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Nanotechnology and Nanomaterials in Dentistry: Present and Future Perspectives in Clinical Applications

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Abstract

Nanotechnology has established its presence in virtually all domains of science and technology. Its applications in healthcare widely range from advanced diagnostics to biosensors and targeted drug delivery. This is because nanomaterials have unique size-dependent properties that significantly improve human life and health when exploited. Dentistry has been no exception and thus seen profound developments, especially in the last decade, with the involvement of such nanomaterials and technology. The number of dental nanomaterials available has risen with time and a wide range of them have been researched for commercial and clinical usage. For example, antimicrobial nanoparticles are being utilized in restorative composite material for the prevention of dental caries. Incorporating nanomaterials into preexisting dental substances has enhanced their biocompatibility. It is predicted that in the future, nanotechnology will also allow the repair and rebuilding of dental hard tissues. This review aims to introduce the concept and development of nanoscience, its involvement in medicine, and summarize the recent research in Nanodentistry. The bibliographic study demonstrates the novelties and applications of nanotechnology in orthodontics prosthodontics, preventive dentistry, restorative dentistry, and periodontics. Subsequently, the future of nanomaterials in oral health and the direction in which research should be focused is also discussed. Thus, the review presents a detailed analysis and a comprehensive study to describe the achievements of nanotechnology in dentistry, the current obstacles, and future predictions.

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1. Introduction

Nanotechnology involves the research, development, and manufacturing of materials and devices measured on the nanometer scale.[1,2] Materials with constituents less than 100 nm in at least one dimension can be classified as nanomaterials.[3,4] Nanotechnology has found its way into commercial applications of cosmetics, food packaging, and disinfectants for the past two decades.[5] In the field of medicine, nanotechnology and nanomaterials are used for prevention, diagnosis, and treatment.[6] Nanomedicine is involved in multiple facets such as drug delivery, surgery, restoration, and replacement of tissues.[5] In dentistry, nanoscience has gained impressive traction in the recent past as it deals with nanostructures for diagnostics and treatment of dental diseases.[3] The aim is to attain perfect oral health with the regeneration of oral tissues using nanomaterials, bioengineering, and nanorobotics.[7-10]

The concept of nanotechnology was first introduced by Richard Feynman in 1959 at a lecture at Caltech where he discussed information on a small scale and the unavoidable use of small robots and computers shortly.[11-13] Since then this discipline has seen advancement in leaps and bounds and in the present day, its footprint is noticed in all spheres of technology. This can be attributed to the fact that nanotechnology and nanodevices have properties that were earlier unachievable by available provisions, and as a result, have produced ground-breaking solutions.[14] What makes nanoparticles remarkable is their unique structure with a higher number of atoms present on the surface in comparison to the core. This generates a stronger and larger number of

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bonds relative to macroparticles that have more atoms in the core than on the surface.[15,16] Nanomaterials may be grouped based on their dimensions. Zero-dimensional nanostructures are called nanoparticles, one-dimensional nanostructures fall under nanowires and nanorods and two-dimensional nanostructures are called thin films.[17,18]

The primary challenge that arises is the manufacture of nanoparticles in large quantities in a controlled and purposeful fashion. Nanoparticles are synthesized via solid, liquid, or gas phase and the method is determined by the type of material (metal, ceramic, or polymer), the kind of shape, size, and distribution required in the final product. Two broad approaches adopted are the top-down and the bottom-up approach.[19]

The top-down approach, which is used to generate ceramic nanoparticles, is classically implemented when larger initial structures are involved.[20] In this method, the main concern lies with the technological and the physical factors. The smaller the particles the stronger they are due to fewer defects and lesser number of grain boundaries. Further, ball mills used to break macro particles have to limit properties of their crushing volume, modulus of elasticity, and Kinetic Energy.[17] The other process, which is the bottom-up method involves the miniaturization of components to an atomic level, combining self-assembly that gives rise to the formation of nanostructures.[21]

While this recent technology has proven to have positive implications in medical science, the debate around the toxicity of nanomaterials prevails. The large surface area to volume ratio leads to high absorption through skin and lungs and can cause damage to the alveoli eventually.[22] However, in dentistry, not much evidence has been gathered on the same. In the past, some investigations have indicated that despite making medical practice simpler, the hazards to health and safety cannot be ignored.[23] While further studies and dedicated research are much required, there are several assured technologies of nano dentistry that are being used today.[21-24] In recent times, a large portion of the research revolves around orthodontics and aesthetics. Attention has also been channelized to nanorobots and tissue engineering with certain developments being carried out in bone augmentation, stem cells, and cartilage regeneration.[25-28]

This review discusses the advancements of nanotechnology and its applications in various facets of dental sciences (Fig. 1). The highlighted studies are orthodontics, prosthodontics, preventive dentistry, restorative dentistry, and periodontics.

