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Review Article

Review On Nanoparticles

Insight on Nanoparticles, Green Synthesis and Applications in Drug Delivery System: A Comprehensive Review

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Abstract: Nanoparticles and other new drug delivery methods like green synthesis are utilized as a physical strategy to change and improve the pharmacodynamic and pharmacokinetic aspects of various therapeutic compounds. Nanotechnology's fast advancement has opened the possibility of deploying designed nanoparticles that, interact with biological surroundings to cure illnesses. Interactions between cells and NPs, as well as the extracellular environment, may cause a cascade of biological consequences. Polymeric carbon nanotubes, NPs, liposomes, quantum dots, dendrimers, polymeric NPs, metallic NPs and green synthesis systems have all brought about recent alteration in drug delivery and the entire service of the medical system. Presently, distinct physical or chemical techniques have been utilized for NPs synthesis. However, most of those techniques are steeply-priced and probably risky for the organisms and environment. Therefore, there is necessity to expand a green and cost-powerful approach of synthesis. Recently, the green synthesis processes are gaining a great attention. From their neighboring niche the microorganisms and plants have mounted the strength to accumulate and devour metal ions. It is confirmed that fungi yeast, bacteria, and plant cells can lessen inorganic metallic ions into metallic via means of their cellular metabolites. Both the stability and yield of biogenic NPs are quite acceptable. This review provides an overview of NPs, including their kinds, highlighted green synthesis, benefits, and drawbacks, features of NPs, NPs preparation methods, and the most relevant uses. It is notably predicted that biogenic NPs might be viable and affordable options for medicating drug resistant infections in near future.

Keywords: Nanoparticles, Drug Delivery, Green Synthesis, Preparations, Application

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1. INTRODUCTION

The name "Nano" is derived from the Greek word nanos , which means "very little" & possesses dimensions in nanometers that vary in size from 0.5 to 100 nm[1, 2]. Solid particles that may or may not be biodegradable are referred to as nanoparticles (NPs) and dissolve, entrap, or bind the drug in the matrix. In nanotechnology, both nanocapsules and nanospheres are referred to as nanoparticles. Nanocapsules are systems of a matrix in which the drug is evenly diffused and is surrounded by a unique polymer membrane; on the other hand, nanosphere is matrix systems in which the drug is limited to a cavity bounded by a membrane of unique polymers[3, 4]. The NPs consist of three layers counting (a) the surface layer, which helps with a range of small molecules (b) the interior layer, which can aid with a variety of tiny molecules, metal ions, polymers, and surfactants. The layer of a shell, which is a chemically distinct substance in every way, and (c) the core, which is the most important element of the nanoparticles[5]. Nanomedicine is a medicine branch that expresses nanotechnology to assist in the diagnosis, prevention, and treatment of human illnesses. The dynamic targeting of synthetic compounds and medication conveyance vehicles, can likewise be utilized to guide synthetics and medication conveyance vehicles to explicit areas for example, those perceived by cell surface receptors: lipoproteins, antibodies, nucleic acids and charged atoms are all are examples of targeting moieties that are frequently used in NP systems[6, 7]. NPs are utilized in the pharmaceutical field to develop various therapies and treatments for various ailments. NPs are employed in a variety of medical fields, and one of the most significant characteristics of these particles is that, they must be biocompatible[8]. In order to solve many problems in drug treatment and targeting, nanomedicine is an important tool to fix such problems because the size, specificity, and composition of nano- particles are very crucial for them[9]. The use of NPs in medicine has the potential to identify and treat diseases in the human body, and many procedures that were just a few years ago considered impossible are already becoming a reality. Size-related characteristics in NPs may or may not vary considerably from those seen in small particles or bulk material[10]. Nanotechnology allows for the development of pharmaceuticals with nanometer-sized molecules that increase performance in a number of dosage forms. The following are some of the benefits of nano-sizing:

- Reduced fasting variability
- Equability in treatment to all patients
- Elevate the solubility of a drug
- Bioavailability of drugs is increased
- Dissolution rate of drug is increased
- surface area is Increased
- Faster start of therapeutic effect[11, 12]

The chemical and physical strategies are popularly in-use for NPs synthesis. The issue of toxicity in NPs is frequent due to hazardous materials like organic solvents, reducing agents, and stabilizers. These substances prevent colloidal agglomeration. Furthermore, the usage of chronic solvents and contaminations by chemicals has limited the application of NPs in different biomedical and clinical applications[13]. Currently, there are a number of explorations devoted to the conflation of NPs by green synthesis. Physical and chemical means are gradually replaced by the technique of green synthesis since issues linked to consumption of large quantities of energy, release of poisonous and dangerous chemicals, and use of complex equipment and conflation conditions[14]. The methods of physical means include ultraviolet radiation, aerosols, thermal decomposition; and require high pressure and temperature (approximately 2400k for NPs production). There is a need to foster a non-poisonous, harmless to the ecosystem NPs creation innovation. A few protected, simple, practical, reproducible, and adaptable green amalgamation approaches for NPs have been created lately, enlivened by the wellbeing-by-plan idea. Accordingly, a few organic frameworks, like yeast, growth, microbes, and plant extricates, are presently widely utilized in green blend approaches for the NPs production[15, 16]. Plant-based NPs, green union is presently viewed as a highest quality level among these green organic strategies inferable from its convenience[17].The green synthesis engages environmentally-friendly and natural substances. Certain green materials can also be utilized as dispersants and end-capping materials at the same time, which not only avoids usage of poisonous and dangerous reagents, but also helps in reducing the energy consumption. At present, green synthesis utilizes extract from flowers, roots, leaves,, shelling, fruits, seeds and microorganisms (bacteria, fungi, and algae)[18,19]. This green material usually contains proteins and polyphenols which helps to replace reducing agents, to get reduced into ions with lower valence state. The green material under favorable conditions (temperature) synthesizes the metal nanoparticles[20]. Sometimes, green synthesized NPs surpass those synthesized by chemical methods in terms of their quality. These have numerous advantages than chemical and physical means[21]. It is pollution-free, non-toxic, and eco-friendly. Still, there are issues in terms of raw materials, response time, and final products quality etc. For example, the raw materials aren't extensively available, the conflation time is long, and product size is extremely homogeneous. This review extends deeper analysis and discussion of NPs, green synthesis, which is implicit for advancement of green exploration in the future[22].

1.1 History and development of NPs and nanostructured materials

NPs and nanostructured materials are two innovative groups of materials that have caught the scientific community's interest due to their distinct physicochemical features. Composition, size, and form; all influence these qualities and uses. The capacity to modify the atomic size, shape, and composition promises to revolutionize many fields of science and industry. Although NPs and nanostructured materials have been in nature for an extended time, their use by humans goes back to primordial times[23]. Weathering, volcanic eruptions, wildfires, and microbiological activities all create naturally occurring NPs, which incorporate organic (e.g., viruses, proteins, polysaccharides) and inorganic (e.g., iron oxyhydroxides, aluminosilicates, metals) material. Ancient Egyptians dyed their hair using nanoparticles based on a manmade chemical procedure, Pb's nanocrystals of 5 nm, since 4000 BC. This might be one of the first instances of man-made NPs in use. Understanding the physical process that allows for this degree of control is one of the biggest issues in nano-science today. Growth control additives are, in fact, employed solely for effective regulation of NPs growth and assembly in innovative nanostructured materials. These additives, on the other hand, have an impact on the surface qualities, processing, and prospective uses of these materials[24, 25]. The area of nanotechnology began to emerge in 1958, and the different phases of development are listed in Table 1.

Table 1: Systematic progress in nanotechnology field [26-28]	
Development in nanotechnology	**Year**
Thought process was grounded by R. Feynman	1959
First time the term nanotechnology was quoted by Taniguchi	1974
Scanning Tunneling Microscope technique was developed by IBM	1981
IBM has used its logo as individual atoms	1989
First time, S. Iijima invented carbon Nanotube	1991
R. Freitas published first book on nano medicine	1999
The National nanotechnology startup was inaugurated for the first time	2000
The nanotechnology Feynman prize was granted for the development of theory of nanometer-scale electrical devices, production of nanowires and carbon nanotubes.	2001
For harnessing DNA to allow the self-assembly of novel structures and improving our capacity to describe machine systems for molecules, the Feynman Prize was given.	2002
Modeling the molecular and electrical architectures of novel materials won the Feynman Prize in Nanotechnology.	2003
The first advanced nanotechnology policy conference was conducted.	2004
3D networking robotics, and active nano goods that alter their state while operation was all created as 3D nano systems.	2005-2010
The era of molecular nanotechnology has begun.	2011
Sir J. Fraser Stoddart, Jean-Pierre Sauvage, and Bernard L. Feringa (The design and synthesis of molecular machines bagged the Nobel Prize in Chemistry).	2016
Objects shrinking to the nanoscale.	2018

1.2 NPs classification

The nanoparticles are classified (Figure 1) into the three major classes (1) NPs with one dimension (2) NPs with two dimensions (3) NPs with three dimensions.

1.2.1. NPs with just one dimension

Thin films (sizes 1–100 nm) or monolayers are widely utilized in the area of solar cells fall in the category of one dimension nanotechnology and the word 'nano' display the number 10^{-9} which displays the one-billionth of any unit, that outcome in the development of one dimension nonmaterial such as thin-film. These NPs generally exist in the needle shaped structure and includenanowiresand nanotubes[, 30].

1.2.2 NPs with two dimensions

These kind of nanomaterials are two dimensional& bigger than nanoscale (100 nm). The common instances of this class are nano-layers, nano-films, and nano-coating. This class of nanomaterials has plate-like designs. Carbon nanotubes are tiny carbon tubes. 2D nanostructures have two aspects which are exterior, the nanometric size scope with a particular shape, and 2D nanomaterials are employed as building blocks for key parts of nanodevices. Two-aspect nanomaterials have usage in nano holder, sensor photo catalysts, nanoreactor, and format for 2D construction[31].

1.2.3 NPs with three dimensions

Nano-materials with three dimensions have each of the three dimensions bigger than 100 nm yet their parts are under 100 nm in size. The particles with nano range meet up to frame three-dimensional nano-materials. These materials are for the most part non porous in nature and have numerous applications. The most widely recognized instances of three-dimensional nano-materials are heaps of nano-fibers, nano-composites, multinanolayer-type . Dendrimers, quantum dots, and fullerenes are all examples of nanomaterials (Carbon 60)[38]. For 10 years, nanomaterials with three-dimensional assemblies have acquired an intriguing clinical science and exploration[32].

1.3 Classification based upon shapes and sizes

1.3.1 Inorganic NPs

The exceptional properties of inorganic NPs have a vital role in current research, particularly in the biotechnology area[33]. The physical properties of inorganic NPs are depending upon size, optical, magnetic, electronic, and catalytic capabilities of NPs are connected with the nanoscale dimension of NPs. Mostly the inorganic NPs are made from various metals, or their combination like, silver, iron oxides, gold, silica, quantum dots etc, and these are segregated into two ways.(1) metal nanoparticles (2) metal oxide NPs. Metal NPs offer a wide range of uses in research due to their excellent optical characteristics[34].By the application of constructive and destructive methods, these NPs are synthesized. The oxides of the metal can also be utilized to synthesize the NPs, and these have enhanced reactivity examples of these are silicon dioxide, iron oxide, and aluminum oxide NPs[35].

