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BIOLOGICALLY EXTRACTED SILVER NANOPARTICLES IN ANTICANCER STUDIES– A REVIEW

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Abstract: With the advances in nanotechnology, its applications in the field of medicine have reached new heights. Nanoparticles bound to various non-reacting metals along with different drugs are used in the treatment of various diseases. Majorly, this technique has been useful in treating cancer, a tumor-inducing disease. Many studies have shown that Silver Nanoparticles (AgNPs) can be used at a large scale in therapeutic applications due to their easier mode of action, specificity to cancerous cells, their function as good carriers, and other biological factors. The biological synthesis of these nanoparticles is a greener approach where they can be extracted through microbial as well as plant sources. These AgNPs are tested both in vitro and in vivo conditions to know the effectiveness of the drugs on the tumor. This paper aims to review AgNPs synthesized from biological sources and their utilization in cancer treatment.

Index Terms **- Anticancer activity, biosynthesis, cancer cells, nanoparticles, silver nanoparticle, targeted chemotherapy.**

I. INTRODUCTION

Treatment of cancer, an uncontrolled cell division, depends on the type and stage of cancer. The primary treatment is a therapy that alone can destroy all the cancer cells and adjuvant treatment is given before or after other methods of primary treatment to increase the effectiveness of the therapy. It can be a combination of surgery, chemotherapy, radiation therapy, stem cell transplant, targeted therapy, hormonal therapy, or immunotherapy [1]. Chemotherapy, which is the most commonly used treatment method, includes using drugs that kill cancer cells or prevent them from dividing. These drugs are administered depending on the type of cancer. For more precise application, the targeted type of chemotherapy is used which includes the use of nanotechnology.

Nanotechnology is the branch of technology that deals with molecules of less than 100 nanometres called nanoparticles. It is a developing technology having several fields like nanoelectronics, nanomedicine, and biomaterials. Nanomedicine is a branch of medicine that applies the knowledge and tools of nanotechnology to the prevention and treatment of disease. It involves the use of metal nanoparticles for diagnosis, delivery, sensing, or actuation purposes in a living organism. Most attention has been paid to gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), and copper nanoparticles (CuNPs), which exhibited extensive applications in anticancer studies, molecular imaging, and as drug carriers. These nanoparticles have been observed to be effective target agents against cancerous cells and hence find extensive application in Targeted chemotherapy.

Nanoparticles make excellent drug delivery platforms as they can release a single or multi-type payload of small molecule chemotherapeutics in the vicinity or interior of a cancer cell. These metal nanoparticles can also be coated with other materials to reduce their toxicity, improve biological retention time, or allow specific targeting of a tissue or cancer cell. Antibodies, proteins, or other biomolecules are frequently used as target ligands, which ensures the accumulation of nanoparticles within the tumor due to the enhanced permeability and retention effect in tumors [2].

Targeted heat therapies are developed using nanoparticles in which they absorb infrared light from the laser turning the light into heat destroying the cells. It is specially developed for breast cancer. Some nanoparticles have a radioactive core with attached molecules that attach to lymphoma tumor cells using radiation to destroy the tumor cells. [3]. Recently a new study has brought the use of magnetic nanoparticles which are heated at a specific temperature that is enough to kill cancer cells without harming healthy cells. This destroys tumors as well as activates the immune system to attack other cancer cells throughout the body [4].

Recent studies show that AgNPs can be used in chemotherapy, bio diagnostics, bioimaging, transfection vectors, and antiviral agents; some of these have entered clinical trials [5]. They exhibit various biological effects such as antibacterial, antifungal, antiviral, anticancer, and anti-inflammatory properties. Taking these functions into consideration it has applications for several purposes such as antimicrobial agents in wound dressings, anticancer agents, electronic devices, and water treatment, etc. [6][7]. Their application as anticancer agents is being studied extensively now.

There are various methods for the synthesis of AgNPs which include chemical, physical, electrochemical, irradiative, photochemical, and biological techniques. But most of the methods are quite expensive and potentially dangerous to the environment. Thus, the biological approach of synthesis has been proved to be cost-effective, environment friendly, and can be used for large-scale synthesis. [8] This paper focuses on reviewing the use of silver nanoparticles (AgNPs) as anticancer agents, their biological extraction, mode of action, and uses.

II. ANTICANCER ACTIVITY OF SILVER NANOPARTICLES WITH SOME CASE STUDIES

Although AgNPs are known to have cytotoxicity against cancer cells, the reason behind this is still not clear. Various studies have been carried out to determine the actual mode of action of AgNPs and various possibilities have been proposed. AgNPs show genotoxicity and cytotoxicity against cancer cells. Moreover, the genotoxicity of AgNPs generates double-stranded breaks along the chromosome that leads to apoptosis. This mechanism implies that AgNPs can be used as DNA-targeting anticancer drugs. These are chemotherapeutic agents which induce cell apoptosis through double-strand DNA breaks, oxidative stress, and chromosomal instability. They regulate p-glycoprotein activity which is responsible for the movement of drugs across the membrane of the cell. This promotes multi-drug resistance by preventing its entry into the cell.

