REVIEW PAPER

The green-synthesized metal and metal oxide nanoparticles in dental implant applications

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ABSTRACT

Surface-modifying biomaterials have the potential to improve both the performance and durability of dental implantable products that are currently in use. Dental implants' surfaces may be modified to improve their biocompatibility and other biologically significant characteristics using metal and metal oxide nanoparticle coatings. The toxicity of the materials used in the synthesis, the requirement for high temperature and energy, and the high cost are just a few of the factors that restrict the use of the various physical and chemical methods for the synthesis of metal nanoparticles. Though, these restrictions can be overcome by developing substitute synthetic approaches that are similar to Green Synthesis and have proven to be more eco-friendly and less toxic, including the use of algae, microorganisms, and plants. Metal ions can be readily reduced into nanoparticles by plants' biomolecules, secondary metabolites, and coenzymes. Although still in its infancy, the use of metal nanoparticles produced through green synthesis in dental implants has the potential to open up new avenues for enhancing the caliber of these goods.

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INTRODUCTION

Nanotechnology and nanoscience involve the study and application of extremely small particles, referred to as nanoparticles, that possess unique physical and chemical characteristics. These properties include their small size, high surface-to-volume ratio, low surface charge, and associated biological properties, which could lead to significant opportunities in various industrial, medical, or dental applications [1-4]. Dental implants, which are alloplastic prosthetic devices placed in the oral tissues beneath the mucosal and/or periosteal layer, as well as on/into the bone, have led to a significant increase in clinical dentistry for patients with edentulous or complete oral health [5, 6]. According to the biology of the peri-implant outer and inner tissues, dental implant surface topography and design are continuously being improved. The word "topography" is used

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to describe both the macroscopic and microscopic features of implant surfaces. The primary objectives of surface texturing or implant surface treatments are the stimulation of cellular activity and bone apposition. [7-9]. The surface topography of an implant can be modified to be either porous or coated with other appropriate materials to promote bone-implant contact, given the unpredictable nature of a bone's anatomic surface [10, 11]. An implant's surface may change in topography and surface chemistry due to the presence of nanoparticles, producing unique and exceptional specifications [12]. Metallic and metallic oxide-based nanoparticles coatings are a potential surface modification for improving the biocompatibility and other biologically relevant qualities of dental implants. Adding numerous functional groups to the nanoparticle can improve the final product's quality [13, 14].

The use of nanoparticles made of metal and metal oxides is a recent development in dentistry. Metal nanoparticles are used in dentistry because of their distinctive shape-dependent properties that improve bio-physio-chemical functionalization, antibacterial activity, and biocompatibility. The physical and chemical possessions of several dental materials, including dental amalgam, restorative cements, adhesives, resins, endodontic-irrigation solutions, obturation materials, dental implants, and orthodontic archwires and brackets, are improved by the use of these nanoparticles [15-17]. An implant's mechanical, electrical, thermal, and biological properties can all be improved by the addition of nanoparticles, which can allow for the application of a large interfacial area [18].

Numerous nano biomaterials for biological and therapeutic applications have been developed as a result of the novel field of nanobiotechnology [19]. The majority of synthesizing technologies are expensive and require a lot of energy to maintain the high pressure and temperature needed to carry out the reaction, which increases the risk of endangering the environment, biological systems, and human health because of the use of toxic and dangerous substances [20, 21]. This is true even though they are widely used, particularly in dentistry and implants. Several initiatives are being evaluated globally to create environmentally friendly technologies that enable the production of non-toxic, sustainable products using green nanotechnology and biotechnological tools. The diverse natural behaviors, stability, and appropriate diameters of nanoparticles produced through biological or green technology can facilitate their one-step synthesis at physiological temperatures, pH, pressure, etc., while also minimizing some of the undesirable processing conditions and incurring a minimal cost [22-24].

Technologies for creating "green" nanoparticles use biological systems like yeast, fungus, bacteria, and plant extracts rather than potentially hazardous chemicals. One of the factors contributing to the success of these products is the availability of a wide range of metabolites with potent reduction potentials, as well as their accessibility, global distribution, safe handling, low waste and energy costs, and safe handling during production [25-27]. This study presents a review on the green-synthesized metal nanoparticles and metal oxide nanoparticles in dental implant applications.

