The Saudi Dental Journal (2024) **36**, 158–167

King Saud University

The Saudi Dental Journal

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ORIGINAL ARTICLE

Local and systemic adverse effects of nanoparticles incorporated in dental materials- a critical review

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Received 22 March 2023; revised 23 August 2023; accepted 28 August 2023
Available online 30 August 2023

KEYWORDS

Nanoparticle;
Adverse effects;
Dental materials;
Cytotoxicity;
Genotoxicity;
Risk assessment

Abstract *Introduction:* Nanotechnology is the science and engineering of nanoparticles whose dimensions range from 1 to 100 nm. Nanoparticles have special characteristics like increased surface area, high reactivity, and enhanced mechanical, thermal, and optical properties that make them attractive for use in dental applications. However, the use of nanoparticles in dental materials can have toxic effects on the human body. The objective of this paper is to discuss the toxic effects of various nanoparticles in dental materials, their adverse effect on human health, and measures to overcome such effects.

Objectives: Nanoparticles are used in the diagnosis, prevention, and treatment of oral diseases like dental caries, pulpo periodontal lesions, oral cancer, denture stomatitis, and candidiasis. Exposure to nanoparticles may occur to the dental professional, and the patient during procedures like restoration, finishing, and polishing. Such exposure to nanoparticles through inhalation, and ingestion causes toxic effects in the lungs, skin, brain, liver, and kidney. Proper risk assessment methods and preventive measures may help reduce these toxic effects to some extent.

Significance: Toxic effects of nanoparticles that are released during dental procedures, their route of exposure, and the concentration at which nanoparticles can induce toxic effects on the human body are discussed in detail in this review. The paper also aims to create awareness among dental professionals, students, and patients regarding nanoparticle exposure and its adverse effects, and methods to prevent and overcome these effects. Currently, it is ignored or taken lightly by the stakeholders and this review may throw light.

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Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

https://doi.org/10.1016/j.sdentj.2023.08.013

1. Introduction

Nanoparticles are incorporated in dental materials to provide antibacterial effects, as fillers to improve the flexural strength of the composites, as a coating on implant surfaces to improve osseointegration, and as local drug delivery systems to provide therapeutic effects (Park, 2007; Kasraei et al 2014) (Niu et al., 2014; Memarzadeh et al., 2015; Palaniraj et al.,2022). However toxic effects can arise from their incorporation in dental materials, as demonstrated by several in vitro as well as animal and human in vivo studies (Kumar et al.,2017; Schmalz et al.,2017). The present review summarizes the adverse effects of nanoparticles incorporated in dental materials, their toxicity mechanism, methods to assess toxicity, and strategies to reduce it.

1.1. Nanoparticles

Nanoparticles are atoms or molecules with sizes in the range of 1–100 nm. They are classified into a range of categories depending on their size, shape, and properties (Bonilla-Represa et al.,2020). In 1974, Norio Taniguchi introduced the term 'nanotechnology' (Sreenivasalu et al., 2022).

Nanoparticles can be mainly synthesized by three methods; chemical, physical, and biological. Chemical synthesis uses reducing agents and stabilizers such as sodium citrate, ascorbate, or sodium borohydride (NaBH4); Physical synthesis employs ultraviolet irradiation, thermal synthesis, and spray pyrolysis; Biological synthesis uses organisms like bacteria, fungi, and Plants as reducing agents (Sarkar et al.,2020).

Nanoparticle size, shape, and surface chemistry affect nanotoxicity (Pan et al.,2007). For example, nanoparticles with a smaller size and greater surface area can penetrate biological membranes more easily, leading to toxicity in various organs and tissues. Similarly, the difference in surface charge between nanoparticle and cell wall leads to toxicity (Bozich et al.,2014; Zhao et al.,2013).

1.2. Applications in dentistry

Nanoparticles are commonly classified into two main classes; Inorganic nanoparticles, such as metal or metal oxides like silver, gold, copper, silica, zinc oxide, titanium oxide, and zirconium oxide, are the most commonly used nanoparticles in dental materials. These nanoparticles can improve the mechanical properties of materials, provide antimicrobial effects, and enhance biocompatibility.

