

Review on Nanoparticle Synthesis by Chemical and Biological Method

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ABSTRACT:

The nanoparticles refer to the particles which range between the dimensions of 1-100nm with unique characteristics of physical, chemical and biological properties. Due to increased surface area and reactivity, there has been great importance of nanoparticles in the field of medicines, drugs delivery, diagnosis, anti-microbials, and tissue engineering. This study is aimed at discussing various methods used in making nanoparticles such as chemical, biological or physical. Chemical synthesis methods include chemical reduction, sol-gel process, coprecipitation, hydrothermal, micro-emulsion and other techniques. Biologically based techniques for nanoparticle synthesis are the green method based on plant, bacteria, fungus, yeast and algae, due to being cost-effective, environmental friendly, non-toxic when compared to traditional methods. Nanoparticles can be divided into several categories such as Silver, Gold, Copper, carbon based, organic, and inorganic nanoparticles and various uses and medicinal value associated with them. Different techniques like UV-Vis, SEM, TEM, XRD, DLS and FTIR can be used in evaluating the quality and efficiency of the nanoparticles.

KEY WORDS:

Nanoparticles, Green synthesis, Chemical synthesis, biological synthesis, silver nanoparticles, gold nanoparticles, Drug delivery, antimicrobial activity, Nanotechnology, Characterization techniques

INTRODUCTION:

There are various simple ways of producing nanoparticles using various methods amongst the various methods that can be used to produce silver nanoparticles. These methods include chemical, electrochemical, radiation, photochemical approaches, Langmuir-Blodgett and biological methods. However, in all the chemical methods that can be used in synthesizing nanoparticles, there is extensive use of highly toxic substances, which may not be environmentally safe. This calls for the production of nanoparticles using environmentally friendly methods such as green synthesis method and biological methods. It is possible that under some conditions, nanoparticle production from plant material and their extracts would be much better compared to nanoparticle production using other biological methods owing to their complexity in cultivating microbes. Amongst the various existing types of nanoparticles, metal-based nanoparticles are known to have remarkable antibacterial properties because of their high surface-to-volume ratio; these have attracted attention of researchers owing to increase in antimicrobial resistance to metals and antibiotics. Silver nanoparticles are considered the best among nanoparticles in the field of nanotechnology because of their non-harmful effects on biological cells, thus eliminating any resistance by the microbes. Silver nanoparticles are thought to bind with the cell wall, making it difficult for these organisms to respire. There are two methods of synthesis of nanoparticles: top-down method and bottom-up method(fig.1).

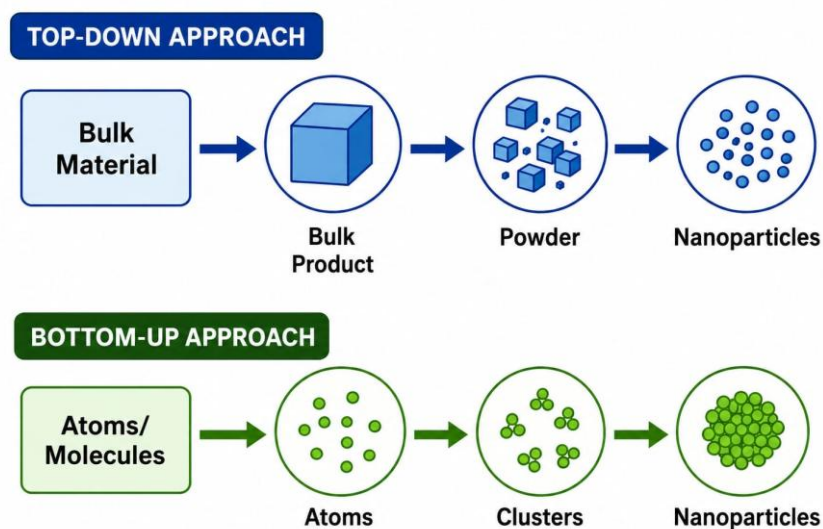


Figure 1: Approaches for the synthesis of nanoparticles

DEFINITION:

Nanoparticles can be described as small particles of matter having a size ranging between 1 and 100 nanometers that possess some physical and chemical attributes other than those displayed by normal bulk materials. Drug delivery system through nanoparticles has been defined using several different terminologies. The mode of delivery of drugs uses nanoparticles having sizes that range between a few nanometers and a few hundred nanometers. Various novel polymers have been developed in an effort to enhance nanoparticles' potential as drug carriers.[2]

NATURE OF NANOPARTICLES:

Nanoparticles are extremely small particles with size in the range of 1-100 nm. They have unique physical, chemical and biological properties.

