Dental Materials xxx (xxxx) xxx

Contents lists available at ScienceDirect

Dental Materials

journal homepage: www.elsevier.com/locate/dental

Physicochemical and biological properties of dental materials and formulations with silica nanoparticles: A narrative review

Larissa Pavanello [a], Iago Torres Cortês [a], Rafaela Durrer Parolina de Carvalho [a], Mayara Zaghi Dal Picolo [b], Vanessa Cavalli [a], Larissa Tavares Sampaio Silva [c], Letícia Cristina Cidreira Boaro [d,*], Polina Prokopovich [e], Karina Cogo-Müller [a,f]

[a] Faculdade de Odontologia de Piracicaba, Universidade Estadual de Campinas, Piracicaba, SP, Brazil
[b] Faculdade São Leopoldo Mandic, Campinas, SP, Brazil
[c] Faculdade de Odontologia, Universidade de São Paulo, São Paulo, Brazil
[d] College of Dentistry, University of Saskatchewan, Saskatoon, Canada
[e] School of Pharmacy and Pharmaceutical Science, Cardiff University, Cardiff, United Kingdom
[f] Faculdade de Ciências Farmacêuticas, Universidade Estadual de Campinas, Campinas, SP, Brazil

ARTICLE INFO

Keywords:
Nanotechnology
Nanoparticles
Silica
Drug delivery
Dentistry

ABSTRACT

Objective: Silica nanoparticles (SNPs) have been extensively studied and used in different dental applications to promote improved physicochemical properties, high substance loading efficiency, in addition to sustained delivery of substances for therapeutic or preventive purposes. Therefore, this study aimed to review the SNPs applications in nanomaterials and nanoformulations in dentistry, discussing their effect on physicochemical properties, biocompatibility and ability to nanocarry bioactive substances.

Data resources: Literature searches were conducted on PubMed, Web of Science, and Scopus databases to identify studies examining the physicochemical and biological properties of dental materials and formulations containing SNPs. Data extraction was performed by one reviewer and verified by another

Study selection: A total of 50 were reviewed. *In vitro* studies reveal that SNPs improved the general properties of dental materials and formulations, such as microhardness, fracture toughness, flexural strength, elastic modulus and surface roughness, in addition to acting as efficient nanocarriers of substances, such as antimicrobial, osteogenic and remineralizing substances, and showed biocompatibility

Conclusions: SNPs are biocompatible, improve properties of dental materials and serve as effective carriers for bioactive substances

Clinical significance: Overall, SNPs are a promising drug delivery system that can improve dental materials biological and physicochemical and aesthetic properties, increasing their longevity and clinical performance. However, more studies are needed to elucidate SNPs short- and long-term effects in the oral cavity, mainly on in vivo and clinical studies, to prove their effectiveness and safety.

1. Introduction

In the last few years, the growing scientific evolution in the field of nanotechnology has brought promising perspectives to modern medicine, allowing greater understanding and agility in the prevention, diagnosis, and treatment of many pathologies at the nanoscale [1,2]. Several nanomaterials are used in biomedical applications because they offer, among other advantages, the ability to signal, transport, and release drugs, genes, and proteins in a controlled and targeted way, overcoming the drawbacks of conventional systemic treatments [1,3]. This is because, at the nanoscale, the particles have a high surface area and small size, which contributes to their reactivity and easy diffusion across biological barriers [4].

Examples of these nanomaterials are organic nanoparticles (NPs),

* Correspondence to: College of Dentistry, University of Saskatchewan, 105 Wiggins Rd, Saskatoon, SK S7N 5E5, Canada.
E-mail addresses: l264473@dac.unicamp.br (L. Pavanello), iagocortes20@gmail.com (I.T. Cortês), r193046@dac.unicamp.br (R.D.P. de Carvalho), mayara_zdp@hotmail.com (M.Z.D. Picolo), cavalli@unicamp.br (V. Cavalli), larissatsampaio@gmail.com (L.T.S. Silva), leticiacidreiraboaro@gmail.com, leticia.boaro@usask.ca (L.C.C. Boaro), prokopovichp@cardiff.ac.uk (P. Prokopovich), karinacm@unicamp.br (K. Cogo-Müller).

https://doi.org/10.1016/j.dental.2024.07.028
Received 25 June 2024; Accepted 25 July 2024

such as liposomes, polymers, dendrimers, and micelles, among others, and inorganic NPs, such as those composed of iron oxide, graphene, gold, silver, titanium, as well as silica nanoparticles (SNPs) [5,6]. Among the inorganic NPs, SNPs have received particular attention for applications in dentistry [7–17], improving physicochemical properties and clinical performance [9,18–21], and promoting high loading efficiency and controlled release of substances with therapeutic and/or preventive effects in materials and formulation, such as antimicrobial [18,22–24] and osteogenic substances [17,25], which can be successfully applied in diagnostic, preventive, restorative, and conservative dentistry [4]. The SNPs have different morphologies, including non-porous, hollow/rattle, mesoporous, amorphous, core-shell, yolk/-shell, Janus, and rod-shaped SNPs (Fig. 1), and can be synthesized using various raw materials and methods, with the Stöber synthesis method [26] being the pioneer and is widely used [26,27].

In this context, this review overviews the perspectives and applications of SNPs in dentistry, subcategorized by their use in (I) dental materials, including dental specialties such as prosthesis, restorative dentistry and orthodontics; and (II) other applications, which include SNPs use in formulations or biomaterials related to specialties such as endodontics, implantology and periodontics, for example, but that do not involve incorporating NPs into dental materials. Furthermore, the general characteristics, such as form, structure and synthesis, and in vitro cellular biocompatibility of SNPs are discussed.

2. Methods

This is a narrative literature review. A search was performed in PubMed, Web of Science and Scopus online databases using the following terms: “silica nanoparticles” and “dentistry” associated with “prosthodontics”, “coating agents”, “composite resin”, “dental adhesive”, “dental cement”, “orthodontics”, “endodontic”, “dental implants” or “periodontics”.

The studies were selected in two stages. In the first stage, a preliminary search was performed based on the titles and abstracts of the articles, followed by the removal of duplicate articles. Then, were considered eligible for the full text reading in vitro and in vivo studies that addressed the use of SNPs in some segments of dentistry. We excluded review articles (narrative and systematic), articles that consisted only of the abstract, without the full text, letters to the editor, editorials and summaries published in the annals of scientific events. There was no restriction on publication date and language. Data regarding the general physicochemical properties and biological activity were extracted from the studies included in this review.

3. Results

692 studies were found, of which 642 were excluded after applying the inclusion criteria and reading the full text, resulting in 50 articles included in results of this narrative literature review (Fig. 2). Based on the studies found, the selected articles were allocated to the following themes: prosthodontics (dental prosthesis), restorative dentistry, orthodontics, and other applications, such as endodontics, dental implants, and periodontics, based on the use of SNPs in dental materials or formulations by dental specialty.

3.1. Use of SNPs in dental materials

Nanoparticles such as SNPs have been extensively studied and used in dentistry, notably in specialty dental biomaterials employed in restorative dentistry, dental implants, orthodontics, and prosthesis. The main purposes of incorporating SNPs in dental materials are to improve their physicochemical properties and interaction with the oral cavity, as well as to act as nanocarriers of therapeutic substances [28]. Their use has also been tested in other formulations as nanocarriers of substances such as antimicrobials and osteogenic substances [17,21,22,29], for example. These topics are discussed in the following sections. Table 1 summarizes the application of SNPs in dental materials focusing on biological activities and mechanical/optical properties presented in the articles discussed in these topics.

3.1.1. Materials used in dental prosthetics

Poly(methyl)methacrylate (PMMA) is widely used for denture base prosthesis and provisional crowns. The material displays inherent favorable features, such as easy handling, low cost, stability in the oral environment, acceptable esthetic results, and color-matching capability [11]. However, PMMA has some drawbacks attributed to inadequate mechanical properties, which allow frequent denture base fracture [30].

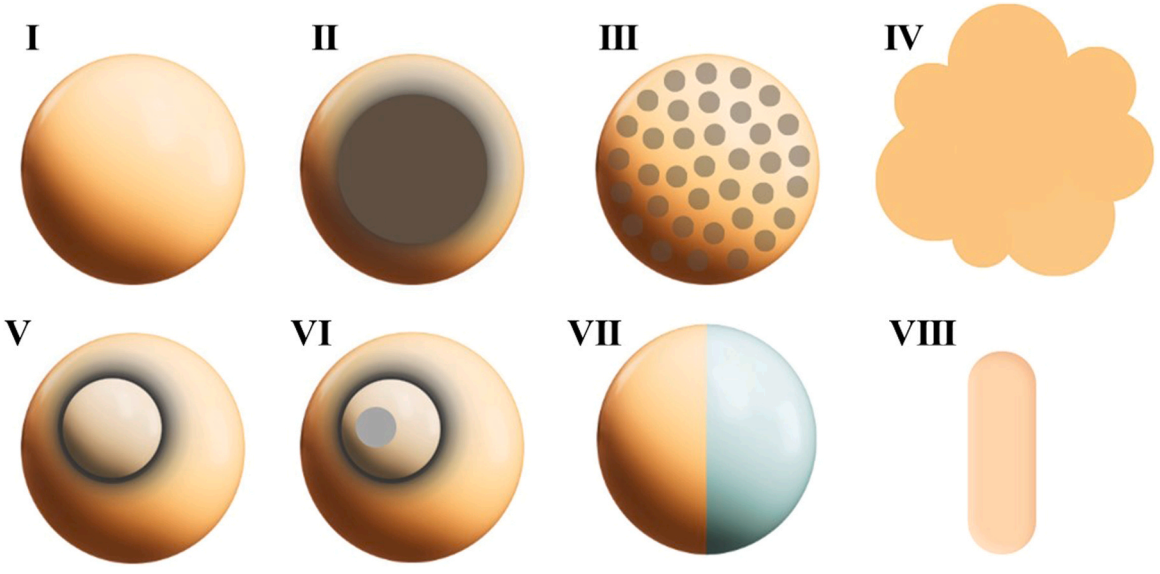

Fig. 1. . Illustration of the different types of SNPs: (I) non-porous (compact NPs, no pores); (II) hollow/rattle (large central cavity); (III) mesoporous (pores with variable and adjustable sizes); (IV) amorphous (shapeless); (V) core-shell (silica core or outer shell); (VI) yolk/shell (hybrid structures with a movable core inside a hollow shell of the same or different material); (VII) Janus (heterogeneous surface); and (VIII) rod-shaped SNPs (flattened, non-spherical NPs). Illustration made by the authors using canva.com.

