# NANO TECHNOLOGY –A NOVEL APPROACH TO DENTISTRY

Nanotechnology can be defined as a technology that deals with small structures or small sized materials.[44]Nanostruc-tures or nanosized materials can be created by two different strategies. The top down strategy starts normally with a bulk material much larger than “nano”, and then uses externally applied forces (mechanical or other), to break the material down for example into nanoparticles. The bottom up strategy, essentially proposed by Feynman, assembles materials or structures atom by atom or molecule by molecule to obtain the desired result. [45]

Nano materials are defined as a natural, incidental or manufactured material containing particles in an unbound state or as an aggregate or as an agglomerate and where 50% or more of the particles in the number size distribution, one or more external dimensions is in the range 1nm-100nm. The Greek word Nano means dwarf. In science nano refers to one billionth (American scale), denoting a factor of $10^{-9}$.

**Production of Nano particles**

Two methods are involved in the production of Nano particles

Conventional- Emulsification/Lyophilisation

Recent- Communition of Larger particles /grinding technique

**Classification:**

Based on their size the particles are classified as ….

Zero dimensional- Eg:nano particles

One dimensional- Eg:Nano rods

Two dimensional- Eg:Thin films

**MECHANISM OF ACTION**

Surface characteristics of nanoparticles plays a vital role in determining their life span and duration of action during circulation. Nanomaterials used invivo has to undergo surface modification with a hydrophilic and biocompatible coating where ligands may be bound on the surface to promote cellular interactions with its receptors.

| MICROPARTICLE | NANOPARTICLE |
| --- | --- |
| Drug is dispersed in a matrix of a biodegradable polymer and the drug is released through a diffusional mechanism. | Particles have a hydrophilic and biocompatible surface and undergoes cellular penetration. |

## APPLICATIONS OF NANO PARTICLES IN DENTISTRY

### NANO PARTICLES IN DIAGNOSIS

- Drug/Gene delivery
- Fluoroscent labelling for imaging
- Detection of Pathogens
- Probing DNA structure
- Tissue engineering
- Tumour destruction.

Nano particles have advantageous application in biomedicine and it can exist in the form of metals/inorganic/polymeric forms. These nanoparticles can be administered Intravenously and can be distributed to organs and tissues and can also used as diagnostic/imaging agent. Behaviour of Nanoparticles are highly dependant on their physicochemical property. Nanoparticles upon intramuscular administration will immediately react with the blood and may induce agglomeration and sequestration.

### NANO MATERIALS IN PERIODONTICS

Commercially available dental prophylactic products containing biomimetic carbonate hydroxyl apatite nanoparticles have been used to fill microdefects on demineralized enamel or dentin surfaces and proved to be effective *in vitro* after a 10 min application. In bone tissue regenaration currently, nanoscale β-TCP has been used for bone tissue regeneration due to its higher compressive strength, degradation rate, osteoconductivity, and protein absorption compared to submicron β-TCP. Commercially available dental prophylactic products containing biomimetic carbonate hydroxyl apatite nanoparticles have been used to fill microdefects on demineralized enamel or dentin surfaces and proved to be effective *in vitro* after a 10 min application.

NANOMATERIALS IN PROSTHODONTICS

A denture base material of choice made of heat-cured acrylic resin, is cheap, biocompatible with good physicochemical properties and acceptable aesthetics .But its surface porosity makes it prone to plaque accumulation , polymer fatigue failure and oral mucosa irritation. impregnation of metal oxide nanoparticles, such as titanium dioxide or iron (III) oxide has been shown to reduce the porosities of PMMA and bacterial attachment.[30,31,32]Studies reveals that embedded titanium dioxide and silver nanoparticles have reduced the adherence of Candida species on denture resins. Silica nanoparticles treated with 3-methacryloxypropyltrimethoxysilane (MPTS) have led to higher bond strength and better adhesion [15], with MPTS aiding the chemical bonding of silica nanoparticle filler to the resin during curing.94

Titanium alloy and chrome cobalt used in removable partial dentures connectors
and fixed prosthesis such as crowns and bridges. However, they are reported to have poor corrosion resistance, causing tooth mobility due to gingival inflammation.(32.33].It is observed that titanium and zirconia nanoparticles have significantly reduced the number of adherent bacteria.[34]Base metal alloys such as Cobalt and cobalt oxide nanoparticles were also recommended for their bactericidal properties.

