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ROLE OF SILVER NANOPARTICLES IN THE TREATMENT OF HYPERLIPIDEMIA

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ABSTRACT

In the recent years, India and other developing nations have seen a quickly raising epidemic of cardiovascular illness. Primary care physicians frequently diagnose and treat hyperlipidemia to avoid cardiovascular disease. The poor absorption characteristics of the active constituents due to their poor water solubility, large molecular sizes which result in a poor diffusion rate. Combining herbal medications with nanotechnology has been advocated because nanostructured systems can overcome the stimulatory effects of plant extracts, reduce the required dose and side effects. Nanoparticles have identified as significant participants in modern medicine, with applications ranging from contrast agents in medical imaging to carriers for gene delivery into individual cells. Silver nanoparticles have tunable physical and chemical properties, so it has been studied widely to improve its applicability. Physicochemical or biological approaches are used to prepare silver nanoparticles, however, each method has its pros and cons. Likewise, biological synthesis is not always reproducible for extensive use but can be a suitable candidate for therapeutic activities like cancer therapy. Excess use of Silver nanoparticles is cytotoxic, and their unregulated discharge in the environment may have effects on both aquatic and terrestrial biota. The research in Silver nanoparticles has always been driven by the need to develop a technology with potential benefits and minimal risk to environmental and human health. In this review, we have attempted to provide an insight into the importance and applications of silver nanoparticles in hyperlipidemia and other pharmacological activities along with the recent synthetic and characterization techniques used for silver nanoparticles.

Keywords - Silver nanoparticles, Nanoparticles, Hyperlipidemia, Antihyperlipidemic activity

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of mortality among adults in the United States and persons with hyperlipidemia are nearly twice as likely as those with normal total cholesterol levels to develop cardiovascular disease (CVD). Primary care physicians frequently diagnose and treat hyperlipidemia to avoid cardiovascular disease (CVD). According to statistics from the Centers for Disease Control and Prevention from a study of 1,492 physicians and it is being observed that hyperlipidemia is only second to hypertension on the list of the ten most frequent serious diseases.[1]

It is a lipid metabolic disorder characterized by higher total cholesterol, total triglycerides, and low density lipoprotein cholesterol in the peripheral blood and decreased high density lipoprotein cholesterol.[2]In recent years, both hyperlipidemia and oxidative stress have become important health concerns. It has become more common in recent years as a result of decreased physical activity and increased consumption of high-calorie, low-fiber fast foods. According to recent research, it is known to be a substantial risk factor for cardiovascular disease.[3]

Human body needs cholesterol which is involved in building the membrane of the cells and hormones like estrogen. Liver is responsible for controlling the content of cholesterol in the blood stream. In the body, liver produces approximately 80% of the cholesterol whereas rest of the cholesterol is obtained from the food like fish, eggs, meat, etc. After having a meal, cholesterol is digested and absorbed in small intestine then the metabolism and storage occurred in the liver. The cholesterol may be secreted by the liver whenever the requirement of cholesterol is needed by the body. Cholesterol is not present in the food which is derived from the plants.[4]

The development of effective safe and adorable nutraceuticals as adjuvant medical therapy to current medications is incredibly challenging. Plant derived bio macromolecules are some of the most promising natural alternatives.[5] In vitro trials have indicated that herbal remedies (plant crude extracts or separated physiologically active ingredients) have good biological activity, but in vivo experiments have not been consistent.[6]

The poor absorption characteristics of the active constituents (flavonoids, tannins, and terpenoids) due to their poor water solubility, large molecular sizes which result in a poor diffusion rate across the membrane and their poor water solubility, which results in reduced dissolution are some of the most common factors that contribute to the poor in vivo efficacy of plant crude extracts or isolated constituents.[7]

The acidic pH of the stomach, as well as the enzymatic conditions of the gastrointestinal system and liver (first-pass metabolism) cause certain compounds to be destroyed and lose their desired effect after administration.[8]Combining herbal medications with nanotechnology has been advocated because nanostructured systems can overcome the stimulatory effects of plant extracts, reduce the required dose and side effects.[9]

Nano drug delivery systems can reintroduce previously discarded components, extend the action of a formulation and successfully combine active ingredients with varying degrees of hydrophilicity and lipophilicity. A Nano-drug delivery system can be utilized to target a particular organ or tissue.[10]The polymeric and co-polymeric nanoparticle systems are the most ideal for screening the hyperlipidemic properties of herbal extracts or their constituents among various nanotechnology-based techniques since these systems are free of lipid extensions.[11]