Organic nanoparticles, on the other hand, include nanotubes, nanofibers, nanocrystals, and solid lipid nanoparticles, such as chitosan and polyethylene glycol. These nanoparticles can provide targeted drug delivery, improve the physical properties of materials, and enhance bioactivity (Mahmud et al., 2022; Priyadarsini et al.,2020).

A range of examples is described in Table 1.

Fig. 1 depicts the number of literature publications on nanomaterials reported over the past 5 years. Nanocomposites and nanotubes have been reported predominantly in dentistry followed by those used as anti-microbial (Jandt and Watts, 2020).

2. Methodology

Literature search was conducted from different scientific publishing websites that include PubMed, Scopus, Web of Science, google scholar, and peer-reviewed online local and international journals. A total of 80 relevant scientific resources were collected to analyze the adverse effects of nanoparticles and measures to control and prevent the adverse effects.

2.1. Nanotoxicology

Nanoparticles incorporated in dental products may enter human cells which causes cell damage and damage to genetic material (Wani et al., 2011; Henshaw & O'Carroll, 2009). Toxicological studies on nanoparticles state that toxicity mainly comes from inhalation and ingestion. Inhaled nanoparticles can be deposited in the lungs, pharyngeal, nasal, tracheobronchial, and alveolar regions, and certain nanoparticle like titanium is found to cause pulmonary toxicity of acute exposure and bronco-alveolar lavage (BAL) inflammation (Grassian et al., 2007a, 2007b). Silver nanoparticles can also cause toxic effects, including argyria and argyrosis, which are characterized by bluish-grey discoloration of the skin and can affect the liver, kidneys, eyes, and intestinal tract (Panyala et al., 2008) (Albanese et al.,2012; Brayner, 2008).

Apart from inhalation and ingestion effects nanoparticles can also have adverse effects on the lymphatic system. Nanoparticles released from implant surfaces enter the lymph nodes and cause DNA damage (Hussain et al.,2001). Fibers from certain nanoparticles like carbon nanotubes are shown to have carcinogenic effects on the lungs of rats. Cardiovascular diseases have also been reported from exposure to nanoparticles (Seato et al., 2019).

Table 1 Applications of nanoparticles in dentistry.

Nanoparticle	Applications in dentistry
Chitosan Nanoparticle	Antibacterial property, Enamel repair, Remineralization, Tissue Engineering.
Silver Nanoparticle	Antimicrobial activity, Prevention of biofilms, Fillers in composite resin.
Titanium oxide Nanoparticle	Osseointegration of implants.
Graphene oxide Nanoparticle	Tissue Engineering, Modification of Glass ionomer cement.
Carbon Nanotubes	Diagnosis of oral cancer.
Silica Nanoparticle	Improves teeth whitening.
Quantum Dots	Nano drug delivery in oral cancer, Nanocarriers to cure periodontal diseases.
Fullerene Nanoparticle	Reduction of friction in Niti wires in orthodontics.

