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AN OVERVIEW OF SILVER NANOPARTICLES

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Abstract:

Nanotechnology refers to the branch of science and engineering dedicated to materials, having dimensions in the order of 100th of nm or less. Cancer in general is a disease which is characterized by the uncontrolled growth and multiplication of cancerous cells. conventional cancer chemotherapy has the therapeutic agents that distribute non-specifically in different tissues of the human body, thus affecting both cancerous as well as normal cells. This non-specific distribution of drugs to normal cells, tissues, and organs causes excessive toxicities; and thereby causing numerous adverse drug reactions including alopecia, weakness, organ dysfunction causing poor quality of life for cancer patients. The pharmaceutical sciences are using nanoparticles to decrease the toxicity and side effects of drugs. Nanoparticles used in the field of biotechnology range in particle size between 10 and 500 nm, seldom exceeding 700 nm. The nanosize of these particles allows various communications with biomolecules on the cell surfaces and within the cells in way that can be decoded and designated to various biochemical and physiochemical properties of these cell. Nanotechnology has emerged as an exciting strategy in the drug development process and among the different nanoparticles; silver nanoparticles were explored for its various medical applications.

Keywords: *Nanotechnology, Nanoparticles, Silver nanoparticles*

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INTRODUCTION:

Nanotechnology is nowadays playing a key role in targeted drug delivery therapy in medicinal field. It deals with the design, production and characterization on ultra-small particles which is ex-tended to broad area in pharmaceutical, medical, chemical and engineering application due to its unique properties. The development of technology occurs at the atomic, molecular or macromolecular range of approximately 1 nm - 100nm to create and use structures that have novel properties. [1]

Cancer, is characterized by the abnormal growth and spread of abnormal cells, is still the second most common cause of death in the U.S. The majority of patients with metastatic tumor eventually developing drug resistance and surrendering to the disease. [2] Chemotherapy Resistance can be divided into two categories i: e intrinsic and acquired. Though chemotherapy is one of the main modes of cancer treatment, its effectiveness is limited by drug resistance. Intrinsic resistance may be due to intra-tumor heterogeneity that a minor drug resistance subpopulation of cells was present in the original tumor. [3] Common cancer chemotherapy has the cancer therapeutic agents distributing non-exceptionally in the human body, therefore these drugs have an impact on both cancerous and normal cells. This non-specific distribution of drugs limits the therapeutic dose within cancer cells while delivering excessive toxicities to normal cells, tissues, and organs; and thereby inflicting number of adverse side effects resulting hair loss, weakness, and organ dysfunction, leading to a low quality of life for cancer patients. [4]

Nanotechnology refers back to the interactions of cell and molecular components and engineered substances-quite often, clusters of atoms, molecules, and molecular fragments into tremendously small particles. [5] The idea of nanoscale devices has ended up to the development of biodegradable self-assembled nanoparticles, which might be being engineered for the targeted delivery of anticancer drugs and imaging distinction agents. Biodegradable nanometer-sized particles have novel physical and structural properties which might be attracting quality interests from prescription drugs for the certain delivery of anticancer medications and imaging distinction dealers. These clever nanoparticles are designed to ferry chemotherapeutic agents or therapeutic or therapeutic genes into malignant cells while sparing healthy cells. Utility of nanotechnology for healing, checking and manage of organic frameworks has as of late been alluded to as "Nano medicine" by the NIH (National Institute of Health). [6]

NANOPARTICLES

Nanoparticles can be defined as being submicron (i.e. less than 1 micrometer) colloidal systems generally made of polymers either biodegradable or non-biodegradable polymer. They can be further classified according to the size and diameter. Fine particles have the range of 100 to 2500 nm or ultrafine particles having the size of 1 to 100 nm. The term “nanoparticles” is used to describe a particle with size in the range of 1nm-100nm, at least in one of the three possible dimensions. [7] In this size range, the physical, chemical and biological properties of the nanoparticles changes in fundamental ways from the properties of both individual atoms/molecules and of the corresponding bulk. Nanoparticles can be made of materials of diverse chemical nature, the most common being metals, metal oxides, silicates, non-oxide ceramics, polymers, organics, carbon and biomolecules. It can exist in several different morphologies such as spheres, cylinders, platelets, tubes etc. Generally, the nanoparticles are designed with surface modifications tailored to meet the needs of specific applications they are going to be used for. The enormous diversity of the nanoparticles arising from their wide chemical nature, shape and morphologies, the medium in which the particles are present, the state of dispersion of the particles and most importantly, the numerous possible surface modifications the nanoparticles can be subjected to make this an important active field of science now-a-days. [8]

