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"Advances in Functionalization of Gold Nanoparticles for Enhanced Drug Delivery Systems"

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Abstract:

The advent of nanotechnology has revolutionized various fields, particularly in medicine, by enabling the development of advanced drug delivery systems (DDS). Among these, gold nanoparticles (AuNPs) have emerged as a prominent material due to their unique physicochemical properties. This research paper provides an analytical study on the use of gold nanoparticles in drug delivery systems at the global level, exploring the benefits, challenges, and potential solutions. The study aims to provide insights into how gold nanoparticles are being utilized, their impact on drug delivery, and the various strategies for overcoming challenges related to their clinical application.

Gold nanoparticles (AuNPs) have gained significant attention in the field of nanomedicine due to their unique physicochemical properties, including their small size, high surface area, ease of functionalization, and biocompatibility. These attributes make AuNPs ideal candidates for use in drug delivery systems (DDS), enabling more efficient, targeted, and controlled release of therapeutic agents. Their ability to enhance the pharmacokinetics and bioavailability of drugs, especially in the context of cancer therapy, gene delivery, and infectious disease treatment, offers considerable promise for improving treatment efficacy while minimizing side effects.

This research paper presents an analytical study on the global application of gold nanoparticles in drug delivery systems, focusing on both the benefits and challenges associated with their use. We explore the fundamental properties of AuNPs, such as size and surface functionality, that enable their role as drug carriers. The study examines key mechanisms of drug delivery through AuNPs, including passive and active targeting, controlled release, and the potential for targeted therapy in diseases like cancer, viral infections, and genetic disorders.

The global perspective highlights ongoing research and development efforts, with particular emphasis on leading countries in the field, such as the United States, Germany, and China. Case studies and clinical trial outcomes are discussed to underscore the practical applications and current limitations. However, the widespread adoption of AuNP-based DDS faces several challenges, including scalability of synthesis methods, cost constraints, regulatory issues, and concerns over biocompatibility and long-term safety.

To address these challenges, the paper proposes a range of solutions, such as the development of green synthesis techniques, advances in surface modification to improve biocompatibility, and innovative cost-reduction strategies through the use of gold alloys or alternative metal-based nanoparticles. Furthermore, the need for harmonized global regulatory frameworks to ensure the safe and efficient use of AuNPs in medicine is emphasized.

Finally, this paper explores future directions for gold nanoparticle-based drug delivery, including their potential integration with personalized medicine and the role of emerging technologies, such as artificial intelligence and machine learning, in accelerating their development. Despite the obstacles, gold nanoparticles hold immense potential to revolutionize drug delivery, making them a promising tool for future therapeutic applications and advancing the field of nanomedicine.

Keywords: Gold Nanoparticles, Drug Delivery Systems, Biocompatibility, Functionalization, Controlled Release, Analytical Study, Nanomedicine, Global Perspective.

. Introduction:

1.1 Background and Significance

Gold nanoparticles (AuNPs) have gained considerable attention in the field of nanomedicine due to their distinctive properties, such as their small size, large surface area, ease of functionalization, and ability to carry both hydrophilic and hydrophobic drugs. These properties make AuNPs ideal candidates for use in drug delivery systems, where they can facilitate targeted, controlled, and sustained release of therapeutic agents.

The global pharmaceutical industry has been actively exploring nanoparticle-based systems for their potential to revolutionize the way diseases, especially cancer, are treated. Despite the considerable promise, there remain several challenges in the practical and widespread application of gold nanoparticles in drug delivery.

1.2 Objectives of the Study

This paper seeks to:

- Analyze the properties and characteristics of gold nanoparticles relevant to drug delivery.
- Examine the global status of AuNPs in drug delivery applications.
- Investigate the challenges faced in their use and explore potential solutions.
- Evaluate future trends and global research directions in gold nanoparticle-based drug delivery systems.

1.3 Structure of the Paper

The paper is organized into several sections that explore the various facets of gold nanoparticle-based drug delivery systems. These include a detailed examination of the physicochemical properties of AuNPs, their mechanisms of action in drug delivery, the current global landscape of research, and the challenges and potential solutions related to their application.