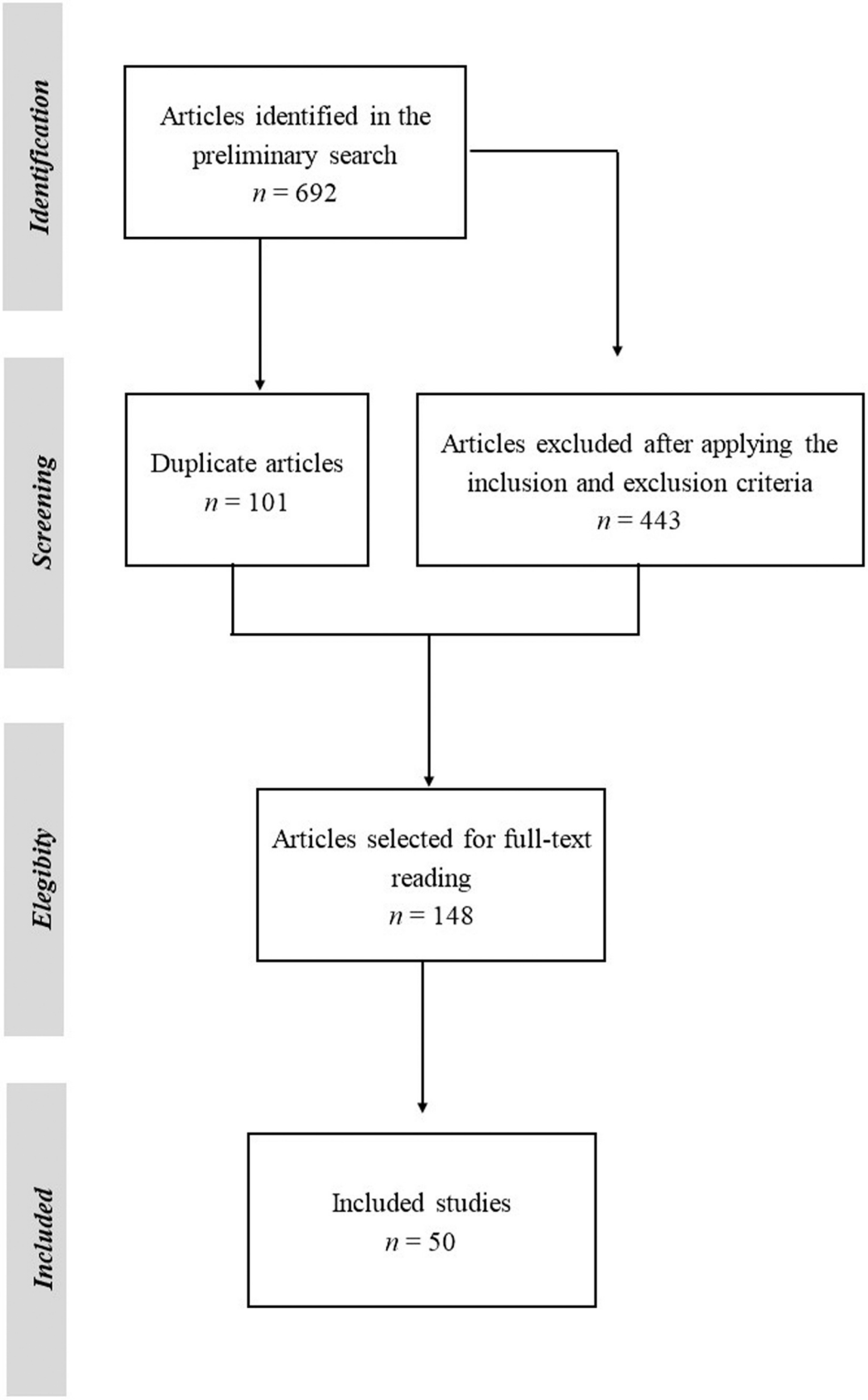

Fig. 2. . Flowchart of the selection process in the literature review.

Table 1
. Application of SNPs on dental materials: biological activities and mechanical/optical properties.

Dental Materials						
Material	NPs	SNPs concentration	Antibacterial activity	Dentin hypersensitivity and remineralization activity	Physicochemical properties	References
PMMA	SNPs	0.023 %	-	-	↑ microhardness, fracture toughness, and did not change the glass transition temperature	[9]
	T-Sil and SNPs pure	0.25 %	-	-	↑ fracture toughness, and dynamic thermomechanical properties. No statistically significant differences were detected among the T-Sil/SNPs oure	[12]
	MPS	1 %	-	-	↑ flexural strength, flexural modulus, fracture toughness, and clinically acceptable color change	[13]
	SNPs	0.05 %	-	-	↑ flexural strength, and flexural modulus	[21]
	SNPs	0.5 %	-	-	↑ hardness and showed acceptable surface roughness and translucence	[31,32]
	SNPs	0.5 %	-	-	↑ flexural strength	[34]
	SNPs	0.05 – 1 %	↓ *C. albicans* adhesion for slide count and direct culture methods	-	↑ surface roughness and surface hardness, ↓ contact angle and translucency (concentration-dependent)	[39]
	SNPs	5 %	-	-	↑ flexural strength, hardness, and resilience, and ↓ surface roughness	[33]
	MSNs with amphotericin B	2.5 – 5 %	↓ *C. albicans* and *S. oralis* adhesion. A long-term antimicrobial effect was observed for 2 weeks (2.5 %)	-	↓ flexural strength, ↑ surface roughness (5 %) and hydrophobicity	[40]
	MSNs with silver-sulfadiazine	0.5, 2.5 - 5 %	Immediate and long-term anti-adhesive effects against *C. albicans* and *S. oralis* (2.5 – 5 %)	-	↑ surface hardness, flexural strength and did not change the flexural modulus (0.5 %)	[41]

Material	NPs	SNPs concentration	Antibacterial activity	Dentin hypersensitivity and demineralization activity	Physicochemical properties	References
PMMA	SNPs	0.5 – 0.75 %	-	-	↑ hydrophobicity, and increased the coating layer durability after brushing-wear simulation	[46]
	SNPs	0.8 %	↓ *S. aureus* adhesion	-	↑ hydrophobicity, and showed good transparency	[44]
	SNPs	2.5 – 10 %	-	-	↑ surface hardness and elastic modulus, and did not change the surface roughness after aging for 6 and 12 months	[47]
Composite resin	UHA-SNPs	5 %, 10 %, 20 % and 30 %	-	-	↑ compressive and tensile strength, microhardness, flexural strength, and flexural modulus. The fillers % did not influence these parameters	[16]
	CHX-SNPs	30 %	Effective against *Streptococcus* genus bacteria	-	↑ flexural strength, flexural modulus and did not interfere the degree of conversion. After water storage ↓ flexural strength	[18]
	SNPs	30 - 40 %	-	-	↑ fracture toughness, flexural strength, and microhardness	[19]
	CHX-MSN	5 %	Effective against plankton and biofilm growth of *L. casei* and *S. mutans*	-	↑ flexural strength, flexural modulus, and constant surface roughness (after 1 month in water)	[22]
	Zn-MSN	15 %	Effective against *S. mutans* (surface plate test and gram staining method)	-	↑ flexural strength, flexural modulus, compressive strength, and microhardness	[24]

Material	NPs	SNPs concentration	Antibacterial activity	Dentin hypersensitivity and demineralization activity	Physicochemical properties	References
Composite resin	Cu-MBGN	5 %	-	-	↑ degree of conversion, flexural strength, flexural modulus, and microhardness	[29]
	QASi	5 %, 8 % and 10 %	-	-	↑ gel effect, degree of conversion, flexural modulus, flexural and compressive strength	[59]
	SNPs	5 – 10 %	-	-	↑ flexural strength, flexural modulus, and wear resistance, and ↓ polymerization shrinkage	[58]
	QASi	-	-	↓ enamel demineralization	-	[61]
Dental adhesives	Silanized SNPs	0.2 %	-	-	↑ flexural strength, fracture toughness and μTBS. Also, showed less roughness and few adhered fragments	[20]
	OCT-MSN	10 %	Effective against biofilm of *S. mutans*	-	-	[53]
	SNPs	15 %	-	-	↑ μTBS and acceptable degree of conversion	[70]
	SNPs	0.2 %	-	-	↑ flexural strength and microshear bond strength	[65]
	MSN/CHX-PLGA	5 %	Effective against biofilm of *S. mutans*	-	↑ μTBS	[66]
	CHX-MSN	5 %	Effective against *S. mutans*	-	↑ MTBS and did not interfere the degree of conversion	[67]

(*continued on next page*)

Table 1 (*continued*)

Material	NPs	SNPs concentration	Antibacterial activity	Dentin hypersensitivity and demineralization activity	Physicochemical properties	References
	silver-loaded SNPs	1 %	No antibacterial activity against *S. mutans*	-	No interference in degree of conversion, shear and complex viscosity, water sorption and linear shrinkage	[68]

Material	NPs	SNPs concentration	Antibacterial activity	Dentin hypersensitivity and demineralization activity	Physicochemical properties	References
Dental adhesives	L-arginine-loaded MSNs	0.5 %	Effective against *S. mutans* and *L. casei*	-	↑ flexural strength, degree of conversion and μTBS	[69]
	Proanthocyanidin-MSN	20 %	-	-	↓ physicochemical properties except μTBS	[71]
Glass ionomer cement	SNPs	0.5 %	-	-	Did not interfere in μSBS	[72]
	HTCC	3 %	↓ growth *S. mutans*	-	↑ flexural strength, flexural modulus, microhardness, and wear resistance	[73]
	SNPs	5 %	-	-	↓ microleakage rates	[74]
	nanoZrO_2–SiO_2– HA	5 %	-	-	↑ compressive and flexural strengths and did not influence surface roughness	[76]
	nanoZrO_2–SiO_2– HA	5 %	-	-	↑ fracture toughness and ↓ water sorption	[77]
DH tratament	$Ca_3(PO_4)_2$-MSNs	-	-	Occluded the dentinal tubules and formed a deeper seal which penetrated about 105 μm deep	-	[81]
	NCMS paste	-	-	Formed a $CaHPO_4{\cdot}2\,H_2O$ precipitation with a 100 μm depth and ↓ dentin permeability	-	[82]
	nHA-MSN	-	-	Completely occluded the dentinal tubules by forming precipitates	Did not influence μTBS between dentin/adhesive	[83]
	Ag-BGN-MSN	3 %	↓ optical density of *L. casei* growth	Occluded the dentinal tubule and formed a membrane-like layer	μTBS similar to the control, but significantly different to the BG and MSN group	[84]
	MSNs with EPD treatment	-	-	Occluded the dentinal tubule with infiltration of 7 – 8 μm and tightly associated with the tubular inwalls	No significant difference for SBS	[85]

Material	NPs	SNPs concentration	Antibacterial activity	Dentin hypersensitivity and demineralization activity	Physicochemical properties	References
Orthodontics						
Composite adhesives	Silver SNPs	250 and 500 ppm	↓ optical density of *S. mutans* and *S. sobrinus*. No inhibition zones observed after 48 h	-	Addition of silver SNPs ↑ surface roughness. No significant difference in SBS and debonding pattern	[88]
TPU	SNPs	1 %	-	-	↑ hydrophobicity, improved elasticity, tension relaxation, and provided shape memory effect	[92]
Orthodontic brackets	Ag-SNPs	1–3 %	↓ *S. mutans* biofilm formation (3 %)	-	↑ SBS (1 %)	[89]
	silica-hydroxyapatite-silver hybrid NPs	2 %	-	-	↑ SBS and did not influence the adhesive remnant index score	[90]
Orthodontic wires	Coating SNPs	-	-	-	↓ frictional resistance, and rough surface and resistance to the friction produced between the wire and the bracket interface	[93]

PMMA - poly(methyl)methacrylate; SNPs – silica nanoparticle; MSNs - Mesoporous silica nanoparticle; T-Sil - silica nanoparticle modified with triethoxyvinylsilane; MPS - γ-methacryloxypropyltrimethoxysilane; UHA-SNPs – urchin-like hudroxyapatite; Cu-MBGN – copper-doped MSN bioactive glass nanospheres; CHX-MSN –chlorhexidine-loaded mesoporous silica nanoparticle; QASi – quartenary ammonium compounds; Zn-MSN – zinc-loaded mesoporous silica nanoparticle; OCT-SNPs – octenidine dihydrochloride-loaded silica nanoparticle; Nano-HA-SiO_2 - nano-hydroxyapatite-silica; MSN/CHX-PLGA - chlorhexidine-loaded mesoporous silica nanoparticle modified with poly-(latic-*co*-glycolic acid); NCMS – calcium oxide-loaded mesoporous silica nanoparticle; HTTC - quaternized chitosan-coated mesoporous silica nanoparticles; EPD – electrophoretic deposition; Ag-BGN-MSN - silver-doped bioactive glass/mesoporous silica nanoparticle; nHA-MSN - nano-hydroxyapatite/mesoporous silica nanoparticle; TPU - Thermoplastic Polyurethane Elastomer, SBS - shear bond strength.

