



Chemical synthesis and applications of Gold nanoparticles

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ABSTRACT: The range of scientific and technical uses for nanoparticles makes it evident how important nanotechnology is in today's world. Gold nanoparticles are among the many metal nanoparticles that can be produced using a variety of methods. This review article emphasizes the fundamental methods of chemical synthesis for gold nanoparticles, exploring their production processes and diverse applications. The data for the research was gathered through a review of existing literature. The Brust-Schiffen method is a significant approach for synthesizing gold nanoparticles (AuNPs). In this technique, two reaction pathways are employed to achieve an efficient surface reaction during the formation and growth process. AuCl₄⁻ is transferred from the aqueous phase to toluene and subsequently reduced by sodium borohydride (NaBH₄) in the presence of dodecanethiol. The adaptable surface chemistry of AuNPs enables them to be coated with small molecules, polymers, and biological recognition molecules, thus expanding their scope of use. They have the ability to accumulate in tumor cells, exhibit optical scattering, and serve as probes for microscopic studies of harmful cells. Additionally, AuNPs are employed in cancer therapy and diagnosis. Furthermore, they hold significant promise in catalysis, as their surfaces facilitate interactions between reactants and the catalytically active sites on gold nanoparticles.

KEYWORDS: Biosensing, Bioimaging, Catalysis, Chemotherapy, Goldnanoparticles.

INTRODUCTION

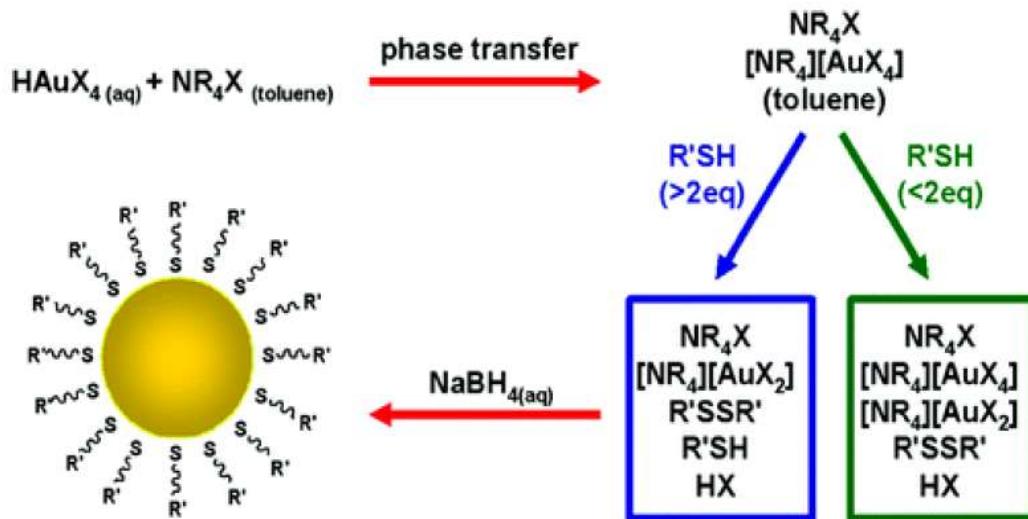
Several methods exist for synthesizing AuNPs, including the "bottom-up" and "top-down" approaches. Significant efforts have been made toward the controlled synthesis of AuNPs, focusing on their size, shape, solubility, stability, and functionality. In general, the synthesis of AuNPs can primarily be divided into chemical, physical, and biological methods (Khanna et al.2019). Metal nanoparticles have garnered significant attention in nanotechnology and Nano medicine because of their distinctive optical, electrical, mechanical, and chemical properties, which differ in size and shape from their bulk metal state (Gopinath et al.2013). A commonly used and more practical approach is the Brust-Schiffen method, a two-phase synthetic technique that leverages strong thiol-gold interactions to stabilize AuNPs with thiol ligands (Amina and Guo.2020). To carry out chemical reduction, a precursor salt and a reducing agent are required. The most commonly used reducing agents include sodium borohydride, dimethyl formamide, sodium citrate, glycerol, and ethylene glycol, among others. Their primary role is to reduce the metal to its natural state (Pal et al.2007). Goldnanoparticles) are typically synthesized in a liquid medium through the reduction of chloroauric acid. Once the acid is dissolved, the solution is quickly stirred together with a reducing agent. This process subsequently reduces Au³⁺ ions to neutral gold atoms. As additional gold atoms are produced, the solution reaches a state of supersaturation. Gold subsequently starts to form as particles at the sub-nanometer scale (Awasthi et al.2020). Recent progress in nanomaterial synthesis and production techniques has enabled precise control over factors like size, shape, composition, and surface chemistry, facilitating the creation of nanostructures with improved stability in biological systems (Siddique and Chow.2020). Numerous studies focus on investigating AuNPs molecules in areas such as biomarking, chemical sensing, human biological medicine, electronic and Thermal Phototherapy, Nanotechnology-based medical imaging, DNA diagnostics of both types, therapeutic transfer methods, and the transfer and attachment of reagents to AuNPs particles for cancer treatment (Mohammed and Algawhari.2020).

