Republic of Iraq
Ministry of Higher Education
and Scientific Research
University of Baghdad
College of Dentistry

Application of silver nano particles in dentistry

A Project Submitted to
The College of Dentistry, University of Baghdad, Department of Restorative & Aesthetic Dentistry in partial fulfillment for the Bachelor of Dental Surgery

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April, 2023 A.D. **1444 A.H.**

Certification of the Supervisor

I certify that this project entitled **"Application of silver nanoparticles in dentistry"** was prepared by the fifth- year student **Mina Ibrahim Shukur** under my supervision at the College of Dentistry / University of Baghdad in partial fulfillment of the graduation requirements for the Bachelor Degree in Dentistry.

Signature

Asst. Prof. Rasha H. Jehad

(The Supervisor)

Date

Dedication

I dedicate this project To my mother who always stand by my side with her limitless love and support at every time .

To my father who believed in me in the hardest times .

To my brothers and sisters who helped me and cheered for me .

To my friends who stood by my side in every step .

Special thanks to my family for all the support they gave me .

Mina Ibrahim

Acknowledgment

In the Name of Allah, the Most Merciful, the Most Compassionate all praise be to Allah, the Lord of the worlds; and prayers and peace be upon Mohamed His servant and messenger.

First and foremost, I must acknowledge my limitless thanks to ***Allah***, the Ever-Magnificent; the Ever-Thankful, for His help and bless.

I owe a deep debt of gratitude to our university for giving us an opportunity to complete this work.

My sincere appreciation is to my supervisor **Asst. Prof. Rasha H. Jehad** for her thoughtful guidance, suggestion, criticism, invaluable help and advice planning and conducting this research.

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Introduction

The use of silver in dentistry has been documented since 1840, mainly in the prevention and treatment of dental caries **(Peng et al. , 2012)** . Initially, it was used as silver nitrate (AgNO3), and then in association with fluorine (AgF). In the 2000s, silver started to be also used in restorative materials such as silver amalgam. In the 20th century, the study of nanomaterials started a new field in health sciences, then named nanotechnology. The nanometric dimension of the particles used in this new field altered the usual properties of biomaterials, showing new characteristics, process ability, and capabilities **(Duran et al. , 2010)**. Among metallic nanoparticles, silver nanoparticles (AgNP) have stood out in scientific research for presenting antimicrobial properties and biological activity against bacteria, fungi, and enveloped viruses **(Gupta et al. , 2016) (Lara et al. , 2011)** . The mechanism of action of AgNPs is mainly associated with the release of cationic silver and its oxidative potential **(Porenczukl et al. , 2019)**. Particle size and shape can also influence the mechanism of action of AgNPs, as well as their synthesis. Therefore, silver nanoparticles emerged as a promising compound to be used in dentistry, since the incorporation of antimicrobial substances in dental biomaterials has been a strategy adopted by some researchers **(Brennan et al. , 2017) (Zhang et al. , 2015)** . Silver nanoparticles have already proved to be effective against several multi-drug-resistant microorganisms **(Lara et al. , 2010) (Panáček et al. , 2018)** . Thus, in dentistry, the direct application of AgNP would be aimed at disinfection and the prevention against pathogenic microorganisms in the oral cavity.

Aims of the review

Highlight the application of silver NPs mainly in operative dentistry which includes :

1- Synthesis of silver nanoparticles

- Physical methods
- Chemical methods
- Biosynthesis

2- Mechanism of action of AgNPs

3-The characterization Of Silver NPs

4-Forms of incorporation

5- The use of silver NPs in dentistry : which include their use in :

- Caries inhibition
- Composite resins
- Endodontic
- Porcelain
- Dental cement

6- Identification of the adverse effects of silver NPs

7- Cytotoxicity

8 -Allergy

Chapter one

Review of Literature

1.1 Nanotechnology

Since the last century, nanotechnology had become a well-known area of research. Feynman (1959) brought a revolution in nanotechnology development. At the nanoscale, nanotechnology has introduced a range of materials. Nanoparticles (NPs) are a broad category of materials that contain unique substances and have at least one dimension of fewer than 100 nanometers **(Laurent et al., 2010)**, since these materials' shapes may be 0D, 1D, 2D, or 3D **(Tiwari et al., 2012)**. The size of the materials will influence the physicochemical properties as well as the optical properties, the significance of these materials is revealed **(Dreaden et al., 2012)**. Since NPs are complex molecules, they have three layers: (a) the surface layer, which can be functionalized with a variety of small molecules, surfactants, polymers, and metal ions; (b) The shell layer, which differs from the core chemically in every way. (c) The core, which refers to the NPs themselves and is the central part of the NPs **(Shin et al., 2016)**.

1.2 Classification of nanoparticles

Different types of NPs can be classified based on their morphology, size, and chemical properties. The popular groups of NPs, as described by **Khanet al. in 2017,** are based on physical and chemical characteristics:

Carbon-based NPs.

● Metal NPs.

● Ceramics NPs.

● Semiconductor.

● Polymeric NP**.**

● Lipid-based NPs.

1.3 Synthesis of nanoparticles

Different methods are used to synthesize NPs, and these methods canbe divided into two categories: (1) Bottom-up strategy (2) Top-down strategy **(Wang and Xia, 2004)**, as shown in Figure (1).

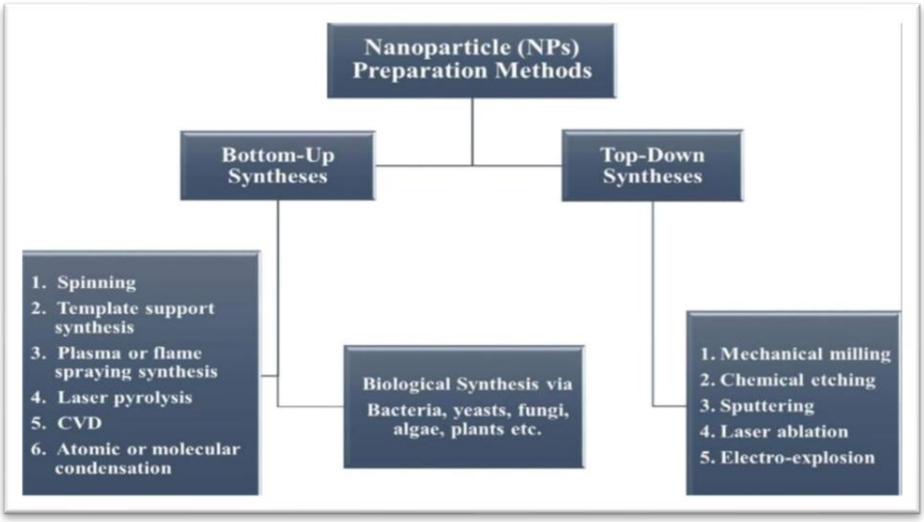

Figure (1): Methods of NPs synthesis (Iravani, 2011)

1.4 Nanomaterials

They are nanoparticle-based materials of at least one nanometer-scale dimension. Nanomaterials are divided into three types: one-dimensional, two-dimensional, and three-dimensional nanostructures, which can be used in the medical and dental fields to diagnose the disease at an early stage. Sheets are one-dimensional nanostructures; nanotubes and nanowires are two-dimensional nanostructures; and quantum dots are three-dimensional nanostructures **(Arora and Kapoor, 2014; Okada and Matsumoto, 2015; Rasheed, et al. 2016)** , (Figure 2) .

Nanomaterials' properties vary from those of other materials for tworeasons: the increase in surface area due to nanoparticles' small size per unit mass, as well as quantum effects **(Bhardwaj et al., 2014)**.

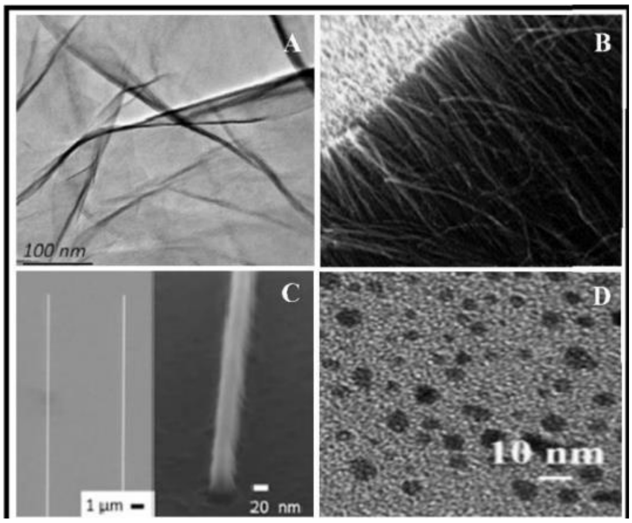

Figure 2 : Highly magnified nanostructures A. nano-sheets, B. nano-tubes, C. nanowires, D. quantum dots (Jurczyk, 2013; Zhu et al., 2014; Li, 2015; Roy et al., 2015).

1.5 Silver nanoparticles in dentistry

Silver nanoparticles (AgNPs) are particles that have the potential to bind to and penetrate both Gram-positive and Gram-negative bacterial cell walls, disrupt cell function by releasing silver ions. As a result, they are used totreat and prevent drug-resistant bacteria, as well as to prevent biofilm formation**(Rai et al., 2012)**.In dental practice AgNPs are used in a variety of ways. When concentrating on AgNPs' antimicrobial properties, they were incorporated into restorative materials and bonding agents to prevent biofilm formation and caries reduction **(Durner et al., 2011; Garcia-Contreras et al., 2011; Cheng et al., 2012)**, in the orthodontic adhesives **(Ahn et al., 2009; Degrazia et al., 2016)** and into the implant materials **(Sheikh et al., 2010; Allaker and Memarzadeh, 2014).**

1.6 Synthesis of silver NPs

Silver nanoparticles are synthesized using a precursor (often silver nitrate), a reducing agent that reduces silver ions from Ag+ to Ag0, and a stabilizing agent that ensures the stabilization of suspended nanoparticles and prevents nucleation and aggregation, since metallic nanoparticles have a high surface energy. Therefore, the synthesis of silver nanoparticles can be chemical, physical, or biological . In dentistry, the most common synthesis is the chemical route **(Fernandes et al. , 2018)** .

1.6.1 Physical methods

Evaporation-condensation and laser ablation are the most important physical approaches. The absence of solvent contamination in the prepared thin films and the uniformity of NPs distribution are the advantages of physical synthesis methods in comparison with chemical processes. Physical synthesis of silver NPs using a tube furnace at atmospheric pressure has some disadvantages, for example, tube furnace occupies a large space, consumes a great amount of energy while raising the environmental temperature around the source material, and requires a lot of time to achieve thermal stability. Moreover, a typical tube furnace requires power consumption of more than several kilowatts and a preheating time of several tens of minutes to reach a stable operating temperature **(Kruis F et al. , 2000) (Magnusson M et al. , 1999)**. It was demonstrated that silver NPs could be synthesized via a small ceramic heater with a local heating area **(Jung J et al. , 2006)**. The small ceramic heater was used to evaporate source materials. The evaporated vapor can cool at a suitable rapid rate, because the temperature gradient in the vicinity of the heater surface is very steep in comparison with that of a tube furnace. This makes possible the formation of small NPs in high concentration. One important advantage of laser ablation technique compared to other methods for production of metal colloids is the absence of chemical reagents in solutions. Therefore, pure and uncontaminated metal colloids for further applications can be prepared by this technique **(Tsuji T et al. , 2002)** . characteristics of produced nano-silver particles depend upon many parameters, including the wavelength of the laser impinging the metallic target, the duration of the laser pulses (in the femto-, pico- and nanosecond regime), the laser fluence, the ablation time duration and the effective liquid medium, with or without the presence of surfactants **(Kim S et al. , 2005) (Kawasaki M et al. , 2006).**

1.6.2 Chemical methods

The synthesis of AgNP is based on the chemical reduction of Ag+1 to Ag0. The differentiation between chemical processes is represented by the reduction agents and stabilizers used, such as sodium citrate, ascorbate, sodium borohydride (NaBH4), elemental hydro- gen, polyol process, Tollens reagent, N,N-dimethylformamide (DMF), and poly (ethylene glycol)-block copolymers. Several protective agents (stabilizers) have been used, such as thiols, amines, acids, alcohols **(Krishnaveni et al. , 2017)** , and polymeric compounds such as chitosan **(Cataldi et al. , 2016) (Freire et al. , 2017) (Santos et al. , 2014)** and polymethylmethacrylate **(Chen et al. , 2018) (Zhang et al. , 2016) (De Matteis et al. , 2019) (Bacali et al. , 2019) (Chen et al. , 2017)**. These agents stabilize dispersive NPs during their synthesis and protect NPs that can be absorbed on, or bind onto, nanoparticle surfaces, avoiding their agglomeration and sedimentation **(Oliveira et al. , 2005)** .

