



## Synthesis Methods of Biocompatible Nanoparticles

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### INTRODUCTION

Nanotechnology has emerged as a revolutionary field in science, particularly in medicine, agriculture, environmental remediation, and biotechnology. Among various nanomaterials, biocompatible nanoparticles are of special importance due to their non-toxic, eco-friendly, and biological safety properties. These nanoparticles can interact safely with living systems without causing adverse effects, making them highly suitable for biomedical and agricultural applications.

Biocompatible nanoparticles are generally made from materials such as gold, silver, zinc oxide, iron oxide, silica, chitosan, and biodegradable polymers (PLA, PLGA). The effectiveness of these nanoparticles largely depends on their size, shape, surface properties, and synthesis method. The synthesis of biocompatible nanoparticles can be broadly classified into physical, chemical, and biological (green) methods. Each method has unique advantages and limitations in terms of cost, scalability, toxicity, and environmental impact.

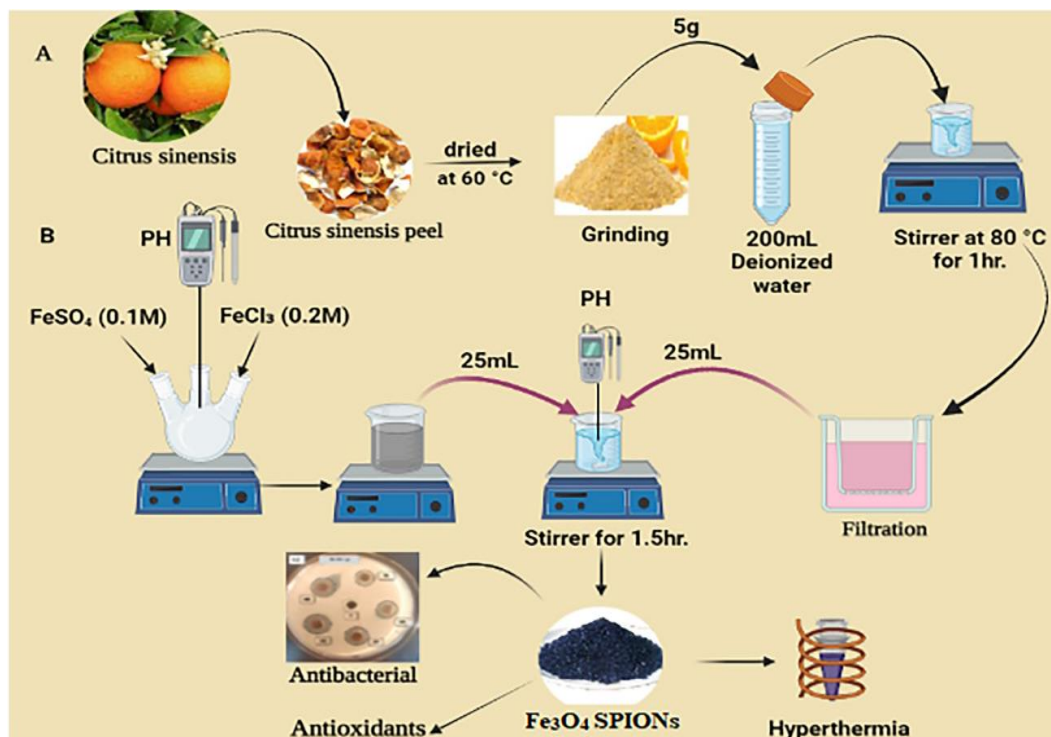
### 2. Concept of Biocompatible Nanoparticles

Biocompatible nanoparticles are nanoscale materials, typically ranging from 1–100 nm, that are designed to interact safely with biological systems without causing toxicity, immune rejection, or adverse physiological effects. These nanoparticles are engineered from materials such as metals, metal oxides, polymers, or biopolymers that are compatible with living organisms.

The key features of biocompatible nanoparticles include their non-toxic nature, high surface area to volume ratio, and ability to interact efficiently at the cellular and molecular levels. They also exhibit controlled drug delivery capability, allowing targeted release of therapeutic agents at specific sites in the body. In addition, they show enhanced cellular interaction and improved stability in biological environments, which increases their efficiency in biomedical applications.

