha Lekhana (tongue scrapping), and Gandoosha (gargling) or even oil pulling and tissue regeneration therapies. Various herbs are widely used in dentistry and they are aloe vera [27], cloves [28], eucalyptus [29], peppermint [30], and turmeric [31].

#### 3.1 Icariin

Icariin, one of the traditional Chinese herbal medicines, possesses significant evidence that it strengthens bones, enhances healing of bone, inhibits osteopenic effect, and inhibits inflammation. This idea made scientists incorporate icariin for better osseointegration of dental implants and shorten the rehabilitation time of patients and the results revealed that. Evaluation of the hypothesis: Limited success has been achieved to help implant surgery in icariin significantly improved the success rate of the dental implant [32].

#### 3.2 Ascorbic acid

Another randomized trial of preparing a biocomposite osteogenic nanofiber was developed with the incorporation of polycaprolactone, hydroxyapatite, dexamethasone, gelatin, beta-glycerophosphate, and ascorbic acid along with titanium implants was developed so that it mimics the bone extracellular matrix and eventually induced osteogenesis in the peri-implant niche and also regenerates the osseous tissue. This implant was worked on rabbit models and the results revealed that a coating of osteogenic nanofibrous tissues significantly increased the magnitude of osteogenesis around the zone of peri-implant tissue and also favored the dynamics of osseointegration [33].

#### 3.3 Cassia Occidentalis

Cassia occidentalis Linn belongs to the family Caesalpiniaceae and is commonly called Kasondi in Hindi. It is mostly grown in the southern parts of India and the plant products have been used for various ailments and have a rich medicinal value [34]. C. occidentalis (CO) contains significant bioactive compounds, such as terpenoids, anthraquinones, and carotenoids. The plant products were reported to stimulate mineralization of the bone and osteoblastic differentiation through the activation of the PI3K-Akt/MAPKs pathway in MC3T3-E1 cells of mice [35].



#### 3.4 Cassia Occidentalis

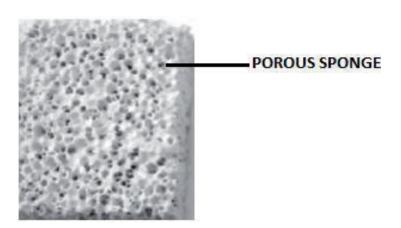
3.4.1 Herbal composite using orange and potato peel, papaya leaf, calendula flower extract

Another novel dental implant synthesized a nanohydroxyapatite using different methods by utilizing the biomolecules from waste products, such as an egg-shell. In this study, an institutional controlled synthesis of nano-sized HAP was performed, which can be employed in the future for another material synthesis thereby an

improved bone bonding was obtained by this novel material [36]. A novel implant synthesized with nano HAP rods was performed by an *in situ* method using poly (vinyl alcohol) (PVA). These PVA nano-sized crystals of HAP obtained were further subjected to *in vitro* analysis using simulated body fluid. The nano-sized crystal of HAP composite improved its hardness when treated with PVA and it overcomes the brittleness of pure HAP [37].

#### 3.4.2 Porous scaffolds

A prepared porous scaffold using nano HAP and nylon 6,6 using a salt-leaching technique was a newly handled technique. Here HAP was dispersed on the pore walls of the scaffold bonds well with nylon 6,6 and it increased the stiffness of the scaffold. This porous scaffold acts to be effective as a three-dimensional substrate for bone tissue engineering [38]. Another method developed on dental implanting includes the synthesis of biphospho-calcium phosphate (BCP) for calcium-deficient apatites, such as enamel, dentin, and bone mineral by a process of sintering. The prepared BCP had controlled bioactivity when the HAP/ $\beta$ TCP ratio was controlled. This form of BCP can be used as carriers for growth factors, drug delivery systems, and in tissue engineering [39].



Another preparation included natural porous bioceramics from processing the cancellous bone. Calcined bovine bone was treated with sodium pyrophosphate and sintered to obtain HAP and was in turn converted to  $\beta$ TCP and BCP. This process was done to improve and increase the bioactivity of the ceramics when placed *in vivo* [40].