1.6.2.1 Photoinduced reduction

Silver NPs can be synthesized by using a variety of photoinduced or photocatalytic reduction methods. Photochemical synthesis is a clean process which has high spatial resolution, convenience of use, and great versatility. Moreover, photochemical synthesis enables one to fabricate the NPs in various mediums including cells, emulsion, polymer films, surfactant micelles, glasses, etc. Nano- sized silver particles with an average size of 8 nm were prepared by photoinduced reduction using poly (styrene sulfonate)/poly (allylamine hydrochloride) polyelectrolyte capsules as microreactors **(Shchukin DG et al. , 2003)**.

1.6.2.2 Polymers and polysaccharides

Silver NPs were prepared using water as an environmentally friendly solvent and polysaccharides as capping/reducing agents. For instance, synthesis of starch-silver NPs was carried out with starch (capping agent) and β-D-glucose (reducing agent) in a gently heated system **(Raveendran P et al. , 2003)**.

1.6.3 Biosynthesis of AgNPs by green synthesis method

Silver nanoparticles are synthesized using a variety of methods **(Tolaymat et al., 2010)**. Reduction in solutions **(Guzma n et al., 2009)**, thermal decomposition of silver compounds **(Navaladian et al., 2007)**, microwave-assisted synthesis **(Sreeram et al., 2008)**, biological reduction process **(Sastry et al., 2003)** are all methods formaking silver nanoparticles. The most common method for the synthesis of nanoparticles is the latest, as it provides a one-step, eco-friendly method **(Das et al., 2013).**

Green synthesis is defined as the production of nanoparticles using environmentally friendly materials such as bacteria, fungi, and plants **(Elavazhagan and Arunachalam, 2011)**. These appealing green strategies are free of the drawbacks that come with traditional synthetic strategies, they are environmentally friendly **(Das et al., 2013)**.

Plants have been found to have a much faster rate of metal ion reduction than microorganisms, and stable metal nanoparticle formation has been recorded. By adjusting the pH, manipulation and modulation of the shape and size of the nanoparticles can be made from plants **(Gardea-Torresedey et al., 2003)**.

1.7 Moringa oleifera plant

Moringa oleifera Lam. is a tree that grows widely in many tropical and subtropical countries. It is known as the drumstick tree based on the appearance of its immature seed pods, the horseradish tree based on the taste of ground root preparations, and the ben oil tree from seed-derived oils. In some areas, immature seed pods are eaten, while the leaves are widely used as a basic food because of their high nutrition content. Seed, leaves, oil, sap, bark, roots, and flowers are widely used in traditional medicine. Moringa leaves have been characterized to contain a desirable nutritional balance, containing vitamins, minerals, amino acids, and fatty acids. Additionally, the leaves are reported to contain various types of antioxidant compounds such as ascorbic acid, flavonoids, phenolics, and carotenoids **(Stohs and Hartman, 2015)**. Isoquercetin, astragalin, and crypto-chlorogenic acid were reported to be major active components in oleifera leaves. Isoquercetin is a powerful natural antioxidant which possesses several potential therapeutic effects including antiasthma and antihypertension. Astragalin is also reported as a natural antioxidant agent exhibiting some biological properties such as attenuation of inflammation, inhibition of dermatitis, and cellular protective effect. Chlorogenic acid and its isomers are esters of quinic and caffeic acids that have abilities to inhibit oxidation and also promote various pharmacological activities such as antiobesity, reduction of plasma and liver lipids, and inhibition of acute lung injury **(Das et al., 2013)**.

Figure 3 : Moringa oleifera plant (Das et al. , 2013)

1.8 Mechanisms of Action of AgNPs

Silver nanoparticles are frequently associated with their antimicrobial and antioxidant activities **(Gupta et al. , 2016)** . The action of silver nanoparticles is mainly related to their nanoscale, which alters the level of silver ion release and interferes with the surface energy **(Porenczukl et al. , 2019)** . Nanoparticles show good antimicrobial effects due to their large surface area, providing high contact with microorganisms when compared to other antimicrobial agents **(Rai et al. , 2009)** . Even multi-resistant bacteria are susceptible to AgNP, which indicates that the mechanisms that confer the resistance of these strains to commercial antibiotics have no protective activity when exposed to nanoparticles **(Lara et al. , 2010)** . One of the most important mechanisms of action of AgNP is represented by the induction of reactive oxygen species (ROS) production, and hydroxyl radicals are the main species responsible for the oxidative damage **(Quinteros et al. , 2018)** . However, it also damages the membrane and cell walls, interferes in the respiratory chain, exhausts the levels of intracellular ATP, and shatters nucleic acids **(Gupta et al. , 2016)** **(Porenczukl et al. , 2019)** . This mechanism of action varies with nanoparticle size and shape, and with the different target species. In Gram-negative bacteria, with Escherichia coli as a representative species, studies have shown action primarily on the outer membrane, resulting in the leakage of cell components.

After entering the cell, it has also been shown that AgNPs inactivate the respiratory chain dehydrogenases, inhibiting cell growth and respiration. In addition, these nanoparticles can act on phospholipids and membrane proteins, causing a breakdown in the plasma membrane and changes in its permeability **(Li et al. , 2010)** . The main responsible for the oxidation of lipids in E. coli is reactive oxygen **(Quinteros et al. , 2018)** . Electron microscopy analyses indicated the fragmentation of E. coli after treatment with silver nanoparticles **(Li et al. , 2010)** . Gram-negative bacteria exhibited no resistance to the antimicrobial action of silver **(Duran et al. , 201)** .The difference between the action of silver nanoparticles on Gram-positive and Gram- negative bacteria is related to the structure of the peptidoglycan cell wall. When comparing inhibition between Escherichia coli and Staphylococcus aureus, the latter being considered as a model microorganism for Gram-positive bacteria studies, it was observed that Gram- negative bacteria are more easily inhibited than Gram-positive ones **(Gomaa , 2017)** . Gram-positive bacteria also show changes in membrane permeability and protein composition in the respiratory chain, and the formation of ROS **(Gomaa , 2017)** . Oxidative stress in Gram-positive bacteria is more abrupt than in Gram-negative ones. As in Gram-negative bacteria, high ROS concentrations lead to protein degradation by activation of the proteolytic pathway and lipid oxidation. However, in S. aureus, the hydroxyl radical is responsible for lipid oxidation. As in Gram-negative microorganisms, there are also changes in membrane potential, as well as DNA degradation in Gram-positive bacteria **(Quinteros et al. , 2018)** . When the mechanism of action of silver nanoparticles in bacteria and fungi is compared, the aggregation of nanoparticles only occurs in eukaryotic cells, resulting in larger particles **(Iravani et al. , 2014)** . In Candida species, it has been shown that the toxic action of AgNP is related both to the ROS-mediated pathway, inducing dysfunctional mitochondrial apoptosis, and to the ROS-independent pathway, culminating in the same cell death outcome **(Radhakrishnan et al. , 2018)** . Similar to the antibacterial action, in Candida species, AgNP acts by interfering with the membrane potential, in its integrity and fluidity, in its growth, and in the cell cycle **(Radhakrishnan et al. , 2018) (Kim et al. , 2009)**. In addition, the synthesis method influences the action of silver nanoparticles, with biosynthesis showing better results **(Ballottin et al. , 2017)** .

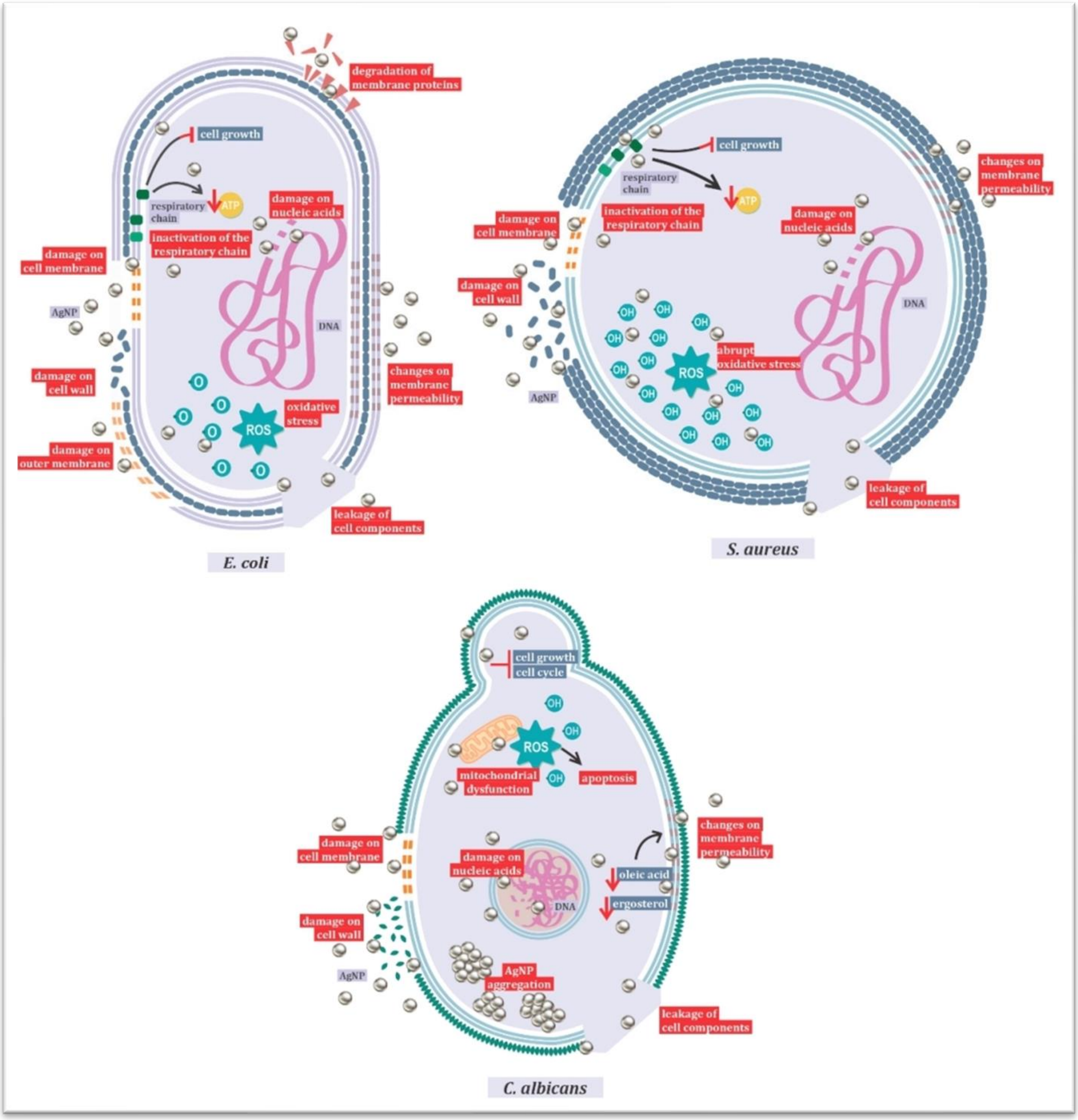

Figure 4 : Mechanism of action of AgNPs against Candida albicans, Escherichia coli, and Staphylococcus aureus (Int. J. Mol. Sci. , 2021)

1.9 Characterization of silver nanoparticles

Characterization of the NPs is important to understand and control the NPs synthesis and applications. Characterization is achieved by using a different techniques such as UV–Vis spectroscopy, atomic force microscopy (AFM), transmission and scanning electron microscopy (TEM, SEM), dynamic light scattering (DLS), powder X-ray diffractometry (XRD), X-ray photoelectron spectroscopy (XPS) and Fourier transform infrared spectroscopy (FTIR) **(Sun et al., 2000; Khomutov and Gubin, 2002; Yeo et al., 2003; Chimentao et al., 2004; Hutter and Fendler, 2004; Zhang et al., 2004; Zhang et al., 2006; Yoosaf et al., 2007; Vilchis-Nestor et al., 2008)**. These techniques are used for detection a several parameters such as particle shape, size, crystallinity, pore size, fractal dimensions, and surface area.

1.10 Forms of Incorporation

AgNPs used in dental materials are incorporated through distinct ways, depending on the type of material. For composite resin and adhesive systems, the most common technique is adding a monomer, usually 2-(tert-butylamino)ethyl methacrylate, in order to improve Ag salt solubility in the resin solution **(Y. J. Cheng et al. , 2011) (F. Li et al. , 2013) (M. A. S. Melo et al. , 2013)** . For dental implants, the process is totally different: Titanium samples are soaked in AgNO3 solutions, rinsed with deionized water, dried, and irradiated with UV light from a high-pressure Hg lamp. This process allows producing samples with different Ag concentrations, depending on the AgNO3 solution concentration **(L. Zhao et al. , 2009)**. Another difference is related to the form of AgNP obtainment. In some studies the particles are commercially avail-able, so they are obtained directly from the producer **(K. Zhang et al. , 2012) (M. A. S. Melo et al. , 2013) (L. Cheng et al. , 2013)**. In others, AgNPs are prepared by reduction of AgNO3, with NaBO4 **(K. Y. Flores et al. , 2010)** , polyvinylpyrrolidone **(K. Y. Nam , 2011)**, sodium citrate **(D. R. Monteiro et al. ,**

2012), and gallic acid **(L. F. Espinosa_cristóbal et al. , 2009)**, among others.

