REVIEW PAPER

ROLE OF NANOTECHNOLOGY IN DENTISTRY: A SYSTEMATIC REVIEW

Akanksha Raj[1], Neetha J. Shetty[1], Ali Atif[2]

[1]Manipal College of Dental Sciences, Mangalore, Manipal Academy of Higher Education, India
[2]Faculty of Dental Sciences, King George Medical University, Lucknow, India

ABSTRACT

Nanotechnology involves physical, chemical, and biological properties of nanoscale structures and their components. Nanotechnology is based on the principle of manipulating atoms and molecules one by one, to create usable structures. Many advances in health sciences as well as materials' science, biotechnology, electronic and computer technology, aviation, and space exploration would be possible because of this technology. The objective of the study was to conduct a systematic review of the literature to evaluate the applications of nano-technology in dentistry. Included studies were systematically analyzed based on PRISMA (preferred reporting items for systematic reviews and meta-analyses), and studies were identified based on PICO (glossary of evidence-based terms, 2007): random clinical trials (RCT), which have been published in last 6 years and in English language only. Electronic database search of PubMed, Medline, Cochrane, and clinicaltrials.gov was performed using MeSH terms: nanotechnology, nanotechnology in dentistry, and nanotechnology in dental practice. Articles published between 2014-2020 were reviewed, and were included based on inclusion and exclusion criteria. The authors assessed individual study bias by using Cochrane risk of bias tool to find bias risk assessment. Based on this systematic review of literature, it can be concluded that advancement in nanotechnology has significantly influenced dental disease prevention and therapy.

Key words: nanotechnology, dentistry, nanodentistry.

J Stoma 2023; 76, 2: 136-140
DOI: https://doi.org/10.5114/jos.2023.125012

INTRODUCTION

"Curiosity is the mother of invention", and it holds true in today's modern era of science and technology. Man's quest to create a new technology, which is better and more efficient, has led to the introduction of nanotechnology, a technology that deals with structures ranging in size of 100 nanometers or less in at least one dimension [1].

The term "nano" is derived from a Greek word meaning "dwarf", and first definition of nanotechnology has been introduced by a Japanese scientist, Dr. Norio Taniguchi in 1974. He defined it as a process of separating, consolidating, and deformating materials by one atom or one molecule [2]. The late Nobel Prize winning physicist Richard P. Feynman, contemplated the potential of nano size devices as early as in 1959. In his historic lecture called "There's plenty of room at the bottom", he concluded by saying: "This is a development, which I think cannot be avoided". The term "nanodentistry" was invented by R.A. Freitas Jr in the year 2000.

The basic idea of nanotechnology is to employ individualatoms and molecules to construct functional structures. Nanotechnology has revolutionized all fields from healthcare to engineering into a new archetype beyond traditional, and dentistry is no exception.

JOURNAL OF STOMATOLOGY
CZASOPISMO STOMATOLOGICZNE

Address for correspondence: Neetha J. Shetty, Manipal College of Dental Sciences, Mangalore, Manipal Academy of Higher Education, India, phone: +91-9880858025, e-mail: neetha.rajesh@manipal.edu

Received: 01.04.2021 • Accepted: 18.04.2021 • Published: 10.02.2023

The aim of this systematic review of the literature was to evaluate and summarize the role of nanotechnology in dentistry.

METHODOLOGY

This systematic review was based on PRISMA (preferred reporting items for systematic reviews and meta-analyses).

FOCUSED QUESTION

Does nanotechnology have an effective role in dentistry for management of oral diseases?

SEARCH STRATEGY

The literature was searched systematically, and studies published between June, 2020 to October, 2020 were taken into consideration. Electronic database search of PubMed, Medline, Cochrane, and clinicaltrials.gov were examined holistically. Key words used for the literature search included "Nanotechnology", "Nanotechnology in dentistry", and "Nanotechnology in dental practice". Articles published in last 6 years, i.e., from 2014 to 2020, were reviewed. Additionalmanual search was also conducted by two authors, Akanksha Raj and Ali Atif, for off-line publications. Duplicated and repeated articles were excluded (Figure 1).

INCLUSION AND EXCLUSION CRITERIA

Random clinical trials (RCT) that have been published in last 6 years and were published in English language only.

Exclusion criteria were articles not relevant to dentistry, letters to editor, short or rapid communications, review articles, observational studies, phase I clinical trials, editorials, case reports, articles published before 2014, and articles published in any other language than English.