NANOPARTICLES IN MEDICAL SCIENCES

In recent years, Nanoparticles have identified as significant participants in modern medicine, with applications ranging from contrast agents in medical imaging to carriers for gene delivery into individual cells. Chemical reactivity, energy absorption, and biological mobility are just a few of the properties that distinguish nanoparticles from bulk materials due to their size. These are the materials whose overall dimensions in the nanoscale is under 100 nm.[12]

Nanoparticles are also referred to as “zero-dimensional” nanomaterials. All of the nanoparticle dimensions are in the nanoscale, as opposed to one-dimensional nanomaterials which have one dimension larger than the nanoscale (such as nanowires and nanotubes) and two-dimensional nanomaterials, which have two dimensions larger than the nanoscale (such as self-assembled monolayer films).[13]

The benefits of nanoparticles to modern medicine are numerous and indeed there are some instances where it enable analyses and therapies. However, it also bring with them unique environmental and societal challenges, particularly in regards to toxicity.[14]

They can provide significant improvements in traditional biological imaging of cells and tissues using fluorescence microscopy as well as in modern magnetic resonance imaging (MRI) of various regions of the body.[15]Among the different application areas of nanoparticles, drug delivery is one of the most advanced. This is large part due to the success of polymer and liposome-based drug delivery systems, many of which are in clinical use today.[13]

Polymer-based drug delivery systems can be categorized as polymeric drugs, polymer-protein conjugates, polymer drug conjugates, and polymeric micelles.[16]Polymers can also be emulsified into nanometer-size particles within which drugs can be trapped. Polymeric drugs are typically natural polymers that are known to have antiviral or antitumor characteristics.

In liposome-based drug delivery systems, liposomes are vesicles formed by the entrapment of fluid by phospholipid molecules which have hydrophobic and hydrophilic components and can form bilayers. A bilayer is formed when two layers of oriented lipid molecules come together such that their hydrophobic sides are in contact with one another. Vesicles can range in size from tens of nanometers to thousands of nanometers. Solid lipid nanoparticles (SLN) are another class of nanoparticles that are made from lipids that are solids at room temperature.[17]

Organic, inorganic as well as hybrid materials, are utilized in nanotechnology. Humankind has been using metals such as silver and copper for ages due to their antimicrobial characteristics, and at present, their applications are being explored in consumer products such as textiles, shampoo, hygiene products and contraceptives.[18]

NANOPARTICLES – NOBLE METALS

Noble metals have been in use from a very long time, dating back to the first Egyptian civilization and have always been viewed as a sign of superior power and wealth.[19]Metal nanoparticles have turned out to be the most commonly and broadly studied because of their impressive physicochemical properties and large surface-to-volume ratio compared to their metal. As for biomedical applications, noble metal nanoparticles became a natural pick due to their resistance to harsh environments. They have been applied in highly sensitive diagnostic assays as a thermal ablation enhancers in radiotherapy and as a drug and gene delivery vehicles.

Noble metals in the colloidal state have been the subject of intensive studies, mainly due to their effectiveness in therapeutics and diagnostics. Generally, silver (Au) and platinum (Pt) nanoparticles are employed in the development of novel biosensors and probes due to their ability to adsorb to the biomolecules along with their supreme conductivity and stability.

Gold nanoparticles (Au) find a wide spread use in biological applications such as cancer therapy, cell labeling, drug delivery and diagnostics. Aluminium (Al) and iron oxide (Fe_2O_3) nanoparticles have been proposed as drug delivery systems. Silver (Ag) nanoparticles are indeed widely used in medicine and in common household products as additives with antimicrobial activity against more than 650 different types of disease-causing organisms, including viruses. Along with Silver (Ag), Titanium dioxide (TiO_2) and Copper (Cu) nanoparticles also show strong antibacterial activity.[20]

SILVER NANOPARTICLES

Silver nanoparticles are the particles of silver with particle size between 1-100 nm. Like gold nanoparticles, ionic silver has a long history and was initially used to stain the glass for yellow. Currently, there is also an effort to incorporate silver nanoparticles into a wide range of medical devices, including bone cement, surgical instruments, surgical masks, etc. Moreover it has also been shown that in the correct quantity, the ionic silver is suitable in treating wounds. In fact, silver nanoparticles are now replacing silver sulfadiazine as an effective agent in the treatment of wounds.