Search strategy and article selection

A non-systematic review of all Dentistry related English language literature published in the last 2 decades was conducted using PubMed and *Google Scholar*. Our search strategy involved creating a search string based on a combination of keywords. These keywords were: 'Nanotechnology', 'Nanodentistry', 'Dentistry', 'Nano Medicine', 'Orthodontics', 'Prosthodontics', 'Restorative Dentistry', 'Preventive Dentistry', 'Periodontics', 'Nano Ceramics'. Original articles published in English were included in this literature review.

Inclusion Criteria:

1. All articles on Nanodentistry, Dentistry, Nanotechnology;
2. Full-text original articles on aspects of diagnosis and treatment.

Exclusion Criteria:

1. Commentaries, reviews, and articles with no full-text context;
2. Animal, laboratory, or cadaveric studies.

2. Spectrum of applications of nanotechnology in dental sciences

2.1. Nanotechnology in orthodontics

Orthodontics is the treatment of and management of malocclusions. It is one of the older specialties in dentistry that has been enormously flourishing under research and development with the discovery of newer materials and diagnostic techniques.[29]

2.1.1 Accelerated tooth movement

The drawback in orthodontics is overcoming the prolonged-time period for the treatment due to slow tooth movement ranging from 2 to 3 years. Apart from causing inconvenience, fixed orthodontic treatment may lead to WSLs (White spot lesions -scars of orthodontic treatment), root resorption, and gingival inflammation.[3] For orthodontic treatment that leads to painless and accelerated tooth straightening, vertical repositioning, and rotation within hours or even minutes, nanorobots can be used to directly manipulate periodontal issues. For this, Optiflex is infused with nanomaterials.[30-32]

2.1.2 Coating of stainless-steel wires and brackets

a. Nano coating in stainless steel wires

Nanoparticles of biocompatible nature are coated on orthodontic stainless-steel wires for friction reduction. For example, inorganic nanosized particles of tungsten disulfide (IF-WS2) that possess effective lubricating properties serve as self-lubricating coatings on orthodontic stainless-steel wires.[32] For antibacterial effects, the silver-zirconia nanocomposite is coated using pulsed laser deposition for stainless steel in bio-implants.[33] The electro-co-deposited inorganic fullerene (IF) - like WS2 coatings consist of a coating of metal composite nanoparticles. This coating isbased on electrodeposited Nickel (Ni) film with IF-like nanospheres which significantly reduce the frictional force on various surfaces, especially on commercially used archwires.[34]