EXTRACTION OF INFORMATION

Data extraction was performed by review author and an assistant researcher after assessing all selected articles, such as RCT to evaluate biasing risk, and data was extracted using data extraction form.

TABLE 1. The domains for the risk of bias assessment

1. Selection bias	Random sequence generation
	Allocation concealment
2. Performance bias	Done by blinding participants
3. Detection bias	Blinding outcome assessors
4. Attrition bias	Outcome data not complete
5. Reporting bias	Selective reporting of outcome

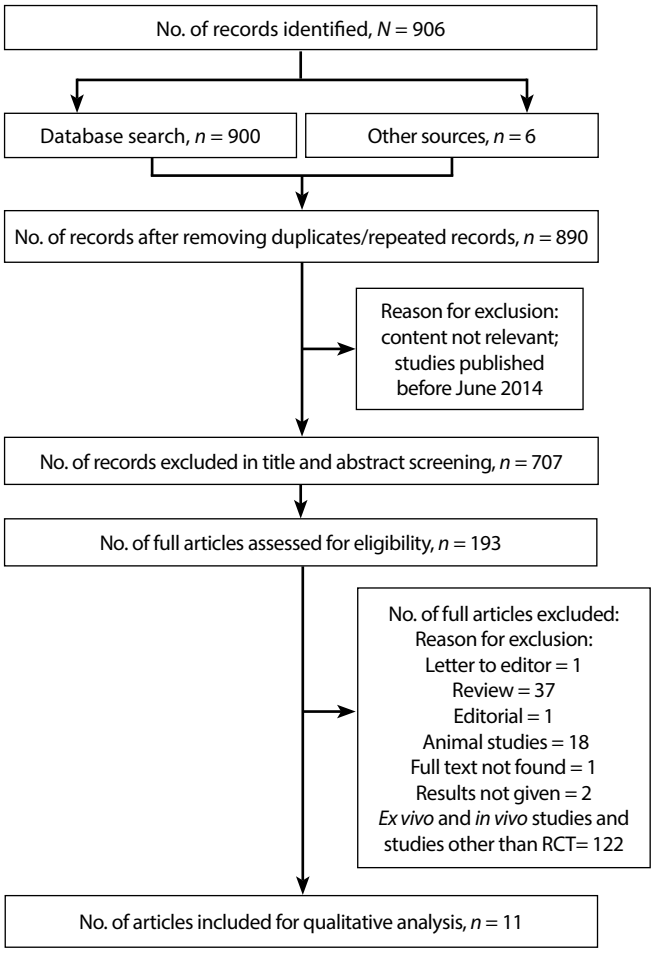

FIGURE 1. Flowchart for the inclusion and exclusion of the articles

RISK OF BIAS ASSESSMENT

Risk of bias assessment was performed according to guidelines issued by Cochrane, and was done under following domains (Table 1). Accordingly, studies were divided into 3 domains (Table 2).

RESULTS

SEARCH RESULTS AND EXCLUDED TRIALS

900 papers were retrieved in initial electronic search, and 6 clinical trials were identified when search was per-

TABLE 2. Criteria for the division of studies based on domain

Good	Low-risk for all domains
Fair	1 or 2 criteria not met, but unlikely to affect quality or outcome of study
Poor	1 or 2 criteria not met and likely to affect quality or outcome of study
	2 or more criteria having high-risk of bias

