Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v29i04.4323

A SYSTEMIC REVIEW ON SILVER NANOPARTICLES: CURRENT PROSPECTIVE AND QUALITY OPTIMIZATION APPROACHES AND APPLICATION

Jiyaul Hak[1*], Dinesh Kumar Sharma[2], Nasiruddin Ahmad Farooqui[3]

[1*]Research Scholar, Sanskriti University, Mathura (U.P.)
[2]Professor, Sanskriti University, Mathura (U.P.)
[3]Professor, Translam Institute of Pharmaceutical Education and Research, Meerut (U.P.)

***Corresponding Author:** Jiyaul Hak
*Research Scholar, Sanskriti University, Mathura (U.P.), Email ID- jiyaultiper@gmail.com

Abstract
In recent years, nanoparticles of noble metals like gold, Palladium, and Silver have drawn immense attention due to the wide range of new applications in pharmaceutical fields as well as other industries. Silver nanoparticles are one of the most beneficial forms of metals in nanotechnology applications. Silver nanoparticles are used in a wide variety of products, including consumer goods, healthcare, catalysts, electronics, and analytical equipment. Silver has a lot of potential in a variety of biological/chemical applications, particularly in the form of nanoparticles (NPs). Silver nanoparticles have anti-inflammatory, anti-cancer, anti-viral, anti-bacterial, and wound-healing activity. The major focus of silver nanoparticles on anti-inflammatory anti-cancer and anti-bacterial capabilities in this review article. We also discuss the properties of AgNPs and methods for their characterization, pharmacokinetics, and pharmacodynamics. More importantly, we extensively discuss the multifunctional bio-applications of AgNPs; for example, as antibacterial, antifungal, antiviral, anti-inflammatory, anti-angiogenic, and anti-cancer agents, and the mechanism of the anti-cancer activity, anti-inflammatory activity and anti-bacterial activity of AgNPs. In addition, we discuss therapeutic approaches and challenges for cancer therapy using AgNPs. Finally, we conclude by discussing the future perspective of AgNPs.
The results show that, depending on a variety of circumstances, silver nanoparticles have varying degrees of anti-inflammatory anti-cancer and anti-bacterial impact. The usage of anti-inflammatory supplements serves as evidence that silver supplements are being used.

Keywords: Silver Nanoparticles, Pharmacokinetic, and Pharmacodynamics, quality optimization approach, therapeutic application, etc.

1. Introduction:

Silver nanoparticles (AgNPs) are increasingly employed in a variety of industries, including medicine, food, health care, consumer goods, and applications in industry [1][2][3][4]. Optical, electrical, heat, and physiological qualities are a few of them, along with strong electrical conductivity. As a result of their uncommon properties, they are utilized for several uses, including antibacterial agents, consumer products, sensors for light, and beauty products, medicine and food

companies, testing, orthopedics, drug delivery, and even chemotherapy drugs, and eventually to boost the tumor-killing effects of anticancer drugs [5][6].

AgNPs are now increasingly found in bandages and medicinal devices. Nano-sized Metallic granules have a variety of purposes due to their extraordinary surface-to-volume ratio and ability to significantly alter physical, chemical, and biological characteristics. A variety of synthetic methods have been employed to produce AgNPs. [7][8][9] Traditional Physical as well as chemical techniques generally appear to be fairly costly and risky. [2] It's noteworthy that biologically generated AgNPs have high yield and solubility. Because a particle's physicochemical qualities may significantly affect those biological properties, detailed particle characterization is required after production. It is crucial to define the produced nanoparticles before use to solve the safety issue and realize the full potential of any nanomaterial for human welfare in Nano pharmaceuticals, healthcare industry etc. Before toxicity or biocompatibility can be assessed, the specific features of nanomaterial, such as size, shape, size distribution, surface area, form, solubility, aggregation, etc. must be investigated. [10] Different techniques for analysis, such as dynamic dispersed light (DLS), X-ray scattering (XRD), Fourier transform infrared spectroscopy (FTIR), and UV- spectroscopy, and have been used to investigate the synthesized nanoparticles. [11]

Due to its special qualities, such as being extremely thermally conductive, antiseptic, antibacterial, anticancer, anti-inflammatory, and anti-diabetic, silver nanoparticles (silver NPs) have gained a lot of interest recently. [12] ([13] [14] Due to their greater surface area, silver nanoparticle drug carriers have an advantage in the treatment of breast cancer because they can demonstrate a stronger therapeutic impact of anticancer medicines on cancer cells. Nanoparticles, fine size, improved enhanced mechanical, magnetic, electrical, optical, and antibacterial characteristics, as well as surface qualities, have novel uses in the realm of catalysis. Have received significant attention due to the growing demand for monodispersed and size-controlled synthesis of nanoparticles in cancer therapy [14], biology, chemistry, engineering, computer science, biology, medicine, and photo detection. [15] By using controlled synthesis and the inclusion of reducing and stabilizing chemicals, it is possible to achieve the quality of NPs with a controlled size that provides a benefit in oral medication administration. [16] AgNPs have a huge potential for commercial application as medical equipment and healthcare goods because of their outstanding features. There are several ways to make silver nanoparticles, including corporal, biochemical and organic techniques. [17] Such as microwave irradiation, opposite micelles, and chemical reduction. [18] [19]

For the production of silver NPs without maintaining an aseptic environment, green synthesis methods using diverse biological components from natural sources are more often utilized. [18]

To create environmentally friendly, biocompatible silver nanoparticles (silver NPs), green synthetic procedures are crucial. [20] [21] With substantial heat conductivity and more stable formulations silver nanoparticles also. [22] The optimum cooling is provided by silver in the form of Nano fluids because they reduce the movement behavior of the fluid, which reduces the width of the warm air layer and increases the heat flow rate. [20][22] The three nanoparticles with the greatest boost, respectively, were Ag, Cu, and Al2O3. [20] Silver NPs have attracted a great deal of interest in a variety of technical applications because of their varied benefits.

2. Pharmaceuticals applications

Silver nanoparticles have an extensive series of applications in the domains of medication, materials science, and catalysis. Due to the unique qualities of their bulk solid, this is the case.

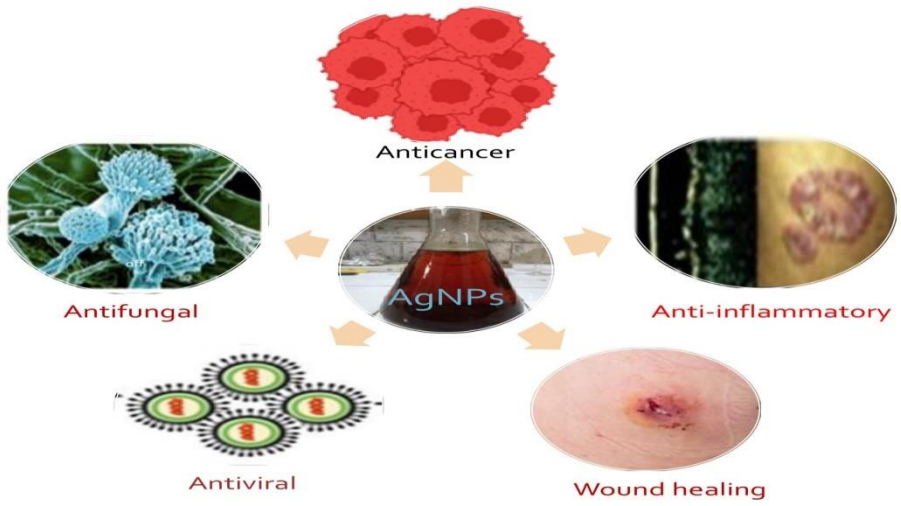

Fig. 1: Application of Silver nanoparticles

2.1 Antifungal Activity of Silver Nanoparticles

AgNPs have demonstrated antifungal activity against forty-four different fungus species strains. AgNPs' activity against Candida albicans may include rupturing the integrity of the cell membrane, which stops the cell from growing. AgNPs may therefore be one of the treatments used to stop fungal infections that affect oral tissues. AgNPs added to resins at a concentration of 1 μg/ml have demonstrated strong antifungal action without causing any cytotoxicity.[23][24][25]