1.11 Application of silver nanoparticles in dentistry

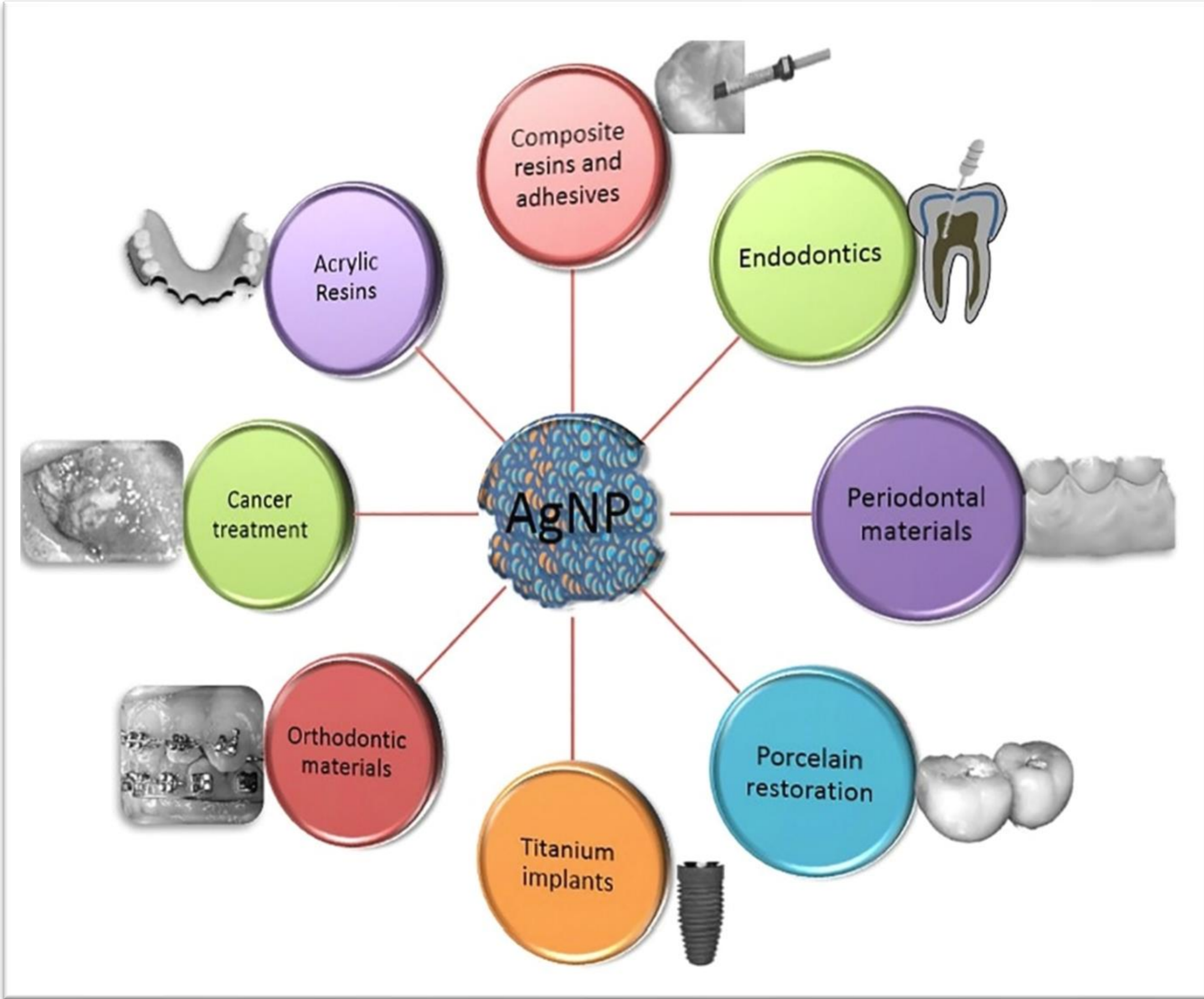

Figure 5 : Applications of silver nanoparticles used for biomaterials (Bapat et al. , 2018).

The use of silver in dentistry dates from the 19th century and has different applications, figure 5 , mainly due to the antimicrobial potential of silver ions **(Peng et al. , 2012)** . However, in the 21st century, the advent of nanotechnology brought a new perspective on the use of silver in dentistry through silver nanoparticles, which have antimicrobial action, Figure 6 .mainly due to the gradual release of silver ions **(Venugopal et al. , 2017) (Fernandes et al. , 2018) (De Matteis et al. , 2019)**

(paiva et al. , 2018). The use of nanoparticles in dentistry over the years is evidenced by the number of articles published in the last ten years .In dentistry, studies have indicated the use of silver nanoparticles in different specialties: oral microbiology, preventive dentistry, prosthodontics, orthodontics, endodontics, and periodontics. In addition, some studies have investigated the potential of using silver nanoparticles by testing their antimicrobial effects against the most common oral pathogens. Considering the use of AgNP in the different dentistry specialties and subsequent fields, the predominant areas are dental prosthesis (25.6%) and oral microbiology (19.5%) Most of the studies have indicated that silver interacts with sulfhydryl groups of proteins and with DNA, altering hydrogen bonding, respiratory processes, DNA unwinding, cell-wall synthesis and cell division **(Kiriyamma et al. , 2013) (De_Deus et al. , 2017)**. At the macro level, these interactions effectively produce bacterial death **(Patil et al. , 2016)** . It is recognized that Ag NPs have antimicrobial activity against Gram-negative bacteria performing 'pits' in the cell wall of the bacteria. Clearly, a membrane with such morphology exhibits a significant increase in permeability, resulting in death of the cell. Overall, silver mainly induces denaturation and oxidization for cell wall which lead to rupture of the internal cell organelles, resulting in bacterial death **(Nozari et al. , 2016) (Besinis et al. , 2014)** . Although bacterial cell lysis could be one of the reasons for the observed antibacterial property, NPs also modulate the phosphotyrosine profile of putative bacterial peptides, which could affect bacterial signal transduction and inhibit the growth of the organisms **(Chladek et al. , 2011)** .

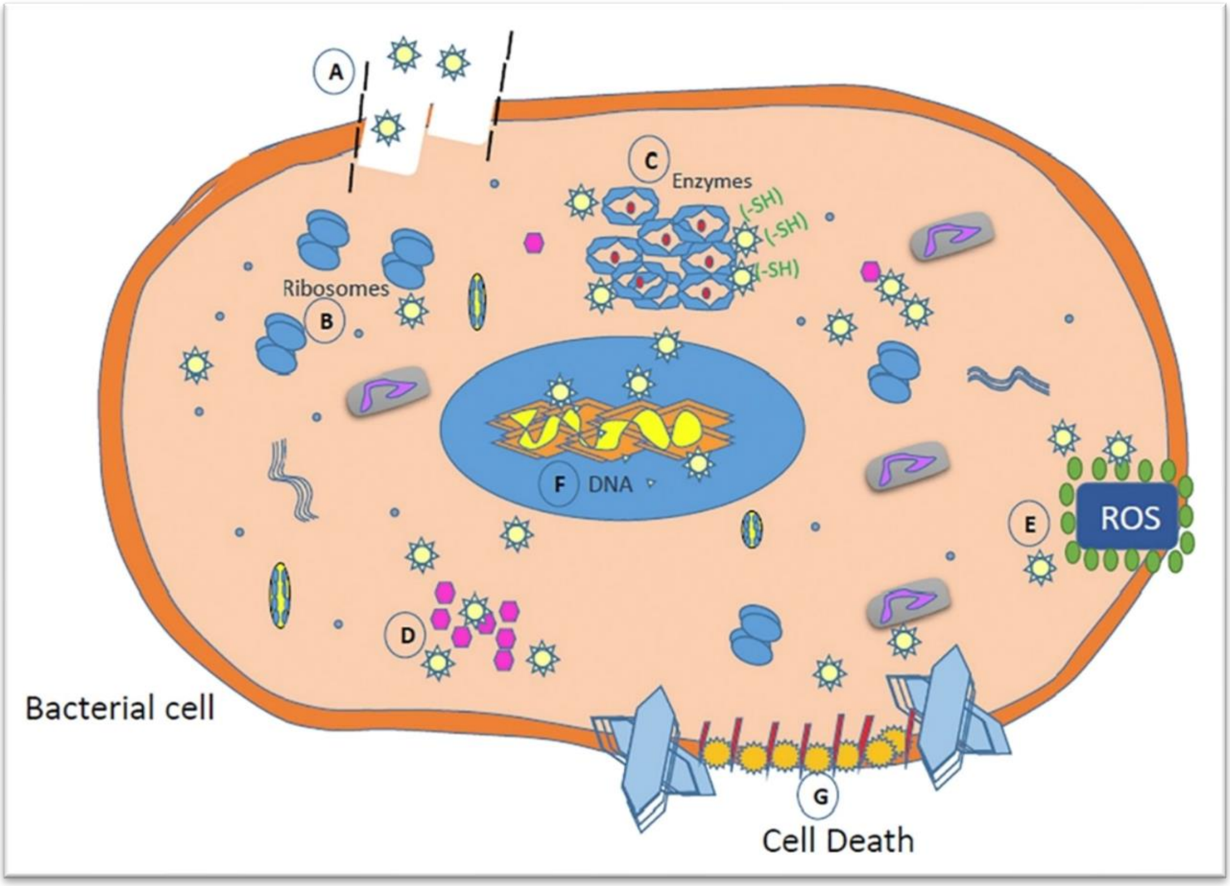

Figure 6 : Steps of antimicrobial action of silver nanoparticles (Bapat et al. , 2018).

(A) AgNPs diffusion and uptake into the bacterial cell: Accumulation and dissolution of AgNPs at plasma membrane cause cell leakage.

(B) Destabilization of Ribosomes: denatures ribosomes inhibiting protein synthesis and plasma membrane degradation.

(C) Enzyme interaction: AgNPs bind with the thiol group (-SH) in the respiratory enzymes and deactivate them.

(D) Interruption of electron transfer chain: AgNPs interfere with electron transport affecting signaling pathway.

(E) Reactive oxygen Species(ROS): Mitochondrial damage induces ROS which oxidizes proteins.

(F) DNA Damage. AgNPs binds with DNA preventing its replication and multiplication causing apoptosis.

(G) Cell Death: Formation of pits and perforations in cell membrane leads to release of cell organelles and cell death.

Likewise, Ag NPs with average size 14 ± 6 nm and Ag^+ ions such as $AgNO_3$, inhibit the growth of Escherichia coli 55 ± 8% and 100%, respectively . Furthermore, silver particles are also used as an alternative radiopacifier to get the necessary radiopacity to calcium silicate cements (CSC) and assess the purity of the radiopacifying agents **(Munikamaiah et al. , 2018)**. These nanomaterials, which can be prepared in a simple and cost-effective manner, may be suitable for the formulation of new types of bactericidal materials **(Patil et al. , 2016)** .

1.11.1 CARIES INHIBITORY PROPERTIES

The most common worldwide oral diseases are dental caries and periodontal diseases, 60–90%, according to the World Health Organization (WHO) **(World health organization , 2011)** . In Mexico, some authors estimate that such diseases affect 90% and 70% of the population, respectively **(de la Fuente_Hernàndez J et al. , 2008)**. In this regard, the use of silver solution, specifically, silver diamine fluoride ($Ag[NH_3]_2F$) has been used as a caries inhibitor. In context, fluoride and silver interact synergistically to form fluorapatite. The first step is the formation of calcium fluoride (CaF_2) and silver phosphate (Ag_3PO_4) in a basic environment, the second reaction is the subsequent dissociation of calcium and fluoride **(Rosenblatt A et al. , 2009)** . Experimental composite adhesives (ECAs) showed slower bacterial growth than those containing conventional adhesives, suggesting that ECAs can help prevent enamel demineralization around their surfaces without compromising physical properties **(Ahn SJ et al. , 2009)** .

1.11.2 Composite resins

AgNPs are combined with different materials due to their antimicrobial effect which decreases biofilm formation and maintenance of better oral health **(M. Rai et al. , 2009) (Y. Zhang et al. , 2015)** . Due to its smaller particle size, AgNPs penetrates through cell membranes more readily, resulting in damage and inactivity ((**H. _J Park et al. , 2013)** . In comparison to other restorative materials, composites exhibit more biofilm formation on its surface in-vivo **(S. Imazato et al. , 1994)** . These biofilms are major reasons for secondary caries formation at the margins of the restoration which leads to failure **(R. L. Sakaguchi , 2005)**. To combat these, formulation of adhesive systems have been developed with antibacterial agents to prevent the issue of secondary caries **(S. Imazato et al. , 2007)** . Evidences suggest that microleakage on restoration margins provides gaps for the colonization by oral bacteria, resulting in secondary caries. This leads to restorative failure and need for restoration replacement. Problem can be averted by incorporation of antimicrobial agents like AgNPs to composite resins and adhesive systems (Fig. 1.7).

