

## Approach of nano materials in pharmaceutical science

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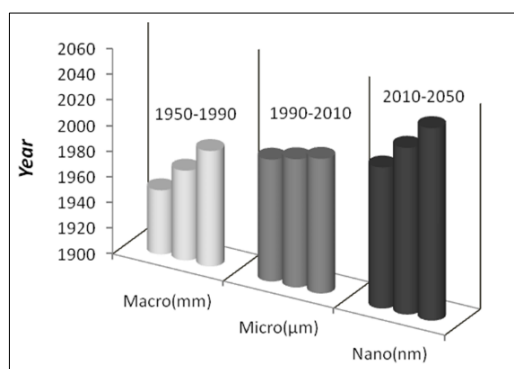
### Abstract

Recent technical advancements have provided proof that evolution in Nano technology and Nano science is the fundamental factor. Physics, chemistry, materials science, and other engineering sciences are all involved in the multidisciplinary field of Nano technology. Nearly all areas of science and technology are seeing significant use of Nano technology. The varieties of Nano particles, as well as their synthesis and characterization methods, were highlighted in this review study. Although various techniques and applications have been described over the previous years, we primarily focused on the general synthetic approaches and uses of Nano materials here in order to give the young researchers a general perspective.

**Keywords:** History of Nano technology; Properties of Nano materials; Synthesis of Nano materials; Characterization methods; Applications

### 1. Introduction

The foundation of Nano science and Nano technology is Nano materials. Nano structure science and technology is a large and interdisciplinary field of study and development that has grown rapidly in recent years around the world. It may revolutionise the processes used to make materials and goods, as well as the types and range of functions that may be accessed. It already has a considerable business influence, which will undoubtedly grow in the future as shown in figure 1[1].



**Figure 1** Evolution of science and technology and the future

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Smart Nano materials, also known as intelligent materials, are gaining popularity due to their versatile and distinct properties. They offer a reliable foundation for a range of applications. During the years of advancement in the field of Nano technology, many smart Nano materials have been created and effectively used in several applications; they are often referred to as 2nd or 3rd generation Nano technology applications [2]. The term "smart materials" was first used to describe materials that responded quickly to environmental factors, but it is now used to describe materials that respond to stimuli that cause a reversible change in their functional qualities. The term "stimuli" refers to variations in environmental variables like temperature, electricity, magnetic field, pressure, tension, etc. All of these will provide the smart Nano materials the essential capabilities they need to develop prospective applications. Smart Nano materials are still challenging to manufacture, but many people are interested in them because of their variety of uses, self-awareness, and self-adaptability, which make them special. They find uses in the fields of biomedicine, energy devices, healthcare, security and defense, and environmental engineering, but the usage of smart Nano materials in the aerospace sector is growing significantly. As a result of their exposure to numerous changes in an open environment, smart Nano particle applications are becoming quite popular in the aircraft industry. Smart Nano materials are therefore becoming quite popular in the aerospace sector [3]. Over time, several Nano materials, including metallic Nano materials, carbon Nano materials, and polymeric Nano fibers, have been discovered that might be employed as intelligent materials that demonstrate cognitive function under environmental changes. The manufacture of fuel cells uses metallic Nano materials with good catalytic characteristics, such as gold Nano particles. Due to their ability to absorb light and produce a variety of colours, silver Nano particles are used to create sensors that can track the performance of structures. The Graphene Nano composites show decent electrical and thermal conductivity therefore they are used as filler in sensor and solar cells.

The article discusses the many smart Nano materials that have been created over time, their characteristics, and their uses. Because of the numerous uses, graphene-based Nano composites are a focus of extensive study. This research is centred on several graphene polymer composites, including those with distinct production processes, functionalization, characterizations, and significant applications. Chemical vapour deposition functionalizations, (CVD)-produced graphene is employed in coating and electrical applications whereas liquid phase exfoliated graphene is used in composite energy storage applications. The graphene metal/ceramic composites demonstrated exceptional mechanical characteristics and ageing resistance. These composites are mostly used in membranes, vehicle parts, sensors, and other products. The project also places a strong emphasis on creating a lightweight structural material that can function in low-temperature environments. Cryogenic fuel tanks made of carbon fibre reinforced polymer (CFRP) can be used instead of metal ones to extend the life of space launch vehicles and cut costs. Due to the thermosetting resins employed as its matrix, the CFRP can be brittle in low temperature conditions and its characteristics can be improved by using certain carbon-based Nano fillers. Thus, structural innovations in graphene-based materials have the potential to significantly alter several fields of research. There are several uses for epoxy Nano composites, particularly in the aircraft industry. Glass transition temperature, as well as mechanical and electrical characteristics, were significantly increased by Nano diamond reinforcement in epoxy composites. Due to their electromagnetic compatibility, shielding properties, and other advantages, these composites are mostly used in electrical equipment. When compared to its other constituents, the ability of Nano diamonds to produce highly tightly spaced particles in the interphase at modest loadings, improving thermal and mechanical strength, makes it a particularly special Nano particle. Particles of Nano scale dimensions are known as Nano materials, and surface and interface features predominate over bulk qualities. Due to their Nano scale dimension, Nano materials might be categorised as ultra-fine particles[4].