2.2 Anti-cancer Activity of silver nanoparticles:

The use of nanoparticles, including silver nanoparticles, in combating dermatophyte infections and exhibiting potential anti-cancer activity is a fascinating and evolving area of research. Here's a sample section for your review article that focuses on the anti-cancer activity of nanoparticles against dermatophyte.[26][27]

2.3 Antiviral activity of silver nanoparticles:

Nanoparticles, including silver nanoparticles, have demonstrated notable antiviral properties through various mechanisms. These mechanisms may include interference with viral entry, inhibition of viral replication, and modulation of host immune responses. Our review critically analyzes existing literature to unravel the intricacies of these mechanisms, providing insights into how nanoparticles combat a broad spectrum of viruses.[28]

2.4 Anti-inflammatory application of silver nanoparticles:

Inflammation is a complex biological response that plays a pivotal role in the immune system's defense against harmful stimuli. However, dysregulated or chronic inflammation is implicated in various pathological conditions. Nanoparticles, owing to their unique physicochemical properties, have garnered considerable attention as potential modulators of inflammatory responses. This review aims to comprehensively examine the mechanisms underlying the anti-inflammatory activity of nanoparticles and their therapeutic implications.[29] [30]

2.5 Anti-wound healing activity of silver nanoparticles:

While silver nanoparticles have gained recognition for their wound-healing potential, it is imperative to critically examine potential challenges and considerations associated with their application in wound care. This section aims to explore any documented instances or concerns related to the anti-wound healing activity of silver nanoparticles, shedding light on factors that warrant careful consideration.[31][32][33]

3. Pharmacokinetics and pharmacodynamics

3.1 Pharmacokinetics

Silver NPs' physicochemical characteristics are essential for modifying PK because they regulate the body's initial pharmacologic reaction after ingestion. "Nano sizing" a pharmaceutical formulation can increase medication absorption and increase drug dissolution rates for drugs with low bioavailability. [34][35]

NPs can also extend the drug's half-life in the bloodstream that would otherwise be quickly eliminated or broken down. Numerous important parameters that have a substantial impact on the PK of NPs are explored because PK has a considerable impact on the cytotoxicity and therapeutic effectiveness of the NPs offered. We concentrate in this section; we focus on the theranostic features of small NPs as opposed to reticuloendothelial system-mediated NP removal. Because bigger NPs are unlikely to be used in clinical settings. The NPs may be quickly removed within the body without cellular internalization or metabolism, limiting body exposure to the NPs, prior studies have demonstrated that A kidney's discharge favored and desired route contrasted with the liver's clearance for Silver NPs. [36] [37]

3.2 Pharmacodynamics

Silver nanoparticles have been used most successfully in cancer research. However, as mentioned above, the majority of NPs should have inert surface coatings with organic polymeric and/or biological components for theranostic and therapeutic objectives. Additionally, customized targeting is a crucial component to overcome a drawback of conventional therapy and reduce any potential adverse effects. Effective tumor targeting may be achieved using two main strategies: Leaky endothelium surrounding cancer cells allows therapeutic NPs to passively target tumors Impact of improved permeation as well as retention (EPR). Active focusing on the other hand depends on the surface of NPs being targeted with ligands like antibodies, aptamers, and peptides so that NPs may bind to the receptors that are overexpressed on cancer cells. In this part, we present some instances of cutting-edge theranostic Nano platforms. [38][39][40]

3.2.1 Pharmacokinetic behavioral approach of Silver nanoparticles

However, excessive distribution to tissues outside the target area may have negative side effects that must be avoided. It is typically desired for drugs or NPs to have a dominating concentration in the target tissue for increased therapeutic benefits. As a result, information on tissue bio-distribution and pharmacokinetics is essential for NP biological applications that are both safe and effective. [41][42][43]

3.3 Absorption

Compared to tiny molecules, the nanoparticle absorbing process is more complicated. In contrast to subcutaneous, intramuscular, or inhaled nanoparticles, which are mostly absorbed by macrophages and lymphatic uptake, through Mouth nanoparticles, transcytosis, M cell adsorption, and Para cellular movement in the GI tract can be absorbed. There are very few studies that offer quantitative data, but many have provided qualitative descriptions of the oral absorption that takes place in humans and other animals. [44][45]

In 1980, looked at the persistence of silver in a 47-year-old patient with argyria. The amount of silver that was kept in the body after an oral intake was discovered to be 18% using a radioactive tracer. It has been demonstrated that silver Nanoparticle was less accessible than silver ionic following oral administration due to increased fecal clearance and lower absolute levels in organs. [46][47]

3.4 Distribution

A few of the multiple transport processes that affect how nanoparticles are distributed in vivo include target-mediated disposal, opsonization, protein corona creation, MPS absorption, enhanced EPR (Effect of Permeability and Resistance), and lymphatic carriage. [48][49]

The hepatic system was identified as the primary organ for Ag dispersion, followed by the spleen and kidneys, regardless of the oral, intravenous, subcutaneous, or inhalation exposure route. Numerous cells, such as sinusoidal endothelium cells, hepatocytes, and Kupffer cells, have been found to accumulate silver in the liver. [50][51]

3.4 Metabolism:

It has been demonstrated that oral contact with electrical and silver nanoparticle solutions causes silver can accumulate in organs like the skin as tiny granules of glomeruli, intestines, and skin surface. These silver, sulfur, and selenium-containing size of nanoparticles are 12 nm were originated in the rat gut. [52][53]

Ag+ and GSH combine to create H+ and GS-Ag, which are then distributed throughout various tissues as Ag-GSH polymer complexes. Ag-thiol complexes may still be transformed into zero-valent AgNPs via UV photodecomposition, but more slowly. AgNPs may also undergo sulphation to generate Ag2S NPs as well as thiols. Additionally, Ag2S NPs can be created through the interaction of Ag2S nanoparticles with Argyrial Ag/Se nanoparticles. [54][55]

3.5 Elimination:

Silvery outflow was determined to be high (63 and 49 % of the day-to-day intake in the Ag NPs and silver acetate groups, respectively) but low (0.1% of 24-hour consumption for both groups) in the faces of rats repeatedly treated for 28 days to fourteen-nm PVP coated AgNPs or silver acetate. [56][57] Following oral administration, it was discovered that 14 nm AgNP had greater fecal excretion rates than ionic silver, at 63 and 49%, respectively. This was related to silver nanoparticles lower bioavailability. [58]

Subsequent oral administration, it was discovered that 14 nm AgNP had greater fecal excretion rates than ionic silver, at 63 and 49%, respectively. This was related to silver nanoparticles lower bioavailability. Urine production a woman excreted between 2 and 104% of a radioactive silver tracer administered orally at 12 hours in her urine, according to East et al. After administering 110 radioactive silver radionuclides orally, Furchner et al. found that Urinary excretion of silver. Eight weeks following consumption of silver particles or nanoparticles of silver found that silver continued to be detectable in the rat brain and testes at (15 and 20 nm). [59][60][61]

4. Rationale of the study

The chemical reduction approach and the green synthesis method were two of the SNPs synthesis methods that garnered the greatest interest because of their ability to effectively manage particle size and shape in various research activities carried out in the field of modified focus. The right nanoparticle size may be produced more quickly with this method. Despite the abundance of data demonstrating Ag NP's antibacterial efficacy against a variety of illnesses. Instead of employing various sizes of SNP, these trials against human pathogenic bacteria used a range of sizes. There was a recent increase in the use of silver nanoparticles to treat cancer, diabetes, and inflammation.