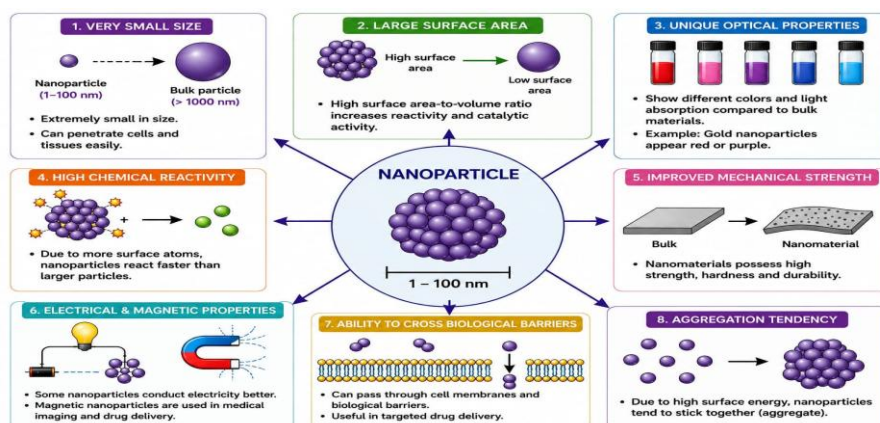


Figure 2: Nature of Nanoparticles

CLASSIFICATION OF NANOPARTICLES:

Based on their composition, NPs are generally placed into three classes: organic, carbon-based, and inorganic [3].

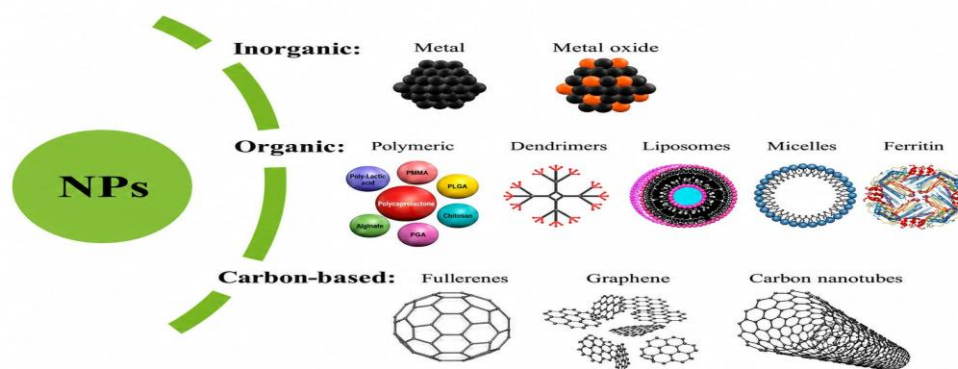


Figure 3: Classification of Nanoparticles

ORGANIC NANOPARTICLES:

Organic nanoparticles comprise proteins, lipids, carbohydrates, and polymers and contain liposomes and micelles. Organic nanoparticles are biodegradable, non-toxic, heat and light sensitive as a result of weak bonds. The major application of organic nanoparticles is delivery of drugs and treating cancer patients.

CARBON BASED NANOPARTICLES:

Carbon based nanoparticles consist of carbon atoms. Carbon fullerenes, carbon black and carbon quantum dots can be named as examples of carbon-based nanoparticles. Due to the nature of carbon bonding at the nanometre scale, carbon-based nanoparticles possess novel physical properties, including electrical, optical, thermal and mechanical properties.