Over the years, many studies have been conducted to improve PMMA properties by adding different types of NPs, such as SNPs [9,12,13,31,32]. The SNPs exhibit high surface activity and solid interfacial interaction with the organic matrix [33] and at specific concentrations can enhance the physical, thermal, and optical properties of the organic polymer [31].

In vitro studies have investigated the most appropriate SNP concentration in PMMA for denture base and provisional crowns to improve general mechanical properties, and most reports suggest the use of low [9,12,21,31,32,34] over the high concentrations [33]. The studies showed that higher concentrations caused extensive agglomeration, whereas not observed with lower concentrations, indicating that low concentrations are prone to a more homogenous distribution of the NPs in the polymer [9,34]. The uniform particle dispersion and impregnation in the matrix is crucial to avoid the development of stress concentration areas, impairing the mechanical properties of the resin [9,35].

To enhance the bonding between the reinforcement particles and the PMMA polymer [36] coupling and reinforcement agents such as

γ-methacryloxypropyltrimethoxysilane (MPS) [13] and triethoxyvinylsilane (T-Sil) [12], can be used. It was observed these agents improved the overall PMMA mechanical properties in low concentrations [12,13], and showed clinically acceptable color change [13].

Since those materials could be placed in esthetic locations, investigating the effects of SNPs incorporation on their optical properties is also important because it is suggested that the shape, size, and distribution of NPs also impact PMMA esthetic properties by influencing the material's translucence [31]. It was noted that incorporating SNPs into acrylic PMMA powder facilitated the filling of cracks and gaps between polymer chains, resulting in a homogeneous PMMA/NPs matrix. However, despite achieving a homogeneous matrix in the modified PMMA, higher concentrations of SNPs led to a reduction in the material's translucency [32]. Therefore, the proportion of the SNPs should be minimum to guarantee uniform distribution without agglomerations. In this context, silanization could enhance the dispersion based on the chemical interactions between the OH– of the SNPs particles and the hydrolysable groups of the silane coupling agent [37].

Another important aspect of SNPs incorporation into PMMA is the antibacterial effects provided by its addition [38], since the potential for biofilm accumulation due to the surface porosities and food-retentive configuration is a common issue faced by patients using PMMA-based prostheses or provisional crowns and bridges. The biofilm formation, in turn, increases the possibility of *Candida albicans* (*C. albicans*) adhesion, eventually leading to denture stomatitis [31]. Therefore, adding NPs with antimicrobial potential is highly desirable. However, the required NPs concentration, type, and overall features to decrease the biofilm formation cannot be detrimental to the mechanical properties. In this context, the nano-filled-reinforced PMMA must exhibit an antimicrobial potential without interfering or, preferably, while increasing the mechanical aspects.

The incorporation of SNPs alone [39] or combined with antimicrobial agents such as amphotericin B [40] and silver-sulfadiazine [41] in PMMA denture-based material decreased C. *albicans* [39–41] and *Streptococcus oralis (S. oralis*) [40,41] adhesion. It is suggested that the effects against *C. albicans* and *S. oralis* can be the direct contact of SNPs with the cell that may inhibit the normal reproduction process since the NPs may cross the fungal cell membrane and disrupt the metabolic pathway, affecting the membrane function and shape [41], and sustained release of silver ion (~ 10 ppm in 28 days) [41], can be potent for achieving long-term microbial anti-adhesive effects. Furthermore, the contact angle of the PMMA nano-filled material decreased, increasing the acrylic resin's wettability and thus reducing *C. albicans*' ability to adhere to a hydrophobic surface [39–41]. Regarding mechanical properties, the incorporating SNPs, and silver-sulfadiazine-MSN (mesoporous silica nanoparticles) increased the surface hardness [39,41], while decreasing flexural strength as particle concentration increased [40]. Moreover, the incorporation of amphotericin B into PMMA increased the surface roughness [39,40], exceeding the 0.2 μm threshold at which biofilm formation tends to occur [42,43].

SNPs were also added to PMMA prosthesis coating agents. The advantage of coating materials is changing the surface properties of denture-based and provisional crowns and bridges, without compromising PMMA bulk, and optical or clinical esthetics properties. Furthermore, investigations have demonstrated that SNPs added to the coating agents can hamper oral biofilm formation, by changing PMMA surface hydrophobicity [44–46], enhancing the mechanical properties of these agents [46,47], without compromising the optical properties [44]. Generally, low concentrations of SNPs were sufficient to promote these properties [44,46]. In the long-term, the coating agent applied to the PMMA surface is expected to wear out due to the intraoral chemical and mechanical degradation. However, another advantage of the coating material is the possibility of reapplying it to the PMMA surface. In this context, incorporating SNPs into PMMA denture base materials seems to be a feasible alternative to extend the SNPs beneficial effects [14].

3.1.2. Materials used in maxillofacial prosthesis

In the field of maxillofacial prosthesis, SNPs have been investigated for their potential to enhance the properties of dental materials and improve the performance of maxillofacial prostheses, used to treat congenital and acquired abnormalities in the head and neck area. Maxillofacial prostheses offer a convenient option, providing patients with a typical appearance, aesthetic appeal, and social recognition [48]. Studies have investigated the effect of SNPs on silicone elastomers, a polymer used in the manufacture of maxillofacial prostheses [10,49]. The results indicate that the nanoparticles increased the mechanical properties of experimental elastomers [10,49], probably due to the reinforcement provided by the effective interaction between the SNPs and the polymeric matrix [10].

Furthermore, when associated with magnesium for biodegradable implants for maxillofacial applications, there was a significant increase in fracture strain and a reduction in the rate of corrosion in lower concentrations. On the other hand, increasing the concentration of nanoparticles did not reduce the cell viability of osteoblastic cell line MC3T3-E1. Additionally, the wettability properties indicated a more hydrophilic surface, which is favorable for cell adhesion and proliferation as it promotes interfacial reactions between the surface and proteins, thereby enhancing cellular response [50].

3.1.3. Materials used in restorative dentistry

For years, dentistry has benefited from materials to restore the aesthetics and function of the dental elements. The clinical performance and longevity of dental restorations depends on the procedure, factors related to the material used, and patient factors [51,52]. In this section, will be discussed the effect of SNPs on material-related factors, such as physicochemical, optical, and antimicrobial properties, in addition to the remineralizing activity of restorative materials.

3.1.3.1. Composite resins. Composite resins have been widely used in restorative dentistry since the 1990s. They offer several advantages, including aesthetic similarity to natural teeth, ease of application, good mechanical properties, and biocompatibility [53,54]. Since the 2000s, pioneering studies [55,56] have investigated the use of SNPs in composite resins to enhance their mechanical properties, longevity, and clinical success. Today, various commercial products incorporate SNPs in their composition [57].

In vitro studies have investigated the influence of silica particles size [58], and different SNPs concentrations on the physicochemical properties of experimental composite resins, alone or combined with other substances [16,18,19,29,59]. In general, it was observed that adding SNPs in higher concentration to composites improved overall mechanical properties compared to silica microparticles [58], but reduced the contrast ratio [60]. Usually, inorganic microparticles have difficulty dispersing homogeneously in the polymeric matrix, generating agglomerates that compromise the mechanical resistance of the material, while SNPs can fill the gaps in the resinous matrix, improving the general properties. Moreover, these findings indicate that the increase in filler particles content generates higher material compaction, reducing crack propagation, but affect the translucency of composites [58,60].

Additionally, studies have been carried out to develop dental composite resins with high clinical performance and antimicrobial activity, by associating SNPs and other substances. SNPs combined with urchin-like hydroxyapatite [16], copper-doped mesoporous bioactive glass nanospheres [29], quaternary ammonium [59,61], zinc [24], and chlorhexidine (CHX) [18,22] promoted antimicrobials activity against oral biofilm adhesion such as *Lactobacillus casei* (*L. casei*) [22] and *Streptococcus* genus bacteria biofilm [18,22,24] without significantly compromising their physicochemical properties [16,18,22,24,59,61]. Additionally, it was observed a sustained release of zinc [24], and CHX [18,22]. These findings are promising because a material that demonstrates potential to reduce oral biofilm adhesion and pathogenicity,

without altering the composite-tooth microbiome and general properties [62], is highly desirable in dentistry because it is known that the acidic by-products generated by oral biofilms influence the balance between demineralization and remineralization of teeth, resulting in surface changes that promote the development of caries [63,64].

3.1.3.2. Dental adhesives. In addition to composite resins, incorporating inorganic filler particles with bioactive substances can be a strategy to increase the physicochemical properties of the adhesive layer and the bond strength of dental adhesives, used mainly to ensure adequate adhesion of restorative composites to tooth structure and to avoid deficiencies that can lead to failure of restorations [65], preventing the onset and progression of oral infections caused by cariogenic bacteria [53,66–69].

Different SNPs concentrations on the physicochemical properties of dental adhesives were investigated and it was observed that low concentrations improve the physicochemical properties [20,65,66,69,70] compared to higher concentrations like PMMA materials. This improvement is attributed to the homogeneous dispersion of nanoparticles at lower concentrations, facilitating the formation of a resilient structure, while higher concentrations tend to form clusters that negatively affect adhesive properties [67]. Similar findings were obtained with the addition of L-arginine-loaded MSNs [69] and chlorhexidine-loaded MSNs [66,67]. Divergently, dental adhesives with low concentrations of silver-loaded SNPs [68] showed no statistical difference for the degree of conversion, shear and complex viscosity, water sorption, linear shrinkage, when compared to the control group (no particles).