Researchers have incorporated AgNP into a resin matrix based on bisphenol A-glycidyl methacrylate/triethylene glycol dimethacry-late (BISGMA/TEGDMA), which is used in restorations of deciduous and permanent dentitions through chitosan polymers. They found antimicrobial activity against S. mitis, pointing out that the coating of restorative materials by this polymer decreases antimicrobial activity **(Cataldi et al. , 2016)**. However, incomplete nanocomposite polymerization (resin + AgNP), along with an increase in the release of unbound monomers, has been demonstrated **(Durner et al. , 2011)**. The literature does not clearly state whether AgNPs can be used with polymer resins in restorative dentistry **(Pal et al. , 2007) (Prabhu and S.; Poulose , 2012)** . The union of AgNP with composite resins did not decrease the marginal infiltration of the material **(Kielbassa et al. , 2020)** . These nanocomposites have their final mechanical properties influenced by the type of polymerization **(Barszczewska_Rybarek and I.; chladek , 2018)** .

The use of photopolymerization for the formation of resins associated with silver nanoparticles did not improve the mechanical properties when compared to commercial resins **(Hanif and A.; Ghani , 2020)** . Dentin adhesives associated with AgNPs increased surface wetting and cohesive failures **(Torres_Mendez et al. , 2017)**.

When self-etching adhesives and AgNP were tested against S. mutans, antimicrobial activity was observed, without compromising the conversion of adhesive into the resin **(Mohammed and H.F.; Riad , 2019)**, and AgNP incorporation made the antibacterial activity more durable. It can be applied for immediate antibacterial needs **(Keskar et al. , 2019)**.

Two-step adhesive systems associated with AgNP showed higher shear strength

results than self-etchers/AgNP **(Fatemeh et al. , 2017)**. AgNP powder showed better results than the alcoholic AgNP solution both in antimicrobial activity and in the degree of conversion of the self-etching adhesive **(Mohammed and H.F.; Riad , 2019)**. AgNP incorporation in disinfectants generated commercial products (Nanocare Gold) with biocompatibility and no cytotoxicity to stem cells from dental pulp **(Porenczuki et al. , 2019)**

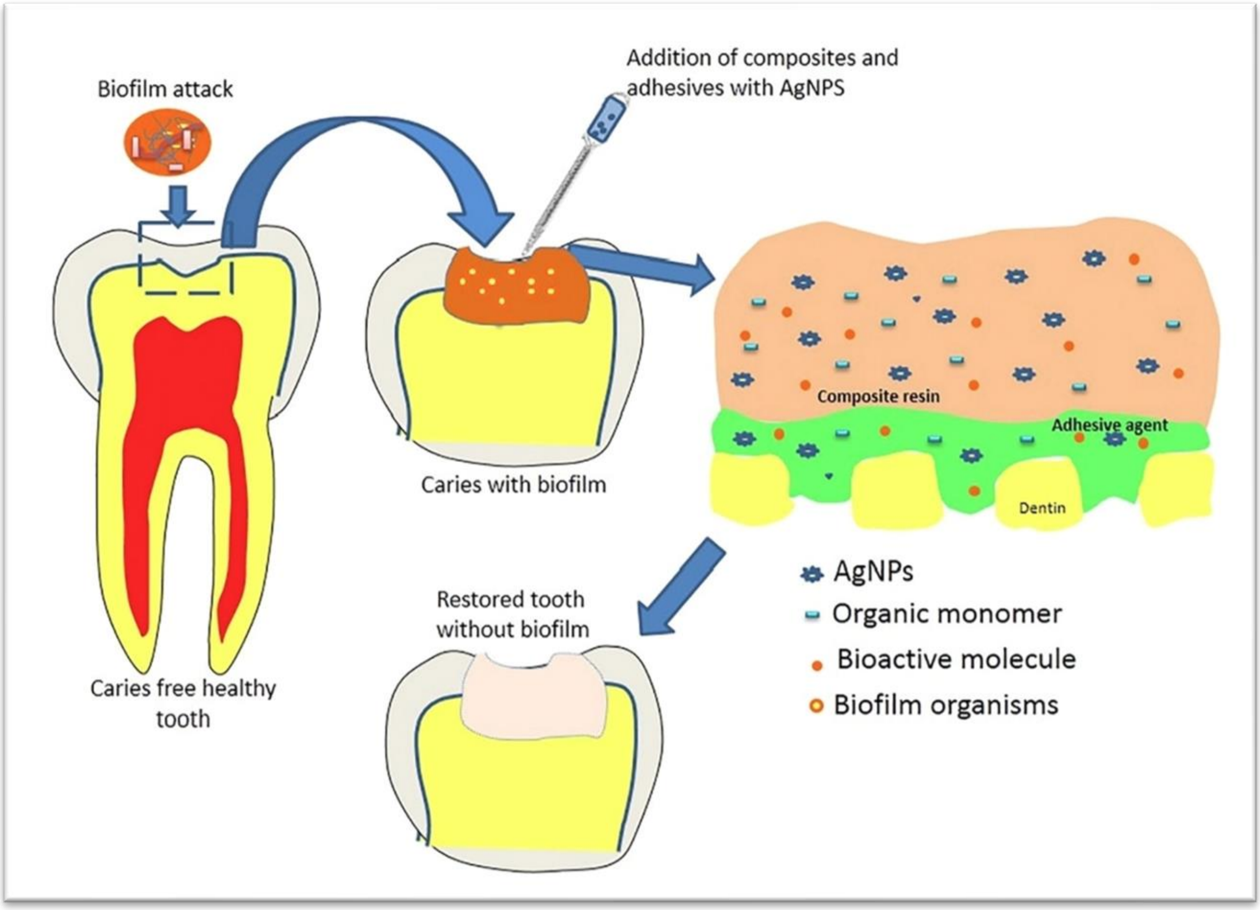

Figure 7 : Incorporation of silver NPs in composite resins and adhesive system (Bapat et al. , 2018).

1.11.3 Incorporation in porcelain

Dental porcelain is the most popular material used for fixed prosthesis due to good biocompatibility, mechanical durability and aesthetics similar to natural teeth **(J. B. Quinn et al. , 1997)** . However, on application of excessive masticatory force, it may chip or fracture due to lack of malleability or ductility. Reinforcing porcelain with metal particles have been recommended to enhance fracture toughness and prevention of crack propagation. This could be due to exchange of ions between reinforced metal particles with porcelain **(K. J. Anusavice et al. , 1992)** .This review attempts to highlight effect of incorporation of AgNPs on mechanical properties of dental porcelain. Thus, studies have demonstrated that incorporation of AgNPs inside porcelain improves its mechanical properties. It improves its fracture resistance and decreases length of the crack . this simply implies that AgNPs have a potential to tackle problems associated with porcelain.

1.11.4 In Endodontics :

The crucial cause of apical periodontitis is inflamed or necrotic pulp, which is a consequence of colonization by microorganisms and can even lead to bone infection **(Kim et al. , 2009)** . Several studies have demonstrated that bacteria are the main etiologic agent of pulpal infection and periradicular lesion formation **(A. Byström and G. Sundqvist , 1981) (L. Fabricius et al. , 1982) (G. Sundqvist et al. , 1998)** . The microbiota of infected root canals is polymicrobial and is dominated by Gram-negative anaerobes **(J. C. Baumgartner and W. A. Falkler , 1991) (J. C. Baumgartner et al. , 2003)** . It has been demonstrated that the presence of residual bacteria in root canal is connected with significantly higher rates of treatment failure **(U. Sjögren et al. , 1997)** . In infected root canals, despite its polymicrobial etiology, Enterococcus faecalis, a facultative anaerobic Gram-positive bacterium, is often present, causing persistent and difficult-to- treat infections. In an effort to improve upon intracanal medicaments in inhibiting the growth of Enterococcus faecalis, the short term and long term effects of calcium hydroxide intracanal medicament with silver nanoparticles suspension was investigated **(Afkhami et al., 2015)**. Its effectiveness against Enterococcus faecalis was superior when compared to calcium hydroxide alone, and calcium hydroxide mixed with chlorhexidine. Nano-silver particles were significantly effective after one week, and showing no significant antibacterial effect after one month in comparison to the other materials used. Researchers, therefore, concluded that nanosilver particles proved to be an effective antibacterial agent specifically against Enterococcus faecalis in short term. The association of AgNP with composites disrupts E. faecalis biofilm through the release of silver ions **(Fan et al. , 2015)** . AgNPs also demonstrated their antimicrobial effect when used as final endodontic irrigators, with the effect similar to the treatment with 2.5% sodium hypochlorite **(Gonzàlez_Luna et al. , 2016)** . Calcium-based cement and mineral trioxide aggregate (MTA) associated with AgNP presented antimicrobial activity against Escherichia coli, Actinomyces spp., Streptococcus mutans, E. faecalis, and

C. albicans isolates. Silver particles can decrease the attachment of microorganisms to the tooth surface and increase the antibacterial properties of endodontic sealers **(Jonaidi_Jafari et al. , 2016)**. These particles also increased the MTA radiopacity **(Mendes et al. , 2017)** .

1.11.5 Nanosilver Application in Dental Cements

The initial adhesion of specific oral bacteria to tooth surfaces or artificial dental substrata is both the primary and the essential prerequisite for the development of Cariopathogenic biofilms **(C. J Whittaker et al. , 1996) (C. Estrela et al. , 2009) (D. R. Monteiro et al. , 2009) (R. P. Allaker , 2010)** . Within the complex formation of such biofilms, Streptococcus mutans is primarily responsible for the initiation of tooth decay as well as for the progression of an established lesion **(R. Bürger et al. , 2009)**. Although the prevalence of primary caries has been on decline worldwide since early 1980s, secondary caries remains an unresolved problem in restorative dentistry **(S. Saku et al. , 2010)** . Ideally, the restorative materials should exhibit antibacterial properties to limit the adhesion and proliferation of pathogens at a very early stage and, therefore, prevent secondary caries **(R. Bürger et al. , 2009)** . In Dentistry there is a wide range of cements with different applications where the antimicrobial activity is relevant. Antibacterial activity of dental luting cements is a very important property when applying dental crowns, bridges, inlays, onlays, or veneers, because bacteria may be still present on the walls of the preparation or gain access to the cavity if there is microleakage present after cementation **(P. Daugela et al. , 2008)** .

Metallic nanoparticles may improve the physicochemical, mechanical and antibacterial properties of dental materials. Silver particles are used as alternative radiopacifier agents in calcium silicate **cements (Camilleri J and Gandolfi MG , 2010)**. Silver (Ag+) added to calcium phosphate bone cements improved physicochemical properties, such as setting time, presented anti-adhesion and antibiofilm activity and showed non- cytotoxic effect with human bone cells **(Jacquart S et al. , 2013)**. A silver alloy powder was formerly added to a restorative glass ionomer cement to make a metal reinforced GIC, which is more complex and more substantial. A silver powder was sintered to glass at high temperatures to obtain cermet cement. It has been claimed that such silver-sintered powder could improve abrasion resistance and durability **(Simmons, 1983; McLean et al., 1994).** Silver nanoparticle incorporation into GIC powder could reduce biofilm formations that would not significantly affect the mechanical and physical properties.Incorporating silver nanoparticles into glass ionomer cements significantly enhanced the material's wear resistance. The main improvement after adding silver nanoparticles was abrasion resistance and radio-opacity to the glass ionomer cement **(McKinney et al., 1988; Xie et al., 2000)**.

1.11.6 Nanosilver fluoride in remineralization of dental caries

Nano-silver fluoride (NSF), a new colloid based on AgNPs, chitosan, and fluoride was developed as a caries arresting agent that comprises both antibacterial and remineralizing properties. **(Sayed et al. , 2020)** Hence, NSF is a promising agent as it overcomes the clinical limitations of Silver diamine fluoride (SDF) as it's less cytotoxic **(Targino et al., 2014)** and causes no carious lesion staining. **(Espíndola_Castro LF et al. , 2020) (Sayed et al. , 2020) (Yin IX et al. , 2020) (Tirupathi S et al. , 2019)** This is due to the size of silver particles and also because the nanoparticles do not undergo oxidation. **(Espíndola_Castro LF et al. , 2020)** This new formulation is safe for use in humans, and controlled clinical trials have shown its anti- caries property. **(Tirupathi S et al. , 2019) (Burns J and Hollands K , 2015) (Santos VE dos Jr et al. , 2014)** The antibacterial properties of nanomaterials have been investigated, and the antibacterial effect showed to come from AgNPs. Chitosan was added to the AgNPs as it acts as a carrier and stabilizes the compound. Further, to make this a more comprehensive agent, fluoride was added to the AgNPs-chitosan compound to fortify the antibacterial properties and prevent demineralization. This new formulation, called NSF, has been reported for caries prevention and arrest.**(Yin IX et al. , 2020)** AgNPs incorporation aims to avoid or at least to decrease the microbial colonization over dental materials increasing oral health levels **(S. Eckhardt et al. , 2013)** . The combination of these strategies may confer a better treatment of the white spot lesion .

