Nanotechnology: A New Strategy to Treat Dental Hypersensitivity

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Abstract

Dental Hypersensitivity is the most commonly encountered dental problems associated with short, sharp pain rising from exposed dentine in response to stimuli such as tactile, osmotic and chemical. Hypersensitivity may present on several teeth, in one area of the mouth, or on one specific tooth. DHS should be differentiated from another tooth sensitivity which may elicit from other clinical conditions such as dental caries, microleakage, cracked tooth or fractured restorations. Several treatment strategies such as desensitization of nerve endings, masking of dentin tubules, occlusion of dentin tubules, and iontophoresis, are prevalent in clinical practices. Stannous ions, most commonly used in toothpastes as stannous fluoride, have been demonstrated to occlude dentine tubules in vitro. SnF2 toothpaste formulations have been used for several decades and are widely accepted as an effective DH treatment. Recently advanced nanotechnology has taken a wide leap in improving the various measures in the treatment of hypersensitivity by its nano particles. Nano structures have superior hardness, elasticity and flexural strength leading to its better application. Biomimetic particles desensitizing effect of nanocrystals which is caused by the progressive closure of the tubular openings of the dentine with plugs. These advancements have progressed the growth in the treatment of Dental Hypersensitivity and have evoked a great amount of attention for improving disease prevention.

Keywords: *Dental Hypersensitivity, Nanotechnology, Stannous Fluoride, Biomimetic Particles.*

Introduction

Dentine hypersensitivity (DHS) is one of the most commonly encountered dental problems. It is characterized by short, sharp pain arising from exposed dentine in response to stimuli, typically thermal, evaporative, tactile, osmotic or chemical and which cannot be ascribed to any other dental defects or pathology [1]. Dentinal hypersensitivity is defined as an exaggerated response to a stimulus that usually causes no response in a healthy tooth & also an exaggerated response to a non-harmful stimulus which evoke pain without causing pathologic alteration to the dentin-pulpo complex. A modification of this definition is usually recommended by the Canadian planning board on Dentinal hypersensitivity in 2003 which suggested that disease should be substituted for pathology. The definition provides the clinical description of the condition & identifies Dentinal hypersensitivity as a distinct clinical identity [2–4]. Others terms to explain DH are created by substituting the word dentinal, adding site descriptors, like cervical or root, and mixing this with either hypersensitivity or sensitivity.

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Hypersensitivity may present on several teeth, in one area of the mouth, or on one specific tooth [5,6]. DHS should be differentiated from another tooth sensitivity which may elicit from other clinical conditions such as dental caries, microleakage, cracked tooth or fractured restorations [3]. The clinical management of DHS has been a challenge for clinician, various treatment modalities are available, but the success of any sound treatment plan is depended on taking a detailed clinical and dietary history, differentially diagnose the condition from other dental pain conditions and identify and manage etiological and predisposing factors[6–9]. Despite the existence of those different terms, various authors prefer the term DH, commonly used and accepted for several decades, to explain a selected painful condition of teeth, which is distinct from others sorts of dentinal pain having different aetiologies.

Prevalence and epidemiology

Various studies highlighted the incidence of DHS in major population ranges between 10-30% of the general population and the age range differs from 20-50 years with the peak incidence present at the end of the third decade and reduces during the fourth and fifth decades of life [10–12]. Such variations were performed to the differences in populations, dietaries, and methods of investigations which are usually through patient questionnaires or clinical examinations. The higher incidence is observed in females than in males which may cause hormonal influence and dietary practices [13,14]. In contrary, one study showed no difference in prevalence of dentine hypersensitivity in either gender, suggesting overall that as many males as females are susceptible. The type of teeth most widely involved, canines and premolars of both the arches are the most affected teeth. It was also reported that buccal aspect of cervical area is the commonly affected site [14].

Pathogenesis

It has been reported in the literature that DH develops in two different phases: lesion localization and lesion initiation [15]. Lesion localization occurs by losing the protective covering over the dentin leading to exposure to external environment. It includes reduction of enamel via tooth wearing problems. Another cause for lesion localization is gingival recession which may flow from toothbrush abrasion, tooth preparation for crown, pocket reduction surgery ,excessive flossing or secondary to periodontal diseases [16]. As stated earlier, not all exposed dentine is sensitive. For DH to occur, the lesion localization has got to be initiated. It occurs after the protective covering of smear layer is removed, resulting to exposure and opening of dentinal tubules.