A case study describes the mode of action of the AgNPs on the MCF-7 tumor cells. The cells that take up the nanoparticles are catabolized to form amino acids and silver ions. These silver ions interact with the macromolecules of the cell, like DNA and proteins, and tend to damage the DNA and also increases mitochondrial permeability. The mitochondrial dysfunction leads to apoptosis which inhibits the proliferation of MCF-7 cells. The cells which uptake the nanoparticles also accumulate and synthesize reactive oxygen species (ROS) causing oxidative stress leading to permanent damage to the structure of proteins and negative regulation of ATP synthesis [8].

In another experiment conducted by Shimpi et al. on A549 cells, the use of AgNPs and Ag+ showed a decrease in mitochondrial activity which was studied using the MTT assay. A549 cells exposed to AgNPs for 24 hrs in a dose-dependent manner (0–20 g/ml) showed a reduction in mitochondrial function. It was found that AgNPs are taken up by the A549 cells resulting in oxidative stress and cell death. Using the 32P photolabeling technique, a dose-dependent increase in the level of bulky DNA adducts after exposure to AgNPs for 24 h was found. From this study, it was concluded that AgNPs decrease mitochondrial activity by giving rise to oxidative stress. [9]

Various in vitro studies have shown that silver nanoparticles can enter cells by endocytosis, enter the mitochondria and produce reactive oxygen species (ROS) by affecting the respiration of cells. Both direct and indirect damage can be caused to the DNA because of these ROS. [10] AgNPs are shown to be toxic and can lead to DNA damage and mitochondrial damage to cancer cells, oxidative stress, and can also induce apoptosis. [11] [12]. Moreover, studies indicate that AgNPs affect the function of the vascular endothelial growth factor (VEGF), also known as the vascular permeability factor, which plays a major role in angiogenesis within tumors. [13] These results hence indicate that AgNPs have anti-cancer properties that can be used as an alternative for traditional chemotherapy. [14]

III. PLANT AND MICROBIAL SOURCES OF NANOPARTICLES

Nanoparticles are created from various sources, using several methods. Two types are the top-down method and the bottom-up method. The top-down method involves breaking larger materials into nanoparticles. An example of this is Attrition or milling, which includes size-reducing types of machinery like a ball mill. And the bottoms-up method has different types like pyrolysis, inert gas condensation, sol-gel fabrication, etc. [15]

The bottoms-up method is used for the biological extraction of the AgNPs. The chemical and physical processes for the synthesis of AgNPs mostly involve hazardous chemicals, high energy requirements, and other strict conditions. On the contrary, the biological method makes use of biological reductants, has low to zero energy requirements, and better characteristics of the metallic silver nanoparticles. It also has the advantage of eliminating the need for toxic chemicals to be used as surfactants or stabilizers since various proteins present in the plant extracts act as reducing as well as capping agents for AgNPs. The sizes and morphologies of AgNPs synthesized from chemical and physical methods are quite variable depending on the conditions and methods applied.

The biological method has been able to biosynthesize silver nanoparticles with better sizes and morphologies. Most of the AgNPs produced were reported to have a predominantly spherical shape. [16] Biological extraction of AgNPs has been done by using bacteria, fungi, and plant extract. Although the use of plant extracts is often preferred because it eliminates the elaborate process of maintaining cell cultures. [6]

Biosynthesis of AgNPs from microbial Source

Microbial species can synthesize predominantly spherical AgNPs within the range of 1 – 70 nm and fungi can produce AgNPs with an average size range of 13 nm, but the mechanism of the reduction process is still unknown. The suggested mechanism for the biosynthesis of intracellular and extracellular AgNPs by bacteria involves reduction of silver by sulphur-containing proteins or DNA, while in the case of fungi the mechanism is thought to occur with the involvement of carboxylic group or through nitrate dependent reductase.

In the case of intracellular synthesis, the downstream processing is difficult and expensive due to the separation and purifying steps involved, thus making extracellular synthesis preferable. Compared with bacteria or algae, biosynthesis of AgNPs from fungi provides a more rational and economical approach because downstream processing and biomass handling much simpler and easier in the case of fungi, also the amounts of proteins known to reduce silver are secreted in much higher amounts, thus increasing the biosynthesis productivity.