Additionally, Samsung has created and marketed a material called “Silver Nano”. It includes silver nanoparticles on the surfaces of household appliances. Moreover, due to their attractive physiochemical properties these nanomaterials have received considerable attention in biomedical imaging. Many targeted silver oxide nanoprobes are currently being developed.

Typically, they are synthesized by the reduction of a silver salt with a reducing agent like sodium borohydride in the presence of a colloidal stabilizer. The most common colloidal stabilizers used are polyvinyl alcohol, poly vinyl pyrrolidone, bovine serum albumin (BSA), citrate and cellulose. Newer novel methods include the use of β-d-glucose as a reducing sugar and a starch as the stabilizer to develop silver nanoparticles ion implantation used to create silver nanoparticles. Also, it is important that not all nanoparticles created are equal. It is observed that the size and shape have an impact on its efficacy.[21]

METHODS FOR SYNTHESIS OF SILVER NANOPARTICLES

5.1Chemical synthesis

The most popular method for synthesizing Silver (Ag) nano particles is the chemical reduction of silver precursors (usually silver salts) by different organic and inorganic reducing agents, often accompanied by stabilization using various capping or stabilizing agents. The shape, size, stability and dispersity of the Silver (Ag) nanoparticles are influenced mainly by the reaction conditions and the nature of reducing and capping agents used.

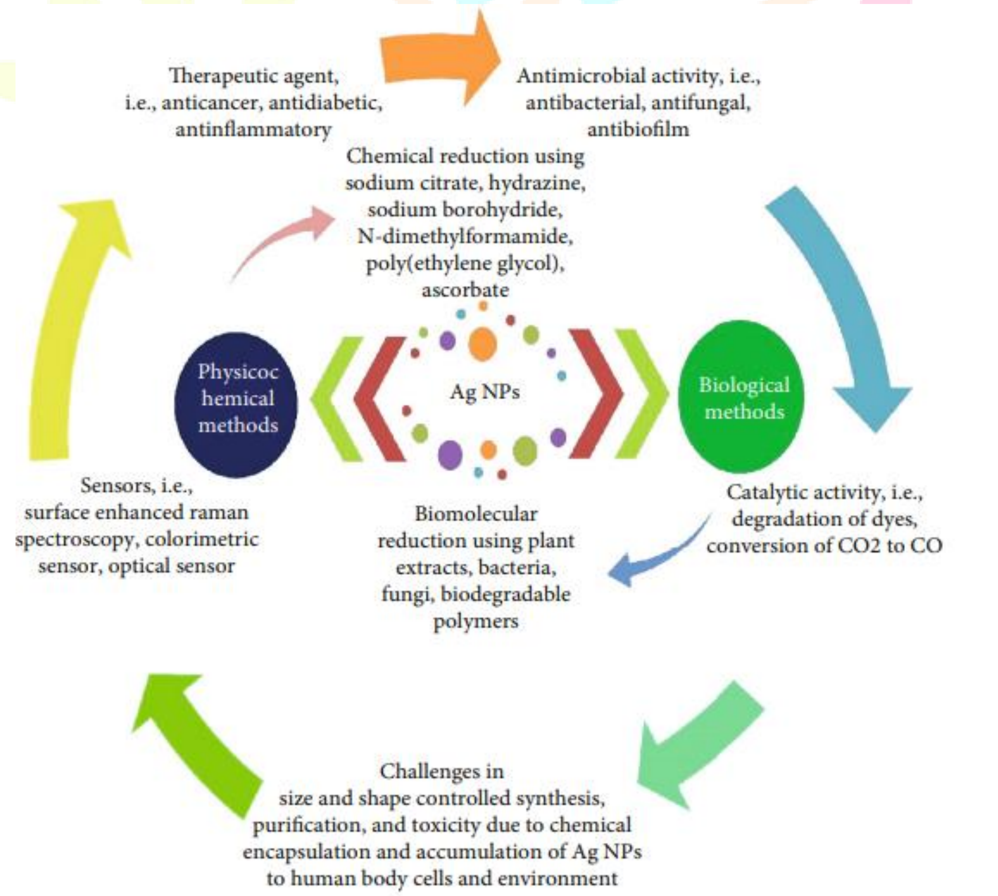

Fig no.1 Synthesis of silver nanoparticles

Chemical synthesis has also been widely used for coating drugs on the surface of Ag NPs. For instance, Masri et al. synthesized stable Vildagliptin-conjugated Silver (Ag) nanoparticles by stirring the 1 : 1 mixture of Vildagliptin and Silver nitrate (Silver nitrate) for 10 minutes, followed by the addition of aqueous Sodium borohydride ($NaBH_4$) solution.