1.3.2 Organic NPs

The NPs existing naturally are otherwise called polymeric NPs. The major state known about natural or polymeric NPs is nanosphere or nanocapsule. The natural NPs incorporate dendrimers, micelles, and liposomes and these are biodegradable, non-poisonous. These embody NMs created largely from organic matter, not including carbon-based NMs. The employment of non-covalent (weak) reactions for the self-assembly and style of molecules assists to remodel the organic NMs into required structures. These exceptional attributes make them an ideal decision for drug conveyance. The medication conveying limit, delivery system, stability, either captured drug or adsorbed drug framework decides their field of uses and their productivity[36].

1.3.3 Polymeric NPs

Consisting of polymers is the main characteristic of such types of NPs. In the current scenario, these sort of NPs have made remarkable progress in the realm of study[37]. For the preparation of such kind of NPs, there are two types of methods, one is the dispersion of polymers and the other one is the polymerization of monomers. The standard size of such NPs lies in the range of 10 to 1000 nanometers[38,39]. The polymeric NPs are shown in Figure 1.

1.3.3.1 Liposomes

Liposomes are NP-based technologies for a variety of applications. Liposomes are sphere-shaped vesicles that are made up of one or more phospholipids bilayers. Liposomes are now employed as a reagent and a tool in a variety of scientific areas[40]. Liposomes have carved out their own niche in the market due to the many qualities they have. Various molecules operate as carriers in the cosmetic and pharmaceutical sectors, while liposomes are used in encapsulation to provide a delivery mechanism that may entrap unstable substances in the food and agricultural industries[41, 42].

1.3.3.2 Dendrimers

Dendrimers[43] are made up of two Greek expressions "Dendron," which means "tree," and "meros," which means "part." Dendrimers have distinct molecular weight, shape, size, and structure, and they are also hyper-branched, globular, mono dispersed, three-dimensional nanoscale synthetic polymers. Dendrites have well-defined features in both molecular and polymer chemistry[44, 45].

1.3.3.3 Micelles Polymers

The polymeric micelles[46] are nanoscopic supramolecular core-shell structures created by copolymers of an amphiphilic block. The polymeric micelles are typical in size (<100nm), and their hydrophilic surface serves to shield them from nonspecific reticuloendothelial absorption[47,48].

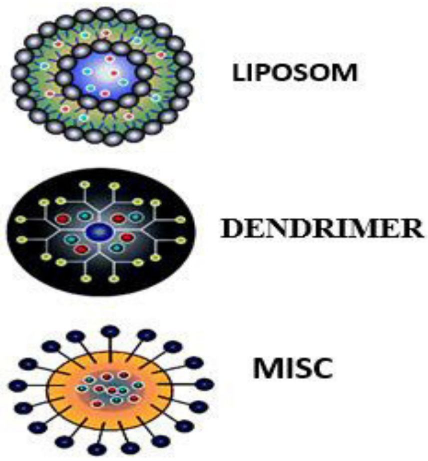

Fig 1: Diagram representing the various types of nanoparticle[44]

1.3.3.4 Ceramic NPs

These are the non-metallic NPs[49] that are synthesized by the heating and cooling process. These classes of NPs exist as porous, amorphous, hollow, or dense forms. These are widely accepted due to their usage in dye photo-degradation. Therefore, these NPs have received gotten nice attention of researchers because of their use in applications like photo-degradation, contact action, photo-catalysis of dyes, and imaging applications.[50, 51]

1.3.3.5 Bio-NPs

These are the molecule or atom assemblies which have been developed in the biological system. This type of NPs exists within the range of 1-100 nm. There exist the two forms which are intracellular intercellular structure and extracellular structures[52,53].

1.4 Green synthesis of NPs

There are two methods used for NPs synthesis namely bottom-up synthesis and top-up synthesis (Figure 2). In the top-down type approach, the large structural units are broken into smaller pieces by the application of the biological, chemical, and physical processes.

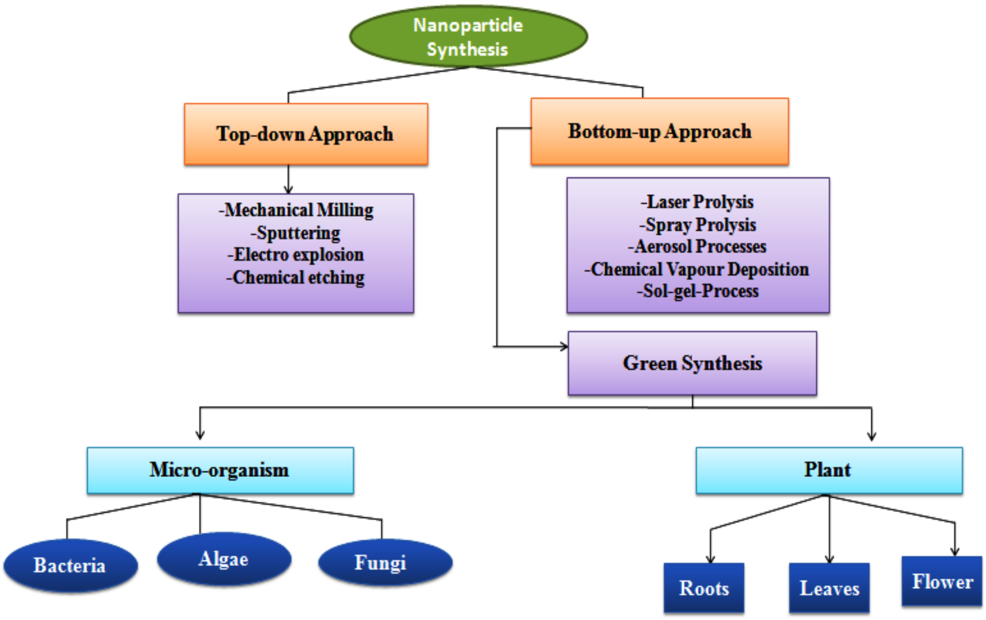

Fig 2. Schematic representation for NPs synthesis[66]

In the case of the bottom-up approach, the NPs are synthesized by the atomic level by applying the physical, chemical, and biological reactions[54, 55]. The primarily customized approach for the synthesis generally utilizes the biological or chemical technique. In nanoparticle synthesis, chemicals that exert toxic effects lead to a hazardous effect like environmental toxicity, carcinogenicity, and toxicity. These type of toxicities generally arise due to the substances like organic solvents solvent, reducing agents, and stabilizers. These types of hazardous effects reduce the usage of NPs, thus a biologically accepted, clean, reliable, environmentally accepted technique is essential for NPs synthesis. The synthesis of the nanoparticle biologically, is an attractive alternative over the other approaches by incorporating the unicellular and multicellular entities like fungi, bacteria, viruses, yeast, and plants[56, 57].

1.4.1 Mechanism for green NPs synthesis

The proteins like phytochelatins and metallothioneins, nitroreductases, NADH-dependent nitrate reductases (NRs), peptide (less molecular weight), glutathione (GSH) and oxidoreductases (enzyme), reductases (NADH- dependent), and cysteine desulfhydrase are accountable for formations of nano-crystal in fungi, yeast, and bacteria. All material with biological properties has unique composition (chemical) and metabolic intricacies, which react in a various way with metal ions, thus controlling and modifying the NPs synthesis. The green NPs synthesis is usually (i) from living cells extracted from biomolecules (ii) extracellular/intracellular living cells (iii) supernatants (cell free)[58].

1.4.2 Green synthesis using biological components

1.4.2.1 Bacteria

Bacterial species were broadly applied for business biotechnological applications which include bioleaching, genetic engineering, and bioremediation. Bacteria own the ability to lessen metallic ions and are critical candidates in NPs production[59]. For metallic and other novel NPs production, an assortment of bacterial types is used. Actinomycetes and prokaryotic microbes[60, 61] have been comprehensively utilized for integrating metal/metal oxide NPs[62]. Organisms interceding biosynthesis of metal/metal oxide NPs[63,64] is likewise an exceptionally effective cycle for the age of monodispersed NPs with defined morphologies (Table 2). They go about as better organic specialists for the planning of metal and metal oxide NPs because of the presence of an assortment of intracellular enzyme[65].

1.4.2.2 Yeast

Successful NPs synthesis via yeast has been mentioned by means of numerous research organizations. The biosynthesis of silver and gold NPs with the aid of Ag-tolerant yeast and broth (saccharomyces cerevisiae) has been suggested[66, 67].

1.4.2.3 Plants

Plants can aggregate specific measures of weighty metals in their assorted parts. There is a range of plants that can be used to lessen and settle the metallic NPs in a "one-pot" combination process (Figure 3). Different plants (Coriandrum sativum, Aloe barbadens is Miller, Avena sativa, Ocimum sanctum, Medicago sativa, Citrus limon, Azadirachta indica, have been employed to produce silver and gold NPs[68-70].

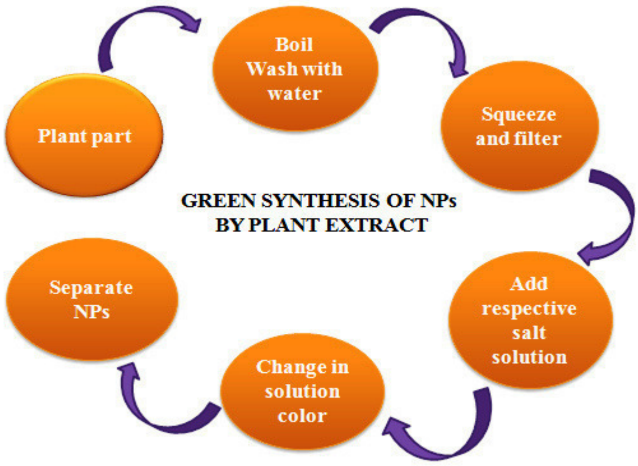

Fig 3: NPs green synthesis from plant extract[65]

1.4.3 Types of NPs and their application

1.4.3.1 Gold (Au) and Silver (Ag) NPs

The Au NPs have considerable potential in the biology and medical field. Granium leaf extract in the year 2003 was firstly used to synthesize Au NP. The terpenoid in the leaf has reduced Au ions into the Au NPs. The various leaf extracts (Azadirachta Indica, neem, aloe vera) were further explored to improve shape and dimension of Au NPs[71]. The alteration in size, shape and Au nanoparticles surface properties makes them veritably salutary for their implicit operations within the area of hyperthermia remedy, biosensors, delivery systems for remedial medicines and inheritable accouterments, as well as anti-bacterial medicine. The gold NPs from rattlebush have revealed the catalytic activity that may be useful in nitro compound depletion in waste decontamination. For the Ag NPs synthesis silver metal ions solution with biological reducing agent used. The simplest way for synthesis is reduction of Ag ions and stabilization by the application of fusion of biomolecules like vitamin, polysaccharide, alkaloid, phenolics, and terpenes[72]. The Ag antimicrobial application is extensively known, and is utilized in multiple medical medications against pathogens. The anti-bacterial application of Ab NPs has been authorized for their use in food storehouses, the health sectors, several environmental operations and textile coatings. Ag NPs produced by the application of Tridax procumbens shows antibacterial exertion toward Shigella dysenteriae, E-coli, and Vibrio cholera. The cone extract (Pinusthun bergii) produced Ag NPs show antibacterial and antifungal effects of Ag NPs has been verified. Their antifungal applications were found to be safer than conventional pesticides[73].

