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A COMPREHENSIVE REVIEW ON THE "NANO ERA OF NANOPARTICLES"

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Abstract:

The application of nanoparticles in cancer therapy is an emerging and promising approach aimed at enhancing the efficacy and selectivity of therapeutic interventions. This strategy seeks to improve treatment outcomes by increasing the potency of drugs while minimizing toxicity to healthy cells. Nanoparticles are categorized into three main types: organic nanoparticles (such as liposomes and polymer-based particles), inorganic nanoparticles (including gold and silica nanoparticles), and hybrid nanoparticles (like lipid–polymer hybrids). These nanomaterials, typically ranging in size from 1 to 100 nanometers, represent a diverse class of materials with unique physicochemical properties. Various methods such as magnetic, electrical, optical, and mechanical techniques can be employed to synthesize nanoparticles for biomedical applications.

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INTRODUCTION:

Breast cancer, a highly heterogeneous malignancy, is often characterized by the expression of specific molecular biomarkers such as estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2/ERBB2). These biomarkers play a pivotal role in tumor classification, prognosis, and the selection of targeted therapeutic strategies. Superparamagnetic iron oxide nanoparticles (spions) have attracted considerable attention for their therapeutic potential in breast cancer treatment, owing to their efficient cellular uptake, prolonged intracellular retention, and intrinsic cytotoxic effects. , SPIONs coated with dimercaptosuccinic acid (DMSA) which confers a negatively charged surface have been effectively studied in MCF-7 breast cancer cell models, demonstrating biocompatibility and favorable cellular interactions, thereby highlighting their promise as a nanotherapeutic platform.

MCF-7(Michigan Cancer Foundation-7) cells, known for their hormone receptor-positive characteristics, serve as a commonly used in vitro model for investigating hormone-sensitive breast cancer. The name of the cell line originates from the institution where it was first developed in 1973, with the number "7" signifying that it was Soule's seventh effort to create a cancer cell line. The MCF-7 cell line, established from a metastatic adenocarcinoma in 1970, is the most extensively researched human breast cancer cell line worldwide. Curcumin, a natural polyphenol derived from the turmeric plant (Curcuma longa), has attracted considerable interest in biomedical research due to its wide range of therapeutic effects, including antimicrobial, antioxidant, anti-inflammatory, and anticancer properties. Nevertheless, curcumin's clinical application is hindered by its poor water solubility and limited bioavailability. To overcome these challenges, solid lipid nanoparticles (SLNs) which are made from biocompatible lipids are utilized as drug delivery systems to encapsulate hydrophobic compounds like curcumin, thereby enhancing their solubility, stability, and bioavailability in the body.

Furthermore, hybrid polymeric nanoparticles have gained prominence as advanced delivery systems for various therapeutic agents, including chemotherapy drugs, genetic materials, and photothermal agents, aimed specifically at targeting breast cancer cells. Among the various biodegradable polymers available, poly(lactic-co-glycolic acid) (PLGA) is one of the most widely used due to its excellent biocompatibility, biodegradability, and tunable degradation properties. Its safety and efficacy have been validated by regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), making it a preferred choice in pharmaceutical and clinical drug delivery research.

Polylactide-co-glycolide (PLGA) can be used for drug delivery over a period ranging from several months to even years, depending on factors such as its molecular weight and the ratio of lactide to glycolide in the copolymer. This property makes PLGA highly suitable for sustained- release drug formulations, where medications are released slowly over an extended time. Such systems offer several benefits, including reduced dosing frequency and enhanced patient adherence to treatment. In breast cancer therapy, PLGA can be used to deliver anticancer drugs like tamoxifen citrate. Tamoxifen citrate, an anti-estrogenic agent, is primarily administered as adjuvant therapy for both premenopausal and postmenopausal women in the early stages of breast cancer. Its key mechanism involves blocking estrogen receptors in breast tissue, thereby inhibiting the estrogen-driven proliferation of cancer cells.

Additionally, gold nanoparticles (GNPs) serve as effective carriers for transporting chemotherapeutic agents, genetic material, and other therapeutic compounds directly to breast cancer cells.

Nanoparticles

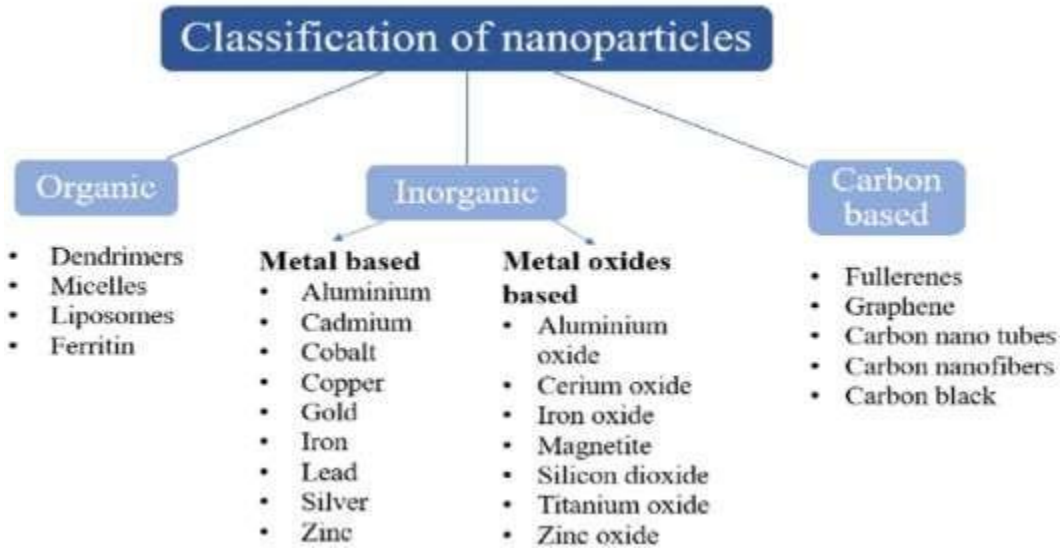
Gold nanoparticles (GNPs) can enhance the effectiveness of radiation therapy in breast cancer by acting as radiosensitizers. When exposed to ionizing radiation, GNPs interact with the radiation field to produce secondary electrons. These electrons increase DNA damage within cancer cells, ultimately leading to cell death. This synergistic effect allows for a lower radiation dose while still achieving effective tumor control.

Some commercially available formulations associated with nanoparticle technology include Doxil®, Lipoplatin®, Onivyde®, Genexol-PM, and Abraxane®. In particular, Abraxane® utilizes nanoparticles to encapsulate hydrophobic drugs like paclitaxel, improving their water solubility and physiological stability. Nanoparticles can be precisely engineered at the nanoscale, making them ideal for cellular uptake and systemic distribution. These particles can also be tailored for controlled and sustained drug release. This is achieved by incorporating materials that respond to physiological stimuli such as changes in pH, temperature, or the presence of specific enzymes to trigger drug release at the desired site.

Doxorubicin is a widely used anticancer agent effective against a broad range of tumors, including breast cancer. However, its use is often constrained by dose-dependent toxicity. Similarly, cisplatin is a potent chemotherapeutic drug effective against several cancers, such as ovarian, testicular, bladder, and lung cancers. Its mechanism involves binding to DNA and causing cross-linking, which leads to DNA damage and apoptosis in fast-dividing cancer cells.

CLASSIFICATION OF NANOPARTICLES

Nanoparticles can be categorized accounting to their shape, size and chemical features.



Classification of nanoparticles.(source – research gate)

Carbon Nanoparticles

Fullerenes and carbon nanotubes are the two main types of carbon-based nanoparticles. Fullerenes are spherical, hollow cage-like structures formed from carbon allotropes, contains organized pentagonal and hexagonal rings of sp^2-hybridized carbon atoms. carbon nanotubes are cylindrical ones with diameters typically ranging from 1 to 2 nms.

Metalnanoparticles

Metal nanoparticles consist solely of metallic elements and are notable for their distinctive electrical properties, largely due to localized surface plasmon resonance (LSPR). Nanoparticles made from metals like copper (Cu), silver (Ag), and gold (Au) exhibit strong absorption in the visible light spectrum. Their size, shape, and crystallographic facets can be precisely controlled during synthesis, making them valuable across various scientific fields.

CeramicNanoparticles

Ceramic nanoparticles are composed of inorganic, non-metallic materials that undergo specialized heat treatments and cooling processes to develop specific characteristics. These particles can have different structures, such as amorphous, polycrystalline, dense, porous, or hollow forms, and are well-known for their heat resistance and robust durability.