DENTAL IMPLANT SURFACE TOPOGRAPHY

Over the past few decades, the use of dental implants to treat partial and complete edentulism and restore function and appearance has increased, improving the quality of life for dental patients [28]. Surfaces contain a vital role in biological and medicinal aspects since most of the biological processes occur at surfaces and interfaces. The design of high surface area geometries can increase the rates of reaction turnovers. Particulate organic environments can improve certain specific reactions and affinities. It is possible to precisely orient and space molecules through the technique of self assembly in the plane of an interface. Specific structures can be oriented to interfaces via surface energy minimization. The execution of molecular recognition as a manifestation of both geometry and chemistry can be simplified by surfaces [29]. The rate of both commercial and scholar investments in dental implant surfaces has been recently increased. According to past studies, implant surface topography was the only factor with a substantial impact on the shear strength and bone-to-implant contact (BIC) of interfaces. These claims were further supported by the results of animal researches, which displayed the favoring attitude of a specific level of surface roughness towards BIC as measured by the removal torque test [30, 31]. Implants with sufficient surface roughness can potentially affect their primary stability, improve BIC, and intensify the removal torque force[32].

As an established fact, biological reactions to an implanted substance are governed by the chemistry, energy, and topography of its surface. The physical characteristics of size, shape, surface roughness, and relative interfacial movement, as well as the linked chemical characteristics to the composition and surface structure, may have a role in tissue responses to a dental (or surgical) implant [7, 33]. In addition, the critical function of implants surfaces in configuring the factors of biocompatibility and bio integration is attributed to their direct contact with tissues [34]. The four material-related parameters that can affect the events of bone-implant interfaces include the composition, energy, roughness, and topography of implant surface. There are proofs on the possibility of successfully altering the reactions of cells and tissues by creating various surface textures, which are divided into the three types of macro, micro, and nano. In comparison to their traditional macro- or micro-scale counterparts, the "nanostructured" materials can display improved mechanical, electrical, magnetic, and/or optical properties. A notable proportion (>50%) of defects in nanostructured (NS) materials is composed of grain boundaries, interphase boundaries, and dislocations that can significantly affect their chemical and physical properties [35, 36]. Nanotechnology can provide surface designs with specific topography and chemical features with the ability to aid the comprehension of biological interactions and the development of novel implant surfaces with predicted tissue-integrative qualities [37, 38]. Nanoscale surface modifications and coating technologies of dental implants can be effective in the adhesion, proliferation, and differentiation of cells, as well as the osseointegration of implants[39].

Nanoscale Surface Modifications

The creation of functional materials, systems, and apparatuses is referred to as nanotechnology. "because it is capable of manipulating matter and exploiting novel physical, chemical, and biological events and properties at the nanoscale (1-100 nm). In this field, materials with nanoscale topographies or products made of materials with nanoscale topographies range in size from 1 to 100 nm. [40]. Various surface treatments were made possible by osseointegrated implant dentistry after a careful analysis of their surface characteristics. The attendance of nanometers in roughness and chemistry can have a significant impact on how proteins and cells interact, and surface properties have a significant impact on biological interactions. A two-dimensional association of surface features is required for the purpose of applying nanotechnology to the surface of dental implants (across and away from the mean surface plane), whereas the manufacturing process determines whether these nano-features are arranged in an organized (isotropic) or disorganized (anisotropic) manner. Anisotropy is frequently discernible in the applied surface topographies on a dental implant surface. Application for isotropic features, such as nanogrooves or nanopits, which are primarily produced by optical processes, is quite difficult for complex screw-shaped items. By applying these concepts to the endosseous implant surface, new physicochemical conduct (like bone bonding) or biochemical events (like protein adsorption or cell adhesion) will be produced, likely on the nanometer scale [35, 38, 41]. There are certain properties to the unique nanostructures of alloplastic surfaces that can affect the type of cells interaction, since the dimensions and densities of nanostructures can impact the behavior of cells[42]. Nanotopography seems to influence cells interactions at the surface of applied materials and also results in changing the cells behavior, which is in contrast to the typical topography of sized units. The cellular protein adsorption can be altered by the nanoscale modification of bulk material. The rate of cell spreading may be accelerated or slowed down in accordance to the exerted nano-architecture. The existence of undefined mechanisms indicates the apparent enhancement of cell proliferation by nanoscale topography. Numerous studies conformed the improving effects of osteoblast differentiation on nanoscale topography [6, 43]. Treated implant surfaces are able to serve with a variety of functions that include the enhancement of biological response of osteogenic cells and increasing the contact area between the implant and host bone. In actuality, the direct contact of implant surface with the host tissue affects the stability of implant and the bone, as well as the cell and biochemical responses. Numerous histomorphometric studies claimed the impact of using rough surfaces on extending the contact of bone-to-implant (BIC)[44, 45]. Surface nano-features, such as coating, patterning, functionalization, and molecular grafting at the nanoscale, enable the development of more promising biomaterials, the planning of improved implant designs, and the preparation of surface