Metal Nano particles, a Faraday discovery, are an essential field of Nano technology due to their exceptional properties optically, thermally, mechanically and electrically. Their thermal properties can be used for electronic wiring and their electrical characteristics for superconductivity materials. In addition to these they serve as excellent catalysts especially gold and silver Nano particles which can be purposeful in fuel cells. The both photolytically and radiolytically synthesised particles lay forward infinite possibilities in various fields. But the disadvantages they possess like the particle instability, impurities building up, coagulation etc should be taken care of for better manipulation of these particles. The gold Nano particles has attracted many researchers due to their high activity even under mild conditions. These highly active Nano particles exhibit excellent catalytic and lubricant properties. Their catalytic property can be used in the removal of carbon monoxide by oxidation thus controlling pollution and emission. Not just carbon monoxide they also detect harmful nitrogen compounds and hence helps to purify air. As we know fuel cells are excellent source of electric power in spacecrafts. The catalytic property of Nano gold can be manipulated in fuel cells. Gold Nano particles are easily available which makes them cost efficient and they also exhibit great stability. They can also be used in sensors to detect poisonous and inflammable gases. The gold Nano particles if manipulated properly can be highly beneficial commercially in lots of fields including medical due their properties [5]. The Nano technology is an emerging field. The application of Nano materials is immense due to their exceptional properties which arise due to their Nano scale dimension. The synthesis of these particles in a befitting manner is highly essential. This paper discusses the various

synthesising methods of Nano scale particles along with their advantages, disadvantages and applications. New methods or improvising the existing methods for the same is regarded important. The Nano fibers synthesized by using electron spinning procedure have weak strength which doesn't allow them to be used for many applications. To improve their properties hierarchical morphology is used which introduces additional structures on electrospun Nano fibers. By controlling electrospinning parameters, we can improve the properties but also eliminate the undesirable properties of the electro spun Nano fibers. Hierarchical electro spun Nano fibers provide a high-porous mesh structure that could be used for energy storage and also increase the multifunctionality of the Nano fibers. The Nano materials have been playing a crucial role in the development of thermal management to create highpowered electronics which are used in aerospace platforms [6].

There are many techniques present to manufacture objects on the scale of 100nm, but one of the main and efficient techniques is lithography, the various processes under the lithography are Ion Beam lithography technique, Electron Beam Lithography technique, Optical Lithography technique. These processes are classified based on radiation used: In the case of optical lithography, we use photons, electrons in the electron beam, and ions in ion beam lithography. The steps involved in the lithography process are, at first, to prepare our desired pattern or structure we take a material called substrate; it is flat shaped material (ex: Silicon Wafer) now we spread a layer of energy sensitive material called resist. Now we expose it to radiation at some well-defined spots to create a chemical change, these steps define the size of the pattern. Now we remove the resist from exposed regions in case of positive resist, but if it is negative resist, we remove the unexposed region. Then after many other techniques can be applied for the transfer of resist onto a substrate such as etching, electroplating, or lift-off. This entire process is called Lithography and is the most widely used technique in the case of large volume printing [7].

Nano technology and current techniques are advancing the pharmaceutical sector toward customised therapy (Table 1). An efficient method for creating highly selective in-vivo imaging agents that specifically target cancer cells and other elements of the tumour microenvironment is Nano particle technology. There are several merits of using Nano particles as imaging agents:

- Massive carrying capacity to enhance the sensitivity of modalities like high-resolution MR.
- Integrating with a variety of imaging techniques to provide non-invasive imaging during surgery to assure total tumour removal and cancer-free margins, and
- Can be utilised as theragnostics to facilitate medication transport to the tumour site monitoring [8].

**Table 1** FDA approved Nano drugs available commercially and in clinical use

Name	Particle type/drug	Approved application	Year of approval(FDA)
ONPATRO patisiran ALN-TTR02(alnylam pharmaceuticals)	LipidNanoparticle RNAi for the knock down of disease- causing TTR protien	Transthyretin-mediated amyloidosis	2018
VYXEOS CPX-351(jiazz pharmaceuticals)	Liposomal formulation of cytarabine daunorubicin	Acute myeloid leukemia	2017
Marqibo(spectrum)	Liposomal irinotecan (PEGylated)	Metastatic pancreatic cancer	2015
Injectaferferinjet(vifor)	Iron carboxymaltose colloid	Iron deficient anemia	2013
Optison(GE healthcare)	Human serum albumin stabilized perflutern microspheres	Untrasound contrast agent	1997

Understanding the tumour microenvironment is necessary for the development of Nano particles that perform as effective therapeutic agents. Complex extracellular fluid, leaky blood arteries, invasive immune cells, and stromal cells surround the cancer or tumour cells. The tumour cells' physiological circumstances are unstable, such as hypoxia and an acidic extracellular pH. This generates a barrier that prevents the regular treatment medicines from efficiently attacking the malignant cells, limiting their potency. The secreted protein acidic and rich in cysteine (SPARC) in prostate cancer cells, which affects cell adhesion otherwise, has been discovered to bind successfully to the functionalized biocompatible, fluorescent iron oxide Nano particles both in vivo and in vitro. Nano particles might therefore be used

in the development of individualised treatment plans. For the treatment of cancer, fluorescent carbon Nano particles can be utilised in conjunction with prescription medications. Due to their high water solubility, flexibility in surface modification with different chemicals, outstanding biocompatibility, lack of toxicity, strong cell permeability, and high photostability, carbon Nano particles function as a viable substitute for modern pharmacological therapy[9].