To improve implant–bone interconnection quality, including mechanical anchorage and bone remodelling, nanotopographies helps by increasing surface wetness, continuous protein adsorption and the formation of blood components at implant interface.[35]Titania nanosheet structures fabricated on titanium surfaces with coatings of HA and alumina nanoparticles provides good osteointegration. Nanocoating with quercitrin, a natural flavonoid reduces osteoclast activity.[36,37,38]Examples of other nanoparticles, are silver, zinc oxide, copper (II) oxide and chlorhexidine nanoparticles have also been used in dental implants fortheir antimicrobial properties.

NANO PARTICLES IN RESTORATIVE DENTISTRY

GIC

GIC also known as polyalkenoate cements has very unique properties like chemical bonding, biocompatible and presents potential for release and uptake of fluoride ions .But its application as a restorative material is limited due to drawbacks such as low fracture toughness , brittle material leading to early bulk fracture when subjected to tensile stress high rate of occlusal wear when compared to amalgam and modern composite resin systems and so not currently recommended for permanent restorations in posterior teeth endodontic disinfection. Salt- or oxide-based nanoparticles added to GIC make them to react with thepolyacrylic acid in the matrix and increase the overall resistance of the material. Additionally, smaller gic fillers makes them capable of filling up interstitial spaces, thereby strengthening the cement even more.

Addition of Nano hydroxyapetite and Nano fluorapetite particles at an average size of 100–200 nm to the powder component of commercial GIC (5 wt%, Fuji II, GC Corp) had a better effect on both the setting reaction mechanism and the degree of polysalt bridge formation, improving the mechanical properties of the cement after its final set. Bond strength to dentine was also improved in the experimental GIC, which could be due to the formation of ionic and hydrogen bonds between GIC and the tooth structure.

Examples of other Nano particles incorporated in GIC were Chlorhexidine hexametaphosphate (CHX-HMP) which showed fluoride release for up to 33 days.[6]

## NANO COMPOSITES

Resincomposites with filler loading smaller than 100 nm are considered as *nanofill* or *nanocomposite.* Restorative composites containing filler particles smaller than100 nm associated with microfillers (particles larger than 0.1 μm) are hybrid materials and maybe considered as *nanohybrids* The types of nanofillers in dental composites include silica,[7,8] tantalum thoxide,[9] zirconia-silica,[10]alumina,[11]nano-fibrillar silicate [12]and titanium oxide[13]among others. Incorporation of nanofillers are advantageous by reducing polymerization shrinkage, maintaining good handling characteristics and manufacturing costs.[14]

## DENTIN BONDING AGENTS

The ideal dentin bonding agent should provide high and stable mechanical properties to the hybrid layer and should have some level of bioactivity, which would decrease the incidence of pulpal damage and occurrence of secondary caries. Disadvantage with the conventional material is that when a dentin bonding agent is applied ,the filler content of the bonding agent agglomerate and forms clusters which then acts as a screener and prevents resin penetration to the underneath dentin.[15]According to Wagner et al, Dentin bonding agents with nano fillers though agglomerates,they are dispersed throughout the adhesive layer instead of being deposited on top of the demineralized dentin.[16] Studies have shown that incorporation of QADM (Quartenary ammonium dimethacrylate)Nano silver particles and Zirconia nanoparticles added in different concentrations to the primer/adhesive of the Adper scotchbond multipurpose,3M had the potential to inhibit S.mutans both on the material surface and away from the surface and doesn't affect the bond strength to dentine as well.

### NANO MATERIALS IN REMINERALISATION

Etiology of hypersensitivity is due to the exposure of dentinal tubules.Remineralisation therapeutic approach involves formation of a remineralised layer on the surface of demineralized dentin which results in mineral deposit or plugs in the dentinal tubules.[15]An emerging view in hypersensitivity treatment is to delaye the restorative approach and to provide maximum possibilities for natural lesion repair and arrest.[16]Recently nanoparticles of hydroxyapatite (HAP), tricalcium phosphate (TCP), and amorphous calcium phosphate (ACP) have been developed as sources to release calcium/phosphate ions and increase the supersaturation of HAP in carious lesions.[17-19] Karlinsey et al,reported that the combination of NaF & *f*TCP in a simple aqueous solution can significantly remineralize white spot enamel lesions relative to that achievable with fluoride alone.[20]

