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Biomedical Applications of Gold & Silver Nanoparticles

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A B S T R A C T

Metallic nanoparticles such as gold & silver nanoparticles hold enormous biomedical applications in the areas of targeted delivery, gene delivery, drug delivery & therapeutics. Researchers are concerned in the nanoscale structures because at this scale these nanoparticles can be utilize as biosensors, for detection of macromolecules, microorganisms, enzyme immobilization, for immunoassay, single nucleotide polymorphisms detection & metal sensors. We have also glanced on biodistribution and toxicity aspects of gold nanoparticles.

The other nanoparticles discussed here is silver nanoparticles on basis of its historical perspective and application as potent antibacterial agent, antifungal agent, antiviral and anti-inflammatory activity. At the nanometer regime, materials demonstrate unique applications in various domains.

Keywords: Metal Nanoparticles, Silver & gold nanoparticles, Applications, Nanoparticles

1. Introduction

1.1. Gold nanoparticles

1.1.1. Ancient perception of gold nanoparticles in medicine

Gold has been explored for its putative medicinal use from ancient times. In medieval Europe it was found that a diverse range of diseases were cured by aurum potabile (drinkable gold). Not until the sixteenth century European alchemists learned to use aqua regia to dissolve gold. Since then, gold had been used in medicinal treatments. Ancient cultures such as those in Egypt, India, and China used gold to treat ailments such as smallpox, skin ulcers, syphilis, and measles [1-4]. Recently, gold is in use in medical devices which including pacemakers and goldplated stents [5,6], for the treatment of heart disease; middle ear gold implants [7], and gold alloys in dental ailments [8,9]. Previously, several organogold complexes have emerged with promising antitumor, antimicrobial, antimalarial, and anti-HIV activities [10,11]. In fact, organogold compounds are now widely used for the treatment of rheumatoid arthritis [12]. Organogold compounds mitigate arthritis symptoms such as joint pain, stiffness, swelling, bone damage, and also reduce the chance of joint deformity and disability. However, many of these compounds have shown reversible dose-dependent toxicities. In particular, at high doses, arthritis patients undergoing chrysotherapy often experience two common side effects: proteinuria and skin reactions.

1.1.2 Biomedical applications of gold nanoparticles

Gold nanoparticles have widely investigated their way from detection to therapeutics in current therapeutics based on the functional moieties and their capabilities. Gold nanoparticles have a significant role in the delivery of nucleic acids, proteins, gene therapy, in- vivo delivery and targeting.

1.1.2.1 Targeted Delivery

Targeted delivery of biomolecules to specific cell and organelles such as the nucleus or mitochondria can be done using gold nanoparticles. A peculiar example of a nuclear drug delivery carrier that penetrates the nucleus of HeLa cells without causing severe cytotoxicity by gold nanoparticles functionalized with PEG and 3-mercaptopropionic acid [13]. Encapsulation of gold nanoparticles by liposomes is similar approach studied for cellular targeting and uptake capacity while carrying drugs or other cargos [14].

1.1.2.2 Gene Delivery

PEGylated gold nanoparticles are one of the most commonly used nanoparticles for gene delivery. Gene expression was enhanced to about 100- fold with DNA-PEGylated gold nanoparticles compared to bare DNA after intravenous injection [15]. The transgenes were stable in circulation and the DNA was released and passed through the cellular membranes. Also, gold nanoparticles functionalized with amino acid have also been used as efficient gene

delivery vectors without causing cytotoxicity [16]. Recently, idodecyldimethylammonium bromide (DDAB, a cationic lipid) coated gold nanoparticles were reported to offer higher efficiency of gene delivery with reduced toxicity. An increase of more than two-times for green fluorescent protein and 48-fold in luciferase gene expression was observed in cells after transfection [17].

1.1.2.3 Drug delivery

Gold nanoparticles are suitable for the cell targeted drug delivery due to their ease of synthesis, functionalization and biocompatibility. Surface functionalized gold nanoparticles with targeted specific biomolecules can efficiently destroy cancer cells or bacteria [18]. Large surface to volume ratio of gold nanoparticles offers a large number of drug molecules being carried by the gold nanoparticles [19]. Gold nanoparticles have been used for the co-administration of protein drugs due to their ability to cross cellular membranes [20] due to the interaction of gold nanoparticles with cell surface lipid. Chitosan capped gold nanoparticles have been used to design high efficiency vectors for DNA vaccine delivery [21]. These DNA conjugated chitosan capped gold nanoparticles have been studied for their efficiency in vitro and in vivo. When delivered intramuscularly to BALB/c mice, these nanoparticles were found more proficient than blank DNA vaccine. These nanoparticles also induced potent cytotoxic T lymphocyte responses at a low dose compared to blank DNA.

