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Review Article

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The Effectiveness of Nanomaterials in the Management of Dentine Hypersensitivity-A Review

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Abstract

Dentin hypersensitivity [DH] associated with short sharp pain is a public health concern with a dire consequence to good oral health hygiene. Although different materials and desensitizing toothpastes have flooded the market with claim to provide relief for DH patients by occluding patent dentinal tubules, their occluding abilities have been limited. As such, a new strategy it's required to effectively manage DH. The use of nanomaterial for dentinal tubules occlusion is predicted to revolutionize the treatment of DH. This article aimed to review the effectiveness of nanomaterials in the management of DH.

Keywords: Dentin Hypersensitivity, Desensitizing Toothpastes, Occlusion, Nanomaterials

Introduction

Dentin Hypersensitivity [DH] is a common occurrence and under extreme conditions when dentine is exposed to the oral cavity patients will experience a short, sharp pain [1-3]. Clinically, patients become more susceptible to external stimuli such as thermal, tactile, osmotic or chemical changes due to open dentinal tubules. More worrisome is that [DH] if left untreated will negatively affect the quality of life the patients [4-6]. In particular, and as pointed out, DH sufferers tend to modify their habits by eliminating certain foods and drinks from their regular diets and they become non-complaint with specific at-home care recommendations such as tooth brushing. They further noted that there is a higher accumulation of dental plaque in patients that are non-compliant with specific at-home care recommendations from their oral care providers. Consequently, caries formation, gingival inflammation and periodontal problems are likely to increase. Given the negative consequence of DH conditions to dental patient's oral health care and hygiene, it is highly sensible to understand the factors that could contribute to the onset of DH. These are highly imperative in order to formulate the best oral health care strategy that would improve the overall quality of life of dental patients.

An Etiology, Histopathology and Management of DH

Dentin Hypersensitivity [DH] primarily develops in two phases, namely: lesion localized and lesion initiation. Studies by, and mooted that lesion localization occurs by loss of protective covering over the dentin [7-9]. They, together with other authors, have elaborated that the dentin covering enamel can be lost through attrition, abrasion (Figure 1A), erosion (Figure 1B), and abreaction [10-12]. Other causes for enamel loss include gingival recession, which can be due to toothbrush abrasion, pocket reduction, toting preparation for crown, excessive flossing or secondary periodontal diseases. The aforementioned authors, however, acknowledged that for DH to occur, the lesion localization has to be initiated.

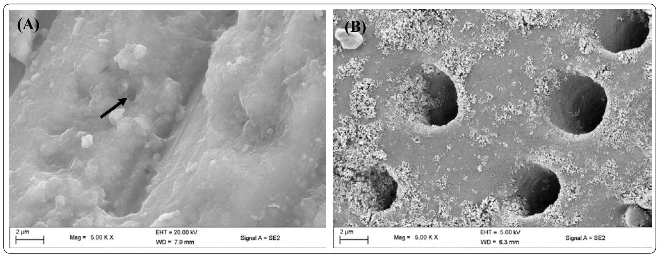

Figure 1: Representative SEM micrograph for (A) Dentine surface abraded with silicon carbide paper for 60s; (B) pre-treatment of dentine surface exposed 1wt. % citric acid solution for 30min. (Original magnification x 5000). Arrows pointing to exposed tubules.

Histopathology of DH

Typically, the human tooth dentin is a hydrated Nano-composite that comprises of hydroxyapatite [$(Ca_2(PO_4)_6(OH)_2)$] mineral crystallite with thickness of (~ 5nm) and (~ 45% by volume) distributed in a scaffold of type 1 collagen fibrils (~ 50-100nm diameter) and about 20% fluid [13-15]. From an anatomical context, dentin consist of microscopic dentinal tubules that are about 2-4 µm in diameter (Figure 2) [16-19]. Literature suggested that for DH to be initiated, the dentinal tubule must be exposed to the external environment, which is caused by the removal of the protective smear layer covering the tubule. Notably, SEM studies have shown that tubules in exfoliated teeth (sensitive tooth) are eight times more numerous, twice larger in diameter and are open, whereas tubules in non-sensitive tooth are less numerous, smaller, and usually blocked [8, 20, 21].

