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An updated review on Emerging recent advances and biomedical application of silver nanocluster

Vaibhavi Vijay Kshatriya*, Manoj Ramesh Kumbhare, Shraddha Vikas Jadhav, Prajakta Jaywant Thorat, Rushikesh Gajanan Bhambarge

Department of Pharmaceutical Chemistry, S.M.B.T. College of Pharmacy, Affiliated to Savitribai Phule Pune University, Dhamangaon, Nashik, M.S. India-422403

***Address for Correspondence:** Department of Pharmaceutical Chemistry, S.M.B.T. College of Pharmacy, Affiliated to Savitribai Phule Pune University, Nandi-Hills,Dhamangaon,Tal-Igatpuri, Dist-Nashik, M.S., India-422403
Email: vaibhavikshatriya5086@gmail.com
Contactno.+91-9762755260

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Abstract Silver nanoclusters (AgNCs) have emerged as versatile nanomaterials with immense potential in theranostic applications, combining therapeutic and diagnostic functions in a single platform. This review provides a comprehensive overview of recent advancements in the synthesis, characterization, and utilization of AgNCs for theranostics. The synthesis of AgNCs has witnessed significant progress, with numerous strategies such as chemical reduction, green synthesis, and templated approaches being employed to control size, shape, and stability. Their unique optical properties, including strong fluorescence and surface-enhanced Raman scattering (SERS) signals, make AgNCs ideal candidates for bioimaging and diagnostic purposes. Additionally, the surface chemistry of AgNCs allows for facile functionalization with targeting ligands and therapeutic agents, enhancing their specificity and efficacy. In the realm of diagnostics, AgNCs have been employed for various imaging modalities, including fluorescence imaging, photoacoustic imaging, and SERS-based sensing. Their excellent photostability and biocompatibility make them suitable for in vitro and in vivo imaging applications, enabling the real-time monitoring of disease progression and treatment response.

Keywords Silver nanoclusters, theranostics, bioimaging, biosensors, targeted therapy, personalized medicine, nanomedicine

Introduction

Atomically precise metal nanoclusters (NCs) are extremely small particles with core dimensions below 2 nm, positioned between the atomic scale and plasmonic metal nanoparticles.[1-7] These metal NCs possess remarkably distinctive electronic and optical characteristics, such as energy gaps reminiscent of molecules, robust photoluminescence (PL), and excellent catalytic capabilities. Noble metal NCs, in particular, have garnered significant attention in the scientific community due to their unique structures and their potential for diverse applications. To prevent aggregation and facilitate the isolation of specific Au and Ag NCs, organic ligands like thiolates, phosphines, and alkynyls are typically employed to cover their surfaces. These ligands not only impact the formation processes of Au and Ag NCs but also play a critical role in determining their sizes, shapes, and ultimate

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properties.[8-15]

Nanotechnology has emerged as a transformative field with diverse applications across various domains, and the development of nanomaterials has been at the forefront of these advances. Among the myriad of nanomaterials, silver nanoclusters (AgNCs) have garnered substantial attention due to their unique size-dependent properties and versatile applications. AgNCs represent a class of nanoscale silver particles with a size typically ranging from a few to several tens of atoms. Their distinctive electronic and optical properties, along with their tunable size and shape, make them particularly intriguing for researchers in disciplines ranging from materials science and chemistry to biomedicine and electronics.

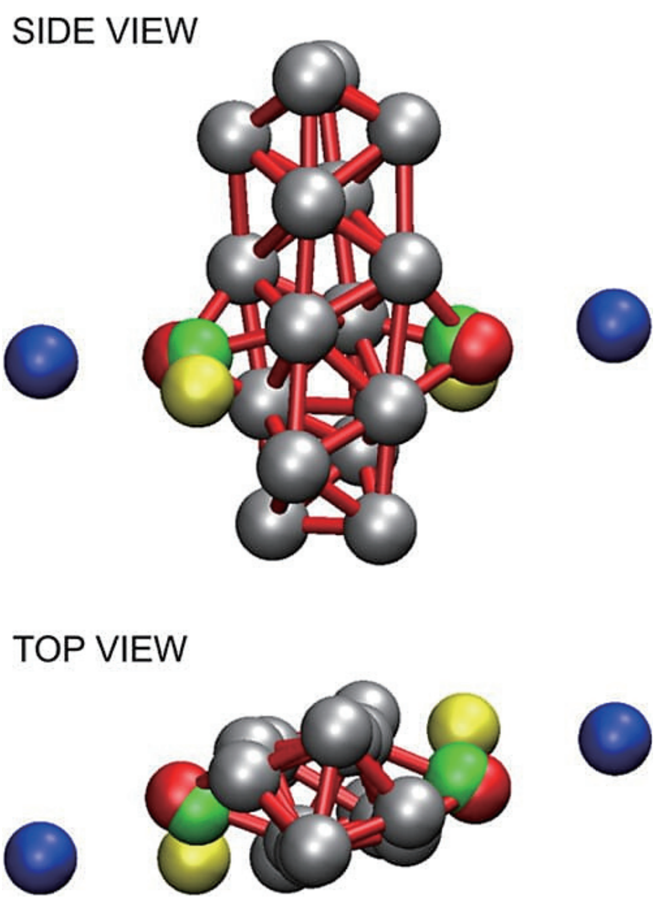

Figure 1: Structure of silver nanocluster

Among the noble metal nanoclusters explored to date, silver nanoclusters (Ag NCs) are particularly appealing due to their distinctive physical attributes, including strong luminescence and extremely small size. These characteristics offer promising platforms for constructing luminescent probes for applications in bio-imaging and sensing.[16] Nevertheless, silver in its zero-valent state is more reactive and prone to oxidation compared to gold. This increased reactivity makes the preparation and study of Ag NCs more challenging when compared to the extensively investigated gold counterparts. Therefore, the availability of high-quality Ag NCs with precisely defined size, structure, and surface characteristics is essential for both fundamental scientific research and practical applications.

The synthesis and study of AgNCs have experienced significant advancements in recent years, enabling precise control over their structural attributes. Various synthesis methods, including chemical reduction, ligand-assisted growth, and template-directed approaches, have been developed to tailor the size, shape, and surface chemistry of AgNCs. These advances have unlocked numerous possibilities for harnessing AgNCs in a wide array of applications .

One of the most remarkable features of AgNCs is their exceptional optical properties. These nanoclusters exhibit size-dependent absorption and fluorescence, giving rise to intense and tunable photoluminescence, which has found applications in areas such as bioimaging, sensing, and optoelectronics. Their strong fluorescence emission, coupled with high photostability, has made AgNCs valuable tools for cellular and molecular imaging, enabling researchers to explore biological processes at the nanoscale with remarkable precision.

In addition to their optical characteristics, AgNCs possess excellent catalytic and antimicrobial properties, making them suitable candidates for catalysis, environmental remediation, and combatting microbial infections. Their capacity to generate reactive oxygen species (ROS) under light irradiation has paved the way for the development of photodynamic therapy (PDT) platforms, offering a non-invasive and targeted approach to cancer treatment.[17]

Lately, numerous effective methods have emerged for producing silver nanoclusters (Ag NCs) with customizable physical and chemical characteristics, and in quantities suitable for practical use. By carefully designing synthesis approaches like direct reduction, chemical etching, and ligand exchange, well-established processes can be employed to craft high-quality Ag NCs with novel and sometimes unprecedented properties. Additionally, various techniques such as UV-vis absorption spectroscopy, photoluminescence emission spectroscopy (PL), electrospray ionization mass spectrometry (ESI-MS), and single crystal X-ray crystallography (SC-XRD) have been employed to analyze the physical and chemical properties and elucidate the complete structures of

Ag NCs, establishing a central avenue of research in the field of nanoscience.[18] The precise atomic-level structures of Ag NCs allow for an exploration of the relationship between their structure and properties, potentially leading to performance enhancements. Among the crucial spectroscopic characteristics, luminescence stands out as particularly valuable in biological applications. Recent reports have highlighted the tunable photoluminescent properties of Ag NCs achieved by controlling the core size and the type of ligands over the past five years.[19,20]

This introduction sets the stage for a comprehensive exploration of silver nanoclusters, delving into their synthesis, structural properties, unique optical features, and their myriad applications across various scientific disciplines. As researchers continue to unravel the potential of AgNCs, it becomes increasingly evident that these nanoscale silver entities hold the key to unlocking innovative solutions in nanotechnology, biomedicine, and beyond. Hence, this review article places its primary emphasis on delivering an extensive examination of both the production and practical use of silver nanoclusters (Ag NCs).