Lipid-basedNanoparticles

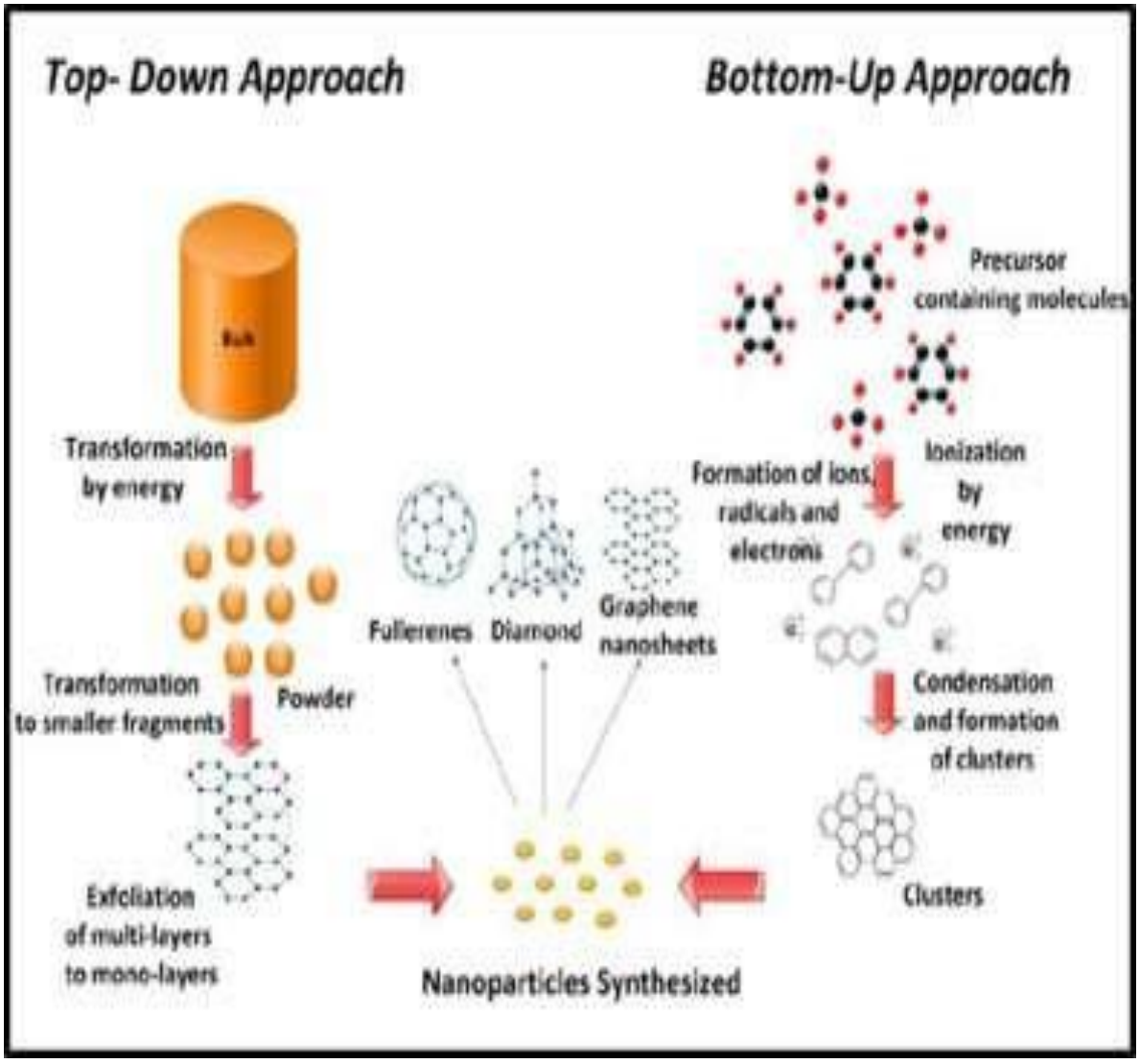
Lipid nanoparticles usually measure between 10 and 1,000 nanometers and are generally spherical in shape. They feature a solid lipid core surrounded by a matrix containing soluble lipophilic molecules, similar in structure to polymeric nanoparticles.

SemiconductorNanoparticles
Semiconductor nanoparticles exhibit properties that fall between metals and non-metals, providing them with unique physical and chemical behaviors. Their capacity to absorb and emit light makes them useful for applications including high-efficiency solar cells and bright light-emitting diodes (LEDs). They also play a role in the creation of smaller, faster electronic devices such as transistors, and are utilized in bioimaging and cancer therapies.

PolymericNanoparticles
Polymeric nanoparticles range from 1 to 1,000 nanometers in size and may have therapeutic agents either adsorbed onto their surface or encapsulated within the polymer matrix. Often referred to as polymer nanoparticles (PNPs), these organic particles commonly exist as nanospheres or nanocapsules.

METHODS OF NANOPARTICLE SYNTHESIS

a. ***Top-down synthesis*:** This approach starts with bulk materials and reduces them into nanosized particles through physical or mechanical means.
b. ***Bottom-up synthesis:*** This method involves assembling nanoparticles from atoms or molecules, gradually building up to create larger nanostructures[1]



Source : researchgate.net

A. Physical methods

- Mechanical Method
- Pulse Laser Ablation
- Pulsed Wire Discharge Method
- Chemical Vapour Deposition
- Laser Pyrolysis
- Ionized Cluster Beam Deposition

B. Chemical methods

- Sol-gel Method
- Sonochemical Synthesis
- Co-precipitation Method
- Inert Gas Condensation Method
- Hydrothermal Synthesis

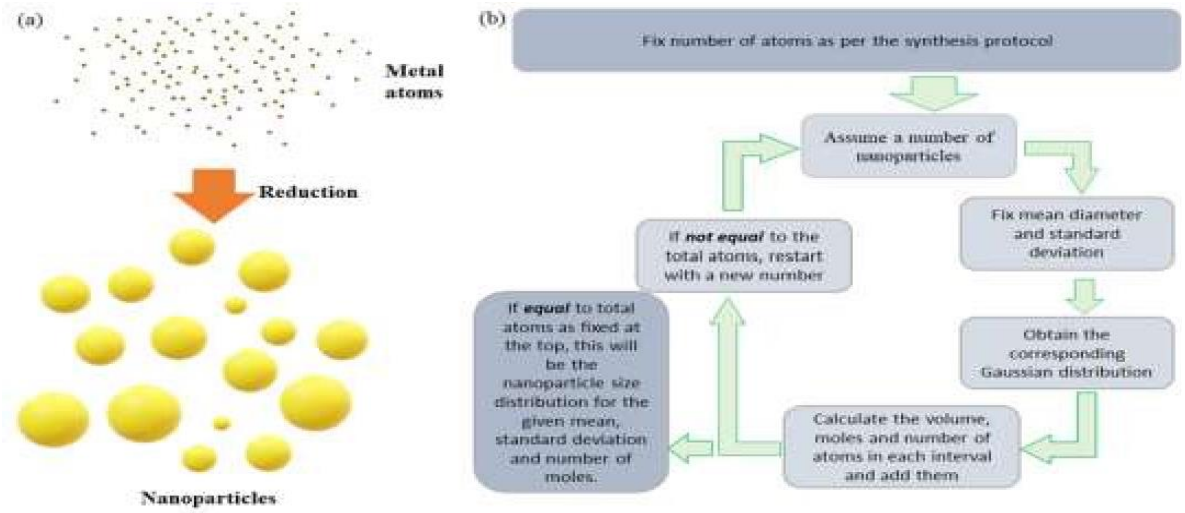
C. Biological methods

- Synthesis Using Microorganisms
- Synthesis Using Plant Extracts
- Synthesis Using Algae

I. **CHEMICAL METHODS**

1. The Polyol Method :

The polyol method is a commonly used technique for synthesizing nanoparticles that utilizes a non-aqueous liquid, known as a polyol, which serves both as a solvent and a reducing agent. One key benefit of using non-aqueous solvents is their ability to reduce surface oxidation and prevent particle agglomeration. This method offers considerable control over the size and shape of the nanoparticles, making it suitable for large-scale production as well. During the synthesis, stabilizing agents are added to inhibit agglomeration, oxidation, and precipitation of the nanoparticles. These stabilizers also play a crucial role in determining the size, shape, and uniformity of the final particles. The polyol process can be considered a type of sol-gel method for synthesizing metal oxides when carried out at moderately elevated temperatures with precise control over particle growth[3]. In this technique, ethylene glycol is the most commonly used solvent due to its strong reducing power, high dielectric constant, and elevated boiling point. Additionally, ethylene glycol acts as a crosslinking agent by binding to metal ions, forming metal glycolates that facilitate oligomerization during the synthesis of metal oxide nanoparticles[4].