Utilizing point-of-care diagnostics, lab-on-chip based Nano devices have shown possibilities in addressing the complex problem of global health, particularly in underdeveloped nations where the largest need for medical technology exists. These are inexpensive, extremely picky, and capable of diagnosing diseases. Strategies utilising lab-on-chip technology have significantly helped the fight against pathogens like ebola and malaria. Heat capacity decreases due to an increase in surface area, resulting in rapid mass/heat transfer and a greater response rate. Diffusion distance also decreases as a result of the increase in surface area. The decreased size also results in lower sample, reagent, energy, and waste creation, as well as a smaller instrument footprint. Under the suitable excitation, Europium (Eu) Nano particles can generate a stable, high-intensity fluorescence. It has been reported that biconjugated Eu Nano particles employed as probes can increase the sensitivity of microchip immunoassays without using labile catalytic enzymes and can detect HIV-1 p24 antigen [10].

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## 2. Different properties of Nano materials

These characteristics of Nano particles differ from those of the bulk substance. Despite the fact that their bulk and macro-structured features are the same. The concentration of particles present on the surface increases as particle size decreases. Surface atoms are more mobile because their coordination number is lower than that of their interior atoms. We may use Nano particles in many different domains, such as catalysis, functional coatings, adsorbents, Nano electronics, and sensors, depending on the surface property. At the Nano -regime, the excitation, emission, chemical reactivity, and stability features are similarly size-dependent. In addition to size, shape also had a significant impact on how successfully a Nano material performed. They display quantum size effects when the Nano particle size is closer to the de Broglie wavelength limit and the diameter is less than the quasiparticle interaction. By adjusting the size of Nano materials as they are being synthesised using various techniques, it is possible to regulate and manipulate their characteristics. They can be used as catalysts since they have a larger surface area. The majority of metal Nano particles may be used as effective catalysts. The following fields can use Nano materials by utilising the surface phenomenon [11].

A metal's electronic band structure determines its electronic properties. The particle size affects the band structure. In the molecular states, the delocalized bands are visible. Nano crystal band structures fall between between continuous bands of crystals and discrete states of atoms (and molecules). The size of the particle affects how far apart the consecutive lines are energetically. The spacing between energy levels expands when size is reduced. The metallic quality eventually quickly turns away to reveal the semiconductor nature. Magnetic materials come in a variety of forms, including dia, para, ferro, antiferromagnetic, and ferromagnetic materials. Depending on their coercivity, soft and hard magnetic materials are various categories of magnetic materials. Soft materials can be magnetised by a weak magnetic field because they have a low coercivity and a tiny hysteresis region. This is in contrast to the hard magnets. Depending on the size of the particles, the coercivity will alter. Coercivity and saturation magnetization typically rise with increasing surface area and decreasing particle size. As a result, Nano particles have more surface area with smaller grain sizes and exhibit strong magnetic properties. Further reduction in particle size will result in instability, which will cause ferromagnetic particles to transform into paramagnetic materials. Superparamagnetic describes the behaviour of these paramagnetic materials, which differ from the behaviour of the bulk material. The use of magnetic materials is possible in many different devices, including actuators, transformers, power generators, and electronic circuits for data storage.

The Nano materials have unique optical characteristics. The optical property of a substance is the way it interacts with light, and it depends on the substance's size, shape, doping, surface properties, contact with the environment, and other factors. Due to their surface plasmon and electron quantum confinement, they have this feature. The surface plasmon resonance energy will be determined by the free electron density and the Nano material's dielectric medium. Silver's surface plasmon resonance band is at 410 nm, whereas gold's is at 520 nm. Dimensional dependence Optical characteristics are size dependent. The size and form of Nano particles are the key determinants of all of their attributes. Therefore, it is feasible to regulate and manipulate the characteristics of Nano materials by varying the methods used to manage their size throughout the production process [12].

### 3. Smart Nano material's

Smart Nano materials are frequently referred to as "bright" or "intelligent" Nano materials since they have intriguing adjustable properties in many media to quickly carry out their specialised duties in the best possible condition with regard to changes in their environment. Smart Nano materials are those that have excellent selectivity, prompt responsiveness, self-actuation, flexibility, and directness as their distinguishing characteristics. Due to these outstanding qualities, researchers have recently focused on using them as promising candidates in the creation of sensing devices for biosensors and other sensing applications[13].

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### 4. Synthesis of Nano materials

Three alternative methods can be used to create Nano particles. They are listed below.

- Biological methods
- Physical methods
- Chemical methods

#### 4.1. Biological methods

The biological technique is straightforward, typically requiring only one step, and environmentally beneficial. In this context, we can create the Nano materials using both microorganisms and various plant parts[14].

##### 4.1.1. Microorganisms are used in the synthesis of Nano materials

From an aqueous solution of metal salts, various microorganisms such as bacteria, fungi, and algae can be employed to create diverse Nano materials.