Recently 5 fluorouracil capped gold nanoparticles were found to be more effective on gram negative bacteria than gram positive due to their easier permeability into the cells. Also, they showed antifungal activity on A. fumigates and A. niger [22]. Cefaclor synthesized gold nanoparticles were further encapsulated with PEI and tested for E. coli growth. These gold nanoparticles inhibited peptidoglycan layer synthesis of E. coli, and increased the cell wall permeability [23]. In another study, gold nanorods functionalized with innate immune response activators were used to inhibit H1N1 influenza virus. Here, single stranded RNA was used to activate retinoic acid-inducible gene I pathogen recognition pathway which increased the expression of IFN-β and other IFN-stimulated resulting in a decrease in the replication of H1N1 influenza viruses [24]. Recently, non-toxic and biocompatible naturally occurring polysaccharides such as chitosan and gellan gum were utilized for rapid synthesis of AuNps and subsequent use for drug delivery applications [25].

1.1.2.4 Diagnostic and therapeutic agents

The use of gold nanoparticles for cancer therapy has been widely investigated in recent years. Gold nanoparticles conjugated with cyclodextrin and admantane has shown photothermal effects against cancer cells [26]. Generally, these nanoparticles can target tumor cells by an accumulation and entrapment process, known as permeation and retention effect imposed by angiogenic vessels and improper lymphatic flow. Therefore, the nanoparticles can accumulate selectively inside the cancerous cells at higher concentrations than the normal cells. Gold nanoparticles functionalized with fluorescently labeled heparin have been investigated for the targeted detection and apoptotic killing of metastatic cancer cells [27] and the rationale behind this study is the over-expression of heparin-degrading enzymes by metastatic cancer cells.

When attached to gold nanoparticles fluorescence of heparin is quenched and upon cleavage by heparinase/heparanase the fluorescence effect is regained and cancer cells can be detected. In another study, gold nanoparticles functionalized with polyamidoamine (PAMAM) dendrimer-folic acid and/or flouresceinisothiocyanate (FITC) conjugates have been utilized for targeting as well as imaging of the tumor cells [28]. Due to surface functionalization properties and acetylation of the terminal amines of these dendrimers, it is possible to synthesize multifunctional gold nanoparticles with several ligands giving rise to multifunctional nanoparticles. Attachment of folic acid helps these nanoparticles target the tumor cells by binding to the folic acid receptors on the cell membrane in vitro. A thiol-PEGylated tamoxifen derivative was developed for selective targeting of gold nanoparticles to the breast cancer cells which indicated 2.7-fold enhanced drug potency in-vitro [29]. Cisplatin and doxorubicin loaded gold nanoparticles targeted nucleus whereas gamitrinibs loaded gold nanoparticles targeted mitochondria of the cancer cells [30]. Gold nanoparticles functionalized with therapeutic agents can be activated through exchange with complementary molecules, thus reducing cytotoxicity, targeting sub-cellular locations and finally release of the drug for desired therapeutic effect [31]. Gold nanoparticles functionalized with coumarin and PEG have been shown to be effectively internalized by the human breast carcinoma cells without causing any toxicity [32]. This dual functionalization of gold nanoparticles involving biomolecules and fluorescent dyes can particularly be used to target cells for bioimaging along with drug delivery purposes. Radioactive gold nanoparticles functionalized with gum arabic glycoprotein were studied for their biocompatibility and cancer therapeutic applications in severely compromised immuno-deficient (SCID) mice [33]. Individual tumour cells were targeted and nanoparticles were able to penetrate through tumor vasculature and pores with minimum or no radioactivity leakage.