A newly evolved technique was prepared by using BCP with different HAP/  $\beta$ TCP ratios and was analyzed for its bioactivity with SBF solution and osteoconductivity in rabbits. The study found that BCP with a HAP/TCP ratio of 60:40 was found to be best in showing the bioactivity and osteoconductivity compared to pure HAP and other BCP ratios. A newly developed implant was created using a coating material for orthopedic metal implants. In this study, a new bioglass was prepared and coated on Ti-based and Co-Cr alloys. This was done to enhance the cell adhesion when placed *in vivo* as a dental implant. This coated metal implant was prepared for dental applications [41].

Another novel implant was prepared by using composite material consisting of poly-L-lactide (PLLA) and bioactive glass by solvent evaporation technique. The composite was bathed and soaked in SBF for 3 days for allowing the HAP deposition on the composite. The dried composite was subjected to various characterization techniques. The study found that the bioactivity of the composite was highly increased and it, in turn, supported the composite to promote bone integration when placed *in vivo* [42].

#### 3.4.3 Chitosan-HAP composite

Another group of researchers synthesized a composite containing chitosan, HAP, and bioglass. Chitosan-HAP composite was prepared using calcium nitrate and orthophosphoric acid in SBF. The novel prepared composite bioactive glass was added to this preparation. *In vitro* bioactivity was determined for the composite and the study found that the addition of bioactive glass improved the compression strength of the material [43]. A prepared HAP-bioglass composite was developed to improve the compression strength of the composite compared to pure HAP. In this study, HAP was synthesized and combined with a varying percentage of bioglass and was pelletized. The biocomposite dental implanting material was characterized using various techniques and the study found that HAP with 10% bioglass was having increased bioactivity and compression strength (**Figure 2**) [44].

#### 3.4.4 Vitamin E

Another implant was prepared with a bioglass composite film consisting of poly (3-hydroxybutyrate) and vitamin E. The incorporation of vitamin E was done to increase the protein adsorption and hydrophilicity on the surface of the film. This composite film was subjected to various characterized studies and the results reported that they can be applied [45] in tissue engineering as a better matrix material for cell adhesion [46]. Chin et al. worked on preparing a novel multicomponent skin substitute by using collagen as a matrix material which typically depicts the normal architecture of the skin. This implanting material has a main advantage in producing a cost-effective bone substitute. A novel prepared magnetic fibrin incorporated with nanoparticles and characterized those nanoparticles by various physicochemical techniques using Saos 2 cells, the cell viability, adhesion, and alkaline phosphatase assay. The study revealed that the [47] material exhibited good osteogenic property and hence it can be used in bone tissue engineering .

#### 3.4.5 Collagen

Auxenfans et al. [48], a researcher investigated a scaffold that contains collagen and glycosaminoglycans (GAG). The matrix was seeded with fibroblast and the study found that it forms a typical reconstructed skin or hemicornea once epithelialization



Figure 2.

Cassia occidentalis.

completes. Another study analyzed the rate of degradation of pure collagen and collagen—HAP beads using collagenase enzyme. This enzyme was able to digest pure collagen quickly compared to collagen-HAP gel beads. The HAP provides resistance for quick degradation and the matrix structure could be maintained for a greater period and it supports the cell to adhere, proliferate, and then differentiate [49].

#### 3.4.6 Gluataraldehyde and barium sulfate

Another research study reported the collagen type II scaffolds by cross-linking with glutaraldehyde and scaffold without cross-linking with glutaraldehyde. The study explained that the scaffolds were seeded with chondrocytes and observed the interaction of cells with the scaffold. The cell adherence on the surface of the scaffold was high which was confirmed by SEM analysis [50]. Another implant using used barium sulfate and zirconia as additives to implant as a bone cement was created to enhance the visualization through X-ray imaging. The incorporation of these additives in bone cement helps to locate the material placed in the bone defect areas [51]. Brown et al. [52, 53] formulated a bone cement consisting of tetra calcium phosphate (TTCP) and dicalcium phosphate (DCPA or DCPD) with a P/L ratio of 4:1 and mixed with water. The mixture was allowed to set for 30 min which formed calcium-deficient HAP. The formed material was hardened and molded and has wide applications in craniofacial surgery. Yamaguchi et al. [54] suggested the inclusion of zinc along with bone cement which induces osteoblast formation at the localized area and eventually new bone formation happens. Another material was developed where Co-Cr alloy was coated with bioactive glass by a process of enameling. The coated alloy was immersed in SBF for 30 days to observe the deposition of HAP on its surface which eventually increases the bioactivity of the material. This has also had wide applications in the tissue engineering field [55].

