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Novel Formulations of Green Synthesized Plant Based Metal Nanoprticles along with their Therapeutic Applications: an Insight to Nano-Green world

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ABSTRACT

Nanoparticles are the most important entity in the widely spread field of nanotechnology. A series of numerous physical and chemical methods are involved in nanoparticle synthesis. Metallic nanoparticle can overcome the issues of highly monodispersed nanoparticles of various sizes, geometries and chemical composition, as they are comparatively smaller in size. Hence chemicals and non-polar solvents are involved in the synthesis of metallic nanoparticles which makes them unsuitable for being used in clinical fields. Therefore, the scientists have developed new aspects of clean, non-toxic, biocompatible and eco-friendly synthesis method for nanoparticles. Metal nanoparticles have attained a special focus attributed to their unique features like size and shape dependant optical, electrical and magnetic properties. The green synthesis using biological molecules obtained from plant sources are quite beneficial over other physical and chemical methods that have been used for metal nanoparticle synthesis and stabilization. This exhaustive review is focused on the metallic nanoparticles, which are synthesized from plant sources and overview of their pharmacological properties.

Key words: Size and shape dependant optical, electrical and magnetic properties, Metallic nanoparticles, Green synthesis.

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INTRODUCTION

FDA approves number of chemically synthesized newer molecules nowadays, which are introduced in the market with wide therapeutic efficacy, but the adverse effects related to these molecules can be harmful for the patients. Due to peak and valley fluctuations, conventional therapy is non- targetable in tissues and organs and high dose frequency is also the main problem associated with allopathic medicines which lead to poor patient compliance [1].

A number of phytoconstituents belonging to nature have different biological activities against chronic diseases and have wide therapeutic potencies. Phytoconstituents are beneficial as they exhibits free from adverse effects treatment where none of the medication can do. Although, some physiochemical factors like less solubility, less permeation and non-targeting at the active site will act as a barrier which create problems to its therapeutic efficacy. Therefore, various novel formulation techniques are discovered to overcome these barriers and achieve uniform drug targeting at the active site in desired concentration and enhanced therapeutic potency. These novel formulation techniques includes emulsion-based formulations, phytosomes, liposomes, microspheres, topical based formulations and nanoparticles which are available in commercial level to enhance the bioavailability of the poorly soluble herbal drug [2].

From the past few decades novel drug delivery system (NDDS) is used and gained the attention related to further development in these novel systems. The two ideal requirements for a system to be novel are:-

- Drug delivery at a predetermined rate and for predetermined span of time;
- Conveying the active entity to the target site.

Currently, there is no such system which can fulfill all these requirements. So a lot of research work is required to accomplish them using novel strategies. These targets can be achieved by studying the drug distribution through unifying drug into a carrier system, modification in molecular drug composition or by controlling drug release in the bioenvironment to achieve desired distribution profile. Novel drug delivery systems can be effectively minimize the side effects and maintain uniform and potent levels of drug in the body. These carriers have the ability to restrict the drug action specifically in diseased tissue or organ or adjacent to it [3].

NANOPARTICLES

The Greek term 'nano' means small in size which is a unit prefix meaning "one billionth" from the range 9 to 10. Particles which have two or more dimensions in the size range as 1 to 100 NM are defined as nanoparticles [4]. A Professor from Tokyo Science University, Dr. Norio Taniguchi was introduced the term Nanotechnology in the year 1974 to explain precise production of materials at the nanometer level [5]. Although a physicist, Professor Richard P. Feynman was the first who use this Nanotechnology concept in his lecture entitled "There's plenty of room at the Bottom" [6]. Nanoparticles are colloidal particles having submicron size ranges from 10 to 1000 nm. Nanospheres are a matrix type of structure which entrapped active pharmaceutical ingredient. Nanocapsules composed from a polymer membrane which contains the API in its polymer core. Nanoparticles are the most suitable delivery tools for encapsulating drugs ranging from small to larger molecular weight compounds. Nanoparticles based on herbal drugs, is the area of thirst in modern era. Nanoparticles can release the drug through bulk erosion from the matrix or through surface erosion within the polymer, which is totally related to the nature of drug and preparation method used [7]. Nanotechnology is very popular nowadays, because of its wide range of applications from cosmetics and skin care products to abrasives, car polishes and drug delivery systems. Nanoparticles made by human are fabricated within the diameter range of < 100 nm, which shows specific physicochemical properties attributed to their small size measurement, large surface-to-volume ratio and also in-creased reactivity [8]. These specific properties of nanoparticles are responsible for the desired result which is given by an almost inert material at nanoscale [9].

USE OF NANOPARTICLES

Nanomaterials have already been exhausted deeply in early 2005 for its capabilities to use in medical and pharmaceutical fields [10]. Nanoparticle has a wide area of applications in energy, nutrition and medicine [11]. Nanotechnology has showed great possibilities nowadays in various areas of technology and science. Pharmaceutical nanotechnology includes various benefits which increasingly gained the attention of a number of budding researchers [12]. The importance of nanomaterials as drug delivery systems has been analyzed from about past twenty years which results in dosage forms with enhanced therapeutic effects as well as improved physicochemical properties [13 and 14]. Therefore, nanoparticles are already recognized as the biomaterials that have a great potential for medical and biological applications. They may be utilized as a contrast agent for medical imaging, or in therapeutic drug delivery, elimination of tumours and labelling of cells. Moreover, biomedical instruments are mostly fabricated by organic and inorganic nanoparticles in the industry, attributed to their easy incorporation in biological processes [9].

A size dependant physicochemical characteristic of nanoparticles is the reason behind its extensive exploration in the area of medicine. The size of nanoparticles and most biological molecules and structures are very similar to each other. This unique property makes them suitable candidate to apply in both *in vivo* and *in vitro* biomedical research. Due to their amalgamation in medicinal field they can be easily applied in imaging, sensing, artificial implants and targeted drug delivery. Nanoparticle used as antimicrobial is another interesting approach for their exploration in medicinal field to target highly pathogenic and drug resistant microbes. However, nanoparticle application in biology is greatly depends upon biocompatibility. Biocompatibility is the ability of material to give therapeutic effect without showing any unwanted local or systemic effects [15].

METAL BASED NANOPARTICLES

From the few past decades, metals are used for treating a number of infectious diseases and due to the emergence of resilient pathogens their antimicrobial potencies are being reevaluated nowadays. The main area of research related to metal efficacy includes their use in topical/therapeutic as well as disinfecting agent to control the bacterial adhesion and transmission. Nanoparticles can be a fascinating candidate in that because of their formulation with a high surface area to volume ratio and with unexpected morphological characters containing sharp edges and corners [16]. The metal nanoparticles have been attracted many researchers and scientists due to their widely uses in industry and medicine [17 and 18]. Antibacterial nanomaterials as compared to antibacterials are become very popular because they have the ability to give better options against antibiotics. They also overcome the problems related to antibiotics. They attributed to combat multidrug-resistant mutants and biofilms of the bacteria [19 and 20].

Metals and their oxides are exhaustively analyzed and reported for having the antibacterial potency [21]. Metals like, zinc (Zn), silver (Ag), copper (Cu), gold (Au) and titanium (Ti) possesses good antibacterial ability and have been used from ancient times [22]. Similarly, the oxides of metals as nanoparticles like iron oxide (Fe_3O_4), zinc oxide (ZnO), silver (Ag), titanium oxide (TiO_2) and copper oxide (CuO) were reported for having potent antibacterial activity [23]. Figure 1 shows various metals used for the synthesis of plant mediated nanoparticles.

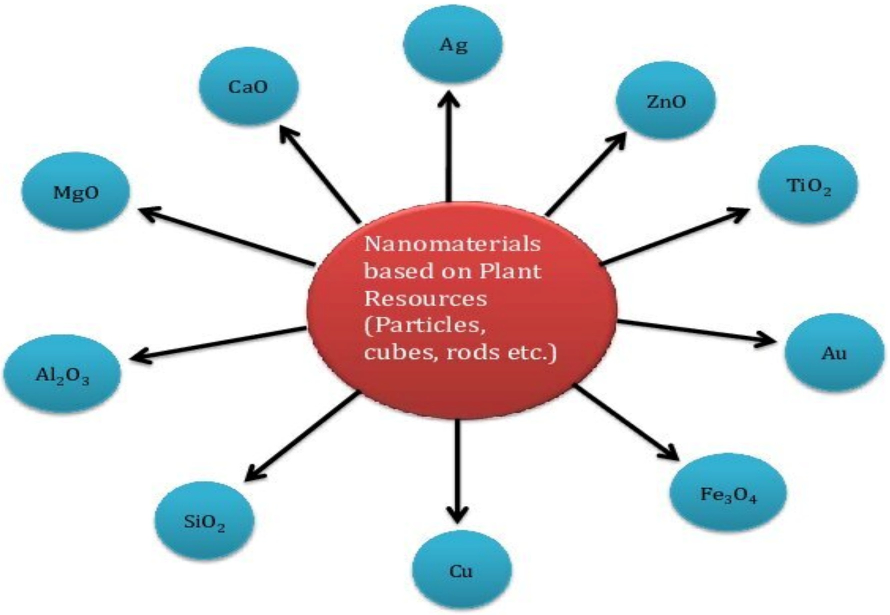

FIGURE1: VARIOUS METAL NANOPARTICLES SYNTHESIZED FROM PLANT RESOURCES [24].

