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"Advances In Nanoparticle-Based Therapeutics: A Review Of Serum Protein Nanoparticles, Gold And Silver Nanoparticles, And Magnetic Nanoparticles - Preparation, Mechanism Of Action, And Function In Pharmacy"

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➢ **ABSTRACT**

The significance of nanoparticles (NPs) in technological advancements is due to their adaptable characteristics and enhanced performance over their parent material. They are frequently synthesized by reducing metal ions into uncharged nanoparticles using hazardous reducing agents. However, there have been several initiatives in recent years to create green technology that uses natural resources instead of dangerous chemicals to produce nanoparticles. In green synthesis, biological methods are used for the synthesis of NPs because biological methods are eco-friendly, clean, safe, cost-effective, uncomplicated, and highly productive. Numerous biological organisms, such as bacteria, actinomycetes, fungi, algae, yeast, and plants, are used for the green synthesis of NPs. Additionally, this paper will discuss nanoparticles, including their types, traits, synthesis methods, applications, and prospects Nanoparticles are tiny particles with unique properties, classified into organic, inorganic, and carbon-based categories.

They have been used for centuries, with ancient civilizations employing them in various applications. The surface characteristics and particle size of nanoparticles can be modified to target medications passively and actively. They offer numerous advantages, including enhanced control over the encapsulated chemicals' release

kinetics, improved drug transportation through cell barriers, and reduced toxicity. However, nanoparticles also exhibit strong reactivity due to
their small size and large surface area, which can lead to biologically harmful effects. Carbon-based nanoparticles, including fullerenes, graphene, carbon nanotubes, and carbon nanofibers, have distinct mechanical, chemical, and physical characteristics. Silver, gold, and copper nanoparticles have also been extensively studied for their antibacterial and antiviral properties. The applications of nanoparticles are diverse, ranging from biomedical and pharmaceutical to environmental and industrial uses. Overall, nanoparticles have the potential to revolutionize various fields, but their development and use must be carefully managed to mitigate their potential risks.

➢ INTRODUCTION

❖ NANOTECHNOLOGY

It is the fascinating branch of Science which encompasses study of systems having nano scale size. The prefix 'nano' comes from Latin word 'nanus' meaning dwarf or tiny. With the convention of International System of Units (SI) it is used to indicate a reduction factor of 109 times (1nm corresponding to 10-9 m). Nobel Laureate Richard P. Feynman first presented 'Nanotechnology' during his well famous 1959 lecture,
'There's Plenty of Room at the Bottom'. Since then, there have been various innovative and revolutionary developments in this field. They may consist of organic material, metal, metal oxide or carbon. Nanoparticles differ in size, shore & dimension in addition to their composition. one-dimensional graphemes, which con only has one parameter, two-dimensional carbon nanotubes, which have both length & breadth, three dimensional gold nanoporficies, which have all these dimensions & zero-dimensional nan dots, which have their length, breadth & height fixed of a single point are just a few examples of the different sizes & shapes of nanoparticles. The range of dimensions, forms & arrangements, such as spherical, cylindrical, tubular, conical, hallow core, spiral, flat, etc. Nanotechnology involves the design, synthesis and use of materials of the atomic, molecular and macromolecular scales in order to produce new Nona sized materials.
Pharmaceutical nanoparticles are solid drug carriers that are sub micron-sized (less than 100nm in diameter) and either biodegradable or Not. Richard Zsigmondy, Nobel Prize Laureate in chemistry in 1925, first suggested the idea of a "nanometer".
He invented the term nanometer specifically to describe particle size & was the first to use a microscope to quantify particle size like gold colloids. Synthesizing using a plant or plant extracts, an enzyme, a fungus & a microorganism.
The development of these eco-freiendly techniques for producing nanoparaticles-especially silver nanoparticles, which have many uses - is emerging as a major field of nanotechnology. There are essentially three different kinds of methods for the synthesis of NPs. Physical, chemical and other techniques. The Physical approach is sometimes referred to as the top-down approach, where as the chemical and biological approaches together are called the bottom-up approach.

❖ History

In 1959, American physicist & Nobel Laureate Richard Feynman introduced the idea of nanotechnology. Feynman gave a talk titled "There's plenty of room at the bottom" at the California Institute of Technology (Caltech) during the annual meeting of the American Physical Society.
After fifteen years, Norio Taniguchi, a Japanese scientist, was the first to use & define the term "nanotechnology" in 1974.

Nanostructures have been used by humans since the 4th century AD by the Romans, which demonstrated one of the most interesting examples of nanotechnology in the ancient world. The Lycurgus cup, from the British Museum collection, represents one of the most outstanding achievements in ancient glass industry.

➢ LITERATURE REVIEW

1. **[10] Pokhroal A, Tripathi G. Evaluation Parameters of Nanoparticles: A Review. Indian Journal of Novel Drug Delivery.**

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2. **Nanoparticles, and Their Applications in Various Fields of Nanotechnology: A Review. Catalysts. 2022;12(11):**

Certain serum proteins, like transferrin, naturally attach to receptors that are overexpressed on diseased tissues or cancer cells.
When utilized as nanoparticles, they reduce side effects by delivering the medication only to these cells through receptor-mediated endocytosis.

3. **[21] Borkar A, Kharbal G, Shende M, Gaikwad P, Bhopale S. A Review on Nanoparticle. Journal of Emerging**

Naturally, occurring serum proteins like albumin, transferrin, and immunoglobulins are used to create serum protein nanoparticles, which are nanoscale particles (usually 1–100 nm).
These proteins are great drug carriers because they are both biocompatible and biodegradable. Serum protein nanoparticles can bind drugs and shield them from degradation. Since they can target specific tissues like tumors, they are frequently used in drug delivery, targeted therapy, and controlled release of medications

4. **Technologies and Innovative Research. 2023;10(6):1-6.**

Nanoparticles bind to cell surface receptors and enter cells through endocytosis once they reach the target tissue. After internalization, they are transported within the cell.