Mechanism of Dentin hypersensitivity

Three major mechanisms of dentinal sensitivity are proposed within the literature (Figure 1):

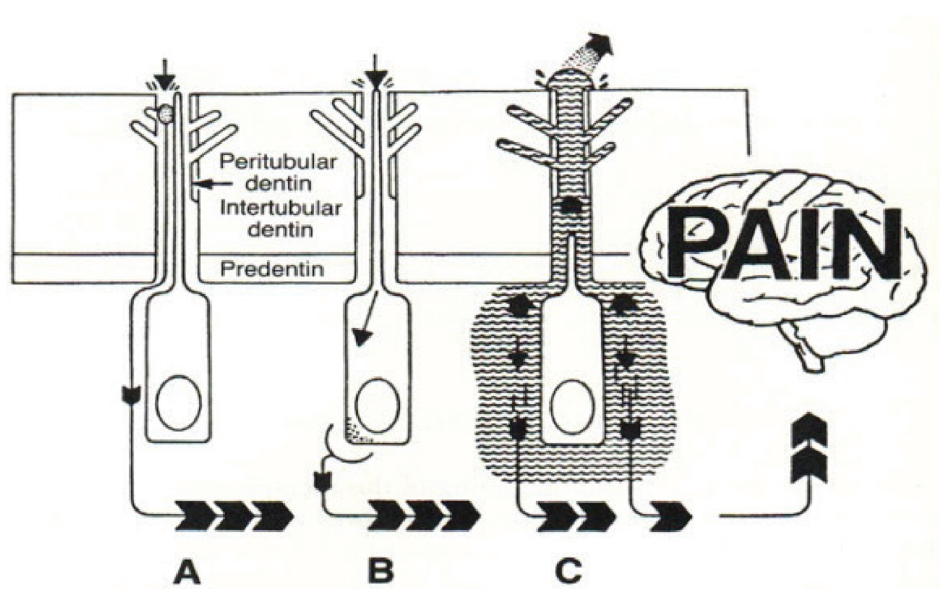

Figure 1. The schematic picture of the proposed theories [16]

- Direct innervation theory
- Odontoblast receptor
- Fluid movement/hydrodynamic theory

As per the direct innervation theory, nerve endings enters through the dentine and hold forth to the dentino-enamel junction [17]. Direct mechanical stimulation of these nerves leads to initiation an action potential. There is no evidence that outer dentin, which is typically the foremost sensitive part, is innervated. Developmental studies have reported that the plexus of Rashkow and intratubular nerves does not establish themselves until the tooth has erupted; whereas the newly erupted tooth is sensitive. Moreover, bradykinin does not induce pain when applied to dentine, and immersing with local anaesthetic solutions shows no signs of prevent pain, which does so when applied to skin.

Odontoblast receptor theory states that odontoblasts acts as receptors and relay the signal to a nerve terminal [18]. But maximum studies have shown that odontoblasts are matrix forming cells and hence they are not considered to be excitable cells, and no synapses are demonstrated between odontoblasts and nerve terminals [3].

Brannstrom (1964) has suggested that dentinal Hydrodynamic theory, proposed by Gysi and explained further by Branstrom[19] remains the most widely credited. Based on this theory, DH reduces with the depletion in fluid flowing within dentinal tubules [20]. Pashley (1986) suggested that DH might be reduced physiologically by the formation of intratubular crystals from dentinal fluids and saliva minerals [21]. Several treatment strategies such as desensitization of nerve endings, masking of dentin tubules, occlusion of dentin tubules, and iontophoresis, are prevalent in clinical practices.

