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Synthesis and Characterization of Novel Nanoparticles for Targeted Cancer Therapy

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Abstract

The use of nanoparticles in carrier-drug systems improves tumour inhibition and lowers drug-related side effects, according to recent studies on silver nanoparticles. The fusion of conventional medicine with nanotechnology presents an opportunity to create novel antimicrobial agents concurrently. This work aimed to identify the pro-apoptotic properties, anticancer, and antibacterial properties of silver nanoparticles (AgNPs) and AgNPs-Car, the latter of which were loaded with carboplatin. DLS, EDX-STEM, and FTIR analysis were used to conduct characterisation studies of the synthesised nanoparticles. The outcomes showed that AgNPs-Car effectively targeted C6 glioma cells by encouraging medication entrance into the cell. Additionally, the toxicity was minimal and the anticancer efficacy against MCF-7 and A549 cells was strong. Silver nanoparticles are the favoured material because of their superior quality and ability to improve medication delivery. Consequently, it is a promising field of study for the focused combat of cancer cells and harmful microbes. Silver nanoparticles are the favoured material because of their superior quality and ability to improve medication delivery. Consequently, it is a promising field of study for the focused combat of cancer cells and harmful microbes.

Keywords: Cancer, Nanomedicine, Targeted Nanoparticles.

1 INTRODUCTION

A class of disorders known as cancer is defined by malignant, aberrant tissue growth, or neoplasia, which produces cells that are devoid of normal form and/or function. These atypical cells have the ability to cause life-threatening malignant tumours by multiplying, performing angiogenesis, tricking the immune system, and even invading other areas of the body. As a result, cancer patients must receive timely and suitable treatment in order to prevent unchecked tumour growth. Bahjat et al., (2021) The growing resistance of tumour cells to chemotherapy, in particular, and the unregulated metastatic cascade of invasion, intravasation, circulation, extravasation, and colonisation hamper cancer treatment, though. Other non-pharmacological treatments include surgery, radiation therapy, heat shock, and stem cell therapy. Combining two or more alternative treatments may also be investigated. Kariper et al., (2020) However, there are a number of disadvantages to each technique, including invasiveness, systemic and local adverse effects, multiple resistance, brief circulation of chemotherapeutic medications, low solubility of the pharmaceuticals, and nonspecific targeting.

One such area of research that has gained increasing interest recently is the use of biosynthesised or biogenic nanotechnology in cancer therapy. Biogenic nanoparticles are microscopic particles that are created by living things, including bacteria or viruses. These particles can be designed to specifically target cancer cells, providing medications or other therapeutic agents directly to the tumour location by sensing, imaging, and delivery. Ebrahimi Shahmabadi et al., (2014) One of the key benefits of biogenic nanotechnology is its ability to target cancer cells accurately. This lowers the risk of toxicity and adverse effects by requiring less of the medication. By endowing biogenic nanoparticles with the ability to respond to certain stimuli, such as variations in pH or temperature, their potential to target cancer cells can also be enhanced (Gupta et al., 2021). The use of nanoparticles functionalised with molecules that bind selectively to cancer cells, enabling targeted drug administration, is one method of using biogenic nanotechnology to treat cancer. These advancements hold enormous promise for enhancing patient outcomes, reducing side effects from conventional cancer treatments, and improving quality of life for patients.

It has also been possible to kill cancer cells and create heat using magnetic nanoparticles. Photothermal therapy is a cancer treatment modality that makes use of carbon nanotubes (CNTs). Cylindrical nanotubes (CNTs) possess axial homogeneity and a thickness of nanometres, making them valuable for both cancer therapy and detection. Mohsen et al., (2020) Depending on their size and form, they can be divided into two types of CNTs: single-walled and multi-walled. CNTs' physical and chemical properties, including their architecture, surface area, high mechanical and metallic activity, thermal conductivity, electrical conductivity, and ultra-lightweight nature, make them a strong candidate for a variety of biological applications. Graphene nanoparticles have the ability to absorb light energy and convert it into heat, which makes them useful for photothermal therapy and targeted drug delivery. Al-Nuairi et al., (2020) Because quantum dots emit fluorescent light, they are useful in cancer therapeutic imaging. In 1980, quantum dots (QDs)—small nanoparticles or semiconductor nanocrystals with dimensions ranging from 2 to 10 nanometers—were produced. Quantum dots (QDs) hold promise as a means of identifying tumour biomarkers, including membrane proteins and other constituents of various cancer specimens.