➢ SERUM PROTEIN NANOPARTICLES

❖ DEFINITION

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❖ MOA OF SERUM PROTEIN NANOPARTICLES

Their mechanism of action involves several key steps:

1. **Drug Encapsulation and Stabilization**

Serum proteins use hydrogen bonds, hydrophobic interactions, and electrostatic forces to bind, entrap, or adsorb drug molecules.

This enhances the drug's stability and solubility while shielding it from deterioration.

2. **Targeted Delivery**

Certain serum proteins, like transferrin, naturally attach to receptors that are overexpressed on diseased tissues or cancer cells.

When utilized as nanoparticles, they reduce side effects by delivering the medication only to these cells through receptor-mediated endocytosis.

3. **Cellular Uptake**

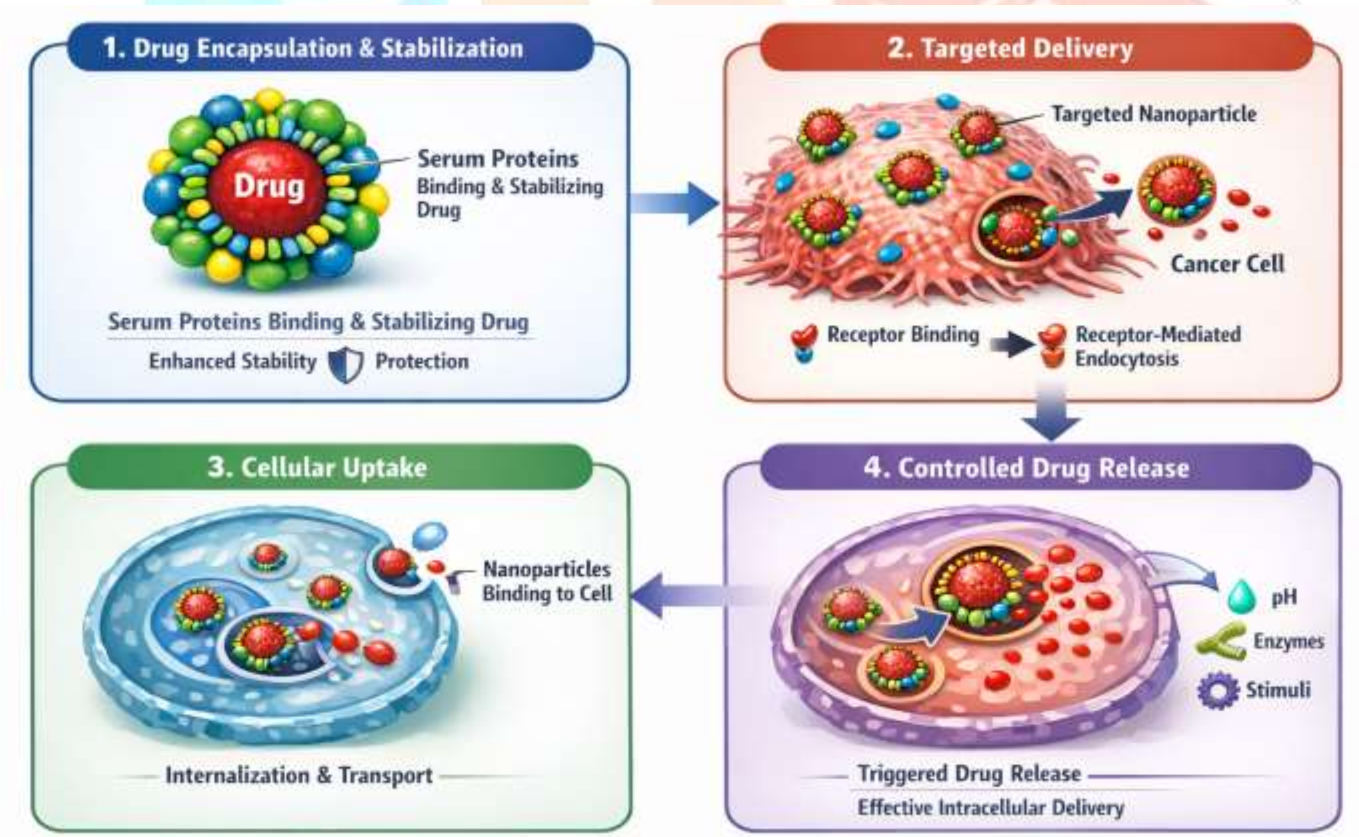
Nanoparticles bind to cell surface receptors and enter cells through endocytosis once they reach the target tissue.

After internalization, they are transported within the cell for further processing.

4. **Controlled Drug Release**

The drug is released from the nanoparticle in response to changes in pH, enzymes, or the intracellular environment.

This increases therapeutic efficiency by ensuring that the medication is released only inside the target cells.



❖ PREPARATION OF SERUM PROTEIN NANOPARTICLES

1. Nanoparticle Formation

The following techniques are used to create nanoparticles:

a) Desolvation / Coacervation

Protein molecules aggregate into nanoparticles when a desolvating agent (such as ethanol or acetone) is added dropwise.

b) Emulsification

An organic phase is used to emulsify the protein–drug solution before it is solidified.

c) Thermal Gelation / pH Induction

Nanoparticle formation is triggered by heat or by a change in pH.