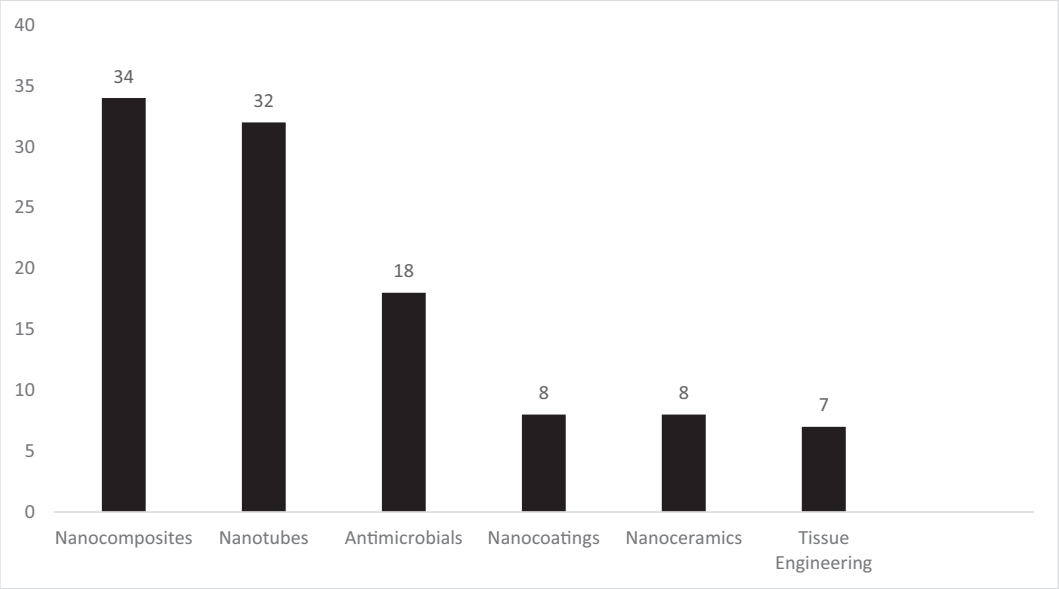

Fig. 1 Tentative Number of studies on nanomaterials in dentistry in the past five years.

Table 2 Evidence for adverse effects of nanoparticles predominantly focusing on dermatology, pulmonary, reproductive, and neurology.

Dermatotoxicity	Pulmonary Toxicity	Reproductive and Developmental toxicity	Neurotoxicity
Silver nanoparticles cause argyrosis (discoloration of the skin) in humans which has toxic effects on the liver, and kidneys. (Sicilia et al., 2008). Titanium oxide nanoparticles cause allergic contact dermatitis in dental personnel and patients. (Kumar et al., 2017)	Silver nanoparticles cause bronchoalveolar inflammation in mice, and rats. (Soto et al., 2007; Carlson et al., 2008) Titanium oxide nanoparticles cause bronchoalveolar inflammation and pulmonary toxicity in mice. (Grassian et al., 2007a, 2007b)	Zinc oxide nanoparticles cause impaired ovary growth in fish embryos. (Yu et al., 1982)Titanium oxide nanoparticles decreased survival, increased morphological abnormalities, and delayed embryo hatching in zebrafish. (Yan et al., 2014)	Titanium oxide nanoparticles cross the placental barrier and cause impairments in the rat fetal brain development (Lockman et al., 2004)Silica nanoparticles cause oxidative stress damage and microglial function alteration in neural cells (in vitro) . (Jallouli et al., 2007)

Table 2 below summarises the nanoparticles and their toxic effects on various systems in the human body. Dermatotoxicity effects, pulmonary toxicity, and developmental and neurotoxic effects of nanoparticles are discussed below (Holmes et al.,2016). However detailed studies, clinical reports, and systematic reviews on nanotoxicity in humans are very limited.

2.2. Mechanism of Nanotoxicity

Nanoparticles can directly interact with cells within organs, causing damage to cell membranes and interrupting normal cellular functions and homeostasis (Chen and Bothun, 2014). Another mechanism is the generation of free radicals which can occur due to high surface chemical reactivity of nanoparticles and through mitochondrial respiration. The increased production of free radicals leads to damage to cellular organelles like mitochondria, DNA, plasma membrane, and cell surface receptors (Zorov et al.,2014).

ROS generation may also affect the cell signaling pathways like nuclear factor kappa-light chain enhancer of activated B cells (NF-κB) which may affect cell differentiation and proliferation (Nishanth et al., 2011). Both ROS and signaling pathways have synergistic effects which result in apoptosis and necrosis of the cells and ultimately lead to organ damage or inflammatory response (Campisi et al.,2014).

2.3. Methods of toxicity Assessment

2.3.1. In-vitro toxicity assessment

Proliferation assay measures cellular metabolism. The advantage of this assay is that results are quick, with minimal manipulation of model cells and reproducible cells. This assay uses tetrazolium salt for the toxicity assessment of nanoparticles. MTT assay, XTT, and WST-1 are various assays used in proliferation toxicity assessment.

Table 3 Types of nanoparticles, experimental models, and toxic effects.