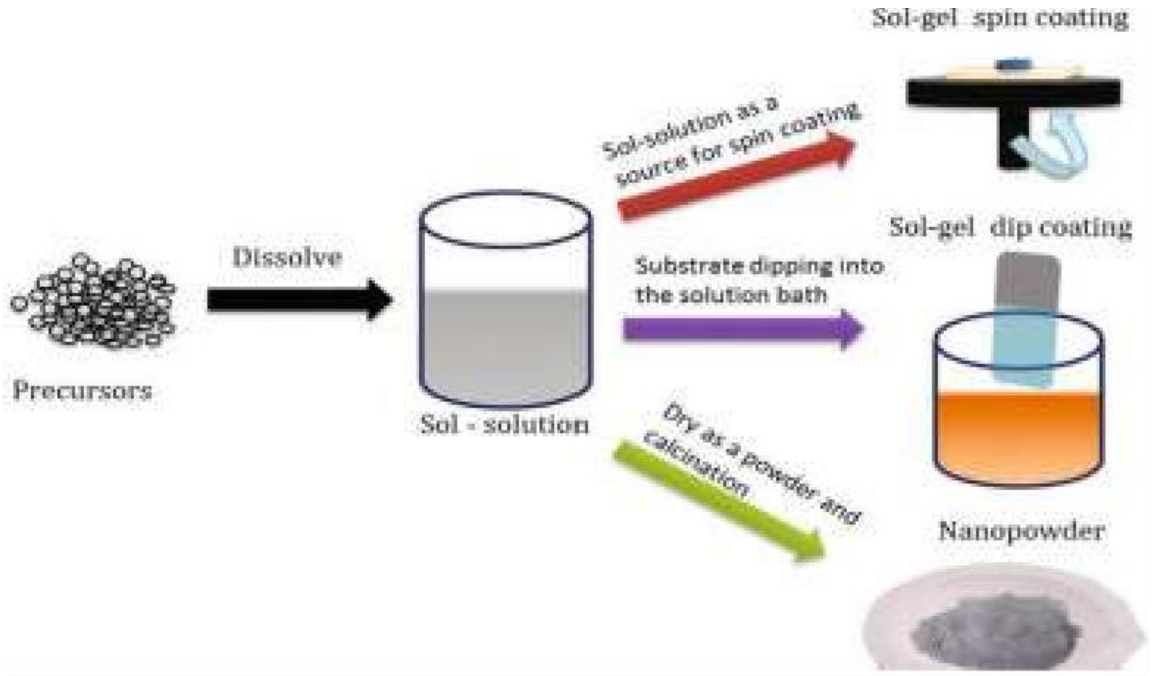


The polyol method [source: researchgate.net]Colloid Synthesis :

Colloids consist of phase-separated particles smaller than a micrometer, which can take various shapes such as spheres, rods, tubes, or plates. These particles are typically suspended within a heated medium. Different types of particles including metals, alloys, semiconductors, and insulators can be produced in either aqueous or non-aqueous environments [5]. Typically, colloidal particles are created within a glass reactor, which allows the introduction of precursors and gases, as well as the monitoring of parameters like temperature and pH throughout the process. Products can be extracted at appropriate times during the reaction. To prevent unwanted oxidation, the reaction is usually performed under an inert atmosphere[6].

2. Sol-Gel method:

It involves two key components: sols, which are tiny solid particles dispersed in a liquid (a type of colloid), and gels, which are three-dimensional networks of these particles with liquid filling the spaces between them. In this method, sols are first formed in a liquid medium, and then the particles link together to create a gel-like structure. By drying out the liquid, the process yields solid products such as powders or thin films.This technique is commonly used to fabricate ceramics and compounds like metal oxides, sulfides, borides, and nitrides. [7].

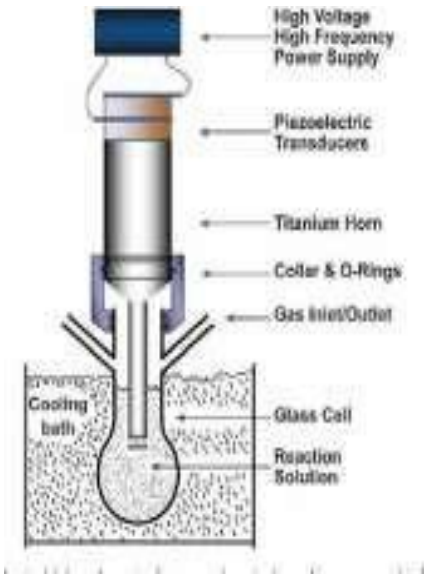


Sol gel method [source: intechopen.com]

3. Sono chemical Method Paragraph:

Ultrasound consists of sound waves with frequencies between 20 kHz and 10 MHz, with the 20 kHz to 1 MHz range commonly applied in sono chemical processes. Sono chemistry relies on a phenomenon known as acoustic cavitation, which involves the rapid formation, expansion, and violent collapse of microscopic bubbles within a liquid. This process generates extreme localized conditions such as high temperatures and pressures that can promote unique chemical reactions and the creation of nanostructures.When exposed to powerful ultrasonic waves, solutions can undergo structural changes that lead to the development of novel nano materials. One such material is copper oxide (CuO), a p-type semiconductor with a narrow band gap of approximately

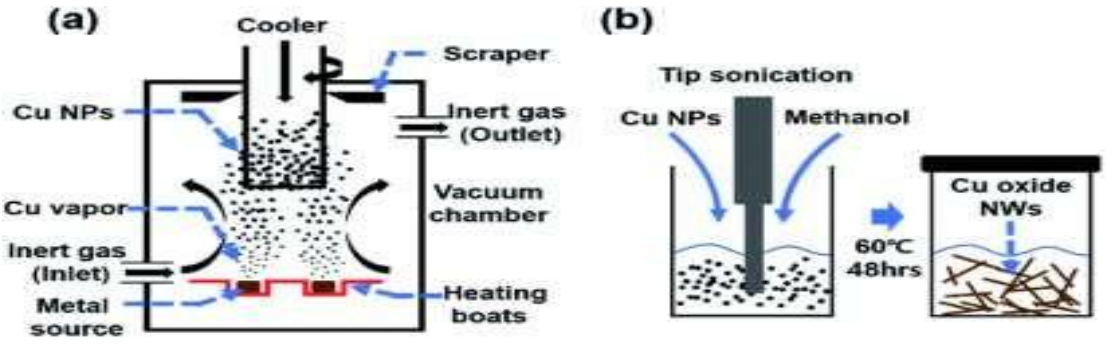
1.2 eV. CuO has attracted significant research interest due to its wide range of applications, including in catalysts, gas detectors, field emission devices, lithium-ion batteries, and dye- sensitized solar cells[8]



Sonochemical synthesis [source: semanticscholar.org]

4. Inert Gas Condensation Method:

Silver nanoparticles were produced using the inert gas condensation technique, where helium gas was introduced into the process chamber to facilitate the synthesis. Key process parameters such as the evaporation temperature and helium gas pressure were varied to observe their impact on particle size, shape, crystallinity, and distribution. Nanoparticles were generated at three different temperatures: 1123 K, 1273 K, and 1423 K, and under helium pressures of 0.5, 1, 5, 50, and 100 Torr.The resulting silver nanoparticles were analysed using X-ray diffraction (XRD) and transmission electron microscopy (TEM), which revealed particle sizes ranging from 9 to 32 nano meters, depending on the synthesis conditions.



Inert Gas Condensation Method. [Source: Researchgate.Net]

5. Hydrothermal Synthesis of Nanoparticles:

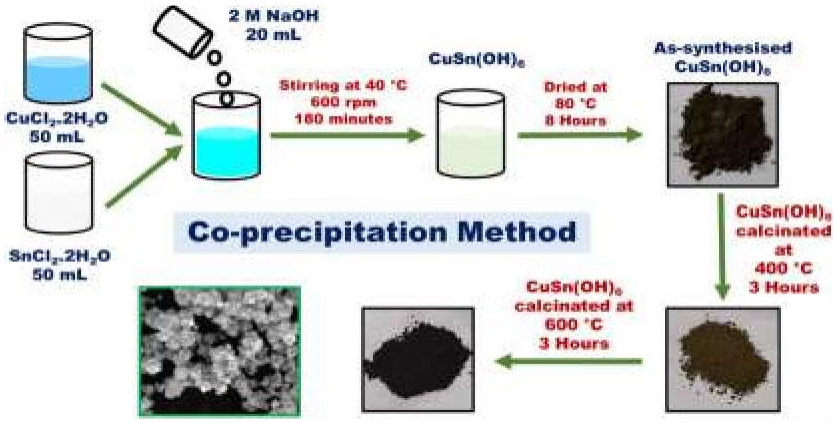
It involves heating an aqueous solution to approximately 200°C inside a sealed vessel known as an autoclave. As the temperature rises, pressure builds up due to the fixed volume of the vessel, leading to enhanced dispersion of the reactants in a compressed liquid phase. This pressurized environment allows chemical reactions to proceed more efficiently, often completing at lower temperatures and within shorter timeframes compared to conventional methods. In addition to water, other solvents can also be used in what is referred to as solvo thermal synthesis, which has gained popularity in recent years. When using water as the solvent, it's important to distinguish between subcritical and supercritical conditions depending on whether the temperature is below or above water's critical point (T_s = 374°C). Operating above the critical temperature can cause pressure in the autoclave to rise uncontrollably, making it difficult to manage the reaction process effectively [10].