1.1.2.5 Biosensors

Biosensors are finding use in various applications: food processing, environmental monitoring, biowarfare defence; to detect bacteria, viruses and biological toxins [34]. Due to their small size, gold nanoparticle based sensors could have an important impact in diagnostics [35]. Gold nanoparticles having special optical and electronic properties can bind the molecules to the particle surface and can change the plasmon resonance frequency directly, which is observable by their scattered light in dark field microscopy, in particular on the single particle level. On the other hand the plasmon resonance frequency is dramatically changed when the average distance between gold nanoparticles is reduced so that they form small aggregates. This effect of plasmon coupling can be used for colorimetric detection of analytes. The method was pioneered by Mirkin and coworkers [36,37] and is nowadays maybe the most well-known example of a gold based sensor. The original assay was developed for the detection of DNA. Gold nanoparticles are conjugated with oligonucleotides that are complementary to the target sequence which is to be detected. Without the presence of the target sequence the gold

nanoparticles are freely dispersed and the colloidal dispersion appears red. In the presence of the target sequence, the gold nanoparticles bind to the target by hybridization of complementary strands of DNA. As each gold nanoparticle is bearing several oligonucleotides, hybridization results in the formation of small aggregates of gold particles, which leads to a change in the plasmon resonance and the colloidal dispersion appears violet/blue colour. When the sample is heated, even single sequence mismatches result in a different melting temperature of the aggregates which causes colour change. Several DNA assays have been derived from this concept and nowadays the method is established in a way that quantitative detection of DNA sequences of very low concentrations is possible.

Gold nanoparticles have been studied and exploited in the development of diverse of biosensors to detect specific biomolecules significant in disease etiology. In a recent study, a simple but significant colorimetric biosensor was developed using gelatin-coated gold nanoparticles with 6-mercaptohexan-1-ol (MCH) for proteinase activity assay where gelatin serves as a proteinase substrate [38]. Proteinase digestion separates gelatin and brings the nanoparticles closer due to the presence of MCH, thereby causing the gold nanoparticles to aggregate and hence change their surface plasmon resonance. The final resultant of the proteinase activity is a shift in the SPR changing colour of the solution which can be easily determined through the change in the absorbance ratio. Such method holds significant promise in the detection of proteinase activity in various biological samples. A colorimetric "universal" biosensor was devised using single stranded DNA, gold nanoparticles and a water-based polyelectrolyte which was found useful in the detection of DNA, proteins, small molecules, ions, etc. [39].

1.1.2.6 Detection

Gold nanoparticles are also being used for detection of various biological molecules including proteins, enzymes, DNA, antigens and antibodies, etc.

a. Detection of biological molecules

Gold nanoparticles have been used for the detection of proteins, based on their characteristic surface plasmon [40]. For this, gold nanoparticles have been functionalized using bi-functional molecules which were conjugated on one side to the gold nanoparticles through their thiol group and on the other side to the electron-rich aromatic side chains of proteins through a diazonium moiety. The model was tested using thrombin as the protein. The vibrations of the diazo-bond formed between the bifunctional molecule and the target protein tends to enhance due to the conjugation of gold nanoparticles constituting the Raman marker. After the functionalized gold nanoparticles interact with antithrombin as a sensitive recognition element, immobilized on a substrate, thrombin can be detected through surface enhance Raman Spectroscopy. In another study, gold nanoparticles functionalized with Trolox, an analogue of vitamin E have been synthesized using self-assembly of thiol ligand, and were evaluated for the free radical scavenging activity. The antioxidant capacity of the gold nanoparticles functionalized with Trolox was observed to be higher than that of Trolox alone, showing a promise of these antioxidant-functionalized gold nanoparticles in the treatment of various diseases [41]. Also, gold nanoparticles have been employed for the detection of aflatoxins which are mycotoxins associated with different pathophysiological conditions in humans. Aflatoxin AFB1 is associated with cancer. Gold nanoparticles functionalized with antibodies against AFB1 have been synthesized by using electro-deposition of these antibodies on cysteamine functionalized gold nanoparticles [42]. These gold nanoparticles were found to detect AFB1 with high efficiency and less response time.

b. Detection of microorganisms

Recently nanotechnology has made it possible to detect microorganisms by using nanoparticles functionalized with oligonucleotides complementary to the gene tags of the microorganisms. In one of the study, gold nanoparticles were used to detect Salmonella enteritidis and Listeria monocytogenes, where gold nanoparticles deposited within the flagella and in the biofilm network [43]. In another study, gold nanoparticles functionalized with hairpin DNA was used to image live HEp-2 cells infected with Respiratory syncytial virus [44]. Another immunoassay based on multi-functionalized gold nanoparticles was developed by using antibodies against protein A, a cell wall protein of the bacterium Staphylococcus aureus, to detect it in food samples [45]. A gold nanoparticle based chemiluminescence assay was designed for the detection of Staphylococcus enterotoxin B (SEB) [46]. Antibody against SEB was bio-conjugated to the gold nanoparticles through physical adsorption followed by adsorption of the complex on a polycarbonate surface. The SEB was then detected based on sandwich type ELISA and chemiluminescence signal arising from the secondary antibody. The method was found to be simple, easy and highly sensitive with a detection limit of ~0.01 ng/mL.