2 RELATED WORK

Created liposomes modified with low molecular weight heparin and alendronate to carry doxorubicin. Heparin lengthens the duration that liposomes spend in the bloodstream and may have antimetastatic properties, while alendronate targets bone and is used to treat osteoporosis. Aparicio-Blanco et al., (2020) The efficiency of the nanosystem against orthotopic osteosarcoma and breast cancer bone metastasis was demonstrated by its strong reduction of tumour growth and metastasis production. Furthermore, the FDA has cleared every part of the system, meaning that the liposomal formulation that has been created has a lot of promise for real-world use. Karuppaiah et al., (2020) The drug doxorubicin was delivered via liposomes. The authors employed PEG-phospholipids with pH-sensitive imine linkages and ammonium bicarbonate liposomes functionalised with folic acid. The nanocarriers demonstrated promising cytotoxicity in mildly acidic media and hyperthermia, along with active targeting capabilities, extended circulation period, improved cellular uptake, and fast intracellular drug release. Liposomes grafted with 3-diethylaminopropylamine (DEAP) and filled with hyaluronic acid were sealed with rituximab through-holes on their surface. The acidic conditions in the TME led to the ionisation of DEAP, which in turn enabled the encapsulated medication to release widely. As a result, the anticancer medication coupled to the CD20 receptor that Burkitt's lymphoma-Ramos cells overexpressed and accumulated at high concentrations in the tumour, improving tumour cell ablation.

These large anionic liposomes have the potential to target TAMs and release resiquimoid when injected intraperitoneally. Through the use of this particular delivery mechanism, the drug induced T cell infiltration and M1 macrophage activation, reduced the proportion of Tregs in the TME, and enhanced the efficiency of PD1 blockade in the fight against syngeneic ovarian cancers. The researchers believe that further liposomal non-vehicle optimisation may lead to a clinically beneficial method for enhancing the immunotherapy given to patients with ovarian cancer in light of these positive results. Mahmood et al., (2022) creation of liposomes modified with low molecular weight heparin and alendronate for the delivery of doxorubicin. While alendronate is a bone-targeting medication and an osteoporosis treatment, heparin may extend liposome blood circulation and possess anti-metastatic qualities. enhanced circulation time, rapid intracellular drug release, and cellular absorption These large anionic liposomes have the potential to target TAMs and release resiquimoid when injected intraperitoneally. Alendronate acts as an osteoporosis treatment and a bone-targeting medication, whereas heparin may extend liposome blood circulation and have anti-metastatic qualities. enhanced cellular uptake, rapid release of drugs within cells, duration of circulation, Alendronate acts as an osteoporosis treatment and a bone-targeting medication, whereas heparin may extend liposome blood circulation and have anti-metastatic qualities. enhanced cellular uptake, rapid release of drugs within cells, duration of circulation.

3 MATERIAL AND METHODS

2 × 10 × 3 M Ag(NO3), 8.6 × 10 × 3 M trisodium citrate, and 4 × 10 × 3 M sodium borohydride were utilised as stock solutions. Weigh out 0.0169 g of Ag(NO3) powder using an analytical balance, then dissolve it in 50 ml of clean water to create an Ag(NO3) stock solution. Using an analytical balance, weigh out 0.1109 g of trisodium citrate powder and dissolve it in 50 ml of pure water to create a trisodium citrate stock solution. Using an analytical scale, weigh out 0.0075 g of sodium borohydride powder, and then dissolve it in 50 ml of pure water to create a sodium borohydride stock solution. Then, for 30 minutes at 60 °C, 12 ml of trisodium citrate, 12 ml of sodium borohydride, and 24 ml of pure water were combined. After the stock solution was heated to 90°C, 48 mL of silver nitrate was added. Five minutes later, the reaction was stopped. The AgNPs stock solution was kept in

a dark, cool environment. A Car stock solution containing 10 mg/10 ml was made. Using a sonicator, a mixture of 1 mL of AgNPs stock solution and 1 mL of Car stock solution was sonicated for 10 s. After that, the mixture is left in the dark for a minimum of thirty minutes.