#### 3.4.7 Agarose and BSA

Another new fabrication was created using a porous scaffold containing foamlike bioglass and poly (lactide-co-glycolide) PLGA. The scaffold showed high microporosity and also the material was favorable for cell adhesion and hence this scaffold was widely applied in tissue engineering [56]. Another researcher [57] also developed a scaffold containing BCP and agarose gel. He analyzed the compression behavior of the scaffold and found that agarose improved the property of BCP by imparting elasticity, ductility, and toughness to the material. Hence, this scaffold could be used in the tissue engineering process. Another researcher [58] too prepared a scaffold comprising of two proteins namely bovine serum albumin and alpha casein by a cold gelation process. The developed scaffold can perform better in its porosity, cytotoxicity, and swelling ratio and the pH changes unalters the scaffold performance. An Indian researcher [59] also prepared bone grafts containing fibrin functionalized graphene oxide (FGO) and graphene oxide (GO) on to which HAP was grown by wet precipitation method. An in vitro analysis was performed to study its biocompatibility, cell viability, alkaline phosphatase activity, and protein expression studies. The graft containing FGO-HAP showed a better osteoconductive compared to the GO-HAP graft and the results clearly indicated that FGO-HAP can be used in repairing bone defects.

#### 3.4.8 Terminalia arjuna bark

Another Indian scientist team [60] prepared a bone substitute with the incorporation of the extracts of *Terminalia arjuna* bark. The bark extracts were collected,

added with BCP, casein gel, and cast into cylindrical bone grafts. The grafts were immersed in SBF for 21 days and analyzed using conventional techniques. The graft was subjected to *in vitro* cell studies to observe its ossification property. The plant bark extract was traditionally used in fracture healing and hence its incorporation in the graft to enhance the osteogenic property of the graft which was evident in *in vitro* studies. Santhosh et al. [61] synthesized a bone graft containing BCP, biocompatible casein, and the extracts of *Myristica fragans*. The prepared graft was analyzed for *in vitro* bioactivity and subjected to *in vitro* cell analysis. The results revealed the deposition of apatite on the graft after immersing in SBF and also the ALP activity was high when treated with MG-63 cells, NIH-3 T3, and Saos 2 cell lines. This study indicates that the inclusion of plant extract enhances the osteogenic property of the graft.

#### 4. Conclusion

The widely used dental implants are known for their unique characteristics. Recently, novel dental implants incorporated with herbal composites were evaluated by research scientists and revealed abundant evidence on such materials. These implants developed enhanced bone healing and strengthens the bone, accelerates osseointegration, inhibits osteopenia, and inhibits inflammation. These novel implants allow good biocompatibility, viability and shorten the rehabilitation time for the patients. The application of herbal composite inclusion in dentistry and its applications has a greater potential to improve the success rate of dental implant and allows the implications of biotechnology in implant dentistry.