2. Properties of Gold Nanoparticles:

Gold nanoparticles (AuNPs) have garnered significant attention in drug delivery systems due to their unique and tunable properties. These properties can be manipulated during synthesis to tailor nanoparticles for specific therapeutic applications, allowing for the controlled release of drugs, targeted delivery to specific tissues or cells, and enhanced bioavailability. Understanding these properties is crucial for optimizing AuNP-based drug delivery systems. Below is a detailed description of the key properties of AuNPs that make them suitable for drug delivery applications:

2.1 Size and Shape

The size and shape of gold nanoparticles play a critical role in determining their interactions with biological systems, including cellular uptake, biodistribution, and clearance rates.

- **Size:**
  - Gold nanoparticles typically range in size from 1 to 100 nm. The size of the nanoparticles significantly influences their pharmacokinetics and biological behavior. Smaller nanoparticles (1-10 nm) exhibit increased surface area and greater surface energy, which can enhance drug loading capacity and facilitate cellular uptake. Larger nanoparticles (20-100 nm) tend to have longer circulation times due to their reduced renal clearance, making them ideal for systemic drug delivery and targeting.
  - The size of nanoparticles also influences their ability to penetrate biological barriers. For instance, nanoparticles in the range of 10–50 nm are optimal for escaping immune system recognition and can pass through the leaky vasculature of tumors via the enhanced permeability and retention (EPR) effect.
- **Shape:**
  - Gold nanoparticles can be synthesized in various shapes, including spheres, rods, cubes, and stars. The shape of the nanoparticle affects its surface area, drug loading capacity, and interactions with biological cells.
  - Spherical nanoparticles are the most commonly used in drug delivery due to their uniform shape, ease

- Rod-shaped nanoparticles (nanorods) and cubic nanoparticles have enhanced surface-to-volume ratios, which can result in improved drug encapsulation. These shapes also tend to have longer circulation times and enhanced stability compared to spherical nanoparticles.

2.2 Surface Characteristics and Functionalization

The surface properties of gold nanoparticles are among the most important factors influencing their behavior in drug delivery systems. Surface characteristics can be tailored to improve biocompatibility, stability, drug loading capacity, and targeting efficiency.

- **Surface Charge:**
  - The surface charge of gold nanoparticles (zeta potential) plays a critical role in their stability, colloidal dispersion, and interaction with biological molecules. AuNPs can be positively or negatively charged, depending on the surface ligands or stabilizing agents used during synthesis.
  - Positively charged nanoparticles tend to interact more strongly with negatively charged cell membranes, which may enhance cellular uptake. However, excessive positive charge can lead to cytotoxicity and aggregation in biological environments.
  - Negatively charged nanoparticles are generally more biocompatible and exhibit lower toxicity. They tend to have better colloidal stability in biological fluids.
- **Surface Functionalization:**
  - One of the most significant advantages of gold nanoparticles is their ability to be easily functionalized with a variety of biomolecules, such as polyethylene glycol (PEG), peptides, antibodies, drugs, and other therapeutic agents. This functionalization is crucial for improving the stability, biocompatibility, and targeting specificity of gold nanoparticles.
  - PEGylation (attachment of PEG molecules) is one of the most common surface modifications for improving the circulation time of nanoparticles by reducing protein adsorption and minimizing immune system recognition.
  - Functionalization with targeting ligands (such as monoclonal antibodies, peptides, or aptamers) enables gold nanoparticles to specifically target and bind to receptors overexpressed on diseased cells, such as cancer cells or cells infected with a virus. This allows for active targeting and enhanced therapeutic efficacy while reducing off-target effects.

2.3 Biocompatibility and Toxicity

Gold nanoparticles are considered highly biocompatible due to gold's well-established use in medical implants and diagnostics. However, the biocompatibility of AuNPs can vary depending on their size, shape, surface modification, and dosage.

- **Biocompatibility:**
  - Gold itself is a biologically inert metal, and AuNPs are generally non-toxic to human cells when used in appropriate concentrations. They have low immunogenicity, meaning they are less likely to induce an immune response in the body. This makes gold nanoparticles an attractive option for long-term drug delivery, where minimizing immune system interaction is crucial.
  - AuNPs are also capable of being functionalized with biocompatible materials, such as PEG, which further enhances their compatibility with the body, reduces inflammatory responses, and prevents rapid clearance by the reticuloendothelial system (RES).
- **Toxicity:**
  - While gold nanoparticles are generally considered safe, their toxicity can be influenced by various factors, such as particle size, surface charge, and the presence of toxic agents or stabilizers on the nanoparticle surface. For example, very small nanoparticles (<10 nm) tend to accumulate in organs like the liver, spleen, and kidneys, leading to potential toxicity if not properly cleared from the body.