The difficulties faced in the case of microorganisms, which include preparation and growth of strain, the isolation of strain which requires too many precautions, maintaining the culture medium, and respective conditions such as pH, temperature, the salinity of the culture, and reaction mixture show the complexity of these techniques to be applied on a large scale. Furthermore, there is also a necessity for the use of complicated equipment in process technology, thus increasing the investment cost. Conversely, in the case of fungi and plants, simple equipment such as a filter press can be used thus promising economic feasibility. [17]

Table 1: Some examples of microbes that can used for Biosynthesis of AgNPs [17]

Bacteria	**Fungi**	**Algae**
Aeromonas sp. SH10	*Fusarium oxysporium*	*Spirulina plantensis*
Klebsiella pneumonia	*Phaeneroechaete chrysosporium*	*Oscillatoria willei*
Lactobacillus strains	*Verticillium* sp.	*Gelidiella acerosa*
Pseudomonas stutzeri AG259	*Aspergillus flavus*	*Spirulina platensis*
Corynebacterium sp. SH09	*Fusarium oxysporum*	
Enterobacter cloacae	*Aspergillus fumigatus*	
	Coriolus versicolor	

Table 2: Notable examples of microbes used for Biosynthesis of AgNPs and the nature of AgNPs produced by them. [17]

Microbial Species	**Nature of AgNPs produced**	**References**
	Bacteria	
Nonpathogenic Bacillus licheniformis	Produce highly stable silver NPs (40 nm)	[18]
B. licheniformis	Well-dispersed silver nanocrystals (50 nm)	[19]
B. subtilis	Monodispersed AgNPs (5-50 nm) produced using supernatants microwave irradiation in water	[20]
Silver-resistant bacterial strain of *P. stutzeri* AG259	Naturally accumulate silver NPs intracellularly (200 nm)	[21]
K. pneumoniae	Increased synthesis of AgNPs (1-6 nm) by exposure to visible-light emissions	[22]
	Fungi	
Fusarium oxysporum	Extracellular synthesis of Silver NPs (5-50 nm)	[23]
Aspergillus flavus	Produce AgNPs stable that are in water for more than 3 months	[24]
Aspergillus fumigatus	Spherical and triangular AgNPs	[25]
Coriolus versicolor	Monodisperse spherical silver NPs.	[26]
	Algae	
Oscillatoria willei NTDM01	Marine cyanobacterium used for synthesis of silver NPs (100-200 nm)	
Spirulina platensis	Extracellular synthesis of spherical silver NPs (7-16 nm) in 120 h at 37 °C, at pH 5.6	[27]

Biosynthesis of AgNPs using plants (an example):

In a research paper by Peter Logeswari et al., five different species of plants, that are the leaves from *O. tenuiflorum* (Tulsi), *S. tricobatum* (Thudhuvalai), *S. cumini* (Naval), *C. asiatica* (Vallarai), and peel from *C. sinensis* (Orange) were taken for the synthesis of AgNPs. In this step of selection and collection, the leaves and peels are washed 2-3 times with deionized water. The next step is the biosynthesis, in this, the leaves and peels are boiled in deionized water and then some amount (1-10ml) of this extract was mixed with the solution containing 2.5ml ammonium and 5 ml of 1mM silver nitrate. The solution was made to 50 ml by adding deionized water. The third step is the characterization of the AgNPs. The extract was observed in UV-Vis spectrophotometer at 300-540nm and deionized water was taken as blank. The maximum absorption shows the maximum production of the AgNPs which were further air-dried for characterization by Atomic Force Microscopy. The antimicrobial activity against pathogenic organisms like *S. aureus, P. aeruginosa, K. pneumoniae*, and *E. coli* was obscured by a well-diffusion method. In this paper, the color change was observed from yellow to dark brown which indicated the formation of the AgNPs, and maximum absorbance was noted at 420 nm. The absorbance increased with the time of incubation. The extract was used further for in vivo and in vitro studies. [28]