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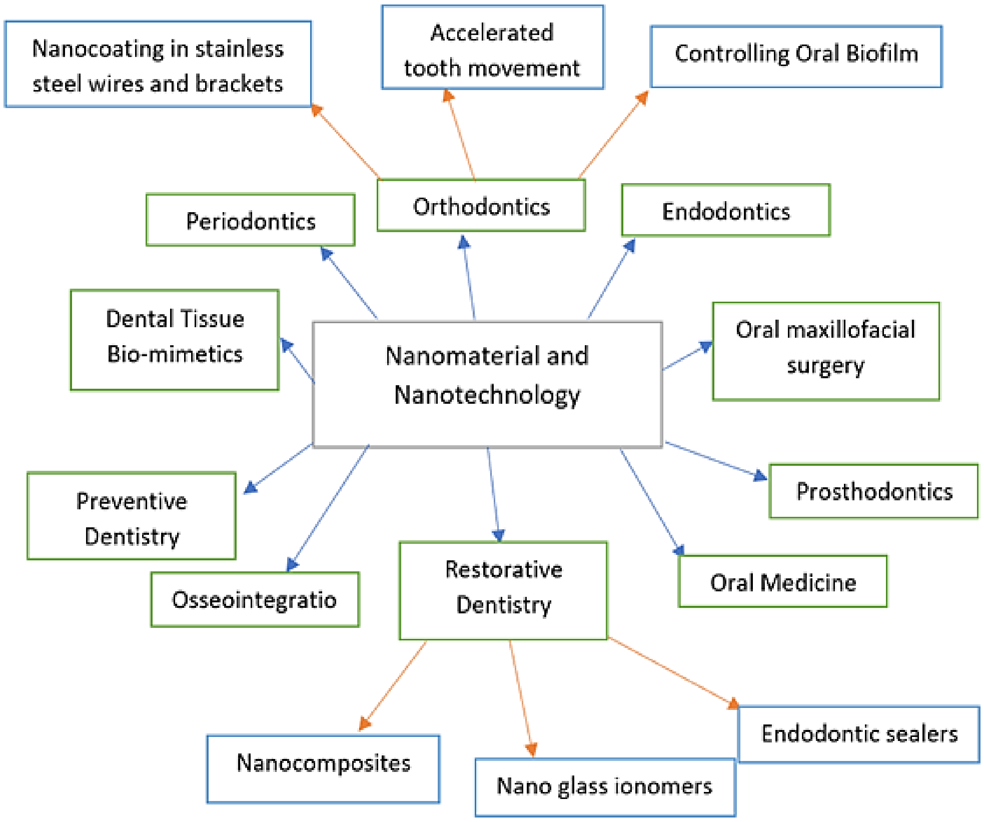

Fig. 1 Nanomaterials and Nanotechnology and their applications in dental sciences.

Titanium dioxide (TiO_2) single layer and Titanium Nitride/Titanium dioxide (TiN/TiO_2) multilayer coatings on stainless steel produce surface wettability that indicates the coatings are hydrophilic. The bacterial adhesion rate for antibacterial coats captured with scanning electron microscopy proved that these coatings effectively reduce bacterial adhesion in biofilms.[33]

b. Nanocoating in stainless steel brackets

Elastomeric ligatures act as a carrier scaffold for nanoparticle delivery with anti-inflammatory, anti-carcinogenic, and/or antibiotic drug molecules embedded within the elastomeric matrix. When medicated wax is coated on orthodontic brackets, pain from mucosal irritation is reduced because the brackets slowly and continually release benzocaine.[36] There is an ongoing attempt to develop brackets that can facilitate three-dimensional (3-D) mechanical sensors in the bases of these brackets to measure the 3-D real-time forces and moments on the teeth. These sensors will allow orthodontists to adjust the forces should they exceed acceptable limits.[37]

2.1.3 Controlling oral biofilms

Biofilm formation in the oral cavity is prevented mainly via two broad approaches, either by combining nanomaterials with traditional dental materials or by adding coatings to surfaces to avoid microbial adhesion.[38] For oral biofilm control, certain nanoparticles have anti-adhesive or biocidal properties and therefore have been incorporated into orthodontic adhesives. These decrease the demineralization around brackets. The inclusion of nanoparticles should however not affect the physical and chemical properties of the orthodontic devices thereby diminishing their performance. It should be ensured that any nanoparticle usage is safe over a clinically relevant period.[39] Usage of appropriate nanotechnological applications that regulate oral biofilm keeps White Spot Lesions (WSL) or orthodontic scars in check.

