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ANTISEPTIC ACTION OF SILVER AND ITS APPLICATION IN DENTISTRY, CARDIOLOGY AND DERMATOLOGY

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Abstract

The problem of antimicrobic resistance is increasingly present and requires the discovery of new antimicrobial agents. The healing features of silver have been recognized since ancient times silver has not been used because of again revealed antibiotics. Because of technology development, a noteworthy step forward has been made in silver nanoparticles study. Silver nanoparticles are a frequent target of investigators to find new and better drugs. There is a need for silver nanoparticles as substitute antiseptic nano biotics. Silver nanoparticles depending on their size and shape have dissimilar antimicrobial movement. AgNPsS can serve as drug delivery systems and have anti-thrombogenic, anti-platelet, and anti-hypertensive assets. They are progressively used in medical medicine and dental medicine.

Keywords: *silver nanoparticles; antiseptic action; dentistry; cardiology; dermatology*

INTRODUCTION

The subject of antimicrobic confrontation is at the top of today's difficulties and is most often the outcome of the illogical use of antibiotics. Resolving this problem should be approached in a multidisciplinary method, counting finding new mediators with disinfectant activity. Silver its antibacterial activity has been recognized since early times and trends in the clinical use of silver are rising. The most general medical forms of silver used in current medicine are silver nitrate, silver sulfadiazine and colloidal silver[1]. The use of products with silver nanoparticles is continuously growing, thus improving the knowledge of the biological interactions of silver nanoparticles and its side effects. Silver nanoparticles have been one of the most popular topics of study in recent decades because they have unresolved antimicrobial activity even at low meditations. Materials with silver nanoparticles are a beneficial choice due to the rising prevalence of bacterial resistance to disinfectant agents. All of this has enthused researchers to study how silver's antimicrobial features could be improved and functional in antimicrobial therapy. The present paper presents the antimicrobial activity of silver and silver nanoparticles (AgNPs) and their application in dental medicine, cardiology, and dermatology. Possible side effects after recurrent and excessive experience to AgNPs were also discussed[2].

History of the Usage of Silver

The history of the use of silver days back to earliest times. It was used as jewellery for body piercings, currency and food treatment. The initial medical use of silver was for water storage to avert decay and keep it fresh for drink. It is recognized that early Greeks and Romans used silver for this purpose. The earliest therapeutic use of silver was noted in 1509 BC in the Han family in China. Silver nitrate is labelled as a medicine in the Pharmacopoeia printed in Rome in 68 BC, maybe to avert and treat wound infections[3]. After the consciousness that microbes cause contagions that came in the 1809s, the medical use of silver as a disinfectant agent was confirmed. It has been used in the treatment of injury damages for over 250 years. Silver nitrate was used for an eye contamination and it was one of the 4 antibiotics selections in the USA in the 1974s. The discovery of penicillin in 1938 by Alexander Fleming, happening the era of modern antimicrobial therapy and until the finding of penicillin silver was commonly used as a disinfectant mediator. Silver sulfadiazine and silver nitrate last to have their place in burn treatment and modern silver bandages have a major role in modern wound healing since the late 21th century[4].

Silver Nanoparticles

Nanotechnology is a rapidly progressing area with various uses in the biomedical sciences and involves manufacturing and manufacture of materials at the atomic and molecular level. It refers to assemblies of 1–120 nm in size which comprise from 30 to 25,000 silver atoms[5]. Dissimilar approaches of silver nanoparticles mixture produce AgNPs of variable size shape, morphology and even steadiness. There are three methods of synthesis: a physical, chemical, and biological mixture. The most extensively used method is the chemical discount of silver salts with sodium citrate or sodium borohydrate. AgNPs are extensively used in biomedical requests because of their antibacterial antiviral, and anti-inflammatory properties. The application of AgNPs is widespread from food packaging, water disinfectants, and sprays, all because of their sterile belongings. AgNPs and silver ions have antimicrobial activity the compensations of AgNPs over silver ions are that AgNPs are less toxic and have increased antimicrobial activity, because because of their size, AgNPs pierce the bacterial cell more effortlessly[6].