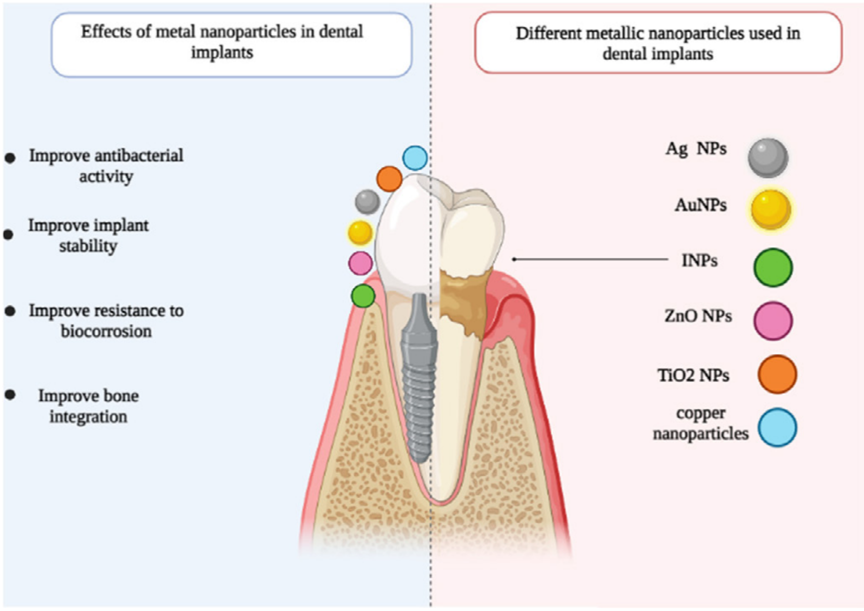

Fig. 1. Surface coating of metal and metal oxide nanoparticles on dental implants

engineering techniques. Medical barriers may be lessened by these characteristics. [46-49].

Surface coating of metal and metal oxide nanoparticles on dental implants

Recognized as the heart of nanotechnology, nanoparticles are extremely small products with diameters in the range of nanometer that can be produced from virtually any biocompatible material and exhibit the materials qualities in a comparable manner to a similar bulk material. In an effort to provide almost perfect oral health, nanoparticles were exploited to increase the bone integration of dental implants, which were also exerted as particle coatings on implants surfaces to enhance soft tissue integration and boost the success of dental implants. Dental implants can be coated with osteoconductive nanoparticles to create a strong biological attachment through the induction of chemical contact with the bone[14, 16, 50-52]. The capability of these materials in generating and regenerating Bone can aid the promotion of developing new bones. It has been revealed that the coating of implant surfaces with bio-nanomaterials may alter their physical characteristics and boost their capacity to promote osteogenic. Additionally, some materials reported to improve the density of osteoblast cells on the implant, which can potentially boost the implant stability[53, 54].