1.4.3.2 Copper and copper oxide NPs

A variety of plant extracts have been utilized for green synthesis of Cu NPs and CuO NPs. The leaf extract of Magnolia kobus and clove (Syzygium aromaticum) found to have wide application in the Cu NPs with size range of 40 to 100 nm. Euphorbia nivulia latex was proved to produce the Cu NPs and Sterculia urens found to have application in the synthesis of Cu O NPs. The Cu O NPs display anti-bacterial, anti-oxidant, and antimicrobial features against pathogenic strains (E-coli and Staphylococcus aureus). These NPs possess decontaminating properties against various microorganisms with the application as bactericidal material[74, 75].

1.4.3.3 Titanium dioxide (TiO_2) NPs

The TiO2 NPs green synthesis from plants is a superior alternative for toxic-free synthesis. Till date, many plants have been utilized for its synthesis where TiO2 salt reacts with plant extract. The color change initially confirms the synthesis of the reaction mixture, and later the spectroscopic and morphological studies authenticate their formation and observed in light green to dark green color. The TiO_2 NPs synthesis is valuable in the papers, plastics, textiles, tints, food stuffs, and cosmetics and reduces toxic chemicals from water[76].

1.4.3.4 Zinc oxide (ZnO) NPs

ZnO green synthesis has been viewed as possibly more valuable and productive than different metals for NPs for clinical utilization. Various investigations confirmed ZnO NPs utilizing different plant extracts. For example plant Cassia auriculata and leaf concentrate of Hibiscus rosa sinensis were utilized as reducing specialists for zinc nitrate to produce ZnO NPs. ZnO NPs integrated by utilizing leaf concentrates of Camellia sinensis, Scadoxus multi florus and Passiflora caerulea showed solid antimicrobial viability against Aspergillus spp, Klebsiella pneumonia, Staphylococcus aureus, and Pseudomonas aeruginosa separately, proposing that therapeutic plant remove interceded blend of ZnO NPs can be extremely helpful for clinical industry[77,78].

Table 2. Green NPs synthesis from various plant and microorganism[77,79]			
Material	**NPs type**	**Size range (nm)**	**Shape**
Plant			
Citrullus colocynthis	Ag	31	spherical
Aloe vera	Ag, Au	50-350	triangular, spherical
Curcuma longa	Pd	15	spherical
Mangnifera indica	Ag	15-20	triangular, spherical
Diopyros Kaki	Pt	15-20	spherical, crystalline
Pistacia altantica	Ag	10-50	spherical
Avena sativa	Au	5-85	spherical, crystalline
Microorganism (Bacteria)			
Sinomonas mesophila	Ag	4-50	spherical
Pseudomonas fluorescence	Au	5-50	spherical
Basillus brevis	Ag	41-68	spherical
Rhodococcus sp	Au	5-15	spherical
Clostridium thermoaceticum	Cds		
Pseudomonas stutzeri	Ag	200	spherical
Actinobacter	Au	19	spherical
Basilus endophyticus	Ag	5.1	spherical
Fungi			
Fusarium oxysporum	Au/Ag	20-50	spherical
Asperigllus fumigates	Ag	-25	spherical
Verticillium	Ag	25±12	spherical
Trichoderma asperellum	Ag	13-18	spherical
Algae			
Chlorella vlugaris	Au	40-60	spherical
Sargassum wightii	Au	9-20	spherical
Ulya fasciata	Ag	28-41	spherical

1.4.4 Metal NPs synthesis by bimolecular route

Biomolecules assume an extremely essential and adaptable route in the NP synthesis. The NPs can be stabilized and functionalized, utilizing these specialists to confer helpful properties by supervising size and morphology. In the perspective on the constraint moved by these synthetic compounds, there is a dire need to utilize climate amicable covering specialists and configuration green biochemical courses at futuristic level for the NPs synthesis[79].

1.4.4.1 Polysaccharide

Polysaccharides are polymeric carbohydrate classes with mono or disaccharides repeating unit connected together by linkages (glycosidic). They react as covering agents in the NPs synthesis as they are minimal expense, stable, hydrophilic, protected, biodegradable and non-poisonous. One of the distinctive highlights of polysaccharides is that they strongly speed up the energy of sol-gel processes because of their reactant impact[79,80]. They not just have been found to change the design and morphology of TiO2, yet have actuated an alternate stage where rutile stage has been found within the sight of chitosan while analyzed within the sight of starch. Dextran is a complex expanded polysaccharide made out of numerous molecules of glucose with chains of changing lengths. It is hydrophilic, biocompatible, non-poisonous and utilized for numerous metal NPs coating. Round Au NPs of size ~ 15 nm were produced in water utilizing regular honey which went about as a capping and reducing agent. Fructose present in the honey should go about as a decreasing specialist while proteins were answerable for the adjustment of the NPs. In this manner, polysaccharides have come up as one of the sustainable green options for the creation of NPs supplanting harmful synthetics, consequently saving the climate from their risky impacts[81].

1.4.4.2 Biomolecules

The homogenous NPs synthesis utilizing biomolecules has newly acquired interest because of their non-poisonous nature, and not including ruthless manufactured methods. Amino acids effectively act as capping agents to produce NPs with extraordinary design. Among 20 distinct amino acids, they took on l-histidine which was observed to reduce tetraauric acid to NPs of Au. The l-histidine amount was found to influence the size of NPs; higher the focus more modest the size of NPs[82].

1.4.5 Factors affecting NPs green synthesis

There are a few factors that influence the NPs synthesis, use and its characterization. Numerous analysts have announced the alteration of nature of the NPs with the kind king of the adsorbate and the movement of the catalyst utilized.

1.4.5.1 pH

The pH is a significant component that impacts the NPs synthesis by green innovation strategies. Scientists have found that pH of the arrangement medium impacts the size and surface of the orchestrated NPs. Thus, NP'S size can be managed by modifying the pH of the media solution.[83]

1.4.5.2 Temperature of reaction

The temperature of reaction is a vital parameter that controls the morphology, size, and synthesis of NPs. The actual physical strategy requires the maximum temperature

(>350°C), though chemical technique need a temperature under 350°C. Mostly, the combination of NPs utilizing green innovation requires temperatures under 100°C. The temperature of the response medium decides the idea of the NPs produced with respect to the size morphology [84,85].

1.4.5.3 Reaction time

The quality and kind of NPs integrated utilizing green innovation are striked by the time span for which the response solution is incubated. The qualities of the integrated NPs were likewise reformed with time, and extraordinarily striked` by the process and light exposure. The varieties in the time might happen in numerous ways, for example, long term storage aggregation; particles might contract or develop during long capacity [86].

1.4.5.4 Other factors

Some other factors like extract volume also impact the metal NPs synthesis as the extract plays a key role in reducing metal ions. Furthermore, the method choice for purification also influences the quantity and quality of the NPs. The separation by utilizing the centrifugation, chromatographic techniques also affects the NPs characteristics [87].

1.4.6 Green NPs toxicity

Green NPs, size and shape have demonstrated to be an aid in a wide scope of applications. Though, these properties might turn unfavorable as properties like antimicrobial effect isn't particular to microorganisms, in this manner delivering a solid chance of their cytotoxic consequences for eukaryotic cells. This is because of the reality that green NPs have the same dimensions as molecules like DNA, proteins, and enzymes, to access the easy way inside cells but get located to the other organs and may lead to damage to membrane cells. The size of the NPs is important in terms of toxicity, as smaller size may lead to DNA damage and also causes toxicity to adjacent cells. Some of the NPs induce toxicity by oxidative stress and result in damage, leakage of cellular components along with the genotoxicity [88].

1.4.7 NPs characterization

Two of the principal boundaries concerned in the NPs characterization are shape and size. We can likewise also quantify distribution of size, surface area, aggregation, surface charge and to some degree assess the chemistry of the surface. All these present on the outer layer of the particles might influence different properties and NPs potential utilization. The estimation strategies for NPs will extraordinarily influence the take-up of these materials in business applications and permit the industry to follow guideline[89].

1.4.7.1 Structural analysis

1.4.7.1.1 Surface morphology

The green NPs primary structural analysis (morphology of surface, visualization, and topography detail) are most frequently examined by the electron microscopy (EM).SEM (Surface electron microscopy) (Figure 4) is a surface delicate imaging methodology with 3-D view which regularly utilizes three modes of examination including backscattered electron, optional electron (SE) mode, and X-beam energy spectroscopy as in TEM.

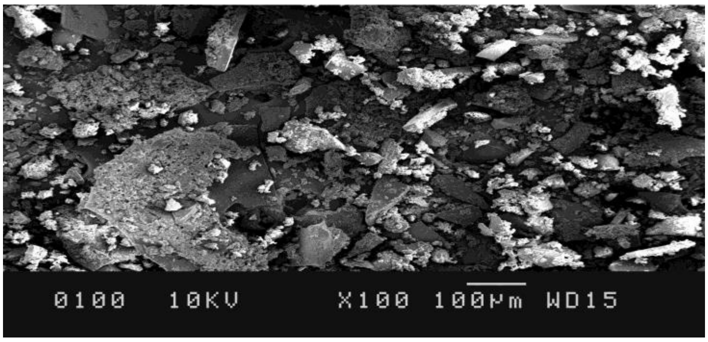

Fig 4: SEM of Ag NPs[90]

Mostly, SEM can't be utilized for cryogenic freeze materials like on account of imaging surface attached to NPs, thus ESEM (environmental surface electron microscope) is utilized for such remarkable cases, in which tests are imaged in their standard state. In the microscope sample chamber, tests imaged by ESEM are seen to have limited partial vapor pressure, protecting the suitable sample conditions, which permits imaging tests in their normal state without modification or arrangement. The BSE with ESEM investigation was important for imaging weighty elements like Au, Pt and Ag with nanomaterial as little as 25 nm at extremely low focus.TEM (Transmission electron microscopy) is generally carried out in contrast to display pictures with crystal planes. The result data displayed by TEM is bright and dark in regards to the microstructure and sample morphology, particularly when joined with X-beam investigation of elemental composition. Atomic force microscopy (AFM) picture gives 3-dimensional shape, distribution and size of NPs. A noticeable distinction in the behavior and morphology of NPs treated chemically can be determined. AFM shows its application in 3D sample mapping, nano-scaled topographical sample resolution, and direct determination of sample in dry state[90].