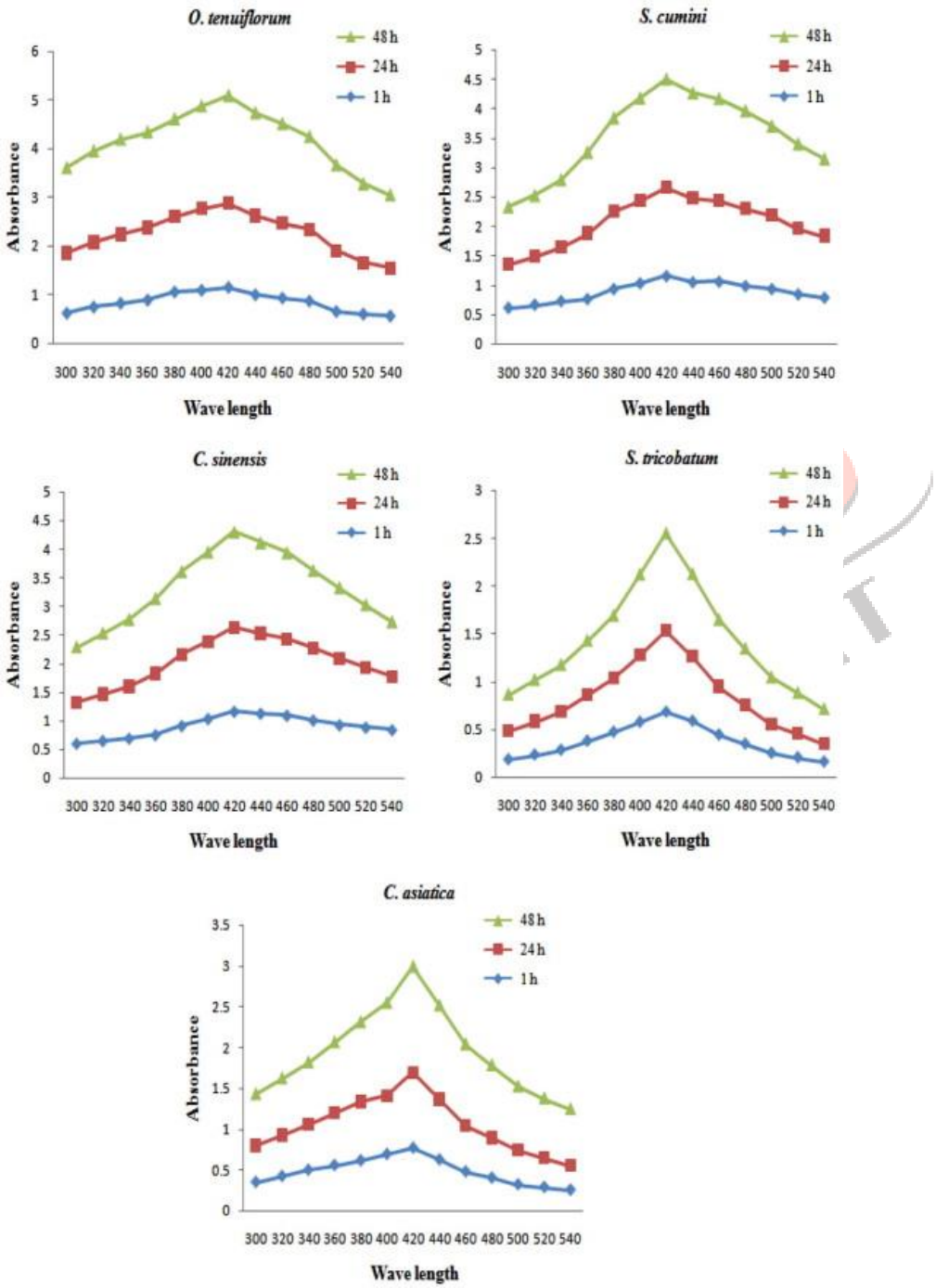

Fig 1: UV–vis spectra of silver nanoparticles synthesized using natural plant extracts [16]

Table 3: Silver nanoparticles from different sources against several cancer cells. [29]

AgNPs	Synthesis Route Tested Cancer Cell
Plant dandelion- *Taraxacum officinale*	Human liver cancer cells (HepG2)
Plant Extract- *Commelina nudiflora L*	HCT- 116 colon cancer cells
plant extracts of guava and clove	Human colorectal adenocarcinoma, the human kidney, human chronic myelogenous, leukemia, bone marrow, and human cervix
Plant Extract- *Nostoc linckia*	MCF-7
Chemical synthesis	A549 (Human lung carcinoma), HeLa (Human cervical adenocarcinoma), MCF7 (Human breast adenocarcinoma), MDAMB231 (Human breast adenocarcinoma), and SKBR3 (Human breast adenocarcinoma) cells
Plant Extract-ethanolic extract of rose *(Rosa indica)* petals	Human colon adenocarcinoma cancer cell line HCT 15

IV. In Vitro Testing Reports of Some Case Studies

As discussed earlier, AgNPs may induce reactive oxygen species and contribute towards cellular damage and cell death processes. [9] This anticancer activity of AgNPs was studied in vitro on various cell lines of different types of cancer [30].

V. Kathiravan et al extracted these silver nanoparticles from *M. dubia* leaves and tested them on Breast cancer MCF-7 cell lines and normal Vero cell lines to determine their cytotoxicity. [8] For normal Vero cell lines, Silver nanoparticles exhibited toxicity at a high concentration of 500 LG/ml as shown in the graph below. The CC50 value indicates the death of 50% of the cell population which is at 500 LG/ml.