SILVER (Ag) and SILVER OXIDE (Ag_2O) NANOPARTICLES

Silver nanoparticles are most popular, among all metal nanomaterials, as potent antimicrobial agent against various bacteria, fungi, and viruses [25]. According to previous literature, the antimicrobial ability of silver nanoparticles is size-dependent, similar to other matal nanoparticles [26]. Previous literatures show that the antibacterial action of silver nanoparticles is attributed to the damage of the outer membrane of bacteria [27]. However few researchers pretend that, silver nanoparticles can create pits and gaps in the bacterial membrane which causes fragmentation of the cell [28 and 29]. The mechanism behind bacterial cell death by silver is that silver ions interact with disulfide or sulfhydryl groups of enzymes results in the interruption in metabolic processes and finally causes the cell death [30]. Jo et al. studied the effect of size reduction on the antimicrobial efficacy of silver nanoparticles. Silver nanoparticles sizes ranging from 20 to 30 nm shows better penetration and can colonize within the plant tissue. According to them, silver nanoparticles can be a great option for inhibition of spore-producing fungal plant pathogens. They give silver nanoparticles more preference over synthetic fungicides in terms of toxicity [31]. Pal et al. compared the shape dependent antibacterial efficacy between spherical, rod-shaped and truncated triangular shaped silver nanoparticles. They concluded that truncated triangular nanoparticles were highly reactive due to their high-atom-density surfaces and hence showed relatively high antimicrobial potency [32].

Silver oxide (Ag_2O) nanoparticles have also been detected for their higher antimicrobial activity [33]. Sondi et al. studied that *E. coli* DNA lost its replication ability when exposed to silver oxide nanoparticles and their cell cycle ceased at the G2/M phase results in DNA damage. Then the cells were affected by oxidative stress, and apoptosis was induced [34].

ZINC (Zn) and ZINC OXIDE (ZnO) NANOPARTICLES

The Zn nanoparticles functionalized with curcumin showed excellent inhibition activity against the microbial strains tested over all [35]. Aqueous extract of *Panax ginseng* roots were used to synthesize zinc nanoparticles, which is considered as the first test that results in remarkable growth reduction of cancer cells *in vitro*, by using zinc nanoparticles of Ginseng (*Panax ginseng*) [36].

ZnO nanoparticles are well known for their antibacterial efficacy against a large variety of microbes and according to reports their activity is attributed to the selected concentrations and particle size [37]. Zinc oxide nanoprticles are comparatively economical [38] and having size dependent efficacy [37] against various species of microorganisms [39 and 40]. These include pathogens such as *Salmonella enteritidis, Listeria monocytogenes* [41], *Klebsiella pneumonia* [42], *Streptococcus mutans, Lactobacillus* [43], and *E. coli* [41 and 44] along with lesser cytotoxicity [45].The properties like white color, UV-protection and bacterial biofilm inhibition are suggested these nanoparticles to be incorporated in facbrics [46] and also in glass [47] industries for coating of medical and related devices. In addition, FDA has also approved the use of zinc as a food additive [48]. These nanoparticles show the activity through membrane binding, inhibiting their potential and integrity, and through facilitating ROS production [41, 44 and 49]. Zinc nanoparticles are also mutagens, but relatively weak ones [50].

TITANIUM OXIDE (TiO_2) NANOPARTICLES

Titanium dioxide (TiO_2) is also one of the metal oxides, which is exhaustively analyzed and shows potent antibacterial effects [33]. This metal oxide was broadly used against both Gram-positive and Gram-negative bacteria since past few decades [51]. These are photocatalytic as they are toxic which is facilitated by visible light, near-UV or UV [19], stimulates ROS burst. The ROS damage the membrane, DNA and many other macromolecules and functions of the bacterial cell [48]. Titanium dioxide is very effective against various highly resistant microorganisms such as bacterial spores of *Bacillus* [52]. The conjugation of titanium or its oxide to other nanomaterials for example silver, possibly shows increased antibacterial activity due to synergism [53, 54 and 55].

GOLD (Au) NANOPARTICLES

Gold nanoparticles act as an antibacterial through attachment to the bacterial membrane, then alter the membrane potential and decreases ATP level, resulting inhibition of tRNA binding to the ribosome [56]. A previous literature shows the efficacy of gold and silver nanoparticles against *E. coli* and *Bacillus Calmette-Guérin* (BCG). They claimed that, Au and Ag nanoparticles exhibited significant antibacterial activity against both Gram negative (E. coli) and the Gram positive bacteria (*Bacillus Calmette-Guérin*). They also formulated gold nanoparticles by using a firmly bound capping agent, poly-allylamine hydrochloride as well as by an infirm bound capping agent, citrate. Due to its positively charged nature, poly-allylamine hydrochloride can make direct contact with the bacterial cell membrane [57 and 58]. Some other studies showed that the gold nanoparticles (5nm) can reduce 90–95% colonies of *Salmonella typhi* and *E. coli*. The investigators finally conclude that, the roughness and the dispersion of the gold nanoparticles on the medium are the main factors which affect their biocidal properties [59].

IRON OXIDE (Fe_3O_4) NANOPARTICLES

Iron oxide is an antibacterial in nano range but it is an inert material in bulk form. Previous microbiological assays conclude the antiadherent properties of iron oxide nanoparticles and its activity against both Gram-negative and Gram-positive bacteria [60]. Gold nanoparticle, conjugated with iron oxide is a newer technique against microbes which is induced by photothermal treatment [61].

COPPER (Cu) and COPPER OXIDE (CuO) NANOPARTICLES

Copper (Cu) nanoparticles due to their unique biological, chemical and physical properties, antimicrobial activities as well as the low cost of preparation, are very fascinating to the investigators [62, 63 and 64]. Usman et al. analysed the antimicrobial potential of Copper-chitosan nanoparticles (2–350 nm). Antifungal and antibacterial efficacies of these nanoparticles were studied on various microorganisms, such as methicillin resistant *S. aureus, Salmonella choleraesuis, B. subtilis, C. albicans* and *P. aeruginosa*. These results show the antimicrobial potency of these nanoparticles [63]. However, on exposure to the air, copper nanoparticles rapidly get oxidation which hinders their application [63 and 65]. Copper (Cu) is comparatively economical than other nano ranged metals and therefore it can be used for increasing efficacy in the form of nanocomposites [23].

Mahapatra et al. analysed the antibacterial potential of copper oxide nanoparticles against various microorganisms like *Salmonella paratyphi, P. aeruginosa, Klebsiella pneumoniae* and *Shigella strains*. According to their report, these nanoparticles indicated suitable antibacterial activity against the mentioned bacteria. They suggested that these nanoparticles can cross through the bacterial cell membrane and causes damage to the vital enzymes and finally trigger cell death. According to them these nanoparticles were also non cytotoxic on HeLa cell line [65]. Azam et al. investigated the antibacterial activity of copper oxide nanoparticles against *B. subtilis* and *S. aureus* (Gram-positive bacteria), and *E. coli* and *Pseudomonas aeruginosa* (Gram-negative bacteria). Their tests show the results that these nanoparticles inhibit the growth of both groups of the above mentioned bacteria. The investigators suggested that bactericidal activity of copper oxide nanoparticles is size-dependent and also affected by its stability and concentration added to the growth medium. The authors believed that the metal nanoparticles can passes through the nanometric pores of the cellular membranes of most bacteria and there by restrict the bacterial growth [66]. Copper oxide (CuO) nanoparticles, like the other metallic nanoparticles, exert their antibacterial activity [67 and 68] by membrane disruption and ROS production

[19]. The bacteria like *B. anthracis and B. subtilis* were more susceptible to Cu nanoparticle [69 and 70]. *B. subtilis*, bacteria with ample proportions of amine and carboxyl groups in its cell walls, can strongly bind to CuO and therefore more sensitive to it [38, 48 and 19]. Hence copper oxide nanoparticles create the impression that, their use in special cases would be more beneficial instead of using other metal nanoparticles [23].