Types of Nanoparticles	Experimental models tested	Toxic Effects
Silver Nanoparticle	Rats, Zebrafish Embryos Human lung cancer cells	Memory impairment (CNS Damage) Placental damage, Foetus death (Muth-Köhne et al., ,2013).
Zinc oxide Nanoparticle	Bacteria, Mammalian cells, Human mesothelioma cello, hepatocytes	Cytotoxicity (Yang et al., 2008)Inflammatory cell infiltration in mice (Yang et al., 2010).
Titanium oxide Nanoparticle	Rat, Mice, Hamsters	Lesions observed in nasal cavity tissue (inhalational toxicity) (Kwon et al., 2012)
Carbon-based Nanoparticles	Lung fibroblast cells	DNA damage, Halts G1 phase (Kisin et al., 2007).
Silica Nanoparticles	Rats, mice, Human bronchoalveolar carcinoma cells, liver cells	Cytotoxicity Duan et al DNA damage (Napierska et al., 2010).
Graphene	Mice fibroblast cells, macrophage cells	Chromosomal alterations in the bone marrow and genotoxic effects on lung cells (El-Yamany et al., 2017).
Quantum dots	Rat adrenal medulla cells, Human endothelial cells	Cell death by cell shrinkage due to Chromatin condensation and membrane blebbing. (Villar et al., 2015).

Apoptosis assay is another method for toxicity assessment where free radicle generation causes apoptosis of cells and DNA damage. Annexin-V assay, Comet assay, and TdT-mediated dUTP-biotin nick end labeling (TUNEL)assay are used for apoptotic assessment. Apoptosis is confirmed by the reduction in cell size and DNA fragmentation.

Necrosis assay determines cell membrane integrity and cell viability. The neutral red and trypan blue dyes diffuse readily into the plasma membrane and enter the liposomes and bind by electrostatic bonds in the liposomal matrix. Any changes in liposomes caused by nanoparticles result in decreased uptake and binding of the dye. This helps to distinguish between live viable cells and dead cells. The oxidative assay uses reactive oxidative stress and reactive nitrogen species to determine the toxic effects (Kumar et al.,2017).

2.3.2. Invivo toxicity Assessment

The in-vivo toxicity assessment includes animal models like rodents and rabbits. Biodistribution, clearance, hematology, serum chemistry, and histopathology involve in vivo assessment of toxicity. Biodistribution is the route of distribution of nanoparticles detected by radiolabels. Clearance is by the excretion of nanoparticles from live animals at various time intervals. Serum chemistry is changing in cell type after exposure to nanoparticles. Histopathology determines the toxicity level of a nanoparticle in tissues (Wani et al., 2011).

Table 3 below summarises the nanoparticles and their toxic effects on various experimental models. However, the majority of the studies are based on cell culture and animal models. These studies do not fully evaluate nanotoxicity in human subjects and hence are limited in predicting nanotoxicity in humans (Holmes et al.,2016).

Table 4 below summarises the nanoparticles used in dentistry, the release of nanoparticles from dental materials, routes of exposure, size, and concentration of nanoparticles causing toxic effects, adverse effects, and methods to overcome the adverse effects of nanoparticles.

3. Methods to overcome nanoparticle toxicity

3.1. Routes of exposure

According to the Centre for Knowledge Management of Nanoscience & Technology (CKMT), the most common routes of exposure to nanoparticles include inhalation, ingestion, and dermal absorption. Inhalation hazard control measures include performing procedures under biosafety cabinets with HEPA filters. Ingestion of nanoparticles may occur in dental supply factory workers if good hygiene is not practiced. Dermal exposure can occur while handling nanoparticle powder and suspensions. Dental factory workers should be provided with gloves, lab coats, and safety goggles while handling nanoparticles. (Guidelines and Best Practices for Safe Handling of Nanomaterials in Research Laboratories and Industries, CKMT).

