

Gold Nanoparticles in Drug Delivery: Innovations, Applications, and Challenges

Poorwi Sahu¹, Palak Jain¹, Purvi Pandey¹, Ara Manya¹, Rishu Kumar¹, Gyanesh Kumar Sahu^{2*}

¹Rungta Institute of Pharmaceutical Sciences ²Rungta Institute of Pharmaceutical Sciences and Research

ABSTRACT

In addition to its special physicochemical characteristics, such as their large surface area, biocompatibility, simplicity of functionalization, and capacity to enable regulated drug release, gold nanoparticles (AuNPs) have drawn a lot of interest in the field of drug delivery. Because of these characteristics, AuNPs are excellent choices for targeted drug administration, improving the stability, bioavailability, and therapeutic effectiveness of a range of medications. Functional groups like antibodies as well as peptides from or small molecules can be added to the surface of metallic nanoparticles to allow for the selective targeting of particular cells or tissues, especially in the treatment of cancer.Furthermore, AuNPs provide flexible drug delivery platforms by encapsulating a variety of therapeutic molecules, such as hydrophobic medications, proteins, and nucleic acids. Enhancing drug release kinetics and reducing adverse effects is made possible by the capacity to adjust the size, influence, and surface properties of AuNPs. There are still issues with the toxicity, flexibility, and long-term biologic compatibility of AuNP-based drug administration systems, despite their encouraging promise. To allay these worries and fully use gold nanoparticles' therapeutic promise in personalized medicine, more investigation is required.

Keywords: Biocompatibility, Functionalization, Nanoparticles, Encapsulating.

1. INTRODUCTION

Considering their distinct physical, chemical, and biochemical properties, metallic nanoparticles (AuNPs) are one of the most researched nanomaterials. These attributes, which make gold nanoparticles extremely useful in a variety of domains, include a huge surface area, ease of functionality, optical features (such surface plasmon resonance), biologic compatibility, and low toxicity. Tiny gold particles, known as gold nanoparticles (AuNPs), usually have a size between one and one hundred nanometres (nm) (<u>1</u>). These nanoparticles' distinct qualities, which set them apart from bulk gold, have attracted a lot of interest in a



variety of scientific and technical domains. Because of their unique optical, electrical, and chemical characteristics, gold nanoparticles may be used in a wide range of fields (2).



(Fig 1 Nanoparticles)

1.1 Gold Nanoparticles Synthesis

Numerous techniques, such as biological reduction, sunlight, and green synthesis methods, can be used to create gold nanoparticles. The most popular technique is chemical reduction, which involves converting gold salts—usually the gold chloride or metal nitrate—to gold nanoparticles while a reducing agent, like sodium citrate, is present (3). Additional techniques that offer greater control over the size and form of the particles are template-assisted synthesis and laser ablation. Green synthesis, which produces nanoparticles using living organisms or plant extracts, is becoming more and more well-liked because of its environmentally benign methodology ($\underline{2}$).

1.2 Gold Nanoparticle Properties

Surface plasmon resonant (SPR), or the communal oscillation of electrons at the nanoparticle surface, is one of the amazing visual features of gold nanoparticles. They are helpful in sensing and imaging applications because of this feature. Gold nanoparticles are also exceedingly versatile for drug administration, diagnostics, and other therapeutic uses since their surface may be readily altered with different functional groups (3). Additionally, gold nanoparticles are comparatively non-toxic and biocompatible, which adds to their appropriateness in biological settings. Their surface may be functionalized with biomolecules like protein chains, antibodies, or nucleic acids, enabling disease detection, tailored treatments, and other cutting-edge medical uses (4).

1.3 Important Features of Gold Nanoparticles:

a) **Size and Shape:** The characteristics of gold nanoparticles vary with their size. Their responsiveness and usefulness are improved by their compact size, which leads to a high dimension to volume ratio.