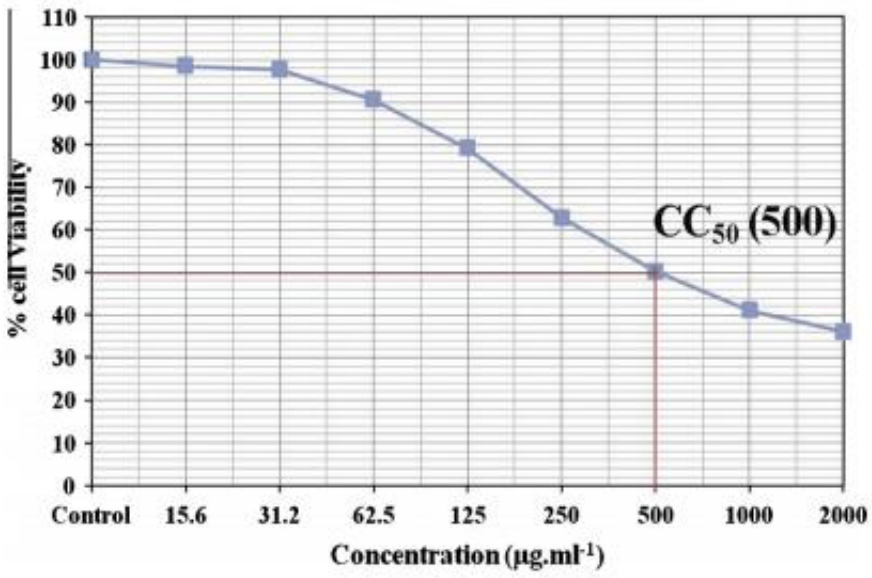

Fig 2: CC50Value of the silver nanoparticles against the Vero cell line which indicates the death of 50% cell population. [8]

The cytotoxicity of silver nanoparticles test solution under low toxic moderately toxic and high concentrations by V. Kathiravan et al is shown in the Figure. It can be inferred that cell death for normal cells does not occur until high concentrations are reached.

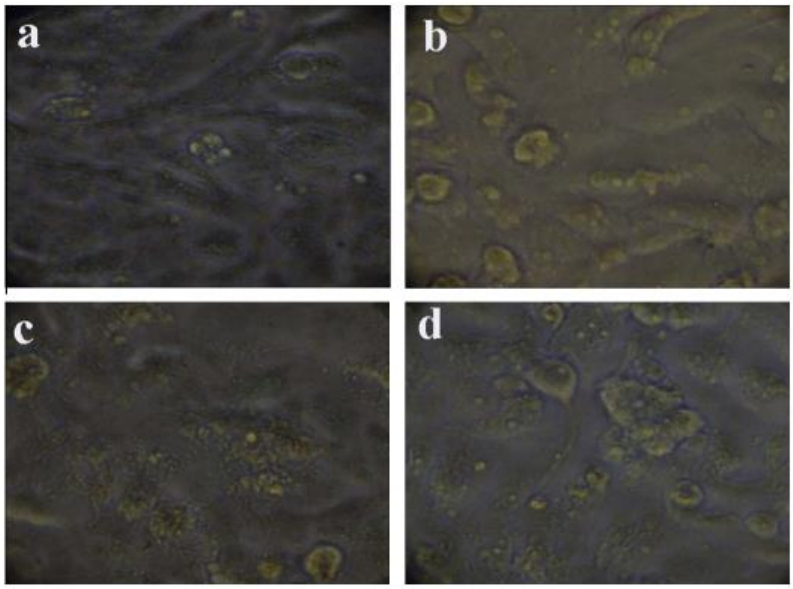

Fig 3: Effect of crude extract from silver nanoparticles on the Vero cell line: (a) controlled, untreated cell line, (b) low concentration treated cell line, (c) medium concentration treated cell, and (d) high concentration treated cell. [8]

In the same study, different concentrations of silver nanoparticles are tested in vitro for anti-breast cancer activity on the MCF-7 cell line. The cancer cell death increased with increasing concentrations of silver nanoparticle solution. The cytotoxicity of silver nanoparticles test solution on MCF-7 cell line is shown in the following Figure. Here, cell death is achieved even at low concentrations.

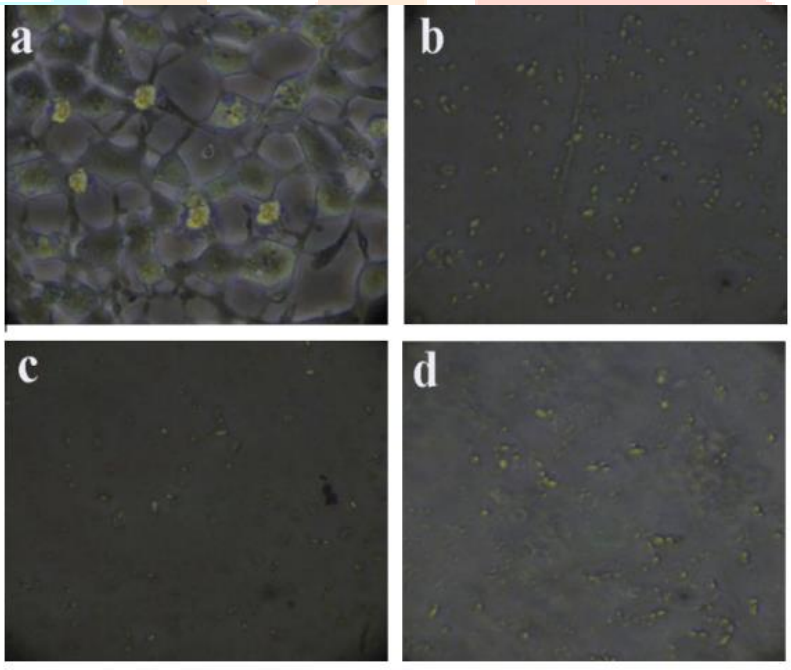

Fig 4: Effect of crude extract from silver nanoparticles on the breast cancer MCF-7 cell line: (a) controlled, untreated cell line, (b) low concentration treated cell line, (c) medium concentration treated cell, and (d) high concentration treated cell. [8]