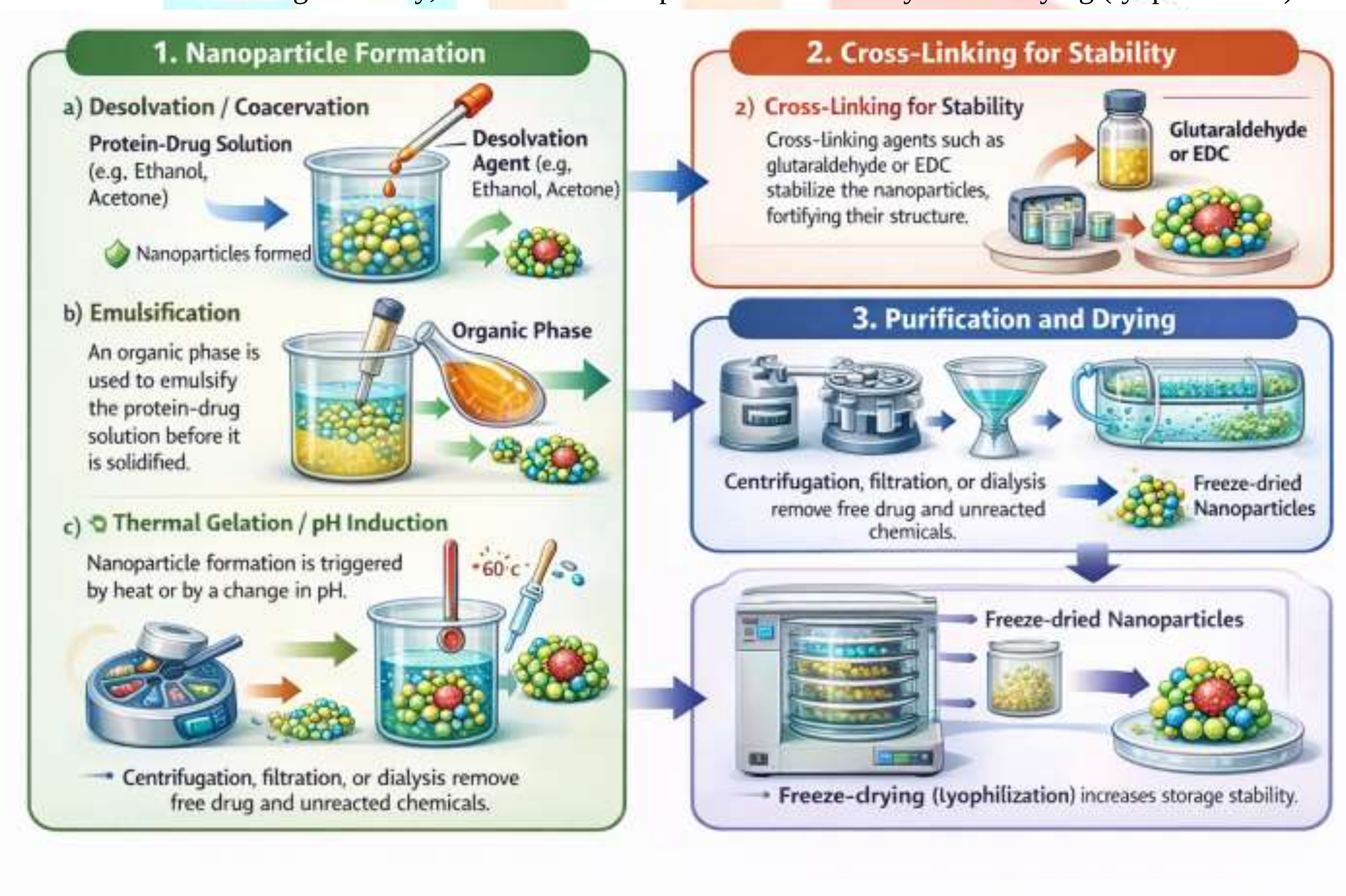
2. Cross-Linking for Stability

.Cross-linking agents such as glutaraldehyde or EDC are added to the nanoparticles to stabilize them. In addition to preventing dissolution, this step fortifies the structure of the nanoparticles.

3. Purification and Drying

Centrifugation, filtration, or dialysis are used to purify the formed nanoparticles in order to eliminate free drug and unreacted chemicals.

To increase storage stability, the finished nanoparticles are dried by freeze-drying (lyophilization).



❖ FUNCTIONS OF SERUM PROTEIN NANOPARTICLES

1. Drug Delivery and Targeting

Through receptor-mediated targeting, serum protein nanoparticles (such as albumin or transferrin nanoparticles) function as carriers that deliver medications directly to particular tissues or cells, particularly in cancer therapy.

2. Improved Drug Solubility and Stability

Serum protein nanoparticles increase the stability and bioavailability of medications by making poorly water-soluble drugs more soluble and by shielding them from degradation and deterioration.

3. Controlled and Sustained Release

Serum protein nanoparticles minimize side effects and reduce the frequency of dosing by releasing the medication gradually and in a controlled manner.

4. Fast Action of Serum Protein Nanoparticles

Serum protein nanoparticles, such as albumin-based nanoparticles, exhibit fast action in pharmacy due to their ability to rapidly transport drugs to the target site. Their nanoscale size facilitates effective cellular uptake and rapid absorption.

Additionally, they ensure quicker release of the drug at the site of action by binding and transporting medications through the bloodstream with ease. Their biocompatibility and reduced clearance from the body help them reach tissues more effectively, leading to a rapid onset of therapeutic activity.

➢ GOLD SILVER NANOPARTICLES

❖ DEFINITION

Gold and silver nanoparticles are minuscule particles of gold (Au) and silver (Ag), usually ranging in size from 1 to 100 nm. In contrast to their bulk forms, they display unique optical, chemical, and physical characteristics at the nanoscale.

These nanoparticles are very useful in medicine, including drug delivery, diagnostics, imaging, and antimicrobial treatments. They also have catalytic applications due to their large surface area and strong surface plasma on resonance.