Although several nanoparticles have been utilized in people to carry drugs, it is still unknown how most proteins will react to them. Understanding how proteins interact with nanoparticles in vivo affects their structure and function is crucial. Understanding how protein structure and biological function are impacted when NP penetrates through the cell membrane and interacts with them is also essential for understanding nanoparticle-mediated cell death.

This is also essential to comprehend how in vivo gene expression levels are impacted by nanoparticles. Because there has been a substantial attempt to increase the activity or expression

level of many enzymes industrially utilizing molecular or chemical guides, most enzymes are expressed at a lower level. However, no such impact has yet been investigated using nanoparticles.

5. Methodology

This study was accompanied by the preferred report from reviews or research articles statements that were published in national and international journals.

6. Search strategy:

For the portion of current and important information for the study, this information was gathered by a prospective complete literature search utilizing more than six electronic databases, including Google Scholar, PubMed, and Elsevier ASC publications from databases between 2001 and 2019. All included papers reference lists and other possibly pertinent citations were examined. Because of the difficulty in communicating, the short turnaround time, and the expensive expense of translation, the study's selection was restricted to publications written in English. The publishing history of the journal was searched as a review using the hyphenated term "Role of Silver nanoparticles in the treatment of inflammation" to obtain a thorough search of pertinent research, and the pertinent data was extended to access in the selection process.

7. Inclusion criteria:

The original study was supplemented by reviews or research papers from national and international publications that addressed the prevalence of silver nanoparticles, molecular approaches to inflammation and cancer, a thorough analysis of the study.

To prevent misuse of comprehensives, studies like duplicate publications, abstracts from studies published before 2019, and unreliable ethnobotanical and ethno medical reports that lacked study areas and locations, informant participation, and information on untargeted diseases were removed.

Study choice by reviewing each records title and abstract and, if required, obtaining the entire text of the studies, each author independently evaluated each study according to their inclusion criteria.

Only high quality indexed journal papers (research and review articles) about silver nanoparticles were chosen for the studies trending input. Based on the titles and abstracts of recognized journal articles, the search results were screened. In addition, only the most pertinent reports out of thousands were downloaded and carefully examined to further the discussion of the preclinical and mechanistic assessment of silver nanoparticles and their strategy for inflammatory illness.

Table No. 1: Silver Nano-particles and quality optimization approaches

Base/polymers	Source	Physiochemical characteristic	Mechanical strength	Applicability	References
Hydroxypropyl methylcellulose	wood pulp and cotton linter (Natural)	Thickening power, tasteless, odorless, non-toxic	Pervasive,	reducing the absorption of oil from fried products	[62]
Polyethylene glycol	petroleum refining	Odorless, colorless, inert, non-toxic	High molecular weight PEG20000 and PEG 35000 formed coherent tablets at low compaction pressure	Swelling behavior controlled release matrices for therapy or,	[63]
Dextran	isolated from different plant sources (e.g., A gave salmiana a nd pummelo)	Soluble in water and electrolyte solution, molecular weight 10000, easily filtered, non-toxic	mechanical strengths as a function of concentrations of MgCl2, GA, and PEG 400, which	Antithrombotic and anti-inflammatory	[64]

			was found to be useful for the evaluation		
Polyethylene glycol	petroleum refining	Odorless, colorless, inert, non-toxic	High molecular weight PEG20000 and PEG 35000 formed coherent tablets at low compaction pressure	Swelling behavior controlled release matrices for therapy or,	[63]
polyvinylpyrrolidone	made from the monomer N-vinylpyrrolidone.	a biocompatible, non-toxic, temperature- and pH-resistant, inert, and biodegradable polymer	Tensile strength of 4.3 MPa and a hardness of 1.3 GPa	Adhesives, ceramics, ink, printing, fibers a nd textiles, personal care goods, water treatment and dialysis films, batteries Semiconductors	[65]
Methacrylic acid	acetone cyanohydrin	colorless transparent liquid at room temperature	Methacrylic acid copolymer containing 4.1 mole % acid units	Protective agents	[65]

Table No. 2: Current Scenario of SNP in Therapeutic Applications

Type of nanoparticle	Route of administration	Animal Model/invitro	Exposure	Effective dose	Therapeutic application	Molecular Approach	References
Silver Nano-particle	Oral	Rat (150-300 g),	Toxicant	1µm/ml /day	antibacterial	Interfere with DNA replication	[66]
Gold Nano-particle	i.v.	Wistar Rat (180-220 g)	Toxicant	0.32 ml/kg	Anti-cancer	Inhibit ATPase activity	[67]
Lipid Nano-particle	parenteral	Rat 180-220 g)	Toxicant	1µm/ml	Anti-cancer	HY1991	[68]
Zinc oxide nanoparticles	i.v.	Rat (180-220)	Toxicant	1000 mg/kg	Anti-bacterial		[69]

Table no. 3: List of types of silver nanoparticles with their Practical Range, concentration and Activity

Types of silver nanoparticles	Practical range	Concentration uses	Activity	Reference
Silver colloid nanoparticles silver nanoparticles	25-450 nm	0.005-0.20 mol L^{-1}	Anti-bacterial	[70]
Cucumis prophetarum silver nanoparticles	25 -40 nm	50,75,100 µg/mL	Anti-bacterial	[71]
Bacillus thuringiensis silver Nanoparticles	50 nm size	25-50 µg/mL	Antibacterial	[72]
Melia Dubai leaf silver Nanoparticles	20-45 nm	5-10 µg/mL	Breast cancer	[73]
Fruit extract of Cleome viscosa Silver Nanoparticles	15-50 nm	20-30 µg/mL	Anti-cancer	[74]
extraction from saliva	a typical size of	50 µg/mL	Inhibiting blood	[74]

officinalis Silver Nanoparticles	sixteen and a half nm x 1.2 nm		vessel formation	
B. licheniformis silver Nanoparticles	40–50 nm	an amount of 50 mg/mL	inhibits endothelial cell migration	[75]
polyvinylpyrrolidone (P VP) coated silver nanoparticles	2–3 nm	levels of 0.5, 1, 5, 10, and 20 grams per milliliter	induced VEGF si gnaling and angio genesis	[76]
Nanoparticles of silver	a typical size of ten millimetres	2.5 and 0.25 grammes per millilitre concentrations	healing of wounds	[77]
Ginseng fresh leaves silver Nanoparticles	10-20 nm	an amount of 100 milligrammes per millilitre	lung cancer	[78]
silver nanoparticles with a spherical form	10 nm	400µg/mL	impeded HUVECs' ability to form tubes	[79]
fruit extract of *Ficus carica* Silver Nanoparticles	10-30 nm	50 ng/mL	impeded HUVECs' ability to form tubes	[80]

8. Mechanism of action of silver nanoparticles:

8.1 Anti-bacterial Mechanism of silver nanoparticles.

Figure 2 was proposed to have a variety of antibacterial activities even though the precise workings of the antimicrobial capabilities is unknown of silver nanoparticles are unclear. The death of bacteria may be attributed to the silver nanoparticles' ability to continuously discharge silver ions. Silver ions can cling to the cell wall and cytoplasmic membrane due to electrostatic attraction and affinity to sulfur proteins. Adherent ions can make the membrane of the cytoplasm more permeable and cause the bacteria's coat to disintegrate. The most important catalyst for the modification of DNA and membrane breakdown might be the reactivity of oxygen species. Pulmonary enzymes may become inactive when free Ag components enter cells, causing a responsive oxygen class and stopping the formation of adenosine triphosphate. Replication of DNA may be hampered by the silver ions' interactions with these substances., hinder cell development, or possibly result in the deaths of microorganisms due to the importance of sulfur and phosphorus in DNA. Silver ions can denaturize cytoplasmic ribosomes, which can also stop the creation of protein.[81][82][83]