## ENDODONTIC APPLICATIONS

### NANOPARTICLES IN IRRIGATION AND INTRACANAL MEDICAMENT

Nanoparticle-based disinfection plays a vital role in root canal disinfection. Materials like Chitosan, zinc oxide, silver and Bioactive glass nano particles have been introduced in endodontics to provide more effective removal of microorganisms.[21]Chitosan, with its polycationic structure, binds to negatively charged bacterial cell walls due to the presence of carboxyl, phosphate and amino groups, altering membrane permeability and attaching to bacterial DNA and inhibiting replication.[22] The more commonly proposed antimicrobial mechanism is contact - mediated killing that involves the electostatic attraction of positively charged chitosan with the negatively charged bacterial cell membrane. This altered cell wall permeability eventually results in rupture.Chitosan also chelates the trace metal elements that combine with cell wall molecules of microorganisms, destabilising the cell wall.Chitosan were found to retain their antibacterial properties after aging for 90 days.[2] of cells and leakage of proteinaceous and other cellular components results in cell death.[3,4]

Zinc oxide nanoparticles under UV illumination generate reactive oxygen species (ROS) including hydrogen peroxide(H2O2),hydroxyl radicalsand superoxide ( Superoxide and hydroxyl radicals, due to their negative charges, stay on the outer surface of the bacteria. Meanwhile, hydrogen peroxide molecules can pass through the cell wall to cause oxidative damage to cellular structures. The uptake of toxic dissolved zinc ions also depletes intracellular ATP production and disrupts DNA replication.[24]

Mechanism of Silver nanoparticles is they anchor and infiltrate bacteria cell wall, then, electrostatic attraction between silver nanoparticles and sulfur-, nitrogen- or oxygen-containing functional groups on the cell membrane causes physical membrane damage and cellular leakage.Silver nanoparticles also produce high levels of ROS, together with dissolved silver ions they can increase cellular oxidative stress in microorganisms.[24,25]

## NANOPARTICLE-INCORPORATED ROOT CANAL SEALERS

Root canal filling done with root canal sealers should eliminate bacteriaremaining in the root canal system and prevent bacterial recolonization in case of leakage. bacterial adhesion and formation of biofilms on gutta - percha could lead to the persistence of infection in the root canals. the common sealers are known to possess antibacterial activity for a maximum period of 1 week. it was observed that the addition of antibacterial NPs in root canal sealers would improve the direct and diffusible antibacterial effects of the root canal sealers and the efficacy of root canal sealers were not lost even after 7 days of setting. The bactericidal effect was mainly by adsorption and penetration through the bacterial cell wall following which they interact with the protein and fat layer in the cell membrane blocking the exchange of essential ions. the destabilization of the cell membrane leads to leakage of intracellular constituents and cell death.[5]

Eg- Quaternary ammonium polyethylenimine nanoparticles(QAPEI), Bioactive glass nano particles(BAG Nps).

## REGENARATIVE ENDODONTIC THERAPY

Nanoparticles were shown to improve SCAP adherence, viability and differentiation of stem cells. Increased surface area of nanoparticles is useful for cell adhesion and biological activity. They can also be developed into a controlled-release system with growth factors to support and regulate the differentiation of stem cells.[25,26] A nanofiber scaffold system of chitosan nanoparticles loaded with dexamethasone sodium phosphate (DEXP) reduces inflammation , and when loaded with bovine serum albumin (BSA)maintains the osmotic pressure and transportation of nutrients into cells for bone tissue regeneration. Similarly, an injectable scaffold of poly-l-lactic acid (PLLA) nanofibrous microspheres with controlled release of bone morphogenic protein 2 (BMP-2) helps in the promotion of SCAP differentiation into odontoblast-like cells.[27,28,29,30]

## NANOMATERIALS IN ORTHODONTICS

In orthodontia,to reduce friction between bracket slot and archwire for efficient tooth movement, inorganic fullerene-liketungsten disulfide (IF-WS2) and molybdenum disulfide (IF-MoS2) nanoparticles have been coated on orthodontic wires as a dry lubricant .[39,40.] To provide a firmer anchorage and increased mechanical strength, a combination of zirconia and titanium dioxide nanoparticles have been added to orthodontic adhesive and alumina nanoparticles have been added to clear plastic polymer braces.[41,42]Orthodontic adhesive with europium-doped zinc oxide nanoparticles increases safety during complete removal of the adhesive after treatment. Shape memory polymer responsive to body temperature or light are modified with photoactive nanoparticles to execute desired geometry and surface characteristics thereby influencing influence tooth movement[.43]