Because of their quick detection times and inexpensive cost, nanoparticles like gold, silver, silica, magnetics, and iron oxide are employed in cancer diagnosis. They also have less negative effects than radiation and chemical-based therapies. Hamed et al., (2020); (Chen et al., 2020) Electrochemical biosensors are a great way to diagnose cancer since they are easy to use, affordable, and very effective (Cesewski et al., 2020). By functionalising them, nanoparticles can be made more effective at detecting cancer. For instance, Jihad et al., (2021) polyethylene glycol (PEG) was coupled with anti-cancer antibodies to identify breast adenocarcinoma cells (Jihad et al., 2021). The sulfur-containing group at the distal end of the PEG linker was subsequently used to attach this antibody–PEG complex to the surface of the nanoparticles.

Mechanistic Insights for Targeted Drug Delivery

Effective drug delivery using nanoparticles to target cancer cells is essential for increasing treatment efficacy, lowering dose-limiting toxicity, and shielding healthy cells from systemic toxicity. Anticancer medications should be delivered to the tumour site utilising nanoparticles in a method that allows them to pass through all phagocytic barriers and enter the tumour tissue with the least amount of blood volume and activity loss. Furthermore, the active form of the medication should only work on cancer cells after being administered intracellularly, with no effect on healthy cells. Currently, there is a lot of research being done on the interaction between nanomaterials and tumour cells with the goal of delving extensively into the subject of targeted medication delivery using nanoparticles. Drug delivery techniques fall into two groups. The first one uses nanoparticles that are devoid of ligands. i.e., passive targeting, whereas ligand-conjugated nanoformulations mediate the latter, active targeting (Figure 1).

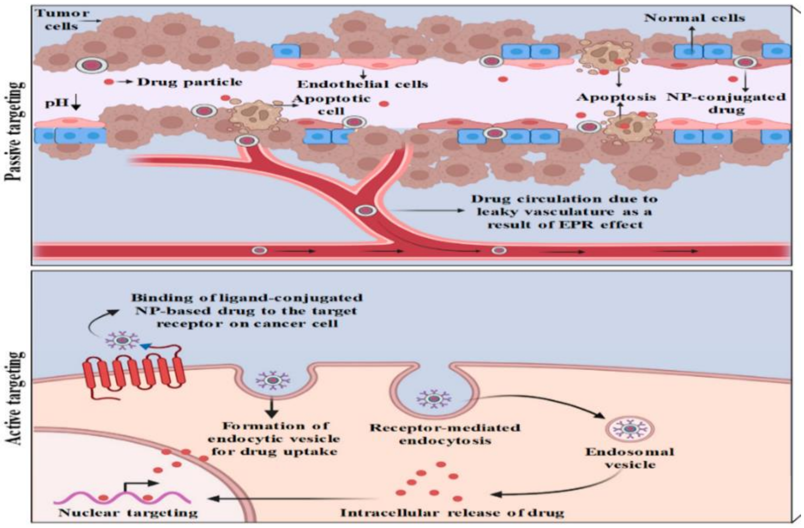

Figure 1: Mechanism of Passive and Active Targeting of NP-Drug Conjugates

Nanotechnology-Mediated Cancer Therapy

The therapy of cancer has greatly advanced because to nanotechnology. New medicines are being developed that leverage the magnetothermal and photothermal effects of specific nanomaterials. Superparamagnetic materials have a high sensitivity and are used for tumour lesion imaging and diagnostics. Furthermore, it is possible to raise the temperature to 40–45 °C in the presence of an external magnetic field in order to kill tumour cells. Certain sophisticated functions, such vascular detoxification, energy generation, and intracellular medication delivery, can be accomplished with non-medical equipment for effective biological treatment and manipulation of medical cells. Each NP in PDT has the potential to deliver a high number of photosensitive molecules, which permits a significant number of photosensitive molecules to be delivered to the tumor site. PDT involves the delivery of numerous light-sensitive chemicals to the tumour in order to kill cancer cells. Many nanomaterials have significant photocatalytic activity, especially those employed in semiconductors such nanoscale zinc oxide (ZnO) and titanium dioxide (TiO2). Compared to conventional photosensitisers, these nanomaterials exhibit superior catalytic performance, greater stability, lower cost, and less cytotoxicity. The ones that can selectively kill tumours while protecting healthy structures, however, are maybe the most significant. PDT expands the use of photosensitisers and is essential in combination therapy for malignant disorders.