1.4.7.1.2 Crystalline analysis

X-beam diffraction (XRD) is perhaps the most widely involved technique for the NPs characterization. Commonly, XRD presents statistics with respect to the crystalline structure, phase nature, and grid boundaries. For specific samples, the parameters are assessed by utilizing the equation by Scherrer using the widening of the intense peak of a XRD measurement. The expanding of XRD tops was chiefly brought about by molecule/crystallite size and strains.

The XRD-displays size is broadly greater than the alleged magnetic size, because more modest regions are accessible in a structure where all moments are adjusted in a similar bearing, regardless of whether the particle is single domain[91].

1.4.7.1.3 *Compositional analysis*

The understanding into the confined composition of surface element/compound and their quantity present in metal NPs and purity characterized by energy dispersive spectroscopy (EDS). It is used to investigate the basic course materials arrangement. The EDS framework can be joined to either TEM or SEM instruments as the capacity of the miniature degree imaging recognizes the example of concern. EDS examination produces information that comprises spectra that display tops connected with the components of the dissected example. EDS is a non-destructive method that can be utilized for subjective, semi-quantitative, and quantitative examination which gives the component appropriation through planning. EDS investigation affirmed the existence of iron in NPs integrated from leaf of Ailanthus excelsa concentrate and peaks of O and Ni uncovered the presence of NiO NPs[90].

1.4.7.2 *Chemical analysis*

FTIR spectroscopy strategy is utilized to record IR spectra of emission or absorption. Light owning the entire recurrence range between 5000-400 cm might be utilized for investigation of the vibration of the functional group (–$CONR_2$, –RNH, –COOH, –NH_2, –$CONH_2$, –CONHR,) related with NPs, as well concerning the estimation of functional group in plants before the green NPs manufacture. NPs of different varieties have been explored and characterized through various spectroscopic strategies in the infrared reach. A recorded range gives the place of groups connected with the strength and nature of bonds, and explicit useful gatherings, giving in this way information concerning subatomic designs (structure) and collaborations[58].

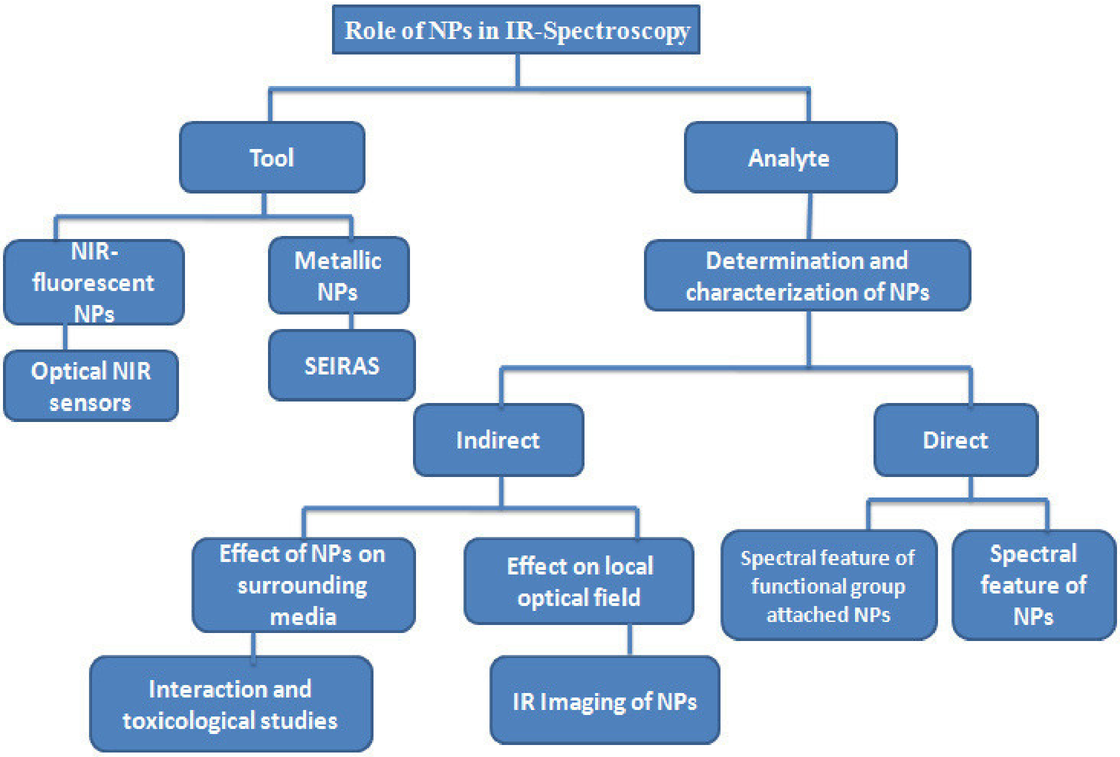

Fig 5: IR different roles in NPs characterization[91]

Nuclear magnetic resonance (NMR) spectroscopy is one more significant scientific procedure in the structural and quantitative assessment of nanoscale materials. It depends on the NMR peculiarity shown by nuclei that have non-zero spin while explored in a high magnetic field, which causes a little energy variation between the spin up and down. It also helps in the confirmation of metabolites like organic acid, carbohydrate, and amino acids by their corresponding peak intensity comparison[58,90,91].

1.4.1 *Physical analysis*

Spectroscopy is the investigation of the light emission or absorption and extra radiation by substances, as an electromagnetic radiation component. Metallic NPs have λ_{max}, and an output of λ_{max} in the scope of 300-800 nm is commonly utilized for affirming individual NPs synthesis. The spectroscopy (UV) applications are for the most part worried about UV (185-400 nm) and visible (400-700 nm) light. Utilizing Beers-Lambert regulation, the centralization of different arrangements can be determined by estimating the absorbed light. Generally, NPs like selenium, iron and others are described by spectroscopy particularly after synthesis as the color of the response combination will change. Every metal outcomes in an alternate arrangement; to give a gold molecule (20 nm), for instance, there is an ascent in red arrangement, which assimilates at 520 nm. Though, having displayed those apparent spectra of gold colloids for sizes 5-80 nm brings about redshift with an expansion in NP distance across. Redshift isn't simply connected with size yet in addition can be associated with shape too. So UV -noticeable estimations are likewise utilized to concentrate on the functionalization of Au NPs like restricting to antibodies or collection[58,92]. DLS is a light dissipating strategy that can be metal oxides, non-oxides, and metallic NPs. This system is based on salt reactions in solvents. The precipitation approach is used to manage the size of this strategy. The essential method enables nanomaterial creation and study in situ, i.e. in the same liquid media, without causing physical changes or aggregation of microscopic crystallites. The solvent displacement technique is a frequently used method for NPs production. This approach involves drug and polymer precipitation from an organic solvent, that has been diffused into an aqueous medium including or lacking the addition of a surfactant[97,98].

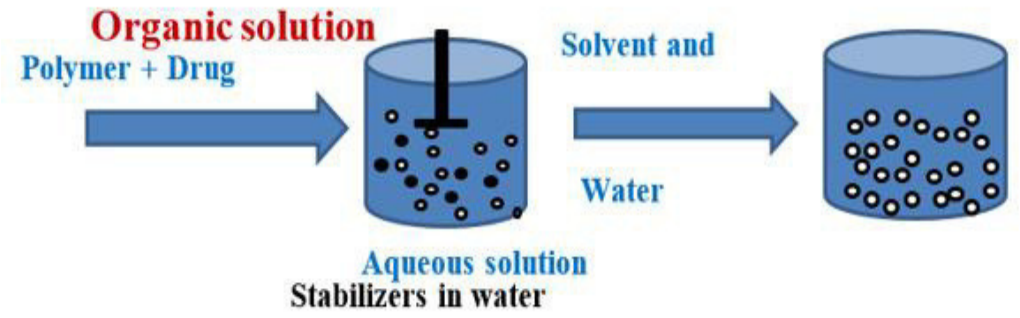

Fig 8: Precipitation technique for nanoparticle preparation[94]

1.5.5 Dialysis

One of the most effective approaches for preparing NPs is dialysis. Polymer and medication are disintegrated in an organic solvent. The solution is then put into a dialysis tube, and dialysis is carried against a non-solvent as shown in figure 9. The displacement of the solvent into the membrane is followed by increasing polymer aggregation owing to solubility loss and the production of homogenous NPs suspensions. The process of NPs production by dialysis is currently unknown. It might be based on a similar process as nano precipitation[99,100].

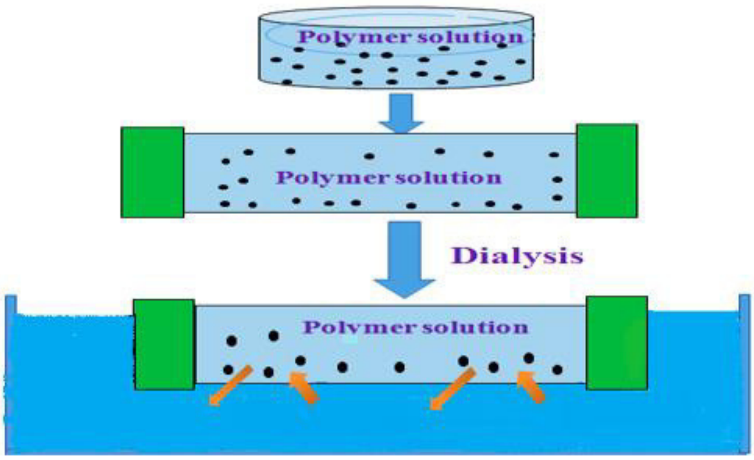

Fig 9. Representation of osmosis based method for preparation of NPs[94]

1.5.6 Supercritical fluid technology

This procedure is carried out above a substance's critical temperature and pressure. The material may exist in equilibrium between vapor and liquid form under these circumstances. The pressure may be raised while the viscosity stays constant to increase the number of dissolved chemicals [101]. Under these circumstances, the fluid may behave as an organic solvent, simply dissolving lipids and other components. Carbon dioxide is often utilized since it is safe, inexpensive, and non-irritating [102,103]. Two primary procedures that employ supercritical fluids are:1) Supercritical anti-solvent (SAS) 2) Rapid expansion of critical solutions (RESS). Liquids are utilized as solvents in the SAS process, and they must be entirely miscible with the supercritical fluid. This method uses a liquid solvent, such as methanol, that is entirely supercritical fluid miscible. The liquid solvent extract causes the solute to precipitate instantly, resulting in the creation of NPs. High levels of supersaturation are achieved in RESS by dissolving a solute in a supercritical fluid to create a solution, then rapidly expanding the solution by a capillary nozzle to ambient air, followed by quick pressure reduction, resulting in the formation of well-dispersed particles[104,105].