Crude extract of silver nanoparticles was found to be potent by V. Kathiravan, as evident by low concentration (< 31.2 ll/ml) at which 50% of cancer cell death occurred.

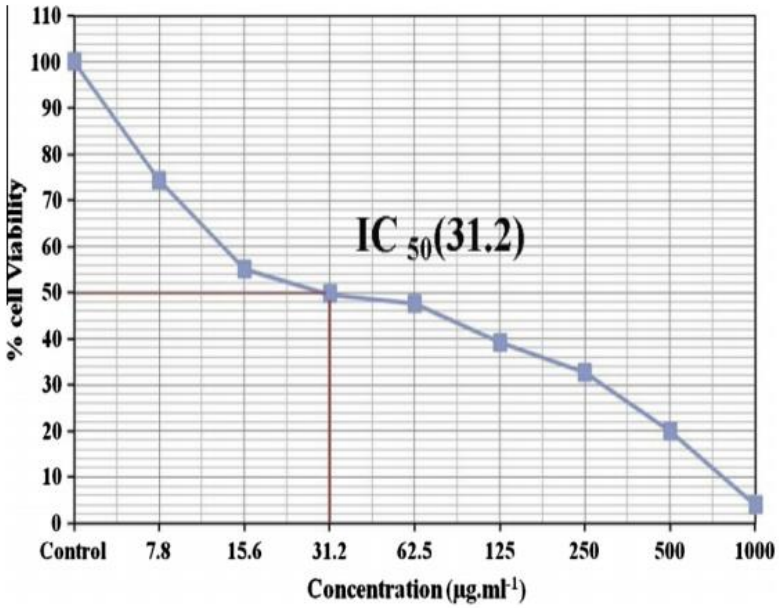

Fig 5: IC50Value of the silver nanoparticles against breast cancer (MCF-7) cell line. [8]

As the AgNP concentration required to kill cancerous cells (31.2 μg/ml) was far too less than the concentration required to kill normal cells (viz 500 μg/ml) they can be successfully used to treat cancer without harming the normal body cells. The therapeutic index (CC50/IC50) for the Breast cancer cell line was hence estimated by the authors to be up to 16.02. The nanoparticles used in these studies were spherical with an average size of 7.3 nm. This work showed the potential application of these AgNPs of M. dubia for in vitro-anticancer activity against human breast cancer cell lines. [8]

In another study conducted by P. V. AshaRani, et al., these AgNPs showed an effect on cell morphology and cell viability. Nanoparticle treated cells were observed to be clustered with a few cellular extensions, and cell spreading patterns were restricted as compared to control cells. This was concluded to be due to disturbances in cytoskeletal functions as an outcome of the nanoparticle treatment. [31]

Similar results were observed by other groups like Pernodet, N. et al. in dermal fibroblast cells treated with citrate-coated gold nanoparticles. [32]. The nanoparticles are absorbed on the cell surface due to which the dark orange patches are observed on the cell surface in the adjoining image. However, the researchers observed only a few floating cells under the microscope, which suggested the absence of widespread cell death due to necrosis. It can be concluded from this study that AgNPs are effective against human cancer cells but the rate of cell death is limited in some cases.

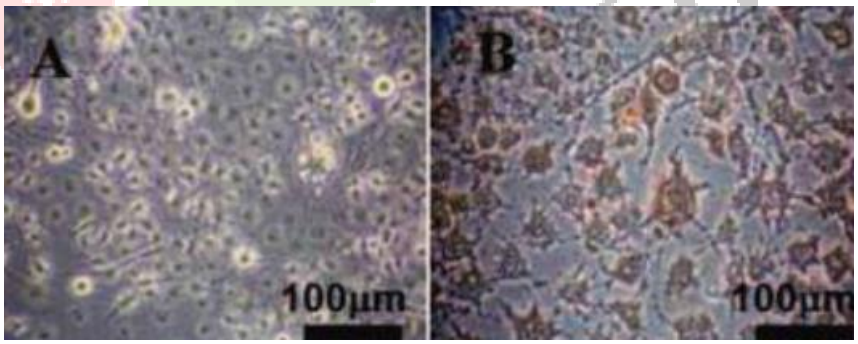

Fig 6: Optical micrographs of U251 cells without any nanoparticle treatment (A) and cells treated with Ag-Starch (200 g/mL) (B) Dark orange patches are visible on the cell surface of the treated cells and remain even after repeated washing. [21]