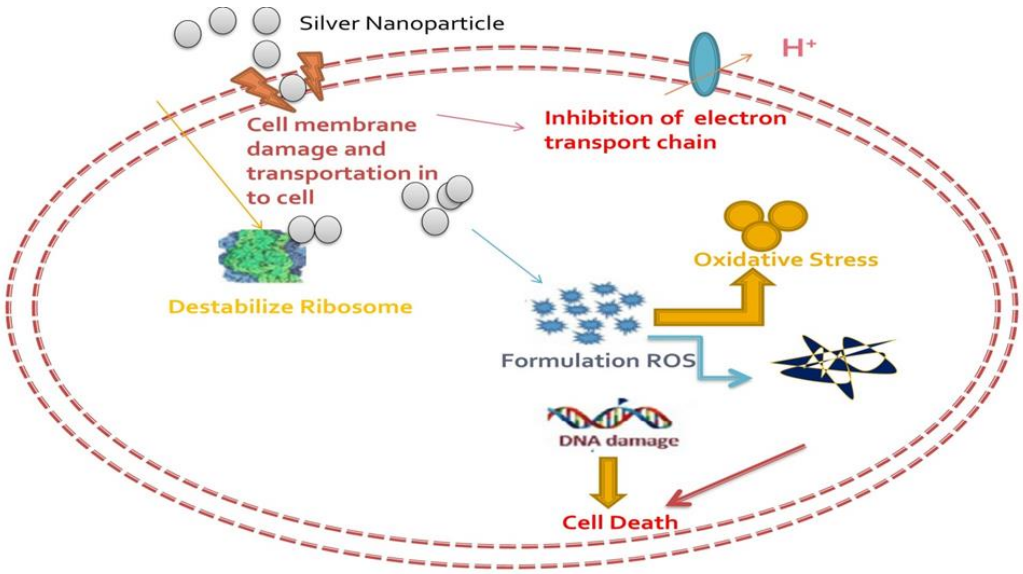

Fig. 2: mechanism of silver nanoparticles:

Cell membrane breakdown is the main way that silver nanoparticles work. [84]. Furthermore, when the silver nanoparticles dissolve, antimicrobial silver ions are released. These silver ions can interact with thiol-containing proteins in the cell wall and alter their activities (fig.2). Silver nanoparticles can attach to proteins when they come into contact with the outer membrane, creating compounds containing molecules of oxygen, nitrogen, phosphorus, or Sulphur as electronic donors. The relationship that exists involving the literature describes these groups as well characterized. Thus, through interactions with disulfide bonds and active site blockage, silver nanoparticles cause the inactivation of membrane-bound enzymes and proteins. [85] According to reports, AgNPs may increase the trans/cis ratio of unsaturated membrane fatty acids, which might modify the fluidity of the membrane and the makeup of the lipid bilayer. It may result in modifications to the membrane's structure that prohibit the membrane from functioning, increasing permeability and deteriorating membrane integrity.

An adequate inflammatory in vitro model should be employed to observe the anti-inflammatory action of AgNPs and their mechanism. A pro-inflammatory cytokine called tumor necrosis factor (TNF) controls cellular responses in a variety of pathological situations, including inflammatory disorders and cancer. [86] TNF's principal cellular reaction, inflammation, is mostly brought on through the NF-KB activation pathway. As a result, the TNF-induced inflammatory response in lung epithelial cells is a good model for investigating how AgNPs work to reduce inflammation.

Therefore, it is essential to create small-sized AgNPs and prevent precipitation or particle clustering. Stable nanoparticle synthesis is difficult and problematic since they naturally aggregate their constituent particles during storage. [20]. Silver nanoparticles (NPs) were mixed inside the clay's exterior surfaces to solve the precipitation problem. [87]. It is the reported method for preventing agglomeration [88] between particles.

Because of its ease of use, inexpensive price, and low toxicity, the reduction process of bio-nano composites is now often employed to create AgNPs without particle aggregation. Size-controlled synthesis of silver NPs is the first choice for higher therapeutic potential. Because of its changed properties, such as stability during extended storage and size or surface volume ratio, the synthesis of AgNPs is a particularly attractive scientific topic. [89]. The antimicrobial characteristics of nanoparticles of silver have drawn a lot of interest, but research on their antiviral capabilities is still in its infancy. [90]

8.2 Anti-cancer Mechanism of silver nanoparticles:

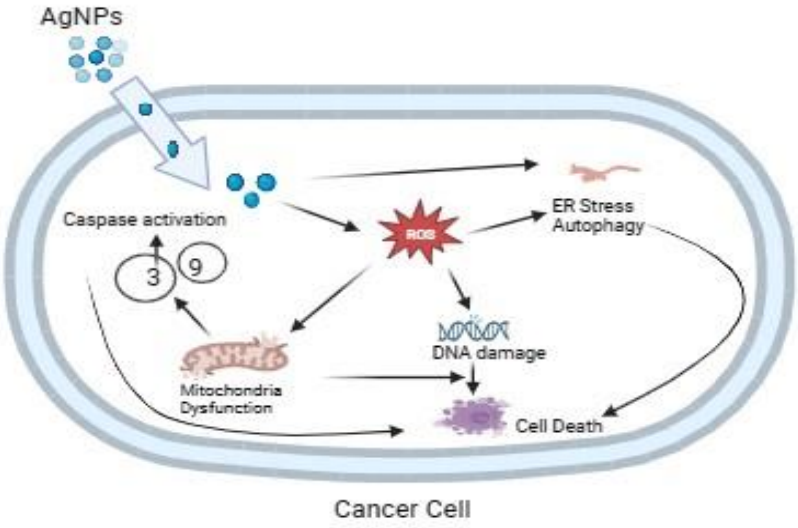

Figure 2: Anti-cancer Mechanism of silver nanoparticles

AgNPs are entering into cancer cells, and ROS are activated. DNA and Mitochondria Dysfunction and Caspase activated. These are the reasons for cell death (Fig. 2).[91][91]

Anti-inflammatory Mechanism of silver nanoparticles:

One of the essential biomedical applications of the nanoparticle is as an anti-inflammatory agent. Sole metallic nanoparticles containing silver have intrinsic anti-inflammatory effects.[92] This activity has been explained in the Figure 3.[93] When it is produced along with plant materials or biological materials, the anti-inflammatory effect shows synergistic action.[94][95]

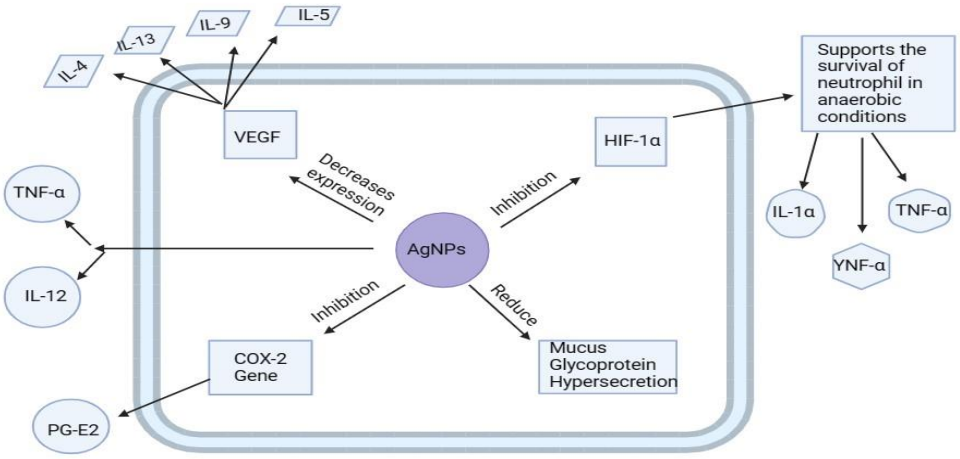

Figure 3: Anti-inflammatory Mechanism of Silver nanoparticles

8.3 Anti-viral mechanism of action of silver nanoparticles:

Nanoparticles, including silver nanoparticles, have demonstrated notable antiviral properties through various mechanisms.[96] These mechanisms may include interference with viral entry, inhibition of viral replication, and modulation of host immune responses. [97]Our review critically analyzes existing literature to unravel the intricacies of these mechanisms, providing insights into how nanoparticles combat a broad spectrum of viruses.[98][99][100]