❖ MECHANISM OF ACTION OF GOLD AND SILVER NANOPARTICLES

1. Cell Membrane Interaction

Gold and silver nanoparticles attach to the microbial or cell membrane due to electrostatic attraction. This interaction damages membrane integrity and increases membrane permeability, resulting in leakage of cellular components and eventual cell death, particularly in bacteria.

2. Generation of Reactive Oxygen Species (ROS)

Silver nanoparticles induce the formation of reactive oxygen species such as superoxide radicals and hydrogen peroxide. These ROS cause oxidative stress, leading to damage of proteins, lipids, and DNA, thereby inhibiting cell growth and inducing apoptosis.

3. Protein and Enzyme Inactivation

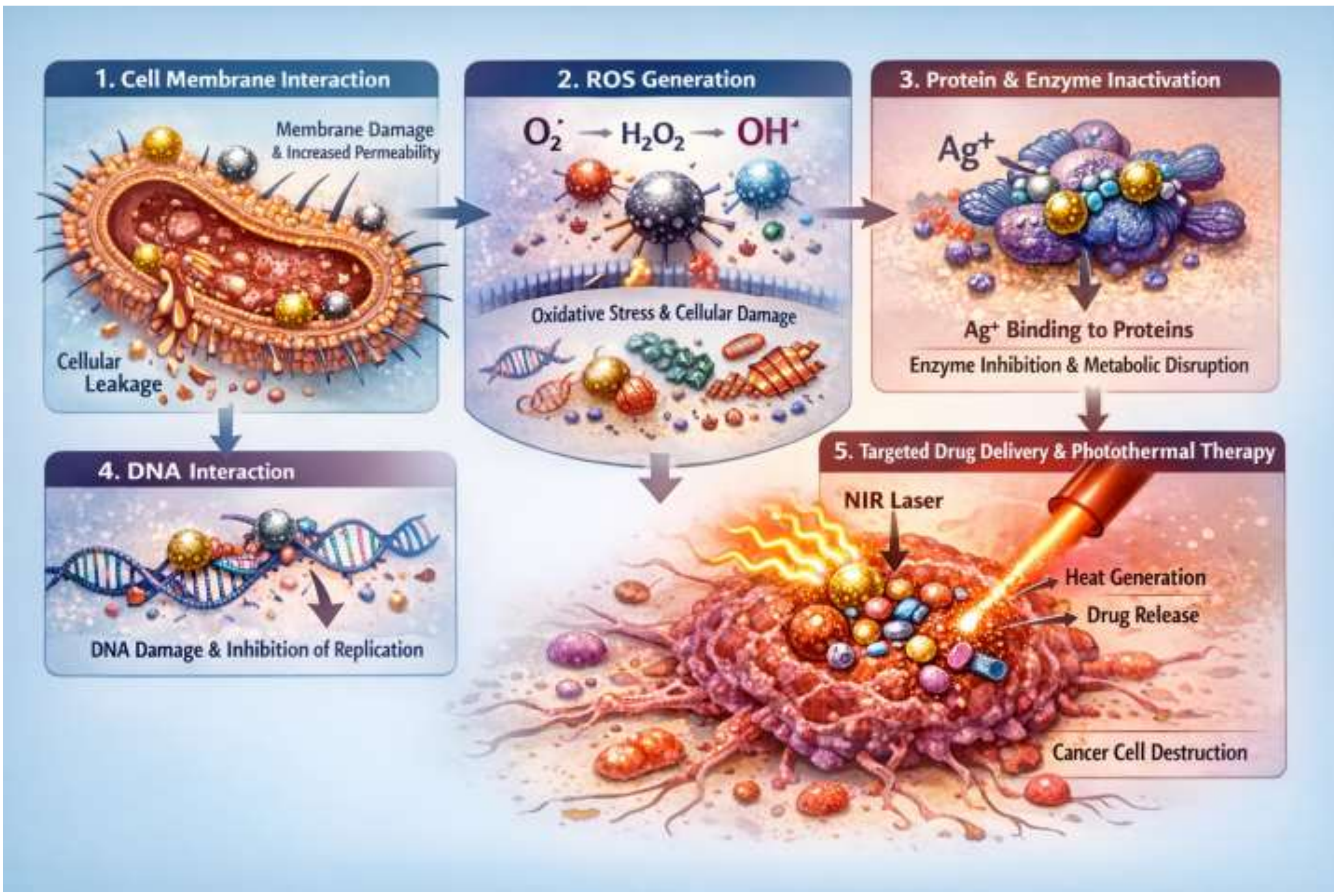
Silver nanoparticles release Ag^+ ions that bind to thiol (–SH) groups of enzymes and proteins. This causes enzyme denaturation and disruption of metabolic pathways. Gold nanoparticles mainly function as carriers and can regulate protein interactions.

4. DNA Interaction and Inhibition

Nanoparticles penetrate the cell and interact directly with DNA. This interaction inhibits DNA replication and transcription, preventing cell division and ultimately leading to cell death.