INORGANIC NANOPARTICLES:

Inorganic nanoparticles refer to metal, ceramic, or semiconductor nanoparticles possessing distinctive optical and electrical characteristics. These nanoparticles' remarkable stability and function have been sources of significant attention for various biomedical, electronic, catalytic, and drug delivery purposes.

METHODS OF NANOPARTICLES:

Nanoparticles are synthesized mainly by three approaches:

1. Chemical methods
2. Biological methods
3. Physical methods

Table 1: Chemical Methods of Nanoparticles:

CHEMICAL METHODS	DESCRIPTION	EXAMPLES OF NANOPARTICLES
Chemical Reduction Method	Metal ions are reduced into nanoparticles using reducing agents	Silver nanoparticles, Gold nanoparticles [4]
Sol–Gel Method	Nanoparticles are formed through hydrolysis and condensation reactions	Silica nanoparticles, Titanium dioxide nanoparticles [4]

Co-precipitation Method	Nanoparticles are produced by precipitation from aqueous solutions	Iron oxide nanoparticles, Magnetic nanoparticles [4]
Hydrothermal Method	Synthesis occurs under high temperature and pressure in an autoclave	Zinc oxide nanoparticles, Ceramic nanoparticles [4]
Microemulsion Method	Nanoparticles are synthesized inside nanosized droplets using surfactants	Semiconductor nanoparticles, Metal nanoparticles [4]

Table 2: Biological Methods of Nanoparticles:

BIOLOGICAL METHODS	DESCRIPTION	EXAMPLES OF NANOPARTICLES
Plant-Mediated Synthesis	Plant extracts are used to reduce metal ions into nanoparticles	Silver nanoparticles, Gold nanoparticles [5]
Bacteria-Mediated Synthesis	Bacteria synthesize nanoparticles through enzymatic reduction	Iron oxide nanoparticles, silver nanoparticles [5]
Fungi-Mediated Synthesis	Fungi produce nanoparticles using extracellular enzymes and proteins	Zinc oxide nanoparticles, silver nanoparticles [5]
Yeast-Mediated Synthesis	Yeast cells convert metal ions into nanoparticles	Cadmium sulfide nanoparticles, silver nanoparticles [5]
Algae-Mediated Synthesis	Algae act as reducing and stabilizing agents for nanoparticle formation	Gold nanoparticles, silver nanoparticles [5]

Table 3: Physical Methods of Nanoparticles:

PHYSICAL METHODS	DESCRIPTION	EXAMPLES OF NANOPARTICLES
Ball Milling Method	Mechanical force is used to break bulk materials into nanoparticles	Ceramic nanoparticles, Metal nanoparticles [6]
Laser Ablation Method	High-energy laser beam vaporizes target material to form nanoparticles	Gold nanoparticles, silver nanoparticles [6]
Evaporation–Condensation Method	Materials are evaporated and condensed into nanoparticles	Metal nanoparticles, Oxide nanoparticles [6]
Arc Discharge Method	Electric arc vaporizes materials to produce nanoparticles	Carbon nanotubes, Metal nanoparticles [6]

SYNTHESIS OF NANOPARTICLES:

Synthesis of nanoparticles is the process of producing particles with sizes ranging from 1–100 nm by physical, chemical, or biological methods [7].

Nanoparticle synthesis aims to control:

- Size
- Shape
- Structure
- Stability
- Purity

➤ Synthesis of nanoparticles by using chemical methods:

1. Chemical reduction method:

Chemical reduction is the most commonly used approach for the preparation of metal nanoparticles. In this technique, metal ions are converted into metal atoms using a chemical agent, which can be sodium borohydride or citrate. The formed metal atoms bind themselves together to produce nanoparticles. Stabilizers are used to avoid agglomeration of the nanoparticles. It is a relatively simple and inexpensive process for preparing silver and gold nanoparticles on a commercial scale.[7]

Steps of chemical reduction method:

- Preparation of metal salt solution
- Addition of reducing agent
- Reduction of metal ions into atoms
- Formation of nuclei
- Growth of nanoparticles