1.1.2.7 Enzyme Immobilization

Immobilization matrices for enzymes is another area where gold nanoparticles have been used. Functionalization of gold nanoparticles with a carboxyl terminated thiol group was performed through the attachment of the enzyme glucose oxidase [47]. Thermally, the immobilized enzyme was found to be more stable as compared to free enzyme. Such immobilized systems can be very useful in several biotechnological processes in food and environment fields.

1.1.2.8 Immunoassay

Different immunoassays have been designed through functionalized gold nanoparticles with antibodies such as human IgG against pathogenic bacteria [48].Instead of traditional mono or polyclonal antibodies, many immunosensors have been recently developed using single chain fragment variable recombinant antibodies (scFv). A colorimetric immunoassay was developed using gold nanoparticles functionalized with engineered scFv containing either cysteine or histidine in its linker region [49].Here, scFvs are, small heterodimers that are composed of the antibody variable heavy and light chains connected by a peptide linker which stabilizes the molecule. Upon addition of rabit IgG, these scFv stabilized gold nanoparticles have been shown a color

change from red to purple. The method showed high sensitivity with very low detection limit. In another study, Protein A was detected using a biosensor which is based on engineered recombinant A10B scFv. It has been developed as a model through self-assembled monolayer formation detected using gold nanoparticles coated with the protein resulted in a 42 fold increase in the detection limit as compared to A10B Fab [50].

1.1.2.9 Single nucleotide polymorphisms detection

The detection of diseases including diabetes mellitus, β-thalassemia, via single nucleotide polymorphisms associated with them is the most effective technique which gives an idea about point mutations or polymorphisms in various genes, which can be easily, detected using complementary single stranded DNA molecules. Gold nanoparticles functionalized with single-strand- specific-nucleases have been utilized for identification of single nucleotide polymorphisms [51].Similarly, development of a simple colorimetric assay was established with the help of DNA functionalized gold nanoparticles for detection of single nucleotide polymorphisms in the human p53 gene [52]. The 12 point mutations were successfully detected in the human p53 gene as compared to wild type technique which displays a simple approach for detection of altered nucleotide sequences.

1.1.2.10 Metal sensors

Complex biophysical techniques such as fluorimetry, ICP-MS and atomic absorption spectroscopy are conventionally used to detect uranium in the environment. However, these methods are difficult to be used on-site. An alternative to the traditional methods is provided by the DNAzyme-gold nanoparticles system. DNAzymes are catalytic DNA molecules developed in vitro with specific affinities to metal cofactors such as Uranyl is the most common bioavailable form of uranium [53]. For the mercury detection, gold nanoparticles functionalized with L-cysteine were used. The detection of these by gold nanoparticles is facilitated in the presence of UV light and mercury as they tend to aggregate which using them as useful biosensor for on-site applications [54]

1.3 Biodistribution study

To understand the intracellular trafficking and fate of nanoparticles in the animal system, biodistribution studies or tissue kinetics are carried out. Recently, in various animal models some studies have been conducted describing the passage and clearance of the nanoparticles in vivo. Geometry and surface chemistry are the factors on which the biodistribution of gold nanoparticles is dependent. The biodistribution has also been attributed to the type of coating or stabilizing agent used in the preparation of the gold nanoparticles as found in a study on swine .The gum arabic stabilized gold nanoparticles were distributed in the liver whereas maltose stabilized gold nanoparticles were distributed in the lungs. The biodistribution actually followed a first round of distribution followed by another round of redistribution and elimination. In the recent study, the gold nanoparticles were shown to cross the blood brain barrier and have a non- saturable deposition in the brain [55,56]. Also, the gold nanoparticles levels were found to decrease over time indicating efficient clearance from the body. Gold nanoparticles accumulated in various organs without significant toxicity, as observed by cyto-pathological examinations in mice. Thus, promising the use of these nanoparticles to target brain and other organs. Also, gold nanoparticles based first generation anticancer drug CYT-6091 HEG-Thiol-TNF α was studied for its biodistribution and drug loading capacity [57]. The gold nanoparticle was found to be mostly distributed in the liver due to its size, after the release of TNFα. However the amount of residual gold nanoparticles decreased over time. The overall effect included an enhanced uptake of TNFα with lesser adverse effects. The biodistribution of the gold nanoparticles in various tissues is also attributed to their interaction with various plasma proteins which affects their biocompatibility and therapeutic efficacy [58]. Gold nanoparticles attached to tumor necrosis factor accumulate mostly in the liver and spleen and did not dissipate even after a month. Also the biodistribution of gold nanoparticles was correlated to the amounts of polyethylene glycol used for functionalization and the injection dose [59]. Biodistribution studies on PEGylated gold nanorods and nanospheres showed their significant deposition in liver and spleen of ovarian tumor bearing mice in vivo. However, in other organs gold nanorods were found to accumulate more than nanospheres and they have reported that nanorods had longer circulation times than the nanospheres [60]. In a size dependent biodistribution study of spherical gold nanoparticles showed that 10 nm size gold nanoparticles were more profoundly distributed in blood, liver, spleen, kidney, testis, thymus, heart, lung and brain in rats, whereas the larger particles were limited to blood, liver and spleen [61].