1.5.7 Salting out method

The solvent-diffusion approach is extremely similar to this method. This approach uses the salting-out phenomenon to separate a solvent that is water-miscible from an aqueous solution. This procedure does not involve toxic solvents. Acetone is often used since it is completely water-miscible and may be readily removed. The method of salting out can also be achieved by aqueous phase saturation with colloidal stabilizers which are dissolved in a solvent and emulsified into an aqueous solution having a salting-out agent. It was diluted utilized to concentrate on little particles' size distribution, in any event, for polymers or atoms in the size of submicron to I nm either in suspension or solution by utilizing a source of monochromatic light. A number of physicochemical attributes of nano materials such as hydrodynamic size, construction, shape, can be found through radiation dissipating strategies. NPs zeta potential is a vital sign of the colloidal dispersion stability. Exceptionally negative or positive charged particles will more oftenly repulse one another, in this manner shaping stable colloidal dispersion. These procedures had all the earmarks of being significant instruments to examine the NPs fate in natural environments. A low incentive for the ζ -capability of a colloidal NP scattering causes the flocculation of the colloids and thus is considered unstable[91,93].

1.5 Preparation methods of NPs

1.5.1 Solvent evaporation

As far as preparation of polymer-based NPs is concerned, the solvent evaporation method is mostly used (Figure 6). This method is further divided into single and double emulsion techniques. One is oil in water emulsions produced single emulsion production, while water in oil in water emulsions is used in double emulsion preparation. To promote the creation of solid NPs, solvents are homogenized and evaporated once they have been suitably prepared. Ultracentrifugation is used to collect solid NPs, which are subsequently rinsed with distilled water to eliminate any remaining surfactants. After that, the mixture is lyophilized. The following is a step-by-step guide to solvent evaporation: Polymers are dissolved in organic solvents, and then the drug of choice is added. The organic mixture is mixed with an emulsifier or stabilizer in a water phase (oil/water). After full homogenization, the solution is agitated continuously for a few minutes to evaporate the organic phase and solidify the freshly created NPs. Finally, the solutions are centrifuged or filtered[94].

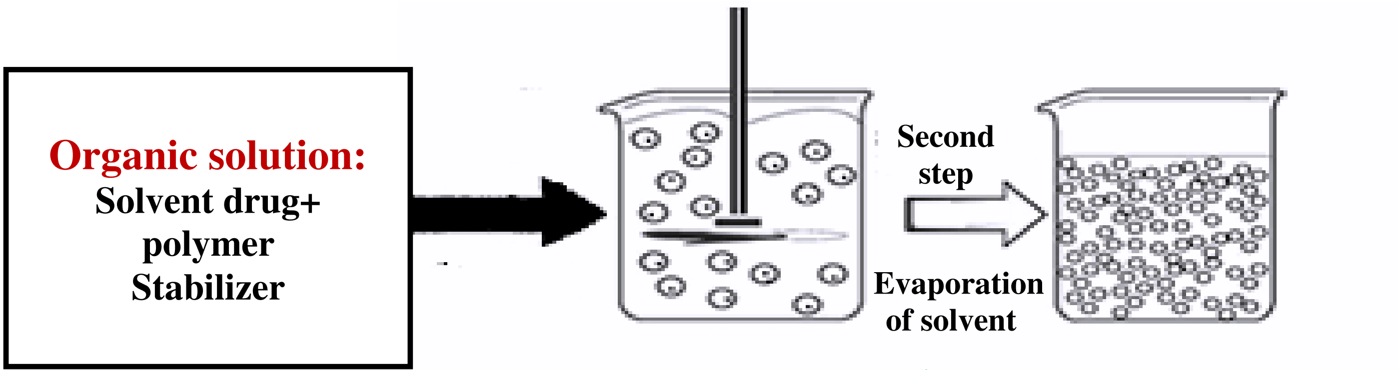

Fig 6: solvent evaporation techniques[94]

1.5.2 Double emulsification method

Because both emulsification and evaporation methods are limited in their ability to entrap hydrophilic medicines, a two foldemulsification procedure was adopted. To begin, make water in oil emulsion by continuously swirling the aqueous drug solution into the organic polymer solution. This created emulsion was then placed in another aqueous phase and vigorously stirred, yielding a w/o/w emulsion. After that, high centrifugation was used to extract the organic solvent [95].

1.5.3 Emulsions - diffusion method

The polymer is disintegrated in a solvent (water-miscible) and then diluted with water. In an aqueous solution with a stabilizer, the water-polymer phase is emulsified. The solvent is then evaporated or filtered out (Figure 7).

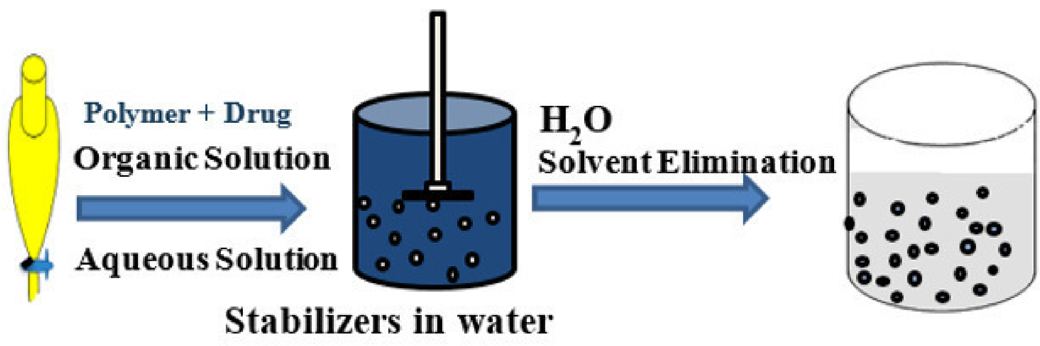

Fig 7: Emulsification-diffusion techniques[96]

Good encapsulation efficiency, the minimal requirement for homogenization, repeatability, simplicity, ease of scale-up, and restricted size distribution are all benefits of this approach. This approach has certain drawbacks, including reduced encapsulation efficiency[96].

1.5.4 Nano precipitation method

The most common manufacturing technique for nanomaterials is the solid precipitation from a solution with metal ions and shown in figure 8. This method may create with water to enable full acetone penetration into the aqueous phase, facilitating the development of nanospheres. This method does not need the higher temperatures and stirring energy necessary for smaller particle sizes. The technique's main drawbacks are applicability limited to lipophilic drugs and the lengthy NPs cleaning procedures [106].

1.5 Genetic engineering method (GEM)

This approach uses drug carriers such as silk-like proteins and elastomer-like proteins to modify the structural and functional characteristics of recombinant proteins. This approach may improve transfection efficiency while also controlling hydrophobicity, molecular weight, secondary structure, and drug conjugate site [107].

1.6 APPLICATION OF NPs

1.6.1 NPs antimicrobial activity

Different investigations have been ended to improve antimicrobial capacities in view of the progressing microbial opposition towards normal antibiotics and antiseptics. As indicated by in-vitro antimicrobial investigations, the metallic NPs actually impede the few microbial species. The antimicrobial adequacy of the metallic NPs relies on two significant boundaries: (a) material utilized for the NPs synthesis and (b) their molecule size. Further, microbial protection from antimicrobial medications has become progressively raised and is in this way a significant danger to general wellbeing. The most encouraging methodology for decreasing or keeping away from microbial medication obstruction is the use of NPs. The Ag NPs made by Pestalotia sp, which was secured from leaves of Syzygium cumini having antibacterial exercises against Homo sapiens microbes. These NPs have inherent effect as an antibacterial specialist[108,109].

1.6.2 Cellular imaging

Study displayed self-bio-imaging (*in-vivo*) of malignant growth cells utilizing fluorescent gold nano-cluster. It was intra cellular intracellularly synthesized by chloro auric acid reduction arrangement inside destructive cell cytoplasm into Au NP. Further, Au NP was in grouped structure with fluorescence which specifically analyzes destructive cells by *in-vivo* imaging (fluorescence). In another report, scientists incorporated carbon NPs utilizing a high level green strategy, which yielded NPs with blue shaded photoluminescence. This NP found to be biocompatible to biocompatible, less cytotoxic, high water solvency and had enhanced quantum yield. It was viewed as a decent contender for cell imaging, as it displayed cell take-up by Human HeLa cells and at 488 nm fluorescence green[58,108].

1.6.3 Catalyst and alternative energy source

The NPs green synthesis has an application as a catalyst and could also act as an alternative energy source. The gold NPs by green technology from egg shell concentrates of Anas platyrhynchos were utilized as catalyst for photo degradation-based expulsion of a poisonous dye (Eosin Y) and results affirmed removal of 96.1% of dye. The synergist conduct of AuNPs was explored for decolonization of two model mixtures in presence of NaBH4. It is clear that AuNPs proficiently catalyzes the decrease of receptive dye within 20 minutes or less[109].Among different substitute energy resources, hydrogenise an encouraging, green and reasonable energy source. Green NPs have been viewed as a reasonable possibility for parting water and creating hydrogen in light of its catalytic conduct. In this interaction, the outer layer of green NPs was utilized to gather energy in the presence of daylight and the collected energy was utilized to part water to oxygen and hydrogen. As daylight photons fall on NPs, electrons get invigorated (valence band) into the conduction band creating positive openings at valence band[58, 110].

1.6.4 NPs in dermatology

Recent breakthroughs in nanotechnology have enabled the production of intricate particles of nanometer-sized for a variety of biological applications. Only a few of these novel uses include controlled medication release to transcutaneous immunization, skin appendages, and transdermal gene therapy. The use of microparticles and nanocarriers to transport drugs via the skin might revolutionize the treatment of a variety of skin ailments [111-113].

1.6.5 Transdermal drug delivery

Solid lipid nanoparticles (SLN) dispersions with minimal lipid content have the lowest particle sizes. The low concentration of distributed lipids, as well as the low viscosity makes dermal administration difficult. Internalization of the SLN dispersion in an ointment or gel is usually required to provide a formulation that may be applied to the skin. The internalization stage suggests that the lipid content will be reduced even further. When the solid lipid content of the SLN dispersion is increased, semisolid, gel-like systems emerge, which may be suitable for direct skin application [114].

1.6.6 Approaches in tumor cells targeting

Cancer cells are more vulnerable to the effects of chemotherapeutic agents than normal cells, and many anticancer medications also harm normal cells. Now, attempts are being made to concentrate on killing malignant cells with more precise targeting while leaving normal cells alone [115]. By restricting medication distribution to the target organ, NPs will lower the drug threat to healthy tissues.

1.6.7 NPs in gene therapy

Polynucleotide vaccines induce an immune response by transferring genes encoding appropriate antigens to host cells, expressed and creating the antigenic protein in the presence of effective antigen-presenting cells. Because intracellular protein synthesis, as an opponent to extracellular deposition, stimulates immune system arms, these vaccines generate both humoral and cell-mediated immune responses [116, 117].