Nanopores, nanotubes, quantum .s, nanoshells, nanospheres, nanowires, nanocaps, dendrimers, nanorods, liposomes, metallic, and metal oxide nanoparticles are just a few examples of the many types of nanoparticles that are frequently used to help diagnose and treat dental diseases. As metals get closer to the nanoscale, their physio-chemical properties change, and nanoparticles have different properties than bulk metal does [55, 56]. MNPs may be viable resolution to the limitations of dental implants (Fig. 1). The increased antibacterial capabilities of certain metal nanoparticles, including gold, silver, platinum, copper, and selenium, led to their application for providing an antibacterial surface coating for traditional dental implants. These nanoparticles can also possess osteointegration property by being incorporated with titanium and hydroxyapatite [57, 58]. Some related studies confirmed the biocompatibility of certain metal nanoparticles such as nanocrystalline titanium-copper alloy. A highly useful orthopedic material, especially for dental implant applications, is required to contain antibacterial, osseointegration, and mechanical qualities[59]. Additionally, it has been demonstrated that some other metal nanostructures, similar to silver nanoparticles that are decorated with graphene nanocomposites, can display osteointegration properties and improved antibacterial activity[60]. According to reports, the combination of metal nanoparticles and metal

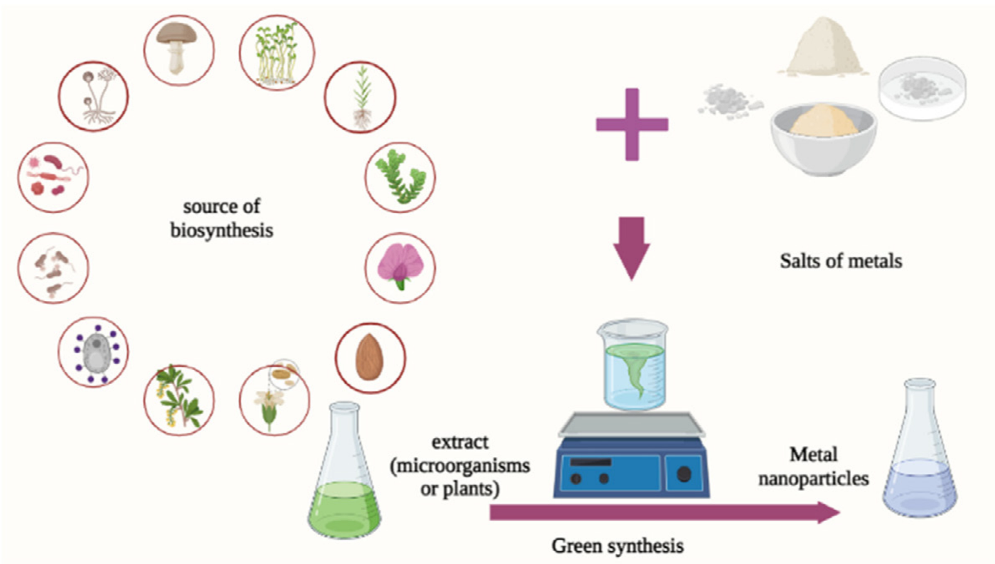

Fig. 2. The green synthesis of metal and metal oxide nanoparticles

oxide nanoparticles with carbon nanomaterials or polymer nanomaterials as nanocomposites leads to retaining their mechanical properties and enhancing their biological features as well [61].

Different physical, chemical, and biological processes can result in the production of metal nanoparticles. In the process of synthesis, specific metal ions from salt solutions are chemically reduced in the attendance of a strong base (reducing agent), like as sodium borohydride or sodium hydroxide, and then another stabilizing factor, also referred to as a capping factor or stabilizer, is added [62]. However, the applied chemicals in the form of reducing agents, as well as the solvents required to dissolve the stabilizers, are commonly hazardous substances. Therefore, the presence of their residues in the final nano systems may cause harmful and detrimental impacts on the health of people and environment[63]. These facts raised the concern of many about the safety of MNP applications that led to the quest of designing novel synthesizing techniques [64]. The green synthesis of MNPs using biological systems, which is based on the ideas of green chemistry, is one of these alternatives [65, 66].