2.2. Nanotechnology in prosthodontics

Prosthodontics involves dental defects and treatments post tooth loss including crowns, onlays, and dentures along with the usage of prostheses for missing teeth and maxillofacial defects in tissues.[40-43] Research of nanomaterials in prosthodontics has been prompt and is focused primarily on two aspects: the creation of new inorganic nanoparticles and surface alteration with inorganic nanofillers to develop a low rate of shrinkage of the repair resin (acrylic resins).[44] With the inclusion of nanomaterials in prosthodontics, modulus of elasticity, polymerization shrinkage, surface hardness, and filler loading properties have been enhanced.[45,46] Denture bases with nanomaterials have better interfacial shear bonds between the nanoparticles and the binding matrix as compared to a conventional resin matrix. This can be attributed to the supermolecular bonding covers or shields created by the nanoparticles that form a thick interface resulting in enhanced bonds and higher molecular weight polymers.[47] By adding 0.4% TiO_2 to a denture base made of three-dimensional (3D) printed poly-methylmethacrylate (PMMA), an improvement in mechanical and antibacterial properties was observed.[48] Heat cured PMMA with 7wt.% of nano zirconium oxide (ZrO_2) possesses significant tribological properties. The addition of zirconium oxide nanoparticles gives denture bases improved hardness, flexural strength, and fracture toughness. The nano zirconium not only adds to the mechanical properties during the construction phase but also magnifies the transverse strength of repaired bases.[49,50] Additionally, the antifungal properties of chlorhexidine coating with various nanoparticle additives were studied, and it proved to inhibit fungal growth in dental silicones commonly adopted in maxillofacial prosthesis and indenture soft liners.[51] Table 1 summarizes the relevant information on nanomaterials used in prosthodontics.

2.3. Nanotechnology in preventive dentistry

Nanoscience provides distinctive strategies in the field of preventive dentistry especially when it comes to controlling bacterial biofilms and remineralization of sub-micrometer tooth decay. By incorporating nanosilver or nanogold colloidal particles between bristles, nano-toothbrushes, as shown in Fig. 2, have been developed for improved mechanical plaque removal along with the antibacterial effects of added gold and silver.[63] For nano modification of oral hygiene products, nano-calcium fluoride has been added to mouthwashes to reduce dentine permeability, and caries activity, and to increase the concentration of labile fluoride in the oral cavity[64] Toothpaste formulations with calcium carbonate nanoparticles and nano sodium trimetaphosphate in 3% appeared to give remineralization of initial carious lesions relative to conventional toothpaste.[65]

Nanosized hydroxyapatite particles can integrate into dentin tubules with ease and protect against external stimuli. This has led to a reduction in hypersensitivity in teeth.[66,67] These particles maintain the enamel on the tooth and protect against erosion due to acidic food and drinks apart from desensitizing.[68] Modified silica nanoparticles also desensitize by lowering the hypersensitivity of dentinal tubules by blocking them.[69]

Table 1. Characteristics of nanomaterials used in prosthodontics.

Dental Material	Material Properties	Advantage	Disadvantage
PMMA	The mechanical behavior of PMMA improved because of TiO_2 reinforcement[52] Better modulus and strength along with improved ductility with well-dispersion nano-ZrO_2 particles[52]	Good aesthetics and biocompatibility. Easy to process and repair[53]	Poor strength and fracture resistance, radio-opacity behavior, and prone to microbial adhesion[43,54-56]
CERAMICS (Ex: Glass-ceramic, Aluminium Oxide-Al_2O_3, ZrO_2)	Nano zirconia ceramics give increased fracture toughness and hardness[57] High corrosion resistance, translucency, and fracture toughness with glass-ceramics of nanosized grains[58]	Good color, high strength, low electrical and thermal conductivity[59]	Brittle with low ductility[59]
METALS (Ex: Cobalt Chrome-CoCr, Cobalt-Chrome-Molybdenum-CoCrMo, alpha-beta Titanium alloy-Ti_6Al_4V	Metals in nanoparticle form and promote osteoblast adhesion, differentiation, proliferation, and mineralization[60-62]	Ti alloy: provides high strength, lightweight, low density with other desirable mechanical properties. CoCr: provides high wear resistance, strength, and less cutting of tooth structure is required. Good biocompatibility. CoCrMo: High gloss with anti-plaque adhesion properties, good ductility	CoCr alloys can result in sensitivity symptoms. There is scope for improvement in the corrosion resistance properties and biocompatibility of Ti and CoCrMo nanophase metals

Fig. 2 Nano-toothbrush with gold, silver, and charcoal particles incorporated.[75]

Akkus *et al*. proved that adding Aluminium oxide (Al_2O_3) nanoparticles to Zinc polycarboxylate cement increased the microhardness and the contact angle.[70] With the addition of nano-hydroxyapatite/fluorapatite to glass ionomer cement, the new materials demonstrated a rise in tensile, compressive, and biaxial flexural strength compared to traditional ones thereby reducing the frequency of treatment.[71,72] An upgrade in tribological properties was seen in the new resin nanoceramic Computer-aided design and computer-aided manufacturing (CAD/CAM) blocks. The Lava^{TM} ultimate resin nanoceramic blocks were manufactured by 3M^{TM} Envision Schools Project Exchange (ESPE), an online workspace to create an open-standard software platform to be used across a range of dental applications that gave better aesthetics and lasted much longer.[73] The blocks made from nanoceramics incorporated with highly cured resin can be modified and customized with ease post milling.[74]

2.4. Nanotechnology in Restorative Dentistry

Nanotechnology has been implemented to develop nano dental composites, glass-ionomer cement, and endodontic sealers for tooth regeneration.