Another approach to improving the physicochemical properties and reducing the hydrolytic degradation of restorative materials is by modifying the SNPs surface to increase the compatibility between the inorganic matrix and the organic matrix [37]. Despite this, the functionalization of MSN with organosilanes and loadeding with proanthocyanidin resulted in decreased overall physicochemical properties of dental adhesive[71]. It is proposed that post-functionalization, certain amino groups from organosilanes may have linked to collagen hydroxyl groups, favoring the interaction of the adhesive with dentin and, as a result, there was high bond strength, but the effect of functionalization in reducing the other properties analyzed is uncertain.

Regarding antimicrobial activity, adhesives containing CHX exhibited a notable reduction in the metabolic activity and cell viability of *Streptococcus mutans* (*S. mutans*) and, proportionally to the increase in the concentration of nanoparticles [66,67]. Interestingly, the release profile of CHX was better at pH 5.0 than at 7.4 from SNPs, suggesting the potential for drug release modulation in response to acidogenesis and bacterial infections [66]. Similar findings were obtained with adhesives containing octenidine dihydrochloride (OCT) [53] and L-arginine, an amino acid that, when metabolized by oral bacteria, neutralizes the acidic environment that contributes to primary or recurrent caries development and progression [69], while silver showed less pronounced effects, possibly due to their lower silver content [68].

3.1.3.3. Glass ionomer cement. Glass ionomer cements have wide application in dentistry due to their characteristics, such as biocompatibility, chemical bonding to the dental substrate and release and recharge of fluorine ions. Despite the benefits, these materials have disadvantages that limit their use in areas with a higher incidence of occlusal forces, such as the formation of marginal gaps in restorations, fractures and wear out [72–77]. To improve the mechanical properties and overcome the main limitations, the addition of SNPs [72,74], quaternized chitosan nanoparticles (HTCC-MSN) [73], and nano zirconia-silica-hydroxyapatite (nanoZrO_2 –SiO_2– HA) [76,77] was investigated in glass ionomer cements.

Adding SNPs to glass ionomer cements resulted in reduced microleakage rate between the tooth surface and the restoration, supposedly due to the formation of siloxane bonds between the SNPs and the organic material of the cement [74]. However, there were no significant differences between the microshear bond strength (μSBS) with low concentration of SNPs [72], suggesting that low SNPs content may not have been enough to increase the μSBS, potentially causing incomplete cement maturation. Therefore, glass ionomer cements containing HTCC-MSN [73] and nanoZrO_2–SiO_2–HA [76,77] exhibited higher mechanical properties at lower concentration, while increasing particle concentration tended to reduce these properties[76,77], reinforcing the findings of other studies in different restorative materials [9,20,32,34,39,65–67,69,70]. Based on these results, it is assumed that SNPs, alone or associated with other substances, can increase the packing density in the cement matrix, generating a homogeneous and resistant material [73,76,77]. In addition to the reinforcement of silica molecules, it is worth highlighting the hardening effect of ZrO_2 and the hydroxyapatite additive, which can contribute to the good results [76,77].

In addition to the mechanical properties, it was also observed that materials with HTCC-MSN inhibited the growth of *S. mutans* in a concentration-dependent manner [73] and that nano-hydroxyapatite-silica (nano-HA-SiO_2) were compatible with the human dental pulp stem cells (DPSC) in 24 h and 72 h between concentrations of 3.125 and 100 mg/mL [75].

3.1.4. Materials used in the treatment of dentin hypersensitivity

Dentin hypersensitivity (DH) is characterized by a sensitivity to non-harmful environmental stimuli, such as thermal, tactile, osmotic, or chemical [78,79] and is a common problem in clinical dentistry with an incidence of 4 to 74 % [80,81]. *In vitro*, the SNPS, particularly MSNs containing calcium oxide [82], calcium phosphate [81], hydroxyapatite [83] and bioactive glass-coated and silver (Ag-BGN-MSN) [84] have been applied to occlusion of dentinal tubules in severe DH treatment, providing acid-fast stability, and promoting tissue remineralization.

Pastes with MSNs containing calcium oxide and calcium phosphate diffused deep into the dentinal tubules and formed calcium phosphate precipitates [81,82] highlighting their therapeutic potential for tissue remineralization. Similarly, pastes with hydroxyapatite-loaded SNPs can act as a calcium phosphate reservoir and contribute to dental mineralization, with low cytotoxicity even at the highest dosage. In addition to completely occluding the dentinal tubules with hydroxyapatite nanocrystals, this particle strongly combines with the tubular wall, which allows greater tubular infiltration [83].

Bioactive glasses containing SNPs showed remineralizing potential due to their osteoconductive effect and ionic dissolution [81,84]. From this dissolution, the formation of apatite hydroxycarbonate precipitates accelerates the occlusion of dentinal tubules [84]. Moreover, dentinal tubules were also effectively occluded by MSNs alone. Using electrophoretic equipment, it was observed that specimens fixed to the positive electrode had an effective occlusion of the dentinal tubules when compared to specimens fixed to the negative electrode, probably due to negative charge of the SNPs. Furthermore, the shear strength between the dentin and the adhesive system was not affected after electrophoretic deposition application [85].

3.1.5. Orthodontics

In the oral cavity, despite the numerous advantages, fixed orthodontic appliances modify the symbiotic microbiome by accumulating cariogenic biofilm that reduces the oral pH to acidic levels which can cause causes dental demineralization, appearance of white spot lesions around the orthodontic brackets, inflammation of the periodontium, and increase in the risk of caries, particularly in patients with poor oral hygiene during treatment [86,87]. Therefore, orthodontic appliances are reported as a risk factor for adhesion and bacterial multiplication, including orthodontic adhesives, that have surface roughness and may have areas with gaps around the brackets at the adhesive-enamel interface. An alternative to this situation is incorporating antimicrobial drugs to orthodontic adhesives to prevent the accumulation of

biofilm without negatively interfering with the mechanical properties of the material [88].

Experimental adhesives with silver nanoparticles associated with SNPs [88] and coated with silica [89], and silica-hydroxyapatite-silver hybrid nanoparticles [90] did not interfere with mechanical properties in low concentrations [88–90]. However, for bonding orthodontic brackets, for example, the use of higher concentrations of particles is recommended due to the lower risks caused to the dental enamel during bracket detachment [90]. In addition, adhesives containing silver exhibited antimicrobial activity against *S. mutans* [88,89] and *Streptococcus sobrinus* (*S. sobrinus*), bacteria associated with the initiation of oral biofilm formation [88]. It can be considered that the antibacterial effect is synergistic, since the silver ions released from the nanoparticles can bind in different structures and cause damage to the bacterial cell and the SNPs can penetrate the bacterial cells and interfere with its metabolism through the interaction of the silane group of the particles with biological molecules of the cell membrane, such as proteins and lipids [91].

The SNPs were also investigated when added to elastomeric ligatures of fixed appliances that hold the orthodontic wire to the bracket [92] and to coating orthodontic wire [93], as an alternative to the main limitations, such as water absorption and tension relaxation [92] and to reduce friction between parts, facilitating orthodontic movement [93]. For successful orthodontic treatment, elastomeric ligatures must provide sufficient strength for corrective tooth movement with a minimal tension relaxation to avoid causing pain to the patient and have acceptable elasticity and stretching to not fail during treatment period [92,94]. Due to conditions of the oral cavity and changes in the molecular structure, elastomeric ligatures may show a reduced viscoelastic strength, which compromise tooth movements and the success of orthodontic treatment. Therefore, materials that have elastic memory effect are clinically desirable for stabilizing the degree of strength for a longer period [94].

Thermoplastic polyurethane (TPU) elastomer with SNPs showed improved properties such as hydrophobicity, elasticity, tension relaxation, and shape memory effect, which are crucial for orthodontic applications. Furthermore, the sample showed an acceptable initial force for tooth [92]. Moreover, coating orthodontic wires with SNPs resulted in a smoother and more resistant surface compared to titanium dioxide coating, reducing friction between the wire and the bracket interface, in dry and wet environments (artificial saliva) [93]. Considering that frictional resistance is a factor that can reduce tooth movement and the surface roughness of the wire can favor the adhesion of oral pathogenic microorganisms, the results obtained are promising.

3.2. Other applications of SNPs in dentistry

In addition to the application of SNPs in dental materials, they can also be used for other purposes in dentistry, performing anti-inflammatory, antimicrobial, osteogenic, as well as improvements in the mechanical properties of implants, and aesthetic and functional materials used extraorally [10,17,49,95,96]. Some examples are MSNs which, when loaded with antimicrobial, anti-inflammatory and osteogenic substances, have shown promising results in the treatment of periodontal disease [8,97] and bone regeneration [17,25].

The association of nanoparticles with bioactive materials for bone metabolism, such as calcium, magnesium and strontium revealed the formation of apatite hydroxycarbonate on their surface and biocompatibility with human periodontal ligament fibroblasts (hPDLFs) [17]. MSN hydrogel loaded with carboxymethyl chitosan and clindamycin exhibited biomineralizing properties and biocompatibility in human mesenchymal stem cells (hMSCs), in addition to antimicrobial activity against *Streptococcus sanguinis* [25]. The mineralization mechanism has not been fully clarified, but it is suggested that after cellular internalization, the nanoparticles may mediate chemical signals that activate gene expression and/or alkaline phosphatase activity, responsible for promoting ideal concentrations of inorganic phosphate and decrease extracellular pyrophosphate, facilitating local mineralization [25,98].

SNPs loaded with curcumin also exhibited biocompatibility in dental pulp stem cells and dose-dependent antimicrobial activity against *Porphyromonas gingivalis*, the bacteria involved in periodontitis. Among other mechanisms, it is presumed that curcumin can damage the bacterial membrane, inhibit bacterial proliferation, or generate the generation of reactive oxygen species (ROS) [97]. Furthermore, MSNs with flavonoids such as baicalein and baicalin were able to down-regulate the expression of pro-inflammatory cytokines. Despite the potential in vitro effect in modulating the immune-inflammatory response, baicalein significantly reduced the viability of primary human gingival epithelial cells (hGECs) in a dose-dependent, with formation of cellular voids. In contrast, baicalin has not been shown to be cytotoxic [8].

SNPs were also tested as components of implant cleaning creams to remove organic residues and reduce the abrasion often caused by conventional toothpastes. The addition of hydrated SNPs in experimental implant paste resulted in greater protection against abrasion and reduction of organic contaminants such as carbon when compared to conventional dentifrices [95]. Conventional toothpastes contain compounds such as organic compounds, fluoride ions and abrasives, which affect surface stability, chemical properties, cause corrosion, increase roughness and cause significant damage to the implant surface [99,100]. For the number of bacteria, both the conventional dentifrices and the cream developed in the study showed significant bacterial removal [95].