9. Future prospective

The nanoparticle drug delivery system manages the many drugs for the treatment of inflammation, cancer, diabetes, and other conditions. Silver nanoparticles reduce inflammation and cancer cells without running the danger of doing significant harm. A clear palliative choice is the only way to manage the increased prevalence of both inflammation and cancer for those who have both illnesses. To further reduce morbidity and mortality among patients with cancer and inflammatory diseases, a multidisciplinary approach is required. Both developed and developing countries see cancer and inflammation as serious public health problems that have a big impact on people all around the world. The largest barriers to reducing people's financial hardship in the treatment of cancer and inflammation may be related to the cost, acceptability, availability, and accessibility of medications. Despite this, many individuals continue to use silver nanoparticles as a kind of treatment since they are convenient, well-liked, and affordable. Even yet, the evaluation of the effectiveness, safety, and quality of silver nanoparticles may contribute to their absence. The emergence of nanoparticle systems with scientific validation and well-known therapeutic and regulatory components can supply and formalize a natural approach that not only decreases the burden of sickness but also raises the medical system to an affordable economic level.

10. Conclusion:

Silver nanoparticles are now frequently used since they have so many uses in so many different sectors. Apart from its widespread use in antibacterial applications, Ag NPs have demonstrated use in gene therapy, antiviral, anti-inflammatory, diagnostic, and imaging fields. AgNPs are now being researched as a possible substitute for current conventional cancer treatments such as radiation, chemotherapy, and other treatments. Given that these AgNPs have anti-angiogenic qualities, treating cancer with them is seen as an interesting approach. It has been demonstrated that cancer therapy is

safe and site-specific. Therefore, it can be said that these AgNPs are a simple, secure, and efficient treatment for a variety of ailments. This study provided a comprehensive overview of the mechanism of action, characterization, and bio applications of silver nanoparticles (AgNPs), with an emphasis on the mechanisms behind AgNPs' anticancer activity and their possible application in cancer therapy. The potential use of AgNPs as a next-generation anticancer therapeutic agent has recently been investigated in research from academic and commercial sources due to the prevalent side effects of radiation therapy and chemotherapy.

11. List of abbreviation:

1	AgNPs	Silver nanoparticles
2	Ag	Silver
3	PVP	Polyvinylpyrrolidone
4	NP	Nanoparticles
5	EPR	Effect of Permeability and Persistence
6	FTIR	Fourier transform infrared spectroscopy
7	Cu	Copper
8	GI tract	Gastro intestinal tract
9	PVP	Polyvinylpyrrolidone

12. Author Contribution:

1. Jiyaul hak (Research Scholar, Sanskriti University, Mathura (U.P.))
All paper writes by Jiyaul hak.
2. Dr. Dinesh Kumar Sharma (Professor, Sanskriti University, Mathura (U.P.))
He guide me how to write the paper
Dr. Nasiruddin Ahmad Farooqui (Professor, Translam Institute of Pharmaceutical Education and Research, Meerut (U.P.)- He Guide me how to make diagram, tables and write the paper.

13. Conflict of interest:

14. Source of Funding: No

15. Acknowledgement:
I would like to express my sincere gratitude to all those who have contributed to the successful completion of this systematic review on silver nanoparticles. First and foremost, I extend my heartfelt appreciation to the researchers and scientists whose groundbreaking work has laid the foundation for the field of nanotechnology and silver nanoparticles. Their dedication to advancing knowledge has been invaluable in shaping the landscape of this study. My sincere thanks go to the authors of the studies and papers included in this systematic review. Their diligent research and comprehensive reporting have greatly enriched our understanding of the subject matter. I would like to express my gratitude to my colleagues who provided valuable insights and feedback during the course of this review. Their constructive criticism and thoughtful suggestions have undoubtedly strengthened the quality and rigor of our work. Special thanks are due to [Name of Mentor or Advisor] for their guidance and mentorship throughout the research process. Their expertise and support have been instrumental in shaping the structure and content of this systematic review. Lastly, I express my heartfelt thanks to my family and friends for their unwavering encouragement and understanding during the challenges of this article. Their support has been a source of inspiration. The successful completion of this systematic review would not have been possible without the collective efforts of all those mentioned above. I sincerely appreciate their contributions and commitment to advancing scientific knowledge in the field of silver nanoparticles.

References

1. S. Gurunathan, J. H. Park, J. W. Han, and J. H. Kim, "Comparative assessment of the apoptotic potential of silver nanoparticles synthesized by Bacillus tequilensis and Calocybe indica in MDA-MB-231 human breast cancer cells: Targeting p53 for anticancer therapy," *Int. J. Nanomedicine*, 2015, doi: 10.2147/IJN.S83953.
2. W. R. Li, X. B. Xie, Q. S. Shi, H. Y. Zeng, Y. S. Ou-Yang, and Y. Ben Chen, "Antibacterial activity and mechanism of silver nanoparticles on Escherichia coli," *Appl. Microbiol. Biotechnol.*, 2010, doi: 10.1007/s00253-009-2159-5.
3. W. R. Li, X. B. Xie, Q. S. Shi, S. S. Duan, Y. S. Ouyang, and Y. Ben Chen, "Antibacterial effect of silver nanoparticles on Staphylococcus aureus," *BioMetals*, 2011, doi: 10.1007/s10534-010-9381-6.
4. P. Mukherjee *et al.*, "Fungus-Mediated Synthesis of Silver Nanoparticles and Their Immobilization in the Mycelial Matrix: A Novel Biological Approach to Nanoparticle Synthesis," *Nano Lett.*, 2001, doi: 10.1021/nl0155274.
5. S. Chernousova and M. Epple, "Silver as antibacterial agent: Ion, nanoparticle, and metal," *Angewandte Chemie - International Edition*. 2013. doi: 10.1002/anie.201205923.
6. R. Preety, R. Anitha, S. Rajeshkumar, and T. Lakshmi, "Anti-diabetic activity of silver nanoparticles prepared from cumin oil using alpha amylase inhibitory assay," *Int. J. Res. Pharm. Sci.*, 2020, doi: 10.26452/ijrps.v11i2.1978.
7. Y. Cao *et al.*, "sRNATarBase: A comprehensive database of bacterial sRNA targets verified by experiments," *RNA*, 2010, doi: 10.1261/rna.2193110.
8. W. Y. Huang, Y. M. Liu, J. Wang, X. N. Wang, and C. Y. Li, "Anti-inflammatory effect of the blueberry anthocyanins malvidin-3-glucoside and malvidin-3-galactoside in endothelial cells," *Molecules*, 2014, doi: 10.3390/molecules190812827.
9. I. Sondi and B. Salopek-Sondi, "Silver nanoparticles as antimicrobial agent: A case study on E. coli as a model for Gram-negative bacteria," *J. Colloid Interface Sci.*, 2004, doi: 10.1016/j.jcis.2004.02.012.
10. M. F. Rahman *et al.*, "Expression of genes related to oxidative stress in the mouse brain after exposure to silver-25 nanoparticles," *Toxicol. Lett.*, 2009, doi: 10.1016/j.toxlet.2009.01.020.
11. S. Gurunathan *et al.*, "Reduced graphene oxide-silver nanoparticle nanocomposite: A potential anticancer nanotherapy," *Int. J. Nanomedicine*, 2015, doi: 10.2147/IJN.S92449.
12. E. Stathatos, P. Lianos, P. Falaras, and A. Siokou, "Photocatalytically deposited silver nanoparticles on mesoporous TiO2 films," *Langmuir*, 2000, doi: 10.1021/la981783t.
13. S. V. Kyriacou, W. J. Brownlow, and X. H. N. Xu, "Using Nanoparticle Optics Assay for Direct Observation of the Function of Antimicrobial Agents in Single Live Bacterial Cells," *Biochemistry*, 2004, doi: 10.1021/bi0351110.
14. X. Feng *et al.*, "Aqueous-organic phase-transfer of highly stable gold, silver, and platinum nanoparticles and new route for fabrication of gold nanofilms at the oil/water interface and on solid supports," *J. Phys. Chem. B*, 2006, doi: 10.1021/jp0609885.
15. Y. Cui, Q. Wei, H. Park, and C. M. Lieber, "Nanowire nanosensors for highly sensitive and selective detection of biological and chemical species," *Science (80-.).*, 2001, doi: 10.1126/science.1062711.
16. W. Zhang, X. Qiao, J. Chen, and H. Wang, "Preparation of silver nanoparticles in water-in-oil AOT reverse micelles," *J. Colloid Interface Sci.*, 2006, doi: 10.1016/j.jcis.2006.06.035.
17. Y. K. Mohanta *et al.*, "Silver nanoparticles synthesized using wild mushroom show potential antimicrobial activities against food borne pathogens," *Molecules*, 2018, doi: 10.3390/molecules23030655.
18. A. Thapliyal, R. K. Khar, and A. Chandra, "Artificial Neural Network Modelling of Green Synthesised Silver Nanoparticles in Bentonite/Starch Bio-Nanocomposite," *Curr. Nanosci.*, 2017, doi: 10.2174/1573413713666171103103141.
19. K. Shameli *et al.*, "Silver/poly (lactic acid) nanocomposites: Preparation, characterization, and