DISINFECTANT MOVEMENT OF SILVER NANOPARTICLES

The chief submissions of silver nanoparticles (AgNPs) in medicine contain their use in the diagnostic measures, but the most important custom is in rehabilitation due to their antimicrobial act. Bactericidal and repressive silver activity on infective bacteria has been proven in many technical studies. Silver has a benefit over the majority of other antimicrobials because it has a giant scope of activity[7]. It is real against various types of bacteria: bacteria, viruses, fungi. Conservative antibiotics have a bactericidal effect on average on six pathogens. AgNPs could have a bactericidal influence on 670 pathogens without indorsing the mechanism of the resistance. Antiseptic activity is more obvious in Gram-negative bacteria than in Gram-positive bacteria. The exact structure of Gram-positive bacteria is a cell wall, which is much thicker, solider, and is constructed of a thick coating of peptidoglycan. Peptidoglycans have a negative charge, which can measure down silver nanoparticles' movements and make bacteria relatively more resilient to silver. The surface charge has shown to play a significant role in the bactericidal response of AgNPs in contradiction of Gram-negative and Gram-positive bacteria. The various silver nanoparticles tested, those with a positive care had the strongest antimicrobial activity against all tested bacterial species. It is vital to remark that numerous researchers have proven the synergistic and preservative silver effects of conventional antibiotics. It needs a lower dose of antibiotics used in therapy reduces the toxic effects of the antibiotic itself. The bactericidal action, constancy, and biocompatibility of silver nanoparticles be contingent on their size. Silver nanoparticles should not be larger than 52 nm, and those of 12 and 18 nm have augmented activity. Lesser AgNPs have a higher surface-to-nanoparticle volume amount, which documents them to subordinate more with cell membranes than greater nanoparticles. The maximum antimicrobial activity has silver nanoparticles in the range of 5 to 15 nm[8].

Instrument of Antibacterial Action of Silver Nanoparticles

There are three devices by which silver performances on bacteria. One mechanism is that silver positive ion enters the cell wall of bacteria and respond with peptidoglycans. Oxidative pressure, which results from the compulsory of AgNPs to a bacterial cell causing the ions' release, is the second procedure of antibacterial act of silver nanoparticles. Silver nanoparticles can quandary to casing proteins, which can meaningfully affect membrane permeability. This may result in leakage of cell fillings, i.e., unrestrained transportation across the cytoplasmic membrane. AgNPs that bind to membrane proteins can move the acceptance and proclamation of phosphate ions and thus disrupt the respiratory chain and energy production. Reserve of record occurs due to the penetration of AgNPs into the cell where they could subordinate with intracellular rudiments such as lipids, proteins, and DNA they damage DNA and act on protein amalgamation[9]. Sensitive oxygen species can be a significant factor in cell membrane disturbance and DNA alteration. AgNPs unceasingly release silver ions, which is estimated to be the mechanism of abolishing microorganisms. The bactericidal activity of AgNPs is an importance of their action on the bacterial cell, subsequent in cell death[10].

Biofilm

Biofilm has been related with many microbial contaminations. The National Institutes of Health, biofilm is present in about 75% of microbial infections and 85% of chronic infections. Bacteria communicate with each other. It is considered by the persistence of infection and confrontation to antimicrobial drugs. Bacteria in its stalkless form are 200 to 2000 times less delicate to antibiotics than planktonic cells. The penetrability of the EPS matrix for antibiotics. The result is a plain danger to public health. Discovery an innovative way of therapy is considered to be the utmost test of the 21st century. The anti-biofilm activity of silver nanoparticles has been confirmed in frequent analyses. The fact that 25.1 ± 1 nm silver nanoparticles efficiently stop Pseudomonas aeruginosa biofilm development and act bactericidal in already formed biofilm structures suggests that they could be used to prevent and treat biofilm-connected contagions[11].