Classification of Desensitizing Agents:

I. Mode of administration

At home desensitizing agents

In-office treatment

II. On the basis of mechanism of action

1. Nerve desensitization

- Potassium nitrate
- Protein precipitation
- Gluteraldehyde
- Silver nitrate
- Zinc chloride
- Strontium chloride hexahydrate

2. Plugging dentinal tubules

- Sodium fluoride
- Stannous fluoride
- Strontium chloride
- Potassium oxalate
- Calcium phosphate
- Calcium carbonate
- Bio active glasses (SiO_2–P_2O_5–CaO–Na_2O)

3. Dentine adhesive sealers

- Fluoride varnishes
- Oxalic acid and resin
- Glass ionomer cements
- Composites
- Dentin bonding agents

4. Lasers

- Neodymium:yttrium aluminum garnet (Nd-YAG) laser
- GaAlAs (galium-aluminium-arsenide laser)
- Erbium-YAG laser

5. Homeopathic medication

- Propolis

At-home therapy:

When the desensitizing tooth pastes were presented on the market for the first time were those which contained strontium salt and fluoride that had the property to occlude dentinal tubules, whereas those which contained formaldehyde, destroy vital elements inside the tubules. A t the present moment most of the desensitizing toothpastes contain potassium salts such as potassium chloride, and potassium nitrate [22]. The studies have revealed that potassium salts move along the dentinal tubules by blocking the axonic action of the intra-dental nerve fibres which reduces the excitability of the tooth [4].

Mouthwashes and chewing gums:

Findings reported that mouthwashes which consisted of potassium nitrate and fluoride reduce DH. A few studies on the chewing gums containing potassium chloride has been reported fair but not much reliable. About 2-4 weeks after at- home therapies, the degree of DH would be reinvestigated. If the pain still existed, the patient should start the next phase of the therapy; in-office therapy [23].

In-office therapy:

Theoretically, in-office therapy of DH should cause prompt relief of the pain. Classification of various types of clinical desensitizing agents depend upon their mechanism of action and includes occluding dentinal tubules and disturbs the transmission of nerve impulses.

Management of Dentine Hypersensitivity focuses on two approaches: occluding dentine tubules or blocking impulse transmission in dentinal nerves. The former depends on ingredients that form hard deposits which partially occlude dentine tubules so external stimuli do not produce substantial shifts within fluid movement. Such agents include strontium or stannous salts, arginine plus insoluble calcium salts. Blocking of impulse transmission has been achieved by potassium ion; however, repeated administration appears to be required before symptomatic relief occur.

Short-term studies have always been positive for SnF2 toothpastes applied using the focused brushing technique, with many demonstrating clinical efficacy versus a control toothpaste.

According to a randomized clinical study conducted by Jonathan et al, DH was assessed using evaporative (Schiff scale) and tactile (Yeaple probe) stimuli. Participants applied toothpaste to two sensitive teeth by fingertip (60 s each); DH was re-assessed, prior to brushing. Test treatment participants brushed their sensitive teeth, with all participants then brushing all teeth for ≥60 s, twice daily for 3 days. DH was re assessed. Data were analysed by study and the pooled analysis indicated test treatment significantly reduced DH versus control, Studies indicated that single, fingertip application of a SnF2 toothpaste reduced DH and provides relief increased over 3 days. Stannous ions, most commonly used in toothpastes as stannous fluoride, have been demonstrated to occlude dentine tubules in vitro. SnF2 toothpaste formulations have been used for several decades and are widely accepted as an effective DH treatment [24].

Recent Advances

Nanotechnology (Nanohydroxyapatite Crystals): Recent Advancement in Treatment of Dentinal Hypersensitivity

Norio Taniguchi in 1974 First elucidated, “Nanotechnology mainly consists of the processing of separation, consolidation, and deformation of material by one atom or one molecule” [25].

Nanotechnology has achieved a phenomenal progress in the last several decades. These are those materials with parts less than 100 nm in at least one dimension, which included clusters of atoms, fibres those are less than 100 nm diameter, grains less than 100 nm in size, films less than 100 nm in thickness, composites and nanoholes. They have evoked a great amount of attention for improving disease prevention, treatment and diagnosis. The definition provided by the National Nanotechnology Initiative, nanotechnology proposed specific phenomena and manipulation of materials over the nanoscale [26]. Nanotechnology, it is the research and production of materials, devices and systems exhibiting physical, chemical, and biological properties which varies from those on a larger scale [25].

Freitas in 2000 proposed the term nano dentistry and stated that “new treatment opportunities, permanent hypersensitivity cure, complete orthodontic realignments during a single office visit, covalently bonded diamondized enamel and continuous oral health maintenance through the use of mechanical dentirobots” [25].

Properties of Nanoparticles:

1. Particles have significant surface, size and quantum effects.

2. They have special properties, including chemical, magnetic, optical and electro-optical properties, which are different from those of individual molecules or bulk species.