THE GREEN SYNTHESIS OF METAL NANOPARTICLES AND METAL OXIDE NANOPARTICLES

Prokaryotic or eukaryotic creatures (including microorganisms, plants), or their different parts, have the potential of being applied in the green synthesis of MNPs (Fig. 2). The Primary and secondary metabolites of biological components act as agents to promote the reduction of a targeted metal ion and lead to the creation of MNPs[67-70]. In the course of MNPs production, these reducing substances or other surrounding molecules may also fabricate a stabilizing layer (coating) on their surface, which can prevent or at least minimize their tendency to agglomerate/aggregate or grow in a disorderly manner[71, 72].

Furthermore, particular experimental parameters, such as temperature, pH, and reagent concentration, can influence the generation and characteristics of produced MNPs through green synthesizing techniques. These nanoparticles can exhibit desirable traits from a sustainable perspective that include being environmentally friendly (exerting less toxic reagents and solvents), biocompatible (Offering the option of direct usage in target applications without prior purification steps), and biodegradable (able to be hydrolyzed by biological pathways), as well as implicating a quick and easy manufacturing (fewer steps), low costs, and high yields [73, 74]. The following sections present discussions on the most critical metal nanoparticles and their based green synthesis and application in dental implants.

Silver nanoparticles (Ag NPs)

Silver (Ag) ions or salts have been utilized for a long time in a variety of medical applications, such as wound dressings, catheters, and prosthetics, due to their broad antibacterial impact. Next to its powerful antimicrobial effects, Ag can offer a number of benefits that include minimal toxicity, strong biocompatibility with human cells, sustained ion release for providing long-lasting antibacterial activity, and low bacterial resistance. There are proofs on the harmless presence of silver in low doses towards human cells. Numerous studies described the biological activity of silver nanoparticles in medical applications by mentioning their anticancer, antioxidant, and antibacterial properties[75-77].

When nanotechnology first emerged, it was possible to create silver nanoparticles (Ag NPs), which have a variety of properties, including a variable surface-area-to-volume ratio that can be helpful in many biological and technological applications. Ag NPs have been widely used in the medical field for things like bone prostheses, endotracheal tubes, and wound sutures because of their capacity to form distinctive interactions with different bacterial and fungal species [78-81]. This product's use was beneficial in a number of dental specialties, including endodontics, dental prosthetics, implantology, and restorative dentistry. Incorporating these NPs is intended to prevent or at least slow down microbial colonization of dental materials, which will improve oral condition and overall characteristic of life. There are a number of theories as to how Ag NPs exert their antibacterial properties, such as their capacity to adhere to bacterial walls and change the composition of the cell membrane, the capacity of free Ag nanoparticle-containing to harm and penetrable the same cell-based membrane, or the discharge of silver ions that interfere with different cell functions [82-85]. The risk of infection from the peri-operation persisting for the duration of the patient's life makes conventional antibacterial methods ineffective in the face of the serious threat posed by peri-implant infection to implant treatment. This is because many people are interested in using different doping techniques to modify implant surfaces with silver nanoparticles due to their safety and potent antibacterial properties [86, 87]. There are disadvantages to the provided wide range of possibilities for developing new antimicrobial materials in nanotechnology such as color alteration that is an important factor for dental materials[88]. Table 1 exhibits some applications of green synthesized silver nanoparticles in dental implants.

Gold Nanoparticles (AuNPs)

A simple, one-step, environmentally friendly chemical process can be used to make AuNPs, a particular variety of nanomaterial. AuNPs can be a formidable competitor for biological applying due to their intriguing characteristics, in addition to their popularity as non-toxic and biocompatible materials [95]. There are numerous therapeutic uses for gold nanoparticles (GNPs) such as protein , gene and drug delivery and biosensor. Despite their availability in different sizes, the achieved GNPs in 20-50 nm proved to contain the highest rate of cellular uptake. These nanoparticles can be identified by their greater surface area in relation to volume, size, and shape, which have been seen in the forms of rods or spheres, triangles, stars, and squares, among others. In light of these facts, their application was suggested in the areas of tissue engineering, periodontology, dental implants, restorative dentistry, and cancer disease diagnosis. To produce various forms of GNPs, various bacteria and fungi were tested [96-100]. The fine biocompatibility and surface specificity of these nanoparticles can facilitate the design of more practical dental implants. Green chemistry-produced plant-mediated AuNPs were reported to be environmentally friendly and biocompatible nano molecules capable of stimulating bone growth, which can be exerted as an active bone inductive substance after implant placement to induce bone formation, reduce bone resorption, and promote bone growth[101]. Table 2 presents certain applications of green synthesized gold nanoparticles in dental implants.