Types of nanoparticles

Nanoparticles can be broadly classified into two, namely, organic nanoparticles which include carbon nanoparticles (fullerenes) while, some of the inorganic nanoparticles include magnetic nanoparticles, noble metal nanoparticles (like gold and silver) and semi-conductor nanoparticles (like titanium oxide and zinc oxide). There is a growing interest in inorganic nanoparticles i.e. of noble metal nanoparticles (Gold and silver) as they provide superior material properties with functional versatility. Due to their size features and advantages over available chemical imaging drug agents and drugs, inorganic particles have been examined as potential tools for medical imaging as well as for treating diseases. Inorganic nonmaterial have been widely used for cellular delivery due to their versatile features like wide availability, rich functionality, good compatibility, and capability of targeted drug delivery and controlled release of drugs. [9]

Advantage of Nanoparticles

Nanoparticles in medication can be utilized for sitecoordinated/focused on medication delivery. Nanoparticles decrease amounts Nano grams since the solution is conveyed/actuated by any of different techniques at the correct site of requirement. Nanoparticles alter the medications to be focus on infections and tumors and allow solid tissue to sit unbothered. This is known as bioavailability: conveying particles to where they are most required, for instance growth drugs authoritative to tumor locales.

Disadvantages of Nanoparticles

Blending nanoparticle tranquilize conveyance frameworks has dependably been muddled by planning a fitting size to convey successful medication/quality payload and capacity to focus to the perfect place. Unseemly size circulation, vague structure/shape, poor biocompatibility, and uncalled for surface science are conceivable hazard figures the organic environment. Creation of nanoparticles with sub-200 nm size requires control over every single stride in the system, which is continually testing. [10]

SILVER NANOPARTICLES

Silver is a soft, white, lustrous transition metal possessing high electrical and thermal conductivity. It has been known longer than the recorded history due to its medical and therapeutic benefits before the realization that microbes are agents for infections. It is used in many forms as coins, vessels, solutions, foils, sutures, and colloids as lotions, ointments. It is the foremost therapeutic agent in medicine for infectious diseases and surgical infections. [11]

Silver nanoparticles are a class of materials with sizes in the range 1–100 nm. They are of particular interest due to their remarkable antimicrobial and localized surface Plasmon resonance properties, which render them unique properties such as broad-spectrum antimicrobial, surface-enhanced Raman spectroscopy (SERS), chemical /biological sensors and biomedicine materials, biomarker. Several physical and chemical methods have been used for synthesizing and stabilizing silver nanoparticle. In recent years, with higher integrated density of electronic components, there are growing demands for the thickness or the width of printed electronic circuits due to considering the space between these circuits. Therefore, the synthesis of silver nanoparticles becomes an important issue in the electronic industry. [12]

Currently, many methods and approaches have been reported for the synthesis of silver nanoparticles by using chemical, physical, photochemical and biological routes. Each method has advantages and disadvantages with common problems being costs, scalability, particle sizes and size distribution. Physical and photochemical methods to prepare nanoparticles are usually need the very high temperature and vacuum conditions, and expensive equipment. Among the existing methods, the chemical methods have been mostly used for production of silver nanoparticles. It is well known that chemical method can successfully produce pure, well-defined nanoparticles and is also the most common method because of its convenience and simple equipment. [13]

Silver nanoparticles have received attention due to their physical, chemical, and biological properties that attributed to the catalytic activity and bactericidal effects and found applications in Nano biotechnological research They are used as antimicrobial agents in wound dressings, as topical creams to prevent wound infections, and as anticancer agents. Although it has been reported that silver nanoparticles have toxic properties that can inhibit bacterial growth, are hazardous to zebrafish and the human reproductive system, and are lethal to cell-based in vitro systems, they are still abundantly utilized in several commercial products such as contraceptive devices and feminine hygiene products. Because of such health concerns, a number of researchers have recently carried out measurements and reported that several consumer products released silver nanoparticles into the environment in large amounts. [14]

CHARACTERISTICS OF SILVER NANOPARTICLES

The main characteristics are

Large surface-area-to-volume ratio as compared to the bulk equivalents;

Large surface energies

The transition between molecular and metallic states providing specific electronic structure (local density of states lodes);