Common reducing agents:

- Sodium borohydride
- Hydrazine
- Citrate
- Ascorbic acid

2. Sol-gel method:

This process involves the processes of condensation, hydrolysis, and thermal degradation of metal alkoxide or metal precursor ions in a liquid medium. A homogeneous solution called the sol is thus created. Through hydrolysis and condensation, a highly viscous gel is developed. Precursor concentration, pH value, and temperature control the size of the particles. It is essential that an aging stage should follow to enable the formation of a solid material; it may take several days during which solvent removal, Ostwald ripening, and phase transformation might occur. The unstable components are eliminated to form nanoparticles [8].

Steps of sol-gel method:

- Preparation of precursor solution
- Formation of sol
- Gel formation
- Drying and calcinations

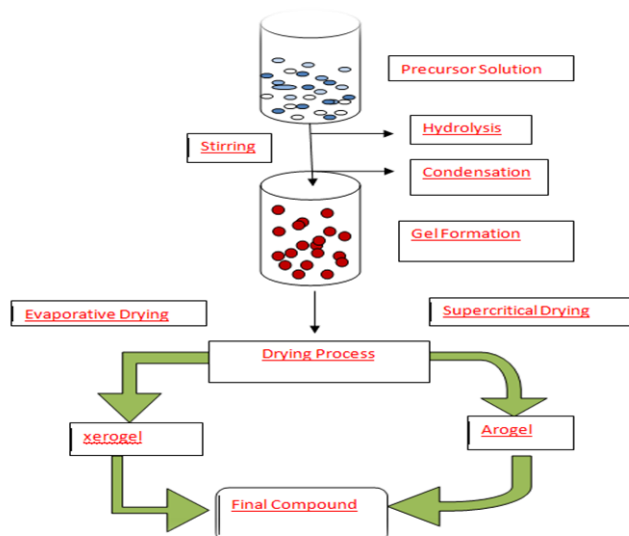


Figure 4: Steps of sol-gel method

3.Co-precipitation method:

Sol–gel process is a synthesis process involving the hydrolysis and condensation of the metal precursor, resulting in the formation of a stable sol, which then transforms into a gel. The diameter of the nanoparticles is regulated via the concentration of the precursor, temperature, and pH. [8]

Steps of co-precipitation method:

- Preparation of metal salt solution
- Add precipitating agent
- Formation of precipitate
- Filtration and drying

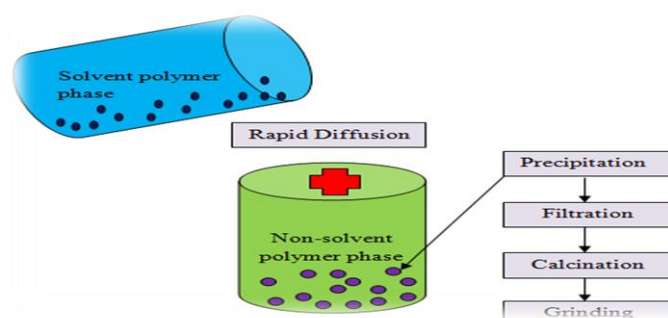


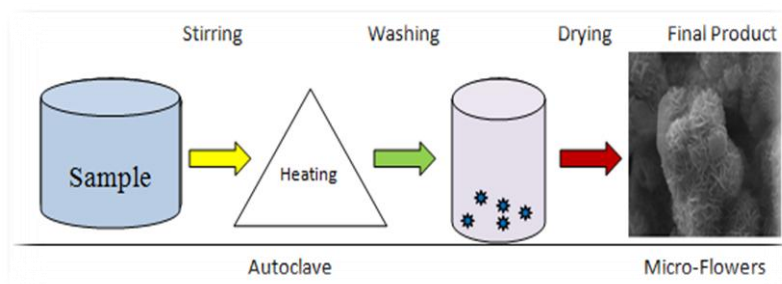
Figure 5: Co-precipitation method

3.Hydrothermal synthesis:

The hydrothermal synthesis method is one of the most common chemical processes of producing nanoparticles at different temperatures. This technique has several benefits compared to physical and biological processes, though the synthesized nanomaterials become unstable at high temperatures [9].