##### Use of bacteria

By employing a protein, living things will help produce the Nano particles through the biomineralization process. For instance, magnetotactic bacteria use magnetosomes, which are protein-coated structures used in the manufacture of Nano sized magnetic iron oxide crystals, to prepare magnetic particles as a compass to the direction of their chosen habitat at the bottom of the sea. The production of homogenous particles with a core diameter of 20–45 nm has been shown to occur in vitro. Despite this, magnetosomes have strong magnetic characteristics in medicinal applications, such as hyperthermia [15]. employing microorganisms that can synthesise light, such as Rhodospseudomonascapsulata He et al. generated 10-20 nm size gold Nano particles extracellularly. The bacterial enzyme Nicotinamide Adenine Dinucleotide Hydride (NADH)-dependent reductase plays a crucial role in the reduction of gold ions to gold Nano particles. They discovered that the pH of the growing media affects the Nano particles' morphology and form. Schluter et al. demonstrated the extracellular synthesis of palladium Nano particles utilising Pseudomonas bacteria from the alpine location [16].

##### Use of fungi

Extracellular silver Nano particles were created using the fungus Fusariumoxysporum. Due to NADH-enzymatic reductase's activity, these Nano particles are long-term stable. In comparison to bacterial cells, more protein is secreted by fungal cells [17]. Trichodermareesei is now widely used in the food, animal feed, pharmaceutical, paper, and textile industries.

##### Use of algae

Extracellular gold Nano particles made from Sargassumwrightii algae were suggested by Singaravelu et al. 95% of the intended yield was produced after 12 hours [18]. There is a lack of further investigation into the synthesis of Nano particles using algae. Some bacteria, fungus, and algae in this process are harmful, thus precautions should be taken to prevent them.

##### Synthesis of Nano materials by the use of biological templates

The synthesis of Nano materials inside the organism can be accomplished by utilizing the biological process. The main methods for achieving this are biological templates. By utilising biological building blocks like DNA and proteins, they create distinctive and sophisticated Nano structures. Through the use of these Nano particles, biosensors, bioNEMS, and bioelectronic systems [19] can be created. The primary building blocks of Nano composite materials are proteins. For

instance, ferritin is the internal iron-storage protein found in prokaryotes and eukaryotes. It accumulates in the form of iron oxide and releases it gradually. When there is an iron deficiency or an iron overload in people, it functions as a buffer and controls. It has an iron oxide core that is encapsulated in a protein shell. The core containing the iron oxide can be selectively degraded to produce apoferritin without harming the protein that surrounds it. Once more, iron oxide or any other desirable Nano particle can be inserted into the vacant core of apoferritin. Now, an inorganic Nano composite protein has been created. Fan et al. created the gold Nano particles using the ferritin found in horse spleen. Wu and his friends produced a yttrium phosphate radionuclide Nano particle inside the apoferritin and coupled it with biotin [20]. The Nano particles can be assembled using the DNA templates as well. The closed circular DNA molecules known as plasmids are present in many bacterial species. The combination of cadmium perchlorate and plasmid DNA can be spin coated to create 5–10 nm CdS DNA Nano particle conjugates.

#### Preparation of Nano materials by using different plant parts

The Nano particles have also been created using plants and plant extracts. The phytochemicals found in plants diminish the metal Nano particles. Phytochemicals such as flavones, organic acids, and quinones naturally function as effective reducing agents for the creation of Nano particles. From the biomass of the *Medicago sativa* (alfalfa) and *Pelargonium graveolens* (geranium) plants, variously shaped gold Nano particles are produced. From the leaves of *Azadirachta indica* (neem), bimetallic Au, Ag, and bimetallic Au core-Ag shell Nano particles are produced. This plant contains terpenoids and/or sugars that function as reducing agents. Aloe vera leaf extract is used to create gold Nano triangles. It is also possible to create silver, nickel, cobalt, zinc, and copper Nano particles by employing a variety of plants, such as *Brassica juncea* (Indian mustard) and *Helianthus annuus* (sunflower) [21].

## 4.2. Physical methods

The physical methods are categorized to “top-down” and “bottom-up” approaches. In “top-down” approach the larger materials are pulverized into smaller particles by mechanical milling technique. The main disadvantage of this method is the toughness of getting the desired particle size and shape. When compared to regular particles of the same size the deviation of magnetic characteristics of the prepared samples by milling process is observed due to the defects of lattice parameters which were developed due to the milling process [22]. In the “bottom-up” method either liquid or gaseous phase, Nano particles are condensed in which the larger materials are formed by the chemical combination of the smaller ions.

### 4.2.1. Laser evaporation method

The promising bottom-up technique for creating magnetic Nano powders is laser evaporation. The raw metal oxides that serve as the foundation for synthesis have been evaporated using a laser. As a result, the sharp temperature differential causes quick condensation and nucleation outside the evaporation zone, which leads to the formation of Nano particles. The size of the particles and magnetic phase can be altered by adjusting the laser intensity and atmospheric composition in the evaporation chamber [23].

### 4.2.2. RF plasma method

The RF Plasma approach, which necessitates a high temperature, is another physical method. The metal is heated beyond its evaporation point using high voltage RF coils wrapped around the evacuated system. The system is then filled with helium gas, which causes the coils to reach a high temperature. Metal vapour begins to form on the atoms of He gas. Diffusion causes it to enter the colder collector rod, where it forms Nano particles [24].