Plasmon excitation;

Quantum confinement;

Short range ordering;

Increased number of kinks;

A large number of low-coordination sites such as corners and edges, having a large number of ″dangling bonds″ and consequently specific and chemical properties and the ability to store excess electrons. [15]

Synthesis of silver nanoparticles

Physical methods

Evaporation-condensation and laser ablation are the most important physical approaches. The absence of solvent contamination in the prepared thin films and the uniformity of NPs distribution are the advantages of physical methods. Physical synthesis of silver NPs using a tube furnace at atmospheric pressure has some disadvantages, for example, tube furnace occupies a large space, consumes a great amount of energy while raising the environmental temperature around the source material, and requires a lot of time to achieve thermal stability. Moreover, a typical tube furnace requires power consumption of more than several kilowatts and a preheating time of several tens of minutes to reach a stable operating temperature. It was demonstrated that silver NPs could be synthesized via a small ceramic heater with a local heating area. The small ceramic heater was used to evaporate source materials. The evaporated vapor can cool at a suitable rapid rate, because the temperature gradient in the vicinity of the heater surface is very steep in comparison with that of a tube furnace. The characteristics of produced Nano-silver particles depend upon many parameters, including the wavelength of the laser impinging the metallic target, the duration of the laser pulses (in the pico- and nanosecond regime), the laser fluency, the ablation time duration and the effective liquid medium, with or without the presence of surfactants.

One important advantage of laser ablation technique compared to other methods for production of metal colloids is the absence of chemical reagents in solutions. Therefore, pure and uncontaminated metal colloids for further applications can be prepared by this technique. Silver Nano spheroids (20-50 nm) were prepared by laser ablation in water with femtosecond laser pulses at 800 nm. The formation efficiency and the size of colloidal particles were compared with those of colloidal particles prepared by nanosecond laser pulses. As a result, the formation efficiency for femtosecond pulses was significantly lower than that for nanosecond pulses. The size of colloids prepared by femtosecond pulses were less dispersed than that of colloids prepared by nanosecond pulses. [16]

Chemical approaches

The most common approach for synthesis of silver nanoparticles is chemical reduction by organic and inorganic reducing agents. In general, different reducing agents such as sodium citrate, ascorbate, sodium borohydride (NaBH4), elemental hydrogen, polyol process, Tollens reagent, N, N-dimethylformamide (DMF), and poly (ethylene glycol)-block copolymers are used for reduction of silver ions (Ag+) in aqueous or non-aqueous solutions. The aforementioned reducing agents reduce silver ions (Ag+) and lead to the formation of metallic silver (Ag0), which is followed by agglomeration into oligomer clusters. These clusters eventually lead to formation of metallic colloidal silver particles. It is important to use protective agents to stabilize dispersive nanoparticles during the course of metal nanoparticle preparation, and protect the nanoparticles that can be absorbed on or bind onto nanoparticle surfaces, avoiding their agglomeration. The presence of surfactants comprising functionalities (*e.g.*, thiols, amines, acids, and alcohols) for interactions with particle surfaces can stabilize particle growth, and protect particles from sedimentation, agglomeration, or losing their surface properties. Recently, a simple one-step process, Tollens method, has been used for the synthesis of silver nanoparticles with a controlled size. In the modified Tollens procedure, silver ions are reduced by saccharides in the presence of ammonia, yielding silver nanoparticle films (50-200 nm), silver hydrosols (20-50 nm) and silver nanoparticles of different shapes. [17]

Biological approaches

In recent years, the development of efficient green chemistry methods employing natural reducing, capping, and stabilizing agents to prepare silver nanoparticles with desired morphology and size have become a major focus of researchers. Biological methods can be used to synthesize silver nanoparticles without the use of any harsh, toxic and expensive chemical substances. The bio reduction of metal ions by combinations of biomolecules found in the extracts of certain organisms (*e.g.*, enzymes/proteins, amino acids, polysaccharides, and vitamins) is environmentally benign, yet chemically complex. Many studies have reported successful synthesis of silver nanoparticle using organisms (microorganisms and biological systems). [18]