SILICON (Si) and SILICON DIOXIDE (SiO_2) NANOPARTICLES

According to some previous studies, nanowires of Silicon (Si) could interface between the living cells and bacteria, and there by it interrupt the bacterial cell growth, adhesion and spreading. Some investigators stated the good antibacterial activity of silver nanoparticles with silicon nanowires in their studies. A fair biocompatibility was also seen between these nanostructures and the human lung adenocarcinoma epithelial cell line A549 [71 and 72]. Fellahi et al. prepared solicon nanowire substrates, decorated with silver and copper nanoparticles and evaluate their antibacterial activity. According to the authors, their prepared nanoparticles revealed strong antibacterial activity against *E. coli*. However the results conclude that silver based silicon nanowires shows biocompatibility with human lung adenocarcinoma epithelial cell line A549, but in case of copper based silicon nanowires, it shows cytotoxicity [71].

Egger et al. studied the antimicrobial activity of novel silver–silicon nanocomposite and concluded that, as compared to conventional materials like silver zeolite and silver nitrate, this nanocomposite has strong antimicrobial capabilities against various microorganisms [73]. At nano-range, SiO_2 more significantly shows antimicrobial efficacy due to the increased surface area [74]. In another study, Mukha et al. formulated Ag/SiO_2 and Au/SiO_2 nanostructures and evaluated their antimicrobial potency. According to their results Ag/SiO_2 nanocomposites found to be a fair antimicrobial agent against *S. aureus*, *C. albicans* and *E. coli*, while Au/SiO_2 nanocomposites did not exhibit any antibacterial activity against the same microorganisms. Hence the investigators recommended these nanocomposites for being useful in medical and pharmaceutical field, and also for water disinfection [75].

The above studies proposed that formulation of silicon nanocomposites by using other metals like silver can be a better alternative for antimicrobial agents. Furthermore, the non-toxicity of silicon nanoparticles is a remarkable factor for being used in biomedical fields [76].

ALUMINUM OXIDE (Al_2O_3) NANOPARTICLES

To establish the ability of aluminum oxide (Al_2O_3) nanoparticles as antibacterial agent requires more research. Though, previous researches shows comparatively mild bactericidal effects of aluminum oxide and their efficacy is largely depends on their higher concentrations [19 and 77] as well as in association with other metal nanoparticles like silver [78]. One more problem associated with them is that, they are capable of promoting horizontal multi resistance gene transfer, mediated by plasmids across genera [77]. Few years ago the mechanism of action of aluminum nano material was reported aginst *E. coli*, which was based on diffusion and accumulation within the bacterial cells followed by pit formation, perforation and membrane disorganization, finally causes death of the cell [79].

MAGNESIUM OXIDE (MgO) NANOPARTICLES

Magnesium (Mg) can be used in various nanoparticles in the form of magnesium oxide (MgO) or MgX_2 [e.g., Magnesium fluoride (MgF_2)] [19 and 80]. Magnesium based nanoparticles are capable of inducing ROS and can also inhibit the essential bacterial enzymes [48].

Magnesium oxide (MgO) has been proven for its bactericidal potency against Gram-positive as well as Gram-negative bacteria [81]. Researches give the proof that, magnesium oxide nanoparticles can disrupt the bacterial cell membrane followed by leakage of intracellular constituents and finally results in cell death [82]. Some studies show that magnesium oxide triggered the alterations in sensitivity within *E. coli* promoted by active oxygen [83]. However, Leung et al. reported that magnesium oxide nanoparticles can exhibit their high antibacterial potency without occurrence of any ROS production. The authors concluded that the antimicrobial mechanism of magnesium oxide nanoparticles depends upon the destruction of bacterial cell membrane [84]. Some researchers studied the antibacterial efficacy of MgO against *E. coli* or *S. aureus*. They proposed that the antibacterial activity of MgO nanoparticles is depend on the factor that active oxygen, such as superoxide, was present on their surface [85].

CALCIUM OXIDE (CaO) NANOPARTICLES

The potent antibacterial property of calcium oxide (CaO) is associated with the alkalinity and also with active oxygen species. The antibacterial mechanism of CaO nanoparticles has been proven that it is attributed to the generation of active oxygen, such as superoxide, which is present on their surface, and additionally to the higher pH values, through the hydration of CaO with water [86]. Jeong et al.

investigated the antimicrobial efficiency of $CaCO_3$ nanoparticles. The authors indicated that, $CaCO_3$ is transformed in to CaO, through the heat treatment. These nanoparticles has good bactericidal efficacy against *B. subtilis, S. typhimurium, E. coli* and *S. aureus* [87]. The above results suggested that CaO nanoparticles alone or in combination with other disinfectants exhibit greater antibacterial properties. CaO nanoparticles are easily available, economic and biocompatible. Hence, these properties make it a promising antibacterial agent [76]. The investigators finally proposed that these nonmaterial's have applications in environmental preservation, food processing and medical treatments [88].

CLASSICAL APPROACHES FOR THE SYNTHESIS OF METAL NANOPARTICLES

Nanoparticles are generally synthesized by two approaches, either top–down or bottom–up approaches [Figure 2]. In top–down approaches, bulk materials are successively breaking down in to nanosized structures by the use of size reduction mechanical methods. Bottom– up approach is based on the assembly of atoms or molecules to molecular structure in nanoscale range [89]. In top–down approaches, nanoparticle synthesis is achieved by size reduction of primary suitable material. This reduction in size may be performed by various physical and chemical treatments. The major drawback associated with this approach, is that the surface structure of the product is found to be non uniform, as in surface chemistry and the other physical properties of nanoparticles, primarily based on the surface structure [90]. The bottom– up approach is based on nanoparticle production by assemblage of small molecules either by joining the atoms or molecules and small structures [91]. In this the nanostructure, building blocks of the nanoparticles are formulated first and then assembled to produce the final particle [90]. The chemical as well as biological methods of metal nanoparticle production are based on the bottom–up approaches [89]. Another approach for metal nanoparticle synthesis is bottom-to-top approach, which involves chemical reduction methods [91]. Bottom-to-top synthesis not only comprises of toxic chemicals but also generates environmentally hazardous byproducts. Considering all the above stated drawbacks, this method is not commonly used for metal nanoparticle synthesis. General methods used for metal nanoparticle synthesis are as follows:

PHYSICAL METHOD OF NANOPARTICLE SYNTHESIS

Physical methods of nanoparticle synthesis involve different techniques like UV irradiation, laser ablation, radiolysis, sonochemistry etc. Physical method involves vaporization of metal atoms followed by condensation on different supports and leads to rearrangement and accumulation of metal atoms to form small clumps of metal nanoparticles [91]. By applying physical approaches, highly pure and definite shaped nanoparticles are obtained. Though, highly sophisticated instruments, chemicals and radiative heating involves in physical approaches, along with high power consumption, this method becomes expensive to operate [92].

CHEMICAL METHOD OF NANOPARTICLE SYNTHESIS

This method comprises of reduction of metal ions within the solution using different chemicals as reducing agents. Small clumps of metals are formed either by nucleation or aggregation process, which is purely based on the conditions of reaction mixture. The chemicals generally used as reducing agents are hydrogen, sodium borohydride and hydrazine [93]. This method also involves various synthetic or natural polymers as stabilizing agents like chitosan, cellulose, natural rubber and co-polymers micelles. Due to the hydrophobic nature of the above chemicals, they needed the addition of some organic solvents such as ethane, toluene, dimethyl formaldehyde and chloroform. These chemicals are toxic in nature and are non-biodegradable, which limit the production scale. Further, nanoparticle surfaces get contaminated by a few toxic chemicals, which leads to their unsuitability for certain biomedical applications [94]. Therefore, due to such major drawbacks associated with physical and chemical methods, an alternative approach for metal nanoparticle synthesis is an area of interest for investigators.

BIOLOGICAL METHOD OF NANOPARTICLE SYNTHESIS

From the past few years, biological synthesis of metallic nanoparticle has attracted considerable attention. Biogenic synthesis process involves plants and microorganisms for synthesizing nanoparticles [95]. Biogenic synthesis process of nanoparticle synthesis has the advantages over other physicochemical methods of formulation, as this method gives nanoparticles with a better defined size and morphology [96]. The nanoparticles synthesized with microorganism is fruitful in context of pharmacological applications, because of its eco-friendly nature, compatibility to use and is also readily scalable, but this process is quite expensive in comparison to the production with plant-based materials. Plant-based synthesis process is more eco-friendly, low-priced and can be easily scale-up for the large-scale synthesis of nanoparticles, therefore it is more beneficial when compared to the traditional physicochemical methods and further, this method doesn't required high temperature, pressure and toxic chemicals [97]. Biogenic production of metal nanoparticles based on microorganisms like algae, bacteria, fungi and plants were reported in plenty of research articles. This is purely attributed to their antioxidant or reducing potencies which are responsible for metal nanoparticle reduction. Further, microbial synthesis needs immense aseptic conditions with sophisticated care and therefore, this method is not suitable for large scale production. On the other hand, plant based synthesis of nanoparticle is quite beneficial over microbes based methods, due to its easy scale-up process with less maintenance of cell culture [98]. Nanoparticle synthesis with plant extract is also fruitful, because it cut down the sophistication, related to isolation of microbes and culture medium preparation, and therefore this method is highly cost-effective and practical when compared to microorganism based synthesis. Plant based synthesis method is a one-step process of synthesis, while microbial synthesis takes long time duration and sometimes unable of producing nanoparticles due to mutation; thus, research on plant is expanding rapidly [99]. Various nanoparticle synthesis methods are discovered such as metal ions chemical reduction within aqueous solutions in presence or absence of stabilizing agents, thermal decomposition with organic solutions. The advantages of green synthesis of nanoparticles over the physical and chemical methods are:

- Clean and eco-friendly approach, as toxic chemicals are not used;
- The active biological component itself act as reducing and capping agent , therefore reduction in the overall cost of synthesis process;
- Can be used at large scale production of nanoparticles;
- External experimental conditions like high energy and high pressure are not required, which leads to energy saving process [100].