Due to these properties, biocompatible nanoparticles are widely used in drug delivery systems, cancer therapy, biosensors for disease detection, plant disease management in

agriculture, and environmental detoxification processes. Their safe interaction with biological systems makes them highly valuable in modern science and technology.



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### 3. Classification of Synthesis Methods

The synthesis methods of biocompatible nanoparticles are broadly classified into two main approaches: **top-down** and **bottom-up**, based on how nanoscale materials are formed from bulk substances or atomic units.

#### 3.1 Top-Down Approach

In the top-down approach, large bulk materials are physically or mechanically broken down into nanosized particles. This method involves techniques such as ball milling, lithography, etching, and laser ablation. Although it is simple and suitable for large-scale production, it often results in irregular particle size distribution and possible surface defects.

#### 3.2 Bottom-Up Approach

In the bottom-up approach, nanoparticles are synthesized by assembling atoms, ions, or molecules through chemical or biological processes. This includes chemical reduction,

sol-gel synthesis, hydrothermal methods, and green synthesis using plant extracts or microorganisms. This method provides better control over particle size, shape, and surface properties.

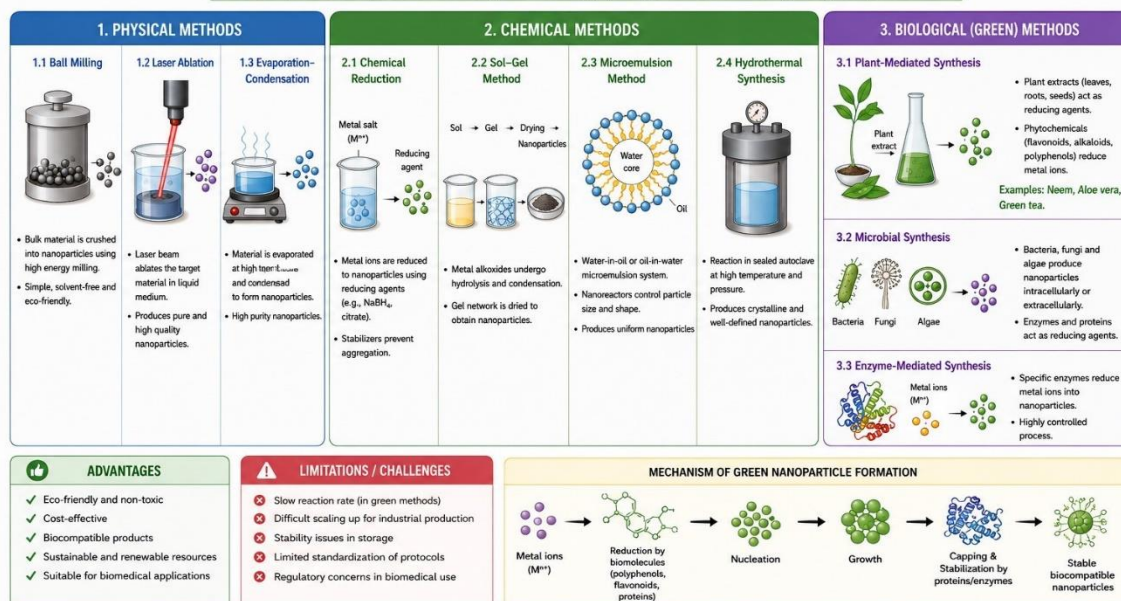
Among these two, the bottom-up approach is more widely preferred for biocompatible nanoparticles because it ensures higher precision, improved uniformity, and better compatibility for biological applications such as drug delivery and medical diagnostics.

### 4. Physical Methods of Synthesis

Physical methods of nanoparticle synthesis involve mechanical or physical processes without the use of chemical reactions. These methods are generally used to produce high-purity nanoparticles, although they may require high energy input and specialized equipment.

## SYNTHESIS METHODS OF BIOCOMPATIBLE NANOPARTICLES

Biocompatible nanoparticles can be synthesized by physical, chemical and biological (green) methods.



### 4.1 Ball Milling

In the ball milling method, bulk materials are mechanically ground into nano-sized particles using high-energy rotating balls in a closed chamber. It is a simple, cost-effective, and widely used technique for producing metal and ceramic nanoparticles. However, particle size distribution may not be very uniform.