1.6.8 NPs in cardiovascular disorders

The study on cardiac ailments is currently underway. NPs are a kind of protein that is formed through translation and is utilized to adhere damaged arteries and break blood clots. Under the influence of a magnetic field, NPs are employed to transport proteins to the correct location in arteries [118-120].

1.6.9 NPS in Diabetics

Insulin is connected to the matrix in the developed NP. The enzymes are connected NPs that enhance insulin secretion and, in turn, control blood glucose levels over more than a few days when blood glucose levels rise[121-122].

1.6.10 NPs as cosmaceuticals

NPs are employed in the cosmetics industry in two ways: as "encapsulation or carrier systems" to help chemicals penetrate deeper into the skin layers and as ideal UV protection filters in sunscreens. Other nano-size materials, such as ceramic NPs, nanoparticulate silver and gold, pigments, minerals, and fullerenes, may be found in cosmetic goods, according to the makers[123,124].

1.6.11 NPs in ocular delivery

Longer residence duration, lesser toxicity, and increased capacity of drug penetration into ocular deeper layers and all advantages of drug-loaded NPs, as are reduced pre-corneal drug loss due to fast tear fluid turnover[125,126].

2. CONCLUSION

Nanotechnology is projected to revolutionize manufacturing in the next few years, with huge implications for life sciences such as medication delivery, diagnostics, NPs, and biomaterial synthesis. Engineered NPs (less than 100 nm) are a critical component in a variety of the aforementioned applications. Nanotechnology's use in medicine, especially medication delivery, is estimated to grow largely. Green NPs have been used in research for decades to lower medication toxicity and adverse effects. The ability of nanoparticulate systems to transform poorly absorbed, poorly soluble, and labile biologically active substances into viable deliverable medications has huge promise. To develop the notion of green NPs technology into a viable practical application as the upcoming generation of medication delivery systems, further progress is required.

3. FUTURE PERSPECTIVES

The majority of commercial NPs with medical uses are designed to transport drugs. NPs have replaced dyes with organic characteristics in bioscience applications that need great photostability. There has been some advancement in remotely directing and managing the operations of nano-probes, such as driving magnetic NPs to the tumor. The main tendency in nano-material development is to build them multifunctional and programmable by external signals or the local environment, thereby transforming them into nanodevices. The nanoparticles have been shown to be an effective medication delivery device. Green NPs provide significant benefits in terms of medication targeting and delivery, as well as the possibility for combined diagnosis and treatment, and are one of the most important nanomedicine tools[127, 128.]

4. AUTHORS CONTRIBUTION STATEMENTS

Mr. Abhishek Sharma conceptualized and collected the data with regards to this work. Mr. Rakesh and Ms. Ashima Verma scripted the article and Dr. R.B Sharma has critically analyzed this review article.

5. CONFLICTS OF INTERESTS

The authors do not have any conflicts of interest

6. REFERENCES

1. Anna PG. Nanotechnology and its applications in medicine. J Chem. 2015;5(2):81-9. Doi:10.4172/2161-0444.1000247.
2. Ingle AP, Shende S, Pandit R, Paralikar P, Tikar S, Kon K, Rai M. Nanotechnological applications for the control of pulmonary infections. The Microbiology of Respiratory System Infections. 2016:223–35. doi: 10.1016/B978-0-12-804543-5.00015-4.
3. Khan I,Saeed K, Khan I. Nanoparticles: properties, applications and toxicities. Arab J Chem. 2019;12(7):908-31. doi: 10.1016/j.arabjc.2017.05.011.
4. Martins P, Fernandess RA, Baptista VP. Nanoparticle drug delivery systems: recent patents and applications in nanomedicine. Bentham Sci Publish J.2013;3(2):1877-9123. http://dx.doi.org/10.2174/18779123046661403040000133
5. Hasan S. A Review on nanoparticles: their synthesis and types biosynthesis: mechanism. 2015;4:9-11.
6. Tai CY, Tai C, Chang M, Liu H. Synthesis of magnesium hydroxide and oxide nanoparticles using a spinning disk reactor. Ind Eng Chem Res. 2007;46(17):5536-41. doi: 10.1021/ie060869b.
7. Jong De HW, Paul B. Drug delivery and nanoparticles: applications and hazards. Int J Nanomedicine.2008;3(2):133-49. doi: 10.2147/IJN.S596.
8. Kumar PR, Sagadevan S, Savitha S. Beneficial applications of nanoparticles in medical field-a review. Int J Pharmatechnol Res.2014;6(5):1711-7.
9. Bhatia S. Natural polymer drug delivery systems. Springer Int Publish Switzerland. 2016.
10. Barhoum A. History and development of nanoparticles and nanostructured materials. Chem Sci J.2016;7(3):1-14.http://dx.doi.org/10.4172/2150-3494.C1.006
11. Heera P, Shanmugam S. Nanoparticle characterization and application: an overview. Int J Curr Microbiol Appl Sci. 2015;4(8):379-86.
12. Asha Spandana KM, Bhaskaran M, Karri VVSNR, Natarajan J. A comprehensive review of nano drug delivery system in the treatment of CNS disorders. J Drug Deliv Sci Technol.2020;57. doi: 10.1016/j.jddst.2020.101628, PMID 101628.
13. Bahadar H, Maqbool F, Niaz K, Abdollahi M. Toxicity of Nanoparticles and an Overview of Current Experimental Models. Iran Biomed J. 2016;20(1):1-11. doi: 10.7508/ibj.2016.01.001.
14. Singh A, Gautam PK, Verma A. Green synthesis of metallic nanoparticles as effective alternatives to treat antibiotics resistant bacterial infections: A review Biotechnol Rep (Amst). 2021;19;29:e00578. doi:10.1016/j.btre.2020.e00427.
15. Oxana VK, Boris IK, Cesar MO, Yolanda PM, Israel L. Green synthesis of chemical compound and

materials. Royal Soc Open Sci. 2019;6(11):1-41.https://doi.org/10.1098/rsos.191378.

16. Kalpana VN, Rajeshwari VD. A review on green synthesis, biomedical application, and toxicity study of ZnO NPs. Bioinorganic Chem Appli.2018:1-12.https://doi.org/10.1155/2018/3569758.
17. Shandilya N,Olivier LB, Martin M. A review on the study of the generation of (Nano) particles Aerosols during the Mechanical Solicitation of Materials. J Nanomat. 2014. https://doi.org/10.1155/2014/289108
18. Andrew JC, Devin TW, Johnathan EZ, Mark ED. CRLX101 nanoparticles localize in human tumors and not in adjacent, non-neoplastic tissue after intravenous dosing. PNAS. 2016;113 (14):3850-3854. https://doi.org/10.1073/pnas.1603018113
19. Munir H, Bilal M, Mulla SI, Khan AH, Iqbal HMN. Plant-Mediated green synthesis of nanoparticles. Adv in Sci, Technol & Innov. 2021;75-89. doi:10.1007/978-3-030-67884-5_4.
20. Rosenholm JM, Eriksson JE, Peuhu E, Sahlgren C, Lindén M. Targeted intracellular delivery of hydrophobic agents using mesoporous hybrid silica nanoparticles as carrier systems. Nano Letters. 2009;9(9):3308-3311. https://doi.org/10.1021/nl901589y
21. Laura C, Subhani B, Marshall J, Tony G, Tony G, Godson O, Aruna W, Peter A, Selamawit W. Foodborne Patho and Dis. 2020.504-511. http://doi.org/10.1089/fpd.2019.2714
22. Benelli G. Green Synthesis of Nanomaterials. Nanomaterials (Basel). 2019;9(9):1275. doi:10.3390/nano9091275.
23. Dada OA, Ojediran OJ, Dada FE, Olalekan AP, Awakan OJ. Green synthesis and characterization of silver nanoparticles using Calotropis Procera extract. J Appl Chem Sci Int. 2017 8(4): 137-143.
24. Dizaj SM, Vazifehasl Zh,Salatin S, Adibkia KH, Javadzadeh Y. Nanosi-zing of drugs: effect on dissolution rate. Res Pharm Sci.2015;10(2):95-108. PMID 26487886.
25. Gwinn MR, Vallyathan V. Nanoparticles: health effects--pros and cons. Environ Health Perspect.2006;114(12):1818-25. doi: 10.1289/ehp.8871, PMID 17185269.
26. Bayda S, Adeel M, Tuccinardi T, Cordani M, Rizzolio F. The history of nanoscience and nanotechnology: from chemical-physical applications to nanomedicine. Molecules. 2019;25(1):112. doi: 10.3390/molecules25010112, PMID 31892180.
27. Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J Nanotechnol.2018;9:1050-74. doi: 10.3762/bjnano.9.98, PMID 29719757.
28. Cooper DL, Conder CM. Nanoparticles in drug delivery: mechanism of action, formulation and clinical application towards reduction in drug-associated nephrotoxicity. Expert Opinion Drug Deliv J. 2014;11(10):1744-7593.http://dx.doi.org/10.1517/17425247.2014.938046.
29. RocoMC. The long view of nanotechnology development: the National Nanotechnology Initiative at 10 years. J Nanopart Res.2011;13(2):427-45. doi: 10.1007/s11051-010-0192-z.
30. Tiruwa R. A review on nanoparticles- preparation and evaluation parameters. Indian J Pharm Bio Res.2015;4(2):27-31. doi: 10.30750/ijpbr.4.2.4.
31. Simko M, Fiedeler U, Nentwich M, Gazso A. Production of nanoparticles and nanomaterials. Nano Trust Dossier.2011.
32. Rajput N. Method of preparation of nanoparticles- a review. Int J Adv Eng Technol.2015;7(4):1806-11.
33. Murthy SK. Nanoparticles in modern medicine: state of the art and future challenges. Int J Nanomedicine. 2007;2(2):129-41. PMID 17722542.
34. Naik J. Nano based drug delivery. International Association of Physical Chemists;2015.
35. Witharana C, Wanigasekara J. Applications of nanotechnology in drug delivery and design - aninsight. Curr Tren Biotechnol Pharm.2016;10(1):78-91.
36. Subbenaik SC, Kole C. Physical and chemical nature of nanoparticles. Springer Int Publish Switzerland. 2016.
37. Dizaj SM, JafariS, KhosroushahiAY. A sight on the current nanoparticle-based gene delivery vectors. Nanoscale Res Lett. 2014;9(1):252. doi: 10.1186/1556-276X-9-252, PMID 24936161.
38. Mody VV, Siwale R, Singh A, Mody HR. Introduction to metallic nanoparticles. J Pharm Bioallied Sci.2010;2(4):282-9. doi: 10.4103/0975-7406.72127, PMID 21180459.
39. Gatoo AM, Naseem S, ArfatMY, Dar MA, Qasim K, Zubair S. Physicochemical properties of nanomaterials: implication in associated toxicm anifestations. J biomedicalres. 2014.
40. Christian P, Von der Kammer F, Baalousha M, Hofmann T. Nanoparticles: structure, properties, preparation and behaviour in environmental media. Ecotoxicology.2008;17(5):326-43. doi: 10.1007/s10646-008-0213-1, PMID 18459043.
41. Soares S, Sousa J, Pais A, Vitorino C. Nanomedicine: principles, properties and regulatory issues. Front Chem.2018;6:360. doi: 10.3389/fchem.2018.00360, PMID 30177965.
42. Nikam AP, Ratnaparkhiand MP, Chaudhari SP. Nanoparticles – an overview. Int J Res Dev Pharm Life Sci.2014;3(5):1121-7.
43. Medina C, Santos-Martinez MJ, Radomski A, Corrigan OI, Radomski MW. Nanoparticles: pharmacological and toxicological significance. Br J Pharmacol.2007;150(5):552-8. doi: 10.1038/sj.bjp.0707130, PMID 17245366.
44. Goud R, Jones R, Banerjee S, Robertson G. Useof nanotechnology to develop multi drug inhibitors for cancer therapy. J Nanomed Nano. 2014;4(6):1-31.http://dx.doi.org/10.4172/2157-7439.1000184
45. Singh S, Pandy VK, Tewari RP, Agarwal V. Nanoparticle based drug delivery system: advantages and applications. Indian J Sci Technol. 2011;4(3):0974- 6846.
46. Kumar P, Kulkarni PK.Anjali and Srivastava A. JChem PharmRes.2015;7(8):703-12.
47. Mukherjee B, Dey NS, Maji R, Bhowmik P, Das PJ, Paul P. Current Status and Future Scope for Nanomaterials in drug delivery. Intech Open journal.doi: 10.5772/58450.