Synthesis of silver nanoparticles by bacteria

The first evidence of bacteria synthesizing silver nanoparticles was established using the *Pseudomonas stutzeri* AG259 strain that was isolated from silver mine. There are some microorganisms that can survive metal ion concentrations and can also grow under those conditions, and this phenomenon is due to their resistance to that metal. The mechanisms involved in the resistance are efflux systems, alteration of solubility and toxicity via reduction or oxidation, bio sorption, bioaccumulation, extracellular complex formation or precipitation of metals, and lack of specific metal transport systems. There is also another aspect that though these organisms can grow at lower concentrations, their exposure to higher concentrations of metal ions can induce toxicity. The most widely accepted mechanism of silver biosynthesis is the presence of the nitrate reductase enzyme. The enzyme converts nitrate into nitrite. In in vitro synthesis of silver using bacteria, the presence of alpha-nicotinamide adenine dinucleotide phosphate reduced form (NADPH) - dependent nitrate reductase would remove the downstream processing step that is required in other cases. [19].

Synthesis of silver nanoparticles by fungi when in comparison with bacteria, fungi can produce larger amounts of nanoparticles because they can secrete larger amounts of proteins which directly translate to higher productivity of nanoparticles. The mechanism of silver nanoparticle production by fungi is said to follow the following steps: trapping of Ag+ ions at the surface of the fungal cells and the subsequent reduction of the silver ions by the enzymes present in the fungal system. The extracellular enzymes like naphthoquinones and anthraquinone are said to facilitate the reduction. Considering the example of F. oxysporum, it is believed that the NADPH-dependent nitrate reductase and a shuttle quinine extracellular process are responsible for nanoparticle formation. Though the exact mechanism involved in silver nanoparticle production by fungi is not fully deciphered, it is believed that the abovementioned phenomenon is responsible for the process. A major drawback of using microbes to synthesize silver nanoparticles is that it is a very slow process when in comparison with plant extracts. Hence, the use of plant extracts to synthesize silver nanoparticles becomes an option that is feasible. [20]

Synthesis of silver nanoparticles by plants:

The major advantage of using plant extracts for silver nanoparticle synthesis is that they are easily available, safe, and nontoxic in most cases, have a broad variety of metabolites that can aid in the reduction of silver ions, and are quicker than microbes in the synthesis. The main mechanism considered for the process is plant-assisted reduction due to phytochemicals. The main phytochemicals involved are terpenoids, flavones, ketones, aldehydes, amides, and carboxylic acids. Flavones, organic acids, and quinines are water-soluble phytochemicals that are responsible for the immediate reduction of the ions. Studies have revealed that xerophytes contain emodin, an anthraquinone that undergoes tautomerization, leading to the formation of the silver nanoparticles. In the case of mesophytes, it was found that they contain three types of benzoquinones: cyperoquinone, dietchequinone, and remirin. It was suggested that the phytochemicals are involved directly in the reduction of the ions and formation of silver nanoparticles.[21]

Drug Delivery system using silver nanoparticles

The drug is incorporated into the liposome binds with their specific cell containing the targeted receptor. After that the drug is released inside the whole body using those infected cell (Figure 1). The Nano sized carriers like micro Nano suspension, liposome, dendrimer, ocular inserts, hydrogels are useful in ocular drug delivery which reduce toxicity. This method of approach will also increase the efficiency of drug delivery than conventional delivery system. [22]