Hydrothermal synthesis of nanoparticles

[source: MDPI]

6. Co Precipitation Method:

Magnetite nanoparticles were synthesized through a chemical co-precipitation technique using ammonium hydroxide as the precipitating agent. Control over particle size was achieved by varying the reaction temperature and applying surface modifications. During the initial crystallization phase, hexanoic acid and oleic acid served as coating agents. The nanoparticles' structure and morphology were characterized using Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), and field- emission scanning electron microscopy (FE-SEM). Their electrical and magnetic properties were evaluated using a conductivity meter and vibrating sample magnetometer (VSM), respectively.Both uncoated and coated magnetite nanoparticles exhibited a cubic spinel crystal structure and spherical morphology. Higher temperatures and surface modifications resulted in increased particle sizes. The nanoparticle size was successfully controlled within the 10 to 40 nm range, making them suitable for various biomedical applications [11].

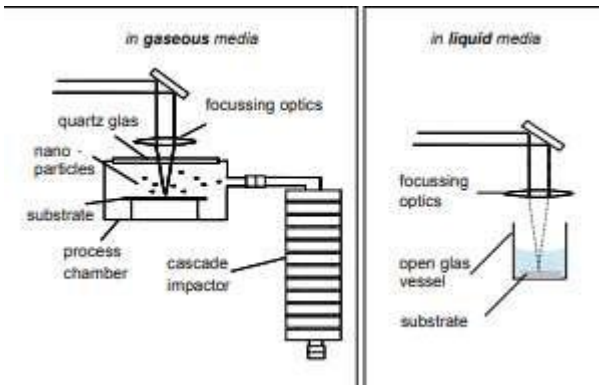


Co precipitation method of nanoparticles [source: vrogue.com]

II. PHYSICAL METHODS

1. **Mechanical methods – mechanical ball milling :**Mechanical milling is a solid-state synthesis method that utilizes ball milling equipment, which can be categorized as either "low-energy" or "high-energy" based on the intensity of mechanical force applied to the powder mixture. This technique is primarily used to reduce the size of particles and to mix them in order to create new phases.In this process, the powder material is loaded into a closed container along with heavy milling balls typically made of steel or tungsten carbide. Through vigorous shaking or high-speed rotation, the powder is subjected to intense mechanical forces from repeated ball collisions, which results in particle refinement and significant changes in material structure[12]

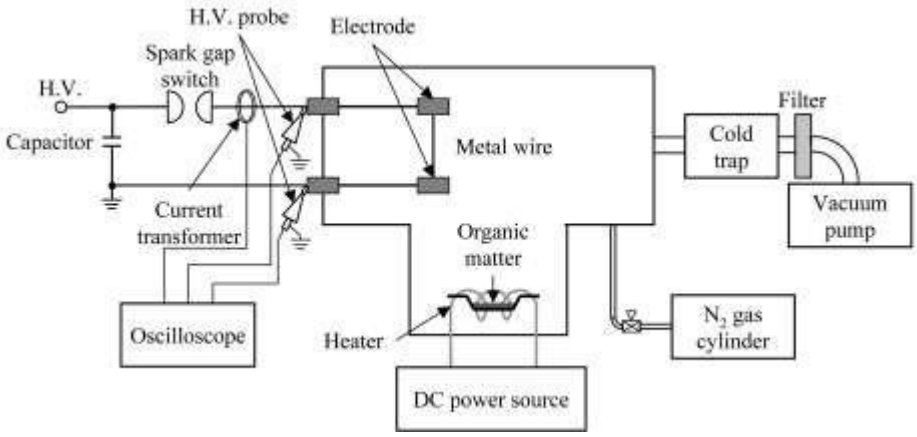
2. **Pulse laser ablation method :** Nanoparticles were synthesized primarily using a commercial femtosecond (fs) laser system that emitted 120-fs pulses at a wavelength of 800 nm, with a maximum energy output of 1 millijoule per pulse and a repetition rate of 1 kHz. A four-axis positioning system from 3D-Micromac was employed for laser micromachining. For ablation of steel samples, an alternative laser source with a shorter pulse duration of 26 femtoseconds was utilized. Liquid-phase ablation experiments were mainly conducted in a 28 mm-diameter glass container. Stabilization of the nanoparticles was examined in real-time using n-hexane as the solvent, with varying concentrations of dodecanethiol added as a stabilizing agent. [13].



Pulse laser ablation method [source: jlps.gr.jp]

3. **Pulsed wire discharge method :**The experimental setup for pulsed wire discharge consisted of a 2.5-liter sealed chamber, an oil-free dry vacuum pump, a powder collection unit (equipped with a cold trap and filter), and a basic discharge circuit comprising a high-voltage power source, a capacitor, and a spark gap switch. A copper wire measuring 25 mm in length and 0.25 mm in diameter was positioned inside the chamber, which was filled with nitrogen gas maintained at an atmospheric pressure of 100 kPa. Prior to initiating the discharge, 15 milligrams of oleic acid were heated to 473 K the compound's boiling point, as determined using a thermogravimetric balance causing it to evaporate and disperse within the chamber. The discharge event was triggered by releasing stored energy from a 10 μF capacitor, previously charged to 5.2 kV. Since the theoretical energy required to fully vaporize the copper wire is approximately 68 joules, the

stored energy was sufficient for complete wire evaporation. The discharge was activated by sending a trigger pulse to close the spark gap switch, which allowed the current to flow through the copper wire. The energy actually delivered to the wire was quantified using voltage and current waveform data. Following the discharge, the chamber was evacuated, and nanoparticles were collected through a membrane filter with a pore size of 0.1 µm (Millipore). Positioned before the filter, a cold trap cooled with liquid nitrogen served to capture any organic vapour or mist. The trap's efficiency was evaluated by monitoring the weight change of the filter in a control test conducted without triggering the discharge. With the cold trap maintained at 77 K, only a minimal amount approximately 0.1 mg of oleic acid was detected on the filter [14].



Pulsed wire discharge [source: psu.edu]

4. Chemical vapour deposition

a. **Methods for Depositing TiO2 Nanoparticles on CNTs and Handling CNT Segments :**The deposition of titanium dioxide (TiO2) nanoparticles onto carbon nanotubes (CNTs) was performed at room temperature inside a fume hood equipped with a humidity control system to monitor and regulate the relative humidity. Liquid titanium tetrachloride (TiCl4) was carefully added into a beaker, where it immediately reacted with the moist air, generating a misty vapor containing TiO2 particles and hydrochloric acid (HCl). Suspended CNT substrates were then exposed to this TiCl4 vapor and TiO2 mist, allowing TiO2 nanoparticles to deposit onto the CNTs. The exposure time typically ranged from 3 to 7 seconds, after which the substrates were removed to halt the deposition. For cutting and transferring CNT segments, the substrate holding the suspended CNTs was positioned on an optical microscope stage. Four probes mounted on two adjustable pedestals were precisely maneuvered in the X, Y, and Z directions using control knobs. These probes were brought into contact with the suspended CNTs, creating two scissor-like setups that enabled the cutting of CNTs. Once a segment was severed, the probes functioned as tweezers to pick up and transfer the individual CNT segment as needed.

b. **Pulling out the inner tube from an individual DWCNT:** When suspended double-walled carbon nanotubes (DWCNTs) decorated with TiO2 nanoparticles were observed under an optical microscope, probes were carefully brought into contact with the suspended nanotubes. By moving the probes in a specific direction, the DWCNTs were stretched, allowing real-time observation of their deformation through the microscope. To quantify the forces exerted on the DWCNTs, AFM cantilevers were attached to the probes using silver paste.