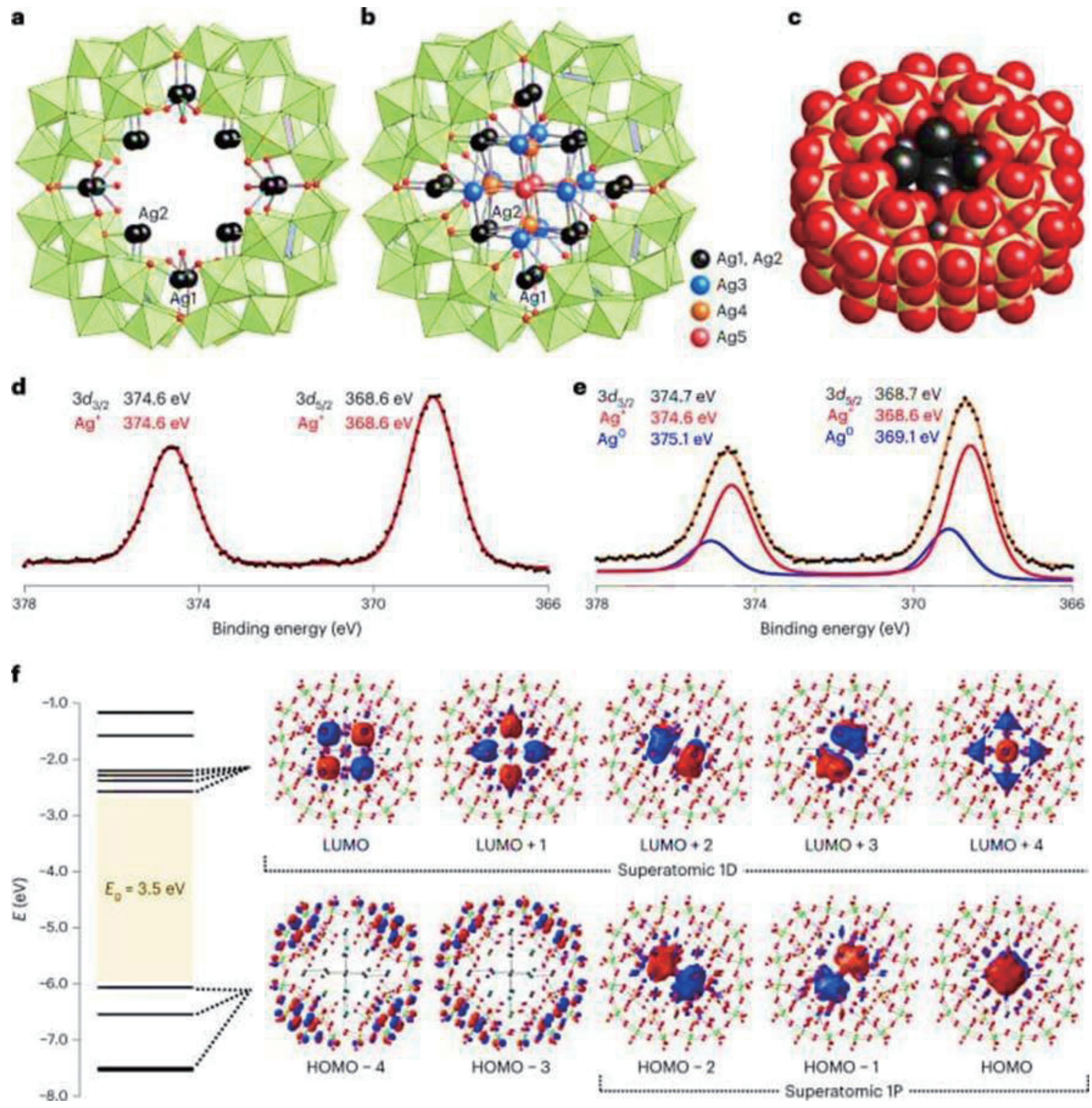

Figure 2: Binding energy of Silver nanocluster

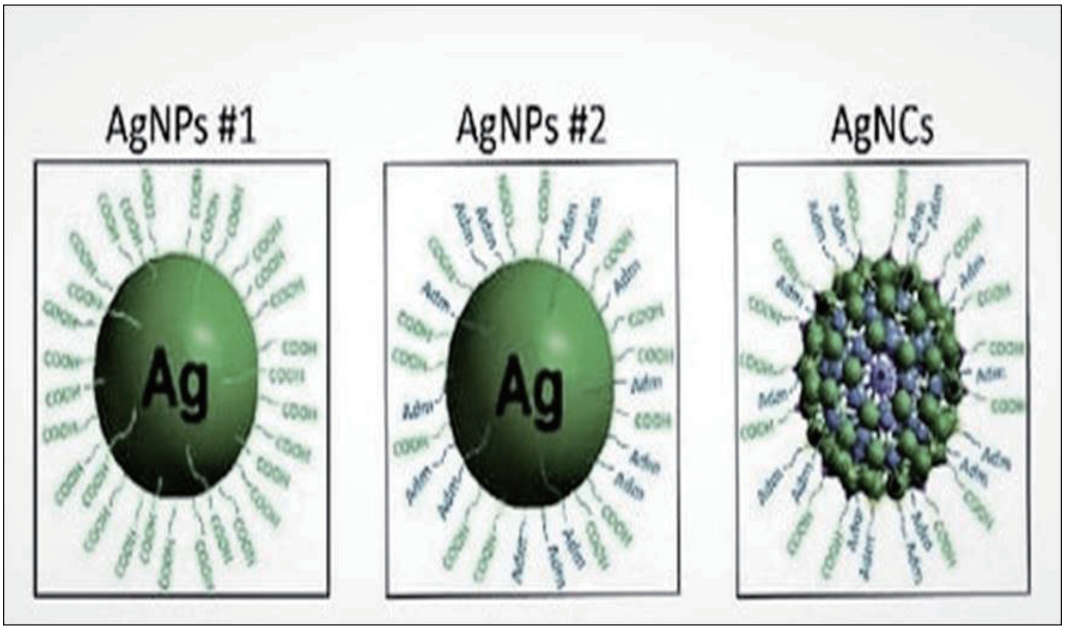

Figure 3: Silver nanoparticle forming nanocluster

Synthesis of Silver Nanoclusters

When compared to the synthesis of gold nanoclusters (Au NCs), crafting silver nanoclusters (Ag NCs) is a more intricate process because of their heightened sensitivity to environmental conditions in solution. Consequently, achieving precise control is essential to generate Ag NCs with well-defined compositions. Recent reports have documented successful endeavors in this regard. Various characterization techniques, including laser desorption ionization (LDI), matrix-assisted laser desorption ionization (MALDI), electrospray ionization (ESI) mass spectrometry (MS), single crystal X-ray crystallography (SC-XRD), and post-synthesis separation methods like size exclusion chromatography (SEC) and polyacrylamide gel electrophoresis (PAGE), are employed to ascertain the compositions and structures of Ag NCs. The synthesis of Ag NCs can be broadly categorized into three main methods: direct reduction of silver precursors in the presence of specific ligands, chemical etching, and post-synthetic ligand exchange.[21,22]

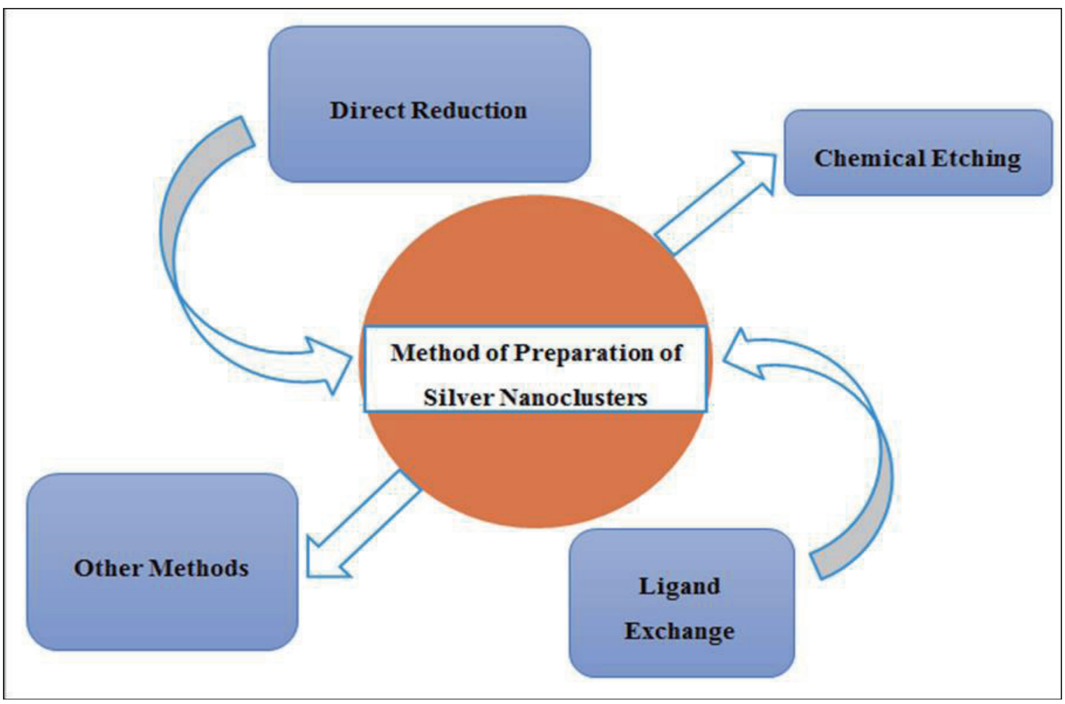

Figure 4: Method of Preparation of Silver Nanoclusters

Direct Reduction

The direct reduction method has proven effective for synthesizing silver nanoclusters (Ag NCs) in both organic and aqueous solutions. This synthetic process involves the rapid growth of intermediate Ag NCs through reduction, followed by a gradual refinement of their size to achieve monodisperse Ag NCs within a reducing agent. Typically, NaBH4 serves as the common reducing agent for the synthesis of Ag NCs, and it can be used alongside various ligands like thiolates, alkynyls, DNAs, peptides, proteins, and polymers. Several Ag NCs, including thiol-protected and alkynyl-protected Ag NCs, have been successfully created using this method. However, NaBH4 is known for its rapid reduction kinetics, which can result in the formation of polydisperse Ag NCs. To counteract this, multiple approaches can be employed to slow down the reduction kinetics of NaBH4. For instance, adjusting the solution's pH, the concentration of reducing agents , and the choice of solvent can all be used to modulate NaBH4's reducing capability. Another efficient method for reducing the rate of Ag NC formation is to substitute NaBH4 with milder reducing agents like formic acid and DMF. Additionally, alternative techniques such as light, ultrasonication, and electrical means can also create a gentle reducing environment conducive to Ag NC formation.[23-25]