### 4.2.3. Thermal decomposition or thermolysis

As a result of chemical bonding, the substance disintegrates into smaller pieces. Hyeon and colleagues used thermal breakdown to produce iron oxide Nano particles. Park et al. created monodispersed heat-induced degradation in a 13 nm scale. It is an endothermic reaction. This heat causes the Nano particles to break. Monodispersed Nano particles are the most useful in biomedicine for the treatment of cancer. Coordination compounds and metallocenes are said to be the optimum precursors for the creation of monodispersed Nano particles by thermal decomposition [25]. The coordination compounds should be subjected to stabilising and capping agents prior to thermal decomposition. The size and morphology can be changed by adjusting the concentration of precursors, the solvents, the time of the reaction, or the stabilising and capping agents. In some cases, the stabilising agent also serves as the capping agent. Lithium azide, for instance, can be used to create LiN<sub>3</sub> tiny lithium particles. The substance is put into an evacuated quartz tube, which is then heated to 400 °C. LiN<sub>3</sub> breaks down at a temperature of about 370 °C, generating N<sub>2</sub> gas. The pressure reduces after all of the N<sub>2</sub> gas has been extracted, which takes a few minutes. The metal colloidal particles are created when the

lithium atoms that are missing mix. This technique can be used to produce the smallest Nano particles, less than 5 nm in size [26].

### 4.3. Chemical methods

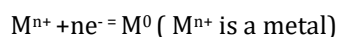
#### 4.3.1. Chemical route of synthesis of Nano materials

The chemical method demonstrates a range of bottom-up synthesis techniques for creating Nano particles. This technique works best with gas or liquid phases. This technique can be used to produce pure, regulated particle sizes. There are numerous ways to prepare Nano particles for the bottom-up approach. The size, kind of Nano material, simplicity of the process, and characteristics of the Nano composite will be used to choose the best preparation strategy. The many synthesis techniques include the sol-gel method, co-precipitation, hydrothermal procedure, solvothermal, sonochemical, pyrolysis, vapour deposition, microemulsion, microwave aided, intercalation, ion-exchange, and reflux.

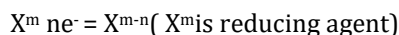
#### Co-precipitation method

This is a widely used, straightforward approach for creating a variety of Nano particles. The aqueous medium is necessary for precipitation in this approach. This method can be used to produce uniform Nano particles. In a nutshell, the coprecipitation process entails combining two or more salts of water-soluble metal ions, often those that are divalent and trivalent. The soluble salts are primarily present in them as trivalent metal ions. These water-soluble salts go through a process and are reduced to create at least one precipitated water-insoluble salt. Continuous stirring of the solution is required, and depending on the reaction circumstances and the reducing agent, it may or may not be heated. This approach typically results in particles with less crystalline character. The degree of crystallinity in the particles can be increased by applying heat energy [27]. By including common reducing agents like ammonia solution, sodium hydroxide, and many others to maintain the proper pH, the entire process is kept running in the alkaline medium. The ratio of salts used, the pH of the solution, the temperature of the reaction medium maintained, and the type of base utilised are some of the variables that affect the size of the Nano particles. The solvent can be removed, further purified, and dried using filtration or centrifugation. Doped ferrites can also be created by doping the ferrites with various rare earth elements. Nano particles of extremely small sizes are required for biomedical applications. So it is possible to manufacture biocompatible Nano particles using this technology. The following processes are used in this method to produce Nano particles: nucleation, growth, coarsening (Ostwald ripening), agglomeration, and stabilising mechanisms. The primary processes in them are nucleation and growth.

The process of the tiniest elementary particles of the new thermodynamic phase forming is called nucleation. The level of supersaturation is the primary determinant of the nucleation process. When a solution is in a supersaturation state, it has more dissolved material in it than the solvent can really dissolve. The solute thus has a solubility greater than equilibrium. The larger particles will eat the smaller ones as they expand in order to minimise their surface energy. The term "coarsening" or "Ostwald ripening" refers to this process. Agglomeration may also happen in order to lower the surface energy. The particles may continue to expand past the Nano scale if the coarsening and aggregation are not controlled. It can be useful to use some stabilising or capping chemicals to stop the growth of Nano materials. Through the chemisorption of charged species, the capping agents bond to the Nano particle surface and create electrostatic (van der Waals) repulsion on its surface. Stable Nano particles will form if the repelling forces are strong, else coagulation will take place [28]. Hydrogen (H<sub>2</sub>), metal borohydrides (NaBH<sub>4</sub>, LiBH<sub>4</sub>), hydrazine hydrate (N<sub>2</sub>H<sub>4</sub>H<sub>2</sub>O), and hydrazine dichloride are a few examples of reducing agents (N<sub>2</sub>H<sub>4</sub>2HCl). The reduced reaction will be as follows:



Simultaneously oxidation reaction also occurs which can be depicted as follows,

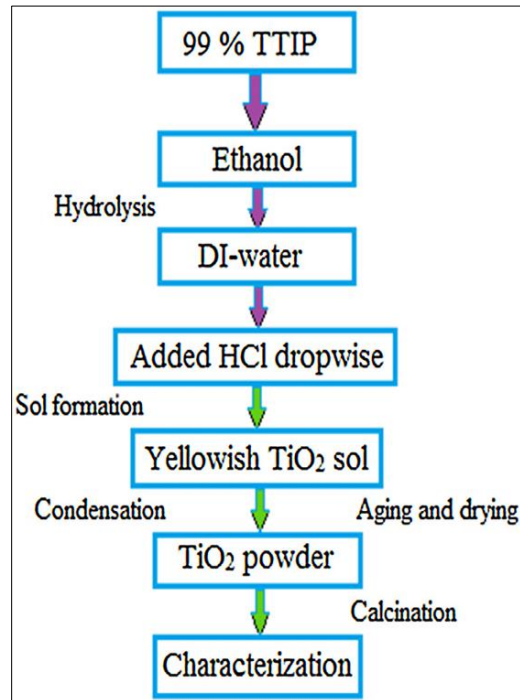


The whole reaction occurs in the liquid state but the final compound collected in the solid state. So this process also called reactive crystallization.

#### Sol-gel method

The sol-gel technique was initially created for the low temperature processing of glass and ceramic materials. This procedure involves first hydrolyzing the metal alkoxide solution with water or alcohols while it is in the presence of an acid or base, followed by polycondensation. The loss of water molecules from the solution and an increase in viscosity caused the liquid phase to shift into the gel phase as a result of polycondensation. The transition from the gel phase to

the powder phase occurs after all of the water molecules have condensed (Fig. 2). To give the powder its fine crystalline character, some further heat is needed [29]. The creation of oxides, composites, and organic/inorganic hybrid materials benefited from the application of this technique. The basis of the sol-gel method is inorganic polymerization reactions. The main advantage of this method is its simple procedure. But the purity is less in this method due to the formation of composites in it. So post-treatment is required for the purification of the sample.



**Figure 2** Schematic representation of sol-gel method

#### Sonochemical method

The most convenient and secure method is sonochemical. By irradiating a liquid medium with ultrasonic energy, this technique creates the cavities (bubbles). The massive energy inside the bubble, which is at a high temperature of almost 5000 K and a pressure of 20 MPa, is increased by the ultrasound energy as it diffuses through the medium. This energy also causes the bubble to spontaneously collapse, which causes the matter inside and around it to become chemically excited. Metals like CoS<sub>2</sub>, alloys, oxides, and selenides like CdSe and ZnSe [30] can all be synthesised using this process.

#### Microwave-assisted synthesis

The microwave aided approach was first used in the 1950s, but it has only recently acquired widespread adoption. By heating the materials with movable electric charges utilising EMR, the microwave radiations are directly transferred to the materials. Here, thermal energy is created by converting electromagnetic energy. Temperatures between 100 and 200 C will rise due to the use of frequencies between 1 and 2.5 GHz. It necessitates a quicker reaction time so that the slower reactions can be finished in a short amount of time. This technique allows for the manufacture of narrowly distributed, small-sized particles. Using this approach, colloidal metals, ferrites, oxides, and selenides [31] are produced. The microwave polyol process, created by Fievet, is the enhanced method of microwave synthesis.

## 5. Characterization of Nano materials

The Nano particles exhibit different physicochemical properties. On varying their size and even a small dimension in Nano scale they will exhibit different properties. To examine their properties characterization of Nano particles wants to be done with different instruments. They are UV Spectrophotometer, Fourier Transform Infrared (FT-IR) Spectroscopy, Atomic Force Microscopy (AFM), Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), Vibrating Sample Magnetometer (VSM), Superconducting Quantum Interference Device (SQUID), Energy Dispersive X-ray Spectroscopy (EDS), X-ray Photoelectron Spectroscopy (XPS), Magnetic Force Microscopy (MFM), Mossbauer Spectroscopy (MS), Electron Paramagnetic Resonance (EPR) and Thermo Gravimetric Analysis (TGA) [32].



### 5.1. Determination of surface morphology, surface area, size and shape of Nano particles

The primary characteristic of a Nano particle that displays the distinct physicochemical character is dependent on their size and form. The AFM, TEM, and FESEM can all be used to examine the surface morphology. The images produced by these approaches will provide information regarding the shape of the Nano particles, including whether they are spherical, rod-shaped, or have pores. The Nano particles' diameter can also be calculated. TEM will provide information on the compositional, morphological, and crystallinity of Nano particles when compared to SEM. In SEM, an electron beam interacts with the sample's atoms to produce a variety of signals. These signals will reveal details regarding the sample's surface topography and composition. Therefore, the samples should at the very least have an electrically conducting surface. Surface coating with an extremely thin electrically conducting substance is required for nonconductive samples. SEM and TEM can also be used, however AFM only works with dry samples. The three main techniques for calculating Nano particle sizes are HRTEM, FESEM, and XRD. In contrast to light microscopes, TEM can take high-resolution pictures. In this way, information about Nano particles will be made clear and thorough. The TEM apparatus can also be used to determine the crystal orientation, aggregation state, electron structure, lattice spacing, and electron phase shift. By employing the TEM, it is simple to determine the Nano particle's size [33]. The Scherrer equation can be used in them to determine size using XRD spectroscopy. The size of Nano particles may easily be determined thanks to the strong XRD peaks. However, the XRD peaks for non-crystalline Nano particles are broad and make size estimation more difficult than with TEM. The size of very small Nano particles cannot be determined by XRD. For calculating the mean particle size and size distribution, three techniques are useful: photon correlation spectroscopy, Mossbauer spectroscopy, and dynamic light scattering (DLS). The BrunauerEmmet Teller (BET) method can be used to calculate a Nano particle's surface area.