2.4.1 Nanocomposites

Nanocomposites were first brought into usage because of the persistent and dissuading problems of low strength, microhardness, polymerization shrinkage, and wear resistance, properties that are vital in occlusal applications.[76] After the advent of nanotechnology in dentistry, composite fillings became an essential piece in restorative dentistry. Resin-based composites in particular have seen great research and development in the past decade. Nanotechnology has encouraged the usage of nanofillers. Currently, the research is focused on polymerization shrinkage, microhardness, and wear resistance along with good aesthetics.[77,78]

Nanocomposites possess good translucency, surface finish, and contouring, and can restore damaged or lost dental tissues. Fig. 3 illustrates the pre-composite and post-composite clinical application of white tooth-colored nanocomposite material for restoration. Adding monovinyl methacrylate to dental resins enhances mechanical properties and polymerization kinetics. These dental resins, also known as ultra-rapid monomethacrylates, are made of secondary and tertiary functionalities like urethanes, carbonates, or cyclic carbonates. Further investigation is being conducted to test the addition of acidic functional groups to monomers.[79]

Fig. 3 Clinical applications of white tooth-colored nanocomposite material for restoration a. pre composite b. post composite.

2.4.2 Nano glass ionomers

The retention of restorations on the teeth prepared is a primary function of dental cement. No cement can fulfill all required applications and so a variety of cement is used and their properties are manipulated to fit the requirements. For permanent restorations of crowns and bridges, long-term cementation is necessary. Compomers, zinc phosphate, zinc polycarboxylate, glass ionomers, and hybrid ionomers are some strong cement applied for long-term cementation.[81,82] Glass ionomers are widely accepted for their biocompatibility, fluoride release, and chemical bonding to the tooth structure. However, they have disadvantages such as poor aesthetics, mechanical properties, prolonged setting reaction, and weaker bond strength.[83] To overcome these shortcomings and improve the characteristics of glass ionomers, active research on the addition of cellulose fibers, hydroxyapatite and fluorapatite needs to be conducted.[71] In recent times, nanotechnology has been implemented to resin-modified glass ionomers in the form of nanomers and nanoclusters in fluoroaluminosilicate (FAS) glass. These have been found in clinical use since 2007 and they have led to improvements in aesthetics of final restoration and polishability.[84,85]

2.4.3 Endodontic sealers

A bioceramic-based nanomaterial (EndoSequence BC sealer) consisting of calcium phosphate, calcium silicate, calcium hydroxide, zirconia, and a thickening agent has been designed for clinical applications. Nano additives improve physical properties and handling. A nanocomposite structure of hydroxyapatite and calcium silicate is formed during the hydration reaction in the root canal. This hydration reaction and the setting time depend on the amount of water available.[86] The setting time may get prolonged if the canals are overly dried. The nano additives facilitate material delivery from 0.012 capillary needles and adapt to irregular dentin surfaces. It sets and hardens quickly, imparting a good seal and dimensional stability. On setting, hydroxyapatite is formed and it provides bioactivity and compatibility. The high pH of 12.8 has antibacterial properties.[86,87] GuttaFlow Sealer, a commonly used silicon-based sealer contains gutta-percha and silver nanomaterials. It comes in the form of a uni-dose capsule that is mixed and injected.[87] This nano-sealer sets within half an hour and has good biocompatibility and dimensionally stability. It is reported to have raised the sealing capacity and gives enhanced resistance to bacterial penetration. Antibacterial activity in endodontic sealers is essential from an infection standpoint. In recent times, antibacterial quaternary ammonium polyethylene (QPEI) has been added to pre-existing sealers like AH plus, GuttaFlow, and Epiphany.[88] The QPEI nanoparticles prolong the antibacterial activity without trading off the mechanical properties.[89] QPEI nanoparticles are very stable, leach no by-products to the surroundings, and do not alter biocompatibility while maintaining high antibacterial activity.[88]