Steps of hydrothermal method:

- Prepare precursor solution
- Transfer into autoclave
- Heat under pressure
- Cool and collect nanoparticles.

**Figure 6: Hydrothermal synthesis****4. Microemulsion Method:**

Microemulsion consists of water, oil, and surfactant mixture, which is a stable solution. Based on how they are arranged, they either form an oil-in-water microemulsion or water-in-oil microemulsion, whereby the surfactant forms a boundary between the two types of phases [9].

Types of microemulsion:

- ✓ **Oil-in-Water (O/W):**
Oil droplets are dispersed in a continuous water phase.
- ✓ **Water-in-Oil (W/O):**
Water droplets are dispersed in a continuous oil phase.

Steps of microemulsion method:

- Prepare microemulsion
- Add precursor solution
- Chemical reaction occurs inside droplets
- Separate nanoparticles

Table 4: Common solvents used in nanoparticle synthesis:[10]

SOLVENTS	EXAMPLE
Water	Silver nanoparticles
Ethanol	Gold nanoparticles
Methanol	Metal oxide nanoparticle
Acetone	Nanoparticle purification
Ethylene glycol	Polyol method

EVALUATION OF NANOPARTICLES:

This is all about examining nanoparticles. It will be necessary to determine the size, shape, and structure of these particles. Their surface characteristics as well as their stability should be examined. This will be required to ensure that these nanoparticles are manufactured properly.[11]

Examples of common evaluation methods are:[12]

- UV–Visible spectroscopy – confirms nanoparticle formation.
- Study size and morphology – SEM and TEM.
- XRD – determines crystalline structure.
- DLS – measures particle size distribution.
- FTIR – surface functional groups.

Evaluation is used in quality control, biomedical applications and nanotechnology research.

➤ **Synthesis of nanoparticles by using biological methods:**

1.Plant-mediated synthesis:

This is an environmentally friendly technique for creating nanoparticles with the help of plant extracts [13]. Flavonoids, phenols, alkaloids, and proteins are some of the natural components of plants that play an important role in the reduction and stabilization of metal ions [14]. In this synthesis process, different parts of the plants including leaves, roots, fruits, and flowers are employed. It is a simple and environmentally friendly procedure that involves minimum costs. Various applications of nanoparticles synthesized from plant sources include pharmaceutical, drug delivery, antimicrobial, and environmental science purposes [15, 17].



Figure 7: Plant-mediated synthesis

Example of plants used for nanoparticle synthesis:

Table 5: Green synthesis of silver nanoparticles using different plant extracts:[18,19]

Plants	Plant parts	Size(nm)	Shape
Prunus yedoensis	Leaf	20-70	Circular,smooth edges
Tephrosia tinctoria	Stem	73	Spherical
Grewia flaviscences	Leaf	50-70	Spherical
Skimmia laureola	Leaf	46	Hexagonal
Clerodendrum serratum	Leaf	5-30	Spherical
Averrhoa carambola	Leaf	14	Spherical
Rosmarinus officinalis	Leaf	10-33	Spherical
Carica papaya	Leaf	50-250	Spherical
Plukenetia volubili	Leaf	4-25	Optical
Cucurbita maxima	Petals	19	Crystalline
Moringa oleifera	Leaf	11	Rectangle
Acorus calamus	Rhizome	19	Spherical
Aristolochia indica	Leaf	30-55	Spherical or cubical
Euphorbia helioscopia	Leaf	2-14	Spherical
Datura metel	Leaf	40-60	Spherical
Momordica cymbalaria	Fruit	15.5	Spherical
Hypnea musciformis	Leaf	40-65	Spherical
Potentilla fulgens	Root	10-15	Spherical
Annona muricata	Leaf	20-53	Spherical
Justicia adhatoda	Leaf	5-50	Spherical
Hemidesmus indicus	Leaf	25.24	Spherical
Emblica officinalis	Leaf	15	Spherical