Materials and Chemical Preparation of AuNPs

Wet chemical methods begin with the reduction of metal ion precursors into metal atoms, which then undergo controlled aggregation to form nanoparticles (Haiss et al.2007). The production of AuNPs with sizes spanning from a few nanometers to several hundred

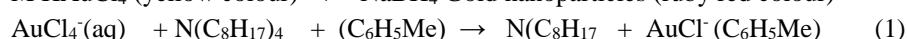


nanometers has been achieved in both aqueous solutions and organic solvents (Corma and Garcia, 2008). Brust and Schiffrin made a significant advancement in the synthesis of AuNPs. They introduced a two-phase synthetic technique, known as the Brust Schiffrin method, which employed strong thiol-gold interactions to stabilize AuNPs with thiol ligands. In this process, AuCl_4^- was moved from the aqueous phase to toluene and then reduced using sodium borohydride (NaBH_4) in the presence of dodecanethiol (Brust et al., 1994)..

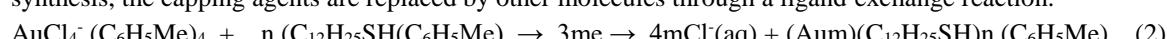


1-Figure: preparation of GPNs by Brust-Schiffrin method (Yu et al, 1997).

The AuNPs were produced with precisely controlled diameters ranging from 1.5 to 5 nm. Thiol-protected AuNPs exhibit excellent stability owing to the robust thiol gold bond, making them easy to handle and further functionalize (Li and Lou, 2020). This approach involves the creation of a hydrophobic mineral group, followed by its dissolution, while preserving the properties of the resulting particles. The Brust-Schiffrin method has gained wider application with the use of 4-mercaptophenol, offering greater stability compared to other approaches. This method is favored for its ability to control particle size by adjusting the ratio of HAuCl_4 to NaBH_4 (Mohammed and Algawhari, 2020). Next, employ chloroauric acid (HAuCl_4) as the reactant and sodium borohydride (NaBH_4) as the reducing agent NaBH_4^+ Deionized water NaBH_4 solution.



The shift in gold's color from yellow to ruby red signifies the formation of gold nanoparticles (Tomar and Garg, 2013). Following synthesis, the capping agents are replaced by other molecules through a ligand exchange reaction.



(Mohammed and Al-Gawhari, 2020).

Application of Goldnanoparticles

Goldnanoparticles exhibit distinctive electric and magnetic properties influenced by their shape and size, making them a focal point of research, particularly in areas such as biological tagging, chemical and biological sensing, opoelectronics, Photothermal therapy, and biomedical imaging. Considering their diverse applications in biosciences, the most significant applications of gold nanoparticles are listed below:

Bio imaging

The primary goal of imaging is to identify and pinpoint specific targets, typically through the accumulation of a particular imaging compound at a specific cell, body region, or disease site, in a safe and non-invasive manner (Smith and Gambhir, 2017). Computed tomography (CT) is a non-invasive technique that utilizes X-ray scanning, tissue attenuation, and computerized image reconstruction to acquire morphological and vascular details of the body (Seeram, 2018). The integration of CT imaging with gold nanoparticles as contrast agents has recently advanced significantly, owing to their strong X-ray attenuation properties and bio-conjugation

capabilities (Meir and Popovtzer, 2018). Gold nanoparticles possess distinctive properties that enable the identification of specific elements within complex biological mixtures. Raman spectroscopy is employed for this purpose. The Raman Effect arises from the scattering of photons as they interact with matter, producing a chemical fingerprint unique to a molecule. This effect is significantly amplified by AuNPs. This effect, known as surface-enhanced Raman scattering (SERS), can be utilized in highly sensitive probes (Wu et al., 2019). Gold nanoparticles, with their dispersed colors, are presently utilized in biological imaging applications. Furthermore, the high density of gold nanoparticles makes them advantageous as probes in transmission electron microscopy (Perrault and Chan, 2010). Gold nanoparticles are utilized in resonance scattering dark-field microscopy to detect microbial cells and their metabolites, visualize tumor cells through bio-imaging, identify surface receptors, and examine the process of endocytosis (Awasthi et al., 2020).