2.5. Nanotechnology in periodontics

The development of nanosensors, nano switches, nanopharmaceuticals, and nano delivery systems has contributed significantly to the field of local or targeted drug delivery. To create a novel intrapocket delivery system for periodontal disease treatment, Pinon-Segundo *et al*. developed and characterized triclosan-loaded nanoparticles with the help of an emulsification-diffusion process. Triclosan is a non-cationic antimicrobial agent with high efficacy against various plaque-forming bacteria. Nanoparticles are prepared using poly (D, L-lactide), poly (D, L-lactide-coglycolide), and cellulose acetate phthalate. Poly(vinyl alcohol) acts as a stabilizer. Solid nanoparticles with diameters less than 500 nm are obtained. Triclosan nanoparticles act as a homogeneous polymer matrix-type delivery system with triclosan or the drug molecularly dispersed. The release kinetics show that the depletion zone shifts towards the device center as the drug is released indicating that the release is controlled by the diffusion.[90,91]

Bioactive glasses have found wide acceptance in the treatment of periodontal defects due to their properties of osteoconduction, osteoinduction, and bone regeneration. Bioactive glass in direct contact with periodontal ligament cells gives rise to increased alkaline phosphate activity, cell viability, and proliferation.[92] Further, studying the behavior of cementoblasts in contact with bioactive glass showed increased cell viability and proliferation.[93]

The highest antimicrobial effect (damage to 95% of cells) by affecting the cell membrane of *S. mutans* was observed in biopolymer nano complexes like chitosan nanocomplexes produced with low molecular weight chitosan.[94] Chitosan nanoparticles can be used as delivery vehicles through toothpaste prepared by glutaraldehyde crosslinking with Sodium fluoride (NaF) or cetylpyridinium chloride (CPC) as drugs.[95] Chitosan can also be used to produce anti-sensitive tripolyphosphate nanoparticles that are loaded with oligonucleotide.[96]

3. Future perspectives

Nanotechnology holds an intriguing future with endless potential to revolutionize healthcare. As discussed, there are several pieces of research in Nano dentistry but challenges inevitably arise when it comes to clinical practice. The aim of future studies should be to improve the available technology and enable easier production and implementation.

In the field of orthodontics, tooth-colored shape-memory polymers that move teeth aesthetically are a viable possibility. For cosmetic applications and durability, it has been proposed that pure nanoscale sapphire and diamonds replace outer enamel layers to impart fracture resistance and high strength. Perhaps the most potential development of nano dentistry is the use of nanoparticulate drug delivery systems to treat oral cancer. Dendrimer nanoparticles that are already in use are expected to be further advanced for drug delivery facilitation. A dendrimer can carry a molecule of an anticancer drug that specifically recognizes and targets cancer cells. These nanoparticles show great promise as drug delivery vehicles that can attack tumors with large doses of anticancer drugs. Nanoshells have a metallic outer layer and silica core. By manipulating the layer thickness, beads to absorb infrared light can be created, thereby generating an intense heat capable of killing cancer cells. In the future, the effort should lie in cultivating the positive effects of nanotechnology while reducing the associated toxicity.

4. Conclusions

A large portion of applied nano dentistry is in its initial stages with most research in the elementary phase. However, the pace at which nanotechnology has been advancing is promising and more applications are anticipated shortly. We expect a unique capacity to provide controlled release devices equipped with autonomous operation as per requirement. There are significant challenges from fundamental engineering problems to economic mass production and biocompatibility. The coordination of a large number of independent micrometer-scale devices needs adequate research before implementation. Nano dentistry can change the way we look at oral health care as it can use natural resources more effectively with reduced environmental pollution. Nanoscience is bound to pave the way for futuristic treatments that will impact oral health care and human life profoundly. The concerns of public acceptance, safety, and ethics should be tackled before nanotechnology becomes mainstream in modern medicine.

Conflict of Interest

The authors declare no conflict of interest.

Supporting information

Not applicable.

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