Table 6: Green synthesis of copper nanoparticles using different plant extracts:[20,21]

Plant name	Part used	Phyto constituents	Precursor	Activity
Allium sativum	Leaves	Steroid saponins	1mmol Copper sulphate	Antibacterial
Allium sativum	Herb	Sulphides, thiosulfinates, vinylthiins	2mmol Copper Chloride	Antibacteria, Anticancer
Zingiber officinale	Rhizome	Phenols and terpenes	2mmol Copper Chloride	Antibacteria, Anticancer
Cissus quadrangularis	Leaves	Quercetin, quercitrin, beta-sitosterol	1mmol Copper Acetate	Antifungal
Moringa oleifera	Leaves	Flavonoids, alkaloids, phenols, vitamins, minerals	0.04M Cu ²⁺ Solution	antifungal, antioxidant Antibacterial
Azadirachta indica	Leaves	Azadirachtin, nimbin, nimbidin, quercetin	0.2M Copper Acetate	Anticancer, Antioxidant
Hibiscus rosa-sinensis	Leaves	Tannins, anthraquinones, quinines, phenols, flavonoids, alkaloids	0.2M Copper Acetate	Anticancer, Antioxidant
Murraya koenigii	Leaves	Polyphenols	0.2M Copper Acetate	Anticancer, Antioxidant
Tamarindus indica	Leaves	Tannins, alkaloid, flavonoids, sesquiterpenes, glycosides	0.2M Copper Acetate	Anticancer, Antioxidant
Eclipta prostrata	Leaves	P-caryophyllene, α -Humulene	3mmol Copper Acetate	Anticancer, Antioxidant
Abutilon Indicum	Leaves	Carbohydrates, steroids, glycosides, flavonoids, tannins, phenolic compound	Copper nitrate	Antibacteria, antifungal, anticancer, antioxidant
Clerodendrum inerme	Leaves	Beta sitosterol	Copper nitrate	Antibacteria, antifungal,
Clerodendrum Infortunatum	Leaves	Saponin	Copper nitrate	Antibacteria, antifungal, anticancer

Table 6: Green synthesis of gold nanoparticles using different plant extracts:[22,23]

Material used	Part used	Phytoconstituents involved in the reduction	Precursor salt	Reaction condition
Persicaria salicifolia	Leaf	Phenolic compounds, flavonoids, Glycosides	HAuCl ₄ .H ₂ O RT	Violet
Curcuma wenyujin	Rhizome	Phenolic compounds, flavonoids, alkaloids, tannins	NaAuCl ₄ Stirring, RT	Purple-red
Tasmannia lanceolata	Leaf	Alkaloids, proteins, phenolic acids, terpenoids, polyphenols	HAuCl ₄ .3H ₂ O Stirring, 15 min	Ruby red

Corchorus olitorius	Leaf	Phenolic compounds, vitamins, fatty acids	HAuCl ₄ .3H ₂ O Stirring, 1 min	Dark red
Linum usitatissimum	Seed	Alkaloids, flavonoids, phenols, proteins, vitamins	HAuCl ₄ .3H ₂ O RT, 6h	Ruby red
Garcinia mangostana	Pericarp	Phenolic acids, xanthones, tannins	HAuCl ₄ .3H ₂ O Incubated, RT, 5 min	Purple
Cibotium	Root	Phenolic acids, flavonoids	HAuCl ₄ 80°C, 1 min	Ruby red
Pituranthos tortuosus	Aerial parts	Flavonoids, tannins, carbohydrates, glycosides, alkaloids, terpenoids, proteins	HAuCl ₄ .4H ₂ O RT, 40 min	Pink
Solanum	Leaf	Flavonoids, saponins, alkaloids, Glycosides	HAuCl ₄ Stirring, RT	Purple
Xanthocarpum	Seed	Terpenoids, thymoquinone, Polyphenols	HAuCl ₄ .3H ₂ O pH 6-10, 0-48h	Purple
Nigella sativa	Seed	Flavonoids, polyphenols, Terpenoids	HAuCl ₄ Stirring, 40 °C, 3 min	Pink
Rosa damascena	Flower	Phenolic compounds, alkaloids	AuCl ₃ Stirring, 1-2h	Pink ruby
Azadirachta indica	Fruit	Flavonoids, chalcones, phenolic Compounds	HAuCl ₄ .3H ₂ O RT	Dark violet
Glycyrrhiza glabra	Root	Phenolic compounds, terpenoids, flavonoids, proteins	HAuCl ₄ Stirring, 30 min and microwave irradiation, 2 min	Ruby red
Trachyspermum Ammi	Seed			