Drug Carriers

Due to their biocompatibility, stability, and non-toxicity, AuNPs serve as an effective Nano carrier in drug delivery systems with minimal side effects. A variety of drugs, including peptides, proteins, and anticancer agents, can be anchored to the surface of AuNP (Zhang et al., 2016). Targeted drug delivery represents one of the most promising and rapidly advancing applications of AuNPs in medicine. Target delivery systems most commonly focus on antitumor agents and antibiotics (Paciotti et al., 2006). Gold nanoparticles are also recognized as carriers for delivering antibiotics and other antibacterial agents. The formation of a stable vancomycin-colloidal gold complex and its effectiveness against various enteropathogenic strains of *Escherichia coli*, *Enterococcus faecium*, and *Enterococcus faecalis* (including strains resistant to vancomycin) has also been confirmed (Gu et al., 2003). Gene therapy refers to a method that involves introducing genetic material into cells and the body for therapeutic use (Zelenin, 2001).

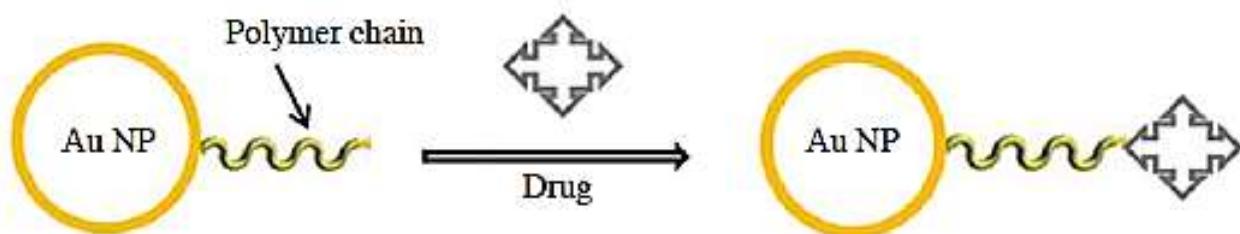


Figure 2: Schematic representation of surface modified Au-NPs (Patra , 2008).

Biosensing

The conductive valence electrons on the surface of the metals oscillate naturally due to the storing attraction effect of the positive charge of the atomic nuclei. The oscillation process causes an electron density waves (surface Plasmon) with characteristic frequency on the surface of the metal. (Nur, 2013). Surface Plasmons (SPs) are a type of Plasmon associated with the surfaces of metals. When a metal absorbs a resonant wavelength of light, it triggers vibrations in the electron cloud, dispersing energy across the material's surface—an effect known as surface Plasmon resonance (SPR) (Kneip et al., 2006). Various Nano-biosensors have utilized the unique properties of AuNPs. Electrochemical sensors rely on the electrical characteristics of bio-functionalized electrodes when interacting with a sample analyte. Electrochemical sensors are categorized into amperometric, impedimetric, potentiometric, and conductometric types. Optical sensors rely on variations in color or surface plasmon resonance (Makhsin et al., 2017).

Therapeutic

In 2003, gold nanoparticles (AuNP) were first utilized as agents in Photothermal therapy, and this approach was later termed plasmonic Photothermal therapy (Huang et al., 2008). When exposed to light at specific wavelengths, AuNPs can absorb the light and generate heat in the area near their surface. Thus, when light is directed at a tumor containing AuNPs during treatment, the particles quickly heat up to destroy the tumor cells, a process referred to as AuNP-based phototherapy (Abad et al., 2005). Therapeutic agents can be attached to the surface of nanoparticles. The high surface area-to-volume ratio of AuNPs allows their surface to accommodate a substantial number of molecules, including therapeutics, targeting agents, and antifouling polymers (Love et al. 2005). When positioned within or near the target cells (achieved by attaching gold particles to antibodies or other molecules), these cells are destroyed (Awasthi et al., 2020).