Understanding how DH is initiated is therefore imperative to develop an effective strategy to mitigate and management its onset. In these end, several hypotheses have postulated in the past decades that explain the mechanism of DH. Currently, the hydrodynamic theory is most extensively used to explain the mechanism of DH [22]. The hydrodynamic theory is premise on the principle that any decrease in dentinal fluid movement should result in reduction of DH [23]. Thus, and as observed by, the most effective strategy in the management of DH is to effectively occlude the dentinal tubules to prevent fluid flow. Bearing these in mind, advocated using a desensitizing paste to physically block the exposed dentine tubules [24].

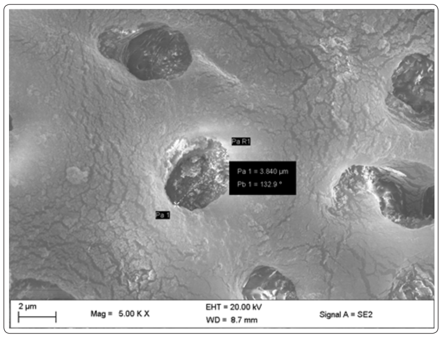

Figure 2: Diameter of open dentin tubules

Management of DH

Traditionally, the first-line of ‘at-home’ treatment is to use over the counter products (OTC) in the form of desensitizing toothpastes noted that these OTC products contain active ingredients that either desensitize the nerve tissue at the base of the dentin tubule or function by promoting dentin tubule occlusion [11, 25, 26]. Over the last decades, the oral care industry have witnessed proliferation of different occlusion materials that claim to occlude open dentin tubules [27]. Among these materials, the use of potassium oxalates, sodium fluoride, strontium salt, amorphous calcium phosphate containing casein phosphopeptide, calcium glycerophosphate, and calcium carbonates (mainly as abrasive agents) have gain significant interest as an occlusion materials [11, 28-31]. Although the aforementioned occlusion materials have been reported to provide some relief to patients, the dentin tubules occluded by some of these materials are reported to be superficial with limited infiltration depth-which could be readily re-exposed in an acidic environment [27, 32].

Furthermore, reported that some common OTC desensitizing pastes (Table 1) that contains above mentioned materials were lacking in terms of their effectiveness in occluding dentin tubules particularly under acidic environment [27]. According to their report, the occlusion abilities of these pastes were easily reopened under erosive attack. The authors concluded that the effectiveness of desensitizing pastes should be in their active ingredients.

Table 1: Common desensitizing tooth paste active ingredients

Product name	Active ingredient	Company
Elmex Sensitive Professional	Pro-Argin, calcium carbonate	GABA
Sensodyne Rapid	Strontium acetate	Glaxo Smith Kline
Sensodyne Repair	Stannous fluoride	Glaxo Smith Kline
BioRepair	Zinc-carbonate hydroxyapatite	Dr. K. Wolff
Colgate Total Sensitive	New silica	Colgate-Palmolive
Dontodent Sensitive	Tetrapotassium pyrophosphate, hydroxyapatite	DM Dogeriemarkt

Given the above drawbacks of many OTC desensitizing pastesto effectively managed DH, literature have assumed that a novel approach in the treatment and management of DH should be the use of various combinations of nanoparticles [32-35]. According to, the idea behind this approach is that nanoparticles can easily penetrate into dentin tubules, which could act as mineralizing agents that block fluid movement within the dentin tubules when combined with various agents [27]. Although there are yet to be established gold standard treatment modalities in the management of DH, the use of tubule blocking agents is a growing area of interest in the healthcare industry as an effective strategy for the management of DH [32]. This review aimed to review the effectiveness of nanomaterials in the management of DH.

Nanomaterials in DH management

In recent years, Nanotechnology particularly as it applies to dentistry “Nano dentistry” has increasingly become a fascinating area of discourse for many researchers. For instance, explicitly noted that the Nano dentistry has the power to completely revolutionize the field of dentistry [35]. The authors predicted that through nanomaterials and manipulating materials at the nanoscale level, painful procedures would become history as nanomaterials could reduce painful dental procedures, help remineralise tooth and associated structures and help maintain oral hygiene. This section illustrates the evidence base for the application of nanomaterials in occluded dentin tubules.