3. Nanostructured materials are the development of self-building an autonomous organization of components into various patterns without human intervention [12].

Fabrication Techniques:

In 'top - down' techniques, the micro-nano dimensions of the hydroxyapatite are obtained by milling larger particles of commercial synthetic hydroxyapatite. Only recently, the development of nanotechnologies has opened new opportunities in obtaining cheap HA micro-nanoparticles using the ''bottom up'' methods, in order to improve the biological responses of natural HA. The bottom-up fabrication technique has been summarized in Figure 2.

Various Nanostructures[25]

1. Nanopores

2. Nanotubes

3. Quantum dots

4. Nano shells

Gary and Leinfelde (2009) have summarized the types of nanoparticles in composite resins as below[26]

Type I: Subtype A: Nanometric particles disseminate as a single unit within the resin matrix.

Type I: Subtype B: Comprises of agglomerated cluster of nanoparticles.

Type II: Consists of cage like formation that is composed of 8 silicon atoms and 12 oxygen atoms.

Characteristics of nanofillers in dental composites make the nanocomposites superior to the traditional composites and blend with natural tooth structure far better.

1. Superior hardness

2. Superior flexural strength

3. Superior modulus of elasticity

4. Superior translucency, excellent colour density, high polish, esthetical appeal and polish retention

5. About 50% depletion in filling shrinkage

6. Good handling properties

Nano-resins are "utility in fielder" with ability to move over the walls of the cavity preparation, dampen the surface of dentine to assure good adaptation. These materials are often used as sealants and also as cement for thin staked porcelain veneers. Septodont's N'Durance- Dimer flow is a latest flowable composite, which features unique chemistry and nanotechnology formulation. They have less shrinkage with simple handling and is a very aesthetic material.

Nanotechnology in Dentistry:

Teeth Remineralization by Nanotechnology:

Hydroxyapatite Ca10(PO4)6(OH)6 building block of enamel, are the most constituent of dental tissues representing in enamel and dentin 95% - 97% wt. and 75 % respectively and responsible for mechanical behaviour of dental tissues. Hydroxyapatite (HA) is the most stable form of calcium phosphate. Enamel prismatic HA crystals consist of a weaving of prisms ranging from 3 to 5 µm in diameter. A single prism reveals a highly organized array of fastened needle like HA crystallites (approximately 30 nm thick, 60 nm wide and numerous mm long). Unlike bone, in enamel and dentine when HA is dissolved or abraded, it cannot spontaneously remineralize because enamel is bereft of deprived of regenerative cells and contrarily dentine apposition occurs only towards the pulp tissues [27].

Biogenic Hydroxyapatite V/S Biomimetic Synthetic:

Hydroxyapatite (Nanohydroxyapatite)

Biogenic carbonate hydroxyapatite (CHA) nanocrystals, constituents' mineral phase of calcified tissues like bone, dentin and enamel. They comprise of 4-8 wt.% of carbonate anions, which is approximately

25 nm wide, 60 nm in long and 2-5 nm thick. They exhibited a nonstoichiometric composition and have considerable low degree of crystallinity. Synthetic biomimetic CHA nanocrystals are similar to biogenic CHA nanocrystals. Biomimetic CHA nanocrystals are synthesized, comprising 4 ± 1 wt.% of carbonate ions, mostly 100 and 20 nm in size with a plate and acicular morphology respectively. They are stoichiometric in large amount of Ca/P molar ratio of about 1.6-1.7 [28]. Synthetic bioresorbable biomimetic hydroxyapatite nano and micro crystals provides good properties like bone filler biomaterial, such as bioactivity, osteoconductive, biocompatibility, direct bonding to bone, etc., exciting new applications of HA in the fields of bone tissue engineering and orthopaedic therapies.