48. Midha K, Diwan P, Mampi D. A recent update on nanoparticles. Advanced research in pharmaceutical and biological an international peer reviewed. J Pharmal Allied Res.2018;8(1):2250-0774.
49. Bose S. Nano drug delivery System in pharmacy and chemistry. J Pharm Biolol Sci.2015;10(5):01-6. doi: 10.9790/3008-10520106.
50. Salata OV. Applications of nanoparticles in biology and medicine. J Nanobiotechnology. 2004;2(1):3. doi: 10.1186/1477-3155-2-3, PMID 15119954.
51. Nasimi P, Haidari M. Medical use of nanoparticles: drugdelivery and diagnosisdiseases. IntJGreen Nanotechnol.2013;1:1-6. doi: 10.1177/1943089213506978.
52. Kaur P, Kaur L, Khan MU. Nanoparticles as novel drug delivery system. Int J Res Pharm Chem.2012;2(3):2231-781.
53. Shah M, Badwaik VD, Kherde Y, WaghwaniHK, Modi T, Aguilar ZP, Rodgers H, Hamilton W, Marutharaj T, Webb C, Lawrenz MB, Dakshinamurthy R. Gold nanoparticles: various methods of synthesis and antibacterial applications. Front Biosci (Landmark Ed). 2014;19:1320-44. doi: 10.2741/4284, PMID 24896353.
54. Gressler S, Fiedeler U, Gazso A, Nentwich M. Nanotechnology in cosmetics. J Nano Trust Dossier. 2010.
55. Ekambaram P, Zarekar NS Shengde RS. Solid lipid nanoparticles. Nano Sci Nanotechnol Res. 2017;4(2):67-72. Doi- 10.12691/nnr-4-2-5.
56. Rizvi SAA, Saleh AM. Applications of nanoparticle systems in drug delivery technology. Saudi PharmJ.2018;26(1):64-70. doi: 10.1016/j.jsps.2017.10.012, PMID 29379334.
57. S Anu Mary Ealia and MPSaravanakumar. A review on the classification, characterization and synthesis of nanoparticle and their application. IOP Conf Ser Mater Sci Eng.2017;263. PMID 032019.
58. Rana A, Yadav K, Jagadevan S, A comprehensive review on green synthesis of nature-inspired metal nanoparticles: Mechanism, application and toxicity, J of Cleaner. https://doi.org/10.1016/j.jclepro.2020.122880
59. Vanlaveni C, Lallianrawna S, Biswas A, Selvaraj M, Changmai B, Rokhum LS. Green synthesis of silver nanoparticle using plant extract and their antimicrobial activity: a review of recent literature. RSV Adv.2021. PMID 112804.
60. Mohanraj VJ, Chen Y. Nanoparticles-a review. Trop J Pharm Res. 2006;5(1):561-73. doi: 10.4314/tjpr.v5i1.14634.
61. Zhang D, Ma XL, Gu Y, Huang H, Zhang G. Green synthesis of metallic nanoparticle and their potential application to treat cancer. Forntier Chem. 2020;8:799.https://dx.doi.org/10.3389%2Ffchem.2020.00799.
62. Ahmad S, Munir S, Zeb N, Ullah A, Khan B, Ali J, Bilal M, Omer M, Alamzeb M, Salman SM, Ali S. Green nanotechnology a review on green synthesis of nanoparticles. Int J Nanomedicine.2019;14:5087-107. doi: 10.2147/IJN.S200254, PMID 31371949.
63. Rauwel P, Kuunal S, Ferdov S, Rauwel E. A review on green synthesis of silver nanoparticle and their morphological studies via TEM.Adv Mat Sci Tech;2015. p. 1-9.https://doi.org/10.1155/2015/682749.
64. Izaj I, Gilani E, Nazir A, Bukhari A. Detailed review on chemical, physical, green synthesis, classification, characterization and application of nanoparticles. Green Chem Lett Rev.2020;13(3):59-81.https://doi.org/10.1080/17518253.2020.1802517.
65. Jadoun S, Arif R, Jangid NK, Meena RK. Green synthesis of nanoparticles using plant extract –a review. Environ Chem Lett.2021;19(1):355-74. doi: 10.1007/s10311-020-01074-x.
66. Singh J, Dutta T, Kim KH, Rawat M, Samdda P, Kumar P. Green synthesis of metals and their oxide nanoparticles application for environmental remediation. J Nanotechnol.2018;16:84.https://doi.org/10.1186/s12951-018-0408-4
67. Castillo-Henríquez L, Alfaro-Aguilar K, Ugalde-Álvarez J, Vega-Fernández L, Montes de Oca-Vásquez G, Vega-Baudrit JR. Green synthesis of gold and silvernanoparticles from plantextracts and theirpossibleapplications as antimicrobialagents in the agriculturalarea. Nanomaterials (Basel). 2020;10(9):1763. doi: 10.3390/nano10091763, PMID 32906575.
68. Okafor F, Janen A, Kukhtareva T, Edwards V, Curley M. Green synthesis of silver nanoparticles, their characterization, application and antibacterial activity. Int J Environ Res Public Health. 2013;10(10):5221-38. doi: 10.3390/ijerph10105221, PMID 24157517.
69. Ahmad S, Munir S, Zeb N, Ullah A, Khan B, Ali J, Bilal M, Omer M, Alamzeb M, Salman SM, Ali S. Green nanotechnology: a review on green synthesis of silver nanoparticles - an ecofriendly approach. Int J Nanomedicine. 2019;14:5087-107. doi: 10.2147/IJN.S200254, PMID 31371949.
70. Zhang D, Ma XL, Gu Y, Huang H, Zhang GW. Green synthesis of metallicnanoparticles and theirpotentialapplications to treatcancer. Front Chem.2020;8:799. doi: 10.3389/fchem.2020.00799, PMID 33195027.
71. Fahmy SA, Preis E, Bakowsky U, Azzazy HME. Platinum nanoparticles: greensynthesis and biomedicalapplications. Molecules. 2020;25(21):4981. doi: 10.3390/molecules25214981, PMID 33126464.
72. Erci F, Cakir-Koc R, Isildak I. Green synthesis of silver nanoparticles using Thymbra spicata L. var. spicata (zahter) aqueous leaf extract and evaluation of their morphology-dependent antibacterial and cytotoxic activity. Artif Cells Nanomed Biotechnol. 2018;46(sup1):150-158. doi: 10.1080/21691401.2017.1415917.
73. Lee SH, Jun BH. Silver Nanoparticles: Synthesis and Application for Nanomedicine. Int J Mol Sci. 2019;20(4):865. doi:10.3390/ijms20040865.
74. Letchumanan D, Sok SPM, Ibrahim S, Nagoor NH, Arshad NM. Plant-based biosynthesis of copper/copper oxide nanoparticles: an update on their applications in biomedicine, mechanisms, and toxicity. Biomolecules. 2021;11(4):564.
75. Rabiee N, Bagherzadeh M, Kiani M. Biosynthesis of copper oxide nanoparticles with potential biomedical applications. Int J Nanomedicine. 2020;15:3983-3999. doi:10.2147/IJN.S255398.
76. Ziental D, Czarczynska-Goslinska B, Mlynarczyk DT, Glowacka-Sobotta A, Stanisz B, Goslinski T, Sobotta L. Titanium dioxide nanoparticles: prospects and

applications in medicine.Nanomaterials(Basel,Switzerland).10(2),387.https://doi.org/10.3390/nano10020387.

77. Shah M, Fawcett D, Sharma S, Tripathy SK, Poinern GEJ. Green synthesis of metallicnanoparticles via biologicalentities. Materials (Basel). 2015;8(11):7278-308. doi: 10.3390/ma8115377, PMID 28793638.

78. Castillo-Henríquez L, Alfaro-Aguilar K, Ugalde-Álvarez J, Vega-Fernández L, Montes de Oca-Vásquez G, Vega-Baudrit JR. Green synthesis of gold and silvernanoparticles from plantextracts and theirpossibleapplications as antimicrobialagents in the agriculturalarea. Nanomaterials (Basel). 2020;10(9):1763. doi: 10.3390/nano10091763, PMID 32906575.

79. Rana A, Yadav K, Jagadevan S. A comprehensive review on green synthesis of nature-inspired metal nanoparticles: mechanism, application and toxicity.Journal of Cleaner Production. *2020;122880–*. doi:10.1016/j.jclepro.2020.122880

80. Nath D, Banerjee P. Green nanotechnology-a new hope for medical biology. Environ Toxicol Pharmacol. 2013;36:997-1014.http://dx.doi.org/10.1016/j.etap.2013.09.002.

81. Ovais M, Khalil AT, Ayaz M, Ahmad I, Nethi SK, Mukherjee S. Biosynthesis of metal nanoparticles via microbial enzymes: a mechanistic approach. Int J Mol Sci. 2018;19(12):4100. doi:10.3390/ijms19124100.

82. Aboyewa JA, Sibuyi NRS, Meyer M, Oguntibeju OO. Green synthesis of metallic nanoparticles using some selected medicinal plants from Southern Africa and their biological applications. Plants (Basel). 2021;10(9):1929. doi:10.3390/plants10091929.