Although the chemical reduction methods are widely used for synthesizing Silver (Ag) nanoparticles , the yield is often too low. Their production can be scaled up using some flow reactors capable of scaled-up production of Silver (Ag) nanoparticles with the narrow-sized distribution.

5.2 Electrochemical and Sonochemical synthesis

In addition to chemical methods, there is a rapidly growing interest in electrochemical and sonochemical methods for synthesizing Ag NPs. These methods do not require chemical oxidants, which benefit from curtailing the purification route of synthesis and the benefit of getting pure materials. Sanchez et al. employed an electrochemical method based on the dissolution of a silver anode in an acetonitrile solution containing tetra butyl ammonium salt to obtain Silver (Ag) nanoparticles with sizes ranging from 2 to 7 nm. One attractive feature of this method is that the size of the Silver (Ag) nanoparticles can be tuned simply by varying the current density when the current density is increased, the overall potential increases and the size of the silver (Ag) nanoparticle decreases.

Besides electrochemical methods, several sonochemical methods for synthesizing Silver (Ag) nanoparticles have been reported. Sarkaret al. reported a sonochemical method for synthesizing Silver (Ag) nanoparticles by decomposing Silver nitrate. In this process, an aqueous Silver nitrate solution was ultrasonicated for an hour in an argon-hydrogen atmosphere to generate amorphous Silver (Ag) nanoparticle (20 nm). Thus, the sonochemical methods offer a nontoxic, environmentally friendly, and economical approach for synthesizing Silver (Ag) nanoparticleat room temperature, but their size-controlling ability is usually less than that of electrochemical methods.

5.3 Nanocage - assisted synthesis

The polymeric matrices, nanocages and supercages present in certain compounds can offer reactive sites to reduce silver ions and impose confinement and protection to the nanoparticles, ultimately leading to size control and stability. Therefore, nanocage-assisted synthesis can be a better strategy to obtain small-sized stable silver nanocomposite materials.

Zhang et al. demonstrated that the ordered arrangement of micropores and nanocages in the zeolites could serve as a sound barrier against the agglomeration of the synthesized Silver (Ag) nanoparticlethrough an electrochemical reduction method on a compact faujasite zeolite film-modified electrodes by an ion-exchange mechanism in an Silver nitrate solution. It was revealed that the size of the Silver (Ag) nanoparticles and the site of formation, inside or outside of the zeolite, can be controlled by changing the extent of silver exchange.

They fabricated a new class of silver nanohybrid particles based on reactive polymeric molecular cages (nanocages) where silver nanohybrid particles were synthesized by the reduction of Silver nitrate with polyamide network polymers (PNP) with an average diameter of 4.34 nm. In any synthetic method after forming nanoparticles, it is essential to transfer them to different bio-physicochemical environments for their practical applications.

But since the Silver (Ag) nanoparticleformed by such nanocage-assisted methods are confined within the polymeric nanocages, it limits their applications usually for catalysis and electronics only.

5.4 Solid Support - assisted synthesis

In recent years, the synthesis of Silver (Ag) nanoparticles mediated by some solid support is emerging as a promising strategy for synthesizing uniformly distributed functionalized Ag NPs.

Zhao et al. reported a facile synthesis of Silver (Ag) nanoparticles on graphene oxide as solid support by microwave-assisted reduction of Silver nitrate in the presence of polyethylene glycol as a stabilizing agent. Graphene oxide provides a fixed platform and anchoring sites for the in situ reductions of silver ions and prevents the aggregation of synthesized Ag NPs.

Similarly, the sol-gel method has been used to develop the highly porous Silver (Ag) nanoparticleby entrapping Ag inside the silica matrix. Here, the reduction of silver salt (Silver nitrate) was made after forming the solid matrix. It has been found that the catalyst has a high surface area and high inner porosity.