CLINICAL APPLICATION OF SILVER

Development in nanotechnology has allowable the application of silver nanoparticles, which has created new healing capacities and a possibly wide range of applications. The use of AgNPs varies count cardiovascular implants, catheters, dental composites, curative drugs, and many others[12].

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Application of Silver Nanoparticles in Dental Medicine[13]

Silver has been used in dentistry for over a century and is a critical component in dental amalgam fillings. It is used in rehabilitative dentistry, as well as in implantology and the manufacture of dentures. Biofilms on the superficial of a dental implant can cause provocative lesions on the peri-implant mucosa, thus increasing the risk of implant failure. The main area of using silver nanoparticles is to stop infection during and after dental surgery, i.e., thanks to their sterile activity, microbial colonization through fixed biomaterials is reduced. The antimicrobial topographies of silver nanoparticles have also been studied in detail in dental medicine. Based on the consequences of the investigate, there is a growing notice in AgNPs. The oral cavity is an active ecology that is often colonized by diverse pathogenic microorganisms, so dental resources and implants have an augmented risk of infection. In vitro examinations show the sole antimicrobial silver nanoparticles' action when bound to dental materials for example nanocomposites, acrylic resins, composite resins, adhesives, intracanal drugs and implant covers. They are also second hand to make membranes for guided tissue renewal in periodontal treatment. Lesser silver nanoparticles have increased antibacterial activity against oral anaerobic infective bacteria. It is important to note that AgNPs, thanks to their anticancer possessions, have shown optimistic results in the treatment of oral cancer. The application of silver arrangements as a microbicide to stop dentin caries is flattering more common. In vitro trials demonstrated the microbicidal effectiveness of silver diamine fluoride (SDF) on cariogenic microorganisms in a human dentin model. Silver nanoparticles have also been recognized in in vitro studies to have a microbicidal impact against growth, adhesion, and biofilm growth of Streptococcus mutans in human dentin models. SDF has an intense antimicrobial result on dental plaque. It reduces the metabolism of carbohydrates in dental plaque and rouses a different equilibrium of plaque flora. SDF has a bactericidal result on cariogenic bacteria, largely S. mutans, constraining the increase in cariogenic biofilms on teeth. SDF rouses remineralization of demineralized enamel or dentin and constrains collagenases and thus defends the collagen in dentin from demolition. AgNPs, in mixture with antibiotics, improves bactericidal features. When inactive antibiotics are joint with AgNPs, they gain strong antibacterial activity in contradiction of multidrug-resistant strains of bacteria. Silver nanoparticles have a healthier bacteriostatic and bactericidal outcome, with five times lower attentiveness than chlorhexidine. When AgNPs are used in the proper attentiveness, it is a safe option than other chemically resulting antimicrobials. Dental materials with AgNPs are biocompatible and have no expressive toxic or mutagenic penalties.

Submission of Silver Nanoparticles in Cardiology[14]

Cardiovascular diseases (CVD) are the most shared cause of human death worldwide. The mainstream of the CVD-related deaths is due to atherosclerotic plaque obstruction. The new approach for the analysis, prevention and action of atherosclerosis involves nanoparticles. The most protruding nanoproduct are silver nanoparticles. Biomaterials play a significant role in cardiology. A coronary artery stent meaningfully enhanced the treatment of heart attack by providing mechanical support to tapering vessels. Silver in cardiology was first used in a silicone heart valve covered with silver to gap bacterial infection and decrease inflammation response. Clinical trials displayed that a heart valve coated with silver reasons side effects. Silver encourages hypersensitivity blocks regular fibroblast activity and causes paravalvular outflow. New nanocomposites with AgNPs and carbon for stents and heart valves have anti-thrombogenic and sterile features. The use of cardiac pacemakers whose surfaces have been treated with AgNPs loopholes the application of antibiotic-encumbered pouches. This approach diminutions the risk of infection in the first few months after surgery and increases the likelihood of an optimistic consequence for patients. The study of de Mel et al. showed that polymeric materials for cardiovascular inserts with integrated AgNPs have antibacterial and anti-thrombogenic possessions. The potential application of AgNPs in cardiology is to use them as a vehicle to deliver drugs at a meticulous site in the organism.