TABLE 3. Summary of the studies included in the review

Study No.	Authors, year [Ref.]	Study title	Aim of the study	No. of participants	Remarks
1	Vano *et al.*, 2014 [6]	Effectiveness of nano-hydroxyapatite tooth-paste in reducing dentin hypersensitivity: a double-blind randomized controlled trial	To compare the efficacy in reducing dentin hypersensitivity of a dentifrice formulation containing nano-hydroxyapatite with a fluoride dentifrice and placebo	105 cases (age range, 20-70 years)	Nano-hydroxyapatite toothpastes showed re-mineralizing effects comparable to fluoride-containing toothpastes
2	Santos *et al.*, 2014 [7]	A new "silver bullet" to treat caries in children-NSF: a RCT	To investigate the effectiveness of a new anti-caries agent, NSF, applied once a year to arrest caries in children	130 teeth in 60 children (age range, 6-7 years)	NSF has shown to have an effective role in arresting caries when applied once a year. Also, it had an advantage as it did not stain dentinal tubules black
3	Pandit *et al.*, 2015 [8]	The use of nano-crystalline and 2 other forms of calcium sulphate in the treatment of infra-bony defect: a clinical and radiographic study	To evaluate efficacy of three forms of calcium sulphate, i.e. Nanogen (nCS), BoneGen, and Dentogen in treatment of infra-bony defects and to compare their efficacy as substitute to bone graft	45 sites in 60 participants (age range, 20-64 years)	Both Nanogen and BoneGen showed effective results in treatment of infra-bony effects
4	Hegazy *et al.*, 2016 [9]	Peri-implant outcomes with laser versus nano-surface treatment of early loaded implant-retaining mandibular overdenture	To compare peri-implant changes seen with 2 early loading protocols for modifying surface treatment of dental implants – one modifying the collar portion and other modifying the implant surface	36 participants (age range, 47-78 years)	Both laser collar and nano-surface-treated implants showed same peri-implant tissue changes with early loading protocols
5	Wang *et al.*, 2016 [10]	Treatment of dentin hypersensitivity using nano-hydroxyapatite pastes: a randomized three-month clinical trial	To test the three-month desensitizing effect of two protocols using nano-hydroxyapatite formulations compared with Pro-Argin and fluoride varnish	28 subjects with 137 teeth	The tested formulation was effective in reducing DHS over duration of 3 months
6	Freire *et al.*, 2017 [11]	AgNPs: The new allies against *Streptococcus mutans* biofilm: a pilot clinical trial and microbiological assay	To evaluate the anti-microbial properties of a new formulation containing silver nano-particles, named 'nano-silver fluoride' (NSF), to inhibit *Streptococcus mutans* biofilm formation on children's dental enamel	12 schoolchildren, aged between 7-8 years	NSF has bactericidal effect against *S. mutans* biofilm, and it may be used for clinical control and prevention of dental biofilm formation
7	Priyadarshini *et al.*, 2017 [12]	One-year comparative evaluation of Ketac Nano with resin-modified glass ionomer cement and Giomer in non-carious cervical lesions: A randomized clinical trial	The purpose of this study was to evaluate the clinical performance of Ketac Nano (Ketac™ N100), RMGIC (Fuji Filling™ LC), and Giomer (Beautifil® II) in non-carious cervical lesions (NCCLs)	20 subjects	Ketac Nano and RMGIC restorations were better retained in NCCLs, while superior color match and surface finish were observed with Giomer restorations
8	Amaechi *et al.*, 2018 [13]	Clinical efficacy in relieving dentin hypersensitivity of nano-hydroxyapatite-containing cream: a randomized controlled trial	The study aimed to investigate the effectiveness of Apadent Pro (Sangi) nano-hydroxyapatite (nHAP) dental cream to relieve dentin hypersensitivity (DHS) compared with a positive control cream containing 20% pure silica (Silica)	56 participants	20% nHAP dental cream is an effective method to promote the relief in DHS symptoms when applied daily
9	Yaberi *et al.*, 2018 [14]	A comparative study of the effect of nano-hydroxyapatite and eggshell on erosive lesions of the enamel of permanent teeth following soft drink exposure: A randomized clinical trial	To compare the effects of nano-hydroxyapatite or eggshell (ES) extract on the micro-hardness of healthy third molar tooth enamel, following soft drink exposure	10 participants (age range, 18-21 years)	The mean tooth enamel micro-hardness was significantly decreased following exposure to delestre, and the mean micro-hardness of demineralized tooth enamel significantly increased after exposure to both nano-hydroxyapatite and eggshell extract
10	Tripathi *et al.*, 2019 [15]	Comparative cariostatic efficacy of a novel nano-silver fluoride varnish with 38% silver diamine fluoride varnish: a double-blinded randomized clinical trial	To evaluate the clinical cariostatic efficacy of a concocted 5% nano-silver incorporated sodium fluoride (NSSF) dental varnish with 38% silver diamine fluoride (SDF) in preventing the progression of dentinal caries of primary molars	50 children	Annual application of 5% NSSF is better than or equal to 38% SDF in preventing the progression of dentinal caries of primary molars. NSSF does not cause dark staining of dentinal tissue compared to the SDF, and the use of NSSF can be recommended in children
11	Fernando *et al.*, 2019 [16]	Self-assembly of dental surface nano-filaments and re-mineralization by SnF_2 and CPP-ACP nano-complexes	To demonstrate that SnF_2 and CPP-ACP interact to form a nano-filament coating on the tooth surface, and that together they are superior in their ability to promote dental re-mineralization	8 healthy controls; age ranging from 18 to 60 years	The combination of CPP-ACP and SnF_2 in oral care products may significantly improve their efficiency in prevention and treatment of dental caries, erosion, and hypersensitivity