5. Targeted Drug Delivery and Photothermal Effect (Gold Nanoparticles)

Gold nanoparticles convert near-infrared (NIR) light into heat, producing a photothermal effect that selectively destroys cancer cells without damaging normal tissues. They also serve as efficient drug delivery systems, enabling controlled and targeted drug release at the site of action



❖ PREPARATION OF GOLD–SILVER NANOPARTICLES

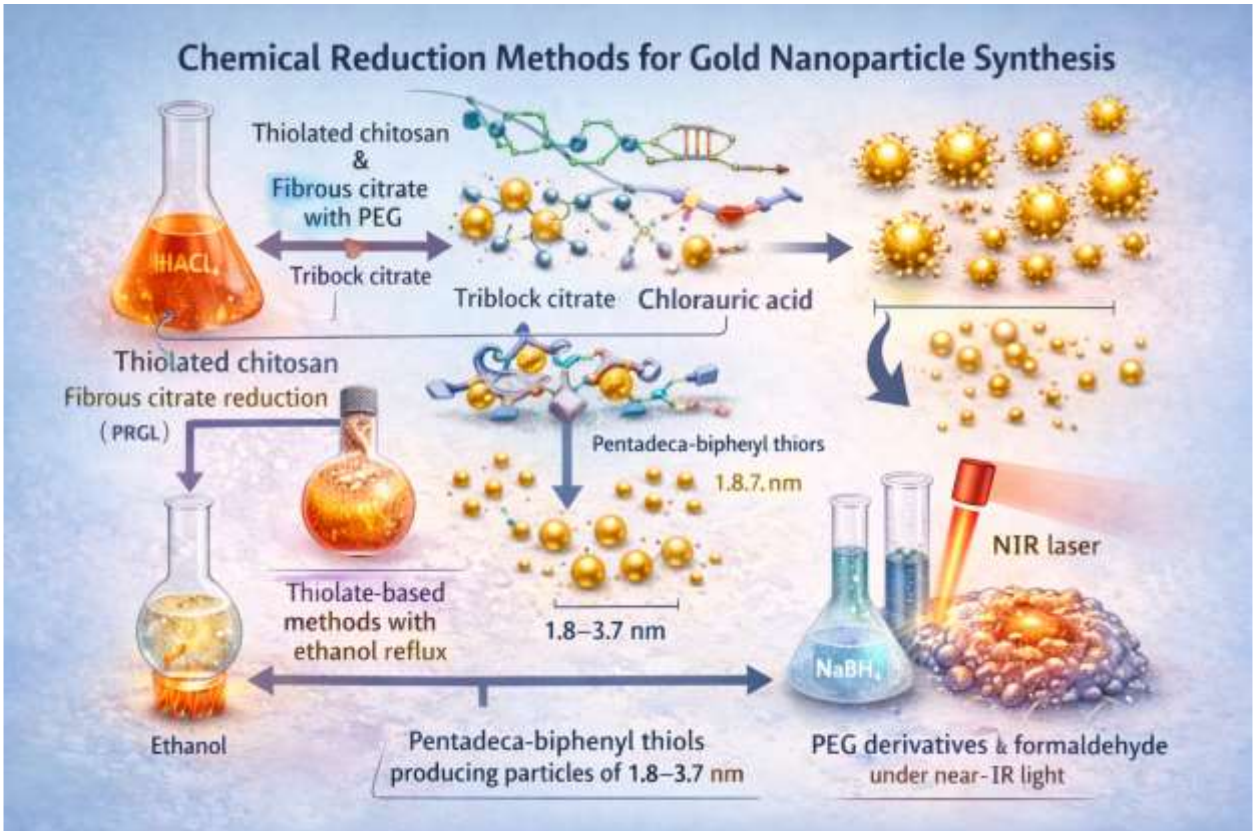
1. Chemical Reduction Method (Wet Chemistry)

The most popular method for creating gold and silver nanoparticles is chemical reduction, also known as the wet-chemical method. This technique uses appropriate reducing agents in the presence of stabilizing (or capping) agents to reduce metal salts such as $HAuCl_4$ and $AgNO_3$.

This method is straightforward, affordable, scalable, and well documented in the literature.