### 5.2. Determination of elemental and mineral composition

Surface morphology analysis and elemental composition determination are both possible when EDS is used in conjunction with SEM and TEM devices. The elemental computation makes use of atomic absorption spectroscopy (AAA) and inductively coupled plasma mass spectroscopy (ICP-MS). However, the solid Nano particles cannot be used directly in AAA spectroscopy. They must dissolve in the right acids or bases before being used. XRD may be used to determine the mineral makeup of the aggregated crystalline Nano particle. XRD can also be used to calculate percentage crystallinity and unit cell dimensions [34]. Additionally, XPS provides data on the elemental composition.

### 5.3. Determination of types of structures and bonds in Nano particles

There are numerous ways to create the desired structure and bonding properties. Common methods including XPS, TGA, FT-IR, RS, and X-ray absorption spectroscopy (XAS) are helpful. The FT-IR and XPS will validate the metal-oxygen bonding. Nano particle surface configuration can benefit from XPS as well. It is possible to capture information on the oxidation state and binding energy of materials with different elemental compositions. Raman spectroscopy is used to determine the compound's structure as well as its spinel lattice. The extensive variety of information provided by XAS includes details on oxidation states, nearby atoms, coordination number, bond length, and the electronic configuration of the needed element [35].

### 5.4. Determination of magnetic properties of Nano particles

In order to better understand the magnetic properties of Nano particles, EPR, VSM, and SQUID are helpful. The EPR technique can be used to find the paramagnetic centres and free radicles. The SQUID device can be used to explore a wide range of materials, including crystals, thin films, powders, liquids, and gases. It is an extremely delicate instrument. SQUID and VSM can be used to calculate the Hs, magnetic saturations, and residual magnetization at a constant applied external magnetic field [36]. Mossbauer Spectroscopy can be used to gather a variety of data. You may find out information about the magnetic properties, covalence, electronegativity, oxidation and spin states, bonding, structural, and magnetic characteristics.

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## 6. Applications of Nano particles

Due to their magnetic, electrical, optical, and chemical capabilities, ferrite Nano particles are practically used in every field. Their uses span current industry and the medical field. They are used in the fields of information technology, wastewater treatment, and biomedicine. In applications where electrochemical, optical, piezoelectric, and magnetic fields are applicable, they are used as sensors and biosensors. They are suitable in the form of electrodes that are necessary for the construction of batteries and supercapacitors in energy storage devices. They are relevant to audio

and video tapes as recording material as well. They are also utilised in circulators, shifters, and isolators. They are helpful in the dyeing business as well as in the treatment of wastewater [37]. They're employed in a microwave device.

### 6.1. In medicine for diagnosis and drug delivery: [application in medicine]

Since 1965, Nano technology has been used in the medical industry. They can be used in medicinal imaging because of their many diverse characteristics. It primarily expands in four areas: pharmaceuticals, tissue engineering at the molecular level, biosensors, and diagnosis. The Nano particle is to the diseases, particularly the cancer tumours, in the targeted pharmaceuticals sector. The Nano particle needs to be the smallest possible size for this application in order to release the medication through blood circulation at the desired spot. Under stimulation, the medicine will be released by the Nano particles at the desired spot. There are numerous sorts of stimuli, including temperature, biological, physical-chemical, and electrical. These cues will determine how the medication is released. The main materials used for medication delivery and targeting are gold, titanium, magnetic Nano particles, and quantum dots. When these Nano particles and polymers are mixed, positive and better results are seen. The gold Nano particles are the ones that target drugs the best out of all the Nano particles. Gold Nano particles have special optical properties that are crucial for both cancer photothermal therapy and diagnostics. Magnetic Nano particles, gold, and silver all function well as Nano carriers. The Nano carriers are made to transport anti-cancer medications to the intended spot [38]. Nano particles have a high degree of penetration and cause less disruption to healthy normal tissues. Thus, the healthy cells will be safeguarded. The Silver Nano particles are crucial to the operation of Drug Delivery. These Nano particles come in a variety of forms, including oxides of Fe, Ni, and Co, some of which are doped with rare earth elements. They can group together due to the magnetic interactions between the dipoles. Additionally used regularly are magnetic core-shell Nano particles and organic or inorganic coatings. For treatments that target tumours, a different type of Nano particles known as QDs is advantageous. QDs are employed as imaging agents and have electrical characteristics. Mesoporous silica Nano particles are extensively used in therapy and diagnosis. This method is useful in targeting medicine delivery for cardiovascular disorders as well [39].