2. Bacteria-Mediated Synthesis:

Nanoparticle synthesis via bacteria is one such eco-friendly process, where nanoparticles are synthesized via the bacteria [24]. Conversion of metal ions to nanoparticles through the use of bacterial enzymes is carried out here. The reason for the popularity of this process is the ease of adoption and low cost involved in it. [25]

Common bacteria used for nanoparticle synthesis: [26,27]

- Bacillus subtilis
- Escherichia coli
- Pseudomonas aeruginosa
- Lactobacillus species

3. Fungi-Mediated Synthesis:

Biological synthesis of nanoparticles utilizes fungi, as they have the potential to synthesize nanoparticles from metal ions [28]. Enzymes, proteins, and metabolic components produced by fungi can lead to the synthesis of nanoparticles [29]. The synthesis of nanoparticles may occur either intracellularly or extracellularly. This is a sustainable and economically viable process for producing nanoparticles industrially [30].

Common fungi used for nanoparticle synthesis:

- Fusarium oxysporum
- Aspergillus Niger
- Penicillium species
- Trichoderma viride

4. Yeast-Mediated Synthesis:

Nanoparticle synthesis through yeast includes synthesis of nanoparticles from metal ions using yeast [31]. Yeast consists of many enzymes and biological active compounds which can be employed for converting metal ions into nanoparticles. It can be accomplished within or out of the cells. This technique is inexpensive and eco-friendly [32, 33].

Common yeast used for nanoparticle synthesis:

- *Saccharomyces cerevisiae*
- *Candida glabrata*
- *Yarrowia lipolytica*
- *Pichia pastoris*

5.Algae-Mediated Synthesis:

Mediated synthesis of nanoparticles by algae implies the preparation of nanoparticles employing metal ions using algae or algae extracts. This process comes under the umbrella term of green synthesis [34]. Various bioactive compounds like proteins, pigments, polysaccharides, and enzymes, which are found in algae, can be employed for reduction and stabilization of the nanoparticles. The process is cost-effective and environmentally friendly [35, 36].

Common algae used for nanoparticle synthesis:

- *Sargassum wightii*
- *Chlorella vulgaris*
- *Spirulina platensis*
- *Ulva lactuca*