5.5 Biological synthesis

The biological approaches follow the principle of utilizing various natural products like phyto chemicals, enzymes and biodegradable polymerase reducing and capping agents to replace potentially hazardous chemicals like sodium borohydride during the synthesis of silver (Ag) nanoparticles and utilizing water as solvent. Reducing agents for the synthesis can be obtained from extracting different parts of the plants (roots, leaf and flower), microorganisms (extracellular and intracellular enzymes, metabolites) and biodegradable polymers.[22]

TOXICITY OF SILVER NANOPARTICLES

Silver nanoparticle causes phytotoxicity in plants to a great extent which can be observed variably by analyzing different physical, physiological, biochemical and structural traits. They damage the cell membranes, interrupt ATP production as well as DNA replication. The enhanced production of reactive oxidant species and subsequent generation of oxidative stress lead to various toxic impacts and may also affect the gene expressions and the demolition of DNA due to enhanced generation of reactive oxidant species.

Toxicity of Silver (Ag) nanoparticles can be seen from seedling growth stage up to a full developed stage of the plants. It generally gives negative impact on the root growth of germinating seedlings and reduces the fresh biomass of the plant through reduction in root elongation and weight. They also induce morphological modifications not only on the contact parts of the roots but also in the stem and leaves. Silver (Ag) nanoparticles modify the expression of several proteins of primary metabolism and cell defense. It also affect the reproductive structure of the plant and reason behind the dreadful toxicity of Silver (Ag) nanoparticles in the plants is its impact on the biochemical properties of plants and inducing free radical generation resulting in induced oxidative stress in plant cells.

Another important toxic effect to be consider is increased generation of the hydrogen peroxide (H_2O_2) in the plants cells which affect the growth and development of the plants and kill the cells. Silver (Ag) nanoparticles may also affect the mitochondrial membrane potential of roots with increasing concentrations. The toxicity of Silver (Ag) nanoparticles is more noticeable in roots as compared to shoots because roots are the main site of interaction while plant's self-defense mechanism involve translocation of the Silver (Ag) nanoparticles from roots to shoots and thus restrict its accumulation in above ground parts completely or partially.

The research is needed to understand the effects of nanoparticles on cellular level and how to reduce nanoparticles inherent toxicity by modifying some cellular processes. One way could be the modification in the osmolyte concentration in the environment for which researches should concern for plasmonic NP–cell interaction as well as internalization dealing with the nanoparticle surface composition. Researcher should also focus on the aggregation behavior of nanoparticles in the cellular environment.

Some researchers have shown the osmolyte-based approach to reduce the toxicity of nanoparticles by surface aggregation on the plasma membrane of the cells without changing the specific surface functionalization. The toxicity may also be reduced by inhibiting protein aggregation through lysozyme – silver nanoparticle interaction.[21]

CHARACTERIZATION OF SILVER NANOPARTICLES

Different analytical and spectroscopic techniques are used to characterize the nature, size, shape, distribution, state of stability or aggregation, morphology, elemental composition, and dispersity (monodisperse or polydisperse) of nanoparticles. It is very characteristic depending upon the shape, size, and distribution of Silver (Ag) nanoparticles due to surface plasma on resonance. The smaller and spherical silver nanoparticles absorb at near 400 nm and have narrow peaks, while larger Silver (Ag) nanoparticles have red shift (absorb at longer wavelength) with broad peaks.

It is also indicative of the stability of Silver (Ag) nanoparticles since the peaks start to decrease in intensity and broaden with the appearance of secondary peaks at higher wavelengths, as particles aggregate. Similarly, the broadening of peaks also provides information about the distribution of Ag NPs. Generally, broad peaks indicate the formation of broader size range distribution (wide dispersity) of Silver (Ag) nanoparticles in solution. The colloidal Silver (Ag) nanoparticles show the size and shape dependent optical properties, i.e., the color of the solution during synthesis is also characteristic of size and shape, and it is possible to perceive and track the progress of synthesis reaction due to the peculiar color of the solution.