T



Additionally, they may be designed into a variety of forms, including stars, spheres, and rods, each of which has special benefits for certain uses (5).

b) **Surface Plasmon Resonance (SPR):** A phenomenon known as surface Plasmon resonance gives gold nanoparticles their remarkable capacity to both absorb and scatter light at particular wavelengths. Because of this, gold nanoparticles have special optical qualities that are frequently used in sensors and testing equipment (5-6).

c) **Chemical Stability:** Although gold is chemically impermeable, gold nanoparticles may withstand a wide range of environmental factors without reacting. They are therefore perfect for applications in biology and medicine.

d) **Simple Functionalization**: To improve gold nanoparticles' interactions with other materials, their surface may be readily altered with a variety of ligands, biomolecules, or polymers. Medication delivery, the detection of bios and other biological applications benefit from this property (7).

1.4 Utilizing Gold Nanoparticles

Gold nanoparticles are widely used in many different sectors, such as:

a) Applications in Biomedicine:

• **Drug Delivery**: By encapsulating medications, AuNPs can enhance their soluble nature, stability, and regulate release. Particularly in cancer treatment, their capacity to target certain cells or tissues improves the accuracy of drug delivery systems (<u>8</u>).

• **Diagnostics & Imaging**: Because of their special optical characteristics, AuNPs are frequently employed in imaging and diagnostic procedures including computed tomography (CT) scans, magnetic resonance imaging (MRI), and surface-enhanced Raman scattering (SERS) (<u>7-9</u>).

• **Therapeutic Applications:** In photothermal treatment, gold nanoparticles are heated with laser light to specifically target and kill cancer cells (<u>10</u>).

b) Cancer Therapy:

As gold nanoparticles may specifically target tumour cells, they have drawn a lot of interest in the treatment of cancer. Gold nanoparticles can be loaded with medications, including RNA-based treatments or chemotherapeutic drugs, and delivered precisely to the tumour location, minimizing adverse effects and enhancing therapeutic results. Gold nanoparticles are also employed in photo thermal treatment, which kills cancer cells via localized heating (by laser irradiation) (<u>11</u>).



c) Gene Delivery:

Target cells are increasingly receiving biological material, such as RNA or DNA, using gold nanoparticles. They may alter their surface such that it binds to amino acids, which are subsequently released into cells. This might be used in the process of gene therapy to treat cancer or hereditary diseases (9, 12).

d) Vaccines:

By acting as adjuvants, gold nanoparticles can improve the immunological response to vaccinations. To encourage a stronger immune response, they can also be utilized to deliver antigens straight to immune cells $(\underline{12})$.

2. Mechanisms of Drug Delivery

According to their design and the kind of therapeutic chemicals they contain, metallic nanoparticles can deliver medications via a variety of mechanisms:

Passive Targeting:

The nanoparticles of gold can passively target malignant tissues because of their tiny size and capacity to accumulate in tumours through their improved permeation and retention (EPR) effect. Drug delivery is improved by nanoparticles accumulating in greater quantities at the tumour location due to the leaky blood arteries around tumours (12-13).

 \blacktriangleright Active Targeting: Gold nanoparticles may be actively targeted to certain cells or tissues by surface functionalization with particular agonists, such as antibodies than others, peptides, or small molecules. This makes it possible to distribute drugs more precisely while minimizing side effects (14).

Controlled and Sustained Release:Small gold particles can be designed to release medications in reaction to particular stimuli, such pH, temperature, or enzyme presence. By ensuring that the medication is administered at the appropriate time and location, this controlled release maximizes therapeutic results (<u>14-</u><u>15</u>).

Combination Therapy: metallic nanoparticles can be utilized to deliver many therapeutic agents at once, such as genetic material and chemotherapeutic medications. In cancer treatment, where combining many medicines can improve overall efficacy and lower the chance of resistance, this strategy is very helpful.

3. Advantages of Gold Nanoparticles in Drug Delivery

> **Targeted Delivery:** By precisely targeting sick tissues or cells, gold nanoparticles can reduce systemic adverse effects and raise a medication's therapeutic index (16).