### 4.2 Laser Ablation

Laser ablation involves focusing a high-energy laser beam onto a solid target material. The intense energy vaporizes the material, and nanoparticles are formed in a surrounding liquid or gas medium. This method produces highly pure nanoparticles with controlled composition and is suitable for advanced applications in medicine and electronics.

### 4.3 Evaporation–Condensation Method

In this technique, the material is first evaporated at high temperatures and then condensed into nanoparticles upon cooling. It is commonly used for synthesizing metallic nanoparticles with good crystallinity.

## 5. Chemical Methods of Synthesis

Chemical methods are widely used for the synthesis of biocompatible nanoparticles because they provide excellent control over particle size, shape, composition, and distribution. These methods generally involve

chemical reactions that convert precursor materials into stable nanoparticles.

### 5.1 Chemical Reduction Method

In this method, metal salts are reduced using reducing agents such as sodium borohydride, citrate, or ascorbic acid. For example, silver nanoparticles can be synthesized from silver nitrate (AgNO<sub>3</sub>). Stabilizing agents or surfactants are added to prevent aggregation and maintain nanoparticle stability.

### 5.2 Sol-Gel Method

Sol→Gel→Drying→Nanoparticles

This process involves the hydrolysis and condensation of metal alkoxides to form a colloidal sol, which gradually transforms into a gel network. The gel is then dried and calcined to obtain nanoparticles. It is widely used for oxide nanoparticle synthesis.

### 5.3 Microemulsion Method

This method uses a water-in-oil or oil-in-water emulsion system where nanoscale droplets act as nanoreactors. These confined spaces control particle growth and produce uniform nanoparticles with narrow size distribution.

### 5.4 Hydrothermal Synthesis

In this technique, reactions occur in a sealed autoclave at high temperature and pressure. It produces highly crystalline nanoparticles with controlled morphology.

## 6. Biological (Green) Synthesis Methods

Green synthesis methods are the most sustainable and eco-friendly approaches for producing biocompatible nanoparticles. These methods use biological resources such as plants, microorganisms, and enzymes as natural reducing and stabilizing agents, eliminating the need for toxic chemicals. As a result, the nanoparticles produced are highly suitable for biomedical, agricultural, and environmental applications.

### 6.1 Plant-Mediated Synthesis

In this method, plant extracts obtained from leaves, roots, stems, seeds, or flowers are used for nanoparticle synthesis. Phytochemicals such as flavonoids, alkaloids, terpenoids, and phenolic compounds act as natural reducing agents that convert metal ions into nanoparticles. For example, neem, aloe vera, and green tea extracts are commonly used for synthesizing silver and gold nanoparticles. This method is simple, rapid, and environmentally safe.

### 6.2 Microbial Synthesis

Microorganisms such as bacteria, fungi, and algae are capable of producing nanoparticles either intracellularly or extracellularly. Enzymes, proteins, and metabolic compounds present in these organisms facilitate reduction and stabilization of nanoparticles. Fungal synthesis is often preferred due to higher production efficiency and ease of handling.

### 6.3 Enzyme-Mediated Synthesis

In this technique, specific enzymes are isolated and used to reduce metal ions into nanoparticles under controlled conditions. This allows precise control over particle size and morphology.

## 7. Mechanism of Green Nanoparticle Formation

In green synthesis of biocompatible nanoparticles, biological molecules play a crucial role as both reducing and stabilizing agents. The formation process is driven by natural compounds present in plants, microorganisms, or enzymes, which facilitate the conversion of metal ions into stable nanoparticles under eco-friendly conditions.

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Polyphenols, flavonoids, and other phytochemicals act as reducing agents by donating electrons to metal ions, thereby converting them into zero-valent nanoparticles. For example, metal salts such as  $\text{Ag}^+$  or  $\text{Au}^{3+}$  are reduced to  $\text{Ag}^0$  or  $\text{Au}^0$  nanoparticles through this biochemical reduction process.

Proteins and other biomolecules act as capping agents that surround the newly formed nanoparticles, preventing aggregation and ensuring stability. These biomolecules also enhance biocompatibility and reduce toxicity. Enzymes further regulate nucleation and growth processes, controlling particle size, shape, and dispersion.