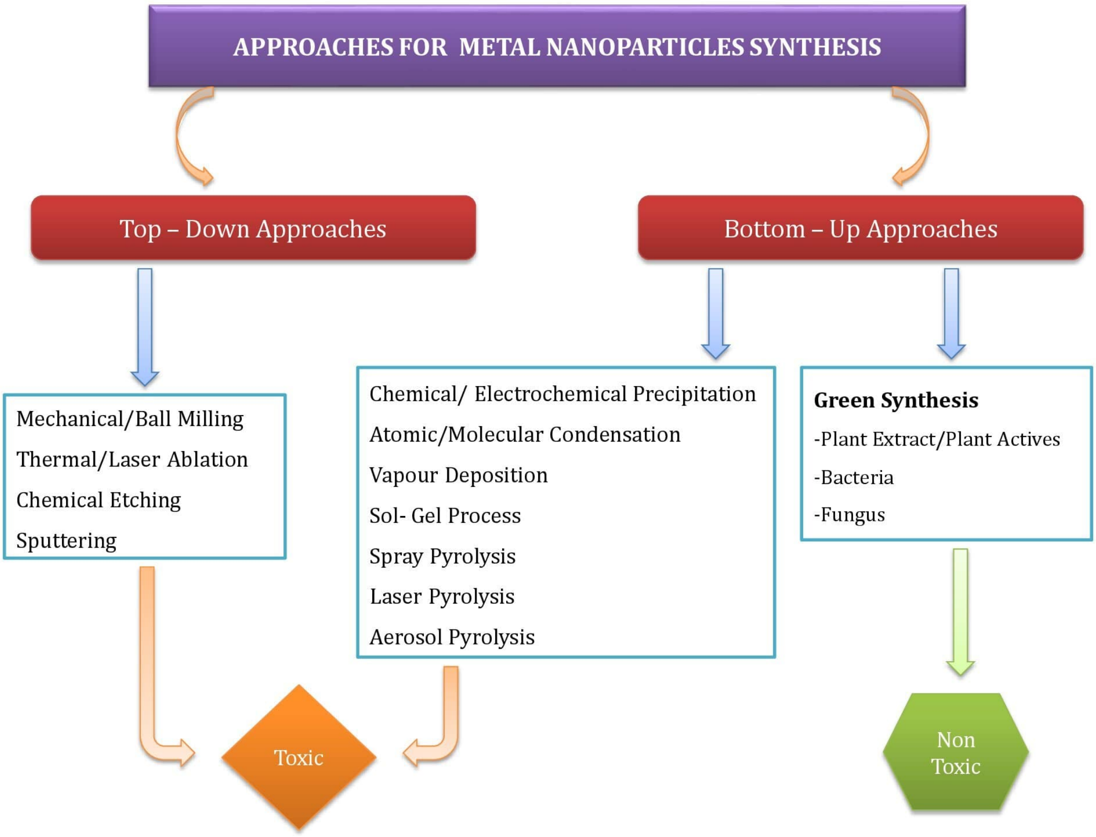

FIGURE2: VARIOUS APPROACHES OF SYNTHESIS OF METAL NANOPARTICLES {Recreated from [101]}.

PLANT EXTRACTS-MEDIATED SYNTHESIS OF NANOPARTICLES

To prepare the plant extract, different parts of the plants are used as fresh or dry material such as the fruit, leaf, peel, petal and shoot. The extraction process includes saturation of the plant material in a green solvent with or without stirring, along with subsequent filtration and centrifugation. The filtered extract is rich in the reducing and capping agents, which required for the bioreduction of metallic ions [Figure 3]. The advantage of using dried plant is that, it has a long shelf life at room temperature, but it is important to store the fresh plant at −20°C to avoid any deterioration. The dry plant material should also be free from seasonal factors that can cause the variations in plant constituents [102 and 103].

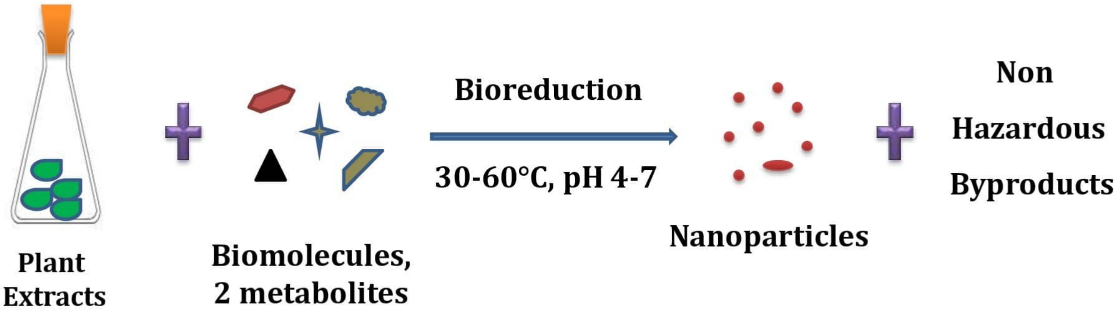

FIGURE3: PROPOSED PROTOCOL FOR SYNTHESIS OF NANOPARTICLES USING PLANT EXTRACTS {Recreated from [24]}.

A number of factors such as temperature, concentrations of the extract, pH and also the metal ions can affect the size and shape of the synthesized nanoparticles [104]. The plant extract based synthesis procedures usually have a high rate of reaction, taking several minutes to several hours for completion, depending on the type and amount of the plant extract. Most plants, especially the perennial plants, are almost always naturally available. Microorganism based nanosynthesis involves heating of the reaction mixture or culture medium, while in case of plant extract mediated synthesis of metallic nanoparticle, there is no need of heating, as it accomplished at room temperature . Plant extract based synthesis includes simple handling and easy reaction conditions, and therefore, it is having more suitability for large-scale production, when compared to microorganism based nanosynthesis [105, 106 and 107]. Table 1 shows various plant resource which are used to synthesize metal nanoparticles.

TABLE1: PLANT RESOURCES BASED METAL NANOPARTICLES.

S.No.	Name of Plant/Plant Active Used	Metal Nanoparticles Made	Parts of Plant Used	Nanoparticle Size (Nm)	Nanoparticle Shapes	Pharmacological Activity	Reference
1.	*Citrus maxima*	Ag	Fruit	11.3–12.8 nm	Spherical	Antimicrobial (evaluated against *Acidovorax oryzae* strain RS-2)	[108]
2.	*Telfairia occidentalis*	AgO	Leaf	15.84 - 19.2 nm	Spherical	Antibacterial (evaluated against *K. Pneumonia*)	[109]
3.	*Vitex negundo L.*	Ag	Leaf	10 – 100 nm	Spherical	Antibacterial (evaluated against *Proteus vulgaris, E. coli, P. aeruginosa, K. pneumonia, Salmonella paratyphi* and *S. aureus*)	[110]
4.	*Eucalyptus globulus*	ZnO	Leaf	40 nm	Needle and Spherical	Antimicrobial (evaluated against , *S. aureus* ATCC 43300, *S. aureus* ATCC 25923, *E. faecalis* ATCC 29212,*E. coli* ATCC 25922,*S. enteritidis* ATCC 13076 and *P. aeruginosa* ATCC 27853, *S. typhimurium, K. pneumoniae*, , *Acinetobacter baumannii* and *Candida albicans*) and Anti-biofilm activity (evaluated against *P. aeruginosa ATCC*	[111]