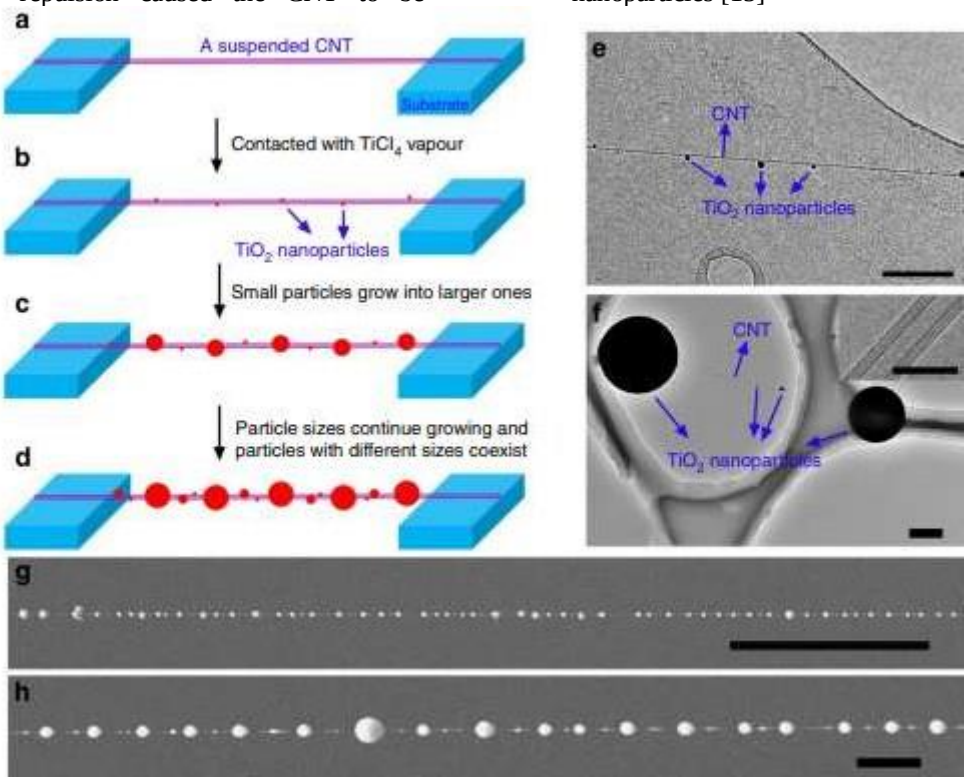
c. **Gas-flow-induced bending of suspended CNTs:** A continuous airflow was directed through a glass tube measuring 5 cm in length and 1 mm in diameter to blow on the suspended CNTs coated with TiO2 nanoparticles. While the ends of the CNTs were held firmly in place, the suspended sections were stretched by the airflow. The elongation of these suspended CNTs was captured using a digital camera. The velocity of the airflow was precisely regulated using a mass flow meter.

d. **Sound-wave-induced oscillation of suspended CNTs:** The suspended CNT/TiO2 hybrid structures were induced to oscillate using sound waves generated by a loudspeaker connected to a signal generator. Their oscillations were captured using a digital

camera.

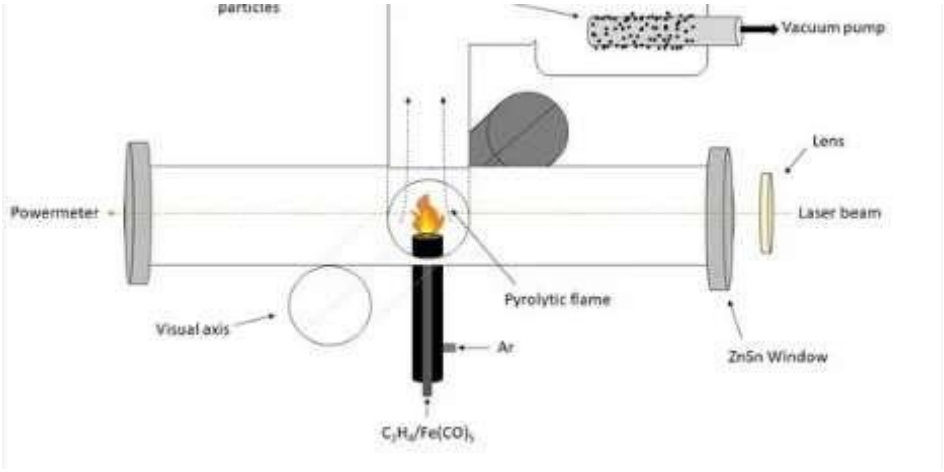
e. **Manipulation of suspended CNTs in an electric field:** A negative voltage was applied to a suspended CNT, while a probe with a positive voltage was used to attract it. Acting as an electric field sensor, the suspended CNT exhibited a rapid response. A 60-mm-long freely hanging CNT was secured to a metal probe, with a second probe positioned 120 mm away. When voltages were applied to both probes (2 V on the left and 2 V on the right), the CNT was immediately drawn toward the left probe. Upon removing the voltage, the CNT returned to its drooping state. However, when identical voltages were applied to both probes (for example, 2 V each), the strong electric repulsion caused the CNT to be pushed away toward the right side. Once the voltages were switched off, the CNT resumed its drooping position. Reapplying a voltage difference between the two probes caused the CNT to be attracted back to the left probe again.

f. **Removing of the Tio2 NPs from CNT:** A substrate containing numerous TiO2 nanoparticles and short carbon nanotubes was immersed in a beaker with 20 ml of 65% sulfuric acid solution. To enhance the dissolution process, 8 g of (NH4)2SO4 powder was added to the acid. The mixture was then heated to boiling and maintained for 2 hours. Afterward, the substrate was removed, resulting in the complete removal of the TiO2 nanoparticles [15]



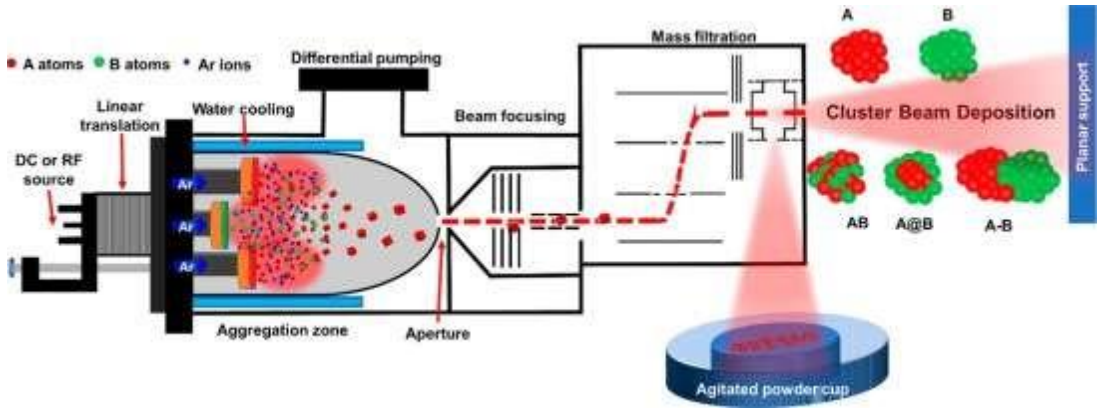
Deposition of Tio_2 [source: nature.com]

5. **Laser pyrolysis :** Iron oxide nanoparticles were produced using laser pyrolysis. The iron source was iron penta carbonyl ($Fe(CO)_5$), while synthetic air served as the oxidizing agent. Ethylene (C_2H_4) acted as the sensitizer, facilitating energy transfer. This technique utilizes a cross-flow reaction chamber design that allows resonance between the emission wavelength of a CO_2 infrared laser and the absorption band of the sensitizer gas, resulting in heating of the reactive gases through collision-induced energy transfer. In brief, the reactant gases flow perpendicularly to a focused continuous-wave CO_2 laser beam (Coherent G Series, max output 400 W, wavelength 10.6 μm). The reactant mixture of synthetic air and Fe $(CO)_5$ vapours, carried by ethylene, is introduced via a central inner tube. A surrounding argon (Ar) flow confines the gas precursors to the flow axis and directs the newly formed nanoparticles toward the collection chamber [16].



Laser pyrolysis [source: MDPI]

6. **Ionized Cluster Beam Deposition:** Although gas-phase synthesis techniques can be technically challenging, the cluster beam deposition (CBD) method has become one of the most promising approaches for creating supported nanoparticle assemblies. Gas-phase synthesis generally involves the homogeneous nucleation of a supersaturated vapor such as metal atoms in a low-pressure rare gas environment followed by particle growth through condensation and coalescence. Among the various CBD techniques, magnetron-sputtering combined with inert-gas condensation stands out for its versatility. This method allows precise control over particle growth by adjusting parameters like magnetron power, inert gas pressure, and aggregation zone length. Additionally, the use of multiple independent targets enables the tailored design and synthesis of multi-metallic nanoparticles with controlled morphology and composition within a single process [17].