## CONCLUSION

Applications of nanotechnology in dentistry is improving day by day.Many pragmatic challenges have hindered the clinical applications of newand emerging nanobiomaterials.On the other hand development of nanotech products in dentistryrequires a complete analysis and full appraisal before they are handed to the clinicians. The scientific hurdle for nanobiomaterials in dentistry lies in understanding theinteraction of materials being developed at the nanolevel with oral and maxillofacialtissues. Nanotechnology also paves the way for development of tools and techniques that will allow clinicians to diagnose, treat, and manage oral conditions at their earliest. Mechanistic research into how nanomaterials can strengthen tooth structure and further exploration of adding physiological function to nanoehnanced dental materials will deliver a paradigm shift in clinical dentisty. Further targeted investigations into the interactions of nanoparticles with oral biofilms are also the current need of time.

## REFERENCES

1) A. Kishen (ed.), Nanotechnology in Endodontics: Current and Potential Clinical Applications, 1 DOI 10.1007/978-3-319-13575-5_1, © Springer International Publishing Switzerland 2015.
2)Shrestha A, Shi Z, Neoh KG, Kishen A.Nanoparticulates for antibiofi lm treatment and effectof aging on its antibacterial activity. J Endod. 2010;36:1030–5.
3)Rabea EI, Badawy ME, Stevens CV, Smagghe G,Steurbaut W. Chitosan as antimicrobial agent:applications and mode of action. Biomacromolecules.2003;4:1457–65.
4) Qi L, Xu Z, Jiang X, Hu C, Zou X. Preparation and antibacterial activity of chitosan nanoparticles.Carbohydr Res. 2004;339:2693–700.
5)Gao B, Zhang X, Zhu Y. Studies on the preparationand antibacterial properties of quaternized polyethyleneimine.J Biomater Sci Polym Ed. 2007;18:531–44.
6)Hook ER, Owen OJ, Bellis CA, Holder JA,O'Sullivan DJ, Barbour ME. Development of anovel antimicrobial-releasing glass ionomer cement functionalized with chlorhexidine hexametaphosphate nanoparticles. J Nanobiotechnol. 2014;12(1):3.
7)Wilson KS, Zhang K, Antonucci JM. Systematic variation of interfacial phase reactivity in dental nanocomposites. Biomaterials. 2005;26(25):5095–103.
8)Chen MH, Chen CR, Hsu SH, Sun SP, Su WF. Low shrinkage light curable nanocomposite for dentalrestorative material. Dent Mater Off Publ AcadDent Mater. 2006;22(2):138–45.
9)Furman B, Rawls HR, Wellinghoff S, Dixon H, Lankford J, Nicolella D. Metal-oxide nanoparticles for the reinforcement of dental restorative resins. Crit Rev Biomed Eng. 2000;28(3–4):439–43.
10)Mitra SB, Wu D, Holmes BN. An application of nanotechnology in advanced dental materials. J AmDent Assoc. 2003;134(10):1382–90.
11)Wang Y, Lee JJ, Lloyd IK, Wilson Jr OC, Rosenblum M, Thompson V. High modulus nanopowder reinforced dimethacrylate matrix composites for dental cement applications. J Biomed Mater Res A. 2007; 82(3): 651–7.
12)Tian M, Gao Y, Liu Y, Liao Y, Hedin NE, Fong H. Fabrication and evaluation of Bis-GMA/ TEGDMA dental resins/composites containing nano fibrillar silicate. Dent Mater Off Publ AcadDent Mater. 2008;24(2):235–43.
13) Xia Y, Zhang F, Xie H, Gu N. Nanoparticle reinforced resin-based dental composites. J Dent.2008;36(6):450–5.
14)Xu HH, Weir MD, Sun L, Moreau JL, Takagi S,Chow LC, et al. Strong nanocomposites with Ca,PO(4), and F release for caries inhibition. J DentRes. 2010;89(1):19–28.