3.2. Classification of exposed people in dentistry

According to the FIDE (Federation of the European Dental Industry), three major categories of people are identified based on exposure to nanoparticles - Direct exposure of users, exposure of patients, and exposure of third parties to dental nanomaterials. Dental personnel, patients, dental laboratory technicians, and dental supply workers are being exposed to the toxic effects of nanoparticles. The lungs of dental personnel are targeted for the toxic effects of nanoparticles. High flow suctions with HEPA filters reduce exposure to nanodust. The high vacuum evacuators have a small square inlet and an oval inlet. The square inlet reduces the suction force and prevents

Table 4 Nanoparticles released from dental materials.

Nanoparticle NP	Dental Material	NP release from Dental Material	Route of exposure	Size and concentration of nanoparticles causing toxicity	Toxic reactions Local/ Systemic	Methods to overcome toxic effects	References
Silver Nanoparticle AgNP	Resin composite, Adhesive systems, Acrylic resin, Titanium implants, Endodontic irrigants	Nanoparticle release during recontouring, finishing, polishing, and removal of the old composite restoration.	Inhalation of nanocomposite dust	The median diameter of nanodust 34–64 nm Chronic inhalation of nano dust (< 5 μm) may cause local and systemic toxicity	*Local:* Allergic contact dermatitis to Methacrylates Systemic: Acute and chronic inflammation of the lungs	High-flow suctioning with HEPA filters, water cooling (water droplets engulf NP and increase size). Particle filtration masks (e.g., FFP (filtering facepiece) masks and Personal Protective Equipment (PPE) worn as protective barriers do not completely prevent inhalation, but provide first base protection. It is recommended to sculpt the uncured composite to reduce excessive contouring with burs.	Assessing Nanoparticle Risks to Human Health - Controlling Nanoparticle Exposures Peter C. Raynor1 and Thomas M. Peters (Van Landuyt et al., 2014). (Schmalz et al., 2017)
AgNP- silver nanoparticle; Nanodust- Nanoparticle release during recontouring, finishing, polishing, and removal of the old composite restoration. HEPA-High efficiency particulate air.							
Zinc oxide Nanoparticle ZnO Np	Polymerised acrylic resin, Resin composite, GlassIonomer Cement (GIC) , Endodontic Nanosealer, Implant coatings, Ortho wires and brackets	Nanoparticles from the denture base are released into oral mucosa and penetrate the tissues inducing toxic effects.	Slow release of zinc oxide nanoparticle from denture base (Denture stomatitis-therapeutic effect)	The concentration used in dental products-2.2–3.5mg/L	No cytotoxic reactions upto 20mg/L Cytotoxicity on Endothelial cells of human blood vessels at a concentration of30 mg/L (Paszek et al., 2012)	ZnO release from dental nanomaterials is only(5.649 mg/mL) .The cytotoxic effect is not observed until the concentration reaches (20 mg/ L) .	(Cierech et al., 2019)
Titanium oxide Nanoparticle TiONP	Dental implants, Dental Ceramics	Small Movements between the implant-abutment connection increase the wear between surfaces and releases metal ions and micro- and nanoparticles into the surrounding tissues	Release of TiO NP after insertion of implants due to corrosion effects	Low doses have no adverse effects on Zebra fish (10–50 mg/L), Higher levels (100–300 mg/ L) had significant adverse effects.	Local Effects: Peri-Implant bone loss -Chronic inflammation around the implant Dermatological:Allergic contact dermatitis (0.6%) of the population of 1500 people	A tight connection between the implant and abutment can prevent micro-movements. Alternative to titanium, Zirconia implants are suggested Epicutaneous testing (ECT)Lymphocyte transformation test (LTT)Memory Lymphocyte Immunostimulation Assay (MELISA) diagnostic test for Ti0NP	(Bressan et al., 2019) (Sicilia et al., 2008)