Chemical Etching

Some silver nanoclusters (Ag NCs) can also be generated using a chemical etching process, wherein relatively larger Ag nanoparticles (NPs) are selectively eroded to form smaller Ag NCs. Compared to the direct reduction method, there have been fewer successful attempts reported for the chemical etching process. This is primarily because the latter method is generally more time-consuming and often yields Ag NCs in lower quantities. However, these limitations can be mitigated to some extent by optimizing the etching conditions, including factors like etching duration, reaction temperature, and the ratio of etching agent to Ag precursors. An effective synthesis approach necessitates a gentle etching environment that enables controlled Ag NC formation within the reaction mixture.[26-28]

For example, one approach involved an interfacial etching process, where initially prepared Ag nanoparticles (Ag@(H_2MSA) NPs) were digested to produce two luminescent Ag NCs protected by mercaptosuccinic acid (H_2MSA). During the reaction, Ag@(H_2MSA) NPs served as starting materials and evolved into a mixture of Ag_8 and Ag_7 NCs in an aqueous-organic biphasic system. This mixture was subsequently separated using gel electrophoresis. Another instance entails the synthesis of red luminescent Ag_{38} NCs through the etching of large citrate-protected Ag@citrate NPs by introducing an excess of mercaptosuccinic acid.

Ligand Exchange

In recent years, the process of inducing size and structure transformation through ligand exchange has gained significant importance. Peripheral organic ligands play a crucial role in determining factors such as nuclearity, geometry, bonding, and electronic transitions within metal nanoclusters. Depending on the specific metal nanocluster being studied, ligand exchange can be partial or complete, and it may or may not affect the metal core itself.

In 2014, Bakr and their colleagues introduced a method for rapidly and completely exchanging thiolate ligands with other thiolates in $Ag_{44}(SR)_{30}$ clusters. Subsequently, they also discovered that the ligand exchange process can efficiently and directly convert $Ag_{35}(SG)_{18}$ clusters (where SG represents glutathionate) into $Ag_{44}(4\text{-FTP})_{30}$ clusters (with 4-FTP being 4-fluorothiophenol), while the reverse transformation occurs slowly and involves intermediate cluster sizes.[29,30]

Other Methods

Alternative approaches for synthesizing silver nanoclusters (Ag NCs) include conducting the reactions in solid-state conditions or within a gel medium. For instance, the Pradeep research group devised a method for producing red-emitting $Ag_9(H_2MSA)_7$ nanoclusters using a solid-state approach . This method is also capable of synthesizing other types of thiolated Ag NCs, including $Ag_{32}(SG)_{1956}$ and $Ag_{152}(PET)_{60}$ (where PET stands for phenylethanethiol), as well as selenolate-protected $Ag_{44}(SePh)_{30}$ NCs. Furthermore, Chakraborty and colleagues employed a gel-based approach to form thiolated $Ag_{25}(SG)_{18}$ NCs with intense red luminescence. Detailed information on the synthesis of Ag NCs can be found in recent reviews.[31-33]

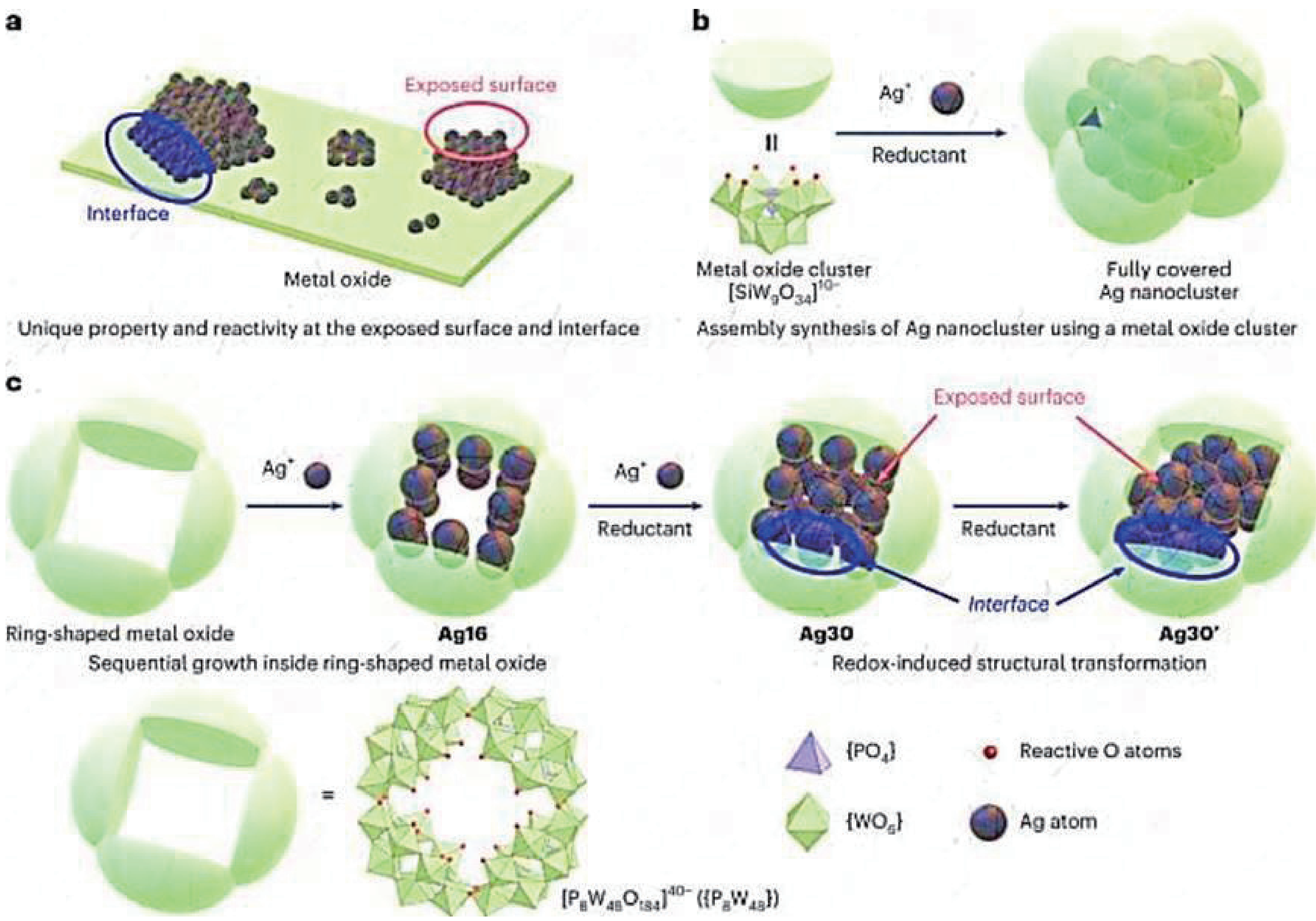

Figure 5: Synthesis of AgNCs using metal oxide cluster

Properties of Silver Nanoclusters

Table 1: Properties of Silver Nanoclusters

Properties	Description
UV-Visible absorption	It is prominently feature the phenomenon known as surface plasmon resonance (SPR), which is characterized by distinctive optical absorption patterns
Photoluminescence	Photoluminescence of silver nanoclusters refers to the emission of light when silver nanoparticles or nanoclusters are exposed to external light sources, such as ultraviolet (UV) or visible light.
Fluorescence's	Fluorescence in silver nanoclusters is a specific type of photoluminescence characterized by the emission of light of longer wavelengths (lower energy) after the absorption of photons from a higher-energy source, such as ultraviolet (UV) or blue light.
Structural	Structural properties in silver nanoclusters refer to the physical and chemical characteristics that define the arrangement of silver atoms within these nanoscale materials.
Biological	The biological properties of silver nanoclusters refer to their interactions with biological systems, including living organisms and biological molecules. These properties are of particular interest due to the potential applications of silver nanoclusters in various fields, including medicine and biology.