Nanomaterials can be classified according to their dimensions (zero-dimensional, one-dimensional, two-dimensional, and three dimensional) or their structures (Nano pores, Nano tubes, quantum dots, Nano shells, dendrimers, liposomes, Nano rods, fullerenes, Nano spheres, Nano wires, Nano balls, Nano rings, Nano cap etc.) [36]. Revealed that nanomaterials have small size, larger surface area, high surface energy, and large proportional of surface atoms [37, 38]. Owing to these unique properties, literature documented that nanoscale materials have attracted interest as a more efficient method of delivering antimicrobials and demineralization agents into dentinal tubules (Figure 3). The size and reactivity of nanoparticles (NPs) may allow them to be delivered further into dentinal tubules, with an enhanced potential for decontamination, remineralisation and reduced sensitization compared with contemporary treatment regimens [37]. In addition, the solubility and reactivity of NPs are significantly increased because of their high surface energy and a large surface [39]. More so, the large surface area of NPs also provides a high affinity and allows them to easily deposit on irregular spaces [40].

Significantly, Tian and his co-authors speculate that due to the superior dispersion of nanomaterials, it can easily enter dentinal tubules of 2–3 µm [32]. The above claim by the aforementioned authors strongly reinforced the superiority of nanomaterials as prime candidates for dentinal tubule occlusion.

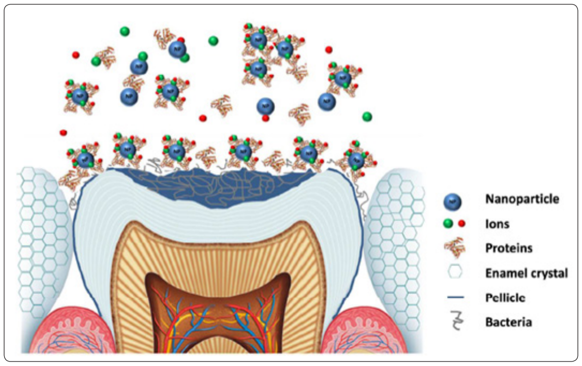

Figure 3: Nanoparticles interaction with tooth surface (Source [Besinis et al., 2015])

Mesoporous silica nanoparticles

In recent time, mesoporous silica nanoparticles (MSNs) have shown promising results as a biomaterial attributed to their stable network structure, large surface area, adsorption performance, thermal, and chemical stability [41]. In terms of the effectiveness of MSNs in occluding dentin tubules, and as highlighted in (Table 2), several studies have been carried out to establish its efficacy as an occluded material either alone or in the modified form with other nanomaterials.

Table 2: Recent studies on MSN occluding abilities

Authors	Particles size	Other materials	Type of study	Model
Tian *et al*. (2014)	50-80nm	Ca^{2+} and PO$_4^{3-}$	In vitro study	Human third molars
Chiang *et al*. (2014)	N/A	Calcium carbonates	In vivo/In vitro study	Animal
Yu *et al*. (2016)	50 nm	Nanohydroxyapatite	In vitro study	Human third molars

In their studies reported on the dentinal tubules occluding abilities of MSNs and or calcium or phosphate modified MSN (Ca^{2+}@ MSN and PO$_4^{3-}$@ MSN) [32]. The authors concluded that MSNs or its modification exhibited superior occluding abilities. It was demonstrated that MSN or Ca^{2+}@MSN and PO$_4^{3-}$@ MS could effectively occlude dentinal tubules at both the exterior open end of dentinal tubules and in the depth of dentinal tubules. Chiang and his co-authors concluded that calcium carbonates (CaCO$_3$) containing MSN mixed with 30% calcium triphosphate (H$_3$PO$_4$) effectively occluded dentin tubules [42]. In a different study, demonstrated that a novel biocompositebased on the medication of nanohdyroxyapatite and mesoporus silica nanoparticles (nHAp@MSN) were highly efficient in occluding dentinal tubule with the occlusion showing a high acid-resistant stability [24]. The authors attributed the acid resistant stability of the bio composite to the unique acid resistance of mesoporous silica. Nevertheless, they noted that intratubular occlusion in the samples treated with MSNsalone were inferior compared to the combination of nHAp@MSN; which they claimed could be washed away be citric acid solution or deionized water. This, they pointed out could be attributed to the particle size differences between the MSNs and nHAp@MSN. More so, it was surmised that the presence of nHAp in the bio composite may lead to favorable blockage insider the tubules which could offer protective effect against acid attack.