						hypersensitivity	
Graphene	Tissue Engineering, Coating of Dental Implants, Denture resins, Fluorinated GIC	Release of Reactive oxidative stress (ROS) from the dissolution of graphene, nanoparticles may induce oxidative stress damage in genetic material, lipoproteins inducing cell death or necrosis.	Graphene nanoparticles cause cell necrosis by mitochondria membrane damage and apoptosis by free Radical generation.	Graphene Nanoparticles with sizes <100 nm can easily enter cells, <40nm enter the nucleus, and <35nm can cross the blood–brain barrier and induce toxicity.	A low concentration of Graphene had no cytotoxic effects at 20 μg/ml (Pang et al.,2017) Cytotoxicity was found when the concentration was up to 50 μg/ml. (Ding et al.,2015).	The threshold limit is 50 ug/ ml	(Ge et al., 2018).
Carbon Nanotube CNT	Multiwalled carbon nanotubes (MWCNT) used in Reinforced GIC, Guided bone regeneration, and as Scaffolds.	Laboratory Ablation facility (particles <100 nm) a dry cutting (Source; respirable fibers) Granulomatous inflammation or alveolar septal thickening is found in the liver, spleen, and lungs due to the accumulation of CNT (Qin Y et al., 2017)	Inhalation route	Single Walled carbon nanotube (SWCNTs) at size (20–50 nm diameter) and Multiwalled carbon nanotube (MWCNT) (diameter: 52–56 nm) cause toxic effects. The recommended exposure limit is given as 1 μg/m3 for respirable size fraction	Increased deposition in the lung; sub pleura observed. SWCNTs showed higher toxicity than MWCNTs in Alveolar macrophages. SWCNT caused inflammation, and progressive fibrosis in mice (Maynard et al., 2004)	Higher molecular weight polyethylene glycol chain attachment to CNTs showed no toxic effects and was easily eliminated from the body, and had very low deposition in the liver and spleen. CNTs coated with CNTs globular heads had no toxic effects.	(Shvedova et al., 2008) (Yang et al., 2008). (Pondman et al., 2015)
Silica Nanoparticle	Silica Nanoparticles are used as fillers in alginate impression mixes, composites, and dental ceramics.	Dental supply factory; Small leaks during manufacturing could expel large amounts of powder which can mix into the ambient air. Silicosis occurs in dental factory workers due to exposure. (de la Hoz et al., 2004)	Inhalation of Silica Nanodust	0.05 mg/m^3 (50 μg/m^3) 10 h/day during a 40-hour workweek [NIOSH 1974].	Silica nanoparticles released from industries induce silicosis as well as lung cancer. They also induce cytotoxicity, genotoxicity, and immunotoxic effects.	Awareness among dental workers regarding silicosis, Exposure monitoring, Proper ventilation and usage of particle filtration masks can reduce the incidence of silicosis and lung cancer.	(Ahmad et al., 2012)
Quantum Dots (QD)	Dental adhesives, Resin composites	Quantum dots core added to composite resins provides fluorescence properties that help to improve the esthetics of natural teeth. (Alves et al., 2010)	Slow release of QDs from dental composites	80 nM of Polyethylene glycol coated -QDs is the maximum permissible dose (Van der Zande et al., 2012)	QDs impair mitochondria damage and induce endothelial apoptosis (Yan et al., 2011)	QDs are stored in micromolar concentrations and will be diluted easily at low concentrations.	(Valizadeh et al., 2012)

(*continued on next page*)

		Quantum dots were added as nonagglomerated nanofillers for adhesive resins. (Garcia et al., 2016)					
Fullerene nanoparticles	Orthodontic wires coated with fullerene nanoparticles	To reduce friction between wires and brackets	Slow release of fullerene nanoparticles from orthodontic wires	Dosage above 2 g/m^3 C_{60} Fullerene is considered toxic. C_{60} is a spherical carbon allotrope With 60 atoms connected by single and double bonds.	C_{60} fullerene nanoparticles may cause pulmonary deposition.	Approximately 2 g/m^3 C_{60} fullerenes had minimal toxicity. (Baker et al.,2008)	(Zhao and Castranova, 2011)
Chitosan Nanoparticles	Endodontic irrigants Antibacterial, (Del Carpio-Perochena et al., 2011) Oral Drug delivery, (Murugesan and Narayan, 2019) Coating of implants, Guided tissue Regeneration.	Irrigation of root canal, local drug delivery system with a sustained release profile, while maintaining intimate contact with the oral mucosa.	Slow release of chitosan from implant coatings.	200 −340nm chitosan nanoparticles	30 mg/L and 40 mg/L concentration causes toxic effects in zebrafish embryos	Chitosan nanoparticle of Size 340 nm had no undesirable effects on zebrafish embryos compared with the 200 nm chitosan nanoparticle.	(Hu et al., 2011)
Zirconium oxide Nanoparticles ZrO NP	Zirconia nanoparticles prevent bacterial adherence to the tooth surface, (Nishakavya et al.,2022) Prevent dental caries.	Dental ceramics	Slow release of ZrONP from dental ceramics. (Inhalation/ Ingestion)	The concentration of (500 mg/kg) had a cytotoxic effect on mice white blood cells. The lethal dose is 600 mg/kg.	Genotoxicity and cytotoxicity in mesothelioma cells of humans and fibroblast cells of rodents.	100–350 mg/kg are safe for clinical use.	(Yang et al.,2019)