> **Decreased Toxicity:** Gold nanoparticles can offer safer substitutes for traditional drug delivery methods due to their biocompatibility and reduced toxicity in a variety of applications, particularly for delicate therapies like cancer therapy.

 \succ Versatility in Functionalization: Gold nanoparticles may be tailored for a variety of drug delivery applications, such as gene delivery and combination therapy, due to their ease of functionalization (<u>15-16</u>).

 \blacktriangleright **Non-invasive Imaging:** By using gold nanoparticles for imaging and tracking, doctors can keep an eye on the whereabouts and concentrations of medications in real time, which is useful for improving treatment plans (<u>16</u>).

4. Challenges in Gold Nanoparticle-Based Drug Delivery

Toxicity at large dosages: Although gold nanoparticles are thought to be biocompatible, there is still some worry about their long-term toxicity and consequences at large dosages or after repeated administrations. Gold nanoparticles' interactions with tissues, proteins, and cells may result in bioaccumulation or unintended immunological reactions (17).

Scalability and Cost: Gold nanoparticle production may be difficult and costly, particularly if size and surface functionalization are precisely controlled. One major obstacle is still scaling up manufacturing for clinical usage (<u>18</u>).

Biodistribution and Clearance: There may be variations in the body's distribution of gold nanoparticles as well as in how easily the liver, spleen, and kidneys remove them. It is crucial to optimize these elements to guarantee that nanoparticles get to the intended site of action and are efficiently removed from the body (16-19).

5. FUTURE PROSPECTIVE

Although gold nanoparticles have a lot of potential, there are several issues that must be resolved. These include worries about their possible toxicity, long-term stability, and effects on the ecosystem. Cost-effectiveness and large-scale manufacturing are still major obstacles to commercial application (20). The goals of ongoing research are to enhance synthesis methods, lower toxicity, and investigate a wider range of uses, especially in medicine. In order to increase the therapeutic potential of gold nanoparticles, their usage in conjunction with other nanomaterials, including liposomes or polymers, is also being investigated (22-23).



6. CONCLUSION

In recognition of their special qualities, such as their flexibility, biocompatibility, and simplicity of functionalization, gold nanoparticles have great potential as drug delivery vehicles (21). Research is still being done to improve and optimize their usage in drug delivery, especially for personalized cancer treatment, and gene delivery, even if issues including toxicity, flexibility, and regulatory approval still exist. Gold nanoparticles have the potential to be a key component of personal healthcare and therapeutic innovation in the future with more developments. Gold nanoparticles are a game-changing technology with enormous potential in a variety of domains, including materials research, healthcare, and environmental monitoring. New developments that fully use the potential of metallic nanoparticles in therapeutic and diagnostic settings are probably going to result from ongoing study into their characteristics, production, and uses (24).

7. **REFERENCES**

 Hayat MA. Colloidal gold: principles, methods, and applications. Academic Press; San Diego: 1989. [Google Scholar]

2. Mirkin CA, Letsinger RL, Mucic RC, Storhoff JJ. Nature. 1996;382:607. doi: 10.1038/382607a0. [DOI] [PubMed] [Google Scholar]

3. Alivisatos AP, Johnsson KP, Peng XG, Wilson TE, Loweth CJ, Bruchez MP, Schultz PG. Nature. 1996;382:609. doi: 10.1038/382609a0. [DOI] [PubMed] [Google Scholar]

4. Xiao Y, Patolsky F, Katz E, Hainfeld JF, Willner I. Science. 2003;299:1877. doi: 10.1126/science.1080664. [DOI] [PubMed] [Google Scholar]

5. Liu J, Lu Y. J Am Chem Soc. 2003;125:6642. doi: 10.1021/ja034775u. [DOI] [PubMed] [Google Scholar]

6. Katz E, Willner I. Angew Chem. 2004;116:6166. [Google Scholar]; Angew Chem Int Ed. 2004;43:6042. [Google Scholar]

7. Faulk WP, Taylor GM. Immunochemistry. 1971;8:1081. doi: 10.1016/0019-2791(71)90496-4. [DOI] [PubMed] [Google Scholar]

8. Connor EE, Mwamuka J, Gole A, Murphy CJ, Wyatt MD. Small. 2005;1:325. doi: 10.1002/smll.200400093. [DOI] [PubMed] [Google Scholar]