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#### References

- [1] https://www.healthline.com/health/deciduous-teeth
- [2] https://my.clevelandclinic.org/ health/ articles/11179-teeth-eruption-timetable
- [3] https://www.who.int/news-room/fact-sheets/detail/oral-health
- [4] Loesche WJ. Microbiology of dental decay and periodontal disease. In: Baron S, editor. Medical Microbiology. 4th ed. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 99. Available from: https://www.ncbi.nlm.nih.gov/books/NBK8259/
- [5] https://www.who.int/oral\_health/media/en/orh\_report03\_en.pdf
- [6] Al-Maskari AY, Al-Maskari MY, Al-Sudairy S. Oral manifestations and complications of diabetes mellitus: A review. Sultan Qaboos University Medical Journal. 2011;11(2):179-186
- [7] http://www.ada.org/~/media/ADA/ Publications/Files/ADA\_PatientSmart\_ Tooth\_Replacement.ashx
- [8] Osman RB, Swain MV. A critical review of dental implant materials with an emphasis on titanium versus zirconia. Materials. 2015;8(3):932-958. DOI: 10.3390/ma8030932
- [9] John WN. Titanium alloys for dental implants: A review. PRO. 2020;2:100-116. DOI: 10.3390/prosthesis2020011
- [10] Ong JL, Chan DCN, Bessho K. HA coatings on dental implants. In: Wise DL, Trantolo DJ, Lewandrowski KU, Gresser JD, Cattaneo MV, Yaszemski MJ, editors. Biomaterials Engineering and Devices: Human Applications. Totowa, NJ: Humana Press; 2000. DOI: 10.1007/978-1-59259-197-8\_3

- [11] Saini M, Singh Y, Arora P, Arora V, Jain K. Implant biomaterials: A comprehensive review. World Journal of Clinical Cases. 2015;3(1):52-57. DOI: 10.12998/wjcc.v3.i1.52
- [12] Kasemo B, Lausmaa J. Biomaterial and implant surfaces: A surface science approach. The International Journal of Oral & Maxillofacial Implants. 1988;3:247-259
- [13] Heydecke G, Kohal R, Gläser R. Optimal esthetics in single-tooth replacement with the Re-Implant system: A case report. The International Journal of Prosthodontics. 1999;**12**(2):184-189
- [14] Kohal RJ, Klaus G. A zirconia implant-crown system: A case report. The International Journal of Periodontics & Restorative Dentistry. 2004;24(2):147-153
- [15] Sennerby L, Dasmah A, Larsson B, et al. Bone tissue responses to surface-modified zirconia implants: A histomorphometric and removal torque study in the rabbit. Clinical Implant Dentistry and Related Research. 2005;7(Suppl 1):S13-S20
- [16] Depprich R, Zipprich H, Ommerborn M, et al. Osseointegration of zirconia implants compared with titanium: An in vivo study. Head & Face Medicine. 2008;4:30
- [17] Piconi C, Maccauro G. Zirconia as a ceramic biomaterial. Biomaterials. 1999;**20**(1):1-25
- [18] Williams DF. Implants in dental and maxillofacial surgery. Biomaterials. 1981;2(3):133-146
- [19] Craig RG. Restorative DentalMaterials. 9th ed. St. Louis, MO, USA:C.V. Mosby; 1993. p. 169

- [20] Lemons JE. In: Lin OCC, Chao EYS, editors. Perspectives on Biomaterials. New York, NY: Elsevier; 1986. pp. 1-13
- [21] Burkhardt F, Harlass M, Adolfsson E, Vach K, Spies BC, Kohal R-J. A novel zirconia-based composite presents an aging resistant material for narrow-diameter ceramic implants. Materials. 2021;**14**(9):2151
- [22] Glantz PO. The choice of alloplastic materials for oral implants: Does it really matter? The International Journal of Prosthodontics. 1998;**11**(5):402-407
- [23] Lemons JE. Dental implant biomaterials. Journal of the American Dental Association (1939). 1990;**121**(6):716-719
- [24] Carvalho TL, Araujo CA, Teofilo JM, et al. Histologic and histometric evaluation of rat alveolar wound healing around polyurethane resin implants. International Journal of Oral and Maxillofacial Surgery. 1997;**26**(2):149-152
- [25] Meijer GJ, Starmans FJ, de Putter C, van Blitterswijk CA. The influence of a flexible coating on the bone stress around dental implants. Journal of Oral Rehabilitation. 1995;22(2):105-111
- [26] Meijer GJ, Dalmeijer RA, de Putter C, et al. A comparative study of flexible (polyactive) versus rigid (hydroxyapatite) permucosal dental implants II. Histological aspects. J Oral Rehabil. 1997;24(2):93-101
- [27] Meena M, Figueiredo NR, Trivedi K. *Aloe vera* An Update for Dentistry. Journal of Dentofacial Sciences. 2013;**2**(4):1-4
- [28] Phyllis B, James B. Prescription for nutritional healing, 3rd ed. Vol. 1. Avery Publishing; 2000. p. 94
- [29] Burrow A, Eccles R, Jones AS. The effects of camphor, eucalyptus and