1.12 ADVERSE EFFECTS

Metal ions are released from casting alloys and cause damage to cell structures and local inflammation. $Ag(NH_3)_2F$ in contact with Human Gingival Fibroblast (HGF) for only one hour induced irreversible cell death, whereas longer duration of contact with AgCl was necessary to induce this same effect. These data suggest the importance of cautious application of $Ag(NH_3)_2F$ into the oral cavity **(Contreras RG et al. , 2010)** . $Ag(NH_3)_2F$ shows much more sensibility as a dose-dependent ion against three normal cells and three cancer line cells than AgCl .Nanotoxicity is the toxicity imposed by nanomaterials **(Fadeel B and Garcia_Bennett , 2010)** . The toxic effects of Ag NPs are proportional to the activity of free Ag^+ ions released by the NPs **(Park EJ et al. , 2010).** Although NPs have tremendous potential for a host of applications, their adverse effects on living cells have raised serious concerns for their use in the healthcare and consumer sectors. For example, NPs may be taken up directly into the brain by trans-synaptic transport and Ag NPs can enter via the blood-brain barrier and accumulate in different regions of the brain and this may be beneficial for drug delivery, increasing a risk to the patient. It has also been reported that nanoparticle exposure can induce impairments to normal neuron- microglia microenviroment and even aggravate the process of brain pathology **(Yang Z et al. , 2010)** . In support of the damage notion, in vitro cell line studies have shown decreased mitochondrial function after exposure to Ag NPs in murine neuroblastoma cells **(Schrand AM et al. , 2008)** , hepatic cells **(Hussain SM et al. , 2005)**, germline stem cells

(Braydich_Stolle L et al. , 2005) , human skin carcinoma **(Arora S et al. , 2008)** and human epidermal keratinocytes and fibroblasts **(Burd A et al. , 2007)** , while in vivo studies showed that exposure to NPs could result in an inflammation, oxidative stress, myocardial infarction and thrombosis .As mentioned above, NPs could alter the permeability of blood brain barrier **(Zhao Y et al. , 2006)**. Exposure to Ag NPs has been associated with tissue damage especially in liver. In rats, a No Observable Adverse Effect Level (NOAEL) of 30 mg ⁄ kg and the Lowest Observable Adverse Effect Level (LOAEL) of 125 mg ⁄ kg has been determined for Ag NPs **(Kim YS et al. , 2010)** . NPs could also damage DNA causing deletions, mutations, single and double strand breakages, adduct formation, and cross linking with proteins. Some studies have confirmed DNA adducts and oxidation and induced DNA fragmentation following exposure to metal oxide NPs. In response to DNA insult, cells attempt to repair damaged DNA but repair failure may lead to cell death (apoptosis) or cell transformation. In the case of severe damage to DNA, cells may die by either necrosis or apoptosis. In this regard, it has been published previously that exposure to certain metal oxide NPs induces apoptosis **(Huang YW et al. , 2010)** . Corrosion and discolorations of dental materials in contact with Ag NPs may be a concern. On the other hand, antibacterial property carries with it a potential environmental risk once these NPs are discharged into the environment. Of particular concern, Ag+ ions from AgNO3 inhibit the algae's photosynthesis around 18 times more than Ag NPs. However, over a long period, the NPs are even more toxic than the ions alone **(Navarro E et al. , 2008)** . These environmental concerns have led to a debate among advocacy groups and governments on whether special regulation of nanotechnology is warranted .

In a pregnant woman :

One of the major concerns regarding the utilization of silver nanoparticles is their use in pregnant women and animals. It was already demonstrated that when pregnant mice were exposed to 18–20 nm AgNP, silver-containing nanoparticles could be detected in the placenta and in the head of the fetus. In the fetus, silver was detected in the ionic form or as nanoparticles with a size less than 13 nm **(Campagnolo et al. , 2017)** , and this situation points to precautions with respect to acute exposure to nanoparticles during pregnancy. This accumulation of silver in the central nervous system has already been shown to induce long-term memory impairments in a mice model **(Antsiferova et al. , 2012)** . In a similar way, phytoreduced silver nanoparticles with polyphenols from Viburnum opulus fruit extract presented testicular toxic effects in offspring during the embryological development of the murine gonad **(Bidia et al. , 2021)** . Therefore, more studies are necessary to evaluate if nanoparticles can be safely administered to pregnant women.

1.13 Cytotoxicity of AgNPs

Low-concentration NPs were found to be non-toxic, while high- concentration NPs demonstrated more pronounced cytotoxicity, according to the researchers **(Hang and Gao, 2014)**, also some researchers discovered that the toxicity of NPs was dose-dependent **(Niska and Knap, 2016; Cao and Zhang, 2018)**. In a previous study, the toxicity of antimicrobial NPs was found to be strongly related to the time rather than the concentration of the antimicrobial NPs **(Dutra-Correa and Leite, 2018)**. According to some studies NP toxicity is influenced by a variety of factors, including dosage, shape, particle size, distribution, time of action, interaction with other materials, and so on. Furthermore, because of their small particle size, NPs can easily enter the body and accumulate in organs, resulting in poisoning symptoms. No human cytotoxicity of NPs studies has been performed to date **(Shrestha and Hamblin, 2014; Chen, and Han, 2017)**.

1.14 Allergy to AgNPs

Increasing evidence on possible interaction between nanoparticles and the immune system has been released lately, however, research data is still limited. Amongst the possible immune-related effects, sensitization as a result of nanoparticle exposure represents a current experimental goal for many research groups. It has been said that NPs may be responsible for inducing allergic sensitization (contact dermatitis). However, it has been said that NPs are unlikely to act as a hapten inducing a specific IgE production **(Di Gioacchino et al., 201**

Chapter two

Discussion

Discussion

In dentistry, only three commercial products with AgNPs in their composition were patented until now: NanoCare Gold DNT™ (Dental Nanotechnology Ltd., Katowice, Poland) **(Porenczukiet al. , 2019) (Mackiewicz et al. , 2014)** ; Novaron AG300 (Toagosei Co Ltd., Tokyo, Japan) **(kiriyama et al. , 2013)** ; and GuttaFlow™ (Coltène-Whaledent, Altstätten, Switzerland) **(De_Deus et al. , 2017) (Patil et al. , 2017)** . However, there is a worldwide growth in publications and technological development on AgNP in the health area, indicat- ing the increase in research on this technology, which has already proven the antimicrobial activity of AgNPs alone, in nanocomposites, or associated to biomaterials. Thus,Ag- NPs emerge as an antimicrobial agent for use in the control of pathogenic bacteria, caries activity, tissue inflammation, and bone loss, when at concentrations presenting low cyto- toxicity to the patient's cells.

Chapter three

Conclusion and Suggestions

Conclusion and Suggestions

In this review, the antimicrobial effect of AgNPs incorporation into dental materials was investigated, such as composite Resin, endodontic materials, porcelain, and dental cement . Several studies have shown that silver, in its nanoparticulated Form, possesses an inhibitory effect against many bacteria and fungi, including S. mutans, C. albicans, P. aeruginosa, E. Faecalis, and S. aureus, among others, which could decrease The occurrence of secondary caries, fungal infection, fails on Endodontic treatment . Incorporation of AgNPs prevents biofilm build up over composite Avoiding microleakage and secondary caries. AgNPs Decreases the microleakage in root canal system and can be used as Canal irrigant similar to sodium hypochlorite. In vitro research depicted that these nanoparticles prevent crack Propagation and improves the fracture toughness with dental ceramics Which will negate the cracking of porcelain restorations with crowns And bridges and veneers. The Risk and toxicity of these nanostructured materials need Extensive research, as well as cost effectiveness and patient Acceptance. Despite the effectiveness that Ag NPs have showed in Dental practice, Ag NPs remain a controversial area of Research with respect to their toxicity in biological and Ecological systems. Therefore any applications of Ag NPs in dentistry requires more clinical study.

References

A

● Afkhami, F., Pourhashemi, S.J., Sadegh, M., Salehi, Y., Fard, M.J.K., 2015. Antibiofilm efficacy of silver nanoparticles as a vehicle for calcium hydroxide medicament against Enterococcus faecalis. J. Dentistry 43 (12), 1573–1579.

● Antsiferova, A.A.; Kopaeva, M.Y.; Kochkin, V.N.; Kashkarov, P.K.; Kovalchuk, M.V. Disturbance in Mammalian Cognition Caused by Accumulation of Silver in Brain. Toxics 2021, 9, 30. [CrossRef]

● Arora, R. and Kapoor, H. (2014). Nanotechnology in dentistry - hope or hype. Ohdm, 13, 928- 933.

● Arora S, Jain J, Rajwade JM et al. Cellular responses induced by silver nanoparticles: in vitro studies. Toxicol Lett 2008 179: 93– 100.

● Ahn, S.J., Lee S.J., Kook, J.K. and Lim, B.S. (2009). Experimental antimicrobial orthodontic adhesives using nanofillers and silver nanoparticles. Dental materials, 25, 206–13.

● Allaker, R.P. and Memarzadeh, K. (2014). Nanoparticles and the control of oral infections. International Journal Of Antimicrobial Agents, 43, 95–104.

● R. P. Allaker, “Critical review in oral biology & medicine: the use of nanoparticles to control oral biofilm formation,” Journal of Dental Research, vol.

89, no. 11, pp. 1175–1186, 2010

● A. Bystrom and G. Sundqvist, “Bacteriologic evaluation of the ¨efficacy of mechanical root canal instrumentation in endodontic therapy,” Scandinavian Journal of Dental Research, vol. 89, no. 4, pp. 321–328, 1981.

B

● Bacali, C.; Badea, M.; Moldovan, M.; Sarosi, C.; Nastase, V.; Baldea, I.; Chiorean, R.S.; Constantiniuc, M. The influence of graphene in improvement of physico-mechanical properties in PMMA Denture Base Resins. Materials 2019, 12, 2335. [CrossRef] [PubMed]

● Besinis, A.; Peralta, T.; Handy, R.D. The antibacterial effects of silver, titanium dioxide and silica dioxide nanoparticles compared to the dental disinfectant chlorhexidine on Streptococcus mutans using a suite of biossays. Nanotoxicology 2014, 8, 1–16. [CrossRef]

● Ballottin, D.; Fulaz, S.; Cabrini, F.; Tsukamoto, J.; Duran, N.; Alves, O.L.; Tasic, L. Antimicrobial textiles: Biogenic silver nanoparticles against Candida and Xanthomonas. Mater. Sci. Eng. C 2017, 75, 582–589. [CrossRef]

● Bhardwaj, A. Bhardwaj, A. Misuriya, A. Maroli, S.Manjula, and S. Singh, A.K. (2014). Nanotechnology in dentistry: present and future. Journal Of International Oral Health, 6, 1-6.

● Bidian, C.; Filip, G.A.; David, L.; Florea, A.; Moldovan, B.; Robu, D.P.; Olteanu, D.; Radu, T.; Clichici, S.; Mitrea, D.R. The impact of silver nanoparticles phytosynthesized with Viburnum opulus L. extract on the ultrastrastructure and cell death in the testis of offspring rats. Food Chem. Toxicol. 2021, 150, 112053. [CrossRef] [PubMed]

● Braydich-Stolle L, Hussain S, Schlager JJ et al. In vitro cytotoxicity of nanoparticles in mammalian germline stem cells. Toxicol Sci 2005 88: 412–419.

● Brennan, S.A.; Fhoghlú, C.N.; Devitt, B.M.; O'mahony, F.J.; Brabazon, D.; Walsh, A. Silver nanoparticles and their orthopaedic applications. Bone Jt. J. 2015, 97, 582–589. [CrossRef]

● Burd A, Kwok CH, Hung SC et al. A comparative study of the cytotoxicity of silver-based dressings in monolayer cell, tissue explant, and animal models. Wound Repair Regen 2007 15: 94–104

● Burns J, Hollands K. Nano silver fluoride for preventing caries. Evid Based Dent 2015;16:8–9

● Barszczewska-Rybarek, I.; Chladek, G. Studies on the curing efficiency and mechanical properties of Bis-GMA and TEGDMA nanocomposites containing silver nanoparticles. Int. J. Mol. Sci. 2018, 19, 3937. [CrossRef]

C

● Camilleri J, Gandolfi MG. Evaluation of the radiopacity of calcium silicate cements containing different radiopacifiers. Int Endod J 2010;43:21-30.

● Campagnolo, L.; Massimiani, M.; Vecchione, L.; Piccirilli, D.; Toschi, N.; Magrini, A.; Bonanno, E.; Scimeca, M.; Castagnozzi, L.; Buonanno, G.; et al.

Silver nanoparticles inhaled during pregnancy reach and affect the placenta and the foetus. Nanotoxicology 2017, 11, 687–698. [CrossRef]

● Cao, W. and Zhang, Y. (2018). Novel resin-based dental material with anti-biofilm activity and improved mechanical property by incorporating hydrophilic cationic copolymer functionalized nanodiamond. J. Mater. Sci. Mater. Med., 29, 162.