						27853 and *S. aureus* ATCC 25923)	
5.	*Solanum nigurum*	Au, Pd and Ag	Leaf	3.46 nm (Ag) 9.39 nm (Au) and 21.55 nm (Pd)	Spherical	Antibacterial, Antimicrobial (evaluated against *Escherichia coli*)	[112]
6.	*Pimpinella anisum*	Ag and Au	Seed	18-22 nm (Ag) 16-22 nm (Au)	Spherical	Antioxidant (evaluated by 1,1-diphenyl-2-picryl-hydrazyl (DPPH)), Antibacterial (evaluated against *S. aureus* and *E. coli*) and Antifungal (evaluated against *Aspergillus flavus* and *Candida albicans*)	[113]
7.	*Aesculus hippocastanum*	Ag	Leaf	50 ± 5 nm	Spherical	Antioxidant (evaluated by 1,1-diphenyl-2-picryl-hydrazyl (DPPH), Reducing power assay, Superoxide anion radical scavenging assay), Antibacterial (evaluated against *Staphylococcus aureus*, *S. epidermidis*, *Listeria monocytogenes*, *Corynebacterium renale*, *Micrococcus luteus*, *Bacillus subtilis*, *B. cereus*, *Enterococcus faecalis, Pseudomonas aeruginosa*, *P. fluorescens*, *Escherichia coli*, *Enterobacter aerogenes*, *Klebsiella pneumonia*, *Proteus mirabilis*, *Candida albicans, C. tropicalis* and *C. krusei*)	[114]
8.	*Phyllanthus emblica*	Ag	Fruit	19 - 45 nm	Hexagonal	Antibacterial (evaluated against *Klebsiella pneumoniae* and *Staphylococcus aureus*)	[115]
9.	*Allium saralicum* R.M. Fritsch	Zn	Leaf	~19 nm	Spherical	Anticancer (evaluated on HUVEC line by MTT assay), Antioxidant (evaluated by 1,1-diphenyl-2-picryl-hydrazyl (DPPH)), Cutaneous wound healing (evaluated on Sprague Dawley rats), Antimicrobial (evaluated against *C. guilliermondii*, *C. krusei*, *C. glabrata*, *C. albicans*, *Staphylococcus aureus* (ATCC No. 25923), *B. subtilis*, *E. coli* O157:H7, *P. aeruginosa*, *Salmonella typhimurium* (ATCC No. 14028) and *Streptococcus pneumonia* (ATCC No. 49619))	[116]
10.	*Averrhoa*	ZnO	Fruit	35.4 - 59.5	Spherical	Antibacterial	[117]

	bilimbi			nm		(evaluated against planktonic and biofilm *Escherichia coli*)	
11.	*Curcuma longa* L.	Ag	Leaf	15 - 40 nm	Spherical	Antimicrobial (evaluated against *S.aureus, S.pyogenes, E.coli, P.aeruginosa,* and *C.albicans*)	[118]
12.	*Echinochloa frumentacea*	ZnO	Grain	35 - 65 nm	Hexagonal	Antibacterial (evaluated against *S. typhi* and *B. pumilus*), Cytotoxicity study (evaluated on E.coli AB 1157)	[119]
13.	*Bergenia ciliata*	ZnO	Root	~30 nm.	Flower-Like	Antimicrobial (evaluated against *Yersenia enterocolitica*, *S. aureus, S. typhi, P. aeruginosa*, , *E. coli*, and *Bacillus Subtilis*), Anticancer (evaluated on HeLa cells of human cervical cancer and Human colon cancer (HT-29) cells by MTT assay), Antioxidant (evaluated by ABTS and 1,1-diphenyl-2-picryl-hydrazyl (DPPH))	[120]
14.	*Crateva adansonii*	ZnO	Leaf	30-55 nm	Hexagonal	Antimicrobial (evaluated against *P. aeruginosa, B. subtilis , S. aureus, and E. coli*)	[121]
15.	*Hibiscus rosasinensis*	Ag	Leaf	15–30 nm	Spherical	Antibacterial, Antimicrobial (evaluated against *S. aureus* and *E. coli*)	[122]
16.	*Allium rotundum l., Ferulago angulate Boiss and Falcaria vulgaris Bernh.*	Ag	Leaf	20.5 nm	Spherical	Antibacterial, Antimicrobial (evaluated against *Pseudomonas aeruginosa* PAO1 and *Staphylococcus aureus* ATCC 25923)	[123]
17.	*Aegle marmelos*	Ag	Fruit	159 - 181 nm	Spherical	Antimicrobial (evaluated against *E. coli, Bacillus cereus, P. aeruginosa, Staphylococcus aureus, S. typhi, Shigella dysenteriae, Yersinia pestis*)	[124]
18.	*Artocarpus Hetrophyllus*	Ag_2O	Leaf	~14 nm	Spherical	Antibacterial, Antimicrobial	[125]
19.	*Azadirachta indica*	Ag and ZnO	Leaf	8 - 50 nm	-	Antibacterial (evaluated against *Bacillus subtilis* (MTCC No.10619))	[126]
20.	*Clitoria ternatea*	Ag and Au	Flower	18-50 nm	-	Antibacterial (evaluated against *E. coli, Streptococcus pyogenes, K. pneumonia and S. aureus*), Antioxidant (evaluated by 1,1-diphenyl-2-picryl-hydrazyl (DPPH))	[127]
21.	Curcumin	SiO_2	-	36 - 40 nm	-	Antimicrobial (evaluated against *P.*	[128]

						aeruginosa and S. aureus)	
22.	*Calotropis gigantea L.*	Ag	Flower	-	-	Antibacterial (evaluated against *Bacillus subtilis, Pseudomonas putida* and *Escherichia coli*)	[129]
23.	*Terminalia belerica, Terminalia chebula, Swertia chiryta, Plumbago zeylanica, Holarrhena antidysenterica*	CuO, ZnO, FeO	Leaf, Stem, Fruit, Root and Bark	2-10 nm (CuO), 2-10 nm (ZnO), 15-23 nm (FeO)	Spherical (CuO). Spherical (ZnO), Spherical (FeO)	Antibacterial (evaluated against *Staphylococcus aureus* (ATCC-6538), *Escherichia coli* (ATCC-8739) and *Salmonella enteric (MTCC-3858)*)	[130]
24.	*Myrtus communis L.*	Ag	Leaf	~15 nm	Spherical	Antibacterial (evaluated against Methicillin-resistantStaphylococcus aureus(MRSA) ATCC 43300andEscherichia coliATCC 35218)	[131]
25.	*Citrullis lanatus var*	Au	Fruit	100-350 nm (Spherical), 200-500 nm (Triangular pyramid)	Spherical, Triangular pyramid	Antibacterial (evaluated against *S. epidermis* and *E. coli*)	[132]
26.	*Ageratum conyzoides*	Fe	Whole Plant	11.45-614.03 nm	Cubic	Antimicrobial (evaluated against *Staphylococcus aureus* (ATCC-25923), *Bacillus subtilis*, *Pseudomonas aeruginosa* (ATCC-27853), *C. albicans* and *Escherichia coli* (ATCC-25922)), Photocatalytic activity (Methylene blue degradation)	[133]
27.	*P. domestica L.(Plum), P. Persia L. (Peach) and A. deliciosa (Kiwi)*	TiO_2	Fruits Peel	47.1-63.2 nm (Plum) 54.1-85.1 nm (Kiwi) 200 nm (Peach)	Cylindrical	Antibacterial (evaluated against *B. substilis, S. aureus*, *P. aeruginosa* and *E. coli*), Antioxidant (evaluated by 1,1-diphenyl-2-picryl-hydrazyl (DPPH), reducing power assays, hydrogen peroxide, and nitric oxide radical scavenging)	[134]
28.	*Prosopis farcta*	Ag	Fruit	10.26-14.65 nm	Spherical	Antioxidant (evaluated by 1,1-diphenyl-2-picryl-hydrazyl (DPPH)), Antimicrobial (evaluated against, *S. pneumonia, S. typhi, S. aureus* and *E. coli*)	[135]
29.	*Camellia sinensis*	Au and Ag	Leaf	~10 nm (Au), ~30 nm (Ag)	Spherical	Antimicrobial [evaluated against *S. aureus* (NBRC 12732) and *K. pneumoniae* (NBRC 13277)]	[136]
30.	*Jatropha curcas*	Ag	Seed	80 nm - 95 nm	Spherical	Antibacterial (evaluated against *P. aeruginosa, B. subtilis* and *E. coli*)	[137]
31.	*Juglans regia*	Ag	Leaf	20–30 nm	Spherical	Antibacterial (evaluated against *K. pneumonia, S. aureus P. vulgaris, P. aeruginosa* and *E. coli*)	[138]
32.	*Embelia ribes* Burm.f.	Ag	Fruit	~30 nm	Spherical	Antibacterial (evaluated against *Bacillus*	[139]