antibacterial activity," *Int. J. Nanomedicine*, 2010, doi: 10.2147/ijn.s12007.
20. K. Thapliyal, R. D. Sharma, and A. Pathak, "Orthogonal-state-based and semi-quantum protocols for quantum private comparison in noisy environment," *Int. J. Quantum Inf.*, 2018, doi: 10.1142/S0219749918500478.
21. P. Shabanzadeh, R. Yusof, and K. Shameli, "Artificial neural network for modeling the size of silver nanoparticles' prepared in montmorillonite/starch bionanocomposites," *J. Ind. Eng. Chem.*, 2015, doi: 10.1016/j.jiec.2014.09.007.
22. M. Turkyilmazoglu, "Condensation of laminar film over curved vertical walls using single and two-phase nanofluid models," *Eur. J. Mech. B/Fluids*, 2017, doi: 10.1016/j.euromechflu.2017.04.007.
23. K. J. Kim, W. S. Sung, S. K. Moon, J. S. Choi, J. G. Kim, and D. G. Lee, "Antifungal effect of silver nanoparticles on dermatophytes," *J. Microbiol. Biotechnol.*, 2008.
24. H. S. Al-Jobory, K. M. A. Hasan, and A. F. Alkaim, "Antifungal effect of silver nanoparticles on dermatophytes isolated from clinicalspecimens," *Plant Arch.*, 2020.
25. F. Noorbakhsh, S. Rezaie, and A. R. Shahverdi, "Antifungal Effects of Silver Nanoparticle alone and with Combination of Antifungal Drug on Dermatophyte Pathogen Trichophyton Rubrum," *2011 Int. Conf. Biosci. Biochem. Bioinformatics.*, 2011.
26. R. Algotiml, A. Gab-Alla, R. Seoudi, H. H. Abulreesh, M. Z. El-Readi, and K. Elbanna, "Anticancer and antimicrobial activity of biosynthesized Red Sea marine algal silver nanoparticles," *Sci. Rep.*, 2022, doi: 10.1038/s41598-022-06412-3.
27. A. K. Lafta, H. A. Ajah, O. A. A. Dakhil, and W. M. Ali AL-Wattar, "Biosynthesis of silver nanoparticles using biomass of Cladosporium cladosporioidesand antifungalactivity against pathogenic fungi causing onychomycosis," *Plant Arch.*, 2019.
28. F. S. AlQahtani, M. M. AlShebly, M. Govindarajan, S. Senthilmurugan, P. Vijayan, and G. Benelli, "Green and facile biosynthesis of silver nanocomposites using the aqueous extract of Rubus ellipticus leaves: Toxicity and oviposition deterrent activity against Zika virus, malaria and filariasis mosquito vectors," *J. Asia. Pac. Entomol.*, 2017, doi: 10.1016/j.aspen.2016.12.004.
29. A. Hebeish, M. H. El-Rafie, M. A. EL-Sheikh, A. A. Seleem, and M. E. El-Naggar, "Antimicrobial wound dressing and anti-inflammatory efficacy of silver nanoparticles," *Int. J. Biol. Macromol.*, 2014, doi: 10.1016/j.ijbiomac.2014.01.071.
30. Z. Hussain, M. A. S. Abourehab, S. Khan, and H. E. Thu, "Silver nanoparticles: A promising nanoplatform for targeted delivery of therapeutics and optimized therapeutic efficacy," in *Metal Nanoparticles for Drug Delivery and Diagnostic Applications*, 2019. doi: 10.1016/B978-0-12-816960-5.00009-4.
31. A. F. Khafaga, H. M. Abu-Ahmed, A. N. El-Khamary, I. M. Elmehasseb, and H. M. Shaheen, "Enhancement of Equid Distal Limb Wounds Healing by Topical Application of Silver Nanoparticles," *J. Equine Vet. Sci.*, 2018, doi: 10.1016/j.jevs.2017.11.013.
32. R. F. Pereira and P. J. Bártolo, "Traditional Therapies for Skin Wound Healing," *Advances in Wound Care*. 2016. doi: 10.1089/wound.2013.0506.
33. A. Hebeish, M. H. El-Rafie, M. A. El-Sheikh, A. Seleem, and M. E. El-Naggar, "More insight on charcterization of nano-sized particles of silver powder and their application in antimicrobial wound dressing and antiinflammatory efficacy," *Egypt. J. Chem.*, 2013, doi: 10.21608/ejchem.2013.1106.
34. S. D. Li, Y. C. Chen, M. J. Hackett, and L. Huang, "Tumor-targeted delivery of siRNA by self-assembled nanoparticles," *Mol. Ther.*, 2008, doi: 10.1038/sj.mt.6300323.
35. A. Elzoheiry, E. Ayad, N. Omar, K. Elbakry, and A. Hyder, "Anti-liver fibrosis activity of curcumin/chitosan-coated green silver nanoparticles," *Sci. Rep.*, 2022, doi: 10.1038/s41598-022-23276-9.
36. E. Phillips *et al.*, "Clinical translation of an ultrasmall inorganic optical-PET imaging nanoparticle probe," *Sci. Transl. Med.*, 2014, doi: 10.1126/scitranslmed.3009524.