● Cataldi, A.; Gallorini, M.; Di Giulio, M.; Guarnieri, S.; Mariggiò, M.A.; Traine, T.; Di Pietro, R.; Cellini, L.; Marsich, E.; Sancilio, S. Adhesion of human gingival fibroblasts/Streptococcus mitis co-culture on the nanocomposite system Chitlac-nAg. J. Mater. Sci. Mater. Med. 2016, 27, e88. [CrossRef]

● Chen, S.; Yang, J.; Jia, Y.G.; Lu, B.; Ren, L. A study of 3D-printable reinforced composite resin: PMMA modified with Silver nanoparticles Loaded Cellulose Nanocrystal. Materials 2018, 11, 2444. [CrossRef] [PubMed]

● Chen, R.; Han, Z.; Huang, Z.; Karki, J.; Wang, C.; Zhu, B.; Zhang, X. Antibacterial activity, cytotoxicity and mechanical behavior of nano-enhanced denture base resin with different kinds of inorganic antibacterial agents. Dent. Mater. J. 2017, 36, 693–699.[CrossRef] [PubMed]

● Chladek, G.; Mertas, A.; Barszczewska-Rybarek, I.; Nalewajek, T.; Zmudzki, J.; Król, W.; Łukaszczyk, J. Antifungal activity of denture soft lining material modified by silver nanoparticles—a pilot study. Int. J. Mol. Sci. 2011, 12, 4735–4744. [CrossRef]

● C. Y. Flores, C. Diaz, A. Rubert et al., “Spontaneous adsorption of silver nanoparticles on Ti/TiO2 surfaces. Antibacterial effect on Pseudomonas aeruginosa," Journal of Colloid and Interface Science, vol. 350, no. 2, pp. 402–408, 2010.

● Chandra, A.; Yadav, R.K.; Shakya, V.K.; Luqman, S.; Yadav, S. Antimicrobial efficacy of silver nanoparticles with and without different antimicrobial agents against Enterococcus faecalis and Candida albicans. Dent. Hypotheses 2017, 8, e94. [CrossRef]

● Chen, R. and Han, Z. (2017). Antibacterial activity, cytotoxicity and mechanical behavior of nano-enhanced denture base resin with

● Cheng, L., Weir, M.D., Xu, H.H., Antonucci, J.M., Kraigsley, A.M., Lin, N.J., Lin-Gibson, S. and Zhou, X. (2012). Antibacterial amorphous calcium phosphate nanocomposites with a quaternary ammonium dimethacrylate and silver nanoparticles. Dental materials, 28, 561–72.

● C. Estrela, G. B. Sydney, J. A. P. Figueiredo, and C. R. De Araujo Estrela, "A model system to study antimicrobial ´ strategies in endodontic biofilms," Journal of Applied Oral Science, vol. 17, no. 2, pp. 87–91, 2009.

● CHIMENTAO, R., KIRM, I., MEDINA, F., RODRI´GUEZ, X., CESTEROS, Y., SALAGRE, P. AND SUEIRAS, J. 2004. Chemical communication. Chem. Commun., 4, 846.

● C. J. Whittaker, C. M. Klier, and P. E. Kolenbrander, "Mechanisms of adhesion by oral bacteria," Annual Review of Microbiology, vol. 50, pp. 513–552, 1996.

● Contreras RG, Sakagami H, Nakajima H et al. Type of cell death induced by various metal cations in cultured human gingival fibroblasts. In Vivo 2010 24:

513–517.

D

● Das, S., Parida, U. K. and Bindhani, B. K. (2013). Green biosynthesis of silver nanoparticles using Moringa oleifera L. leaf. Int J Nanotechnol Appl, 3, 51-62.

● De Matteis, V.; Cascione, M.; Toma, C.C.; Albanese, G.; De Giorgi, M.L.; Corsalini, M.; Rinaldi, R. Silver Nanoparticles Addition in Poly (Methyl Methacrylate) Dental Matrix: Topographic and Antimycotic Studies. Int. J. Mol. Sci. 2019, 20, 4691. [CrossRef]

● Di Gioacchino, M. Petrarca, C. Lazzarin, F. Di Giampaolo, L. Sabbioni and E. Boscolo, P. Et Al., (2011). Immunotoxicity Of Nanoparticles. Int J Immunopathol Pharmacol, 24, 65s–71s.

● Duran, N.; Marcato, P.D.; Conti, R.D.; Alves, O.L.; Costa, F.; Brocchi, M. Potential Use of Silver Nanoparticles on Pathogenic Bacteria, their Toxicity and Possible Mechanisms of Action. J. Braz. Chem. Soc. 2010, 21, 949–959. [CrossRef]

● Dutra-Correa, M. and Leite, A. (2018). Antibacterial effects and cytotoxicity of an adhesive containing low concentration of silver nanoparticles. J. Dent. 77, 66–71.

● De-Deus, G.; Brandão, M.C.; Fidel, R.A.S.; Fidel, S.R. The sealing ability of GuttaFlow™ in oval-shaped canals: An ex vivo study using a polymicrobial leakage model. Int. Endod. J. 2017, 40, 794–799. [CrossRef] [PubMed]

● de la Fuente-Herna´ndez J, Gonza´lez de Cosı´o M, Ortega-Maldonado M et al. [Dental decay and tooth loss at the high school level in Mexican students]. Salud Publica Mex 2008 50: 235–240.

● Dreaden, E.C., Alkilany, A.M., Huang X., Murphy C.J. qnd El-Sayed, M.A. (2012). The golden age: gold nanoparticles for biomedicine. Chem. Soc. Rev., 41, 2740–2779.

● Durner, J., Stojanovic, M., Urcan, E., Hickel, R. and Reichl, F.X. (2011). Influence of silver nano-particles on monomer elution from light-cured composites. Dental materials, 527, 631–6

● D. R. Monteiro, L. F. Gorup, A. S. Takamiya, A. C. Ruvollo-Filho, E. R. D. Camargo, and D. B. Barbosa, "The growing importance of materials that prevent microbial adhesion: antimicrobial effect of medical devices containing silver," International Journal of Antimicrobial Agents, vol. 34, no. 2, pp. 103–110, 2009.

E

● Elavazhagan, T. and Arunachalam, K.D. (2011). Memecylon edule leaf extract mediated green synthesis of silver and gold nanoparticles. International Journal Of Nanomedicine, 6, 1265.

● Espíndola-Castro LF, Rosenblatt A, Galembeck A, Monteiro G. Dentin staining caused by nano-silver fluoride: A comparative study. Oper Dent 2020;45:435–441

F

● Fadeel B, Garcia-Bennett AE. Better safe than sorry: understanding the toxicological properties of inorganic nanoparticles manufactured for biomedical applications. Adv Drug Deliv Rev 2010 62: 362–374.

● Fatemeh, K.; Mohammad, J.; Samaneh, K. The effect of silver nanoparticles on composite shear bond strength to dentin with different adhesion protocols. J. Appl. Oral Sci. 2017, 25, 367–373. [CrossRef]

● Fernandes, G.L.; Delbem, A.C.B.; Do Amaral, J.G.; Gorup, L.F.; Fernandes, R.A.; de Souza Neto, F.N.; Souza, J.A.S.; Monteiro, D.R.; Hunt, A.M.A.; Camargo, E.R.; et al. Nanosynthesis of Silver-Calcium Glycerophosphate: Promising Association against Oral Pathogens. Antibiotics 2018, 7, 52. [CrossRef]

● Fan, W.; Wu, D.; Ma, T.; Fan, B. Ag-loaded mesoporous bioactive glasses against Enterococcus faecalis biofilm in root canal of human teeth. Dent. Mater. J. 2015, 34, 54–60. [CrossRef] [PubMed]

● F. Li, M. D. Weir, J. Chen, and H. H. K. Xu, "Comparison of quaternary ammonium-containing with nano-silver-containing adhesive in antibacterial properties and cytotoxicity," Dental Materials, vol. 29, no. 4, pp. 450–461, 2013.

● Freire, P.L.L.; Albuquerque, A.J.R.; Sampaio, F.C.; Galembeck, A.; Flores, M.A.; Stamford, T.; Rosenblatt, A. AgNPs: The New Allies against S. Mutans Biofilm Radhakrishnan—A Pilot Clinical Trial and Microbiological Assay. Braz. Dent. J. 2017, 28, 417–422. [CrossRef]

G

● Garcia-Contreras, R., Argueta-Figueroa, L., Mejia-Rubalcava, C., Jimenez-

Martinez, R Cuevas-Guajardo, S., Sanchez-Reyna, P.A. and Mendieta-Zeron, H. (2011). Perspectives for the use of silver nanoparticles in dental practice. International dental journal, 61, 297–301.

● Gardea-Torresedey, J.L., Gombez, G., Jose-Yaceman, M., Parsons, J.G., Peralta-Videa, J.R., Tioani, and Jose-Yacaman M. (2003). Alfalfa sprouts: a natural source for the synthesis of silver nanoparticles. Langmuir ,19, 1357–1361.

● Gupta, S.; Jangir, O.P.; Sharma, M. The green synthesis, characterization and evaluation of antioxidant and antimicrobial efficacy of silver and gold nanospheres synthesized using wheat bran. Asian J. Pharm. Clin. Res. 2016, 9, 103–106. [CrossRef]

● Gomaa, E.Z. Silver nanoparticles as an antimicrobial agent: A case study on Staphylococcus aureus and Escherichia coli as models for Gram-positive and Gram-negative bacteria. J. Gen. Appl. Microbiol. 2017, 63, 36–43. [CrossRef]

● González-Luna, I.V.P.; Martínez-Castañón, G.A.; Zavala-Alonso, N.V.; Patiño-Marin, N.; Niño-Martínez, N.; Móran-Martínez, J.; Ramírez-González, J.H. Bactericide effect of silver nanoparticles as a final irrigation agent in endodontics on Enterococcus faecalis: An ex vivo study. J. Nanomater. 2016, 2016, 7597295. [CrossRef]

● G. Sundqvist, D. Figdor, S. Persson, and U. Sjögren, “Microbiologic analysis of teeth with failed endodontic treatment and the outcome of conservative re-treatment,” Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics, vol. 85, no. 1, pp. 86–93, 1998.

● Guzma´ N, M.G., Dille, J. and Godet, S. (2009). Synthesis of silver nanoparticles by chemical reduction method and their antibacterial activity. Int. J. Chem. Biol. Eng. 2, 104–111.

H

● Hang, R. and Gao, A. (2014). Antibacterial activity and cytocompatibility of cu-ti-o nanotubes. J. Biomed. Mater. Res., 102, 1850–1858.

● Hanif, A.; Ghani, F. Mechanical properties of an experimental resin based composite containing silver nanoparticles and bioactive glass. PaK J. Med. Sci. 2020, 36, 776–791. [CrossRef] [PubMed]

● Hernández-Sierra, J. F., Galicia-Cruz, O., Salinas-Acosta, A., Ruíz, F., Pierdant-Pérez, M., and Pozos-Guillén, A. (2011). In vitro cytotoxicity of silver nanoparticles on human periodontal fibroblasts. Journal of Clinical Pediatric Dentistry, 36, 37-42.

● Huang YW, Wu C, Aronstam RS. Toxicity of Transition Metal Oxide Nanoparticles: recent Insights from in vitro Studies. Materials 2010 3: 4842–4859.

● Hussain SM, Hess KL, Gearhart JM et al. In vitro toxicity of nanoparticles in BRL 3A rat liver cells. Toxicol In Vitro 2005 19: 975–983.

● HUTTER, E. AND FENDLER, J.H., 2004. Exploitation of Localized Surface Plasmon Resonance. Adv. Mater. 1685, 16.

● H.-J. Park, S. Park, J. Roh, S. Kim, K. Choi, J. Yi, Y. Kim, J. Yoon, Biofilm-in-
activating activity of silver nanoparticles: a comparison with silver ions, J. Ind.

Eng. Chem. 19 (2013) 614–619, http://dx.doi.org/10.1016/j.jiec.2012.09.013.

I

● Iravani, S.; Korbekandi, H.; Mirmohammadi, S.V.; Zolfaghari, B. Synthesis of silver nanoparticles: Chemical, physical and biological methods. Res. Pharm. Sci. 2014, 9, 385–406.

J

● Jacquart S, Siadous R, Henocq-Pigasse C, Bareille R, Roques C, Rey C, et al.. Composition and properties of silver-containing calcium carbonate-calcium phosphate bone cement. J Mater Sci Mater Med 2013;24:2665-2675.

● J.B. Quinn, G.D. Quinn, On the hardness and brittleness of ceramics, Key Eng. Mater. 132–136 (1997) 460–463, http://dx.doi.org/10.4028/www.scientific.net/KEM.132-136.460 .

● J. C. Baumgartner and W. A. Falkler, "Bacteria in the apical 5 mm of infected root canals," Journal of Endodontics, vol. 17, no. 8, pp. 380–383, 1991.

● J. C. Baumgartner, S.-U. Khemaleelakul, and T. Xia, "Identification of spirochetes (treponemes) in endodontic infections," Journal of Endodontics, vol. 29, no. 12, pp. 794–797, 2003.