15)Kasraei ShA M, Khamverdi Z, Khalegh NejadS. Effect of nanofi ller addition to an experimental dentin adhesive on microtensile bond strength to human dentin. J Dent (Tehran). 2009;6:91–6.
16)Wagner A, Belli R, Stotzel C, Hilpert A, Muller FA, Lohbauer U. Biomimetically- and hydrothermallygrown HAp nanoparticles as reinforcing fi llers fordental adhesives. J Adhes Dent. 2013;15(5):413–22.
17)Zhou H, Bhaduri S. Novel microwave synthesis of amorphous calcium phosphate nanospheres.J Biomed Mater Res B Appl Biomater. 2012;100(4):1142–50.
18)Sun L, Chow LC, Frukhtbeyn SA, Bonevich JE. Preparation and properties of nanoparticles of calcium phosphates with various Ca/P ratios. J ResNatl Inst Stan. 2010;115(4):243.
19)Xu HHK, Moreau JL, Sun L, Chow LC. Nanocomposite containing amorphous calcium phosphate nanoparticles for caries inhibition. Dent Mater. 2011;27(8):762–9.
20)Karlinsey RL, Pfarrer AM. Fluoride plus functionalized β-TCP a promising combination for robust remineralization.Advan Dent Res. 2012;24(2):48–52.
21)Markan, S., Lehl, G. and Kapoor, S. (2017) Recent advances of nanotechnology in endodontics, conservative and preventive dentistry-a review. J. Dent.Oral Biol. 2, 1067 http://www.remedypublications.com/journal-of-dentistry-and-oral-biologyabstract.php?aid=4692
22)Yilmaz Atay, H. (2019) Antibacterial activity of chitosan-based systems. In Functional Chitosan (Jana, S. and Jana, S., eds), pp. 457–489, Springer,Singapore.
23)Damm, C., Münstedt, H. and Rösch, A. (2008) The antimicrobial efficacy of polyamide 6/silver-nano- and microcomposites. Mater. Chem. Phys. 108,61–66 https://doi.org/10.1016/j.matchemphys.2007.09.002.
24) Qing, Y., Cheng, L., Li, R., Liu, G., Zhang, Y., Tang, X. et al. (2018) Potential antibacterial mechanism of silver nanoparticles and the optimization oforthopedic implants by advanced modification technologies. Int. J. Nanomed. 13, 3311–3327 https://doi.org/10.2147/IJN.S165125.
24)Sirelkhatim, A., Mahmud, S., Seeni, A., Kaus, N.H.M., Ann, L.C., Bakhori, S.K.M. et al. (2015) Review on zinc oxide nanoparticles: antibacterial activityand toxicity mechanism. Nano Micro Lett. 7, 219–242 https://doi.org/10.1007/s40820-015-0040-x
25)Keller, L., Offner, D., Schwinté, P., Morand, D., Wagner, Q., Gros, C. et al. (2015) Active nanomaterials to meet the challenge of dental pulp regeneration. Materials 8, 7461–7471 https://doi.org/10.3390/ma8115387.
26)Shrestha, S., Torneck, C.D. and Kishen, A. (2016) Dentin conditioning with bioactive molecule releasing nanoparticle system enhances adherence, viability, and differentiation of stem cells from apical papilla. J. Endod. 42, 717–723.https://doi.org/10.1016/j.joen.2016.01.026.
27)Boroojeni, F.R., Mashayekhan, S. and Abbaszadeh, H.-A. (2019) The controlled release of dexamethasone sodium phosphate from bioactive electrospun .PCL/gelatin nanofiber scaffold. Iran. J. Pharm. Res. 18, 111–124 PMID:31089349.
28)Vakilian, S., Mashayekhan, S., Shabani, I., Khorashadizadeh, M., Fallah, A. and Soleimani, M. (2015) Structural stability and sustained release of protein

from a multilayer nanofiber/nanoparticle composite. Int. J. Biol. Macromol. 75, 248–257 https://doi.org/10.1016/j.ijbiomac.2015.01.051.

29) Liu, W., Sun, J., Sun, Y., Xiang, Y., Yan, Y., Han, Z. et al. (2020) Multifunctional injectable protein-based hydrogel for bone regeneration. Chem. Eng. J.394, 124875 https://doi.org/10.1016/j.cej.2020.124875.

30) Wang, W., Dang, M., Zhang, Z., Hu, J., Eyster, T.W., Ni, L. et al. (2016) Dentin regeneration by stem cells of apical papilla on injectable nanofibrous microspheres and stimulated by controlled BMP-2 release. Acta Biomater. 36, 63–72 https://doi.org/10.1016/j.actbio.2016.03.015.

31)Alp, G., Johnston, W.M. and Yilmaz, B. (2019) Optical properties and surface roughness of prepolymerized poly(methyl methacrylate) denture base materials. J. Prosthet. Dent. 121, 347–352 https://doi.org/10.1016/j.prosdent.2018.03.001.