TABLE 4. Results

Study No.	Authors	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting	Overall risk assessment
1	Vano *et al.*, 2014	√	√	√	√	No dropouts	√	Low
2	Santos *et al.*, 2014	√	√	√	√	Sample size adjustment done	√	Low
3	Pandit *et al.*, 2015	√	×	√	√	No dropouts	√	Unclear
4	Hegazy *et al.*, 2016	√	×	×	×	Sample size adjustment done	√	At risk, but unlikely to affect outcomes
5	Wang *et al.*, 2016	√	×	√	√	Sample size adjustment done	√	Unclear
6	Freire *et al.*, 2017	√	√	√	√	×	√	Unclear
7	Priyadarshini *et al.*, 2017	√	√	×	√	Sample size adjustment done	√	Low
8	Amaechi *et al.*, 2018	√	√	√	√	Sample size adjustment done	√	Low
9	Yaberi *et al.*, 2018	√	×	√	√	×	√	Unclear
10	Tripathi *et al.*, 2019	√	√	√	√	Sample size adjustment done	√	Low
11	Fernando *et al.*, 2019	√	√	√	√	Sample size adjustment done	√	Low

√ – done; × – not estimated/not mentioned

formed by review authors manually. In first stage of screening, 194 papers were selected based on the title and abstract. 14 clinical trials were selected, but only 11 were identified for inclusion, as for 2 clinical trials data was insufficient due to results not given and for 1 clinical trial, full text could not be found. 38 review articles, 18 animal studies, and 1 letter to editor, along with 1 editorial were excluded. *In vitro* studies and *ex vivo* studies were also excluded. Summary of studies are presented in Table 3.

Risk of bias assessment was also performed according to guidelines given in Cochrane handbook, and results are presented in Table 4.

DISCUSSION

Nanotechnology has an effective role in the management of the following oral diseases:

1. A study evaluating effectiveness of nano-hydroxyapatite (nHA) toothpaste in reducing dentinal hypersensitivity problem was conducted, and results showed that nHAP toothpastes had better re-mineralization effects than fluoridated toothpastes [6]. Other study showed that 20% nHA toothpaste or dental cream has an effective role in treating dentinal hypersensitivity when applied daily [10].
2. In a double-blinded randomized controlled clinical trial conducted on 20 teeth of 10 patients of age 18-21 years, showed that 10% of nHA solution has an effective role in increasing micro-hardness of enamel in permanent teeth, following exposure to soft drinks [14].
3. A study done on 159 lesions in 50 children of age 6-10 years concluded that effect of applying 5% nano-silver fluorides annually has same effect as that of 38% silver diamine fluoride in prevention of caries progression in primary molars, and also concluded that its' application does not stains dentinal tubules [7].
4. In cross-over clinical trials, nano-sodium fluoride (nNaF) can be used as an anti-biofilm, as it has proven to have bactericidal effects against *Streptococcus mutans*. Hence, nNaF can be used in clinical control as well as in prevention of oral biofilm formation [11].
5. Nanogen and BoneGen TR can be used to treat infrabony periodontal defects as stated by authors, who conducted their study on 16 individuals in age range of 20-64 years [8].
6. Nano-surface-treated implants: Results have shown that no statistically significant difference was found when comparing laser collar and nano-surface-treated implants in terms of PD, including probing depth, modified bleeding index, and assessment of implant mobility at different follow-up intervals. Amount of bone loss observed was consistent with peri-implant tissue stability observed at 12 months. Also, bone loss had not caused any implant mobility [9].

LIMITATIONS

For the present systematic review, articles published in English language only were considered, which may lead to biasing in results and interpretations.

Due to non-availability of sufficient number of clinical trials, effective assessment of various interventions could not be done.

CONCLUSIONS

It can be concluded that nanotechnology has a pivotal role in prevention and management of oral diseases. The use of nanotechnology in treatment of dental diseases has been extended to treat dentinal hypersensitivity, dental tissue re-mineralization, treatment of dental implant's surface, prevention of formation of oral biofilm, and prevention of progression of dental caries [17]. Nanotechnology in dentistry may have an important role in maintaining oral health, but the risk and toxicity associated with these nano-therapeutics may need extensive research for better understanding [18, 19].