Shimpi et al measured the cytotoxicity of synthesized AgNPs against A549 cells by sulforhodamine B (SRB) assay [9]. For this assay, the A549 cells were grown in RPMI 1640 medium containing 10% fetal bovine serum and 2ml L-glutamine. The cells were inoculated into 96 well microtiter plates in 100µL medium. After cell inoculation, the microplates were incubated at 37 °C in 5 % CO2, 95% air, and 100 % relative humidity for the next 24 hours. To evaluate the anticancer activity of AgNPs from *T. divaricata*, the cultured cells were treated in separate plates with different concentrations of silver nanoparticles, and plates were incubated at standard conditions for 48 hours and the assay was terminated by the addition of cold TCA. Cells were fixed in situ by the gentle addition of 50µl of cold 30% (w/v) TCA (final concentration, 10% TCA) and incubated for 60 minutes at 4 °C.

This group concluded that the presence of bioactive compounds present in *T. divaricata* leaves extract was responsible for the enhanced cytotoxic effect. The in-vitro cytotoxic activity of AgNPs synthesized by using *T. divaricata* leaves extract was tested on A549 human lung cancer cell lines by Sulforhodamine B (SRB) assay. Different concentrations of colloidal silver nanoparticles were able to reduce cell viability of the A549 human lung cancer cell line, in a dose-dependent manner. A dose-

dependent decrease in the viability of A549 human lung cancer cells was observed on treatment with AgNPs. Morphological variations such as retardation in cell growth, loss of membrane stability, cell shrinkage, and cell death were observed in the A549 human lung cancer cell line treated with colloidal AgNPs. [9]

It was observed by Corina Danciu et al. that PEG-capped AgNPs show high selective toxicity at low doses on murine melanoma cells (B16 melanoma 4A5 and B16 ova) in vitro and a lack of toxicity for healthy cells (human keratinocytes and melanocytes) as compared to AgNPs not capped with PEG. Although an increased dosage of these PEG-capped AgNPs invalidated the selectivity on tumor cells, and also showed toxicity towards healthy cells.
Hence AgNPs can be combined with other substances to increase their selectivity although further research is required in this aspect. [33]

V. IN VIVO TESTING REPORTS, SOME CASE STUDIES

Polymeric nanoparticles (PNPs) are optimal nanocarriers for targeted drug delivery (TDD) due to the small size and can also entrap the drug molecules effectively. The radio-labeled PNPs were injected intravenously in the tail vein in healthy Swiss albino mice and severe immunodeficient mice bearing U87MG tumor. Animals were anesthetized using appropriate anesthetizing solutions through injecting it in an intraperitoneal way. No treatment was seen in the control group. Tumour was obtained in vivo using AgNPs-chlorotoxin. In some cases, the tumor size was observed to be too large.

A case study in which AgNPs were formed by phycocyanin pigment extracted from *Nostoc linckia*. These particles had sizes in the range of 9.39 to 25.89nm. The AgNPs showed high antitumor activity for decreasing size in Ehrlich ascites carcinoma-bearing mice. The total WBC count was found to be increased in EAC and control (15.06±1.34 103 /mm^3) which decreased significantly in the mouse treated with AgNP (8.45±1.16 103 /mm^3) and was (9.32±1.01 103 /mm^3) for 5-5-5 fluorouracil. [34]

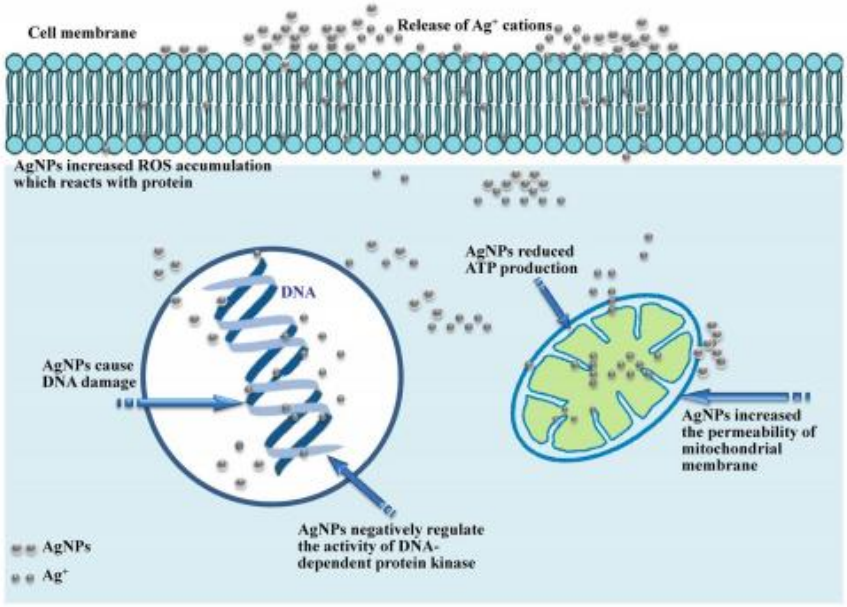

Fig 7: Schematic representation of the proposed mode of action of AgNPs on MCF-7 cells. [24]