IMPORTANCE OF SILVER NANOPARTICLES IN HYPERLIPIDEMIA

Silver (Ag) nanoparticles particularly has attracted lots of interests and has been applied in many areas of medical field for their antibacterial properties amidst their good electrical conductivity, chemical stability and catalytic properties. The In vivo toxicity studies of silver (Ag) nanoparticles in rats has demonstrated that the administration of silver (Ag) nanoparticles are consequently found in the blood and affects several organs including the lung, liver, kidney, intestine, and brain due to their toxic chemical effects. However, the toxic effects of silver (Ag) nanoparticles has been found to be lower in silver nanoparticles that are synthesized using plant extracts, which then compensates the toxicity.

The elevated levels of serum lipids such as total cholesterol, triglycerides, LDL and VLDL were reduced after the treatment of silver (Ag) nanoparticles whereas the level of HDL increased. Periyasamy Karuppannan et al., concluded that the biosynthesized silver (Ag) nanoparticles possess antihyperlipidemic activity against STZ-induced hyperlipidemic condition in diabetic rats which might be useful for the treatment of cardiovascular diseases after advanced clinical evaluation.[23]

APPLICATIONS

Anti-bacterial properties

The silver (Ag) have been demonstrated as an effective biocide against a broad-spectrum bacteria including both Gram-negative and Gram-positive bacteria, in which there are many highly pathogenic bacterial strains. It was reported that the antibacterial activity of silver (Ag) nanoparticles against Gram-negative bacteria divided into three steps:

(i) Nanoparticles mainly in the range of 1-10 nm attach to the surface of the cell membrane and

drastically disturb its proper functions, such as permeability and respiration,

(ii) they are able to penetrate inside the bacteria and cause further damage by possibly interacting

with sulfur- and phosphorus-containing compounds such as DNA,

(iii) nanoparticles release silver ions, which will have an additional contribution to the bactericidal effect of silver (Ag) nanoparticles.s

In another report, Shrivastava et al described the strong antibacterial potency of novel silver (Ag) nanoparticles in the range of 10-15 nm with increased stability against some strains of non-resistant and drug-resistant bacteria. It was concluded that the antibacterial effect is dose-dependent and is more pronounced against Gram-negative than Gram-positive bacteria and independent of acquisition of resistance by the bacteria against antibiotics. It was also suggested that the major mechanism in which silver (Ag) nanoparticles manifested antibacterial properties was by anchoring to and penetrating the bacterial cell wall and modulating cellular signaling by dephosphorylating putative key peptide substrates on tyrosine residues.

Recently, the increasing number of drug-resistant bacteria has become a major challenge endangering human health. Silver (Ag) nanoparticles have been also demonstrated as an effective biocide. Silver (Ag) nanoparticles have been suggested as effective broad-spectrum biocides against a variety of drug-resistant bacteria and a potential candidate for use in pharmaceutical and medical products in order to prevent the transmission of drug-resistant pathogens in different clinical environments.

Antifungal Properties

Fungi are increasingly recognized as major pathogens in critically ill patients, especially nosocomial fungal infections. The antifungal activity of silver (Ag) nanoparticles against *C. albanicans* could be exerted by disrupting the structure of the cell membrane and inhibiting the normal budding process due to the destruction of the membrane integrity. More recently, Pamacek et al investigated the antifungal activity of silver (Ag) nanoparticles prepared by the modified Tollens process. Results also revealed the minimum inhibition against C. albicans growth using silver (Ag) nanoparticles modified with sodium dodecyl sulfate (SDS). Silver (Ag) nanoparticles have also been revealed as potential biocide against fungal strains, and could help to prevent fungal infections for protection of human health.

Antiviral Properties

In recent years, there was an increase in reported numbers of emerging and re-emerging infectious diseases caused by viruses such as SARS-Cov, influenza , influenza A/H1N1, Dengue virus, HIV, HBV, and new encephalitis viruses etc. These viral infections are likely to break out into highly infectious diseases endangering public health. Ag-NPs have shown effective activities against microorganisms including bacteria and fungi.

Elechiguerra et al have investigated the interaction between silver (Ag) nanoparticles and HIV-1. It was reported that silver (Ag) nanoparticles undergo a size-dependent interaction with nanoparticles exclusively in the range of 1–10 nm attached to the virus. It was also suggested that silver (Ag) nanoparticles interact with the HIV-1 virus via preferential binding to the exposed sulfur-bearing residues of the gp120 glycoprotein knobs, resulting in the inhibition of the virus from binding to host cells.