3.3. Biocompatibility and toxicity of SNPs

As the use of SNPs has expanded to various applications, including in medicine, the potential exposure of humans to these substances has increased. It is therefore important to ensure that SNPs are biocompatible and safe for use in humans [101,102]. Studies to date are inconclusive and, in some cases, controversial. Cohesive data on pharmacokinetics is lacking, considering the different variables that interfere with biological effects [2,5,6]. Furthermore, the production method and physicochemical properties of SNPs, particularly their nanometric particle size, have been cited as potential factors that may negatively impact human safety and health [101,102].

The particle size is very important to measure the biocompatibility of nanomaterials and nanoformulations. The basis of this hypothesis is that NPs with smaller sizes have greater cytotoxicity since they diffuse more rapidly to tissues. However, there is no consensus on the effect of size on toxicity [101]. Table 2 shows results from SNPs biocompatibility in dentistry, associating the NPs size, time, and exposure dose with relative cytotoxicity. The SNPs mean size ranged from 52.85 to 425 nm and no study observed cytotoxicity for the investigated nanoparticles. These findings confirm the uncertainty about the nanoparticle size effect on in vitro and in vivo biocompatibility. In addition, generally, studies included in this review focus on evaluating physicochemical properties and short-term nanocarriers of substances. Note that few in vitro studies address biocompatibility in oral cells and, consequently, in vivo evidence to support SNPs clinical safety is lacking.

Although not well established, the main mechanism involved in the cytotoxicity of SNPs is believed to be the induction of oxidative stress (generation of reactive oxygen species – ROS), which oxidize the polyunsaturated fatty acids of the cell membrane, leading to cell necrosis or apoptosis. The shape, particle, and pore size in turn influence the level of intracellular ROS and, consequently, toxicity [6,102].

The systematic review by Murugadoss et al. [102] found that in vitro, SNPs showed cytotoxicity and genotoxicity in different cell lines and induced ROS, apoptosis, and autophagy (intrinsic or mitochondrial pathway) in a size and dose-dependent manner. Furthermore, SNPs induced ROS and adversely affected the cardiovascular system, resulting in platelet, aggregation, endothelial dysfunction with pro-inflammatory signs, and red blood cell hemolysis. *In vivo*, rats and mice were exposed to SNPs by the administration routes – oral, inhalation, topical, and parenteral, single dose or long-term. The administration route and the

Table 2
Summary of studies on SNPs biocompatibility and toxicity.

Material type	SNPs type	Cell or animal species studied	Particle* /pore size• (nm)	Exposure dose and exposure time	Experimental methods	Results	Reference
-	MSNs – MCM−41 (nano-BE and nano-BA)	Human gingival epithelial cells	367 ± 94 *	12.5, 25, 50, 100, and 200 μg mL^{-1} 24 h rated	CCK−8	Biocompatible *	[8]
Superhydrophobic coating material for denture surface	Not specified	Dental pulp cells	Not informed	0.5, 0.8, or 1.0 % 24, 48, and 72 h rated	MTT	Biocompatible	[14]
-	MSN (MSN Mg- and Sr-doped NPs for moxifloxacin)	Periodontal ligament fibroblasts	151.9 to 534.7 *	60, 125, and 250 μg mL^{-1} 24 h rated	MTT	Biocompatible	[17]
Composite resins	MSN (Zn-MSN)	Osteoblasts MC3T3-E1	138 *	0 %, 2 %, 5 %, 10 % and 15 % 1, 3, and 5 days rated	Live/Dead staining and MTT	Biocompatible	[24]
PMMA	MSN with amphotericin B	Immortalized human oral keratinocytes	85.2 ± 7.7 * 3.54 ± 0.41•	0, 0.5, 1, 2.5 or 5 % 24 h rated	WST	Biocompatible	[40]
PMMA	Silver-sulfadiazine-loaded MSN	Immortalized human oral keratinocytes	85.2 ± 7.7 * 3.54 ± 0.41 to 3.50 ± 0.31•	0.5, 1, 2.5, or 5 % 24 h rated	WST	Biocompatible	[41]
Dental Adhesive	Octenidine dihydrochloride-loaded MSN	Human gingival fibroblasts	424 ± 75 *	0, 5, 15, or 50 ng mL^{-1} 24 h rated	WST	Biocompatible	[53]
Dental Adhesive	CHX/MSN-PLGA	Dental pulp stem cells	~ 78 *	5 or 10 % Exposure time uninformed	MTT	Biocompatible	[66]
Glass ionomer cement	nano-HA-SiO_2	Human Dental Pulp Stem Cells	Not informed	5 % 24 h	MTT	Biocompatible	[75]
Biocomposite	MSN (nHA@MSN)	Human dental pulp cells	150 – 350 *	0, 10, 20, 40, 80, 160, 320, 640 μg mL^{-1} 24 h rated	CCK−8	Biocompatible	[83]
-	MSN (Ag-BGN@MSN)		100 – 350 *	1 %, 3 % and 5 % 24, 48 and 72 h rated	MTT	Biocompatible	[84]
Composite hydrogels	Clindamycin-releasing mesoporous silica/ carboxymethyl chitosan	Human mesenchymal stem cells	1,33 cm3g−1•	1, 2 and 7 days	MTT	Biocompatible	[25]
-	Curcumin-loaded silica nanoparticles	Dental pulp stem cells	110 ± 1,23 *	24 h	MTT	Biocompatible	[97]
-	Magnesium-loaded silica nanoparticles	MC3T3-E1	16 – 25 μm*	0.5 %, 1 %, and 1.5 % 1, 3 and 5 days	Live/Dead staining	Biocompatible	[50]

Experimental methods: MTT – [3-(4,5-dimethylthyazol-2-yl)−2,5-diphenyltetrazolium] bromide, WST-1 – water-soluble tetrazolium, CCK-8 – Cell Counting Kit-8; LDH – Pierce lactate dehydrogenase. MSNs - Mesoporous silica nanoparticle; MSN/CHX-PLGA - chlorhexidine-loaded mesoporous silica nanoparticle modified with poly-(latic-*co*-glycolic acid); Zn-MSN – zinc-loaded mesoporous silica nanoparticle; Ag-BGN-MSN - silver-doped bioactive glass/mesoporous silica nanoparticle; Ag-MSN – silver-doped mesoporous silica nanoparticle; Nano-BA and Nano-BE - baicalein and baicalin encapsulated in amine-modified MSNs; nano-HA-SiO_2 – nano-hydroxyapatite-silica; nHA@MSN – nanohydroxyapatite/mesoporous silica nanoparticles.
*At high concentrations (200 μg mL^{-1}), nano-BE reduced cell viability, but biocompatibility was confirmed by the stability of the LDH (Pierce Lactate Dehydrogenase) test

SNPs physicochemical properties influenced the toxicokinetic with adverse effects mainly on the lungs, kidneys, liver, and brain. Interestingly, toxic effects occurred in animals exposed to a single dose whereas those exposed chronically showed no local or systemic toxicity. The authors conclude that the correlation between the findings remains unestablished due to the different methodologies used [102].

Indeed, adverse immune reactions and the production of inflammatory mediators have been observed in response to SNPs, and the extent of these effects can depend on various factors such as size, dose, surface charge of the nanoparticles, and the type of immune cell. Larger pore sizes (> 30 nm) induce less intracellular ROS in macrophages and have fewer pro-inflammatory effects in both cell culture and animal models [6]. Overall, the effects of SNPs on the immune system are complex and can vary depending on many factors. Further research is needed to fully understand the immunological effects of SNPs and to guide their safe use in various applications.

4. Discussion

Research on SNPs, especially MSN, has become an emerging field over the years, due to their promising physicochemical properties, uniform pore distribution (pore diameters between 2 and 50 nm), and in vitro and in vivo biocompatibility. In addition, these nanoparticles have the advantages of simple and economical synthesis, easy scale-up, and the possibility of surface modification with functional molecules to improve stability [103–105]. Several studies have synthesized and characterized SNPs and given their potential use in a wide range of areas, investigated their effect on dental materials and formulations [10,32,46,65,72,89,90,95].

The first reason for this is that SNPs can be synthesized by different methods, such as Stöber, sol-gel and microemulsion methods, using different materials, which results in particles with different morphologies [3,26,101,106,107]. Secondly, SNPs have characteristics that favor their use for various purposes. In the field of dentistry, significant research has been dedicated to enhancing the overall properties of intraoral [9,16,18,31,37,58,73,94] and extraoral dental materials [10,

49,50]. These improvements aim to benefit various dental applications, including prosthetics, restorative dentistry, orthodontics, and addressing oral conditions such as dentin hypersensitivity and periodontitis. Researchers have also explored the use of SNPs as nanocarriers for adsorbing or loading hydrophilic and hydrophobic bioactive substances [22,25,40,61,67,68,83] for the prevention and treatment of oral conditions within the dental field.

The addition of SNPs can impact the mechanical properties of materials, with a positive effect depending on the concentrations used. In general, low concentrations of SNPs were more appropriate to improve the physicochemical properties of PMMA-based dental prostheses [9,31, 32,34,39], maxillofacial prostheses [10,49], adhesives [20,65–67,69, 70], cements [76,77] and orthodontic materials [89] as they present a more homogeneous distribution in the matrices, being able to provide greater reinforcement and resistance to the experimental materials. On the contrary, with higher concentrations of SNPs there was a tendency for agglomeration with heterogeneous distribution of particles in the matrices and, consequently, impairment of physicochemical properties [9,19,20,34,39,40,65,67,76,77,88,90].

Furthermore, SNPs associated or not with other substances have demonstrated potential for the treatment of painful symptoms in dentistry, such as dentin hypersensitivity due to obliteration of dentinal tubules [81–84], remineralizing ability [17,25,81–83], anti-inflammatory activity [8] and antimicrobial activity against oral bacteria [25,53,66,67,69,73,88,89,95,97].

Although often desirable, it is worth noting that the addition of nanoparticles to dental materials to obtain antimicrobial properties often results in a reduction in physicochemical properties [22]. Because of this, the development of dental materials that present antimicrobial activity to reduce the pathogenicity of oral biofilm with adequate general properties, without drastically altering the microbiome and the viability of oral cells, is the target of many studies [22,52]. To the best of our knowledge, only one self-etching adhesive (CLEARFIL SE Protect) with antimicrobial activity has been marketed to date. However, this product does not have SiNPs in its formulation as described by the company. Indeed, there is a challenge in translating in vitro studies into materials that can be clinically used while maintaining quality standards and promoting antimicrobial activity.

While in vitro studies have yielded promising results and significantly contributed to our comprehension of particle behavior in materials, formulations, oral tissues, and microorganisms, thus advancing the potential therapeutic application of SNPs in dentistry, it is crucial to acknowledge that this study method is confined to controlled experimental variables. Consequently, it may not fully represent the real oral conditions that materials and formulations will encounter. Hence, it is noted that there exists a substantial gap in the literature concerning the actual short-term and long-term impact of SNPs within the oral cavity. This is due to the scarcity of in vivo studies, with only one such study discovered [61]. Additionally, this study was confined to assessing tooth enamel demineralization over a four-week period.