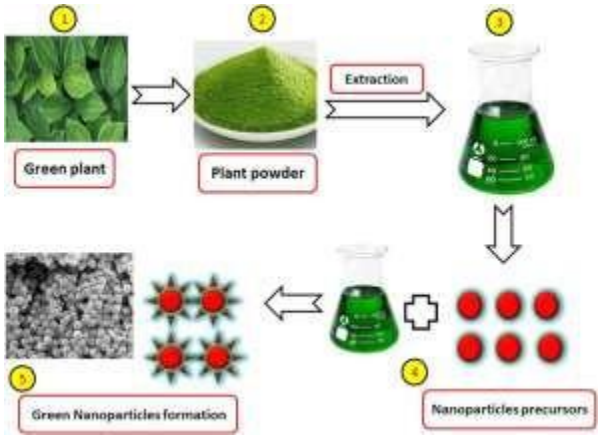


Ion cluster beam deposition [source: pubs.acs.org]

III. BIOLOGICAL METHODS

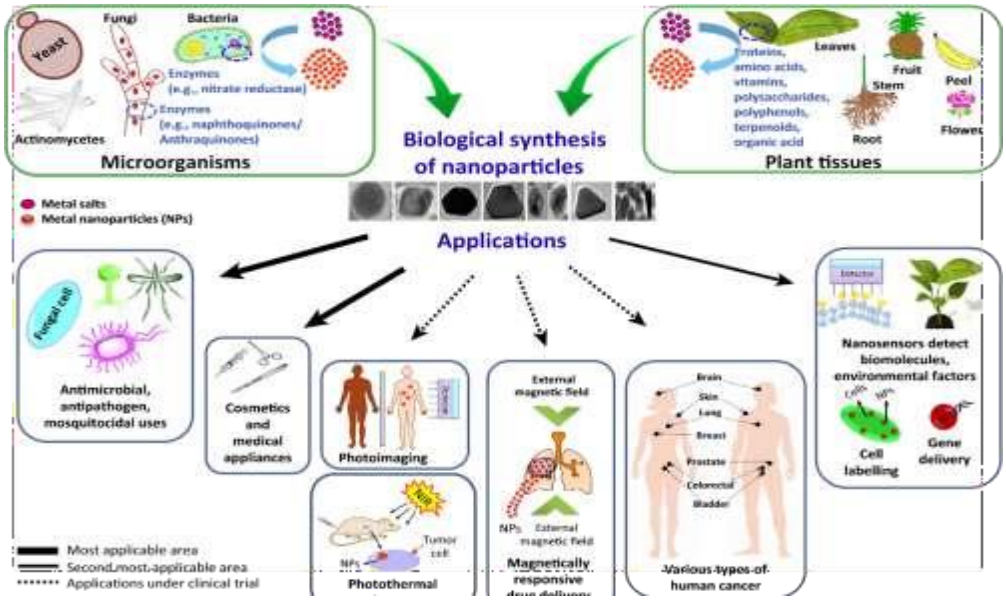
1. **Synthesis of Nanoparticles Using Plant Extracts** :Biosynthesis of nanoparticles via plant extracts often called photosynthesis of nanoparticles is gaining attention as an eco-friendly alternative that merges nanotechnology with biotechnology. Gold nanoparticles synthesized using plant extracts have become particularly popular due to their strong antibacterial properties and the ease of reducing gold salts biologically. Medicinal plants such as *Cucurbita pepo* and *Malva crispa* have been used to produce gold nanoparticles with potent antibacterial effects against food spoilage pathogens. Similarly, aqueous leaf extracts of *Acalypha indica* have been shown to rapidly synthesize gold nanoparticles measuring 20–30 nm, utilizing bio-reductants present in the extract.A novel approach involves synthesizing triangular gold core-silver shell nanoparticles by reducing gold ions with lemongrass extract, followed by electrostatic complexation of silver ions with the negatively charged gold nanoparticles, and subsequent reduction of surface-bound silver ions using ascorbic acid. Leaf extracts of *Cymbopogon citratus* have been reported to act as both reducing and capping agents in the synthesis of gold nanoparticles. Other plants have also been explored for nanoparticle synthesis. For instance, *Zingiber officinale* leaf extract has

been used to produce gold nanoparticles around 10 nm in size, while *Syzygium cumini* fruit extract has been employed for synthesizing silver nanoparticles sized 10–15 nm. The aqueous seed extract of *Abelmoschus esculentus* has been utilized for gold nanoparticle synthesis, which exhibited antifungal activity against pathogens like *Puccinia graminis tritici*, *Aspergillus flavus*, *Aspergillus niger*, and *Candida albicans*, highlighting the potential for drug development against fungal diseases.Stable gold nanoparticles of various sizes have been produced using extracts from *Pelargonium graveolens* leaves and its endophytic fungi through extracellular synthesis. For example, nanoparticles with triangular and spherical shapes averaging 50 nm and 100 nm, respectively, were synthesized using leaf extract of *Nepenthes khasiana*, confirmed by scanning and transmission electron microscopy.Other notable examples include gold nanoparticles synthesized from fruit peel extract of *Punica granatum* for targeted cancer drug delivery, and *Hibiscus* leaf extract, which produced gold nanoparticles with diverse shapes and an average size of 13 nm. Silver nanoparticles synthesized using shadow-dried *Stevia rebaudiana* leaf extract ranged from 2 to 50 nm with an average size of 15 nm. Leaf broths from *Magnolia* and *Persimmon* have also been used to produce gold nanoparticles, with reaction rates increasing significantly at elevated temperatures (up to 95°C), matching the speeds seen in chemical synthesis methods. The particle sizes ranged from 5 to 300 nm in these cases.Additionally, grape waste has been used as a sustainable source for synthesizing gold nanoparticles averaging 20–25 nm, providing a valuable method for utilizing agricultural waste. Gold nanoparticles have also been synthesized at room temperature using aqueous extract of *Hovenia dulcis* fruit, yielding spherical and hexagonal particles about 20 nm in size [18].



Synthesis of nanoparticles from plant extract. [source: researchgate.net]

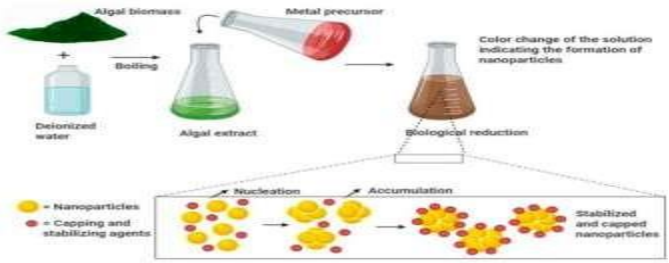
2. **Microbial Synthesis of Nanoparticles :**Microbial synthesis of gold nanoparticles (AuNPs) provides a green, cost-effective alternative to conventional chemical methods. One of the first documented mechanisms involved the formation of AuNPs in *Bacillus subtilis* 168 under ambient temperature and pressure, where incubation with Au^{3+} ions led to the in vitro generation of octahedral nanoparticles (5–25 nm) along the cell wall. This process is thought to be facilitated by organic phosphate compounds acting as complexing agents between the bacteria and gold ions. *Shewanella algae* has shown the ability to reduce Au^{3+} ions under anaerobic conditions. In the presence of hydrogen gas, complete reduction of gold ions occurs, producing nanoparticles between 10–20 nm in size. In *Escherichia coli* and *Desulfovibrio desulfuricans*, hydrogen gas serves as the electron donor, with periplasmic hydrogenases likely playing a role in the reduction process and nanoparticle accumulation. In *E. coli*, engineered expression of cysteine-rich thiol groups in the flagellar protein (FliC) has been shown to enhance gold ion binding and promote the formation of 20–25 nm nanoparticles on the flagellar surface.The filamentous cyanobacterium *Plectonema boryanum* UTEX 485 can also precipitate cubic AuNPs when exposed to aqueous gold chloride. Initially, amorphous gold sulfide forms on the cell wall, followed by the deposition of metallic gold both at the surface and in the surrounding solution. This process can take up to a month at temperatures between 25°C and 100°C but is completed within a day at 200°C [19].



Synthesis of nanoparticles from microorganisms. [source: newsciencetopics.blogspot.com]