UV-Visible absorption

The UV-visible absorption spectra of silver nanoparticles (Ag NPs) prominently feature the phenomenon known as surface plasmon resonance (SPR), which is characterized by distinctive optical absorption patterns as shown in Table 1.[34-36] Typically, the SPR peak for Ag NPs appears around 400 nm. In contrast, silver nanoclusters (Ag NCs) exhibit several discernible absorption peaks within the UV-visible range. These distinct optical absorption profiles of Ag NCs and Ag NPs originate from different factors and are located at different wavelengths. Such spectral data can serve to validate the successful synthesis of Ag NCs and the transformation of small Ag NCs into larger plasmonic Ag NPs. Alterations in the protective ligands and cluster size, both of which influence behavior in the excited state, lead to changes in electronic transitions.[37]

Photoluminescence

Photoluminescence (PL) is an exceptionally captivating property of nanomaterials due to its wide range of potential applications. When silver nanoclusters (Ag NCs) are excited from their ground state, they release excess energy as they return to their ground state, resulting in PL. However, Ag NCs typically exhibit low quantum yield (QY), and there are still unresolved questions regarding the fundamental aspects of their PL properties. Several factors influence the PL of Ag NCs, including their cluster size, the type of protective ligands, and the presence of heterometal atoms. Additionally, the PL behavior is highly sensitive to factors such as the number of valence electrons, the oxidation state of the metal, crystal structure, temperature, and pH, all of which play essential roles in regulating the PL characteristics.[38-40]

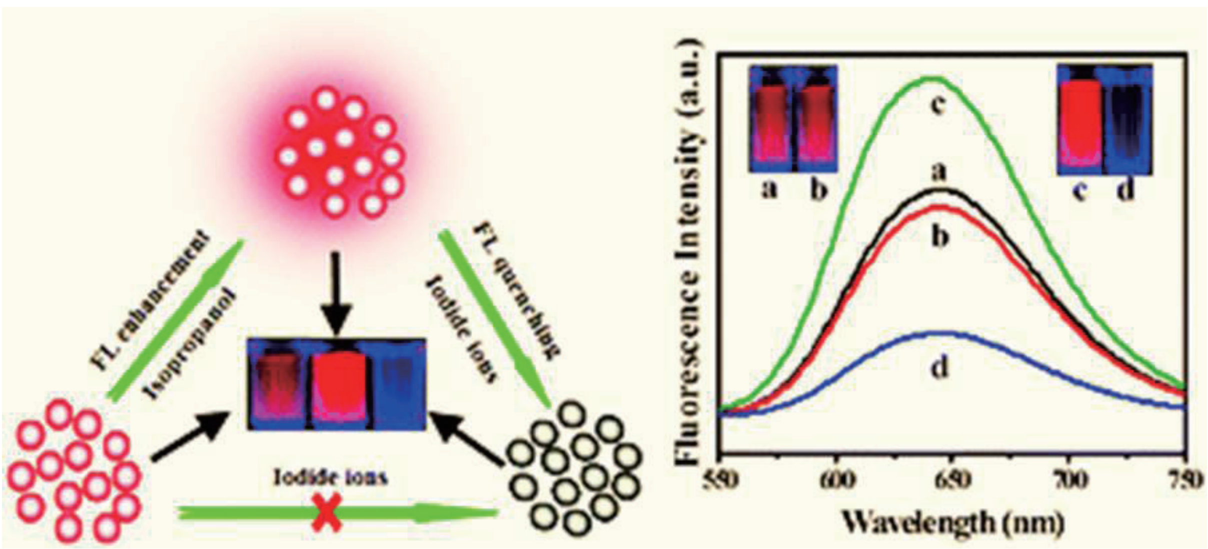

Figure 6: UV absorption of AgNCs

Fluorescence's

Fluorescence is an intriguing property of silver nanoclusters (Ag NCs) that has garnered significant attention in the field of nanomaterials and nanophotonics. These clusters exhibit unique and tunable fluorescence properties, making them promising candidates for various applications.[40-45]

1. Size-Dependent Fluorescence

The fluorescence properties of Ag NCs are highly dependent on their size and structure. As the size of the nanocluster changes, so does its fluorescence emission wavelength. This size-dependent fluorescence is a result of quantum confinement effects, where the confinement of electrons and holes within the nanocluster leads to discrete energy levels and, consequently, specific emission wavelengths. This tunability in emission makes Ag NCs versatile for applications in fluorescence-based sensing and imaging.

2. Intense Emission

Ag NCs are known for their intense and sharp fluorescence emission, which is often characterized by a narrow emission peak. This high brightness is

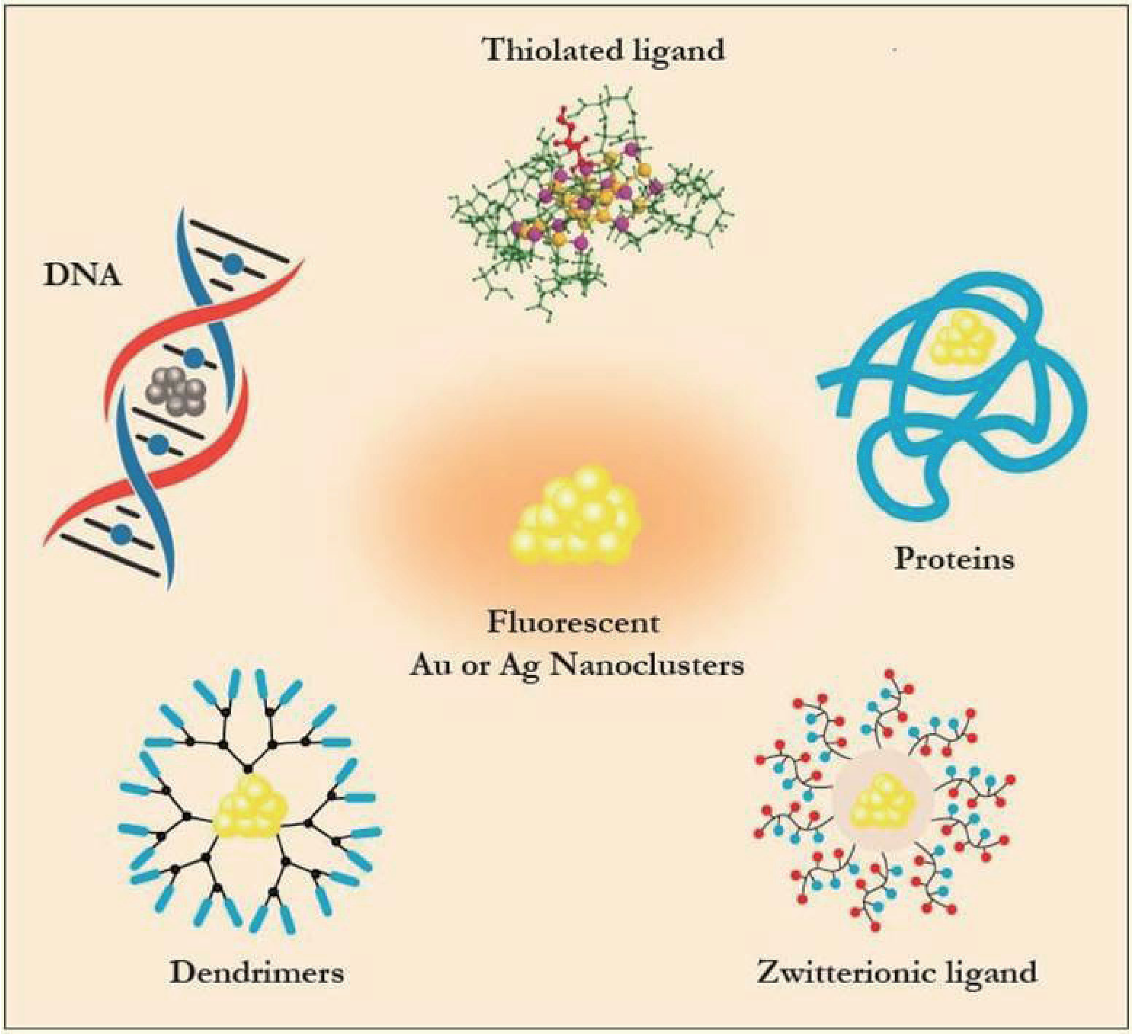

Figure 7: Fluorescence of AgNCs

advantageous for fluorescence-based assays and bioimaging, where strong signals are desirable for detecting and tracking biomolecules and cellular structures.

3. Photostability

Silver nanoclusters exhibit remarkable photostability, meaning they can emit fluorescence for extended periods without suffering from photobleaching or degradation. This property is especially valuable for long-term imaging and tracking experiments, as it ensures the reliability of fluorescence signals over time.

4. Environment Sensitivity

Ag NC fluorescence is highly sensitive to its local environment, including factors like temperature, pH, and the presence of specific molecules or ions. This sensitivity can be harnessed for sensing applications, where changes in the environment result in measurable shifts in the fluorescence emission spectra of Ag NCs.

5. Biocompatibility

Ag NCs can be easily functionalized with biocompatible ligands, allowing them to be used in biological applications. Their small size and excellent fluorescence properties make them suitable for labeling and imaging various biological structures and processes, both in vitro and in vivo.