Presently, synthetic CHA biomimetic nanocrystals proven to produce, In Vitro, re-mineralization of the altered enamel surfaces and closure of dentinal tubules, thus providing a prospective use in desensitizing dentifrices. Hefferren et al. have suggested that, increased

re-mineralization occurs frequently with apatite particles sizes <4 μm [29]. There is a potentially desensitizing effect of biomimetic CHA nanocrystals, is caused by the progressive closure of the tubular openings of the dentine with plugs within a few minutes until the regeneration of a mineralized layer has occurred within a few hours. Natural hypersensitive teeth have 8 times higher surface density of dentinal tubules and diameter with twice as large than non-sensitive teeth [14]. Reconstructive dental nanorobots, using native biological materials, could selectively and precisely occlude specific tubules within minutes, offering patients a quick and permanent cure [30]. Field Emission Scanning Electron Microscope (FE-SEM) observation of the nano-HAP-treated dentine surface showed that nano-HAP uniformly occluded the dentinal tubules with a dentinal plug and a protective layer on the surface of the dentine was also formed [31].

Challenges Faced by Nanodentistry:

• Accurate positioning and assembly of molecular scale part

• Economical nanorobot mass production technique

• Biocompatibility

• Simultaneous coordination of activities of large numbers of independent micron-scale robots

• Social issues of public acceptance, ethics, regulation and human safety

Conclusion

Dentinal hypersensitivity is a relatively common and significant dental problem which can be successfully managed by a very wide variety of procedures, agents and formulations applied locally either "in office" or "at home". These hydroxyapatites are surface nanostructured and have higher surface area and consequently higher reactivity, allowing them to bind to enamel and dentine apatite producing a biomimetic coating on enamel, contrasting plaque formation and sealing dentine tubules and annulling hypersensitivity. Advancements in the management of dental hypersensitivity is slowly taking a new step into technological development.

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Conflict of Interest - NIL

References

1. Dowell P, Addy M. Dentine hypersensitivity--a review. Aetiology, symptoms and theories of pain production. *J Clin Periodontol*. 1983;10(4):341-350. doi:10.1111/j.1600-051x.1983.tb01283.x
2. Mantri V, Maria R, Alladwar N, Ghom S. Dentin Hypersensitivity: Recent Concepts in Management. Kailasam S, ed. *JIAOMR*. 2011; 23:115-119. doi:10.5005/jp-journals-10011-1108
3. Miglani S, Aggarwal V, Ahuja B. Dentin hypersensitivity: Recent trends in management. *J Conserv Dent*. 2010;13(4):218-224. doi:10.4103/0972-0707.73385
4. Davari A, Ataei E, Assarzadeh H. Dentin Hypersensitivity: Etiology, Diagnosis and Treatment; A Literature Review. *J Dent (Shiraz)*. 2013;14(3):136-145.
5. Renton T. Dental (Odontogenic) Pain. *Rev Pain*. 2011;5(1):2-7. doi:10.1177/204946371100500102
6. Lin YH, Gillam DG. The Prevalence of Root Sensitivity following Periodontal Therapy: A