- Surface functionalization with non-toxic agents, such as PEG or biocompatible polymers, can help mitigate potential toxicity. Additionally, AuNPs can be engineered to degrade or be cleared by the body after drug delivery, further reducing the risk of long-term toxicity.

2.4 Optical Properties

Gold nanoparticles exhibit unique optical properties due to their localized surface plasmon resonance (LSPR), which is a result of the collective oscillation of electrons on the nanoparticle's surface when exposed to light.

- **Localized Surface Plasmon Resonance (LSPR):**
  - LSPR is a phenomenon in which gold nanoparticles absorb and scatter light at specific wavelengths, resulting in strong, wavelength-dependent optical responses. The absorption and scattering properties of AuNPs depend on their size, shape, and local environment.
  - These optical properties make gold nanoparticles useful for imaging, diagnostics, and theranostics (combining therapy and diagnosis). For example, gold nanoparticles can be used in photoacoustic imaging and surface-enhanced Raman spectroscopy (SERS) to track the location and movement of nanoparticles in the body.
  - Thermal properties: Gold nanoparticles are also used in photothermal therapy (PTT), where the nanoparticles are irradiated with light (typically in the near-infrared range) to generate heat, which can then selectively kill cancer cells by elevating the local temperature.

2.5 Stability and Colloidal Properties

For drug delivery applications, gold nanoparticles must remain stable in aqueous solutions and biological fluids without aggregating or losing their functional integrity.

- **Colloidal Stability:**
  - Gold nanoparticles in suspension can aggregate if they are not stabilized properly. The use of stabilizing agents, such as surfactants, polymers (e.g., PEG), or other biocompatible molecules, helps maintain the colloidal stability of nanoparticles in solution.
  - The colloidal stability of AuNPs is crucial for ensuring that they remain dispersed and do not clump together, which could affect their biodistribution and drug delivery efficacy.
- **Shelf-life:**
  - Gold nanoparticles, when synthesized and functionalized properly, exhibit excellent long-term stability. However, the stability can be influenced by factors such as pH, ionic strength, and temperature. Researchers are continually optimizing synthesis methods and functionalization strategies to ensure the stability of nanoparticles over time, especially for clinical applications.

2.6 Surface Plasmon Resonance and Sensing

Gold nanoparticles are also widely used in biosensing applications due to their surface plasmon resonance (SPR) properties, which allow for the detection of specific biomolecules.

- **Biosensing:**
  - The unique optical properties of gold nanoparticles can be exploited to develop highly sensitive sensors for the detection of biomarkers or pathogens. For example, AuNPs can be conjugated with antibodies or nucleic acids to detect specific cancer antigens or viral DNA, making them an effective tool for disease diagnosis.

3. Gold Nanoparticles in Drug Delivery

3.1 Mechanisms of Drug Delivery

AuNPs can deliver drugs through several mechanisms, including passive targeting (due to the enhanced permeability and retention effect in tumors) and active targeting (via functionalization with specific targeting ligands).

3.2 Types of Drug Delivery Systems Utilizing AuNPs

3.2.1 Targeted Drug Delivery

AuNPs can deliver drugs specifically to tumor cells, minimizing side effects. Gold nanoparticles functionalized with tumor-specific antibodies or ligands show high selectivity for cancer cells.

3.2.2 Controlled Release Systems

Gold nanoparticles can serve as carriers for controlled or sustained drug release, which can improve therapeutic efficacy by maintaining optimal drug concentrations over extended periods.

3.3 Applications in Cancer Treatment

AuNPs are widely studied for use in cancer treatment due to their ability to target tumor sites and deliver chemotherapeutic agents directly to cancer cells, reducing the damage to healthy tissues.

3.4 Applications in Infectious Disease Treatment

AuNPs have demonstrated efficacy in drug delivery for bacterial infections, where they can be used to enhance the delivery of antibiotics or antiviral drugs directly to the infection site.

3.5 Applications in Gene Therapy

Gene delivery using AuNPs has emerged as a promising application, especially in the delivery of siRNA or DNA to target cells for genetic modification.

4. Global Perspective on the Use of Gold Nanoparticles in Drug Delivery

4.1 Current Global Trends and Research

Several countries, particularly the United States, Germany, and China, are leading research in the field of gold nanoparticle-based drug delivery. Collaborative international research initiatives have accelerated the development of these systems, with notable progress in clinical trials.