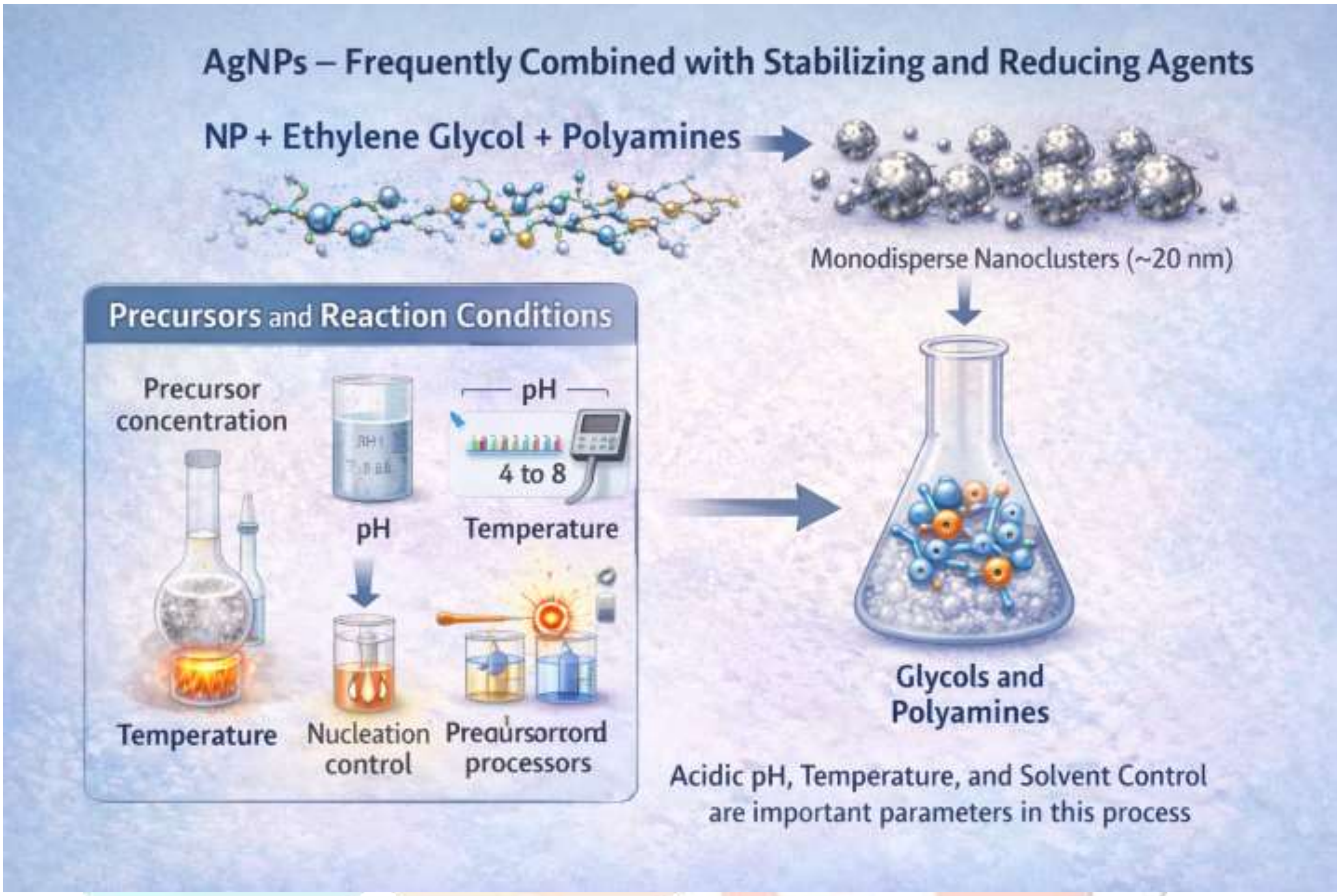
❖ **Gold Nanoparticles**

Several chemical reduction methods, such as the reduction of $HAuCl_4$ using thiolated chitosan and fibrous citrate reduction with PEG, triblock citrate, or chloroauric acid, can be used to create gold nanoparticles.
Other techniques include:
Thiolate-based methods with ethanol reflux Dodecanethiol to obtain particles under 10 nm
Pentadeca-biphenyl thiols, producing particles of 1.8–3.7 nm
Sodium borohydride reduction and PEG derivatives with formaldehyde under near-IR light are also used to synthesize nanoparticles.



❖ **Silver Nanoparticles**

AgNPs – Frequently Combined with Stabilizing and Reducing Agents
To create silver nanoparticles in aqueous solution, monodisperse nanoclusters (~20 nm) are produced by the polyol process using NP and ethylene glycol, along with polyamine-protective systems. Acidic pH, temperature, and solvent control are important parameters in this process.
Precursors and Reaction Conditions Precursor concentration, pH, Temperature, Nucleation control.



❖ FUNCTION OF GOLD SILVER NANOPARTICLES IN PHARMACY

1. **Antimicrobial Agent**:

Gold–silver nanoparticles have strong antiviral, antifungal, and antibacterial qualities. Gold nanoparticles increase stability and biocompatibility and aid in the prevention of drug-resistant infections. Silver nanoparticles produce reactive oxygen species (ROS) that harm microbial cell membranes.

2. **Drug Delivery System**:

By improving drug solubility, stability, and targeted delivery, Au–Ag nanoparticles function as efficient drug carriers. Because of their small size, they allow for controlled and prolonged drug release, which minimizes side effects and lowers dosage frequency.

3. **Diagnostic and Imaging Applications**:

Gold–silver nanoparticles are frequently utilized in biosensors and diagnostic tests because of their surface plasmon resonance characteristics. They are helpful in medical imaging methods and increase the sensitivity and accuracy of disease detection.

4. Anticancer Activity:

Through the production of ROS, gold–silver nanoparticles can preferentially accumulate in cancer cells and cause apoptosis. They are useful in cancer treatment because they increase the efficacy of anticancer medications. Photo thermal therapy is used in cancer treatment to kill cancer cells. Gold acts as a catalyst in reactions involving oxidation and reduction, particularly at the nanoscale. Used in electronics devices like sensors, conductive inks, and nanoelectronics.

➢ MAGNETIC NANOPARTICLES

❖ INTRODUCTION OF MAGNETIC NANOPARTICLES

Magnetic nanoparticles are particles usually ranging in size from 1–100 nanometers. Magnetic nanoparticles have special magnetic characteristics because of their nanoscale size. These materials behave differently from their bulk counterparts and are frequently made of iron, cobalt, nickel, or their oxides such as magnetite (Fe_3O_4) and maghemite (Y-Fe_3O_4).

Due to their easy surface functionalization, controllable size and shape, high surface-to-volume ratio, and sensitivity to magnetic fields, magnetic nanoparticles have garnered a lot of interest. These characteristics allow for effective separation procedures, targeted delivery, and precise manipulation.

These benefits have led to the widespread use of magnetic nanoparticles in biomedicine, hyperthermia treatment, environmental remediation, catalysis, data storage, and sensing technologies. Research and innovation in nanoscience and nanotechnology are still fueled by their adaptability and tunable properties.

❖ HISTORY OF MAGNETIC NANOPARTICLES

1. First Discovery:
In the 1950s, magnetite (Fe_3O_4) nanoparticles in bacteria (magnetotactic bacteria) were the first natural examples of magnetic materials at the nanoscale.
When scientists found that iron oxide particles smaller than about 100 nm exhibit superparamagnetism, they started synthesizing and studying magnetic nanoparticles (MNPs) in the 1970s and 1980s.
Due to their biocompatibility, early research concentrated on iron oxide nanoparticles such as magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3).

2. Why Magnetic Nanoparticles Were Developed:
Magnetic nanoparticles were developed to overcome the limitations of conventional drug delivery and diagnostic systems.
To overcome the drawbacks of traditional medication delivery and diagnostics, magnetic nanoparticles were created.
To make the use of an external magnetic field for targeted drug delivery possible.
To reduce medication side effects and systemic toxicity.
To increase the precision of imaging and diagnosis.
To enable site-specific therapy and regulated drug release.
They have a large surface area for drug loading and surface modification due to their small size

3. Recent Impact in the Pharmaceutical Industry:

Targeted administration of drugs:

An external magnetic field can be used to guide drugs attached to magnetic nanoparticles to particular organs or tumors.