Moreover, there has been limited exploration of the biocompatibility of SNPs in oral cells, with all the available studies being conducted exclusively in vitro (Table 2). Although silica is considered a non-cytotoxic substance for the organism and is already used in several areas, at the nanoscale, it is suggested that the particles diffuse more quickly into tissues, potentially contributing to greater cytotoxicity [99, 106], although there is no consensus on the effect of particle size on toxicity [101]. The studies included in this review showed SNPs with different sizes, ranging between ~78 nm [66] and ~424 nm [53] were not cytotoxic to oral cells, and also the size of the particles did not seem to interfere with the physicochemical and antimicrobial properties.

Although SNPs have shown promise in dentistry, more in vivo studies are needed to elucidate the physicochemical and biological effects of SNPs in the oral cavity. Additionally, there is a need for more long-term studies evaluating the safety and biocompatibility of SNPs in vivo. This includes studying the potential accumulation of nanoparticles in tissues and organs, as well as their potential toxicity and inflammatory responses over time. The development of standardized protocols for testing and evaluating the safety of SNPs is also necessary to ensure their safe and effective use in various applications.

5. Conclusions

The potential applications of SNPs in dental materials are vast and promising, and further research is needed to fully explore and optimize their properties for these applications. It will be important to carefully evaluate the biocompatibility and safety of these materials through in vitro and in vivo studies before they can be used in clinical practice, in addition to studies to verify their long-term biological and physicochemical properties in nanomaterials and nanoformulations, intraorally or extraorally,

Acknowledgments

This work was supported by the following Brazilian research agencies: National Council for Scientific and Technological Development (CNPq), and Coordination of Superior Level Staff Improvement (CAPES), Support Fund for Teaching, Research and Extension – FAEPEX – University of Campinas (grant#2393/19) and São Paulo Research Foundation (FAPESP) (grant# 2019/09010–5 and 2023–11067-0), who we thank for the financial support. The first author was funded by the grant #132616/2020–3 (CNPq). Dr Prokopovich would like to thank her funding: CONFAP - CNPq - The UK Academies 2018; and FAPESP-CARDIFF – SPRINT 1/2019. In addition, the authors thank Espaço da Escrita – Pró-Reitoria de Pesquisa – UNICAMP – for the language services provided.

References

[1] Manzano M, Vallet-Regí M. Mesoporous silica nanoparticles in nanomedicine applications. J Mater Sci Mater Med 2018;29. https://doi.org/10.1007/s10856-018-6069-x.
[2] Li Z, Mu Y, Peng C, Lavin MF, Shao H, Du Z. Understanding the mechanisms of silica nanoparticles for nanomedicine. Wiley Inter Rev Nanomed Nanobiotechnol 2021;13. https://doi.org/10.1002/wnan.1658.
[3] Gonçalves MC. Sol-gel silica nanoparticles in medicine: A natural choice. design, synthesis and products. Molecules 2018:23. https://doi.org/10.3390/molecules23082021.
[4] Jandt KD, Watts DC. Nanotechnology in dentistry: Present and future perspectives on dental nanomaterials. Dent Mater 2020;36:1365–78. https://doi.org/10.1016/j.dental.2020.08.006.
[5] Mebert AM, Baglole CJ, Desimone MF, Maysinger D. Nanoengineered silica: Properties, applications and toxicity. Food Chem Toxicol 2017;109:753–70. https://doi.org/10.1016/j.fct.2017.05.054.
[6] Hosseinpour S, Walsh LJ, Xu C. Biomedical application of mesoporous silica nanoparticles as delivery systems: a biological safety perspective. J Mater Chem B 2020;8:9863–76. https://doi.org/10.1039/d0tb01868f.
[7] Murugan B, Krishnan UM. Differently sized drug-loaded mesoporous silica nanoparticles elicit differential gene expression in MCF-7 cancer cells. Nanomedicine 2021;16:1017–34. https://doi.org/10.2217/nnm-2020-0375.
[8] Li X, Luo W, Ng TW, Leung PC, Zhang C, Leung KCF, et al. Nanoparticle-encapsulated baicalein markedly modulates pro-inflammatory response in gingival epithelial cells. Nanoscale 2017;9:12897–907. https://doi.org/10.1039/c7nr02546g.
[9] Balos S., Pilic B., Markovic D., Pavlicevic J., Luzanin O. Poly(methyl-methacrylate) nanocomposites with low silica addition Balos et al. n.d.
[10] Zayed SM, Alshimy AM, Fahmy AE. Effect of surface treated silicon dioxide nanoparticles on some mechanical properties of maxillofacial silicone elastomer. Int J Biomater 2014;2014. https://doi.org/10.1155/2014/750398.
[11] Gad MM, Fouda SM, Al-Harbi FA, Näpänkangas R, Raustia A. PMMA denture base material enhancement: a review of fiber, filler, and nanofiller addition. Int J Nanomed 2017;12:3801–12. https://doi.org/10.2147/IJN.S130722.
[12] Topouzi M, Kontonasaki E, Bikiaris D, Papadopoulou L, Paraskevopoulos KM, Koidis P. Reinforcement of a PMMA resin for interim fixed prostheses with silica nanoparticles. J Mech Behav Biomed Mater 2017;69:213–22. https://doi.org/10.1016/j.jmbbm.2017.01.013.
[13] Jiangkongkho P, Arksornnukit M, Takahashi H. The synthesis, modification, and application of nanosilica in polymethyl methacrylate denture base. Dent Mater J 2018;37:582–91. https://doi.org/10.4012/dmj.2017-142.
[14] Chen F, Zhao ER, Hableel G, Hu T, Kim T, Li J, et al. Increasing the efficacy of stem cell therapy via triple-function inorganic nanoparticles. ACS Nano 2019. https://doi.org/10.1021/acsnano.9b00653.