Systematic Review. *Int J Dent*. 2012; 1(1):1-12. doi:10.1155/2012/407023

7. Porto ICCM, Andrade AKM, Montes MAJR. Diagnosis and treatment of dentinal hypersensitivity. *J Oral Sci*. 2009;51(3):323-332. doi:10.2334/josnusd.51.323
8. Dowell P, Addy M, Dummer P. Dentine hypersensitivity: aetiology, differential diagnosis and management. *Br Dent J*. 1985;158(3):92-96. doi:10.1038/sj.bdj.4805542
9. Holland GR, Narhi MN, Addy M, Gangarosa L, Orchardson R. Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *J Clin Periodontol*. 1997;24(11):808-813. doi:10.1111/j.1600-051x.1997.tb01194.x
10. Flynn J, Galloway R, Orchardson R. The incidence of "hypersensitive" teeth in the West of Scotland. *J Dent*. 1985;13(3):230-236. doi:10.1016/0300-5712(85)90004-1
11. Irwin CR, McCusker P. Prevalence of dentine hypersensitivity in a general dental population. *J Ir Dent Assoc*. 1997;43(1):7-9.
12. Bartold PM. Dentinal hypersensitivity: a review. *Aust Dent J*. 2006;51(3):212-218; quiz 276.
13. West NX, Sanz M, Lussi A, Bartlett D, Bouchard P, Bourgeois D. Prevalence of dentine hypersensitivity and study of associated factors: a European population-based cross-sectional study. *J Dent*. 2013;41(10):841-851. doi:10.1016/j.jdent.2013.07.017
14. Addy M, Mostafa P, Newcombe RG. Dentine hypersensitivity: the distribution of recession, sensitivity and plaque. *J Dent*. 1987;15(6):242-248. doi:10.1016/0300-5712(87)90045-5
15. Orchardson R, Gillam DG. Managing dentin hypersensitivity. *J Am Dent Assoc*. 2006;137(7):990-998; quiz 1028-1029. doi:10.14219/jada.archive.2006.0321
16. Dababneh RH, Khouri AT, Addy M. Dentine hypersensitivity - an enigma? A review of terminology, mechanisms, aetiology and management. *Br Dent J*. 1999;187(11):606-611; discussion 603. doi:10.1038/sj.bdj.4800345
17. Gillam D, Chesters R, Attrill D, et al. Dentine hypersensitivity--guidelines for the management of a common oral health problem. *Dent Update*. 2013;40(7):514-516, 518-520, 523-524. doi:10.12968/denu.2013.40.7.514
18. Irvine JH. Root surface sensitivity: a review of aetiology and management. *J N Z Soc Periodontol*. 1988;(66):15-18.
19. Brännström M, Lindén LA, Aström A. The hydrodynamics of the dental tubule and of pulp fluid. A discussion of its significance in relation to dentinal sensitivity. *Caries Res*. 1967;1(4):310-317. doi:10.1159/000259530
20. Pereira JC, Segala AD, Gillam DG. Effect of desensitizing agents on the hydraulic conductance of human dentin subjected to different surface pre-treatments--an in vitro study. *Dent Mater*. 2005;21(2):129-138. doi:10.1016/j.dental.2004.02.007
21. Pashley DH. Dentin permeability, dentin sensitivity, and treatment through tubule occlusion. *J Endod*. 1986;12(10):465-474. doi:10.1016/S0099-2399(86)80201-1
22. Cummins D. Recent advances in dentin hypersensitivity: clinically proven treatments for instant and lasting sensitivity relief. *Am J Dent*. 2010;23 Spec No A:3A-13A.
23. Gillam DG, Seo HS, Bulman JS, Newman HN. Perceptions of dentine hypersensitivity in a general practice population. *J Oral Rehabil*. 1999;26(9):710-714. doi:10.1046/j.1365-2842.1999.00436.x
24. Creeth J, Maclure R, Seong J, et al. Three randomized studies of dentine hypersensitivity reduction after short-term SnF2 toothpaste use. *J Clin Periodontol*. 2019;46(11):1105-1115. doi:10.1111/jcpe.13175
25. Kampschulte M, Langheinirch AC, Sender J, et al. Nano-Computed Tomography: Technique and Applications. *Rofo*. 2016;188(2):146-154. doi:10.1055/s-0041-106541
26. Dang Y, Zhang Y, Fan L, Chen H, Roco MC. Trends in worldwide nanotechnology patent applications: 1991 to 2008. *J Nanopart Res*. 2010;12(3):687-706. doi:10.1007/s11051-009-9831-7
27. Roveri N, Foresti E, Lelli M, Lesci I. Recent Advancements in Preventing Teeth Health Hazard: The Daily Use of Hydroxyapatite Instead of Fluoride. *BIOMENG*. 2009;2(3):197-215. doi:10.2174/1874764710902030197
28. Orsini G, Procaccini M, Manzoli L, Giuliodori F, Lorenzini A, Putignano A. A double-blind randomized-controlled trial comparing the desensitizing efficacy of a new dentifrice containing carbonate/hydroxyapatite nanocrystals and a

sodium fluoride/potassium nitrate dentifrice. *J Clin Periodontol*. 2010;37(6):510-517. doi:10.1111/j.1600-051X.2010.01558.x

29. Hefferren JJ. A laboratory method for assessment of dentrifrice abrasivity. *J Dent Res*. 1976;55(4):563-573. doi:10.1177/00220345760550040301

30. Kunam D, Manimaran S, Sampath V, Sekar M. Evaluation of dentinal tubule occlusion and depth of penetration of nano-hydroxyapatite derived from chicken eggshell powder with and without addition of sodium fluoride: An in vitro study. *J Conserv Dent*. 2016;19(3):239-244. doi:10.4103/0972-0707.181940

31. Saravana KR, Vijayalakshmi R. Nanotechnology in dentistry. *Indian J Dent Res*. 2006;17(2):62-65. doi:10.4103/0970-9290.29890