Iron Nanoparticles

The utilization of iron nanoparticles (INPs) in dental implants is a topic of interest due to their exceptional physicochemical, magnetic, and microwave absorption characteristics, as well as their low toxicity and high catalytic activity. Iron oxide-hydroxide (FeOOH), magnetite (Fe3O4, Fe2O3, and Maghemite (Fe2O3)), and zero-valent iron (ZVI) nanoparticles are the three main types of iron nanoparticles (IONPs). The applications of these particles include drug delivery, magnetic targeting, stem cell research and manipulation, genome editing and etc [105, 106].

The wide range of IONPs applications in

Table 1. green synthesized silver nanoparticles in dental implants

Nano particle	source of biosynthesis	Outcome	Reference
Ag NP	*Panax ginseng*	Antibacterial properties	[89]
Chitosan based silver impregnated nanoparticles	*Green tea extract*	Antimicrobial property	[90]
silver nanoparticles	*Green tea*	Antimicrobial activity of silica-coated silver nanoparticles for esthetic dental applications	[91]
silver nanoparticles (Ag NPs)	*Mangifera indica (Mango leaves)*	To promote the mechanical bonding and hardness of dentally applied glass ionomer cement (GIC) Antibacterial peformance	[92]
silver nanoparticles (Ag NPs)	*Salix alba bark extract*	Antimicrobial influence Against Bacteria procured from Dental Plaque	[93]
silver nanoparticles (Ag NPs)	*Starch+glucose*	The antibacterial performances Ag NP-modified hydrogel coatings	[94]

Table 2. green synthesized gold nanoparticles in dental implants

Nano particle Objective	source of biosynthesis	Outcome	Reference
Gold nanoparticles (GNPs)	*Salacia chinensis bark*	An efficient bone inductive ingredient throughout dental implant therapy	[101]
AuNPs	*Anogeissus latifolia (A. latifolia)*	To reduce pain in nursing care for dental tissue implantation usage	[102]
AuNP	*Turmeric*	Antioxidant, anti-inflammatory, and antibacterial performance versus a variety of oral pathogens	[103]
AuNP	*Justicia glauca*	AuNPs and drug-conjugated AuNPs showed impending efficacy versus oral infections	[104]

biomedicine includes diagnosis and treatments. These magnetic nanoparticles can be used in imaging for contrast purposes. Due to their magnetic properties, low cost, and great biocompatibility, IONPs can also be used as nanocarriers for in vivo therapeutic drugs delivery towards targeted cells [107]. In recent years, a lot of interest was invested in iron oxide nanoparticles (IONPs), which include

Table 3. green synthesized iron nanoparticles (INPs) in dental implants

Nano particle	source of biosynthesis	Outcome	Reference
Iron Nanoparticles (FeNP)	*Syzygium aromaticum (Clove) buds, Azadirachta indica (Neem) leaves and Camellia sinensis (Green tea)*	For enhanced Antimicrobial Activity	[110]
PLGA(Ag-Fe3O4)	*Bacterial cellulose (BC) nanofibers*	Antimicrobial activities	[111]
Iron oxide nanoparticles	*Swertia chirata extract*	As a potent anti-corrosive agent which can protect the metal surface from further deterioration in harsh body environments	[112]
Iron oxide nanoparticles	*Grey mangrove Avicennia marina*	As a potential antibiofilm agent	[113]

the exploitation of magnetite and maghemite magnetic nanoparticles in dentistry. In conformity to related researches, iron oxide nanoparticles are frequently used to eliminate biofilms from dental implants and provide resistance against biocorrosion[108, 109]. Table 3 displays Some applications of green synthesized iron nanoparticles (INPs) in dental implants.