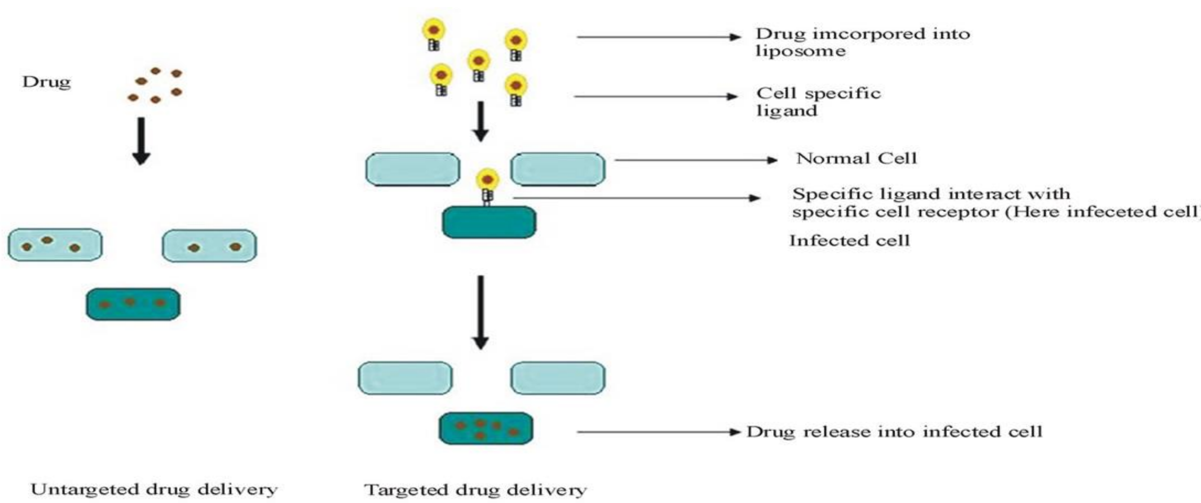

Figure 1: Drug delivery using nanotechnology

Role of Nanoparticles as Medicine

Nanotechnology contributes in management of lung, blood disease and also it counters multiple drug resistance in leukemia by blocking drug efflux from cancer cells and induce efficient delivery of RNA in to lymphocytes to block apoptosis in sepsis. NPs based thrombocyte agent have potential to improve effectiveness of clot removal and also used in nanodentistry in treatment like dention renaturalization, permanent hyper sensitivity, complete orthodontic realignments and covalently bonded diamondized enamel. Nano silver which is a Nano product of 100 nm contains 20-15:000 silver atoms that have strong antibacterial activity which used in wounds and burn healing. Nanocrysalin silver have the property of inhibiting antibiotic resistance and antiseptic resistance microbes. Dendrimers is a novel polymer with well-defined structure, high molecular uniformity and low polydispersity property that makes them more attractive in development of nanomedicine. Dendrimers based delivery system trans-ports drug across cellular barrier efficiently. Mesoporous silica particle (MSP), layered double hydroxide (LDHS) are used for efficient drug delivery. NPs based drug deliveries can target intracellular infection like tuberculosis and also polymeric NPs employing polylactide coglycolide have more potent anti-tubercular activity. [23]

Worldwide silver nanoparticle suppliers [24]

Company name	Size (nm)	Phase	Specification
ABC Nanotech	15-35	Suspension	Dispersed in alcohol; solid content <10 wt.%
Applied Nanotech Holdings	45	powder	P (>99%)
Auto Fibre Craft	30-54	powder	Dry, uncoated
Chengdu Alpha Nano Technology	30-50	powder	P (>99.9%) w/0.3% PVP
Cline Scientific	30	suspension	Citrate stabilized in Milli-Q, spherical
EPRUI	20-80	powder	P (99%); spherical
Inframat Advanced Materials LLC	127	powder	P (99.95%)
IoLiTec	35	powder	P (99.5%)
Kemix	90	powder	P (>99.9%)
Microspheres-Nano spheres	2-250	suspension	Spherical sizes available from 2 to 250 nm
MKnano	90	powder	P (99.9%)
MTI Corporation 55 Powder	55	powder	
NaBond	25	powder	P (>99.9%)
Nano Ocean Tech	6	powder	Surface ligand dodecanethiol

RECENT ADVANCES IN SILVER NANOPARTICLES

Colloidal silver (a colloid consisting of silver particles suspended in liquid) and formulations containing silver salts were used by physicians. Colloidal silver has again been marketed as an alternative medicine, often with extensive "cure-all" claims. Colloidal silver products remain available in many countries as dietary supplements and homeopathic remedies, although they are not effective in treating any known condition and carry the risk of both permanent cosmetic side effects such as argyria and more serious ones such as allergic reactions, and interactions with prescription medications.

The incorporation into wound dressings, creams, and as an antibiotic coating on medical devices. While wound dressings containing silver sulfadiazine or silver nanomaterials may be used on external infections, there is little evidence to support such use. There is tentative evidence that silver coatings on urinary catheters and endotracheal breathing tubes may reduce the incidence of catheter-related urinary tract infections and ventilator-associated pneumonia, respectively The silver ion (Ag^+) is bioactive and in sufficient concentration readily kills bacteria *in vitro*. Silver exhibits low toxicity in the human body, and minimal risk is expected due to clinical exposure by inhalation, ingestion, dermal application. Silver and silver nanoparticles are used as an antimicrobial in a variety of industrial, healthcare and domestic applications.