Drawing from the above, it is not surprising to note that the synergetic effect of the various nanomaterials reported offers in-depth occlusion and acid resistant stability. This goes a long way in supporting the proposition made by other scholars that the combination of nanomaterials offers better treatment strategy for the management of DH [33, 34].

Nano hydroxyapatites crystals

Nanohydroxyapatie (nHAp) is one of the main structure of the dental hard tissues expressed chemically asCa10 (PO4)6, (OH) 2. According to, the biocompatible and bioactive nature of nanohydroxyatite material has endeared its acceptance in medicine and dentistry [43]. In dentistry for example, Nano hydroxyapatite has been extensively investigated for its demineralization potentials (Table 3). For instance, observed the surface of dentin specimens treated with Nan hydroxyapatite using Field Emission Scanning Electron Microscope (FE-SEM) [44]. Their study revealed 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. Similarly, Tschoppe and his colleague investigated the in vitro effects of Nano hydroxyapatites (nHAp) toothpastes on demineralization of bovine tooth [45]. They observed an increased in demineralization of dentin and enamel with toothpastes containing nHAp compared with amine fluoride toothpastes. Due to the positive occlusion notice in the study, the authors reasoned that nHAp can promote remineralization.

Furthermore, and in a separate study, reported on the occluded potentials of nHAp with or without laser CO2 treatment [46]. The authors concluded that the combination of nHAp paste and a CO2laser of moderate power density occluded the dentinal tubules and reduced the permeability of exposed dentin. In addition, Beglar and his team revealed that pure nHAp as well as combination of nHAp in 1%, 2%, and 3% fluoride exhibited strong resistance to degradation. The authors found that nHAp together with the doped fluoride were strongly effective in covering the dentin surface and also showed plugging effects on the tubules [47].

The above mentioned effectiveness of nHAp in the management of DH is further supported by numerous clinical studies [26, 48-50]. Browning and his team investigated the effect nHAp paste on bleaching-related tooth sensitivity [48]. The authors observe that the use of a toothpaste containing nHAp can decrease tooth sensitivity in individuals undergoing bleaching without any desensitizing agent. Equally, Vano and co-authors reported that nHAp provides quick relief from dentin related sensitivity symptoms which was higher than fluoride containing toothpaste [49]. In another clinical study, assessed the ability of a toothpastes containing nHAp together with potassium nitrate, sodium monoflurophoshate, antioxidants phloretin, ferulic and silymarin in reducing tooth pain associated with DH measured using a visual analog scale (VAS) [26]. The authors speculate that when applied daily, the synergetic effect of nHAp and other mentioned constituents can significantly and quickly reduce DH. It was also found that the outstanding results of speed and effectiveness of the toothpastes was related to the activity of nHAp as well as the antioxidants. In a more recent clinical study, Vano and his team objectively (airblast and tactile test) and subjectively (VAS) measured the effectiveness of the effectiveness of nHAp to occlude dentin tubules. The authors found that that the application of 2% nano-hydroxyapatite was effective desensitizing agent providing relief from symptoms after 2 and 4 weeks [50].

In light of the positive reports from the use of nHAp in dentin treatment, the early prediction of Khetawat and Lodha that in near future new products containing nHAp would be a breakthrough in the treatment of dentinal hypersensitivity resonates further. This, and according to may be related to the high biological activity and reactivity of nHAp which enable it to bind to dentin apatite and infiltrate the dentinal tubules [51, 52].

Table 3: Recent studies on Nano hydroxyapatites occluding abilities

Authors	Type of study	Model
Ohta *et al.* (2007)	*In vitro* study	Human molars
Tschoppe *et al.* (2011)	*In vitro* study	Bovine incisors
Browning *et al.* (2012)	Clinical	Humans
Vano et al. (2014)	Clinical trial	Humans
Al-maliky *et al.* (2014)	*In vitro* study	Human molars
Low et al. (2015)	Clinical trial	Humans
Vano et al. (2018)	Clinical trial	Humans
Beglar et al. (2018)	In vitro study	Human molars

Conclusion

Nano dentistry through the modification and manipulation of nanomaterials presents a potent technology for better and improved oral health care services. This new technology appears to be highly effective in the management of pain associated with dentin hypersensitivity. In particular, the use of mesoporous silica and hydroxyapatite nanomaterial holds the future for effective treatment of DH. In vitro, in vivo and clinical trials strongly support their application in consumer toothpastes formulation.

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