Zinc Oxide Nanoparticles (ZnO NPs)

Zinc oxide nanoparticles (ZnO NPs) have numerous applications due to their excellent biocompatibility, high stability, low cost, and low toxicity. They also have excellent physicochemical qualities and a high level of safety. The biocompatible semiconductor metal Zinc Oxide (ZnO) is used to make a number of dental products, including amalgam, ceramics, dental cements, and zinc oxide eugenol. The Food and Drug Administration also gave this substance its seal of approval as one of the safest substances used in the pharmaceutical sector [114, 115]. The wide bandgap, high exciton binding energy, electrical conductivity, nontoxicity, and chemical toughness of nanosized ZnO are among the many intrinsic properties that have garnered industrial interest. A green synthesis of zinc oxide nanoparticles could make it easier to produce in large quantities. Phytochemicals like terpenoids, polysaccharides, vitamins amino acids and alkaloids may be released by plants to reduce the concentration of metal ions or metal oxides. Through electrostatic, steric, hydraulic, and van der Waals forces, phenols and flavones, which are used as reducing agents in extracts from tobacco like pipettes and carpet fibers, can also be used to stabilize NPs [116, 117]. To prevent the development of pathogens that cause periimplantitis, which is believed to be caused by this condition, they used biogenic zinc oxide nanoparticles (ZnPs) derived from Andrographis paniculata leaves (APLAE) to produce an aqueous extract. The obtained results demonstrated that periimplantitis-causing bacteria (E. coli and S. aureus) and thus made the biosynthesis of ZnPs by APLAE a workable technique [118]. Due to the buildup of bacterial biofilms that are frequently resistant to conventional antimicrobials, dental implants are vulnerable to failure. In this respect, the application of nanoparticles as implant coatings may make it easier to control infection for an extended period of time. Through electrohydrodynamic deposition, zinc oxide (nZnO), hydroxyapatite (nHA), and their combination (nZnO + nHA) metal oxide nanoparticles were applied to Ti discs. Coriandrum sativum extract was used on all three of the nano-coated surfaces to create zinc oxide nanoparticles, which were then applied. On nZnO and composite (nZnO + nHA) coated surfaces at 96 h, as opposed to nHA coated and uncoated titanium, a higher proportion of non-viable microorganisms was seen. These surfaces also showed the greatest effectiveness in the results of the biofilm thickness comparison [119].

Titanium Oxide Nanoparticles (TiO2)

The primary uses of titanium oxide (TiO2) nanoparticles are in photocatalytic, tinting, textiles, papers, plastics and cosmetics products, food products and antibacterial and anthelmintic applications. In order to transform the precursor metal salt into the appropriate nanoparticles, a variety of biological entities are involved in the green synthesis of these nanoparticles. The processes of bio-reduction and capping are thought to be mediated by the secondary metabolites already present in organisms, such as plants or microbes [120]. Through the mechanisms of reduction and stabilization, plant components like proteins, enzymes, phenolic acids, and carbohydrates control the synthesis of NPs and produce the various forms of TiO2 NPs [121]. Green titanium dioxide (TiO2) nanoparticles, which were achieved by the aqueous leaf extract of As a reducing and manufacturing agent, Aloe barbadensis' aqueous leaf extract produced green titanium dioxide (TiO2) nanoparticles that were highly effective against P. aeruginosa by successfully preventing planktonic cells from adhering to the substrate. Thus, these NPs might be useful for managing bacterial infections that are linked to biofilm [122]. New coating materials can be produced by utilizing SiC-TiO2-Graphene and different concentrations of Azadirachta indica (Neem) extract in coating nanomembranes. Potential applications for the synthesized nanomembranes include dental implants [123].

CONCLUSION

Scientists from a variety of fields, particularly dentistry, have become interested in the green synthesis of nanostructures. Due to their therapeutic benefits, the phytometabolites of medicinal plants are currently being studied and utilized for the benefit of mankind. In terms of creating metal nanoparticles, this method has shown to be capable of producing favorable and environmentally friendly results. The potential of green synthesized metal nanoparticles in dental implants may lead to a reduction in the negative aspects of traditional implants and an improvement in their quality, potentially elevating patient quality of life in society. The physical modifications, ability to promote osteogenesis, density enhancement of osteoblast cells, and potential stability enhancement through a metal and metal oxide nanoparticle surface can be achieved through dental implant technology.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest

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