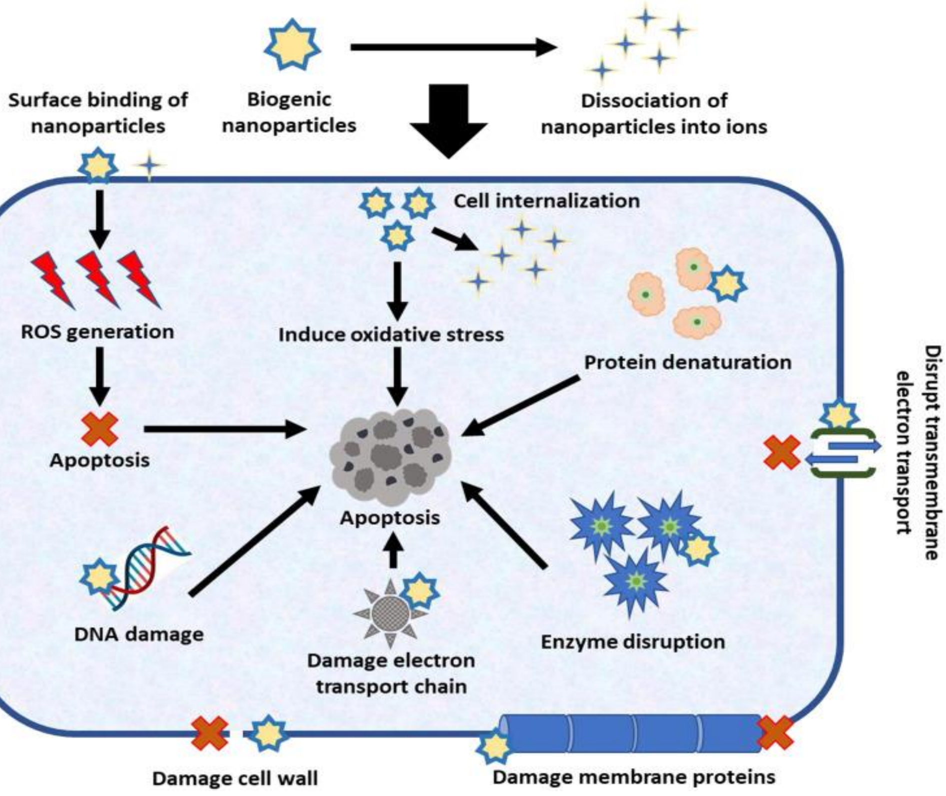

Figure 2: Anticancer Mechanism of Biogenic Nanoparticles.

Semiconductor nanoparticles can be used as a photosensitiser in tumour photodynamic treatment (PDT) because of their generally strong photocatalytic activity. PDT is starting to play a big role in cancer care. By increasing the generation of ROS and ALA peptide in conjunction with a photosensitiser, photodynamic therapy (PDT) can employ a selective photodynamic response to eradicate local aberrant tissue, including tumours (Figure 2). The primary mechanism is the activation of the photosensitiser positioned on the targeted molecules, which releases reactive oxygen species (ROS) including oxygen-free and single oxygen radicals. ROS in tumour tissues and cells can interact with a wide range of biological chemicals, leading to the development of cytotoxicity and ultimately the death of tumour cells and the removal of tumour tissues.

Figure 2 shows two possible anticancer processes that most bio-nanoparticles have in common. The first approach to cancer therapy involves using nanoparticles to directly suppress cancer cells by destroying their cell walls and membrane proteins, inhibiting transmembrane electron transport, or releasing reactive oxygen species (ROS) that promote cell death. Smaller nanoparticles have the ability to enter cancer cells, change DNA, electron transport chains, enzymes, proteins, and reactive oxygen species (ROS), as well as induce oxidative stress and ultimately induce cancer cells to undergo apoptosis. The second method involves isolating the nanoparticles into ions and endowing the resulting isolated nanoparticle ions with anticancer capabilities (Sezari Hamankoh et al., 2021).