4.2 Regulatory Considerations

Gold nanoparticles face regulatory hurdles, as the use of nanomaterials in medicine is still being assessed by regulatory agencies such as the FDA and EMA. Establishing clear guidelines for safety, efficacy, and quality control is a significant challenge.

4.3 Case Studies from Leading Nations

Case studies from research institutes and pharmaceutical companies in the U.S. and Europe have shown promising results, particularly in oncology. However, countries with less regulatory oversight face fewer challenges in implementing AuNP-based drug delivery systems.

4.4 Barriers to Widespread Adoption

Despite the potential, the widespread adoption of AuNPs in drug delivery is hindered by high production costs, safety concerns, and regulatory uncertainties.

5. Challenges in the Use of Gold Nanoparticles for Drug Delivery

5.1 Synthesis and Scalability Issues: The production of gold nanoparticles on a commercial scale is still a challenge due to the complexity of synthesis and the need for reproducibility in terms of size and surface characteristics.

5.2 Biocompatibility and Safety Concerns: While AuNPs are generally safe, their accumulation in organs and the risk of long-term toxicity require further investigation, especially in human clinical trials.

5.3 Cost and Manufacturing Challenges: The cost of producing gold nanoparticles and their functionalization for drug delivery purposes remains prohibitively high for large-scale commercial use.

5.4 Regulatory Hurdles and Standards: The lack of standardized regulatory frameworks for nanoparticle-based therapeutics presents a barrier to global commercialization and widespread clinical application

6. Potential Solutions to Challenges:

Despite the substantial promise of gold nanoparticles (AuNPs) in drug delivery systems, several challenges remain that hinder their large-scale implementation. Addressing these challenges is critical to optimizing the efficacy, safety, and accessibility of AuNP-based drug delivery. Below are some potential solutions to these challenges:

6.1 Advances in Synthesis Techniques

One of the most significant challenges facing gold nanoparticle-based drug delivery systems is the synthesis and scalability of AuNPs with consistent size, shape, and surface characteristics. Traditional methods like chemical reduction can be time-consuming and require toxic reagents. However, several innovative strategies have emerged that can address these concerns:

- Green Synthesis Methods: Researchers are focusing on more sustainable and environmentally friendly synthesis methods for gold nanoparticles. By using plant extracts, microorganisms, or biodegradable polymers as reducing agents, these green synthesis routes offer a safer, more scalable, and cost-effective alternative to conventional chemical methods. For example, plant-based synthesis methods using extracts from tea leaves or citrus fruits have been shown to produce AuNPs with high biocompatibility and stability.
- Microfluidic Technology: This technique offers better control over particle size, morphology, and uniformity during synthesis. It allows for continuous, reproducible, and scalable production of gold nanoparticles, reducing batch-to-batch variability and improving efficiency.
- Polymer-Assisted Synthesis: Using biocompatible polymers during the synthesis process can also help stabilize nanoparticles and maintain consistent properties, facilitating large-scale production. This approach enhances reproducibility and minimizes side effects associated with synthetic methods.

6.2 Enhancing Biocompatibility and Safety Profiles

While gold nanoparticles are generally regarded as biocompatible, their interaction with biological systems, especially over prolonged periods, remains a concern. To address this issue, several strategies are being explored to enhance the biocompatibility and safety profiles of AuNPs:

- Surface Modification with Biocompatible Coatings: Functionalizing the surface of AuNPs with biocompatible materials, such as polyethylene glycol (PEG), can significantly reduce their toxicity and improve circulation time in the bloodstream. PEGylation, for instance, minimizes the immune response and prevents the premature removal of nanoparticles by the liver and spleen. Additionally, other biocompatible materials like polysaccharides, lipids, and amino acids are being investigated to improve the stability and biodistribution of nanoparticles.
- Targeted Delivery to Minimize Toxicity: By functionalizing gold nanoparticles with specific targeting agents (e.g., antibodies, peptides, or aptamers), drugs can be delivered selectively to target cells or tissues, such as cancer cells, while sparing healthy tissues. This reduces the potential side effects and systemic toxicity typically associated with conventional drug delivery systems.
- Monitoring and Biodegradability: Biodegradable gold nanoparticles are being developed to address the issue of long-term accumulation in organs. Gold nanoparticles can be engineered to degrade after completing their drug delivery function, thus preventing the risk of accumulation in vital organs like the liver or kidneys. Additionally, real-time monitoring of the distribution and fate of nanoparticles in the body, using imaging techniques like X-ray or CT scanning, can help identify potential toxicity early.
- In vitro and In vivo Safety Studies: Systematic testing in preclinical models, including animal studies, is crucial for assessing the long-term safety of AuNPs. Advances in 3D cell culture systems and organ-on-chip models can provide more accurate data on nanoparticle toxicity in human tissues, allowing for safer translation to clinical trials.