Catalytic

Nanostructures based on AuNP have been effectively synthesized through various chemical methods and utilized as catalysts. As reactions catalyzed by AuNPs primarily occur on their surface, the surface characteristics of the synthesized AuNPs are considered to have a significant impact on the catalytic process. In chemical synthesis, incorporating stabilizer or linker molecules ensures successful and consistent experimental protocols, along with stable gold nanoparticles (AuNPs) during both synthesis and catalysis. However, it has been observed that these stabilizing molecules on the nanoparticle surface can hinder reactants from accessing the active sites of the nanoparticles (Lopez et al., 2011). Gold nanoparticles demonstrate remarkable activity in CO oxidation at temperatures below room temperature, and since then, gold-based heterogeneous catalysis has garnered significant interest from both academia and industry. Gold nanoparticles supported on various materials have a wide range of applications, including environmental management, chemical synthesis, energy production and conversion, as well as materials processing, offering promising commercial potential. The use of AuNPs as catalysts in selective hydrogenation and oxidation reactions has been extensively documented. For instance, in the catalytic oxidation of alcohols using AuNPs with H₂O₂, the role of H₂O₂ is to function as a hydrogen scavenger and aid in the removal of the α -hydrogen from the alcohol substrate, resulting in the formation of an alcoholate species as the initial reaction step. Subsequently, the Au-alcoholate complex can undergo further interaction with H₂O₂.

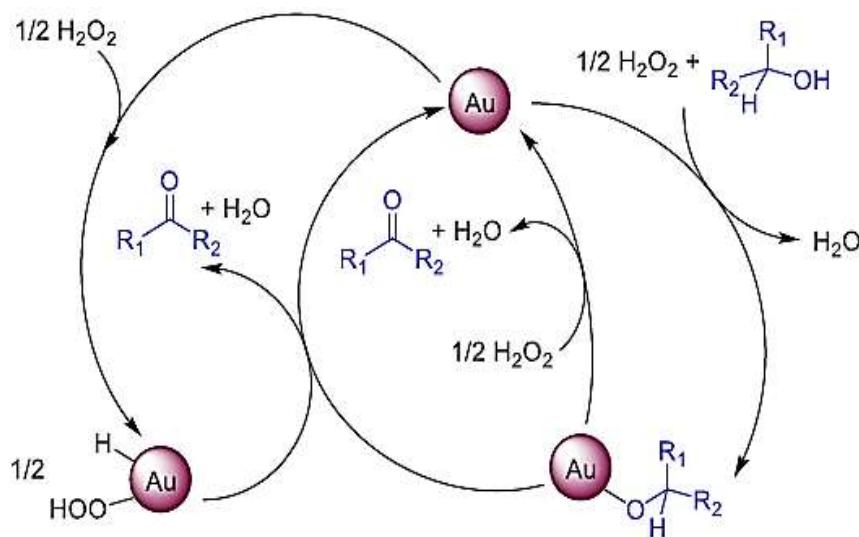


Figure 3: Proposed mechanism for alcohol oxidation with H₂O₂ on AuNPs (Haruta, 2003).

or with the Au-hydroperoxide complex formed through the reaction between Au(0) and H₂O₂, resulting in the production of the final carbonyl compound through a β -elimination mechanism. The use of AuNPs as catalysts in selective hydrogenation has been extensively recognized (Haruta, 2003).

Summary of Findings from Literature

The Brust-Schiffman method occurs in two steps: the first step involves the reduction of metal ion precursors into metal atoms, while the second step focuses on controlling the aggregation of these atoms to form gold nanoparticles (AuNPs). The resulting AuNPs are easy to handle and can be further functionalized. This method is widely used due to its ability to control the size and shape of the particles. Gold nanoparticles (AuNPs) possess distinctive physical and chemical properties that make them highly versatile in various applications. Due to their low toxicity and adjustable physical and chemical characteristics, they can interact with a wide range of organic molecules. This has enabled their use as therapeutic agents or drug carriers, targeting specific cells to enhance drug efficacy.

CONCLUSION

The advancement of various technologies for functionalizing AuNPs with different molecules, enabling stabilization in vivo and direct interaction with biological targets, along with their inherent toxicity, multifunctionality, high surface area, photophysical, and



optical properties, has resulted in their extensive applications across various fields, including drug delivery, chemotherapy, bioimaging, biosensing, and catalysis.

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