						subtilis), Anticancer (evaluated by MTT assay on MCF-7 cell lines)	
33.	*Cardiospermum halicacabum*	ZnO	Leaf	~48 nm	Cubic	Antibacterial (evaluated against*, P. aeruginosa, S. saprophyticus, B. subtilis* and *E. coli*)	[140]
34.	*Panax ginseng*	Zn	Root	45 nm - 85 nm	Spherical	Anticancer (evaluated by MTT assay on L20B tumor cell lines)	[141]
35.	*Ocimum americanum L.*	ZnO	Leaf	~21 nm	Spherical	Antimicrobial (evaluated against *K. pneumonia, B. cereus, S. typhi, S. aureus, V. parahaemolyticus, Xanthomonas citri , P. aeruginosa, E. coli, Aspergillus parasiticus, C. albicans,* Antioxidant (evaluated by 1,1-diphenyl-2-picryl-hydrazyl (DPPH))	[142]
36.	*Terminalia arjuna*	Au	Leaf	15 - 30 nm	Spherical	Antibacterial (evaluated against *S. typhimurium*, *P. aeruginosa* and *S. aureus*)	[143]
37.	*Berberis vulgaris*	Ag	Leaf and Root	30 - 70 nm	Spherical	Antibacterial (evaluated against *E. coli* and *S. Aureus*)	[144]
38.	*Cressa cretica*	Au	Leaf	15-22 nm	Spherical, pentagonal, rod and hexagonal	Antibacterial (evaluated against *S. aureus, S. pyogenes, K. pneumonia* and *E. coli*), Catalytic efficacy (4-nitrophenol reduction)	[145]
39.	*Cassia siamea*	ZnO	Leaf	below 100 nm	Slightly Ellipsoidal/ Spherical	Antimicrobial (evaluated against *Pseudomonas aeruginosa*, *Staphylococcus saprophyticus*, *Streptococcus pyogenes* and *Proteus mirabilis*)	[146]
40.	Hesperidin and Naringin	Ag and Au	-	100–225 nm	Spherical	Antibacterial (evaluated against neuropathogenic *E. coli* and methicillin resistant *S. aureus*)	[147]
41.	Citric Acid, Eugenol, Scopolamine, D-Glucose, Khelin Coumarin, Sucrose, Thymol and L-Asorbic	Au	-	30-80 nm (glucose), 150 nm (eugenol), 230 nm (thymol)	Spherical	Antibacterial, Anticancer, Antifungal	[148]
42.	*Catha edulis Forsk (Khat)*	CuO	Leaf	-	-	Antibacterial (evaluated against *S. typhimurium* and *E. coli*)	[149]
43.	*Rhizophora apiculata*	Ag	Leaf	-	-	Hepatoprotective (evaluated on hepatotoxin-induced liver damage in male Swiss albino mice)	[150]
44.	*Annona reticulata*	Ag	Leaf	6.48 - 8.13 nm	Cubic	Mosquito Larvicidal bioassay (evaluated on vector of dengue *Aedes aegypti*), Antibacterial (evaluated against *E. coli, Bacillus*	[151]

						cereus *S. aureus* and *P. aeruginosa*)	
45.	*Cleome viscosa*	Ag	Fruit	20 - 50 nm	Spherical	Antibacterial (evaluated against *B. subtilis, K. Pneumonia, E. coli* and *S. aureus*), Anticancer (evaluated on PA1-Ovarian teratocarcinoma cell line and A549-Human lung adenocarcinoma by MTT assay)	[152]
46.	*Carissa carandas*	Ag	Fruit	10–60 nm	Spherical	Antibacterial (evaluated against *Aeromonas hydrophila, Acinetobacter sp.,* and *Staphylococcus aureus*)	[153]
47.	*Nyctanthes arbor-tristis*	ZnO	Flower	12–32 nm	-	Antifungal (evaluated against *Aspergillus niger, Penicillium expansum, Alternaria alternata, Botrytis cinerea* and *Fusarium oxysporum*)	[154]
48.	*Crocus sativus L.*	Ag	Flower	12–20 nm	Spherical	Antibacterial (evaluated against *Bacillus subtilis, E. coli, K. pneumonia, P. aeruginosa* and *Shigella flexneri*)	[155]
49.	*Ocimum Sanctum,* Quercetin	Ag	Leaf	14.6 nm (Tulsi extract) 11.35 nm (Quercetin)	Spherical	Antibacterial (evaluated against *Escherichia coli*)	[156]
50.	*Angelicae Pubescentis Radix*	Ag and Au	Root	12.48 nm (Ag), 7.44 nm (Au)	Quasi-spherical(Ag), Spherical Icosahedral (Au)	Antioxidant (evaluated by 1,1-diphenyl-2-picryl-hydrazyl (DPPH), Antimicrobial (evaluated against *S. aureus, Salmonella enterica, E. coli* and *P. aeruginosa*)	[157]

CONCLUSION

A number of metals used for plant resources based green synthesis of nanoparticles like gold (Au), silver (Ag), zinc oxide (ZnO), copper (Cu), titanium (Ti), nickel (Ni), platinum (Pt), selenium (Se), cobalt (Co), palladium (Pd) and magnetite (Fe_3O_4) have already been reported, and have been proved as a potent remedy against different infectious diseases including other acute ailments [158, 24 and 159]. The plant mediated metal nanoparticles have been shown to possess various therapeutic activities such as antioxidant, antimicrobial, anti-inflammatory, anticancer, antidiabetic and immunomodulatory [160, 161, 162 and 163]. Some previous studies suggested that, various phytochemicals such as flavonoids, sugars, alkaloids, proteins, phenols and terpenoids are responsible for bioreduction, capping and stabilization of metal ions during nanoparticle synthesis [164 and 165].

Despite the ease involved in the purification of nanoparticles synthesized using only one single active substance in plant extract, it is important to further study the metal nanoparticles with a biomedical perspective for the treatment of particular diseases. At present, limited information is available in the scientific literature regarding the use of a single substance from plant extract for the synthesis of metal nanoparticles. Recent studies suggested that the flavonoids, due to its ample presence in the plant extracts, have a big contribution toward the bioreduction, capping and stabilization of metal ions into nanoparticle formation [156, 166, 167, and 168].

This exhaustive compilation work will be beneficial for researchers, as using plant sources for metal nanoparticle synthesis is energy efficient, cost effective, protecting human health and environment leading to lesser waste and safer products. Plant resources can act as both reducing and capping agent during nanoparticle synthesis, and thus stabilizes the metal nanoparticles in shape and size controlled manner. This environment-friendly approach could be a competitive alternative to the traditional physical and chemical approaches used for synthesis of metal nanoparticle and thus has a potential to use in biomedical applications like in the field of cosmetics, medical devices, food industries, pharmaceuticals, opto-electronics and thus will definitely lead into a highly productive and innovative phase of research in near future.