Silver ions, usually in the form of a silver salt, demo much higher poisonousness than any size of AgNPs. Ag ionic form for example silver chloride and silver nitrate, caused cardiac changes in rats such as left ventricular hypertrophy causation hypersensitivity and inhibiting regular fibroblast function and causing paravalvular discharge in patients. AgNPs are secure and inoffensive in biomedical implants, as opposed to silver ions. AgNPs are also partly soluble and release Ag ions. Cationic coatings for AgNPs cause higher toxicity than anionic and neutral coatings. AgNPs could be noticed in the cardiovascular system after breath dermal exposure oral exposure, or through injection. Gasped AgNPs which infiltrate in circulation are associated with cardiovascular functions such as cardiac beat disorders and coagulation. The consequence of AgNPs depend on their size dose and experience time. Data on AgNPs' effects are dubious because they defined potential toxicity and likely compensations. Some studies presented that AgNPs have antiplatelet properties. AgNPs stimulates the cohort of vascular endothelial growth factor (VEGF), which is connected with the manufacture of new blood vessels or angiogenesis. Another possible of AgNPs is the introduction of endothelial vasodilatation and therefore better-quality blood flow in the heart. It could be used as a possible antihypertensive agent. The nanocomposite with AgNPs and multilayer films covering AgNPs have antibacterial, mechanical, and hemodynamic possessions in cardiovascular implant coating. The toxicity of AgNPs is not only linked with the release of silver from the nanomaterials. Both oxidative stress and manufacture of reactive oxygen species (ROS) have central role in AgNPs poisonousness[15].

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AgNPs injury cellular components and lead to DNA damage, and damage to the cell membrane which are the seals of early apoptosis. AgNPs increase the ROS production which is accountable for myocardial damage and simultaneously reduces the manufacture of nitric oxide. Silver nanoparticles indorsed oxidative stress and DNA destruction in human endothelial cells. Those data propose that the AgNPs were toxic to endothelial precursors that participate in angiogenesis. ROS could damage the heart muscle and lead to inflammation and oxidative stress in rats. AgNPs encouraged erythrocytes haemolysis, platelet aggregation, and procoagulant beginning. Exposure to AgNPs could cause primary atherosclerosis. Exposure to AgNPs might cause injury to the heart bone and kidney. The raised dermal request of AgNPs induced distortion of the cardiocytes and inflammation. AgNPs are hazardous to cardiac electro-physiology and can bring about lethal bradyarrhythmia and cardiac arrest. Cardiovascular disorders for example hypertension may affect the harmful consequences caused by AgNPs. Studies on animals exposed that inhaled AgNPs are disseminated to all body organs. AgNPs increased heart rate and summary dilation of the artery. AgNPs can induce vasodilation or vasoconstriction in unglued rat aortic rings. AgNPs could pass the blood–brain barrier inducing necrosis and neuronal deterioration. AgNPs affect the start of fish embryos development. It causes chromosomal aberrations and DNA damage and stop the generation of zebrafish. Those data show that AgNPs might have likely teratogenic penalties in human. AgNPs triggers apoptosis through increased caspase three activity. A crucial evaluation of the advantages and disadvantages of AgNPs is needed to ensure their care as a therapeutic agent[16].

Application of Silver Nanoparticles in Dermatology[17]