damage to the soft tissues (Maumoun et al., 2011; van Landuyt et al., 2014). Maintaining proper ventilation in dental laboratories is of high importance in preventing the occurrence of adverse effects. (Van Landuyt et al., 2014).

4. Methods to prevent nanoparticle toxicity

Patients to be previously informed on the adverse effects of nanoparticles and the inclusion of toxic effects in the consent form should be made mandatory. Dental workers should be properly trained in the safe handling of nanomaterials. Standard operating procedures should be implemented during the training period (Raynor and Peters, 2016). Exposure levels should be measured during the usage of nanoparticle-based products (OSHA guidelines). Control Banding is a risk assessment method to assess the exposure rate of nanoparticles in dental laboratories and clinics. The risk assessment for specific nanoparticles will depend on various factors like emission potential, the quantity of nanoparticles used, the rate of nanoparticle exposure, and protocols used for control measures. These factors will be assessed by the occupational hygienist and a risk management strategy will be implemented (Riediker et al 2012; Yang et al.,2021).

Storage of metal nanoparticles should be done under inert gas or liquid bath to prevent exposure to air. Nanoparticle spill kits containing gloves, particulate respirators, absorbent material, plastic bags, wipes, and walk-off mats should be kept readily available in dental clinics and manufacturing units. Before discarding the nanoparticles, they should be aggregated into bulk particles, labeled, and then disposed of as hazardous waste.

Workshops to educate patients and dental professionals on the adverse effects of nanoparticles are to be conducted. Overall, the implementation of these strategies can help mitigate the adverse effects of nanoparticles in dental materials and promote safer and more effective dental care (Egbuna et al., 2021).

5. Strategies to reduce nanotoxicity and future trends

Nanoparticles bind to the cell surface (positive charge) and induce toxicity. Altering the surface charge of nanoparticles to negatively charged ligands can reduce nanotoxicity. Nanoparticles undergo dissolution and release toxic ions; the dissolution of nanoparticles can be reduced by coating the nanoparticles with shell-like materials made of polymers. The polymeric coating acts as a barrier and prevents nanoparticle dissolution. Nanoparticles induce toxicity by free Radical generation. This can be prevented by coating the nanoparticles with antioxidants which can scavenge the reactive oxygen species (Buchman et al.,2019).

The introduction of new methods in toxicity assessment like the production of 3D tissue models which can mimic the complex structure and function of human tissues, explains nanoparticles reaction with cells and tissues. Lab-on-a-chip technologies can enable the rapid and sensitive detection of nanoparticle toxicity in saliva, which is a non-invasive and easily accessible biological fluid.

Immunotoxicity from nanoparticle incorporation can be avoided by Polymeric coatings, Cell-derived plasma membranes, and patient protein-derived nanoparticles. Since these nanoparticles are biodegradable, they do not cause any immunotoxic effects. Lipid NPs also offer an alternative that can be explored for delivering active compounds in a targeted manner, using safe natural compounds.

6. Conclusion

This review concludes that nanoparticles released from dental materials have toxic effects on animals and human health. The lack of data on nanotoxicology may act as a barrier to the progress of nanomaterials in dentistry. This article highlights the importance of awareness and caution while using dental materials containing nanoparticles, and the need for further research to prevent the undesired effects of these materials on humans.

Acknowledgments

Source of Funding: NIL.

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