- menthol vapour on nasal resistance to airflow and nasal sensation. Acta Oto-Laryngologica. 1983;**96**(1-2): 157-161
- [30] Crowell PL. Prevention and therapy of cancer by dietary monoterpenes. The Journal of Nutrition. 1999;**129**(3): 775S-7758S
- [31] Chainani-Wu N. Safety and antiinflammatory activity of curcumin: A component of turmeric (Curcuma longa). Journal of Alternative and Complementary Medicine. 2003;**9**:61-68
- [32] Wang Q, Wang X, Xu X. Icariin: Can an herbal extract enhance dental implant outcomes? Dental Hypotheses. 2012;**3**(4):133-137
- [33] Das S, Dholam K, Gurav S, et al. Accentuated osseointegration in osteogenic nanofibrous coated titanium implants. Scientific Reports. 2019;**9**:17638
- [34] Mohammed M, Aboki MA, Saidu HM, Victor O, Tawakalitu A, Maikano SA. Phytochemical and Some Antmicrobial Activity of *Cassia* occidentalis L. (Caesalpiniaceae). Int J Sci Technol. 2012;**2**(4)
- [35] Lee SU, Shin HK, Min YK, Kim SH. Emodin accelerates osteoblast differentiation through phosphatidylinositol 3-kinase activation and bone morphogenetic protein-2 gene expression. International Immunopharmacology. 2008;8:741-747
- [36] Nayar S, Guha A. Waste utilization for the controlled synthesis of nanosized hydroxyapatite. Materials Science and Engineering C. 2009;29:1326-1329
- [37] Rajkumar M, Meenakshi Sundaram N, Rajendran V. In-situ preparation of hydroxyapatitenanorod embedded poly (vinyl alcohol) composite and its characterization. International Journal of Engineering

- Science and Technology. 2010;**2**(6):2437-2444
- [38] Nasr-Esfahani M, Mehrabanian M. Production of Bone-like 40% nylon 6,6-Nano Hydroxyapatite Scaffold via Salt-Leaching/Solvent Casting Technique. 2nd International Conference on Chemistry and Chemical Engineering IPCBEE, Barcelona, Spain. Vol. 14; 2011. pp. 40-44
- [39] LeGeros RZ, Lin S, Rohanizadeh R, et al. Biphasic calcium phosphate bioceramics: Preparation, properties and applications. Journal of Materials Science: Materials in Medicine. 2003;14:201-209. DOI: 10.1023/A:1022872421333
- [40] Lin EK, Kolb R, Satija SK, Wu W-L. Reduced polymer mobility near the polymer/solid interface as measured by neutron reflectivity. Macromolecules. 1999;32:3753-3757
- [41] Lopez-Estebana S, Saiza E, Fujinob S, Okuc T, Suganumac K, Tomsiaa AP. Bioactive glass coatings for orthopedic metallic implants. Journal of the European Ceramic Society. 2003;23:2921-2930
- [42] Zhou G, Li Y, Zhang L, Zuo Y, Jansen JA. Preparation and characterization of nanohydroxyapatite/chitosan/konjac glucomannan composite. Journal of Biomedical Research. 2007;83(4):931-939. DOI: 10.1002/jbm.a.31427
- [43] Liu A, Hong Z, Zhuang X, Chen X, Cui Y, Liu Y, et al. Surface modification of bioactive glass nanoparticles and the mechanical and biological properties of poly(L-lactide) composites. Acta Biomaterialia. 2008;4:1005-1015
- [44] Kapoor S, Batra U. Preparation and bioactivity evaluation of bone like hydroxyapatite bioglass composite. International Journal of Chemical and Biological Engineering. 2010;3(1):24-28