Therapy for cancer (Magnetic Hyperthermia):

Magnetic nanoparticles (MNPs) selectively destroy cancer cells by producing heat in an alternating magnetic field.

Imaging for diagnostics:

Iron oxide nanoparticles are frequently used as contrast agents for magnetic resonance imaging (MRI).

Theranostics:

In a single system, magnetic nanoparticles integrate diagnosis and treatment.

Delivery of genes and proteins:

Magnetic nanoparticles are utilized in magnetofection to effectively transfer genes.

Clinical and regulatory use:

The pharmaceutical significance of iron oxide nanoparticles has increased as a number of their formulations have advanced to clinical trials and have been approved for medical use.

❖ PREPARATION OF MAGNETIC NANOPARTICLES:

1. Co-precipitation Method:

Principle:

Fe^{2+} and Fe^{3+} salts precipitate simultaneously in an alkaline medium.

Water dissolves ferrous (Fe^{2+}) and ferric (Fe^{3+}) salts in a 2:1 ratio.

Stirring is done while adding a base such as NaOH or NH_4OH.

Fe_3O_4 nanoparticles precipitate in black form.

After washing, stabilizers such as dextran, PEG, and chitosan are applied to the nanoparticles.

2. Thermal Decomposition Method:

Principle:

Iron precursors break down in organic solvents at high temperatures.

Procedure:

Surfactants are used to heat iron salts such as iron acetylacetonate.

Uniform nanoparticles are produced at high temperatures (200–300 °C).

3. Microemulsion Method:

Principle:

Creation of nanoparticles within nanoscale water-in-oil microemulsion droplets.

Procedure:

Microemulsion droplets contain dissolved iron salts.

Nanoparticles are created when a base is added.

Droplet size determines the nanoparticle size.

4. Sol–Gel Method:

Principle:

Metal alkoxides undergo hydrolysis and condensation to create a gel.

Procedure:

Sol formation occurs from iron precursors.

To create nanoparticles, the gel is dried and calcined.

5. Green / Biological Method

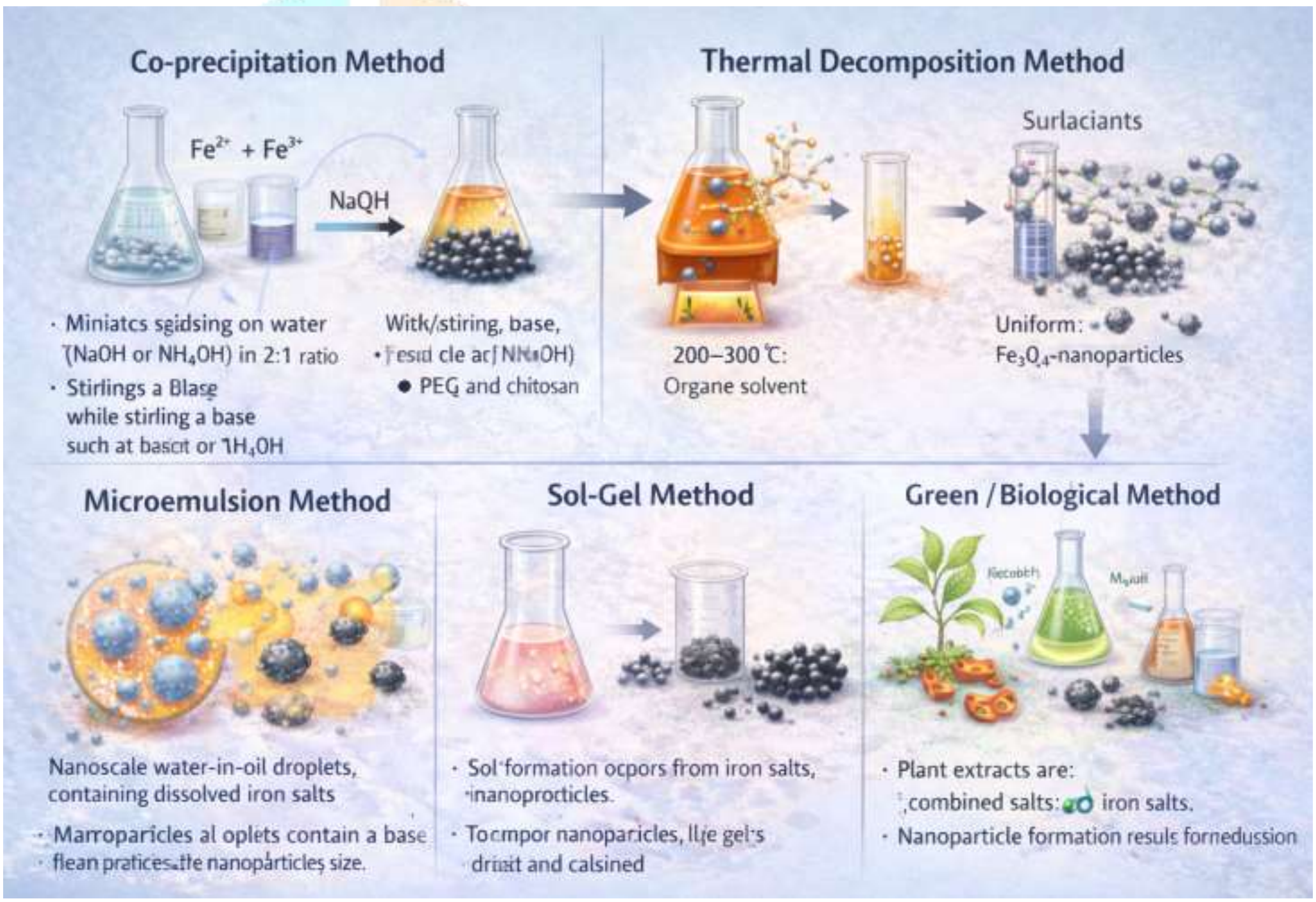
Principle:

Utilizing microbes or plant extracts as stabilizing and reducing agents.