37. NA, "Textbook Section 15.1 Seven-Transmembrane-Helix Receptors Change Conformation in Response to Ligand Binding and Activate G Proteins," *Ncbi.Nlm*, 2002.
38. L. S. Li, J. Hu, W. Yang, and A. P. Alivisatos, "Band Gap Variation of Size- and Shape-Controlled Colloidal CdSe Quantum Rods," *Nano Lett.*, 2001, doi: 10.1021/nl015559r.
39. V. K. Sharma, R. A. Yngard, and Y. Lin, "Silver nanoparticles: Green synthesis and their antimicrobial activities," *Advances in Colloid and Interface Science*. 2009. doi: 10.1016/j.cis.2008.09.002.
40. S. Singla, A. Jana, R. Thakur, C. Kumari, S. Goyal, and J. Pradhan, "Green synthesis of silver nanoparticles using Oxalis griffithii extract and assessing their antimicrobial activity," *OpenNano*, 2022, doi: 10.1016/j.onano.2022.100047.
41. G. Bachler, N. von Goetz, and K. Hungerbühler, "A physiologically based pharmacokinetic model for ionic silver and silver nanoparticles," *Int. J. Nanomedicine*, 2013, doi: 10.2147/IJN.S46624.
42. L. L. Aylward, G. Bachler, N. von Goetz, D. Poddalgoda, S. M. Hays, and A. Nong, "Biomonitoring Equivalents for interpretation of silver biomonitoring data in a risk assessment context," *Int. J. Hyg. Environ. Health*, 2016, doi: 10.1016/j.ijheh.2016.05.005.
43. Z. Lin, N. A. Monteiro-Riviere, and J. E. Riviere, "Pharmacokinetics of metallic nanoparticles," *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*. 2015. doi: 10.1002/wnan.1304.
44. W. Lou, L. Wang, S. Dong, Z. cao, J. Sun, and Y. Zhang, "A facility synthesis of bismuth-iron bimetal MOF composite silver vanadate applied to visible light photocatalysis," *Opt. Mater. (Amst).*, 2022, doi: 10.1016/j.optmat.2022.112168.
45. S. M. Attia, M. S. Abdelfatah, and M. M. Mossad, "Characterization of pure and composite resorcinol formaldehyde aerogels doped with silver," in *Journal of Physics: Conference Series*, 2017. doi: 10.1088/1742-6596/869/1/012036.
46. T. Liu *et al.*, "Preparation of silver nano-composites with photosynergistic antibacterial action," *Hecheng Shuzhi Ji Suliao/China Synth. Resin Plast.*, 2022, doi: 10.19825/j.issn.1002-1396.2022.06.01.
47. N. N. Al-Dabbagh, F. A. Z. Fattima, and N. K. K. Hindi, "Antimicrobial effect of sliver nanoparticles synthesized by chemical reduction on some bacteria and fungi," *Int. J. Appl. Eng. Res.*, 2017.
48. Q. Zhang, H. Liu, X. Wang, X. Shi, and X. Duan, "Fabrication and characterization of mano silver powder prepared by spray pyrolysis," *J. Wuhan Univ. Technol. Mater. Sci. Ed.*, 2009, doi: 10.1007/s11595-009-6871-x.
49. B. Suman *et al.*, "EFFECT OF SILVER NANO PARTICLES SYNTHESIZED OF TRICHODESMA INDICUM AGAINST NAJA NAJA (COBRA) VENOM," *Int. J. Pharm. Sci. Res.*, 2018.
50. T. A. A. Hussian, G. S. Jaber, and A. T. Hassan, "Radioactive Waste Management Using Ag\CNTs Composite Prepared by Laser Ablation in Liquid," *NeuroQuantology*, 2022, doi: 10.14704/nq.2022.20.4.nq22112.
51. B. Tang, G. Chen, Q. Chen, and J. Tai, "Preparation of sliver nanoparticles by liquid chemical reduction method," in *International Conference on Digital Printing Technologies*, 2011. doi: 10.2352/issn.2169-4451.2011.27.1.art00021_2.
52. M. Salah Abdel-Hamid *et al.*, "Biogenic and characterizations of new silver nanoparticles stabilized with indole acetic acid derived from Azospirillum brasilense MMGH-SADAT1, their bioactivity, and histopathological assessment in rats," *Ecotoxicol. Environ. Saf.*, 2021, doi: 10.1016/j.ecoenv.2021.112521.
53. Y. Huang, X. Lü, R. Chen, and Y. Chen, "Comparative study of the effects of gold and silver nanoparticles on the metabolism of human dermal fibroblasts," *Regen. Biomater.*, 2020, doi: 10.1093/RB/RBZ051.
54. K. Pietrzak, M. Twaruzek, A. Czyzowska, R. Kosicki, and B. Gutarowska, "Influence of silver

nanoparticles on metabolism and toxicity of moulds," *Acta Biochim. Pol.*, 2015, doi: 10.18388/abp.2015_1146.
55. M. J. Lee *et al.*, "Silver nanoparticles affect glucose metabolism in hepatoma cells through production of reactive oxygen species," *Int. J. Nanomedicine*, 2015, doi: 10.2147/IJN.S94907.
56. M. Van Der Zande *et al.*, "Distribution, elimination, and toxicity of silver nanoparticles and silver ions in rats after 28-day oral exposure," *ACS Nano*, 2012, doi: 10.1021/nn302649p.
57. F. Ribeiro *et al.*, "Uptake and elimination kinetics of silver nanoparticles and silver nitrate by Raphidocelis subcapitata: The influence of silver behaviour in solution," *Nanotoxicology*, 2015, doi: 10.3109/17435390.2014.963724.
58. I. L. Bergin *et al.*, "Effects of particle size and coating on toxicologic parameters, fecal elimination kinetics and tissue distribution of acutely ingested silver nanoparticles in a mouse model," *Nanotoxicology*, 2016, doi: 10.3109/17435390.2015.1072588.
59. A. Pasricha *et al.*, "Comparative study of leaching of silver nanoparticles from fabric and effective effluent treatment," *J. Environ. Sci.*, 2012, doi: 10.1016/S1001-0742(11)60849-8.
60. F. Afkhami, P. Ahmadi, N. Chiniforush, and A. Sooratgar, "Correction to: Effect of different activations of silver nanoparticle irrigants on the elimination of Enterococcus faecalis (Clinical Oral Investigations, (2021), 25, 12, (6893-6899), 10.1007/s00784-021-03979-5)," *Clinical Oral Investigations*. 2022. doi: 10.1007/s00784-021-04351-3.
61. F. Afkhami, P. Ahmadi, N. Chiniforush, and A. Sooratgar, "Correction to: Effect of different activations of silver nanoparticle irrigants on the elimination of Enterococcus faecalis," *Clin. Oral Investig.*, 2022, doi: 10.1007/s00784-021-04351-3.
62. K. Khwaldia, "Physical and mechanical properties of hydroxypropyl methylcellulose-coated paper as affected by coating weight and coating composition," *BioResources*, 2013, doi: 10.15376/biores.8.3.3438-3452.
63. M. A. Al-Nasassrah, F. Podczeck, and J. M. Newton, "The effect of an increase in chain length on the mechanical properties of polyethylene glycols," *Eur. J. Pharm. Biopharm.*, 1998, doi: 10.1016/S0939-6411(97)00151-3.
64. K. S. Hwang *et al.*, "Ca-Doped ZrO2 Thin Films Deposited by Using the Spin-Coating Pyrolysis Process with a Metal Naphthenate Precursor," *J. Korean Phys. Soc.*, 2003, doi: 10.3938/jkps.43.754.
65. K. M. Koczkur, S. Mourdikoudis, L. Polavarapu, and S. E. Skrabalak, "Polyvinylpyrrolidone (PVP) in nanoparticle synthesis," *Dalt. Trans.*, 2015, doi: 10.1039/c5dt02964c.
66. N. Durán, M. Durán, M. B. de Jesus, A. B. Seabra, W. J. Fávaro, and G. Nakazato, "Silver nanoparticles: A new view on mechanistic aspects on antimicrobial activity," *Nanomedicine: Nanotechnology, Biology, and Medicine*. 2016. doi: 10.1016/j.nano.2015.11.016.
67. M. Bednarski *et al.*, "The influence of the route of administration of gold nanoparticles on their tissue distribution and basic biochemical parameters: In vivo studies," *Pharmacol. Reports*, 2015, doi: 10.1016/j.pharep.2014.10.019.
68. S. Sheoran, S. Arora, R. Samsonraj, P. Govindaiah, and S. vuree, "Lipid-based nanoparticles for treatment of cancer," *Heliyon*. 2022. doi: 10.1016/j.heliyon.2022.e09403.
69. H. J. Ryu *et al.*, "Evaluation of silica nanoparticle toxicity after topical exposure for 90 days," *Int. J. Nanomedicine*, 2014, doi: 10.2147/IJN.S57929.
70. M. Sivera *et al.*, "Silver nanoparticles modified by gelatin with extraordinary pH stability and long-term antibacterial activity," *PLoS One*, 2014, doi: 10.1371/journal.pone.0103675.
71. Hemlata, P. R. Meena, A. P. Singh, and K. K. Tejavath, "Biosynthesis of Silver Nanoparticles Using Cucumis prophetarum Aqueous Leaf Extract and Their Antibacterial and Antiproliferative Activity against Cancer Cell Lines," *ACS Omega*, 2020, doi: 10.1021/acsomega.0c00155.
72. M. Pandurangan, G. Enkhtaivan, and D. H. Kim, "Anticancer studies of synthesized ZnO nanoparticles against human cervical carcinoma cells," *J. Photochem. Photobiol. B Biol.*, 2016, doi: 10.1016/j.jphotobiol.2016.03.002.