REFERENCES

1. Jin, J., Sklar, G. E., Oh, V. M. S., & Li, S. C. (2008). Factors affecting therapeutic compliance: A review from the patient's perspective. *Therapeutics and clinical risk management*, *4*(1), 269.
2. Singh, D. (2015). Application of novel drug delivery system in enhancing phytoconstituents. *Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm*, *9*(4).
3. Patel, R., Singh, S. K., Singh, S., Sheth, N. R., & Gendle, R. (2009). Development and characterization of curcumin loaded transfersome for transdermal delivery. *Journal of pharmaceutical sciences and research*, *1*(4), 71.
4. Alanazi, F. K., Radwan, A. A., & Alsarra, I. A. (2010). Biopharmaceutical applications of nanogold. *Saudi Pharmaceutical Journal*, *18*(4), 179-193.
5. Taniguchi, N. (1974). On the basic concept of nanotechnology. *Proceeding of the ICPE*.
6. Feynman, R. P. (1959). There's plenty of room at the bottom. *Engineering and science*, *23*.
7. Rao, J. P., & Geckeler, K. E. (2011). Polymer nanoparticles: preparation techniques and size-control parameters. *Progress in polymer science*, *36*(7), 887-913.
8. Gupta, T., & Jayatissa, A. H. (2003, August). Recent advances in nanotechnology: key issues & potential problem areas. In *2003 Third IEEE Conference on Nanotechnology, 2003. IEEE-NANO 2003.* (Vol. 2, pp. 469-472). IEEE.
9. Parham, S., Wicaksono, D. H., Bagherbaigi, S., Lee, S. L., & Nur, H. (2016). Antimicrobial treatment of different metal oxide nanoparticles: a critical review. *Journal of the Chinese Chemical Society*, *63*(4), 385-393.
10. Kreuter, J. (2007). Nanoparticles—a historical perspective. *International journal of pharmaceutics*, *331*(1), 1-10.
11. Chandran, S. P., Chaudhary, M., Pasricha, R., Ahmad, A., & Sastry, M. (2006). Synthesis of gold nanotriangles and silver nanoparticles using Aloevera plant extract. *Biotechnology progress*, *22*(2), 577-583.
12. Adibkia, K., Omidi, Y., Siahi, M. R., Javadzadeh, A. R., Barzegar-Jalali, M., Barar, J., ... & Nokhodchi, A. (2007). Inhibition of endotoxin-induced uveitis by methylprednisolone acetate nanosuspension in rabbits. *Journal of Ocular Pharmacology and Therapeutics*, *23*(5), 421-432.
13. Adibkia, K., Javadzadeh, Y., Dastmalchi, S., Mohammadi, G., Niri, F. K., & Alaei-Beirami, M. (2011). Naproxen–eudragit® RS100 nanoparticles: Preparation and physicochemical characterization. *Colloids and Surfaces B: Biointerfaces*, *83*(1), 155-159.
14. Sabzevari, A., Adibkia, K., Hashemi, H., Hedayatfar, A., Mohsenzadeh, N., Atyabi, F., ... & Dinarvand, R. (2013). Polymeric triamcinolone acetonide nanoparticles as a new alternative in the treatment of uveitis: in vitro and in vivo studies. *European journal of pharmaceutics and biopharmaceutics*, *84*(1), 63-71.
15. Samia, A. C., Dayal, S., & Burda, C. (2006). Quantum dot-based energy transfer: perspectives and potential for applications in photodynamic therapy. *Photochemistry and photobiology*, *82*(3), 617-625.
16. Whitehead, K. A., Vaidya, M., Liauw, C. M., Brownson, D. A. C., Ramalingam, P., Kamieniak, J., ... & Banks, C. E. (2017). Antimicrobial activity of graphene oxide-metal hybrids. *International Biodeterioration & Biodegradation*, *123*, 182-190.
17. Liu, H. L., Hua, M. Y., Yang, H. W., Huang, C. Y., Chu, P. C., Wu, J. S., ... & Wei, K. C. (2010). Magnetic resonance monitoring of focused ultrasound/magnetic nanoparticle targeting delivery of therapeutic agents to the brain. *Proceedings of the National Academy of Sciences*, *107*(34), 15205-15210.
18. Sharifi-Rad, J., Hoseini-Alfatemi, S. M., Sharifi-Rad, M., & Iriti, M. (2014). Antimicrobial synergic effect of Allicin and silver nanoparticles on skin infection caused by methicillin resistant Staphylococcus aureus spp. *Annals of medical and health sciences research*, *4*(6), 863-868.
19. Pelgrift, R. Y., & Friedman, A. J. (2013). Nanotechnology as a therapeutic tool to combat microbial resistance. *Advanced drug delivery reviews*, *65*(13-14), 1803-1815.
20. Zhang, L., Pornpattananangkul, D., Hu, C. M., & Huang, C. M. (2010). Development of nanoparticles for antimicrobial drug delivery. *Current medicinal chemistry*, *17*(6), 585-594.
21. Loomba, L., & Scarabelli, T. (2013). Metallic nanoparticles and their medicinal potential. Part I: gold and silver colloids. *Therapeutic delivery*, *4*(7), 859-873.
22. Malarkodi, C., Rajeshkumar, S., Paulkumar, K., Vanaja, M., Gnanajobitha, G., & Annadurai, G. (2014). Biosynthesis and antimicrobial activity of semiconductor nanoparticles against oral pathogens. *Bioinorganic chemistry and applications*, *2014*.
23. Beyth, N., Houri-Haddad, Y., Domb, A., Khan, W., & Hazan, R. (2015). Alternative antimicrobial approach: nano-antimicrobial materials. *Evidence-based complementary and alternative medicine*, *2015*.
24. Kuppusamy, P., Yusoff, M. M., Maniam, G. P., & Govindan, N. (2016). Biosynthesis of metallic nanoparticles using plant derivatives and their new avenues in pharmacological applications–An updated report. *Saudi Pharmaceutical Journal*, *24*(4), 473-484.
25. Rai, M., Yadav, A., & Gade, A. (2009). Silver nanoparticles as a new generation of antimicrobials. *Biotechnology advances*, *27*(1), 76-83.

26. Poulose, S., Panda, T., Nair, P. P., & Theodore, T. (2014). Biosynthesis of silver nanoparticles. *Journal of nanoscience and nanotechnology*, *14*(2), 2038-2049.
27. Lok, C. N., Ho, C. M., Chen, R., He, Q. Y., Yu, W. Y., Sun, H., ... & Che, C. M. (2006). Proteomic analysis of the mode of antibacterial action of silver nanoparticles. *Journal of proteome research*, *5*(4), 916-924.
28. Yun, H., Kim, J. D., Choi, H. C., & Lee, C. W. (2013). Antibacterial activity of CNT-Ag and GO-Ag nanocomposites against gram-negative and gram-positive bacteria. *Bull Korean Chem Soc*, *34*(11), 3261.
29. Iavicoli, I., Fontana, L., Leso, V., & Bergamaschi, A. (2013). The effects of nanomaterials as endocrine disruptors. *International journal of molecular sciences*, *14*(8), 16732-16801.
30. Egger, S., Lehmann, R. P., Height, M. J., Loessner, M. J., & Schuppler, M. (2009). Antimicrobial properties of a novel silver-silica nanocomposite material. *Applied and environmental microbiology*, *75*(9), 2973-2976.
31. Jo, Y. K., Kim, B. H., & Jung, G. (2009). Antifungal activity of silver ions and nanoparticles on phytopathogenic fungi. *Plant disease*, *93*(10), 1037-1043.
32. Pal, S., Tak, Y. K., & Song, J. M. (2007). Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the gram-negative bacterium Escherichia coli. *Applied and environmental microbiology*, *73*(6), 1712-1720.
33. Allahverdiyev, A. M., Abamor, E. S., Bagirova, M., & Rafailovich, M. (2011). Antimicrobial effects of TiO2 and Ag2O nanoparticles against drug-resistant bacteria and leishmania parasites. *Future microbiology*, *6*(8), 933-940.
34. Sondi, I., & Salopek-Sondi, B. (2004). Silver nanoparticles as antimicrobial agent: a case study on E. coli as a model for Gram-negative bacteria. *Journal of colloid and interface science*, *275*(1), 177-182.
35. Jayandran, M., Haneefa, M. M., & Balasubramanian, V. (2015). Synthesis, Characterization and antimicrobial activities of turmeric curcumin and curcumin stabilized zinc nanoparticles-A green approach. *Research Journal of Pharmacy and Technology*, *8*(4), 445-451.
36. Owaid, M. N., Zaidan, T. A., Muslim, R. F., & Hammood, M. A. (2019). Biosynthesis, characterization and cytotoxicity of zinc nanoparticles using Panax ginseng roots, Araliaceae. *ACTA Pharmaceutica Sciencia*, *57*(1).
37. Palanikumar, L., Ramasamy, S. N., & Balachandran, C. (2014). Size-dependent antimicrobial response of zinc oxide nanoparticles. *IET nanobiotechnology*, *8*(2), 111-117.
38. Huh, A. J., & Kwon, Y. J. (2011). "Nanoantibiotics": a new paradigm for treating infectious diseases using nanomaterials in the antibiotics resistant era. *Journal of controlled release*, *156*(2), 128-145.
39. Huang, Z., Zheng, X., Yan, D., Yin, G., Liao, X., Kang, Y., ... & Hao, B. (2008). Toxicological effect of ZnO nanoparticles based on bacteria. *Langmuir*, *24*(8), 4140-4144.
40. Chakraborti, S., Mandal, A. K., Sarwar, S., Singh, P., Chakraborty, R., & Chakrabarti, P. (2014). Bactericidal effect of polyethyleneimine capped ZnO nanoparticles on multiple antibiotic resistant bacteria harboring genes of high-pathogenicity island. *Colloids and Surfaces B: Biointerfaces*, *121*, 44-53.
41. Jin, T., Sun, D., Su, J. Y., Zhang, H., & Sue, H. J. (2009). Antimicrobial efficacy of zinc oxide quantum dots against Listeria monocytogenes, Salmonella enteritidis, and Escherichia coli O157: H7. *Journal of food science*, *74*(1), M46-M52.
42. Reddy, L. S., Nisha, M. M., Joice, M., & Shilpa, P. N. (2014). Antimicrobial activity of zinc oxide (ZnO) nanoparticle against Klebsiella pneumoniae. *Pharmaceutical biology*, *52*(11), 1388-1397.
43. Kasraei, S., Sami, L., Hendi, S., AliKhani, M. Y., Rezaei-Soufi, L., & Khamverdi, Z. (2014). Antibacterial properties of composite resins incorporating silver and zinc oxide nanoparticles on Streptococcus mutans and Lactobacillus. *Restorative dentistry & endodontics*, *39*(2), 109-114.
44. Liu, Y. J., He, L. L., Mustapha, A., Li, H., Hu, Z. Q., & Lin, M. S. (2009). Antibacterial activities of zinc oxide nanoparticles against Escherichia coli O157: H7. *Journal of applied microbiology*, *107*(4), 1193-1201.
45. Reddy, K. M., Feris, K., Bell, J., Wingett, D. G., Hanley, C., & Punnoose, A. (2007). Selective toxicity of zinc oxide nanoparticles to prokaryotic and eukaryotic systems. *Applied physics letters*, *90*(21), 213902.
46. Dastjerdi, R., & Montazer, M. (2010). A review on the application of inorganic nano-structured materials in the modification of textiles: focus on anti-microbial properties. *Colloids and surfaces B: Biointerfaces*, *79*(1), 5-18.
47. Applerot, G., Lellouche, J., Perkas, N., Nitzan, Y., Gedanken, A., & Banin, E. (2012). ZnO nanoparticle-coated surfaces inhibit bacterial biofilm formation and increase antibiotic susceptibility. *Rsc Advances*, *2*(6), 2314-2321.
48. Blecher, K., Nasir, A., & Friedman, A. (2011). The growing role of nanotechnology in combating infectious disease. *Virulence*, *2*(5), 395-401.
49. Pati, R., Mehta, R. K., Mohanty, S., Padhi, A., Sengupta, M., Vaseeharan, B., ... & Sonawane, A. (2014). Topical application of zinc oxide nanoparticles reduces bacterial skin infection in mice and exhibits antibacterial activity by inducing oxidative stress response and cell membrane disintegration in macrophages. *Nanomedicine: Nanotechnology, Biology and Medicine*, *10*(6), 1195-1208.
50. Pan, X., Redding, J. E., Wiley, P. A., Wen, L., McConnell, J. S., & Zhang, B. (2010). Mutagenicity evaluation of metal oxide nanoparticles by the bacterial reverse mutation assay. *Chemosphere*, *79*(1), 113-116.
51. Wang, L., Hu, C., & Shao, L. (2017). The antimicrobial activity of nanoparticles: present situation and prospects for the future. *International journal of nanomedicine*, *12*, 1227.
52. Hamal, D. B., Haggstrom, J. A., Marchin, G. L., Ikenberry, M. A., Hohn, K., & Klabunde, K. J. (2010). A multifunctional biocide/sporocide and photocatalyst based on titanium dioxide (TiO2) codoped with silver, carbon, and sulfur. *Langmuir*, *26*(4), 2805-2810.
53. Reddy, M. P., Venugopal, A., & Subrahmanyam, M. (2007). Hydroxyapatite-supported Ag–TiO2 as Escherichia coli disinfection photocatalyst. *Water research*, *41*(2), 379-386.