Antibacterial cream

A 2012 systematic review reported that topical silver showed significantly worse healing time compared to controls and showed no evidence of effectiveness in preventing wounds infection. A 2010 Cochrane systematic review concluded that "There is insufficient evidence to establish whether silver-containing dressings or topical agents promote wound healing or prevent wound infection". The US Food and Drug Administration has approved a number of topical preparations of silver sulfadiazine for treatment of second- and third-degree burns.

Dressings

A 2012 systematic review found that silver-containing dressings were no better than non-silver-containing dressings in treating burns A 2012 Cochrane review found that silver-containing hydrocolloid dressings were no better than standard alginate dressings in treating diabetic foot ulcers. Silver-containing foam resulted in a greater reduction in wound size and more effective control of leakage and odor than non-silver dressings.

Endotracheal tubes

Limited evidence suggests that endotracheal breathing tubes coated with silver may reduce the incidence of ventilator associated pneumonia (VAP) and delay its onset, although no benefit is seen in the duration of intubation, the duration of stay in intensive care or the mortality rate.

Urinary catheters

Tentative evidence supports a decreased risk of urinary tract infections when silver-alloy catheters are used. [25]

Application of silver nanoparticles

Nanotechnology is contributed to sustainable competitiveness and growth in several fields of industrial application. The chemical and physical properties of nanoparticles provide useful functions that are being rapidly exploited in different areas such as in the medicine, biotechnology, material science and energy sectors. On the other hand, biotechnology engages on the molecular, genetic and cellular processes to develop the synthesis of medicines for agricultural purpose. These promising developments in the agricultural sector have their own contribution to overcome the challenges of climate change on food security. Agriculture is the backbone of developing countries, 60% of the population depending on the livelihood. Nanotechnology holds the potential to manage, detect the disease and enhancing the plants to absorb nutrients among other technology. Nanotechnology can improve our understanding of the potential of various crops and enhances the yields or nutritional values. Novel applications of nanoparticles and nonmaterial are growing rapidly on various faces due to their size, distribution, and morphology. Green nanotechnology is expanding its limit in the world of science and technology and same times they call it “the miracle of science”.

The great evolution of expanding the nanotechnologies had opened new fundamental innovations for a number of applications. This includes the synthesis physicochemical and optoelectronic properties of nanoscale materials. Nanostructures widely used for the applications of nanotechnology where the shape and size of the NPs used to determine their characteristic properties. Since the production of the synthesis of NPs is cost-effective and eco-friendly; its demand increases for numerous purposes. As reported by the physical and chemical synthesis of Nano particles introduced toxic and hazardous materials during the use for antimicrobial activity. Additionally, Biological methods for plant extraction reveled more effective than the chemical and physical. This is because the shape and size of nanoparticle using chemical and physical methods for NPs cannot fit with physicochemical methods.

Currently, new disease-causing organisms such as Avian influenza, HIV/AIDS, the Middle East respiratory syndrome (MERS), Ebola virus, Zika virus are exposed on daily basis, this new disease were difficult to overcome their treatment. To overcome these diseases, using AgNPs as the tool is focus many researchers due to their unique physical-chemical and biological properties. Synthesis of nanoparticle using biological methods such as microorganisms, enzymes, fungus and plant or plant extracts have been proposed as a possible environmental friend who is alternative to chemical and physical methods. Synthesis of silver nanoparticles is extensively used to eliminate the possibility since the extraction of plant for the synthesis of green, silver nanoparticles is cost-effective, simple and eco-friendly method.

Researchers are giving attention on metallic nanoparticles due to its growing microbial resistance against metal ions, antibiotics and development of resistant strains. In the field of nanotechnology AgNPs gained unlimited focus because of its unique property. The chemical stability and catalytic effect of silver nanoparticles have an advantage over the other metallic nanoparticles for antibacterial, antiviral, anticancer antifungal and to anti-inflammatory activities. Silver has long been recognized as having an inhibitory effect on microbes present in a medical and industrial process. [26]

CONCLUSION:

Silver nanoparticles are the most important nanoparticles because of their applications. These nanoparticles have many important applications that include spectrally selective coating for solar energy absorption and intercalation material for electrical batteries, as optical receptors, polarizing filters, catalysts in chemical reaction, biolabelling and as antimicrobial agents. During the past few years the synthesis and development of Nano material has drastically put an effect to work as a next-generation anticancer therapeutic agent. The silver Nano particles can overcome poor delivery and the problem of drug resistance. The method of production bio-distribution, stability, accumulation, controlled release, cell specific targeting and toxicological issues in human too.

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