1.4 Toxicity of gold nanoparticles

In spite of their extraordinary capacity to bio-conjugate to various molecules, there have been studies showing gold nanoparticles to be cytotoxic due to their inherent physio-chemical properties. In previous study, sodium citrate reduced gold nanoparticles elicited toxicity in alveolar cell lines in vitro [62]. Sodium citrate not only compromised cell viability but also affected cell proliferation. However, these nanoparticles remained localized into the membrane bound vesicles and were not freely dispersed in the cytoplasm.

Depending upon their size and shape, the possibility of their internalization differs and so does their cytological effects. 13 nm sized gold nanoparticles coated with PEG (MW5000) in an in-vivo study in mice induced acute inflammation and apoptosis in the liver [63]. Cytotoxic effect of polycaprolactone (PCL) coated gold nanoparticle was evaluated on ECV-304 cells [64]. In comparison to PCL coated gold nanoparticles, bare gold nanoparticles were shown to have significant changes in the cell morphology and cytoskeleton. Also PCL coated gold nanoparticles were shown to be lesser cytotoxic as compared to bare gold nanoparticles. In order to study the possibility of using colloidal AuNps for drug delivery and biomedical applications, it becomes important to carry out its in-vitro and in-vivo toxicity studies.

1.5 Silver nanoparticles

1.5.1 Historical perspective of silver nanoparticles (AgNPs)

The recent advancements of nanotechnology have endowed a novel therapeutic modality in silver nanoparticles for use in medicine. Silver powder was asserted by Hippocrates, to possess beneficial healing and anti-disease characteristics and catalogued as a regimen for ulcers. But it was mainly silver compounds that actually entered medical practice in World War I until the advent of antibiotics. Metallic silver is subjected to new engineering technologies resulting in extraordinarily novel morphologies and characteristics. Instead of being made "bulk form", metallic silver is engineered into ultra fine nanoparticles whose size is in nanometers range [65-67]. At the nanoscale, like other nanomaterials and primarily by virtue of extremely small size, silver particles display remarkably unusual auxiliary physicochemical properties and biological activities. These distinctive characteristics enhance its application in antibacterial, antifungal, anti-viral and anti-inflammatory therapy.

1.5.2 Biomedical applications of silver nanoparticles

1.5.2.1 Potent antibacterial agent

Silver nanoparticles have been known to have inhibitory and bactericidal effects and thus extend its application as an antibacterial agent [68-70]. The combined effect of silver nanoparticles with antibiotics has proven to be fruitful. Such effects were first observed in Staphylococcus aureus and E. coli using disk diffusion method. In the presence of silver nanoparticles, penicillin G, amoxicillin, erythromycin, clindamycin, and vancomycin exhibited an increased antibacterial activities against both test strains. The same effect was not observed in the case of antibiotics tested. The effects of silver nanoparticles on the antibacterial activity of the aforementioned antibiotics for E. coli were lower than S. aureus. In contrast, the most synergistic activity was observed with erythromycin against S. aureus [71]. The antibacterial activity of silver nanoparticles can be extended to the Textile Industry as well. The biologically synthesized silver nanoparticles could be of immense use in medical textiles for their efficient antimicrobial function [72]. Sterile cloth and materials play an important role in hospitals, where often wounds are contaminated with microorganisms, in particular fungi and bacteria, like S. aureus [73]. Thus, for the reduction and prevention of infections, various antibacterial disinfections techniques have been developed for all types of textiles. The silver nanoparticles were incorporated in cotton and silk cloths. Anti-bacterial activity was observed when silver nanoparticles were incorporated in cotton cloth [74]. Buchholz and Engelbrecht (1970) were the first to load bone cement with antibiotics to reduce infection rates in arthroplasty [75]. The first significant reduction of infection rate by the use of gentamicin loaded bone cement compared to plain PMMA cement and it was confirmed significant difference in antimicrobial activity between antibiotic-loaded and plain PMMA cement in a prospective study [76]. The effect of using silver nanoparticles along with bone cement was found to inhibit the proliferation of the bacterial cells. The increase in concentration of silver increased the antibacterial effect. The cytotoxic levels of the silver nanoparticle bound cement were found to be very less significant and thus it was recommended for treatment of joint arthroplasty.