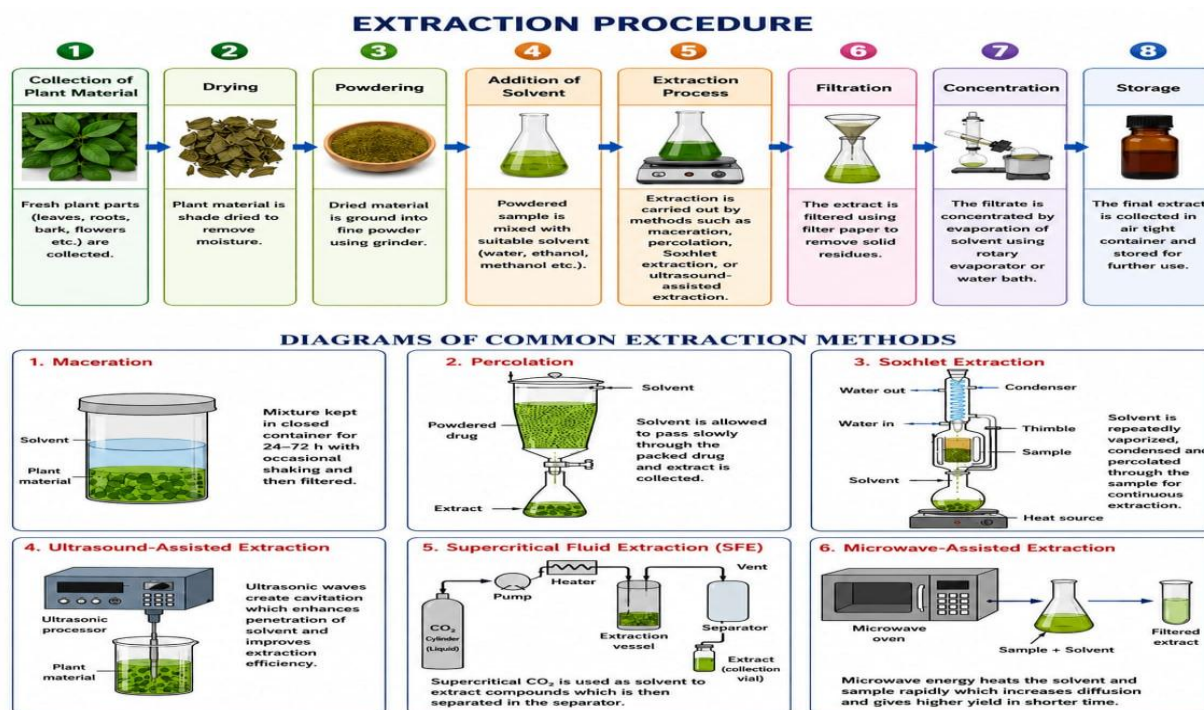
EXTRACTION PROCEDURE:[37]

Figure 8: Extraction process

Table 7: application of nanoparticle in medicinal field:

Medical application	Body part\Organ	Activity of Nanoparticles
Drug Delivery	Whole body\Target organs	Drugs are targeted to specific cells or tissues via nanoparticles. This enhances the effectiveness of the drug and minimises side effects [38].
Cancer Therapy	Tumors,Breast, Lung,Liver	Nanoparticles are used in targeted cancer therapy to deliver an anticancer drug to tumour cells, while sparing normal cells [38].
Diagnostic Imaging	Brain,Heart,Liver	MRI, CT scan and imaging using gold nanoparticles and magnetic nanoparticles are used for better disease diagnosis [39].
Gene Therapy	Cells,Nucleus	Nanoparticles can carry DNA, RNA or genes into cells for use in gene therapy [39].
Antimicrobial Treatment	Skin,Wounds	Their antibacterial, antifungal and antiviral properties are high, and they are applied to wound dressings and coatings [40].
Wound Healing	Skin,Tissues	Nanoparticles aid in wound healing, reduce infections and enhance tissue regeneration [40].
Biosensors	Blood,Body fluids	Biosensors for detecting biological molecules including glucose, cholesterol, pathogens and others are made with the help of nanoparticles [41].
Vaccine Delivery	Immune system	Nanoparticles have been shown to enhance vaccine stability and facilitate efficient vaccine delivery into the body [41].
Tissue Engineering	Bone,Skin, Cartilage	Scaffolds and biomaterials are used for regeneration of damaged tissues and organs with the help of nanoparticles [42].
Pulmonary Drug Delivery	Lungs	Delivers drugs directly through inhalation therapy[42].

Conclusion:

Nanoparticles are an important advancement in the field of nanotechnology due to their unique physical, chemical, and biological properties. Different synthesis methods such as chemical, physical, and biological techniques are used to prepare nanoparticles. Among these methods, green synthesis has become more popular because it is eco-friendly, cost-effective, and less toxic. Plants, bacteria, fungi, yeast, and algae are commonly used in green synthesis. Nanoparticles like silver, gold, and copper show excellent medicinal applications. They are widely used in drug delivery, cancer therapy, antimicrobial treatment, wound healing, and diagnostic imaging. Proper evaluation and characterization methods are necessary to ensure their stability, quality, and effectiveness. Overall, nanoparticles have great potential in medicine and future research may lead to safer and more advanced therapeutic applications.

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