Silver has well-established use in dermatology. It is an energetic antimicrobial agent with broad-spectrum activity, so it is used to prevent and treat infections in acute wounds and chronic wounds. When in interaction with wound fluid, metallic silver salt and highly active against bacteria. The ionized form of silver has desired antiseptic properties interaction with wound fluid is necessary if the cause is metallic silver. Silver has been combined into various dressing products in addition to creams gels and barricade protectants which vary in their solubility and the rate at which silver ions are released into the wound bed. Nanocrystalline silver bandages were launched commercially as antimicrobial dressings in 1999. They are designed for sustained silver release cathartic antibacterial silver levels for 4–8 days resulting in less recurrent re-application of silver preparations or dressings. Advantage of silver use in modern wound management is the availability of various products for different wound situations. Wound features which determine the choice of suitable dressing are: amount of exudate bleeding and pain. If a moist wound environment is an essential principle of wound healing. Silver dressings look to decrease matrix metalloproteinases that are upregulated in non-healing chronic wounds. They may also promote cellular propagation and re-epithelialization by inducing the production of metallothionein by epidermal cells. Metallothionein upsurges zinc- and copper-dependent enzymes required for cellular proliferation and matrix remodelling. The use of silver dressings can reduce the treatment time and thus lead to cost savings likened to the treatment of silver-free dressings. Published reviews found dissimilar results regarding their effectiveness. Silver-containing dressings recover the likelihood of healing venous leg ulcers, as long-established by the 2019 Cochrane review. Considering all that and their comparatively high price in modern wound management the use of silver dressings is supported only if there are indications of wound infection. Up-to-date silver preparation, silver sulfadiazine (SSD) as a 2% cream, applied once to twice a day, is usually used in partial-thickness and full-thickness burns. SSD is no longer so often optional as it used to be. There is also a risk of toxicity to host cells. Silver sulfadiazine 2% cream is sulfa-drug, a group of synthetic antibiotics containing the sulphonamide molecular structures. Allergic reactions to sulfa drugs are among the most shared drug allergies, so they should be prescribed with caution. Other uncommon adverse belongings of silver sulfadiazine are haemolysis in patients with glucose-6-dehydrogenase (G6PD) lack methemoglobinemia and leukopenia (neutropenia) in children. These conditions are rescindable once the cream is discontinued. Silver sulfadiazine has a low toxicity profile but the request to large burn sites or prolonged use in bullous disorders should be avoided. Argyria is a blue-purple-gray staining of the skin produced by silver deposition and can be localized or generalized. Argyria is not remediable or reversible. There are also a few reported cases of argyria subordinate to silver dressings.

Topical combination of silver into the skin depends on the vehicle used particle size and shape, material type. Smaller nanometer particles are healthier able to penetrate the skin than larger particles. Another silver preparation that has extensive use in dermatology is silver nitrate ($AgNO_3$). It is used for its caustic actions in solid form or solutions more hard-wearing than 10%. It is often used to treat small intractable ulcerations or to diminish excess granulation tissue also called hypergranulation which can harmfully influence wound healing. Silver nitrate is also used effectively to treat warts and molluscum contagiosum which are shared viral infections especially among children. 329 successive patients with molluscum contagiosum were prescribed 30% silver nitrate paste with an excellent cure rate. Silver nitrate is also second hand to stop bleeding in small superficial wounds after curettage or shaving grazes in dermatological surgery. It is used because of its astringent and caustic features caution is wanted because the depth of injury can be increased. Silver also has anti-inflammatory belongings and may have angiogenic properties. Its action on the cytokine system arbitrates the anti-inflammatory properties of silver[18].