- [45] Chin CD, Khann K, Samuel K. Biomed microdevices: A microfabricated porous collagen-based scaffold as prototype for skin substitutes. Biomaterials. 2008;**10**:456-454
- [46] Misra SK, Ansari T, Mohn D, Valappil SP, Brunner TJ, Stark WJ, et al. Effect of nanoparticulate bioactive glass particles on bioactivity and cytocompatibility of poly(3hydroxybutyrate) composites. J R Soc Interface. 2010;7(44):453-465. DOI: 10.1098/rsif.2009.0255
- [47] Periyathambi P, Vedakumari WS, Baskar SK, Bojja S, Sastry TP. Osteogenic potency of magnetic fibrin nanoparticles a novel perspective in bone tissue engineering. Materials Letters. 2014;139:108-111
- [48] Auxenfans BV, Andre CA, Lequeux S, Rose F, Braye J, Fradette, et al. Porous matrix and primary-cell culture: A shared concept for skin and cornea tissue engineering. Pathologie et Biologie. 2009;57(4):290-298
- [49] Wu TJ, Huang HH, Lan CW, Lin CH, Hsu FY, Wang YJ. Studies on the microspheres comprised of reconstituted collagen and hydroxyapatite. Biomaterials. 2004;25:651-658
- [50] Shields KJ, Beckman MJ, Bowlin GL. Mechanichal properties and cellular proliferation of electrospun collagen type II. Tissue Engineering. 2004;**10**:1510-1517
- [51] Gillani R, Ercan B, Qiao A, Webster TJ. Nanofunctionalized zirconia and barium sulfate particles as bone cement additives. International Journal of Nanomedicine. 2010; 5:1-11
- [52] Brown WE, Chow LC. Dental restorative cement pastes. U.S. Patent No. 4,518, 430, May. 1985

- [53] Brown WE, Chow LC. A new calcium phosphate water setting cement. In: Brown PW, editor. Cements Research Progress. Westerville, USA: American Ceramic Society; 1986. pp. 352-379
- [54] Yamaguchi M, Oishi H, Suketa Y. Stimulatory effect of zinc on bone formation in tissue culture. Biochemical Pharmacology. 1987;**36**(22):4007-4012
- [55] Fujino S, Tokunaga H, Saiz E, Tomsia AP. Fabrication and characterization of bioactive glass coatings on Co-Cr implant alloys. Materials Transactions. 2004;45(4):1147-1151
- [56] Boccaccini AR, Maquet V. Bioresorbable and bioactive polymer/ Bioglass® composites with tailored pore structure for tissue engineering applications. Composites Science and Technology. 2003;63:2417-2429
- [57] Puertolas JA, Vadillo JL, Sanchez-Salcedo S, Nieto A, Gomez-Barrena E, Vallet-Regi M. Compression behavior of biphasic calcium phosphate-agarose scaffolds for bone regeneration. Acta Biomaterialia. 2011;7:841-847
- [58] Novaes AB Jr, Scombatti de Souza SL, Martins de Barros RR. Influence of implant surfaces on osseointegration. Brazilian Dental Journal. 2010;21(6):471-481
- [59] Deepachitra R, Nigam R, Purohit SD, Kumar BS, Hemalatha T, Sastry TP. In vitro study of hydroxyapatite coatings on fibrinfunctionalized/pristine graphene oxide for bone grafting. Mater. Manufact. Process. 2015;30:804-811. DOI: 10.1080/10426914.2014.994758
- [60] Krithiga G, Jena A, Selvamani P, Sastry TP. In vitro study on biomineralization of biphasic calcium phosphate biocomposite crosslinked

- with hydrolysable tannins of Terminalia chebula. Bulletin of Materials Science. 2011;**34**(3):589-594
- [61] Santhosh Kumar B, Muthukumar T, Deepachitra R, Charumathy RK, Hemalatha T, Sastry TP. In-vitro evaluation of biphasic calcium phosphate/casein incorporated with Myristica fragrans for bone tissue engineering. Ceramics International. 2014;41(1):1725-1734