73. C. Wang *et al.*, "Rapid green synthesis of silver and gold nanoparticles using Dendropanax morbifera leaf extract and their anticancer activities," *Int. J. Nanomedicine*, 2016, doi: 10.2147/IJN.S97181.
74. G. Lakshmanan, A. Sathiyaseelan, P. T. Kalaichelvan, and K. Murugesan, "Plant-mediated synthesis of silver nanoparticles using fruit extract of Cleome viscosa L.: Assessment of their antibacterial and anticancer activity," *Karbala Int. J. Mod. Sci.*, 2018, doi: 10.1016/j.kijoms.2017.10.007.
75. K. Kalishwaralal *et al.*, "Silver nanoparticles inhibit VEGF induced cell proliferation and migration in bovine retinal endothelial cells," *Colloids Surfaces B Biointerfaces*, 2009, doi: 10.1016/j.colsurfb.2009.04.025.
76. T. K. Trinh and L. S. Kang, "Response surface methodological approach to optimize the coagulation-flocculation process in drinking water treatment," *Chem. Eng. Res. Des.*, 2011, doi: 10.1016/j.cherd.2010.12.004.
77. J. Franková, V. Pivodová, H. Vágnerová, J. Juráňová, and J. Ulrichová, "Effects of silver nanoparticles on primary cell cultures of fibroblasts and keratinocytes in a wound-healing model," *J. Appl. Biomater. Funct. Mater.*, 2016, doi: 10.5301/jabfm.5000268.
78. P. Singh, Y. J. Kim, D. Zhang, and D. C. Yang, "Biological Synthesis of Nanoparticles from Plants and Microorganisms," *Trends in Biotechnology*. 2016. doi: 10.1016/j.tibtech.2016.02.006.
79. B. Liu *et al.*, "Prognostic value of inflammation-based scores in patients with osteosarcoma," *Sci. Rep.*, 2016, doi: 10.1038/srep39862.
80. L. A. S. Kurban *et al.*, "Pathological nature of renal tumors - does size matter?," *Urol. Ann.*, 2017, doi: 10.4103/UA.UA_17_17.
81. I. X. Yin, J. Zhang, I. S. Zhao, M. L. Mei, Q. Li, and C. H. Chu, "The antibacterial mechanism of silver nanoparticles and its application in dentistry," *International Journal of Nanomedicine*. 2020. doi: 10.2147/IJN.S246764.
82. M. Khubchandani, N. R. Thosar, S. Dangore-Khasbage, and R. Srivastava, "Applications of Silver Nanoparticles in Pediatric Dentistry: An Overview," *Cureus*, 2022, doi: 10.7759/cureus.26956.
83. L. M. Stabryla *et al.*, "Role of bacterial motility in differential resistance mechanisms of silver nanoparticles and silver ions," *Nat. Nanotechnol.*, 2021, doi: 10.1038/s41565-021-00929-w.
84. J. S. McQuillan, H. Groenaga Infante, E. Stokes, and A. M. Shaw, "Silver nanoparticle enhanced silver ion stress response in Escherichia coli K12," *Nanotoxicology*, 2012, doi: 10.3109/17435390.2011.626532.
85. K. B. Holt and A. J. Bard, "Interaction of silver(I) ions with the respiratory chain of Escherichia coli: An electrochemical and scanning electrochemical microscopy study of the antimicrobial mechanism of micromolar Ag," *Biochemistry*, 2005, doi: 10.1021/bi0508542.
86. N. G. Dengler and H. Tsukaya, "Leaf morphogenesis in dicotyledons: Current issues," *Int. J. Plant Sci.*, 2001, doi: 10.1086/320145.
87. A. R. Harifi-Mood, A. Habibi-Yangjeh, and M. R. Gholami, "Solvent effects on kinetics of the reaction between 2-chloro-3,5- dinitropyridine and aniline in aqueous and alcoholic solutions of [bmim]BF 4," *Int. J. Chem. Kinet.*, 2007, doi: 10.1002/kin.20282.
88. B. Ahmad and J. J. Nieto, "Existence results for nonlinear boundary value problems of fractional integrodifferential equations with integral boundary conditions," *Bound. Value Probl.*, 2009, doi: 10.1155/2009/708576.
89. P. Shabanzadeh, N. Senu, K. Shameli, and M. M. Tabar, "Artificial intelligence in numerical modeling of silver nanoparticles prepared in montmorillonite interlayer space," *J. Chem.*, 2013, doi: 10.1155/2013/305713.
90. Z. A. Ratan *et al.*, "Silver nanoparticles as potential antiviral agents," *Pharmaceutics*. 2021. doi: 10.3390/pharmaceutics13122034.
91. E. O. Mikhailova, "Functional Biomaterials Review Silver Nanoparticles: Mechanism of Action

and Probable Bio-Application," *J Funct Biomater.*, 2020.
92. A. de Souza *et al.*, "SilverSol® a Nano-Silver Preparation: A Multidimensional Approach to Advanced Wound Healing," in *Wound Healing Research: Current Trends and Future Directions*, 2021. doi: 10.1007/978-981-16-2677-7_12.
93. a. Chmielowiec-Korzeniowska, L. Krzosek, L. Tymczyna, M. Pyrz, and a. Drabik, "Bactericidal, fungicidal and virucidal properties of nanosilver. Mode of action and potential application. A review.," *Ann. Univ. Mariae Curie-Sklodowska*, 2013.
94. M. P. Patil and G. Do Kim, "Eco-friendly approach for nanoparticles synthesis and mechanism behind antibacterial activity of silver and anticancer activity of gold nanoparticles," *Applied Microbiology and Biotechnology*. 2017. doi: 10.1007/s00253-016-8012-8.
95. A. Jain, R. Anitha, and S. Rajeshkumar, "Anti inflammatory activity of silver nanoparticles synthesised using cumin oil," *Res. J. Pharm. Technol.*, 2019, doi: 10.5958/0974-360X.2019.00469.4.
96. F. Arshad *et al.*, "Bioinspired and Green Synthesis of Silver Nanoparticles for Medical Applications: A Green Perspective," *Applied Biochemistry and Biotechnology*. 2023. doi: 10.1007/s12010-023-04719-z.
97. R. V. & Rai and J. A. Bai, "Nanoparticles and their potential application as antimicrobials," *Formatex*, 2011.
98. A. Luceri, R. Francese, D. Lembo, M. Ferraris, and C. Balagna, "Silver Nanoparticles: Review of Antiviral Properties, Mechanism of Action and Applications," *Microorganisms*. 2023. doi: 10.3390/microorganisms11030629.
99. A. Salleh *et al.*, "The potential of silver nanoparticles for antiviral and antibacterial applications: A mechanism of action," *Nanomaterials*. 2020. doi: 10.3390/nano10081566.
100. R. Jamunkar *et al.*, "Application of Silver Nanoparticles as a New Alternative Antiviral Agent for SARS-CoV-2: A Review," *Curr. Nanosci.*, 2021, doi: 10.2174/1573413717666211118105415.