Most publications have suggested that silver (Ag) nanoparticles could bind to outer proteins of viral particles, resulting in inhibition of binding and the replication of viral particles in cultured cells. Although the antiviral mechanism of silver (Ag) nanoparticles has not been fully known yet, Ag-NPs are still suggested as potential antiviral agents in the future.

Antimicrobial Properties

Silver (Ag) nanoparticles were used as antimicrobial coatings in medical devices to reduce nosocomial infections at hospitals. Catheters were coated with silver (Ag) nanoparticles and silver released from the catheters was determined in vitro and in vivo using radioactive silver. Silver-coated catheters showed significant in vitro antimicrobial activity and prevented bio film formation against pathogens most of them involved in catheter-related infections. These catheters are non-toxic and are capable of targeted and sustained release of silver at the implantation site. Because of their demonstrated antimicrobial properties, they may be useful in reducing the risk of infectious complications in patients with indwelling catheters.

In addition, silver (Ag) nanoparticles were also used in therapeutics, especially for treating burn wounds. In order to develop this test, a gel formulation containing silver nanoparticles (S-gel) was developed. The antibacterial spectrum of S-gel was found to be comparable to that of a commercial formulation of silver sulfadiazine, albeit at a 30-fold less silver concentration. As part of toxicity studies, localization of silver (Ag) nanoparticles in Hep G_2 cell line, cell viability, biochemical effects and apoptotic/necrotic potential were assessed. It was found that silver (Ag) nanoparticles get localized in the mitochondria. Further, it was obvious that silver nanoparticles induced apoptosis at higher concentrations, which could favor scarless wound healing. Acute dermal toxicity studies on silver (Ag) nanoparticle gel formulation (S-gel) in Sprague-Dwaley rats showed complete safety for topical application. These results clearly indicated that silver nanoparticles could provide a safer alternative to conventional antimicrobial agents in the form of a topical antimicrobial formulation.[24]

CONCLUSION

Metabolic syndrome is a complex disorder comprising hyperlipidemia, insulin resistance, hyperinsulinemia, and impaired glucose tolerance. There is a need for an effective strategy to treat the complications in the pathophysiology of metabolic syndrome. Despite extensive research on the therapeutic effects of plant derived bioactive compounds, their delivery and bioavailability are always troublesome. Over the past few years, the use of silver nanoparticles in nanoformulations has revolutionized the pharmaceutical and clinical industries.

Silver nanoparticles have been the topic of interest for researchers for a long time because of its tunable properties. The nanoparticles are usually synthesized by reducing silver salts with appropriate reducing agents like sodium citrate, ascorbate, and sodium borohydride, and metabolites from biological sources. However, more research is needed to use the particles beyond the laboratory. Synthesizing cost-effective, evenly distributed, well-dispersed nanoparticles is always challenging as not a single synthesis method is perfect. Similarly, the impact of silver nanoparticles on the environment and health may pose a problem in its widespread applications, so investigation on the accumulation and mechanism of action of silver nanoaparticles inside the human body is required.

In the field of nanotechnology, the development of reliable and eco-friendly methods for the synthesis of nanaoparticles is crucial. The conventional methods for the synthesis of nanoparticles are costly, toxic, and not ecofriendly. To overcome these issues, natural sources such as plant, bacteria, fungi, and biopolymers have been used to synthesize silver nanoparticles. Recently, silver nanoparticles have been utilized as delivery vehicles for therapeutic agents, including antisense oligonucleotides and other small molecules. Small metal nanoparticles offer many advantages as drug carriers, including adjustable size and shape, enhanced stability of surface-bound nucleic acids, high-density surface ligand attachment, transmembrane delivery without harsh transfection agents, protection of the attached therapeutic from degradation, and potential for improved controlled intracellular release. Transformation of nanoparticles is an essential property to consider when assessing their environmental impact or toxicity. For instance, sulfurization of silver nanoparticles greatly reduced their toxicity due to the lower solubility of silver sulphide. These nanosystems have improved not only the bioavailability but also the efficacy, stability, and solubility of plant extracts. Hyperlipidemia is a challenging and problematic disease, however, nano-formulations of plant extracts have shown remarkable antihyperlipidemic effects. The delivery of phytochemicals by utilizing nanotechnology facilitated conventional medicines to link with modern techniques and improve their therapeutic efficacy.

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