6. Versatile Applications

Due to their unique fluorescence properties, Ag NCs have found applications in diverse fields such as biological imaging, sensors for environmental monitoring and disease diagnosis, and materials science. They are also being explored for use in optoelectronic devices and as components in nanoscale photonic systems. In summary, the fluorescence properties of silver nanoclusters make

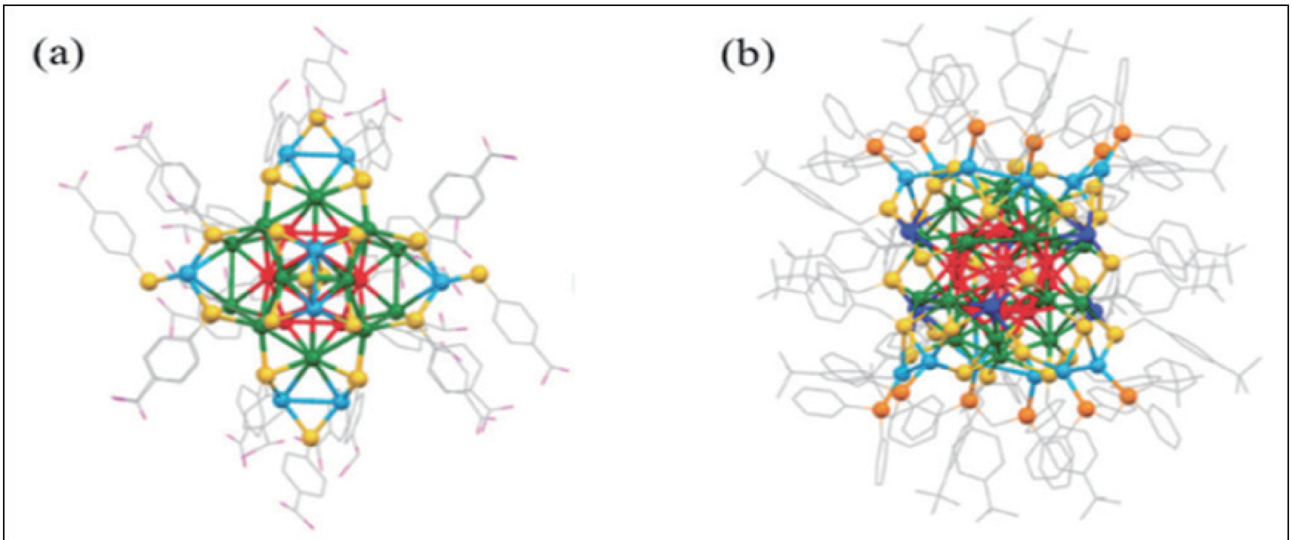

Figure 8: Crystal structures of the $Ag_{44}(SPhCO_2H_2)_{30}$ and the $Ag_{50}(TBBM)_{30}$-$(dppm)_6$ nanoclusters (Copyright 2017, American Chemical Society)

them a fascinating and valuable class of nanomaterials. Their tunable emission, high brightness, photostability, and sensitivity to environmental changes enable a wide range of applications, from advanced imaging techniques to cutting-edge sensing technologies.

Structural

Silver nanoclusters (Ag NCs) exhibit a fascinating array of structural properties that are closely related to their size, composition, and ligand environment. Understanding these properties is crucial for tailoring their behavior and applications.[46-50]

1. Size-Dependent Structures

One of the most prominent structural properties of Ag NCs is their size-dependent atomic arrangement. As the number of silver atoms in the cluster changes, the arrangement of these atoms can transition from compact to hollow structures or even from planar to three-dimensional geometries. For example, Ag25(SG)18 nanoclusters, where SG represents glutathionate, exhibit a well-defined icosahedral geometry with a central Ag13 core surrounded by a shell of Ag12 atoms.

2. Ligand-Induced Structures

The choice of ligands can significantly influence the structural properties of Ag NCs. Organic ligands not only stabilize the clusters but can also dictate their shapes. For instance, thiolate ligands can lead to the formation of symmetric and well-defined structures, while different ligands might induce distinct cluster geometries.

3. Lattice Imperfections

Ag NCs can also possess lattice imperfections, such as stacking faults, vacancies, or twinning, which affect their electronic and optical properties. These imperfections can arise due to growth processes or ligand-induced effects, and they contribute to the unique properties of individual Ag NCs.

4. Core-Shell Structures

Some Ag NCs exhibit core-shell structures where a silver core is surrounded by a layer of ligands. The core-shell architecture can lead to interesting optical and electronic properties. For example, Ag2(SR)2 nanoclusters consist of a silver dimer core protected by two thiolate ligands.

5. Surface Atoms

The properties of Ag NCs are often dominated by their surface atoms. These atoms have a high surface-to-volume ratio, leading to unique chemical reactivity and optical behavior. Surface atoms play a crucial role in the interaction of Ag NCs with other molecules and materials.

6. Chirality

Some Ag NCs can exhibit chirality, which is a structural property related to their handedness. Chiral Ag NCs have been of particular interest due to their potential applications in chiral sensing and catalysis.

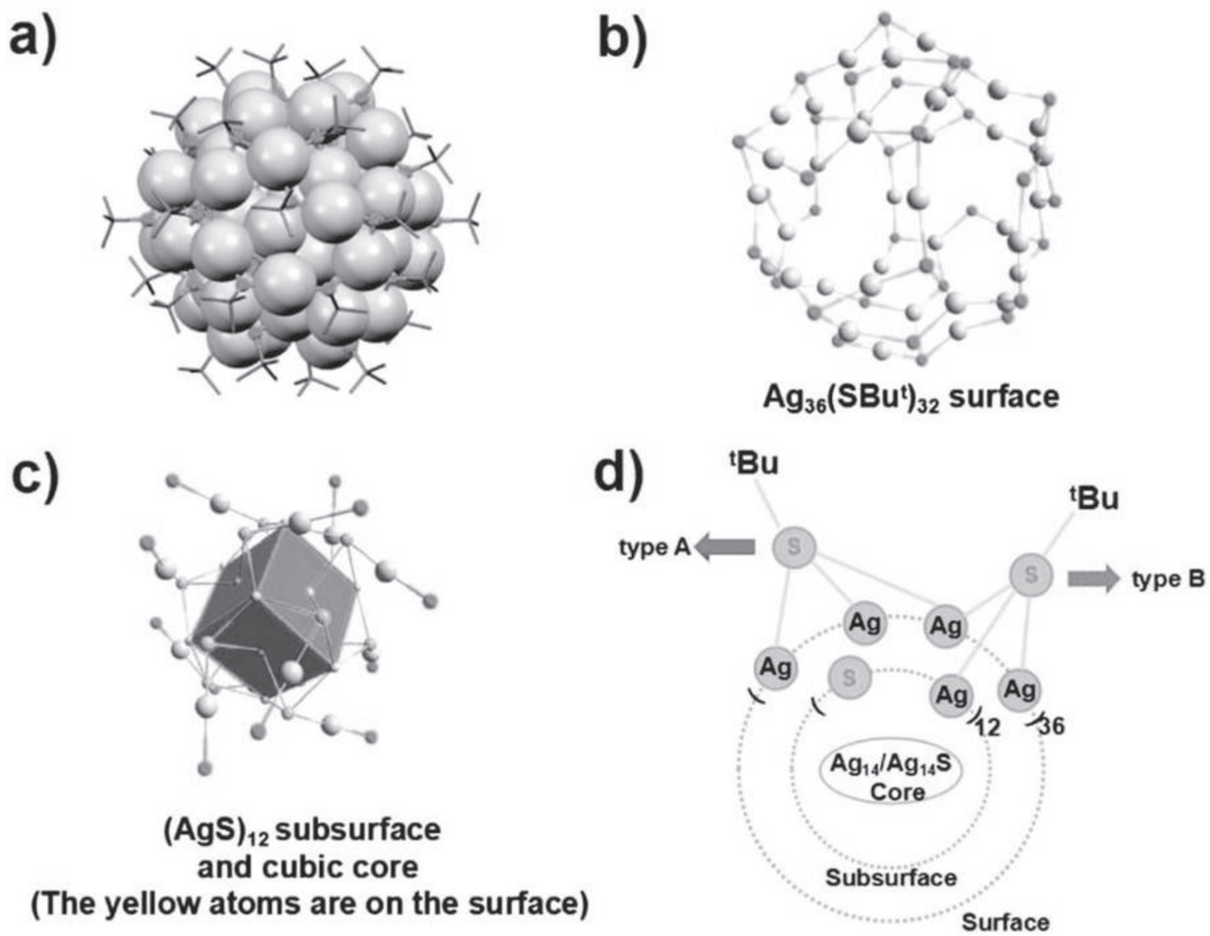

Figure 9: Surface structure of AgNCs

Biological

Silver nanoclusters (Ag NCs) have garnered significant interest in the field of biomedicine and biology due to their unique biological properties, including their biocompatibility, fluorescence, and potential therapeutic and imaging applications.[51-53]

1. Biocompatibility

Ag NCs are generally considered to be biocompatible, making them suitable for various biological applications. They exhibit low cytotoxicity and can be functionalized with biocompatible ligands, enabling their use in vivo and in vitro studies. For example, Ag NCs stabilized with bovine serum albumin (BSA) have been shown to be biocompatible and suitable for cellular imaging.