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Acne is a continuing inflammatory disorder of the pilosebaceous units, and the Gram-positive Propionibacterium acnes bacterium is supposed to have a crucial function in the pathophysiology. Because of the blend of anti-inflammatory and antimicrobial activity, it was expected that topical silver preparations would benefit acne vulgaris. A small number of trainings were conducted to test this hypothesis. Soaps with nanosilver are broadly practical in the medication of acne. In conclusion, silver preparations are often secondhand “off-label” in this indication due to the low possibility of developing bacterial resistance, the nonappearance of irritation, and the preservation of the skin fence. Atopic dermatitis (AD) is the most widespread chronic inflammatory skin disease noticeable by pruritus and relapsing course. It is also recognized as eczema and atopic eczema. More than 70% of patients with atopic dermatitis have skin colonized with Staphylococcus aureus, associated to about 15% of the unaffected individuals. Silver has an excellent antibacterial consequence on S. aureus, so it is supposed to enhance AD’s clinical signs and symptoms. The use of silver-coated textiles in patients with AD was analysed. Most of them demonstrated that about seven days of wearing such textiles could significantly diminish S. aureus density and improve AD symptoms likened with wearing cotton. It has its difficulties. Washing of silver-infused fabrics is one of them. The quantity of silver lost from textiles can range from 80% loss after four washes to less than 5%. There is a possibility that textile silver ends up in the water supply, reducing the number of helpful bacteria used to treat it. The increasing resistance of fungal strains with dermatophyte strains. There is a vital need for novel antifungals. The antifungal activity of AgNPs has been verified. It was effective against Trichophyton violaceum but not in contradiction of Microsporum canis or Microsporum gypseum. M. canis was more resilient to silver nanoparticles. The growing reserve of the silver nanoparticles on Trichophyton mentagrophytes and Candida albicans. Some researchers also likened the antifungal activity of AgNPs with the current antifungals. Mousavi et al. originate that griseofulvin had higher anti-dermatophyte activity than silver nanoparticles. Silver nanoparticles had superior efficiency compared with fluconazole and less antifungal competence than griseofulvin[19].

They also presented that the antifungal outcomes of fluconazole and griseofulvin were enhanced in the presence of the silver nanoparticles. The antifungal activity of AgNPs is yet to be confirmed with more like studies[20].

SIDE EFFECTS OF SILVER NANOPARTICLES[21]

Silver nanoparticles have many compensations and numerous biomedical applications, but their side effects have been progressively studied. Different studies on the side effects of silver nanoparticles conducted in dissimilar biological systems have contradictory and different results. AgNPs can stimulate the creation and intracellular accumulation of reactive oxygen species, leading to mitochondrial membrane penetrability and DNA damage. Oxidative stress caused by silver nanoparticles could result in inflammatory replies. AgNPs’ side effects are related with free silver ions, although AgNPs could cross the blood–brain barrier and have damaging effects on short- and long-term memory. Inhalation of AgNPs accrues in the blood, liver, lungs, kidneys, stomach, testes, and brain, but AgNPs do not have energetic genotoxicity after oral administration of AgNPs. Smaller silver nanoparticles have more important side effects than larger ones due to larger surface area and reactivity. AgNPs could experience different alterations before they end up in the environment. Adverse biotoxic effects of silver are founded on the type of silver compound present in the environment. AgNPs are well-organized in destroying microorganisms. It could cause the same damage to healthy cells and the ecosystem if not rummage-sale under supervision and without a thorough risk assessment. The clinical position of the possible toxicity of AgNPs remains unexplained. Clinical evidence is contradictory and further research is wanted.

ASSUMPTIONS

The antimicrobial action of AgNPs is very pronounced and it is mainly significant that they can overcome the usual mechanisms of resistance formation. Collective with conventional antibiotics they have a synergistic and preservative effect on bacteria showing specific effectiveness against multidrug-resistant bacteria and are useful against biofilm. It is these two sections that represent the most significant problems of modern medicine. The occurrence of silver nanoparticles in dentistry is increasing. It is used in graft treatment as well as in orthodontic, endodontic, restorative, prosthetic, and periodontal treatment. Anti-caries action as well as antitumor activity in the oral cavity were also experiential. Silver is used in modern wound management in the form of silver dressings that are real and with notable regenerative potential. Different silver preparations are used in everyday practice due to its astringent and caustic topographies. Because of the mentioned qualities silver-based products also have great possible in therapy for various skin conditions: acne, eczema, fungal infections, etc. Cardiovascular implants polymeric materials with integrated AgNPs are used because they have sterile and anti-thrombogenic properties. All drugs and medical devices a crucial calculation of the advantages and disadvantages of AgNPs is needed to ensure their safety as a healing agent. The long-term belongings of the use or exposure to AgNPs could be harmful[22].

AgNPs should only be used when there is a total need for it or when silver is immobilized and there is no risk from toxic free silver ions. Seeing that AgNPs are cheap and have low cytotoxicity, they represent an alternative antimicrobial nanobiotic[23].

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