Size and Shape of the Nanoparticles

The size and shape of nanomaterials determine how much they accumulate in tumors and how they are biologically distributed. The size of nanomaterials also determines the drug uptake by cells and their interaction with specific tissues for therapeutic purposes. Furthermore, the size and shape of nanomaterials affect the stability, drug loading and release. Recent studies have shown that the efficacy of small interfering RNA (siRNA) transfection is influenced by the size and shape of gold (Au) nanoparticles. To confirm this dependency, we created three different sizes and two different shapes of siRNA-conjugated gold nanoconstructs (13 nm spheres, 50 nm spheres, and 40 nm starburst morphologies) to study the expression of isocitrate dehydrogenase and the in vitro response of U87 glioma cells to be evaluated (Zhan et al., 2018). Compared to 13 nm spheres, larger particles (50 nm spheres and 40 nm stars) showed higher cellular uptake, suggesting that the size and shape of the nanoconstructs affect both intracellular distribution and cellular uptake kinetics. A study investigating the penetration and localization of very small Au nanoparticles coated with tiopronin in the size range of 2-15 nm into breast cancer cells showed that the smaller nanoparticles accumulated in the tumor tissue of mice. HeLa cells were tested for the uptake of mesoporous silica nanoparticles of different diameters (280, 170, 110, 50, and 30 nm). 50 nm mesoporous silica nanoparticles were found to show the highest cellular uptake, indicating their suitability as drug carriers.

Drug Targeting Strategies

Most nanosystems will simply collect in a particular region and have a prolonged blood circulation time in vivo because of the balance between diffusion mechanisms and vascular haemodynamic factors. Chemotherapy frequently uses passive drug targeting because bloodstream-circulating nanoparticles can localise in tumour tissues due to their well-known increased permeability and retention properties. Tumour microvasculature anatomy is characterised by aberrant branching and larger interendothelial gaps, which are linked to the breakdown of the basement membrane and disruption of tight connections between endothelial cells.63 The wide spaces created by these endothelial cells allow particles to pass through. material seeping into the tumour from the nearby blood vessels. In contrast to the vasculature of healthy tissues, the weakly differentiated vasculature of immature tumours has pore diameters of less than 400 nm, which allows for the extravasation and selective accumulation of nanoparticles in the tumour interstitium through passive targeting mechanisms. to the resulting isolated nanoparticle ions.It is crucial to remember that the effects of increased permeability and retention are highly variable and might differ significantly between patients and tumours.66 Consider the fact that even while examining a single tumour model, there are several variations. in the permeability of the veins. For example, particles with a diameter of more than 200–300 nm may escape, yet in another section of the same tumor, molecules merely a few nanometers in size may have trouble passing through the interstitium.

Anticancer Activities

Clinically authorised anticancer medications are transferred via nanocarrier systems (NCs), which are engineered to address drug solubility issues, enhance circulation times, and facilitate controlled drug release. Furthermore, active targeting or passive (EPR impact) encourage medication accumulation at the tumour location. This finding demonstrates the safety of artificial nanoparticles in terms of size and physical characteristics as well as their potential applications in the treatment of cancer.

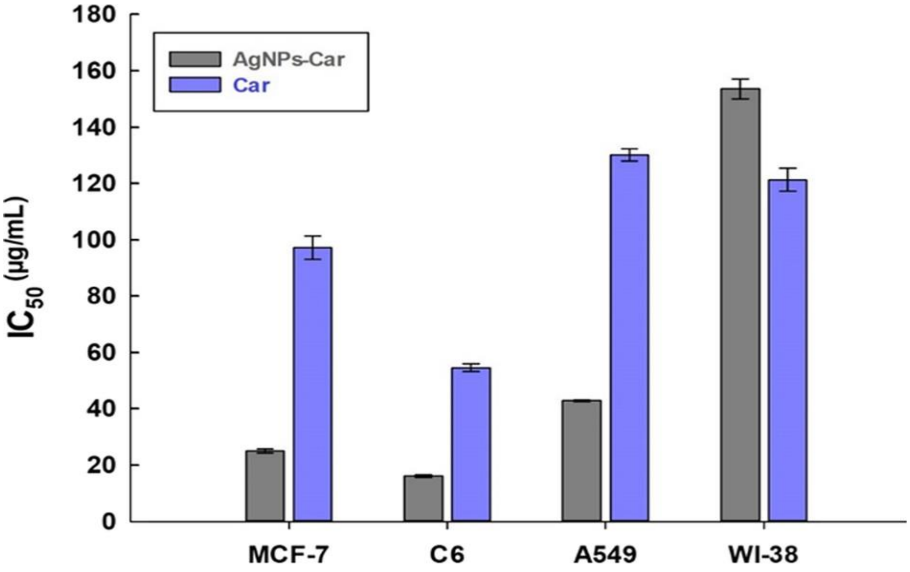

Figure 3: IC50 Results of the AgNPs-Car and Carboplatin

On the other hand, compared to carboplatin alone, AgNPs-Car demonstrated greater activity in all cancer cells, resulting in lower IC50 values and higher cell viability (Figure 3). By measuring the SI index, we were able to determine that AgNPs-Car was more effective in the C6 cell line than in other cancer cells. The low toxicity of AgNPs-Car in the healthy WI-38 cell line is another important advantage.