2. Fluorescence Imaging

Ag NCs exhibit strong and tunable fluorescence emission, making them valuable for biological imaging. Their fluorescence properties, including quantum yield and emission wavelength, can be controlled by adjusting the size and ligands of the nanoclusters. For instance, Ag2(SR)2 nanoclusters have been used for cellular imaging due to their bright and stable fluorescence.

3. Sensing and Detection

Ag NCs have been employed as biosensors for the detection of various biomolecules and ions. Their fluorescence properties are highly sensitive to changes in their local environment, allowing for the detection of specific analytes. Functionalized Ag NCs have been used for the detection of DNA, proteins, and metal ions in biological samples.

4. Drug Delivery

Ag NCs can serve as drug carriers for targeted drug delivery. Their small size and surface functionalization capabilities allow for the attachment of therapeutic agents, enabling controlled and targeted release. This property has potential applications in cancer therapy and other medical treatments.

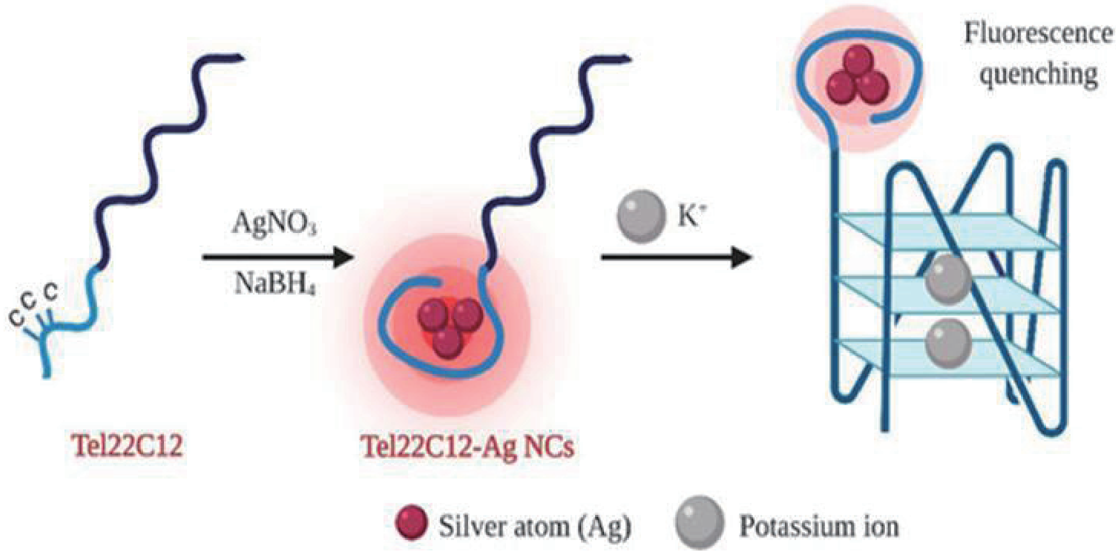

Figure 10: Illustration shows the working idea of Fluorescent –AgNCs

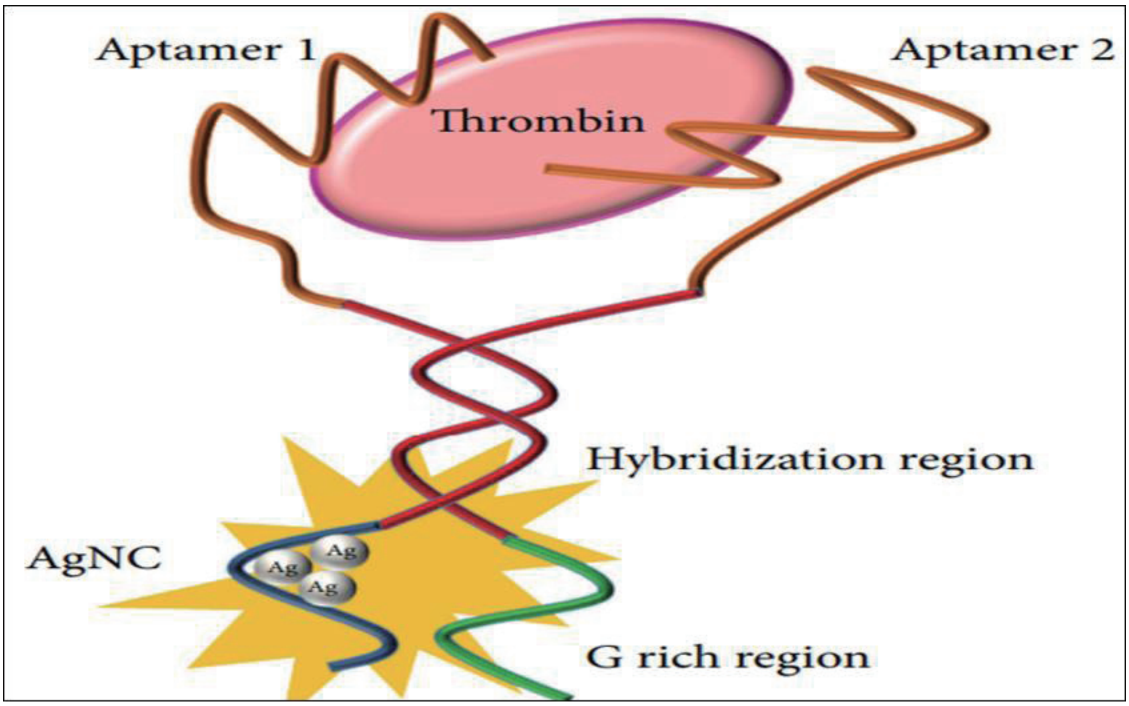

Figure 11: Principle of binding-induced fluorescence turn-on assay for protein detection

5. Antimicrobial Activity

Silver ions released from Ag NCs have intrinsic antimicrobial properties. Ag NCs have been investigated for their potential as antimicrobial agents to combat bacterial infections and as coatings for medical devices to reduce microbial contamination.

Application of Silver Nanoclusters

The figure 3 explained different application of silver nanocluster.[54,55]

Biomedical Application

The silver clusters readily engaged with single-stranded DNA, effectively stabilizing them in the conducted experiments. When interacting with