CONFLICT OF INTEREST

The authors declare no conflict of interest.

References

1. Kovvuru SK, Mahita VN, Manjunata BS, Babu BS. Nanotechnology: the emerging science in dentistry. J Orofac Res 2012; 2: 33-36.
2. Kong LX, Peng Z, Li SD, Bartold PM. Nanotechnology and its role in the management of periodontal diseases. Periodontol 2000 2006; 40: 184-196.
3. Wahajuddin XX, Arora S. Superparamagnetic iron oxide nanoparticles: magnetic nanoplatforms as drug carriers. Int J Nanomedicine 2012; 7: 3445-3471.
4. Bhardwaj A, Bhardwaj A, Misuriya A, Maroli S, Manjula S, Singh AK. Nanotechnology in dentistry: present and future. J Int Oral Health 2014; 6: 121-126.
5. Freitas RA Jr. Nanodentistry. J Am Dent Assoc 2000; 131: 1559-1565.
6. Vano M, Derchi G, Barone A, Covani U. Effectiveness of nanohydroxyapatite toothpaste in reducing dentin hypersensitivity: a double-blind randomized controlled trial. Quintessence Int 2014; 45: 703-711.
7. Santos VE Jr, Vasconcelos Filho A, Targino AG, et al. A new "silver-bullet" to treat caries in children–nano silver fluoride: a randomised clinical trial. J Dent 2014; 42: 945-951.
8. Pandit N, Sharma A, Jain A, Bali D, Malik R, Gugnani S. The use of nanocrystalline and two other forms of calcium sulfate in the treatment of infrabony defects: a clinical and radiographic study. J Indian Soc Periodontol 2015; 19: 545-553.
9. Hegazy S, Elmekawy N, Emera RM. Peri-implant outcomes with laser vs nanosurface treatment of early loaded implant – retaining mandibular overdentures. Int J Oral Maxillofac Implants 2016; 31: 424-430.
10. Wang L, Magalhães AC, Francisconi-Dos-Rios LF, et al. Treatment of dentin hypersensitivity using nano-hydroxyapatite pastes: a randomized three-month clinical trial. Oper Dent 2016; 41: E93-E101.
11. Freire PLL, Albuquerque AJR, Sampaio FC, et al. Agnps: the new allies against S. mutans biofilm – a pilot clinical trial and microbiological assay. Braz Dent J 2017; 28: 417-422.
12. Priyadarshini BI, Jayaprakash T, Nagesh B, Sunil CR, Sujana V, Deepa VL. One-year comparative evaluation of ketac nano with resin-modified glass ionomer cement and giomer in noncarious cervical lesions: a randomized clinical trial. J Conserv Dent 2017; 20: 204-209.
13. Amaechi BT, Lemke KC, Saha S, Gelfond J. Clinical efficacy in relieving dentin hypersensitivity of nanohydroxyapatite-containing cream: a randomized controlled trial. Open Dent J 2018; 12: 572-585.
14. Yaberi M, Haghgoo R. A comparative study of the effect of nanohydroxyapatite and eggshell on erosive lesions of the enamel of permanent teeth following soft drink exposure: a randomized clinical trial. J Int Oral Health 2018; 10: 176-179.
15. Tirupathi S, Svsg N, Rajasekhar S, Nuvvula S. Comparative cariostatic efficacy of a novel nano-silver fluoride varnish with 38% silver diamine fluoride varnish a double-blind randomized clinical trial. J Clin Exp Dent 2019; 11: e105-112.
16. Fernando JR, Shen P, Sim CPC, et al. Self-assembly of dental surface nanofilaments and remineralisation by snf2 and CPP-ACP nanocomplexes. Sci Rep 2019; 9: 1285. doi: 10.1038/s41598-018-37580-w.
17. Liao J, Shi K, Ding Q, Qu Y, Luo F, Qian Z. Recent developments in scaffold-guided cartilage tissue regeneration. J Biomed Nanotechnol 2014; 10: 3085-3104.
18. Abou Neel EA, Bozec L, Perez RA, Kim HW, Knowles JC. Nanotechnology in dentistry: prevention, diagnosis, and therapy. Int J Nanomedicine 2015; 10: 6371-6394.
19. Narang RS, Narang JK. Nanomedicines for dental applications-scope and future perspective. Int J Pharm Investig 2015; 5: 121-123.