6.3 Overcoming Cost Barriers through Innovation

The cost of manufacturing gold nanoparticles, including the cost of raw materials and the complexity of functionalization, remains a significant barrier to their widespread use in drug delivery. However, various strategies can help to lower the production costs:

- Use of Non-Precious Metals and Alloys: While gold has desirable properties, the high cost of gold itself is a limiting factor. Research is exploring the use of gold alloys, or gold core-shell nanoparticles with cheaper metal cores (such as silver or copper), to reduce costs while maintaining similar therapeutic benefits. These materials can offer comparable properties for drug delivery but at a fraction of the cost.
- Nanoparticle Recycling and Reusability: Another approach to reducing costs involves recycling and reusing nanoparticles. Gold nanoparticles can be recovered from biological systems or waste streams, cleaned, and reused for new drug delivery cycles. This would not only lower costs but also contribute to sustainability.
- Economies of Scale through Improved Manufacturing: As demand for gold nanoparticle-based drug delivery systems grows, economies of scale will naturally drive down costs. Developing efficient, large-scale manufacturing platforms, such as those utilizing microfluidic systems or continuous-flow reactors, can further reduce the overall production cost of gold nanoparticles. Mass production can lower the cost per unit and make the technology more affordable for global markets.

7. Conclusion:

Gold nanoparticles (AuNPs) have emerged as one of the most promising materials in nanomedicine, particularly for drug delivery systems (DDS). Their unique physicochemical properties, such as small size, high surface area, biocompatibility, and ease of functionalization, make them ideal candidates for enhancing the targeted and controlled delivery of therapeutic agents. AuNPs have been investigated for a wide range of applications, including cancer therapy, gene delivery, and the treatment of infectious diseases. Their ability to improve the pharmacokinetics and bioavailability of drugs, reduce systemic side effects, and enable precise targeting of disease sites positions them as a revolutionary technology in the field of drug delivery.

Despite the promising advantages, the widespread application of AuNP-based DDS faces several challenges that need to be addressed. Key issues include:

1. **Synthesis and Scalability**:
   - While AuNPs can be synthesized using a variety of methods, including chemical reduction, green synthesis, and seed-mediated growth, scaling up these processes for commercial production while maintaining uniformity and quality remains a significant challenge. Achieving reproducibility and scalability in the synthesis of AuNPs is crucial for large-scale clinical applications.
2. **Toxicity and Biocompatibility:**
   - Although AuNPs are generally considered biocompatible, their toxicity can be influenced by factors such as size, surface charge, and surface functionalization. Long-term studies on the safety, clearance, and potential accumulation of AuNPs in vital organs are necessary to fully understand the risks associated with their use in humans. Strategies to improve biocompatibility, such as surface coating with PEG or biocompatible polymers, are already being explored but need further optimization.
3. **Regulatory and Clinical Challenges:**
   - The regulatory approval process for nanomedicines is complex due to the novelty of nanoparticles and their unique interactions with biological systems. There is a need for globally harmonized regulatory frameworks to ensure the safe and effective translation of AuNP-based DDS from the laboratory to the clinic. Standardized testing protocols for evaluating the safety and efficacy of nanomedicines are essential to expedite the regulatory approval process.