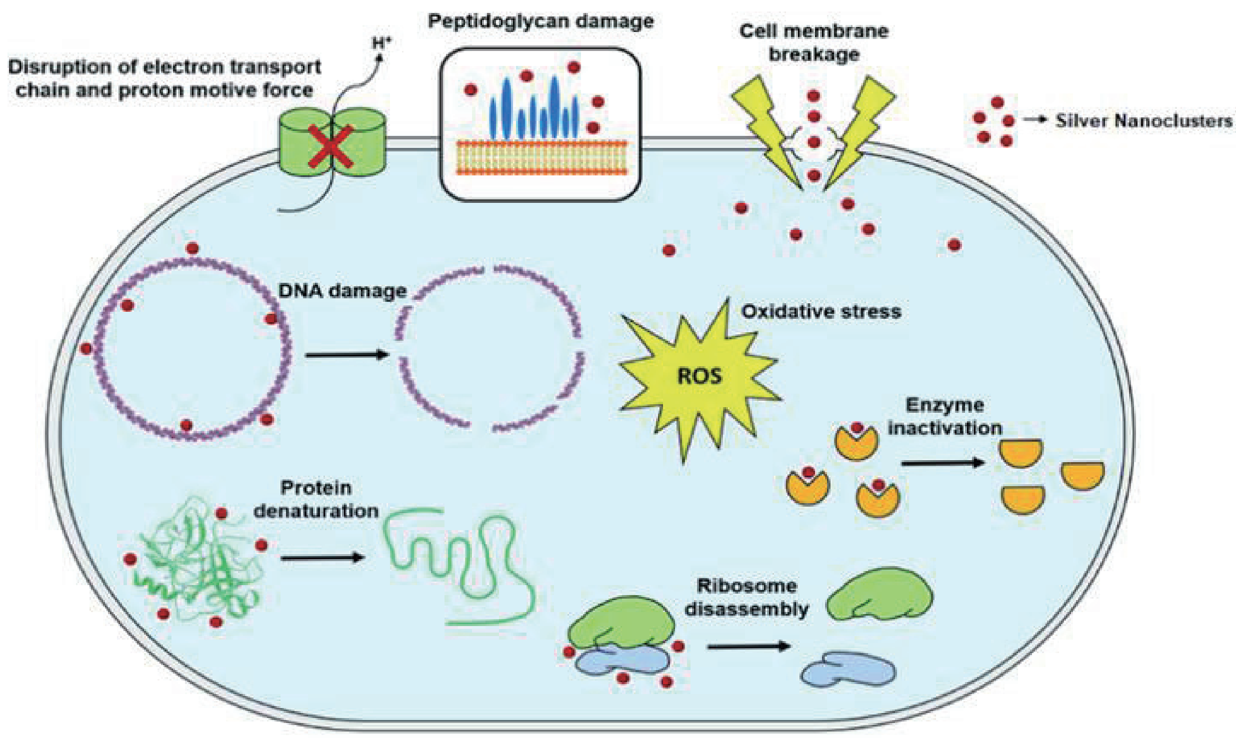

Figure 12: Mechanisms of AgNC antimicrobial activity

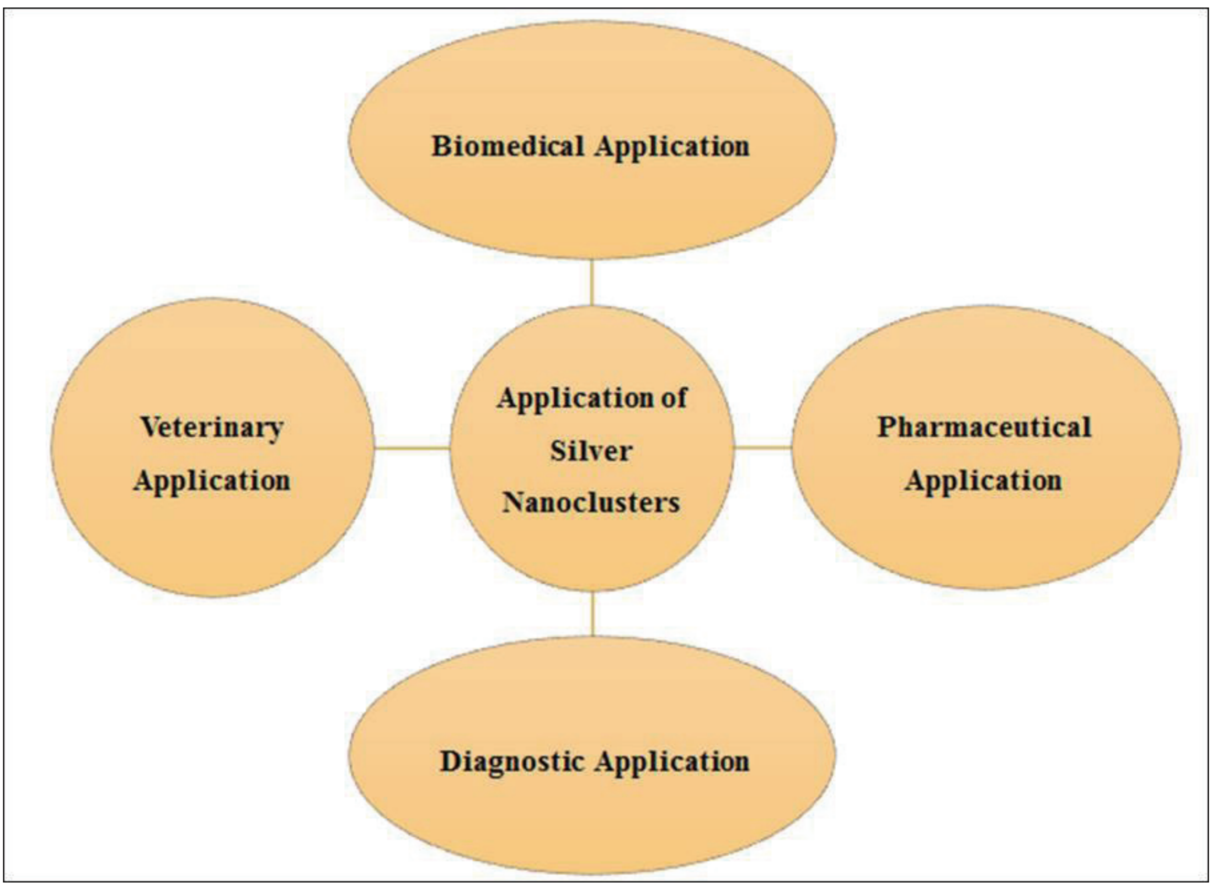

Figure 13: Application of Silver Nanocluster

rhodamine 6G, these structures formed self-assembled complexes that emitted light in the blue part of the spectrum. However, the presence of the fluorescent dye slightly diminished the inherent fluorescence of the clusters. Interestingly, this fluorescence was further diminished upon the introduction of melamine into the aqueous suspension, ultimately disrupting the self-assembled complex.[56]

A biosensor designed for the detection of a crucial RNA protein comprised two distinct sections of a DNA tetrahedral framework. These sections were composed of sequences of four nucleic acids (NAs), forming a scaffold that could be easily switched, along with a photo-induced electron-transfer pair serving as a fluorescence converter. When combined with an Ag cluster, this DNA complex, with or without the presence of the protein in question, produced fluorescence in a transduced manner following two distinct models. This innovative sensor enabled the detection of this specific protein, even within individual cells, for the purpose of diagnosing HIV.[57]

A novel approach for modulating the fluorescence intensity of silver nanoparticle aggregates using DNA has been employed to identify cases of hepatitis B virus in samples. The fluorescence intensity significantly amplified when multilayer complexes were formed between the nanoparticles and the target DNA, subsequently immobilizing the captured samples.

A hydrogel made from poly(ethylene glycol) that emits fluorescence was effectively utilized as a versatile foundation for highly sensitive microRNA detection. In this scenario, the introduction of Ag+ into the hydrogel triggered a significant cation exchange process while also promoting the hybridization of DNA strands. Notably, the hydrated hydrogel medium itself mitigated the risk of fluorescence quenching, streamlining the experimental setup.[58]

Another remarkably selective method for swiftly detecting microRNA in complex biological solutions harnessed the fluorescence properties of Ag nanoclusters. The response of these nanoclusters to the presence of microRNA was also observed to increase dramatically.

Furthermore, a bimetallic electrochemical autosensor was proposed, featuring an outer shell composed of gold nanoparticles that served as a conduit for transmitting signals from Ag nanoclusters to Au nanoclusters. This innovative sensor exhibited

Figure 14: Applications of Silver nanocluster

the capability for ultrasensitive and highly selective detection with a low detection threshold for two distinct types of microRNA, potentially indicative of sarcoma. The sensor platform incorporated a covalent-organic lattice constructed from nanowires, which was synthesized via the condensation of 1,3,6,8-tetra(4-carboxyphenyl)pyrene and melamine. Additionally, this lattice was utilized to capture single strands of DNA helices, with hybridization occurring alongside complementary probes targeting these microRNA variants.[59]

Pharmaceutical Application Antimicrobial Agents

One of the most well-established applications of AgNCs in pharmaceuticals is their use as antimicrobial agents. AgNCs exhibit potent antimicrobial properties against a broad spectrum of microorganisms, including bacteria, viruses, and fungi. This capability stems from AgNCs' ability to release silver ions, which disrupt microbial cell membranes, interfere with DNA replication, and induce oxidative stress in microbes. AgNCs have been incorporated into pharmaceutical formulations to develop effective antimicrobial agents. For example, researchers have demonstrated the use of AgNCs in wound dressings to prevent and treat bacterial infections. Additionally, AgNCs have been employed in the development of antimicrobial coatings for medical devices, reducing the risk of healthcare-associated infections.[60]

Drug Delivery Systems

AgNCs have shown immense potential as drug delivery systems in the pharmaceutical industry. Their small size, high surface area, and ability to carry various payloads make them suitable candidates for encapsulating and delivering drugs to specific target sites AgNCs can enhance the stability and bioavailability of pharmaceutical compounds, improving their therapeutic efficacy while minimizing side effects. In a study by Sengupta et al., silver nanoparticles, including AgNCs, were utilized as drug carriers for the delivery of antimicrobial agents. The researchers demonstrated the synergistic potential of AgNCs in combination with pharmaceutical compounds, highlighting their role in enhancing drug delivery systems.[61]

Cancer Therapeutics

AgNCs have gained attention as potential tools in cancer therapeutics. Their unique properties make