Table 4: Effect of silver nanoparticles and 5-FU on hematological parameters, tumour parameters (volume and cell count) and body weight of EAC bearing mice. [34]

Group	Hb (g/dl)	RBC Count ($10^6/mm^3$)	Total WBC ($10^3/mm^3$)	Tumor volume (mL.)	Tumor cell count (10^6/mL)	Bodyweight (g)
Normal Control	13.53 ± 0.65	5.23 ± 0.28	4.97 ± 0.93	--	--	24.2 ± 1.9
EAC Control	8.10 ± 0.79	3.36 ± 0.36	15.06 ± 1.34	7.6 ± 1.8	49.15 ± 9.62	37.7 ± 3.1
5-FU	12.97 ± 1.03	4.52 ± 0.51	9.32 ± 1.01	1.5 ± 0.6	13.24 ± 7.10	28.6 ± 2.3
AgNPs	13.86 ± 1.10	4.71 ± 0.42	8.45 ± 1.16	1.3 ± 1.2	12.41 ± 8.43	26.5 ± 2.8

Another study includes the synthesis of Silver Nano-particles using *Melia azedarach* (Chinaberry). In vivo, it was used to study the cytotoxicity against Dalton's ascites lymphoma in mice. A significant increase in life span was observed in vivo DAL mice model. Apoptosis induced was scanned by acridine orange and ethidium bromide (AO and EB) staining. [35]

The next study observed was the anti-tumor activity of green synthesized AgNPs against lung cancer. The animal used was a female severe combined immunodeficient (SCID) mouse. The tumor was injected subcutaneously into the back of the mice. The tumor size and body weight were measured. Tumour was measured using the length and width. Two groups containing eight mice each was taken, one group receiving IP vehicles and the other receiving AgNPs. A Mann– Whitney test and analysis of variance

(ANOVA) were used for the comparison of effects between different groups. The effect was seen in the mice, the tumor growth was decreased noticeably. High-dosed mice showed some side effects like irritation with rectal prolapse and a red ass. According to the ANOVA test the initial tumor size in the AgNPs treated group was lowered than in that of the control group. This study concludes that the IP injection of AgNPs had a significant effect in preventing tumor growth. This implies that the Silver Nano-Particles have an anticancer effect against Non-small Lung Cancer cells in vivo. [36]

VI. CURRENT SCENARIO, HUMAN TESTING AND SUCCESS RATE

Nanoparticles generated during the fire, asbestos nanofibres, and micron-sized quartz particles have proven harmful to health. The nanoparticles can enter our system through ingestion, inhalation, or by coming in contact with the skin. The size of nanoparticles is similar to the cell pores and large proteins which generates a possibility of toxicity in the metabolic reactions of the body. So, it is necessary to test the toxicity of nanoparticles *in vitro* as well as *in vivo* before their use, also comparing it in various sizes as well as concentrations. [37]

Maintaining the size and concentration of these AgNPs is extremely essential when administering them for Anticancer purposes.

Currently, studies are going on the AgNPs and clinical trials are in progress. The researchers at MIT and Brigham and Women's Hospital in Boston carried out the human trials where the AgNPs were used to carry docetaxel drugs in treating lung, prostate, and breast cancers. The results were positive and also safe for use. The tumors shrank even at a lower drug concentration. Previous trials were not successful due to difficulty in the design and scaling-up process, but knowing the right combination of properties of the particles and concentration of the target molecules makes them effective to use. The phase I trials have 17 patients already gone through traditional chemotherapy. During the first phase, the concentration of docetaxel was found to be 100 times higher when targeted through the BIND-014 nanoparticles and also the side effects of the drug were milder. The phase I trials are still in the process with increasing concentration levels. BIND Biosciences is planning on Phase II trials to investigate the treatment of a large number of patients. [38]

VII. CONCLUSION

The use of AgNPs in anticancer studies proves to be a promising approach. Biological extraction of the AgNPs reduces the hazardous chemicals, high energy requirements, and other risks that are involved in the process of synthesis of AgNPs by other physical and chemical approaches. The different methods of synthesis also affect the size and cytotoxicity of the nanoparticles. The use of plant extracts for AgNP biosynthesis has a low production cost and less complexity is hence preferred to the use of microbial cells.

The in vitro and in vivo studies showed reduced tumor growth and also indicated the use of AgNPs as carriers for targeted drug delivery. This makes AgNPs promising anticancer agents. Although their mode of action is not quite clear which restricts further formulation.

Various challenges on AgNP synthesis and use as an anticancer agent provide several potential avenues for further work to promote safer and more efficient use of AgNPs.

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