32) Coutinho, I.F., Aras, M.A. and D'souza, K.M. (2018) Nanomaterials and their application in prosthodontics: a review. J. Res. Dent. 6, 124 https://doi.org/ 10.19177/jrd.v6e62018124-131.

33)Acosta-Torres, L., López-Marín, L.M., Núñez-Anita, R.E., Hernández-Padrón, G. and Castaño, V.M. (2011) Biocompatible metal-oxide nanoparticles:nanotechnology improvement of conventional prosthetic acrylic resins. J. Nanomater. 2011, 941561 https://doi.org/10.1155/2011/941561.

33)Arafa, K.A.O. (2016) Comparing the effects of titanium alloy and chrome cobalt in removable partial denture connectors on tooth mobility, bone loss and tissue reaction. Saudi J. Dent. Res. 7, 112–117 https://doi.org/10.1016/j.sjdr.2016.01.001.

34) Priyadarsini, S., Mukherjee, S., Bag, J., Nayak, N. and Mishra, M. (2020) Application of nanoparticles in dentistry: current trends. In Nanoparticles inMedicine (Shukla, A.K., ed.), pp. 59, Springer, Singapore.

35)Kopf, B.S., Ruch, S., Berner, S., Spencer, N.D. and Maniura-Weber, K. (2015) The role of nanostructures and hydrophilicity in osseointegration: In-vitro protein-adsorption and blood-interaction studies. J. Biomed. Mater. Res. A 103, 2661–2672 https://doi.org/10.1002/jbm.a.35401

36)Fujio, M., Komasa, S., Nishizaki, H., Sekino, T. and Okazaki, J. (2017) Biocompatibility of titanium surface nanostructures following chemical processing and heat treatment. Front. Nanosci. Nanotechnol. 3, 1–10 https://doi.org/10.15761/fnn.1000143.

37) Parnia, F., Yazdani, J., Javaherzadeh, V. and Maleki Dizaj, S. (2017) Overview of nanoparticle coating of dental implants for enhanced osteointegration and antimicrobial purposes. J. Pharm. Pharm. Sci. 20, 148–160 https://doi.org/10.18433/J3GP6G.

38) Córdoba, A., Manzanaro-Moreno, N., Colom, C., Rønold, H.J., Lyngstadaas, S.P., Monjo, M. et al. (2018) Quercitrin nanocoated implant surfaces reduce osteoclast activity in vitro and in vivo. Int. J. Mol. Sci. 19, 3319 https://doi.org/10.3390/ijms19113319

39)Katz, A., Redlich, M., Rapoport, L., Wagner, H.D. and Tenne, R. (2006) Self-lubricating coatings containing fullerene-like WS2 nanoparticles for orthodontic wires and other possible medical applications. Tribol. Lett. 21, 135–139 https://doi.org/10.1007/s11249-006-9029-4.

40) Gracco, A., Dandrea, M., Deflorian, F., Zanella, C., de Stefani, A., Bruno, G. et al. (2019) Application of a molybdenum and tungsten disulfide coating to improve tribological properties of orthodontic archwires. Nanomaterials 9, 753 https://doi.org/10.3390/nano9050753.

41)Felemban, N.H. and Ebrahim, M.I. (2017) The influence of adding modified zirconium oxide-titanium dioxide nano-particles on mechanical properties of orthodontic adhesive: an in vitro study. BMC Oral Health 17, 43 https://doi.org/10.1186/s12903-017-0332-2.

42)Universidad Carlos III de Madrid - Oficina de Información Científica (2012) Nanoparticles provide reinforcement for invisible braces in orthodontics. In: ScienceDaily. https://www.sciencedaily.com/releases/2012/10/121029081839.htm. Accessed 14 Aug 2020.

43)Subramani, K., Huja, S., Kluemper, G.T., Morford, L. and Hartsfield, J.K. (2012) Nanotechnology in orthodontics-1: the past, present, and a perspective of the future. In Nanobiomaterials in Clinical Dentistry (Subramani, K. and Ahmed, W., eds), pp. 231–247, Elsevier Inc

44)Cao G, Wang Y. Nanostructures and nanomaterials. 2nd ed.New Jersey: World Scientific; 2011.

45)Feynmann RP. There’s plenty of room at the bottom. Eng Sci1960;23:22–36.