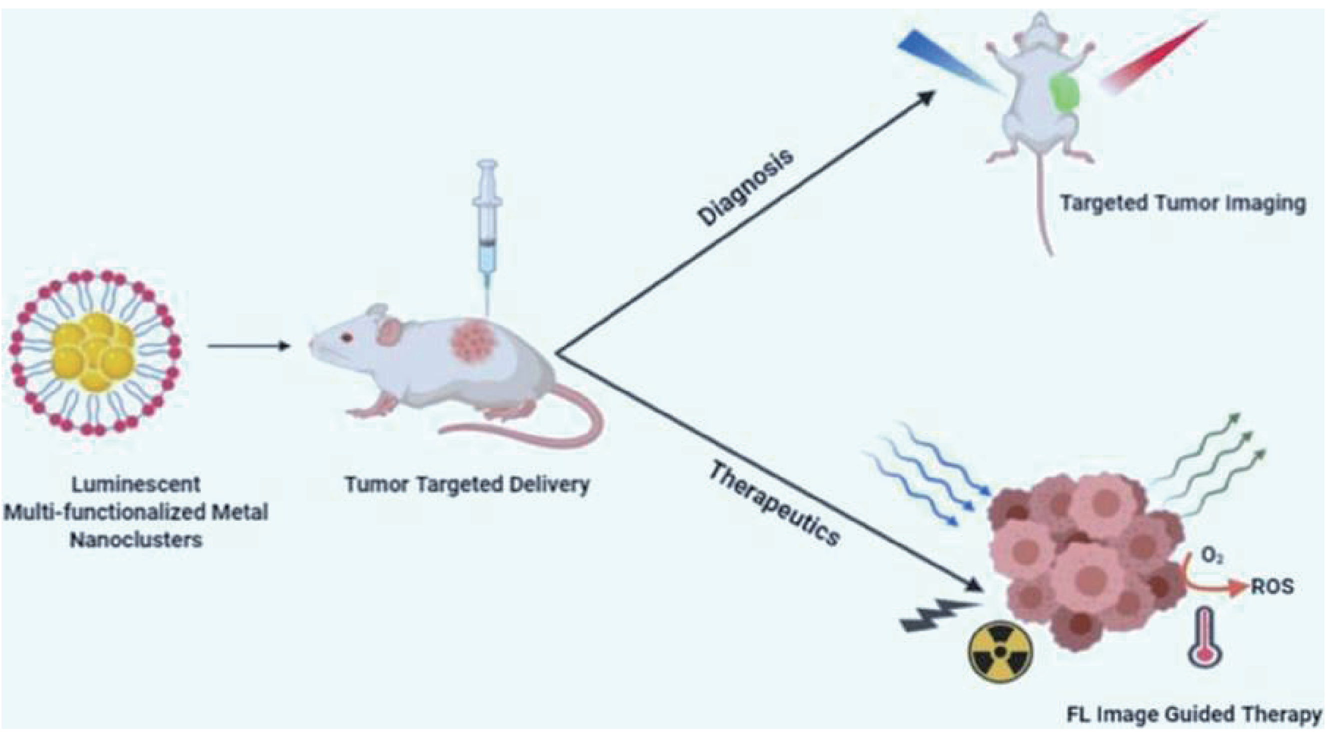

Figure 15: Cancer Therapy

them attractive candidates for selective cancer cell targeting and therapy. AgNCs can be designed to preferentially accumulate in tumor tissues, allowing for the specific destruction of cancer cells while sparing healthy ones. In addition to targeted drug delivery, AgNCs have been explored for their photothermal therapy applications. When exposed to near-infrared light, AgNCs can absorb the energy and generate heat, which can be used to selectively destroy cancer cells through hyperthermia.[62]

Anti-inflammatory Agents

The anti-inflammatory properties of AgNCs have opened up new possibilities in pharmaceutical research. Inflammation plays a crucial role in various diseases, including rheumatoid arthritis and inflammatory bowel disease. AgNCs can be incorporated into pharmaceutical formulations to alleviate inflammation and provide relief to individuals suffering from these conditions. Li et al. emphasized the anti-inflammatory potential of AgNCs in a review article, underlining their role in reducing inflammation in different disease contexts. This highlights AgNCs as promising candidates for the development of anti-inflammatory pharmaceutical products.[63]

Gene Delivery

AgNCs have shown promise as gene delivery vehicles, a crucial aspect of gene therapy in pharmaceutical applications. By functionalizing AgNCs, therapeutic genes can be loaded onto their surfaces, allowing for targeted delivery into specific cells or tissues. This targeted gene delivery approach holds great potential for the treatment of genetic disorders and other diseases. A comprehensive review by Li et al. delves into the synthesis and properties of silver nanoparticles, including AgNCs, for gene delivery applications, providing insights into their potential in pharmaceutical gene therapy.[64]

Radiation Enhancers

In cancer treatment, AgNCs have been explored as radiation enhancers. When combined with radiation therapy, AgNCs can increase its effectiveness by enhancing the radiation's ability to damage cancer cells. This approach improves the therapeutic outcomes of radiation therapy while minimizing damage to surrounding healthy tissues. Zhang et al. conducted a study on the size-dependent radiosensitization of gold nanoparticles, highlighting the potential of similar approaches using AgNCs in cancer radiation therapy.[65]

Diagnostic Application

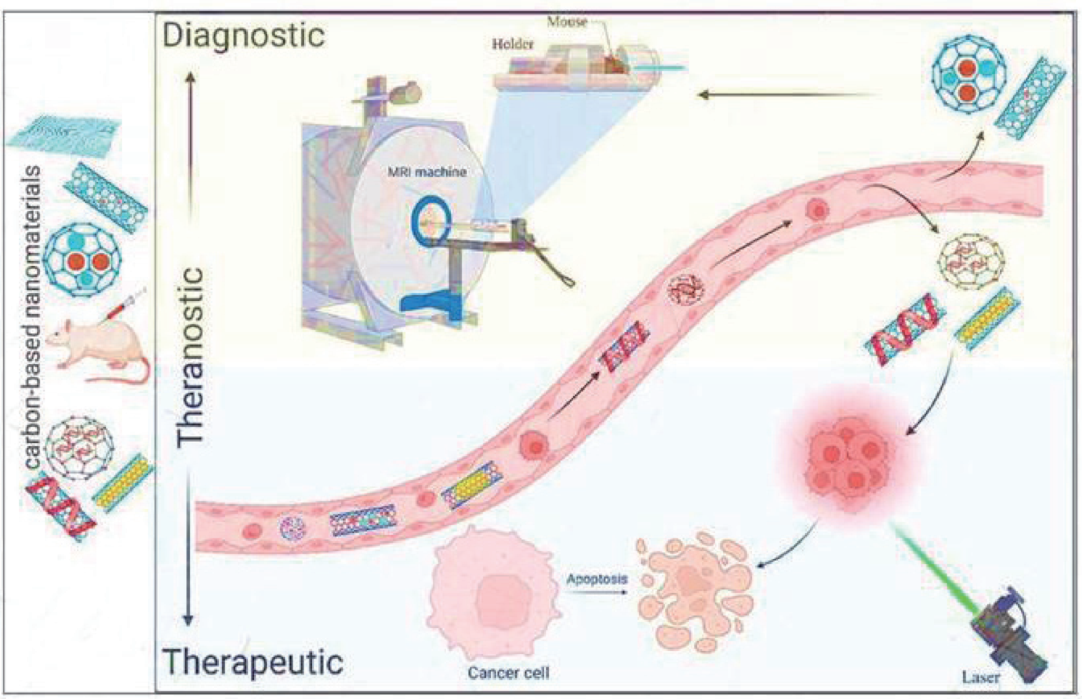

Figure 16: Application in AgNCs in diagnosis

Functionalized AgNCs have found applications as diagnostic tools in pharmaceutical research. By modifying AgNCs with specific ligands or antibodies, they can be tailored to detect biomarkers associated with various diseases. This customization enables the development of highly sensitive and rapid diagnostic tests, contributing to early disease detection and monitoring. In the field of pharmaceutical analysis, aptamer-based fluorescent biosensors have been developed using AgNCs. These biosensors can detect specific biological molecules, providing valuable insights into disease diagnosis and pharmaceutical research.[66]

Veterinary Application

One of the primary applications of AgNCs in veterinary science is their role as effective antimicrobial agents. AgNCs exhibit strong antibacterial, antiviral, and antifungal properties, making them valuable tools in preventing and treating infectious diseases in animals. These nanoparticles can target a wide range of pathogens, including drug-resistant strains. In veterinary medicine, wound management is a crucial aspect of animal healthcare. AgNCs have been used to accelerate wound healing in animals due to their antimicrobial properties and ability to stimulate tissue regeneration. They can be integrated into wound dressings and gels to provide an environment conducive to wound closure. AgNCs have found applications in veterinary diagnostics. They can be functionalized with specific ligands or antibodies to detect pathogens, biomarkers, or antibodies in animals. These functionalized AgNCs can be used in assays and point-of-care diagnostic tests, enabling rapid and sensitive detection of diseases.[67]

Conclusion

In conclusion, the utilization of silver nanoclusters (AgNCs) in theranostic applications represents a promising and rapidly evolving field of nanomedicine. AgNCs offer unique advantages, including their tunable optical properties, biocompatibility, and facile functionalization, making them versatile candidates for integrated diagnostics and therapy. The synthesis techniques for AgNCs have advanced significantly, allowing precise control over their size, shape, and surface chemistry. These capabilities enable tailored design for specific theranostic purposes and contribute to their multifunctionality. AgNCs have shown great promise in diagnostics, offering various imaging modalities with exceptional sensitivity, enabling early disease detection and real-time monitoring of treatment responses. Furthermore, AgNCs possess intrinsic antimicrobial properties and can be harnessed for photodynamic therapy, offering effective therapeutic approaches for combating infections and cancer. When combined with targeted drug delivery systems, AgNCs enhance drug delivery precision, improving therapeutic outcomes while minimizing side effects. Nevertheless, several challenges remain, including the need for rigorous biocompatibility assessments, long-term toxicity studies, and regulatory considerations to ensure the safe translation of AgNC-based theranostics to clinical applications. The balance between therapeutic efficacy and potential cytotoxicity must be carefully evaluated. In summary, the continued exploration of silver nanoclusters in theranostic applications holds great promise for personalized medicine and disease management. Future research efforts should focus on addressing safety concerns, optimizing AgNC-based theranostic platforms, and advancing their clinical translation to harness their full potential in improving patient care.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships.

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