3. SYNTHESIS OF NANOPARTICLES USING ALGAE

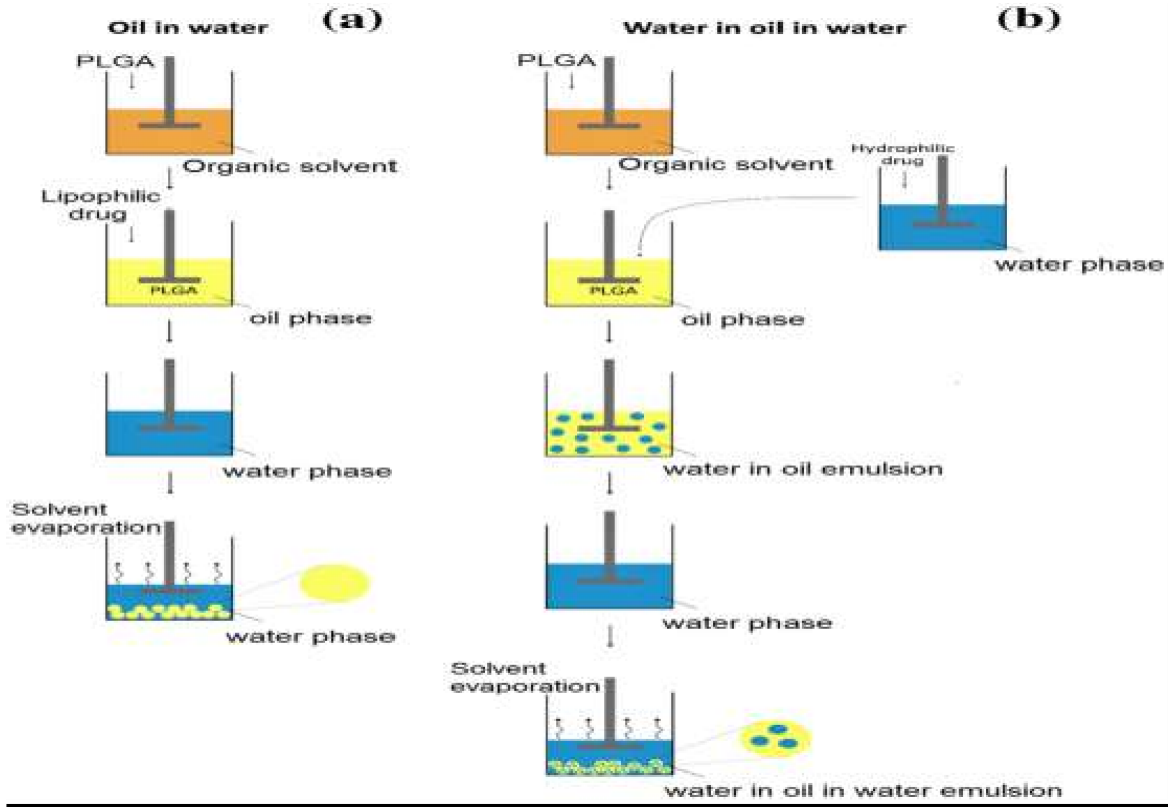
a. **Microbial Synthesis of Nanoparticles Using Cyanobacteria and Algae**: The cyanobacterium *Nostoc ellipsosporum* was among the first microorganisms used in laboratory settings for the intracellular biosynthesis of gold nanorods. When cultured in a gold solution at a concentration of 15 mg/L and a pH of 4.5, the cells produced nanorods within 48 hours at 20°C. Gold nanoparticles (AuNPs) can be synthesized through various methods, and their wide-ranging applications in industrial and medical fields continue to drive interest in sustainable production techniques.Algae, particularly those thriving in environments contaminated with both metallic and non-metallic pollutants, have shown remarkable tolerance to high concentrations of toxic substances. This resistance is attributed to the development of adaptive defense mechanisms that help minimize the harmful effects of metal ions, enhancing their survival. Due to their natural abundance in both marine and freshwater ecosystems, cost-effectiveness, reusability, and exceptional metal-binding abilities, algae serve as excellent biosorbents. Metallic nanoparticles can be synthesized using live microalgal cells in a single-step process. In this approach, an aqueous solution of metal salts is added directly to the growing algal culture. The cells absorb the metal ions and facilitate their reduction into nanoparticles, which are then released into the culture medium. These particles often become embedded in a biological matrix that promotes colloid formation. Due to their density, the nanoparticles settle at the bottom of the photobioreactor. This biosynthetic process can be repeated by replenishing the culture medium, allowing for multiple production cycles. Furthermore, microalgae retain their ability to synthesize nanoparticles even when encapsulated within organic vesicles. In some cases, biomolecules extracted from algal cells have also been used to drive the biosynthesis of nanomaterials, highlighting the potential of algae as bio-factories for sustainable nanotechnology applications [20].



Synthesis of nanoparticle from algae [source : mdpi.com]

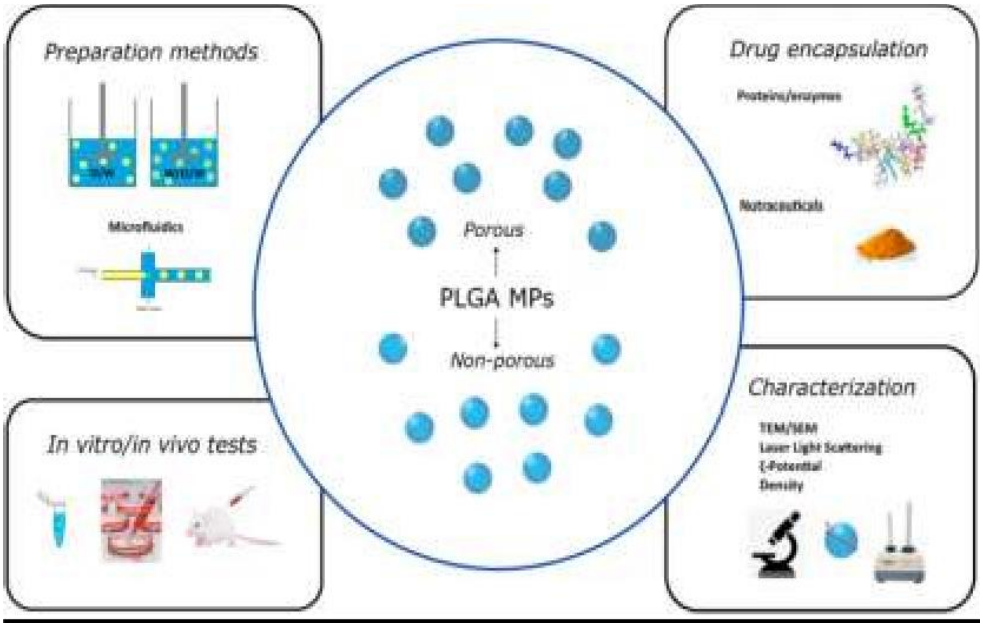
RECENT APPROACHES IN THE FORMULATION OF PLGA MICROPARTICLES FOR CONTROLLED DRUG DELIVERY

1. **Poly(lactic-co-glycolic acid) (PLGA) in Drug Delivery** :Poly(lactic-co-glycolic acid) (PLGA) is among the most extensively used biodegradable polymers in the biomedical field, particularly for drug delivery applications. Its widespread use is largely due to its biocompatibility and safe degradation profile. Upon hydrolysis, PLGA breaks down into lactic acid and glycolic acid—both endogenous metabolites that are naturally processed and eliminated via the Krebs cycle, resulting in minimal systemic toxicity. PLGA has received regulatory approval from both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for use in various human drug delivery systems. It is commercially available in a range of molecular weights and monomer ratios, which directly influence its degradation kinetics. Depending on these factors, PLGA can degrade over time spans ranging from several months to several years.The composition of PLGA is typically represented by the ratio of its monomers. For example, PLGA 50:50 denotes a copolymer containing equal proportions of lactic acid and glycolic acid. In contrast, poly(lactic acid) (PLA), composed solely of lactic acid, has more limited use in drug delivery due to its slower degradation rate [21].
2. **Single Emulsion Technique**



The single emulsion technique [source: springer.com] Single Emulsion Technique for Drug Encapsulation

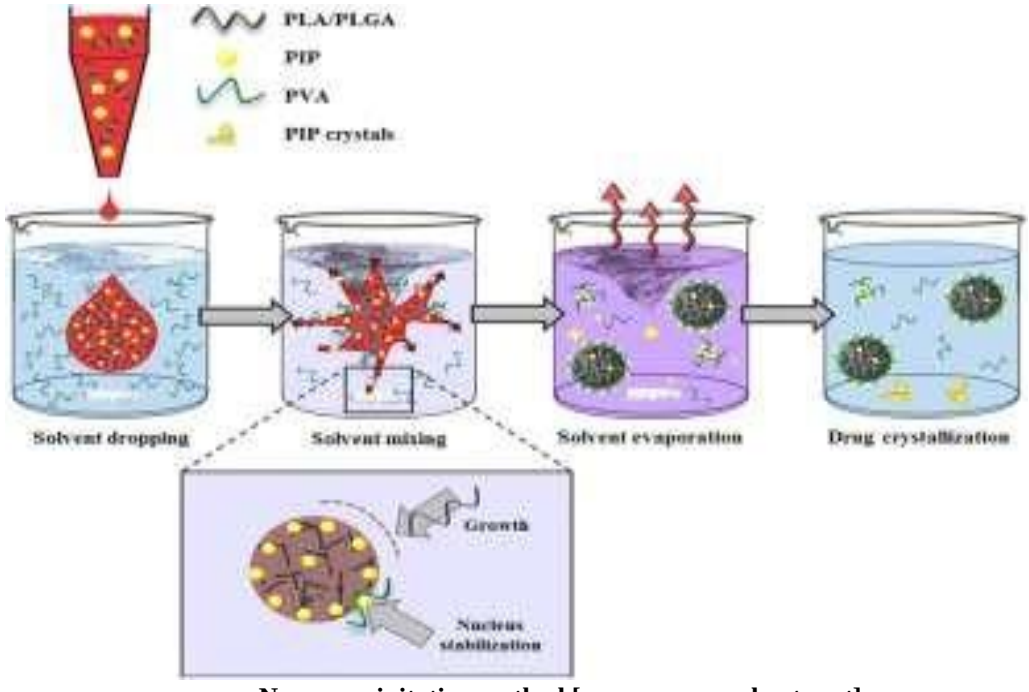
This process involves the creation of an oil-in-water (O/W) emulsion, where both the drug and polymer are dissolved in an organic solvent, forming the oil phase. Commonly used solvents include halogenated compounds with low boiling points such as dichloromethane, chloroform, and hexafluoro-isopropanol as well as non-halogenated alternatives like ethyl acetate, isopropanol, methyl ethyl ketone, acetone, and benzyl alcohol. Mixed solvents are also sometimes employed. This oil phase is then emulsified into an aqueous phase containing a surfactant or emulsifier, such as polyvinyl alcohol (PVA), Tween (polyethylene glycol sorbitan monolaurate), Span (sorbitan monooleate), or sodium dodecyl sulfate (SDS), typically using sonication or high-speed homogenization. The final emulsion is stabilized as the solvent gradually evaporates, a step that is aided by continuous stirring or vacuum-assisted solvent removal. This results in the formation of mature microparticles (MPs) [22].