### 6.2. Nano particles as catalysts

Lowering the activation energy, attaching to reagents to polarise the bonds, putting the reactive species close to one another to achieve effective collisions, and increasing product yield are the primary methods by which the catalytic reaction occurs. Catalysts aid in lowering the temperature of the process by minimising the incidence of side reactions. The tiniest Nano particles increase the surface area per unit mass. This increases the surface area available for catalysing chemical reactions. Therefore, Nano catalytic processes have better reactivity than traditional catalytic reactions that utilise bulk materials. Nano catalysts come in a variety of forms, including carbon-based, metal-based, thin-layer, core-shell, and ceramic Nano catalysts [40]. Core-shell ferrites, cobalt ferrites, nickel ferrites, copper ferrites, and zinc ferrites are a few examples of metal-based catalysts.

#### 6.2.1. Cobalt ferrite Nano particles

These can be made utilising the co-precipitation method and also without the use of any surfactants. When tert-butyl peroxide, which is easily recovered by employing an external magnet, is present, these ferrites are utilised as a catalyst for the oxidation of a number of alkenes. Cobalt ferrite Nano particles are used as a catalyst in the oxidation of styrene, and the influence of the solvent is also seen [35]. The sonochemical and co-precipitation processes are combined in an aqueous medium without the use of a capping agent to produce cobalt ferrite magnetic Nano particles that are then retrieved by an external magnet during the aldol reaction in ethanol.

#### 6.2.2. Copper ferrite Nano particles

These ferrites are employed in the process of converting CO into CO<sub>2</sub>. These ferrites are employed as a reusable heterogeneous initiator in the synthesis of 1,4-dihydropyridines. This ferrite in ethanol, which may also be recovered, is used in the reactions of substituted aromatic aldehydes, ethyl acetoacetates, and ammonium acetate at room temperature. The same copper ferrite Nano material created in the aforementioned technique can be used as a heterogeneous initiator without a cocatalyst at room temperature for the synthesis of beta-alpha unsaturated ketones and allylation to acid chlorides in THF. At room temperature, using water as the solvent, it is utilised as a heterogeneous initiator for the synthesis of aaminonitrile by one-pot reaction of various aldehydes with amines and trimethylsilylcyanides[41].

#### 6.2.3. Nickel ferrites

Nickel ferrites are employed as a catalyst in photocatalytic water oxidation by using [Ru(bpy)<sub>3</sub>]<sup>2+</sup> as a photosensitizer and S2O<sub>8</sub><sup>2-</sup> as a sacrificial oxidant. [42]

#### 6.2.4. Zinc ferrites

The co-precipitation method can be used to make these. These serve as a catalyst in the production of naphthol by the Prins condensation of  $\beta$ -pinene and paraformaldehyde. [43].

### 6.3. In fuel cell application

By electrochemical reaction fuel cell converts the chemical energy into electrical energy. In a fuel cell, oxygen and hydrogen get reacted and generate electricity without carbon oxide emission. Now a day's fuel cell is observed in all vehicles and instruments like airplanes, cars, ships, submarines, and weapons. The different types of fuel cells are Proton Exchange Membrane Fuel Cell (PEMFC), Direct Methanol Fuel Cell (DMFC), Alkaline Fuel Cell (AFC), Phosphoric acid Fuel Cell (PAFC), molten carbonate fuel cells (MCFC), and solid oxide fuel cells (SOFC) [44]. Platinum (Pt) dependent catalysts are too expensive which is a main drawback for the fuel cells application. Still, the researchers are incomplete in the complete replacement of the platinum metal. The other catalysts of platinum dependent one are Pt-Mn, Pt-Fe, Pt-Ir, Pt-Co, Pt-Ru, Pt-Cu and many more. The other type of catalysts like transition metal oxides, iron-based catalysts, carbon-based catalysts. In carbon-based catalysts graphene [45], carbon Nano tubes (CNT), carbon Nano fibers are extensively using. The research is still continuing in this area.

### 6.4. In electronic devices

Researchers were drawn to Nano particles because of their magnetic, electrical, optical, and chemical capabilities, which led them to discover a variety of uses for them. These have a wide range of applications in electronic devices, including memory units, sensors, biosensors, computer units, antenna cores, high-density storage, in recording media, and transformer cores. Only when they exhibit particular qualities will they fulfil. For use in magnetic recording, for instance, ferrite Nano particles with high  $H_s$  can be used. By demonstrating the protection against demagnetization of high  $H_s$ .  $\text{Loss } H_s$  is preferred in transformers. They need to have a high  $M_s$  and  $H_s$  and a low residual magnetization when used in recording media like audio and video tapes. The usage of Nano particles in magnetic fluids, data processing circuits, digital computers, and digital recordings is widespread. The magnetic ferrites exhibit strong electrical resistance and magnetic permeability, making them suitable for use in biological fields and magnetic recording media. Good magnetic and electrical properties are displayed by cobalt ferrites [46]. The polymers' electrical and magnetic characteristics were enhanced by the addition of ferrites.

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## 7. Conclusion

New Nano materials are being created on a daily basis. Additionally, the mixed-composition Nano materials are being created to make a case for several fields. The simple synthesis techniques will result in Nano particles with the desired size, shape, and properties that can endure the environment, but they still require some refinement. Although there is now a lot of research being done in the disciplines of biomedicine, electronic storage devices, and sensors, these subjects still have room for further improvement. Consequently, the current review paper will give readers a chance to learn more about Nano particles in general.

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## Compliance with ethical standards

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No conflict of interest.

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