Table 1: Application of Other Forms of Nanoparticles in Cancer Therapy

Nanoparticle	Cancer Type	Application
miRNA	Colorectal cancer (CRC)	It is a circulating biomarker that can be utilised for CRC early diagnosis (in vitro).
Raman-active nanoprobe (RAN)	Circulating cancer stem cells (CCSCs)	enhanced imaging to identify cancer cells utilising the Raman imaging technique
Fumed silica nanoparticles	Detecting cancer pathways	For more accurate cancer detection, nanoparticles can bind to multi-site phosphorylated peptides.

These nanoparticles' functionality is determined by their size, kind, and structure. After talking about the most prevalent kinds of nanoparticles, it is evident that there are a variety of other nanoparticles, like amino acid and semiconductor nanoparticles, which differ greatly from typical particles. This is shown in the table below. Nanorobots may also be used in the detection and treatment of cancer. Because of their small size and ability to interface with cell membranes, nanorobots—controlled devices composed of components at the nanoscale offer a direct line of communication with cells. By administering cutting-edge biomedical therapies with less intrusiveness, nanorobots can increase the effectiveness of treatment. Furthermore, 12 different types of cancer cell detection is currently possible with nanorobots. The impact of nanoparticles on different forms of cancer cells, including brain tumors, liver cancer, pancreatic cancer, bladder cancer, colon cancer, glioblastoma and melanoma, neuroblastoma, breast, cervical, lung, prostate, and oral squamous cell carcinoma. Table 1 provides an overview of the uses of different kinds of nanoparticles in cancer treatment.

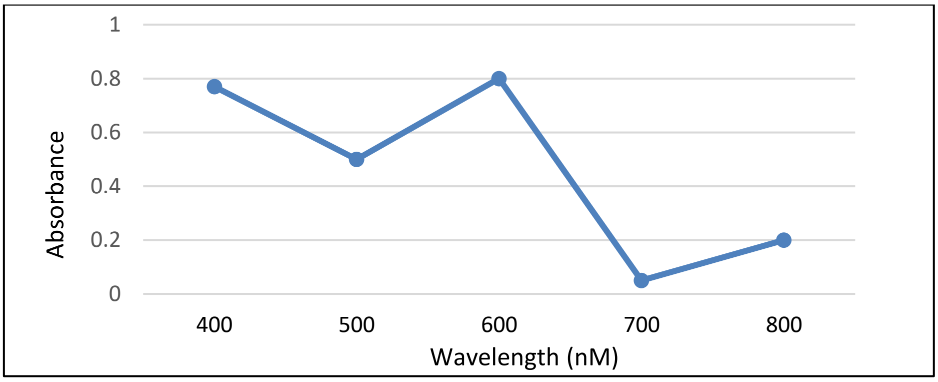

Figure 4: TEM Scans Revealed that AuNPs

The AuNPs' uniform size, low aspect ratio, and good monodispersity were revealed by TEM scans. The UV-Vis spectrum displayed a distinctive absorption peak at 520 nm, and the narrow spectral bandwidth demonstrated the monodisperse condition of the AuNPs (Figure 4).

4 CONCLUSION

Based on our research, it appears that synthetic AgNPs and AgNPs-Car hold great potential as treatments for a variety of malignancies, including brain tumors. When tested on cancer cell lines, AgNPs and AgNPs-Car had anticancer effects that altered the mechanism of death. Furthermore, studies using AgNPs and AgNPs-Car against both Gram-positive and Gram-negative bacteria demonstrated their potent antibacterial properties. medications can be more precisely delivered to the infection site by conjugating silver nanoparticles, which have been shown to have antibacterial activity, with the medications. The employment of drug-loaded AgNPs also presents a significant opportunity to address the escalating microbial resistance problem. Many pharmaceutical uses, such as antibacterial and anticancer treatments, are possible with AgNPs and AgNPs-Car. AgNPs and AgNPs-Car safety aspects require more research to be elucidated.

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