Procedure:

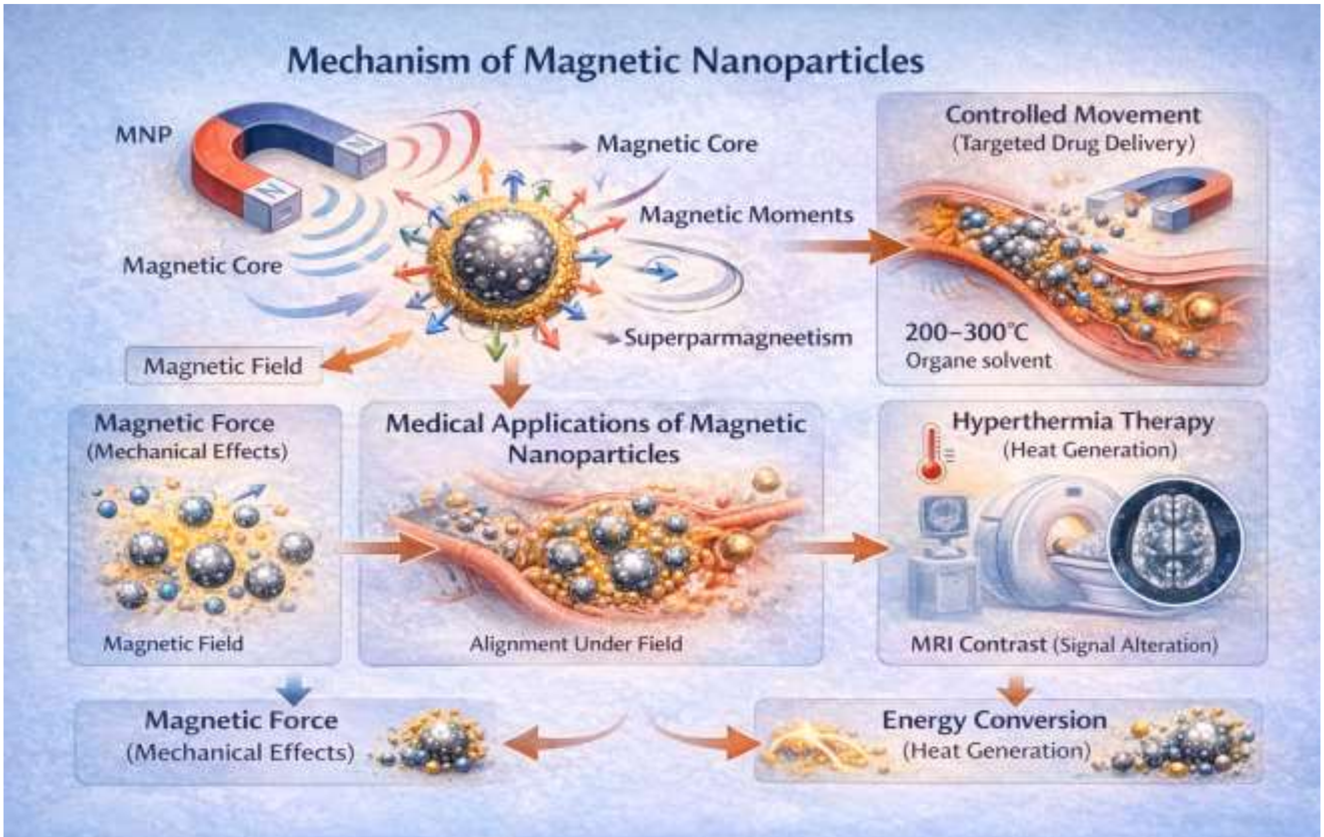
Plant extracts are combined with iron salts.

Nanoparticle formation results from reduction



❖ MECHANISM OF ACTION OF MAGNETIC NANOPARTICLES:

The mechanism of magnetic nanoparticles (MNPs) involves their unique magnetic behavior (like superparamagnetism) and interaction with external fields, allowing for controlled movement, heating (hyperthermia), or signal alteration (MRI contrast) by aligning their magnetic moments (from electrons/ions) under fields, leading to applications in targeted drug delivery, imaging, and therapy, utilizing phenomena like magnetic force for mechanical effects or energy conversion for heat generation.



❖ FUNCTION OF MAGNETIC NANOPARTICLES IN PHARMACY

They enhance image contrast by changing water proton relaxation times near the particles, highlighting diseased areas.

Cellular Manipulation: Mechanical forces from rotating MNPs can influence cell signaling or aid in gene transfection (gene delivery).

Drug Delivery: MNPs carry drugs, guided by magnets to a tumor. The AMF can trigger localized drug release or hyperthermic cell killing.

MRI Contrast: They enhance image contrast by changing water proton relaxation times near the particles, highlighting diseased areas.

Cellular Manipulation: Mechanical forces from rotating MNPs can influence cell signaling or aid in gene transfection (gene delivery).

In essence, magnetic nanoparticles leverage their tunable magnetic properties, especially superparamagnetism, to respond to external magnetic fields for targeted and controlled biomedical interventions.

➢ CONCLUSION

By reviewing different nanoparticles we conclude that nanoparticles have shown great promise in biomedical research, and ongoing studies are focused on exploring their potential applications and addressing the challenges associated with their development and use.

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