9. Tkachenko AG, Xie H, Coleman D, Glomm W, Ryan J, Anderson MF, Franzen S, Feldheim DL. J Am Chem Soc. 2003;125:4700. doi: 10.1021/ja0296935. [DOI] [PubMed] [Google Scholar]

 Jiang Y, Zhao H, Lin YQ, Zhu NN, Ma YR, Mao LQ. Angew Chem Int Ed. 2010;49:4800–4804. doi: 10.1002/anie.201001057. [DOI] [PubMed] [Google Scholar]



11. Huang CC, Chang HT. Chem Commun. 2007:1215–1217. doi: 10.1039/b615383f. [DOI] [PubMed] [Google Scholar]

12. Liu DB, Qu WS, Chen WW, Zhang W, Wang Z, Jiang XY. Anal Chem. 2010;82:9606–9610. doi: 10.1021/ac1021503. [DOI] [PubMed] [Google Scholar]

13. Liu XJ, Cheng XH, Bing T, Fang CL, Shangguan DH. Anal Sci. 2010;26:1169–1172. doi: 10.2116/analsci.26.1169. [DOI] [PubMed] [Google Scholar]

 14.
 Joyce
 GF.
 Annu
 Rev
 Biochem.
 2004;73:791–836.
 doi:

 10.1146/annurev.biochem.73.011303.073717.
 [DOI]
 [PubMed]
 [Google Scholar]
 doi:

15. Lee JH, Wang ZD, Liu JW, Lu Y. J Am Chem Soc. 2008;130:14217–14226. doi: 10.1021/ja803607z. [DOI] [PMC free article] [PubMed] [Google Scholar]

16. Li XK, Wang JN, Sun LL, Wang ZX. Chem Commun. 2010;46:988–990. doi: 10.1039/b920135a. [DOI] [PubMed] [Google Scholar]

17. Kado S, Furui A, Akiyama Y, Nakahara Y, Kimura K. Anal Sci. 2009;25:261–265. doi: 10.2116/analsci.25.261. [DOI] [PubMed] [Google Scholar]

18. Garcia-Etxarri A, Aizpurua J, Molina-Aldareguia J, Marcilla R, Pomposo JA, Mecerreyes D. Front Phys China. 2010;5:330–336. [Google Scholar]

19. Daniel WL, Han MS, Lee JS, Mirkin CA. J Am Chem Soc. 2009;131:6362–6363. doi: 10.1021/ja901609k. [DOI] [PubMed] [Google Scholar]

20. Matsui J, Akamatsu K, Nishiguchi S, Miyoshi D, Nawafune H, Tamaki K, Sugimoto N. Anal Chem. 2004;76:1310–1315. doi: 10.1021/ac034788q. [DOI] [PubMed] [Google Scholar]

21. Liang XS, Wei HP, Cui ZQ, Deng JY, Zhang ZP, You XY, Zhang XE. Analyst. 2011;136:179–183. doi: 10.1039/c0an00432d. [DOI] [PubMed] [Google Scholar]

22. Mirkin CA, Letsinger RL, Mucic RC, Storhoff JJ. Nature. 1996;382:607–609. doi: 10.1038/382607a0. [DOI] [PubMed] [Google Scholar]

23. Li JH, Chu X, Liu YL, Jiang JH, He ZM, Zhang ZW, Shen GL, Yu RQ. Nucleic Acids Res. 2005;33:9. doi: 10.1093/nar/gni163. [DOI] [PMC free article] [PubMed] [Google Scholar]

 24.
 Chen CE, Song GT, Yang XJ, Ren JS, Qu XG. Biochimie. 2010;92:1416–1421. doi:

 10.1016/j.biochi.2010.07.004. [DOI]
 [PubMed]
 [Google Scholar]

Т