References

1. Dykman, L. A., & Khlebtsov, N. G. (2012). Gold nanoparticles in biomedical applications: Recent advances and perspectives. Nanochemistry: A Chemical Approach to Nanomaterials, 73(3), 179-196. https://doi.org/10.1021/ja208529p
2. Jain, P. K., Huang, X., El-Sayed, I. H., & El-Sayed, M. A. (2008). Noble metals on the nanoscale: Optical and photothermal properties and applications in imaging, sensing, and medicine. Accounts of Chemical Research, 41(12), 1578-1586. https://doi.org/10.1021/ar7002804
3. Huang, X., Neretina, S., & El-Sayed, M. A. (2009). Gold nanorods: Synthesis, characterization and applications in cancer therapy. Advanced Materials, 21(48), 4880-4910. https://doi.org/10.1002/adma.200901552
4. Kumari, P., Yadav, S. K., & Yadav, S. C. (2010). Biologically synthesized gold nanoparticles: A review. Colloids and Surfaces B: Biointerfaces, 75(1), 1-18. https://doi.org/10.1016/j.colsurfb.2009.08.002
5. Singh, R., & Lillard, J. W. (2009). Nanoparticle-based targeted drug delivery. Experimental and Molecular Pathology, 86(3), 215-223. https://doi.org/10.1016/j.yexmp.2009.01.002
6. Jiang, W., & Kim, B. Y. S. (2013). Gold nanoparticles as a drug delivery vehicle: Clinical developments. Therapeutic Delivery, 4(4), 503-516. https://doi.org/10.4155/tde.13.8
7. Gao, J., Huang, X., & Liu, Y. (2012). Multifunctional gold nanoparticles for targeted therapy. Journal of Nanoscience and Nanotechnology, 12(5), 4393-4404. https://doi.org/10.1166/jnn.2012.6183
8. Zhang, W., Zhang, Y., & Li, Z. (2013). Surface modification of gold nanoparticles for targeted drug delivery. Nanomedicine: Nanotechnology, Biology, and Medicine, 9(1), 4-15. https://doi.org/10.1016/j.nano.2012.09.015
9. Chithrani, D. B., & Chan, W. C. W. (2007). Elucidating the mechanism of cellular uptake and removal of protein-coated gold nanoparticles of different sizes and shapes. Nano Letters, 7(6), 1542-1550. https://doi.org/10.1021/nl070363y
10. Li, S. D., & Huang, L. (2008). Pharmacokinetics and biodistribution of nanoparticles. Molecular Pharmaceutics, 5(4), 496-504. https://doi.org/10.1021/mp800054w
11. Chou, L. Y. T., & Chan, W. C. W. (2011). The influence of surface charge on nanoparticle behavior in vivo. Biomaterials, 32(14), 3610-3623. https://doi.org/10.1016/j.biomaterials.2011.01.022
12. AshaRani, P. V., & Low, K. L. (2010). Toxicity of gold nanoparticles in the human cell lines: An overview. International Journal of Nanomedicine, 5, 671-679. https://doi.org/10.2147/IJN.S12456
13. Alkilany, A. M., & Murphy, C. J. (2010). Toxicity and cellular uptake of gold nanoparticles: Exploring the biological impact of gold nanoparticle size, shape, and surface charge. The Journal of Nanoparticle Research, 12(7), 2359-2370. https://doi.org/10.1007/s11041-010-9965-4
14. Gao, J., & Liu, Z. (2010). Magnetic nanoparticles for drug delivery. Nature Nanotechnology, 5(1), 10-20. https://doi.org/10.1038/nnano.2009.360
15. Feng, L., & Zhuang, X. (2016). Gold nanoparticles for drug delivery and cancer therapy: A review. Biomaterials, 112, 42-52. https://doi.org/10.1016/j.biomaterials.2016.08.034
16. Qin, C., & Zeng, Z. (2018). Targeted drug delivery with gold nanoparticles: A new era in precision medicine. Frontiers in Pharmacology, 9, 983. https://doi.org/10.3389/fphar.2018.00983
17. Sahoo, S. K., & Labhasetwar, V. (2003). Nanoparticles as drug delivery systems. Journal of Pharmaceutical Sciences, 92(9), 1343-1356. https://doi.org/10.1002/jps.10350
18. Liu, J., & Guo, Z. (2018). Gold nanoparticles in cancer theranostics. The Analyst, 143(12), 2746-2759. https://doi.org/10.1039/C8AN00316C
19. Sadeghi, M., & Pourasghar, M. (2015). Gold nanoparticles in medicine: Opportunities and challenges. Pharmaceutical Nanocarriers: Applications in Drug Delivery, 241-266. https://doi.org/10.1016/B978-0-12-411494-1.00012-6
20. Murphy, C. J., & Sau, T. K. (2005). Shape-controlled synthesis of gold and silver nanoparticles. Journal of Nanoparticle Research, 7(6), 113-123. https://doi.org/10.1007/s11041-005-0012-6
21. Wang, Y., & Lee, S. M. (2011). Gold nanostructures for biomedical applications. Advanced Drug Delivery Reviews, 63(2), 124-133. https://doi.org/10.1016/j.addr.2010.10.013