[15] Gad MM, Abualsaud R, Alqarawi FK, Emam ANM, Khan SQ, Akhtar S, et al. Translucency of nanoparticle-reinforced pmma denture base material: An in-vitro comparative study. Dent Mater J 2021;40:972–8. https://doi.org/10.4012/dmj.2020-296.
[16] Liu F, Sun B, Jiang X, Aldeyab SS, Zhang Q, Zhu M. Mechanical properties of dental resin/composite containing urchin-like hydroxyapatite. Dent Mater 2014;30:1358–68. https://doi.org/10.1016/j.dental.2014.10.003.
[17] Pouroutzidou GK, Liverani L, Theocharidou A, Tsamesidis I, Lazaridou M, Christodoulou E, et al. Synthesis and characterization of mesoporous Mg-and sr-doped nanoparticles for moxifloxacin drug delivery in promising tissue engineering applications. Int J Mol Sci 2021;2021:577. https://doi.org/10.3390/ijms.
[18] Larissa P, Gambrill B, de Carvalho RDP, Picolo MZD, Cavalli V, Boaro LCC, et al. Development, characterization and antimicrobial activity of multilayer silica nanoparticles with chlorhexidine incorporated into dental composites. Dent Mater 2023;39:469–77. https://doi.org/10.1016/j.dental.2023.03.005.
[19] Hosseinalipour M, Javadpour J, Rezaie H, Dadras T, Hayati AN. Investigation of mechanical properties of experimental Bis-GMA/TEGDMA dental composite resins containing various mass fractions of silica nanoparticles. J Prosthodont 2010;19:112–7. https://doi.org/10.1111/j.1532-849X.2009.00530.x.
[20] Mazloom-Jalali A, Taromi FA, Atai M, Solhi L. Dual modified nanosilica particles as reinforcing fillers for dental adhesives: Synthesis, characterization, and properties. J Mech Behav Biomed Mater 2020;110. https://doi.org/10.1016/j.jmbbm.2020.103904.
[21] Alzayyat ST, Almutiri GA, Aljandan JK, Algarzai RM, Khan SQ, Akhtar S, et al. Effects of SiO 2Incorporation on the Flexural Properties of a Denture Base Resin: An in Vitro Study. Eur J Dent 2022;16:188–94. https://doi.org/10.1055/s-0041-1732806.
[22] Zhang JF, Wu R, Fan Y, Liao S, Wang Y, Wen ZT, et al. Antibacterial dental composites with chlorhexidine and mesoporous silica. J Dent Res 2014;93:1283–9. https://doi.org/10.1177/0022034514555143.
[23] Stewart CA, Finer Y. Biostable, antidegradative and antimicrobial restorative systems based on host-biomaterials and microbial interactions. Dent Mater 2019;35:36–52. https://doi.org/10.1016/j.dental.2018.09.013.
[24] Bai X, Lin C, Wang Y, Ma J, Wang X, Yao X, et al. Preparation of Zn doped mesoporous silica nanoparticles (Zn-MSNs) for the improvement of mechanical and antibacterial properties of dental resin composites. Dent Mater 2020;36:794–807. https://doi.org/10.1016/j.dental.2020.03.026.
[25] Sungkhaphan P, Thavornyutikarn B, Kaewkong P, Pongkittiphan V, Pornsuwan S, Singhatanadgit W, et al. Antibacterial and osteogenic activities of clindamycin-releasing mesoporous silica/carboxymethyl chitosan composite hydrogels. R Soc Open Sci 2021;8. https://doi.org/10.1098/rsos.210808.
[26] Narayan R, Nayak UY, Raichur AM, Garg S. Mesoporous silica nanoparticles: a comprehensive review on synthesis and recent advances. Pharmaceutics 2018;10. https://doi.org/10.3390/pharmaceutics10030118.
[27] Ghimire PP, Jaroniec M. Renaissance of Stöber method for synthesis of colloidal particles: new developments and opportunities. J Colloid Interface Sci 2021;584:838–65. https://doi.org/10.1016/j.jcis.2020.10.014.
[28] Patel E, Pradeep P, Kumar P, Choonara YE, Pillay V. Oroactive dental biomaterials and their use in endodontic therapy. J Biomed Mater Res B Appl Biomater 2020;108:201–12. https://doi.org/10.1002/jbm.b.34379.
[29] Marovic D, Haugen HJ, Negovetic Mandic V, Par M, Zheng K, Tarle Z, et al. Incorporation of copper-doped mesoporous bioactive glass nanospheres in experimental dental composites: Chemical and mechanical characterization. Materials 2021;14. https://doi.org/10.3390/ma14102611.
[30] Vojdani M, Bagheri R, Khaledi AAR. Effects of aluminum oxide addition on the flexural strength, surface hardness, and roughness of heat-polymerized acrylic resin. J Dent Sci 2012;7:238–44. https://doi.org/10.1016/j.jds.2012.05.008.
[31] Gad MM, Abualsaud R, Al-Thobity AM, Baba NZ, Al-Harbi FA. Influence of addition of different nanoparticles on the surface properties of poly (methylmethacrylate) denture base material. J Prosthodont 2020;29:422–8. https://doi.org/10.1111/jopr.13168.
[32] Gad MM, Abualsaud R, Alqarawi FK, Emam ANM, Khan SQ, Akhtar S, et al. Translucency of nanoparticle-reinforced pmma denture base material: An in-vitro comparative study. Dent Mater J 2021;40:972–8. https://doi.org/10.4012/dmj.2020-296.
[33] Cevik P, Yildirim-Bicer AZ. The effect of silica and prepolymer nanoparticles on the mechanical properties of denture base acrylic resin. J Prosthodont 2018;27:763–70. https://doi.org/10.1111/jopr.12573.
[34] Sodagar A, Bahador A, Khalil S, Saffar Shahroudi A, Zaman Kassaee M. The effect of TiO2 and SiO2 nanoparticles on flexural strength of poly (methyl methacrylate) acrylic resins. J Prosthodont Res 2013;57:15–9. https://doi.org/10.1016/j.jpor.2012.05.001.
[35] Zheng Y, Zheng Y, Ning R. Effects of nanoparticles SiO2 on the performance of nanocomposites. Mater Lett 2003;57:2940–4. https://doi.org/10.1016/S0167-577X(02)01401-5.
[36] Chan KS, Lee YD, Nicolella DP, Furman BR, Wellinghoff S, Rawls R. Improving fracture toughness of dental nanocomposites by interface engineering and micromechanics. Eng Fract Mech 2007;74:1857–71. https://doi.org/10.1016/j.engfracmech.2006.07.013.
[37] Kotanidis A, Kontonasaki E, Koidis P. Color alterations of a PMMA resin for fixed interim prostheses reinforced with silica nanoparticles. J Adv Prosthodont 2019;11:193–201. https://doi.org/10.4047/jap.2019.11.4.193.
[38] Al Thaher Y, Yang L, Jones SA, Perni S, Prokopovich P. LbL-assembled gentamicin delivery system for PMMA bone cements to prolong antimicrobial activity. PLoS One 2018;13. https://doi.org/10.1371/journal.pone.0207753.
[39] Alzayyat ST, Almutiri GA, Aljandan JK, Algarzai RM, Khan SQ, Akhtar S, et al. Antifungal efficacy and physical properties of poly(methylmethacrylate) denture base material reinforced with SiO2 nanoparticles. J Prosthodont 2021;30:500–8. https://doi.org/10.1111/jopr.13271.
[40] Lee JH, El-Fiqi A, Jo JK, Kim DA, Kim SC, Jun SK, et al. Development of long-term antimicrobial poly(methyl methacrylate) by incorporating mesoporous silica nanocarriers. Dent Mater 2016;32:1564–74. https://doi.org/10.1016/j.dental.2016.09.001.
[41] Jo JK, El-Fiqi A, Lee JH, Kim DA, Kim HW, Lee HH. Rechargeable microbial anti-adhesive polymethyl methacrylate incorporating silver sulfadiazine-loaded mesoporous silica nanocarriers. Dent Mater 2017;33:e361–72. https://doi.org/10.1016/j.dental.2017.07.009.
[42] Bollenl CML, Lambrechts P, Quirynen M. Comparison of surface roughness of oral hard materials to the threshold surface roughness for bacterial plaque retention: A review of the literature 1997;vol. 13.
[43] Köroğlu A, Şahin O, Dede DÖ, Deniz ŞT, Karacan Sever N, Özkan S. Efficacy of denture cleaners on the surface roughness and Candida albicans adherence of sealant agent coupled denture base materials. Dent Mater J 2016;35:810–6. https://doi.org/10.4012/dmj.2016-103.
[44] Cheng Q, Cao D, Liu X, Zheng Y, Shi Z, Zhu S, et al. Superhydrophobic coatings with self-cleaning and antibacterial adhesion properties for denture base. J Mech Behav Biomed Mater 2019;98:148–56. https://doi.org/10.1016/j.jmbbm.2019.06.006.
[45] Kaizer MR, Almeida JR, Gonçalves APR, Zhang Y, Cava SS, Moraes RR. Silica coating of nonsilicate nanoparticles for resin-based composite materials. J Dent Res 2016;95:1394–400. https://doi.org/10.1177/0022034516662022.
[46] Yoshizaki T, Akiba N, Inokoshi M, Shimada M, Minakuchi S. Hydrophilic nano-silica coating agents with platinum and diamond nanoparticles for denture base materials. Dent Mater J 2017;36:333–9. https://doi.org/10.4012/dmj.2016-243.
[47] Choi JJE, Uy CE, Ramani RS, Waddell JN. Evaluation of surface roughness, hardness and elastic modulus of nanoparticle containing light-polymerized denture glaze materials. J Mech Behav Biomed Mater 2020;103. https://doi.org/10.1016/j.jmbbm.2019.103601.
[48] Cevik P. Evaluation of Shore A hardness of maxillofacial silicones: the effect of dark storage and nanoparticles. Eur Oral Res 2019:99–104. https://doi.org/10.26650/eor.2018.469.
[49] Cevik P, Eraslan O. Effects of the addition of titanium dioxide and silaned silica nanoparticles on the mechanical properties of maxillofacial silicones. J Prosthodont 2017;26:611–5. https://doi.org/10.1111/jopr.12438.
[50] Prasadh S, Manakari V, Parande G, Wong RCW, Gupta M. Hollow silica reinforced magnesium nanocomposites with enhanced mechanical and biological properties with computational modeling analysis for mandibular reconstruction. Int J Oral Sci 2020;12. https://doi.org/10.1038/s41368-020-00098-x.
[51] Marghalani HY. Resin-based dental composite materials. Handbook of Bioceramics and Biocomposites. Springer International Publishing,; 2016. p. 357–405. https://doi.org/10.1007/978-3-319-12460-5_22.
[52] Tammaro L, Di Salle A, Calarco A, De Luca I, Riccitiello F, Peluso G, et al. Multifunctional bioactive resin for dental restorative materials. Polym (Basel) 2020;12. https://doi.org/10.3390/polym12020332.
[53] Stewart CA, Hong JH, Hatton BD, Finer Y. Responsive antimicrobial dental adhesive based on drug-silica co-assembled particles. Acta Biomater 2018;76:283–94. https://doi.org/10.1016/j.actbio.2018.06.032.
[54] Ardestani SS, Bonan RF, Mota MF, Farias RM, da C, Menezes RR, et al. Effect of the incorporation of silica blow spun nanofibers containing silver nanoparticles (SiO2/Ag) on the mechanical, physicochemical, and biological properties of a low-viscosity bulk-fill composite resin. Dent Mater 2021;37:1615–29. https://doi.org/10.1016/j.dental.2021.08.012.
[55] Wilson KS, Zhang K, Antonucci JM. Systematic variation of interfacial phase reactivity in dental nanocomposites. Biomaterials 2005;26:5095–103. https://doi.org/10.1016/j.biomaterials.2005.01.008.
[56] Chen MH, Chen CR, Hsu SH, Sun SP, Su WF. Low shrinkage light curable nanocomposite for dental restorative material. Dent Mater 2006;22:138–45. https://doi.org/10.1016/j.dental.2005.02.012.
[57] Mitra SB, Wu D, Holmes BN. An application of nanotechnology in advanced dental materials. J Am Dent Assoc 2003 Oct;134(10):1382–90. https://doi.org/10.14219/jada.archive.2003.0054. PMID: 14620019.
[58] Wang X, Cai Q, Zhang X, Wei Y, Xu M, Yang X, et al. Improved performance of Bis-GMA/TEGDMA dental composites by net-like structures formed from SiO2 nanofiber fillers. Mater Sci Eng C 2016;59:464–70. https://doi.org/10.1016/j.msec.2015.10.044.
[59] Nikolaidis AK, Koulaouzidou EA, Gogos C, Achilias DS. Synthesis of novel dental nanocomposite resins by incorporating polymerizable, quaternary ammonium silane-modified silica nanoparticles. Polym (Basel) 2021;13. https://doi.org/10.3390/polym13111682.
[60] Kim JJ, Moon HJ, Lim BS, Lee YK, Rhee SH, Yang HC. The effect of nanofiller on the opacity of experimental composites. J Biomed Mater Res B Appl Biomater 2007;80:332–8. https://doi.org/10.1002/jbm.b.30601.
[61] Rechmann P., Le C.Q., Chaffee B.W., Rechmann B.M.T. Demineralization prevention with a new antibacterial restorative composite containing QASi nanoparticles: an in situ study 2021. ⟨https://doi.org/10.1007/s00784–021-03837–4/Published⟩.
[62] Spencer P, Ye Q, Misra A, Goncalves SEP, Laurence JS. Proteins, pathogens, and failure at the composite-tooth interface. J Dent Res 2014;93:1243–9. https://doi.org/10.1177/0022034514550039.
[63] He L, Hao Y, Zhen L, Liu H, Shao M, Xu X, et al. Biomineralization of dentin. J Struct Biol 2019;207:115–22. https://doi.org/10.1016/j.jsb.2019.05.010.