83. Shah M, Fawcett D, Sharma S, Tripathy SK, Poinern GEJ. Green synthesis of metallic nanoparticles via biological entities. Materials (Basel). 2015;8(11):7278-7308. doi:10.3390/ma8115377

84. Rajashekar K, Nandita D, Sudip D. Nanoparticulate systems for therapeutic and diagnostic applications. Emer Nanotechnolos Diagn Drug Delivand Med Devi. 2017:105-44.

85. Bhardwaj B, Singh P, Kumar A, Kumar S, Budhwar V. Eco-friendly greener synthesis of nanoparticles. Adv Pharm Bull. 2020;10(4):566-576. doi:10.34172/apb.2020.067.

86. Kumari B. A review on nanoparticle: their preparation method and classification. Ind Res J Pharm Sci. 2018;5(2).

87. Merlin JJ, Rajan SS. A review on synthesis and preparation of nanoparticles. J Cancer Sci Treat. 2020;2(1):87-9.

88. Nagavarma BVN, Hemant KS, Yadav Ayuz A, Vasudha LS, Shivakumar HG. Different techniques for preparation of polymeric nanoparticles - a review. Asian J Pharm Clin Res. 2012;5:1-8.

89. Joachim A. Synthesis of organic and bioorganic nanoparticles: an overview of the preparation methods. London: Springer-Verlag;2013. p. 27-30.

90. Mourdikoudis S, Pallares RM , Thanh NTK . Characterization techniques for nanoparticles: comparison and complementarity upon studying nanoparticle properties. Nanoscale. 2018;13;10(27):12871-12934. doi: 10.1039/c8nr02278j.

91. Shnoudeh A, Hamad I, Abdo RW, Qadumii L, Jaber AY, Surchi HS, Alkelany SZ. Synthesis, characterization, and applications of metal nanoparticles. Biomat Bionanotechno.2019;528-585. https://doi.org/10.1016/B978-0-12-814427-5.00015-9

92. Sovan LP, Utpal J, Manna PK, Mohanta GP, Manavalan R. Nanoparticle: an overview of preparation and characterization.J Appl Pharm Sci.2011;1(6):228-34.

93. Tyagi PK, Quispe C, Herrera-Bravo J, Tyagi S, Mrunal B, Kumar M. Synthesis of Silver and Gold Nanoparticles: Chemical and Green Synthesis Method and Its Toxicity Evaluation against Pathogenic Bacteria Using the Tox Trak Test. 2021;1-12. https://doi.org/10.1155/2021/3773943

94. Katmis A, Fide S, Karaismailoglu S, Derman S. Synthesis and characterization method of polymeric nanoparticle. Chara Appl Nnano. 2018;1:1-9. doi:10.24294/can.v1i2.791.

95. Kaur LS, Sandeep K, Punam G. An overview, preparation, characterization and application of nanoparticles. J Drug Deliv Ther. 2020;10(6-s):159-67.

96. Guo S, Fu D, Utupova A, Sun D, Zhou M, Jin Z, Zhao K. Application of polymer based nanoparticle in vaccine field. Nanotechnol Rev. 2019;8:143-155. https://doi.org/10.1515/ntrev-2019-0014

97. Pal S, Jana U, Manna PK, Mohanta GP, Manavalan R. Nanoparticle: an overview of preparation and characterization. J Appl Pharm Sci.2011;1(6):228-34.

98. Jeevanandam J, Barhoum A, Chan YS, Dufresne A, Danquah MK. Review on nanoparticles and nanostructured materials: history, sources, toxicity and regulations. Beilstein J Nanotechnol.2018;9(9):1050-74. doi: 10.3762/bjnano.9.98, PMID 29719757.

99. Beena K. A review on nanoparticles: their preparation method and applications. Ind Res J PharmSci. 2018;5(2):1420-6.

100. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov. 2021;20(2):101-24. doi: 10.1038/s41573-020-0090-8, PMID 33277608.

101. Baig N, Kammakakam I.FalathW.Nanomaterials: a review of synthesis methods, properties, recent progress, and challenges. Matern Advan. 2021;2:1821.https://doi.org/10.1039/D0MA00807A.

102. Xiaopei H, Yuting Z, Tingting D, Jiang L, Hang Z. Multifunctional gold nanoparticles: A novel nano material for various medical applications and biological activities. Front Bioeng Biotechnol.2020.https://doi.org/10.3389/fbioe.2020.00990

103. Dawadi S, Katuwal S, Gupta A, Lamichhane U, Thapa R, Jaisi S, Lamichhane G, Bhattarai DP, Parajuli N. Current research on silver nanoparticles: synthesis, characterization, and applications. Journal of Nanomaterials. 2021;2021:1-23. doi: 10.1155/2021/6687290.

104. SimS, WongNK. Nanotechnology and its use in imaging and drug delivery (Review). BiomedRep. 2021;14(5):42. doi: 10.3892/br.2021.1418, PMID 33728048.

105. Krishna RN, Gyathri R, Priya V. Nanoparticles and their applications- a review. J Pharm Sci Res.2017;9(1):24-7.

106. Antonio JR, Antônio CR, Cardeal IL, Ballavenuto JM, Oliveira JR. Nanotechnology in dermatology. An Bras Dermatol.2014;89(1):126-36. doi: 10.1590/abd1806-4841.20142228, PMID 24626657.
107. DeLouise LA. Applications of nanotechnology in dermatology. J Invest Dermatol vol. 132.2012;2(3 Pt 2):964-75. doi: 10.1038/jid.2011.425, PMID 22217738.
108. Sharma A, Harikumar SL. Qualiy by design approach for development and optimization of nitrendipine loaded niosomal gel for accentuated transdermal delivery. Int J Appl Pharm.2020;12(5):181-9.https://doi.org/10.22159/ijap.2020v12i5.38639
109. Sharma A, Singh AP, Harikumar SL. Development and optimization of nanoemulsion based gel for enhanced transdermal delivery of nitrendipine using box-behnken statistical design. Drug DevIndPharm.2020;46(2):329-42. doi: 10.1080/03639045.2020.1721527, PMID 31976777.
110. Jin C, Wang K, Oppong-Gyebi A, Hu J. Application of nanotechnology in cancerdiagnosis and therapy - Amini-review. Int J Med Sci.2020;17(18):2964-73. doi: 10.7150/ijms.49801, PMID 33173417.
111. Yao Y, Zhou Y, Liu L, Xu Y, Chen Q, Wang Y, Wu S, Deng Y, Zhang J, Shao A. Nanoparticle-Based drug delivery in cancer therapy and its role in overcoming drug resistance. Front Mol Biosci.2020;7:193. doi: 10.3389/fmolb.2020.00193, PMID 32974385.
112. Mullaicharam AR. Nanoparticles in drug delivery system. Int J Nutr Pharmacol Neurol Dis.2011;1(2):103-21. doi: 10.4103/2231-0738.84194.
113. YuZ, GaoL, ChenK, Zhang W, Zhang Q, Li Q, Hu K. Nanoparticles: A new approach to upgrade cancer diagnosis and treatment. NanoscaleRes Lett.2021;16(1):88. doi: 10.1186/s11671-021-03489-z, PMID 34014432.
114. Herranz F, Almarza E, Rodríguez I, Salinas B, Rosell Y, Desco M, Bulte JW, Ruiz-Cabello J. The application of nanoparticles in gene therapy and magnetic resonance imaging. Microsc Res Tech.2011Jul;74(7):577-91. doi: 10.1002/jemt.20992, PMID 21484943.
115. Tomoda K, Makino K. Nanoparticles for transdermal drug delivery system (TDDS). Colloid Interface Sci Pharm Res Develop. 2014:131-47.
116. KafshdoozT, KafshdoozL, AkbarzadehA, HanifehpourY, JooSW. Applications of nanoparticle systems in gene delivery and gene therapy. Artif CellsNanomed Biotechnol. 2016;44(2):581-7. doi: 10.3109/21691401.2014.971805, PMID 25365242.
117. KelesE,SongY,DuD,DongW-J, LinYuehe. Recent progress in nanomaterials for gene delivery applications.Biomater Sci.2016;4(9):1291-309. doi: 10.1039/c6bm00441e, PMID 27480033.
118. Hashim PW, Nia JK, Han G, Ratner D.Nnaoparticle in dermatology surgery. J AcadDermatol. 2020;83(4):1144-9.https://doi.org/10.1016/j.jaad.2019.04.020
119. Fan C, Joshi J, Li F, Xu B, Khan M, Yang J, Zhu W. Nanoparticle-mediated drug delivery for treatment of ischemic heart disease. FrontBioengBiotechnol. 2020;8:687. doi: 10.3389/fbioe.2020.00687, PMID 32671049.
120. Pala R, Anju VT, Dyavaiah M, Busi S, Nauli SM. Nanoparticle-mediated drug delivery for the treatment of cardiovascular diseases. Int J Nanomedicine. 2020;15:3741-69. doi: 10.2147/IJN.S250872, PMID 32547026.
121. DiSanto RM, Subramanian V, GuZ. Recent advances in nanotechnology for diabetes treatment. Wiley Inter discip Rev Nanomed Nanobiotechnology. 2015;7(4):548-64. doi: 10.1002/wnan.1329, PMID 25641955.
122. He Y, Al-Mureish A, Wu N. Nanotechnology in the treatment of diabetes complications: a comprehensive review. J Diabetes Res.2021:1-11.https://doi.org/10.1155/2021/6612063.
123. Guerrero Correa M, Martínez FB, Vidal CP, Streitt C, Escrig J, de Dicastillo CL. Antimicrobial metal-based nanoparticles: a review on their synthesis, types and antimicrobial action. Beilstein J Nanotechnol.2020;11:1450-69. doi: 10.3762/bjnano.11.129, PMID 33029474.
124. Sharmin S, Rahaman MM, Sarkar C, Atolani O, Islam MT, Stephen O. Nanoparticles as antimicrobial and antiviral agents: A literature-based perspective study. Heliyon. 2021, 2021:7(3).https://dx.doi.org/10.1016%2Fj.heliyon.2021.e06456
125. Omerović N, Vranić E. Application of nanoparticles in ocular drug delivery systems. Health Technol. 2020;10(1):61-78. doi: 10.1007/s12553-019-00381-w.
126. Zhou HY, Hao JL, Wang S, Zheng Y, Zhang WS. Nanoparticles in the ocular drug delivery. Int J Ophthalmol.2013;6(3):390-6. doi: 10.3980/j.issn.2222-3959.2013.03.25, PMID 23826539.
127. Karthikeyan RD, Amaldas J. Green synthesis and characterization of silver nanoparticle (agnps) using Artemisia annua l. and its antibacterial, antifungal activity. Int J Pharma Bio Sci. 2018;9(4):111-121. DOI:http://dx.doi.org/10.22376/ijpbs.2018.9.4.p111-121.
128. Thakur S, Mohan GK. Green synthesis of silver nanoparticles of boswellic acid and its in-vitro anticancer activity. Int J Pharma Bio Sci. 2019;10(3):92-100. http://dx.doi.org/10.22376/ijpbs.2019.10.3.p92-100