1.5.2.2 Antifungal agent

In the recent years fungal infections have become more common. Particularly, the frequencies of fungal infections are more in patients who are immune compromised because of cancer chemotherapy, or organ or human immunodeficiency virus infections [77]. The availability of the antifungal drugs is limited because prophylaxis with antifungal may lead to the emergence of resistant strains. The antimicrobial effects of silver nanoparticles have seen in most of the studies, but the effects of silver nanoparticles against fungal pathogens are mostly unknown. The antifungal effects of silver nanoparticles and their mode of action were investigated. Antifungal effects on fungi tested with low hemolytic effects against human erythrocytes were observed. Amphotericin B, an antifungal agent used to treat serious systemic infections was used as a positive control to compare with silver nanoparticles [78]. Silver nanoparticles showed significant antifungal activity against T. Mentagrophytes and Candida species. Towards all fungal strains, silver nanoparticles exhibited similar activity with amphotericin B, but more potent activity than fluconazole. Transmission Electron Microscope was used to document the ability of silver nanoparticles to disrupt the fungal envelope structure. Significant damage was seen in the treated fungal cells, with the formation of a "pit" in their cell walls and pores in their plasma membrane. The intracellular physiology is elicited by the study on the effects of cell cycle in the fungal cells. In the presence of silver nanoparticles, an increase in the percentage of cells in the G2/M phase by 15%, while significant decrease in the G1 phase by about 20% was observed.

1.5.2.3 Antiviral agent

Silver nanoparticles have been used to exhibit the antimicrobial efficacy against viral particles. Monkeypox virus (MPV), an orthopoxvirus similar to variolavirus, is the causative agent of monkeypox in many species of non- human primates [79]. Silver nanoparticles have been shown to exhibit promising cytoprotective activities towards HIV-infected T-cells; however, the effects of these nanoparticles towards other kinds of viruses remain largely

unexplored. In another study, silver nanoparticles could also inhibit the in vitro production of HBV RNA and extra-cellular virions. It has been proposed that the direct interaction between these nanoparticles and HBV double-stranded DNA or viral particles is responsible for their anti-viral mechanism [80].

1.5.2.4 Anti-inflammatory activity

In 1998, nanocrystalline silver dressings were introduced commercially as antimicrobial dressings and showed improved wound healing [81], which may result from potent anti-inflammatory activity. This unusual activity of nanocrystal is said to occur due to its small size [82]. Nanocrystalline silver has unique dissolution behavior, releasing Ago into solution [83]. This species (Ago) is said to exhibit anti-inflammatory activity and this was illustrated when it was tested on animal models [84]. Silver nanoparticles suppress the activity of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) while relieving rheumatoid arthritis symptoms, indicating it may have an anti-inflammatory effect [85]. The treatment of murine infected burns with silver nanoparticles was found to increase the rate of healing and decrease the scarring in comparison with silver sulfadiazine. This was accompanied by increased expression of IL-10, vascular endothelial growth factor, and interferon-Y, with reduced IL-6 expression. In a porcine infected wound model, nanocrystalline silver treatments enhanced tissue regeneration while decreasing erythema and edema relative to silver nitrate (AgNO3) treatments [86]. In dinitronitrofluorobenzene-induced mouse ear rashes, an emollient cream-based nanocrystalline silver treatment significantly reduced erythema, edema, and expression of IL-12 and TNF-α, while increasing apoptosis in inflammatory cells. The anti-inflammatory effect of silver nanoparticles was checked on porcine skin, an excellent model of human skin. Inflammation was induced by means of DNCB and the control was compared to that of the ones treated with Saline (0.9%), AgNO3 (0.5%) and nanocrystalline silver. Day by day observations were made and it was observed that the wound healing was much more significant.

This review emphasizes the brief overview of diagnostic and biomedical applications of gold and silver nanoparticles. The research on metal nanoparticles, their biocompatibility and applications in drug delivery are interesting areas for researchers.

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