[Source: springer.com]

3. NANO PRECIPITATION METHOD

Nanoprecipitation Technique for Nanoparticle Preparation :Nano precipitation is a simple and efficient method for producing nanoparticles (NPs), particularly suited for encapsulating hydrophobic drugs. In this approach, a solution containing the polymer, drug, and a water-miscible organic solvent is slowly introduced into an aqueous phase. This induces the spontaneous precipitation of nanoparticles through rapid solvent exchange. The method is a one-step, reproducible process that requires minimal energy input and is easily scalable for large-scale production. Using this method, various types of PLGA nanoparticles including surface-modified forms such as PEG-ylated PLGA and ligand-targeted formulations have been successfully developed for targeted drug delivery, especially in cancer therapy.To enhance encapsulation efficiency, several optimizations have been explored. For instance, adjusting the pH from 5.8 to 9.3 and replacing procaine hydrochloride with procaine dehydrate significantly improved drug entrapment efficiency, increasing it from 11.0% to 58.2%. Additionally, a modified Nano precipitation approach using dimethyl sulfoxide (DMSO) as the solvent and poloxamer as the aqueous stabilizer has achieved DNA encapsulation efficiencies exceeding 95%.



Nano precipitation method [source: researchgate.net]

4. MICROFLUIDICS-ASSISTED METHOD

a. Microfluidic-Based Synthesis of PLGA Nanoparticles :Microfluidic systems facilitate the precise manipulation of micro- to nanoliter volumes of liquids within microscale channels, offering significant advantages over conventional bulk methods for nanoparticle synthesis. Based on fluid flow dynamics, these systems are generally categorized into two types:

1. Continuous-phase flow**,** and
2. Segmented (droplet-based) flow microfluidics.

For producing PLGA nanoparticles (NPs), continuous-phase flow microfluidics is particularly effective at achieving nanoscale particle sizes, whereas segmented flow systems typically yield microparticles. In continuous-flow microfluidic synthesis, an organic solution containing both the polymer and drug is introduced into a central channel, flanked by aqueous streams. As the fluids interact, nanoprecipitation occurs within the organic phase, leading to the formation of PLGA NPs.

This approach offers several key advantages:

- Precise control over particle size and distribution
- High reproducibility across batches
- Improved heat and mass transfer efficiency
- Tunable reaction parameters (e.g., flow rate, temperature)
- Faster production times

Additionally, nanoparticles produced via microfluidic techniques often possess compact and uniform morphologies, which can mitigate the initial burst release of the encapsulated drug [23].

CONCLUSION:

Nanoparticles have emerged as powerful tools across various fields, including vaccine delivery, cancer therapy, and numerous other biomedical and industrial applications. While the production of nanoparticles can be technically challenging, the development of innovative and scalable synthesis techniques both at the laboratory and commercial levels has significantly advanced the field. As research continues to refine these methods, the role of nanoparticles in improving therapeutic outcomes and enabling targeted delivery systems is becoming increasingly prominent. Their growing integration into daily life highlights their vital importance in modern science and technology.

REFERENCES:

1. Patil N, Bhaskar R, Vyavhare V, Dhadge R, Khaire V, Patil Y. Overview on methods of synthesis of nanoparticles. International Journal of Current Pharmaceutical Research. 2021;13(2):11-6.
2. Meshesha BT, Barrabés N, Medina F, Sueiras JE. Polyol mediated synthesis and characterization of Cu nanoparticles: Effect of 1-hexadecylamine as stabilizing agent. In: Proceedings of the 1st WSEAS International Conference on Nanotechnology (NANOTECHNOLOGY'09); 2009
3. Caroline Q, Bernard S, Miele P. Synthesis of praseodymium oxide nanoparticles. In: Nanomaterials and Nanotechnology. Vol. 4. No. Godište 2014; 2014. p. 1+
4. Sun YG, Yin YD, Mayers BT, Herricks T, Xia YN. Uniform silver nanowires synthesis by reducing AgNO3 with ethylene glycol in the presence of seeds and poly(vinyl pyrrolidone). Chemistry of Materials. 2002;14:4736-4745
5. S. D. Jadhav1, I A Shaikh2 Synthesis of Nanoparticles an Overview, a Review Article | Mar-Apr 2019
6. Petr Slepička,1,* Nikola Slepičková Kasálková,1 Jakub Siegel,1 Zdeňka Kolská,2 and Václav Švorčík1 Methods of Gold and Silver Nanoparticles Preparation Published online 2019 Dec
7. Hasan S. A review on nanoparticles: their synthesis and types. Res. J. Recent Sci. 2015;2277:2502.
8. Rudramurthy GR, Swamy MK. Potential applications of engineered nanoparticles in medicine and biology: an update. JBIC Journal of Biological Inorganic Chemistry. 2018 Dec;23:1185-204.
9. Dmitry Bokov Nanomaterial by Sol-Gel Method: Synthesis and Application december 2021.
10. Wongpisutpaisan N, Charoonsuk P, Vittayakorn N, Pecharapa W. Sonochemical synthesis and characterization of copper oxide nanoparticles. Energy Procedia. 2011 Jan 1;9:404-9.
11. Raffi M, Rumaiz AK, Hasan MM, Shah SI. Studies of the growth parameters for silver nanoparticle synthesis by inert gas condensation. Journal of Materials Research. 2007 Dec;22(12):3378-84.
12. Schmidt R, Prado-Gonjal J, Morán E. Microwave assisted hydrothermal synthesis of nanoparticles. arXiv preprint arXiv:2203.02394. 2022 Mar 4.
13. Petcharoen K, Sirivat AJ. Synthesis and characterization of magnetite nanoparticles via the chemical co-precipitation method. Materials Science and Engineering: B. 2012 Mar 25;177(5):421-7.
14. Murai K, Watanabe Y, Saito Y, Nakayama T, Suematsu H, Jiang W, Yatsui K, Shim KH,

Niihara K. Preparation of copper nanoparticles with an organic coating by a pulsed wire discharge method. Journal of Ceramic Processing Research. 2007 Jan 1;8(2):114.
15. Zhang R, Zhang Y, Zhang Q, Xie H, Wang H, Nie J, Wen Q, Wei F. Optical visualization of individual ultralong carbon nanotubes by chemical vapour deposition of titanium dioxide nanoparticles. Nature communications. 2013 Apr 16;4(1):1727.
16. Lungu II, Andronescu E, Dumitrache F, Gavrila-Florescu L, Banici AM, Morjan I, Criveanu A, Prodan G. Laser Pyrolysis of Iron Oxide Nanoparticles and the Influence of Laser Power. Molecules. 2023 Oct 26;28(21):7284.
17. Palmer RE, Cai R, Vernieres J. Synthesis without solvents: the cluster (nanoparticle) beam route to catalysts and sensors. Accounts of Chemical Research. 2018 Sep 6;51(9):2296-304.
18. Ikram S. Synthesis of gold nanoparticles using plant extract: an overview. Nano Res. 2015;1(1):5.
19. Shedbalkar U, Singh R, Wadhwani S, Gaidhani S, Chopade BA. Microbial synthesis of gold nanoparticles: current status and future prospects. Advances in colloid and interface science. 2014 Jul 1;209:40-8.
20. Mukherjee A, Sarkar D, Sasmal S. A review of green synthesis of metal nanoparticles using algae. Frontiers in Microbiology. 2021 Aug 26;12:693899.
21. Lagreca E, Onesto V, Di Natale C, La Manna S, Netti PA, Vecchione R. Recent advances in the formulation of PLGA microparticles for controlled drug delivery. Progress in biomaterials. 2020 Dec;9:153-74.
22. Danhier F, Ansorena E, Silva JM, Coco R, Le Breton A, Préat V. PLGA-based nanoparticles: an overview of biomedical applications. Journal of controlled release. 2012 Jul 20;161(2):505-22.
23. Rezvantalab S, Drude NI, Moraveji MK, Güvener N, Koons EK, Shi Y, Lammers T, Kiessling F. PLGA-based nanoparticles in cancer treatment. Frontiers in pharmacology. 2018 Nov 2;9:1260.