## 8. Characterization of Nanoparticles

After synthesis, nanoparticles are characterized using advanced techniques:

- ❖ UV-Visible Spectroscopy (optical properties)
- ❖ X-Ray Diffraction (XRD) (crystallinity)
- ❖ Scanning Electron Microscopy (SEM) (shape and morphology)
- ❖ Transmission Electron Microscopy (TEM) (size analysis)
- ❖ Dynamic Light Scattering (DLS) (particle distribution)

## 9. Applications of Biocompatible Nanoparticles

Biocompatible nanoparticles have a wide range of applications across medicine, agriculture, environment, and industry due to their small size, high reactivity, and safe interaction with biological systems.

### 9.1 Medicine

In the medical field, biocompatible nanoparticles are extensively used for targeted drug delivery systems, where drugs are delivered directly to diseased cells, reducing side effects. They are also applied in cancer therapy for selective tumor targeting and in antimicrobial treatments to control bacterial and viral infections. Additionally, nanoparticles are used in biosensors for early disease detection and diagnostic imaging.

## 9.2 Agriculture

In agriculture, nanoparticles play an important role in nano-fertilizers that improve nutrient efficiency and plant growth. Nano-pesticides provide effective pest control with reduced chemical usage. They are also used for plant disease management by enhancing plant immunity and reducing pathogen attacks.

## 9.3 Environment

Biocompatible nanoparticles are used in water purification systems, wastewater treatment, and removal of heavy metals and toxic pollutants. They help in environmental detoxification and improve ecosystem health.

## 9.4 Industry

In industrial applications, nanoparticles are used as catalysts to enhance chemical reactions, in sensors for detecting gases and chemicals, and in coatings for improving durability, corrosion resistance, and surface properties.

## 10. Advantages of Biocompatible Nanoparticles

Biocompatible nanoparticles offer several important advantages that make them highly valuable in biomedical, agricultural, and environmental applications. One of the main benefits is their high efficiency in biological systems due to their extremely small size and large surface area, which allows better interaction at the cellular and molecular levels.

Another key advantage is reduced toxicity, as these nanoparticles are designed to be safe and compatible with living organisms, minimizing harmful side effects. They are also environmentally safe, especially those synthesized through green methods, which avoid toxic chemicals and reduce ecological pollution.

Biocompatible nanoparticles exhibit target-specific action, meaning they can be engineered to act on specific cells, pathogens, or tissues without affecting surrounding healthy systems. This improves precision in drug delivery and disease treatment.

In addition, they provide enhanced stability and solubility of drugs and active compounds, improving their effectiveness and

bioavailability. Due to these combined properties, biocompatible nanoparticles are considered highly promising tools for sustainable development in modern science and technology.

## 11. Limitations and Challenges (100 words)

Biocompatible nanoparticles face several limitations despite their wide applications. High production cost is a major issue, especially in advanced physical and chemical synthesis methods. Scaling up laboratory processes to industrial levels is difficult and often results in inconsistent quality. Stability during storage is another challenge, as nanoparticles may aggregate or lose functionality over time. Lack of standardized protocols for synthesis and characterization leads to variability in results. In biomedical applications, strict regulatory approval and safety assessments are required due to concerns about toxicity and long-term effects. Therefore, improved, cost-effective, and standardized methods are needed for large-scale use.

## 12. Future Prospects

The future of biocompatible nanoparticle synthesis is highly promising due to rapid advances in green nanotechnology, artificial intelligence, and biotechnology. Plant-based and microbial synthesis will play a key role in developing eco-friendly nanoparticles. AI-driven design will enable precise control over particle size, shape, and function. In medicine, precision drug delivery and targeted therapy will improve treatment efficiency with minimal side effects. Nano-bio hybrid systems will enhance diagnostic and therapeutic applications. Sustainable industrial nanoprocessing will reduce cost, waste, and environmental impact. Overall, integration of nanoscience, biotechnology, and AI will make nanoparticle synthesis safer, smarter, and more efficient.

## CONCLUSION

Biocompatible nanoparticles represent a major advancement in nanotechnology with wide applications in medicine, agriculture, and

environmental science. Their synthesis methods—physical, chemical, and biological—offer different advantages, but green synthesis methods are the most sustainable and eco-friendly. Continuous research in nanoparticle synthesis will enhance their safety, efficiency, and large-scale applicability in the future.

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