[64] Dayo AF, Wolff MS, Syed AZ, Mupparapu M. Radiology of dental caries. Dent Clin North Am 2021;65:427–45. https://doi.org/10.1016/j.cden.2021.02.002.
[65] Azad E, Atai M, Zandi M, Shokrollahi P, Solhi L. Structure–properties relationships in dental adhesives: Effect of initiator, matrix monomer structure, and nano-filler incorporation. Dent Mater 2018;34:1263–70. https://doi.org/10.1016/j.dental.2018.05.013.
[66] Akram Z, Daood U, Aati S, Ngo H, Fawzy AS. Formulation of pH-sensitive chlorhexidine-loaded/mesoporous silica nanoparticles modified experimental dentin adhesive. Mater Sci Eng C 2021;122. https://doi.org/10.1016/j.msec.2021.111894.
[67] Yan H, Wang S, Han L, Peng W, Yi L, Guo R, et al. Chlorhexidine-encapsulated mesoporous silica-modified dentin adhesive. J Dent 2018;78:83–90. https://doi.org/10.1016/j.jdent.2018.08.012.
[68] Kreutz M, Kreutz C, Kanzow P, Tauböck TT, Burrer P, Noll C, et al. Effect of Bioactive and Antimicrobial Nanoparticles on Properties and Applicability of Dental Adhesives. Nanomaterials 2022;12. https://doi.org/10.3390/nano12213862.
[69] López-Ruiz M, Navas F, Fernández-García P, Martínez-Erro S, Fuentes M, aV, et al. L-arginine-containing mesoporous silica nanoparticles embedded in dental adhesive (Arg@MSN@DAdh) for targeting cariogenic bacteria. J Nanobiotechnol 2022;20. https://doi.org/10.1186/s12951-022-01714-0.
[70] Alhenaki AM, Attar EA, Alshahrani A, Farooq I, Vohra F, Abduljabbar T. Dentin bond integrity of filled and unfilled resin adhesive enhanced with silica nanoparticles—an sem, edx, micro-raman, ftir and micro-tensile bond strength study. Polym (Basel) 2021;13. https://doi.org/10.3390/polym13071093.
[71] Alkhazaleh A, Elfagih S, Chakka LRJ, Armstrong SR, Comnick CL, Qian F, et al. Development of Proanthocyanidin-Loaded Mesoporous Silica Nanoparticles for Improving Dental Adhesion. Mol Pharm 2022;19:4675–84. https://doi.org/10.1021/acs.molpharmaceut.2c00728.
[72] Bagher Rezvani M, Atai M, Safar Alizade H, Mohammadi Basir M, Koohpeima F, Siabani S, et al. The effect of incorporation of 0.5 %wt. silica nanoparticles on the micro shear bond strength of a resin modified glass ionomer cement. J Dent Shiraz Univ Med Sci 2019;20:124–30. https://doi.org/10.30476/DENTJODS.2019.44923.
[73] Elshenawy EA, El-Ebiary MA, Kenawy ER, El-Olimy GA. Modification of glass-ionomer cement properties by quaternized chitosan-coated nanoparticles. Odontology 2023;111:328–41. https://doi.org/10.1007/s10266-022-00738-0.
[74] Sundari I, Diansari V, Rahmayani L, Septiani D, Ginting DA. Study of microleakage between teeth and glass ionomer cement modified with 5% silica from sea sand. J Biomim, Biomater Biomed Eng 2020;48:1–9. https://doi.org/10.4028/www.scientific.net/JBBBE.48.1.
[75] Noorani TY, Luddin N, Ab, Rahman I, Masudi SM. In vitro cytotoxicity evaluation of novel nano-hydroxyapatite-silica incorporated glass ionomer cement. ZC105–9 J Clin Diagn Res 2017;11. https://doi.org/10.7860/JCDR/2017/24753.9739.
[76] Sajjad A, Bakar WZW, Mohamad D, Kannan TP. Characterization and enhancement of physico-mechanical properties of glass ionomer cement by incorporating a novel nano zirconia silica hydroxyapatite composite synthesized via sol-gel. AIMS Mater Sci 2019;6:730–47. https://doi.org/10.3934/matersci.2019.5.730.
[77] Aldhuwayhi SD, Sajjad A, Bakar WZW, Mohamad D, Kannan TP, Moheet IA. Evaluation of fracture toughness, color stability, and sorption solubility of a fabricated novel glass ionomer nano zirconia-silica-hydroxyapatite hybrid composite material. Int J Polym Sci 2021;2021. https://doi.org/10.1155/2021/6626712.
[78] Moraschini V, da Costa LS, dos Santos GO. Effectiveness for dentin hypersensitivity treatment of non-carious cervical lesions: a meta-analysis. Clin Oral Invest 2018;22:617–31. https://doi.org/10.1007/s00784-017-2330-9.
[79] Liu XX, Tenenbaum HC, Wilder RS, Quock R, Hewlett ER, Ren YF. Pathogenesis, diagnosis and management of dentin hypersensitivity: An evidence-based overview for dental practitioners. BMC Oral Health 2020;20. https://doi.org/10.1186/s12903-020-01199-z.
[80] Jung JH, Park SB, Yoo KH, Yoon SY, Bae MK, Lee DJ, et al. Effect of different sizes of bioactive glass-coated mesoporous silica nanoparticles on dentinal tubule occlusion and mineralization. Clin Oral Invest 2019;23:2129–41. https://doi.org/10.1007/s00784-018-2658-9.
[81] Tian L, Peng C, Shi Y, Xuan G, Zhong B, Qi J, et al. Effect of mesoporous silica nanoparticles on dentinal tubule occlusion: An in vitro study using sem and image analysis. Dent Mater J 2014;33:125–32. https://doi.org/10.4012/dmj.2013-215.
[82] Chiang YC, Chen HJ, Liu HC, Kang SH, Lee BS, Lin FH, et al. A novel mesoporous biomaterial for treating dentin hypersensitivity. J Dent Res 2010;89:236–40. https://doi.org/10.1177/0022034509357148.
[83] Yu J, Yang H, Li K, Lei J, Zhou L, Huang C. A novel application of nanohydroxyapatite/mesoporous silica biocomposite on treating dentin hypersensitivity: An in vitro study. J Dent 2016;50:21–9. https://doi.org/10.1016/j.jdent.2016.04.005.
[84] Jung JH, Kim DH, Yoo KH, Yoon SY, Kim Y, Bae MK, et al. Dentin sealing and antibacterial effects of silver-doped bioactive glass/mesoporous silica nanocomposite: an in vitro study. Clin Oral Invest 2019;23:253–66. https://doi.org/10.1007/s00784-018-2432-z.
[85] Zhang L, Sun H, Yu J, Yang H, Song F, Huang C. Application of electrophoretic deposition to occlude dentinal tubules in vitro. J Dent 2018;71:43–8. https://doi.org/10.1016/j.jdent.2018.01.012.
[86] Pourhajibagher M, Bahador A. Enhanced reduction of polymicrobial biofilms on the orthodontic brackets and enamel surface remineralization using zeolite-zinc oxide nanoparticles-based antimicrobial photodynamic therapy. BMC Microbiol 2021;21. https://doi.org/10.1186/s12866-021-02324-w.
[87] Govindaraj A, Dinesh SPS. Effect of Chlorhexidine Varnish and Fluoride Varnish on White Spot Lesions in Orthodontic Patients- a Systematic Review. Open Dent J 2021;15:151–9. https://doi.org/10.2174/1874210602115010151.
[88] Ahn SJ, Lee SJ, Kook JK, Lim BS. Experimental antimicrobial orthodontic adhesives using nanofillers and silver nanoparticles. Dent Mater 2009;25:206–13. https://doi.org/10.1016/j.dental.2008.06.002.
[89] De Oliveira Aguiar RC, Nunes LP, Batista ES, Viana MM, Rodrigues MC, Bueno-Silva B, et al. Experimental composite containing silicon dioxide-coated silver nanoparticles for orthodontic bonding: antimicrobial activity and shear bond strength. Dent Press J Orthod 2022;27. https://doi.org/10.1590/2177-6709.27.3.e222116.oar.
[90] Biglar N, Chaychi Raghimi E, Sadighian S, Karamitanha F, Zajkani E, Nourian A. Effect of incorporating silica-hydroxyapatite-silver hybrid nanoparticles into the resin-modified glass ionomer on the adhesive remnant index score and shear bond strength of orthodontic metal brackets: an in vitro study. Int Orthod 2023;21. https://doi.org/10.1016/j.ortho.2023.100761.
[91] Slowing II, Wu CW, Vivero-Escoto JL, Lin VSY. Mesoporous silica nanoparticles for reducing hemolytic activity towards mammalian red blood cells. Small 2009;5:57–62. https://doi.org/10.1002/smll.200800926.
[92] Mehrbakhsh E, Rezaei M, Babaie A, Mohammadi A, Mayan Sofla RL. Physical and thermo-mechanical properties of shape memory polyurethane containing reversible chemical cross-links. J Mech Behav Biomed Mater 2021;116. https://doi.org/10.1016/j.jmbbm.2021.104336.
[93] da Silveira RE, Elias CN, do Amaral FLB. Assessment of frictional resistance and surface roughness in orthodontic wires coated with two different nanoparticles. Microsc Res Tech 2022;85:1884–90. https://doi.org/10.1002/jemt.24049.
[94] Dadgar S, Sobouti F, Armin M, Ebrahiminasab P, Moosazadeh M, Rakhshan V. Effects of 6 different chemical treatments on force kinetics of memory elastic chains versus conventional chains: An in vitro study. Int Orthod 2020;18:349–58. https://doi.org/10.1016/j.ortho.2020.02.003.
[95] Al-Hashedi AA, Laurenti M, Amine Mezour M, Basiri T, Touazine H, Jahazi M, et al. Advanced inorganic nanocomposite for decontaminating titanium dental implants. J Biomed Mater Res B Appl Biomater 2019;107:761–72. https://doi.org/10.1002/jbm.b.34170.
[96] Götz W, Gerber T, Michel B, Lossdörfer S, Henkel KO, Heinemann F. Immunohistochemical characterization of nanocrystalline hydroxyapatite silica gel (NanoBone®) osteogenesis: a study on biopsies from human jaws. Clin Oral Implants Res 2008;19:1016–26. https://doi.org/10.1111/j.1600-0501.2008.01569.x.
[97] Shirmohammadi A, Maleki Dizaj S, Sharifi S, Fattahi S, Negahdari R, Ghavimi MA, et al. Promising antimicrobialaction of sustained released curcumin-loaded silica nanoparticles against clinically isolated porphyromonas gingivalis. Diseases 2023;11. https://doi.org/10.3390/diseases11010048.
[98] Vimalraj S. Alkaline phosphatase: structure, expression and its function in bone mineralization. Gene 2020;754. https://doi.org/10.1016/j.gene.2020.144855.
[99] Stájer A, Ungvári K, Pelsoczi IK, Polyánka H, Oszkó A, Mihalik E, et al. Corrosive effects of fluoride on titanium: Investigation by X-ray photoelectron spectroscopy, atomic force microscopy, and human epithelial cell culturing. J Biomed Mater Res A 2008;87:450–8. https://doi.org/10.1002/jbm.a.31764.
[100] Fais LMG, Fernandes-Filho RB, Pereira-Da-Silva MA, Vaz LG, Adabo GL. Titanium surface topography after brushing with fluoride and fluoride-free toothpaste simulating 10 years of use. J Dent 2012;40:265–75. https://doi.org/10.1016/j.jdent.2012.01.001.
[101] Tang F, Li L, Chen D. Mesoporous silica nanoparticles: synthesis, biocompatibility and drug delivery. Adv Mater 2012;24:1504–34. https://doi.org/10.1002/adma.201104763.
[102] Murugadoss S, Lison D, Godderis L, Van Den Brule S, Mast J, Brassinne F, et al. Toxicology of silica nanoparticles: an update. Arch Toxicol 2017;91:2967–3010. https://doi.org/10.1007/s00204-017-1993-y.
[103] Song Y, Li Y, Xu Q, Liu Z. Mesoporous silica nanoparticles for stimuli-responsive controlled drug delivery: advances, challenges, and outlook. Int J Nanomed 2017;12:87–110. https://doi.org/10.2147/ijn.s117495.
[104] Wuttke S, Lismont M, Escudero A, Rungtaweevoranit B, Parak WJ. Positioning metal-organic framework nanoparticles within the context of drug delivery – A comparison with mesoporous silica nanoparticles and dendrimers. Biomaterials 2017;123:172–83. https://doi.org/10.1016/j.biomaterials.2017.01.025.
[105] Arriagada F, Morales J. Limitations and opportunities in topical drug delivery: interaction between silica nanoparticles and skin barrier. Curr Pharm Des 2019;25:455–66. https://doi.org/10.2174/1381612825666190404121507.
[106] Croissant JG, Fatieiev Y, Almalik A, Khashab NM. Mesoporous silica and organosilica nanoparticles: physical chemistry, biosafety, delivery strategies, and biomedical applications. Adv Health Mater 2018;7. https://doi.org/10.1002/adhm.201700831.
[107] Aquib M, Farooq MA, Banerjee P, Akhtar F, Filli MS, Boakye-Yiadom KO, et al. Targeted and stimuli–responsive mesoporous silica nanoparticles for drug delivery and theranostic use. J Biomed Mater Res A 2019;107:2643–66. https://doi.org/10.1002/jbm.a.36770.