● Jonaidi-Jafari, N.; Izadi, M.; Javidi, P. The effects of silver nanoparticles on antimicrobial activity of ProRoot mineral trioxide aggregate (MTA) and calcium enriched mixture (CEM). J. Clin. Exp. Dent. 2016, 8, e22. [CrossRef] [PubMed]

● Jung J, Oh H, Noh H, Ji J, Kim S. Metal nanoparticle generation using a small ceramic heater with a local heating area. J Aerosol Sci. 2006;37:1662-1670.

K

● Kawasaki M, Nishimura N. 1064-nm laser fragmentation of thin Au and Ag flakes in acetone for highly productive pathway to stable metal nanoparticles. Appl Surf Sci. 2006;253:2208-2216

● Keskar, M.; Sabatini, C.; Cheng, C.; Swihart, M.T. Synthesis and characterization of silver nanoparticle-loaded amorphous calcium phosphate microspheres for dental applications. Nanoscale Adv. 2019, 1, 627–635. [CrossRef]

● Kiriyama, T.; Kuroki, K.; Sasaki, K.; Tomino, M.; Asakura, M.; Kominami, Y.; Takahashi, Y.; Kawai, T. Antibacterial properties of a self-cured acrylic resin composed of a polymer coated with a silver-containing organic composite antibacterial agent. Dent. Mater. J. 2013, 32, 679–687. [CrossRef] [PubMed]

● Kim, K.J.; Sung, W.S.; Suh, B.K.; Moon, S.K.; Choi, J.S.; Kim, J.G.; Lee, D.G. Antifungal activity and mode of action of silver nanoparticles on Candida albicans. Biometals 2009, 22, 235–242. [CrossRef]

● Kim YS, Song MY, Park JD et al. Subchronic oral toxicity of silver nanoparticles. Part Fibre Toxicol 2010 7: 20.

● Kim S, Yoo B, Chun K, Kang W, Choo J, Gong M, et al. Catalytic effect of laser ablated Ni nanoparticles in the oxidative addition reaction for a coupling reagent of benzylchloride and bromoacetonitrile. J Mol Catal A: Chem. 2005;226:231-234

● Kielbassa, A.M.; Leimer, M.R.; Hartmann, J.; Harm, S.; Pasztorek, M.; Ulrich, I.B. Ex vivo investigation on internal tunnel approach/internal resin infiltration and external nanosilver-modified resin infiltration of proximal caries exceeding into dentin. PLoS ONE 2020, 15, e0228249. [CrossRef]

● K.J. Anusavice, C. Shen, R.B. Lee, Strengthening of feldspathic porcelain by ion
exchange and tempering, J. Dent. Res. 71 (1992) 1134–1138,
http://dx.doi.org/10.1177/00220345920710050101 .

● Khan, I., Saeed, K. and Khan, I. (2017). Nanoparticles: properties, applications and toxicities. Arabian Journal Of Chemistry,.05.011.

● KHOMUTOV, G. AND GUBIN, S. 2002. Antimicrobial activity of silver nanoparticles synthesized using medicinal plant. Mater. Sci. Eng. 22, 141.

● Kruis F, Fissan H, Rellinghaus B. Sintering and evaporation characteristics of gas-phase synthesis of size-selected PbS nanoparticles. Mater Sci Eng B. 2000;69:329-334.

● K. Zhang, M. A. S. Melo, L. Cheng, M. D. Weir, Y. Bai, and H. H. K. Xu, "Effect of quaternary ammonium and silver nanoparticle-containing adhesives on dentin bond strength and dental plaque microcosm biofilms," Dental Materials, vol. 28, no. 8, pp. 842–852, 2012.

● K.-Y. Nam, "In vitro antimicrobial effect of the tissue conditioner containing silver nanoparticles," Journal of Advanced Prosthodontics, vol. 3, no. 1, pp. 20–24, 2011.

● Krishnaveni, T.; Ramasubbu, A. Synthesis and characterization of biomimetic hydroxy apatite-silver impregnated soy protein isolate nanocomposites for dental implantations. Asian J. Chem. 2017, 29, 2634–2638. [CrossRef]

L

● Lara, H.H.; Garza-Treviño, E.N.; Ixtepan-Turrent, L.; Singh, D.K. Silver nanoparticles are broad-spectrum bactericidal and virucidal compounds. J. Nanobiotechnol. 2011, 9, e30. [CrossRef]

● Lara, H.H.; Ayala-Nuñez, N.V.; Turrent, L.D.C.I.; Padilla, C.R. Bactericidal effect of silver nanoparticles against multidrug-resistantbbacteria. World J. Microbiol. Biotechnol. 2010, 26, 615–621. [CrossRef]

● Laurent, S., Forge, D., Port, M., Roch, A., Robic, C., Vander Elst, L. and Muller, R.N. (2010). Magnetic iron oxide nanoparticles: synthesis, stabilization, vectorization, physicochemical characterizations, and biological applications. Chem. Rev., 110,2574–2574.

● L. Fabricius, G. Dahlen, A. E. Ohman, and A. J. M ´ oller, ¨ "Predominant indigenous oral bacteria isolated from infected root canals after varied times of closure," Scandinavian Journal of Dental Research, vol. 90, no. 2, pp. 134–144, 1982.

●Li, W.R.; Xie, X.B.; Shi, Q.S.; Zeng, H.Y.; You-Sheng, O.Y.; Chen, Y.B. Antibacterial activity and mechanism of silver nanoparticles on Escherichia coli. Appl. Microbiol. Biotechnol. 2010, 85, 1115–1122. [CrossRef] [PubMed]

● L. Cheng, K. Zhang, M. D. Weir, H. Liu, X. Zhou, and H. H. K. Xu, "Effects of antibacterial primers with quaternary ammonium and nano-silver on Streptococcus mutans impregnated in human dentin blocks," Dental Materials, vol. 29, no. 4, pp. 462–472, 2013.

● L. F. Espinosa-Cristobal, G. A. Mart ´ ´ınez-Castan˜on, R. E. ´ Mart´ınez-Mart´ınez, J. P. Loyola-Rodr´ıguez, J. F. Reyes-Mac´ıas, and F. Ruiz, "Antibacterial effect of silver nanoparticles against Streptococcus mutans," Materials Letters, vol. 63, no. 29, pp. 2603–2606, 2009.

● L. Sintubin, B. De Gusseme, P. Van Der Meeren, B. F. G. Pycke, W. Verstraete, and N. Boon, "The antibacterial activity of biogenic silver and its mode of action," Applied Microbiology and Biotechnology, vol. 91, no. 1, pp. 153–162, 2011.

● L. Zhao, P. K. Chu, Y. Zhang, and Z. Wu, "Antibacterial coatings on titanium implants," Journal of Biomedical Materials Research Part B: Applied Biomaterials, vol. 91, no. 1, pp. 470–480, 2009.

M

● Magnusson M, Deppert K, Malm J, Bovin J, Samuelson L. Gold nanoparticles: production, reshaping, and thermal charging. J Nanoparticle Res. 1999;1:243-251.

● M. A. S. Melo, S. F. F. Guedes, H. H. K. Xu, and L. K. A. Rodrigues, "Nanotechnology-based restorative materials for dental caries management," Trends in Biotechnology, vol. 31, no. 8, pp. 459–467, 2013.

● M. A. S. Melo, L. Cheng, M. D. Weir, R.-C. Hsia, L. K. A. Rodrigues, and H. H. K. Xu, "Novel dental adhesive containing antibacterial agents and calcium phosphate nanoparticles," Journal of Biomedical Materials Research, Part B: Applied Biomaterials, vol. 101, no. 4, pp. 620–629, 2013.

● McKinney, J. E., Antonucci, J. M., and Rupp, N. W. (1988). Wear and Microhardness of a Silver-Sintered Glass-Ionomer Cement. J. Dent Res. 67, 831–835. doi:10.1177/00220345880670050701

● Mclean, J. W., Nicholson, J. W., and Wilson, A. D. (1994). Proposed Nomenclature for Glass-Ionomer Dental Cements and Related Materials. Quintessence Int. 25, 587–589.

● Mendes, M.S.; Resende, L.D.; Pinto, C.A.; Raldi, D.P.; Cardoso, F.G.; Habitante, S.M. Radiopacity of Mineral Trioxide Aggregate with and without Inclusion of Silver Nanoparticles. J. Contemp. Dent. Pract. 2017, 18, 448–451. [CrossRef] [PubMed]

● Munikamaiah, R.L.; Jain, S.K.; Pal, K.S.; Gaikwad, A. Evaluation of Flexural Strength of Polymethyl Methacrylate modified with Silver Colloidal Nanoparticles subjected to Two Different Curing Cycles: An in vitro Study. J. Contemp. Dent. Pract. 2018, 19, 262–268. [CrossRef]

● Mackiewicz, A.; Olczak-Kowalczyk, D. Microscopic evaluation of surface topography and chemical composition of Nanocare Gold. J. Stomatol. 2014, 67, 826–840. [CrossRef]

● M. E. Samberg, P. E. Orndorff, and N. A. Monteiro-Riviere, "Antibacterial efficacy of silver nanoparticles of different sizes, surface conditions and synthesis methods," Nanotoxicology, vol. 5, no. 2, pp. 244–253, 2011.

● Mohammed, H.F.; Riad, M.I. The effect of silver nanoparticles incorporation in the self-etch adhesive system on its antibacterial activity and degree of conversion: An in-vitro study. F1000Research 2019, 8, e244. [CrossRef]

● M. Rai, A. Yadav, A. Gade, Silver nanoparticles as a new generation of anti-microbials, Biotechnol. Adv. 27 (2009) 76–83, http://dx.doi.org/10.1016/j. biotechadv.2008.09.002.

N

● Navarro E, Piccapietra F, Wagner B et al. Toxicity of silver nanoparticles to Chlamydomonas reinhardtii. Environ Sci Technol 2008 42: 8959–8964.

● Nozari, A.; Ajami, S.; Rafiei, A.; Niazi, E. Impact of Nano Hydroxyapatite, Nano Silver Fluoride and Sodium Fluoride Varnish on Primary Teeth Enamel Remineralization: An In Vitro Study. J. Clin. Diagnostic. Res. 2017, 11, zc97–zc100. [CrossRef]

● Navaladian, S., Viswanathan, B., Viswanath, R.P., and Varadarajan, T.K. (2007). Thermal decomposition as route for silver nanoparticles. Nanoscale res. Lett. 2, 44–48.

● Niska, K. and Knap, N. (2016). Capping agent-dependent toxicity and antimicrobial activity of silver nanoparticles: an in vitro study. Concerns about potential application in dental practice. Int. J. Med. Sci., 13,772–782.

O

● Oliveira, M.; Ugarte, D.; Zanchet, D.; Zarbin, A.J. Influence of synthetic parameters on the size, structure, and stability of dodecanethiol-stabilized silver nanoparticles. J. Colloid Interface Sci. 2005, 292, 429–435. [CrossRef]

P

● Park EJ, Yi J, Kim Y et al. Silver nanoparticles induce cytotoxicity by a Trojan-horse type mechanism. Toxicol In Vitro 2010 24: 872–878.

● Panáˇcek, A.; Kvítek, L. Bacterial resistance to silver nanoparticles and how to overcome it. Nat. Nanotechnol. 2018, 13, 65–71. [CrossRef]

● Peng, J.Y.; Botelho, M.G.; Matinlinna, J.P. Silver compounds used in dentistry for caries management: A review. J. Dent. 2012, 40, 531–541. [CrossRef] [PubMed]

● Paiva, L.; Fidalgo, T.K.S.; da Costa, L.P.; Maia, L.C.; Balan, L.; Anselme, K.; Ploux, L.; Thiré, R.M.S.M. Antibacterial properties and compressive strength of new one-step preparation silver nanoparticles in glass ionomer cements (NanoAg-GIC). J. Dent. 2018, 69, 102–109. [CrossRef] [PubMed]

● Patil, P.; Rathore, V.P.; Hotkar, C.; Savgave, S.S.; Raghavendra, K.; Ingale, P. A comparison of apical sealing ability between GuttaFlow and AH plus: An in vitro study. Int. Soc. Prev. Community Dent. 2016, 6, e377. [CrossRef]

● Pal, S.; Tak, Y.K.; Song, J.M. Does the antimicrobial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the Gram-negative bacterium Escherichia coli. Appl. Environ. Microbiol. 2007, 73, 1712–1720. [CrossRef]

● Porenczukl, A.; Grzeczkowicz, A.; Maciejewska, I.; Goła´s, M.; Piskorska, K.; Kolenda, A.; Gozdowski, D.; Kope´c-Swoboda, E.; Granicka, L.; Olczak-Kowalczyk, D. An initial evaluation of cytotoxicity, genotoxicity and antibacterial effectiveness of a disinfection liquid containing silver nanoparticles alone and combined with a glass-ionomer cement and dentin bonding systems. Adv. Clin. Exp. Med. 2019, 28, 75–83. [CrossRef] [PubMed]

● Prabhu, S.; Poulose, E.K. Silver NPs: Mechanism of antimicrobial action, synthesis, medical applications, and toxicity effects. Int. Nano Lett. 2012, 2, e32. [CrossRef]

● P. Daugela, R. Oziunas, and G. Zekonis, "Antibacterial potential of contemporary dental luting cements," Stomatologija, vol. 10, no. 1, pp. 16–21, 2008.

Q

● Quinteros, M.A.; Viviana, C.A.; Onnainty, R.; Mary, V.S.; Theumer, M.G.; Granero, G.E.; Paraje, M.G.; Páez, P.L. Biosynthesized silver nanoparticles: Decoding their mechanism of action in Staphylococcus aureus and Escherichia coli. Int. J. Biochem. Cell B 2018, 104, 87–93. [CrossRef] [PubMed]

R

● Rai, M.; Yadav, A.; Gade, A. Silver nanoparticles as a new generation of microbials. Biotechnol. Adv. 2009, 27, 76–83. [CrossRef] [PubMed]

● Rai, M.K., Deshmukh, S.D., Ingle, A.P. And Gade, A.K. (2012). Silver nanoparticles: the powerful nanoweapon against multidrug-resistant bacteria. Journal of applied microbiology, 112, 841–52.

● Radhakrishnan, V.S.; Mudiam, M.K.R.; Kumar, M.; Dwivedi, S.P.; Singh, S.P.; Prasad, T. Silver nanoparticles induced alterations in multiple cellular targets, which are critical for drug susceptibilities and pathogenicity in fungal pathogen (Candida albicans). Int. J. Nanomed. 2018, 13, 2647–2663. [CrossRef]

● Raveendran P, Fu J, Wallen SL. Completely "green" synthesis and stabilization of metal nanoparticles. J Am Chem Soc. 2003;125:13940-13941.

● R. Burgers, A. Eidt, R. Frankenberger et al., "The anti- ̈ adherence activity and bactericidal effect of microparticulate silver additives in composite resin materials," Archives of Oral Biology, vol. 54, no. 6, pp. 595–601, 2009.

● Rosenblatt A, Stamford TC, Niederman R. Silver diamine fluoride: a caries 'silver-fluoride bullet'. J Dent Res 2009 88: 116–125.

● R.L. Sakaguchi, Review of the current status and challenges for dental posterior restorative composites: clinical, chemistry, and physical behavior considerations. Summary of discussion from the Portland Composites Symposium (POCOS) June
17–19, 2004, Oregon Health and Science University, Portland, Oregon, Dent. Mater. 21 (2005) 3–6, http://dx.doi.org/10.1016/j.dental.2004.10.008.

● R. P. Allaker, "Critical review in oral biology & medicine: the use of nanoparticles to control oral biofilm formation," Journal of Dental Research, vol. 89, no. 11, pp. 1175–1186 . 2010

● R. A. Bapat et al. , Materials Science & Engineering C 91 (2018) 881–898

S

● Sastry, M., Ahmad, A., Khan, M.I., and Kumar, R. (2003). biosynthesis of metal nanoparticles using fungi and actinomycete. Curr. Sci. 85, 162–170

● Santos VE dos Jr, Vasconcelos Filho A, Targino AGR, Flores MAP, Galembeck A, CaldasAF Jr, et al. A new “silver-bullet” to treat caries in children--nano silver fluoride: a randomised clinical trial. J Dent 2014;42:945–951

● Santos, V.E., Jr.; Vasconcelos Filho, A.V.; Targino, A.G.R.; Flores, M.A.P.; Galembeck, A.; Caldas, A.F., Jr.; Rosenblatt, A. A new silver-bullet to treat caries in children Nano Silver Fluoride: A randomised clinical trial. J. Dent. 2014, 42, 945–951. [CrossRef] [PubMed]

● Sayed M, Hiraishi N, Matin K, Abdou A, Burrow MF, Tagami J. Effect of silver-containing agents on the ultra-structural morphology of dentinal collagen. Dent Mater 2020;36:936–944

● S. Eckhardt, P.S. Brunetto, J. Gagnon, M. Priebe, B. Giese, K.M. Fromm, Chem. Rev. 113, 4708 (2013).

● Shchukin DG, Radtchenko IL, Sukhorukov G. Photoinduced reduction of silver inside microscale polyelectrolyte capsules. Chem Phys Chem. 2003;4:1101–1103.

● Simmons, J. J. (1983). The Miracle Mixture. Glass Ionomer and Alloy Powder. Tex. Dent. J. 100 (10), 6–12.

● Shin, W.K., Cho, J., Kannan, A.G., Lee, Y.S. and Kim, D.W. (2016). Cross-linked composite gel polymer electrolyte using mesoporous methacrylate-functionalized sio2 nanoparticles for lithium-ion polymer batteries. Sci. Rep., 6, 26332.

● SHEIKH, F.A., BARAKAT, N.A., KANJWAL, M.A., NIRMALA, R. LEE, J. H., KIM, H., KIM, H. Y. 2010. Electrospun titanium dioxide nanofibers containing hydroxyapatite and silver nanoparticles as future implant materials. Journal of Materials Science. Materials in Medicine. 21, 2551–9.

● Schrand AM, Braydich-Stolle LK, Schlager JJ et al. Can silver nanoparticles be useful as potential biological labels? Nanotechnol 2008 19: 104–119.

● Shrestha, A. and Hamblin, M.R. (2014). Photoactivated rose Bengal functionalized chitosan nanoparticles produce antibacterial/biofilm activity and stabilize dentin-collagen. Nanomedicine, 10, 491–501.

● Sreeram, K.J., Nidhin, M. and Nair, B.U. (2008). Microwave assisted template synthesis of silver nanoparticles. Bull. Mater. Sci. 31, 937–.942

● Stohs, S.J. and Hartman, M.J., 2015. Review of the safety and efficacy of Moringa oleifera. Phytotherapy Research, 29(6), pp.796-804.

● Soekanto, S.A., Marpaung, L.J., Djais, A.A. and Rina, R. (2017). Efficacy of propolis fluoride and nano silver fluoride for inhibition of streptococcus mutans and enterococcus faecalis biofilm formation. International Journal Of Applied Pharmaceutics, 9, 51-54.

● SUN, S., MURRAY, C., WELLER, D., FOLKS, L. AND MOSER, A. 2000. Science, 1989, 287.

● S. Imazato, M. Torii, Y. Tsuchitani, J.F. McCabe, R.R. Russell, Incorporation of
bacterial inhibitor into resin composite, J. Dent. Res. 73 (1994) 1437–1443, http://dx.doi.org/10.1177/00220345940730080701.

● S. Imazato, F.R. Tay, A.V. Kaneshiro, Y. Takahashi, S. Ebisu, An in vivo evaluation of bonding ability of comprehensive antibacterial adhesive system incorporating MDPB, Dent. Mater. 23 (2007) 170–176, http://dx.doi.org/10.1016/j.dental. 2006.01.005

T

● Targino, A. G. R., Flores, M. A. P., Dos Santos Junior, V. E., Bezerra, F. D. G. B., De Luna Freire, H., Galembeck, A. and Rosenblatt, A. J. J. O. M. S. M. I. M. (2014). An innovative approach to treating dental decay in children. A new anti-caries agent. Journal Of Materials Science: Materials In Medicine,25, 2041-2047.

● Tirupathi S, Svsg N, Rajasekhar S, Nuvvula S. Comparative cariostatic efficacy of a novel Nano-silver fluoride varnish with 38% silver diamine fluoride varnish a double-blind randomized clinical trial. J Clin Exp Dent 2019;11:105–112

● Tiwari, J.N., Tiwari, R.N. and Kim, K.S. (2012). Zero-dimensional, One-dimensional, two-dimensional and three-dimensional nanostructured materials for advanced electrochemical energy devices. Prog. Mater sci. 57, 724–803.

● Tolaymat, T.M., El Badawy, A., Genaidy, M.A., Scheckel, K.G., Luxton, T.P. and Suidan, M. (2010). An evidence-based environmental perspective of manufactured silver nanoparticle in synthesis and applications: a systematic review and critical appraisal of peer-reviewed scientific papers. Sci. Total

Environ. 408, 999–1006.

● Torres-Mendez, F.; Martinez-Castanon, G.A.; Torres-Gallegos, I.; Zavala-Alonso, N.V.; Patino-Marin, N.; Nino-Martinez, N.; Ruiz, F. Effects of silver nanoparticles on the bonding of three adhesive systems to fluorotic enamel. Dent. Mater. J. 2017, 36, 266–274. [CrossRef] [PubMed]

● Tsuji T, Iryo K, Watanabe N, Tsuji M. Preparation of silver nanoparticles by laser ablation in solution: influence of laser wavelength on particle size. Appl Surf Sci. 2002;202:80-85

U

● U. Sjögren, D. Figdor, S. Persson, and G. Sundqvist, "Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis," International Endodontic Journal, vol. 30, no. 5, pp. 297–306, 1997.

V

● Venugopal, A.; Muthuchamy, N.; Tejani, H.; Gopalan, A.I.; Lee, K.P.; Lee, H.J.; Kyung, H.M. Incorporation of silver nanoparticles on the surface of orthodontic microimplants to achieve antimicrobial properties. Korean J. Orthod. 2017, 47, 3–10. [CrossRef]

● VILCHIS-NESTOR, A., SA´NCHEZ-MENDIETA, V., CAMACHO-LO´PEZ, M., GO´MEZ-ESPINOSA, R., CAMACHO-LO´PEZ, M. AND ARENAS-ALATORRE, J. 2008. Solventless synthesis and optical properties of Au and Ag nanoparticles using Camellia sinensis extract. Mater. Lett. 62, .3103

W

● Wang, Y. and Xia, Y. (2004). Bottom-up and top-down approaches to the synthesis of monodispersed spherical colloids of low melting-point metals.Nano lett., 4, 2047–2050.

● World Health Organization. 2011. Available from: http:// www.who.int/mediacentre/factsheets/fs318/en/index.html. Accessed 31 May 2011, 18:04 PM

X

● Xie, D., Brantley, W. A., Culbertson, B. M., and Wang, G. (2000). Mechanical Properties and Microstructures of Glass-Ionomer Cements. Dental Mater. 16 (2), 129–138. doi:10.1016/s0109-5641(99)00093-7

Y

● Yang Z, Liu ZW, Allaker RP et al. A review of nanoparticle functionality and toxicity on the central nervous system. J R Soc Interface 2010 7(Suppl. 4): S411–S422.

● YEO, S., LEE, H. AND JEONG, S. 2003. Preparation of nanocomposite fibers for permanent antibacterial effect. J. Mater. Sci. 38, 2143.

● Yin IX, Zhao IS, Mei ML, Lo ECM, Tang J, Li Q, et al. Synthesis and characterization of fluoridated silver nanoparticles and their potential as a non-staining anti-caries agent. Int J Nanomedicine 2020;15:3207–3215

● Y. J. Cheng, D. N. Zeiger, J. A. Howarter et al., “In situ formation of silver nanoparticles in photocrosslinking polymers,” Journal of Biomedical Materials

Research–Part B Applied Biomaterials, vol. 97, no. 1, pp. 124–131, 2011.

● YOOSAF, K., IPE, B., SURESH, C.H. AND THOMAS, K.G. 2007. In Situ Synthesis of Metal Nanoparticles and Selective Naked-Eye Detection of Lead Ions from Aqueous Media. J. Phys. Chem. C., 1287, 111.

● Y. Zhang, T.P. Shareena Dasari, H. Deng, H. Yu, Antimicrobial activity of gold nanoparticles and ionic gold, J. Environ. Sci. Health C 33 (2015) 286–327, http://dx.doi.org/10.1080/10590501.2015.1055161

● Yin IX, Zhao IS, Mei ML, Li Q, Yu OY, Chu CH. Use of silver nanomaterials for caries prevention: A concise review. Int J Nanomedicine 2020;15:3181–3191

Z

● Zhang, Y.; Zheng, Y.; Li, Y.; Wang, L.; Bai, Y.; Zhao, Q.; Xiong, X.; Cheng, Y.; Tang, Z.; Deng, Y.; et al. Tantalum nitride-decorated titanium with enhanced resistance to microbiologically induced corrosion and mechanical property for dental application. PLoS ONE 2015, e0130774. [CrossRef]

● ZHANG, J., CHEN, P., SUN, C. AND HU, X. 2004. Sonochemical synthesis of colloidal silver catalysts for reduction of complexing silver in DTR system. Appl. Catal. A., 266, 49.

● ZHANG, W., QIAO, X., CHEN, J. AND WANG, H. 2006. Preparation of silver nanoparticles in water-in-oil AOT reverse micelles. J. Colloid InterfaceSci. 302, 370.

● Zhang, N.; Melo, M.A.S.; Antonucci, J.M.; Lin, N.J.; Lin-Gibson, S.; Bai, Y.;

Xu, H.H.K. Novel dental cement to combat biofilms and reduce acids for orthodontic applications to avoid enamel demineralization. Materials 2016, 9, 413. [CrossRef]

● Zhao Y, Nalwa HS. Nanotoxicology. Stewenson Ranch, USA: American Scientific Publishers; 2006.