54. Gomathi Devi, L., & Nagaraj, B. (2014). Disinfection of E scherichia Coli Gram Negative Bacteria Using Surface Modified TiO2: Optimization of Ag Metallization and Depiction of Charge Transfer Mechanism. *Photochemistry and photobiology*, *90*(5), 1089-1098.
55. Ungureanu, C., Popescu, S., Purcel, G., Tofan, V., Popescu, M., Sălăgeanu, A., & Pîrvu, C. (2014). Improved antibacterial behavior of titanium surface with torularhodin–polypyrrole film. *Materials Science and Engineering: C*, *42*, 726-733.
56. Cui, Y., Zhao, Y., Tian, Y., Zhang, W., Lü, X., & Jiang, X. (2012). The molecular mechanism of action of bactericidal gold nanoparticles on Escherichia coli. *Biomaterials*, *33*(7), 2327-2333.
57. Zhou, Y., Kong, Y., Kundu, S., Cirillo, J. D., & Liang, H. (2012). Antibacterial activities of gold and silver nanoparticles against Escherichia coli and bacillus Calmette-Guérin. *Journal of nanobiotechnology*, *10*(1), 19.
58. Goodman, C. M., McCusker, C. D., Yilmaz, T., & Rotello, V. M. (2004). Toxicity of gold nanoparticles functionalized with cationic and anionic side chains. *Bioconjugate chemistry*, *15*(4), 897-900.
59. Lima, E., Guerra, R., Lara, V., & Guzmán, A. (2013). Gold nanoparticles as efficient antimicrobial agents for Escherichia coli and Salmonella typhi. *Chemistry Central Journal*, *7*(1), 11.
60. Anghel, A. G., Grumezescu, A. M., Chirea, M., Grumezescu, V., Socol, G., Iordache, F., ... & Holban, A. M. (2014). MAPLE fabricated Fe3O4@ Cinnamomum verum antimicrobial surfaces for improved gastrostomy tubes. *Molecules*, *19*(7), 8981-8994.
61. Huang, W. C., Tsai, P. J., & Chen, Y. C. (2009). Multifunctional Fe3O4@ Au nanoeggs as photothermal agents for selective killing of nosocomial and antibiotic-resistant bacteria. *Small*, *5*(1), 51-56.
62. Ahamed, M., Alhadlaq, H. A., Khan, M. A., Karuppiah, P., & Al-Dhabi, N. A. (2014). Synthesis, characterization, and antimicrobial activity of copper oxide nanoparticles. *Journal of Nanomaterials*, *2014*.
63. Usman, M. S., El Zowalaty, M. E., Shameli, K., Zainuddin, N., Salama, M., & Ibrahim, N. A. (2013). Synthesis, characterization, and antimicrobial properties of copper nanoparticles. *International journal of nanomedicine*, *8*, 4467.
64. Wu, H. Q., Wei, X. W., Shao, M. W., Gu, J. S., & Qu, M. Z. (2002). Synthesis of copper oxide nanoparticles using carbon nanotubes as templates. *Chemical physics letters*, *364*(1-2), 152-156.
65. Mahapatra, O., Bhagat, M., Gopalakrishnan, C., & Arunachalam, K. D. (2008). Ultrafine dispersed CuO nanoparticles and their antibacterial activity. *Journal of Experimental Nanoscience*, *3*(3), 185-193.
66. Azam, A., Ahmed, A. S., Oves, M., Khan, M. S., & Memic, A. (2012). Size-dependent antimicrobial properties of CuO nanoparticles against Gram-positive and-negative bacterial strains. *International journal of nanomedicine*, *7*, 3527.
67. Esteban-Tejeda, L., Malpartida, F., Esteban-Cubillo, A., Pecharromán, C., & Moya, J. S. (2009). Antibacterial and antifungal activity of a soda-lime glass containing copper nanoparticles. *Nanotechnology*, *20*(50), 505701.
68. Taran, M., Rad, M., & Alavi, M. (2017). Antibacterial activity of copper oxide (CuO) nanoparticles biosynthesized by Bacillus sp. FU4: optimization of experiment design. *Pharmaceutical Sciences*, *23*(3), 198-206.
69. Pandey, P., Packiyaraj, M. S., Nigam, H., Agarwal, G. S., Singh, B., & Patra, M. K. (2014). Antimicrobial properties of CuO nanorods and multi-armed nanoparticles against B. anthracis vegetative cells and endospores. *Beilstein journal of nanotechnology*, *5*(1), 789-800.
70. Ruparelia, J. P., Chatterjee, A. K., Duttagupta, S. P., & Mukherji, S. (2008). Strain specificity in antimicrobial activity of silver and copper nanoparticles. *Acta biomaterialia*, *4*(3), 707-716.
71. Fellahi, O., Sarma, R. K., Das, M. R., Saikia, R., Marcon, L., Coffinier, Y., ... & Boukherroub, R. (2013). The antimicrobial effect of silicon nanowires decorated with silver and copper nanoparticles. *Nanotechnology*, *24*(49), 495101.
72. Lv, M., Su, S., He, Y., Huang, Q., Hu, W., Li, D., ... & Lee, S. T. (2010). Long-term antimicrobial effect of silicon nanowires decorated with silver nanoparticles. *Advanced materials*, *22*(48), 5463-5467.
73. Egger, S., Lehmann, R. P., Height, M. J., Loessner, M. J., & Schuppler, M. (2009). Antimicrobial properties of a novel silver-silica nanocomposite material. *Applied and environmental microbiology*, *75*(9), 2973-2976.
74. Dhapte, V., Kadam, S., Pokharkar, V., Khanna, P. K., & Dhapte, V. (2014). Versatile SiO2 nanoparticles@ polymer composites with pragmatic properties. *International Scholarly Research Notices*, *2014*.
75. Mukha, I., Eremenko, A., Korchak, G., & Michienkova, A. (2010). Antibacterial action and physicochemical properties of stabilized silver and gold nanostructures on the surface of disperse silica. *Journal of Water Resource and Protection*, *2010*.
76. Dizaj, S. M., Lotfipour, F., Barzegar-Jalali, M., Zarrintan, M. H., & Adibkia, K. (2014). Antimicrobial activity of the metals and metal oxide nanoparticles. *Materials Science and Engineering: C*, *44*, 278-284.
77. Ding, C., Pan, J., Jin, M., Yang, D., Shen, Z., Wang, J., ... & Li, J. (2016). Enhanced uptake of antibiotic resistance genes in the presence of nanoalumina. *Nanotoxicology*, *10*(8), 1051-1060.
78. Buckley, J. J., Gai, P. L., Lee, A. F., Olivi, L., & Wilson, K. (2008). Silver carbonate nanoparticles stabilised over alumina nanoneedles exhibiting potent antibacterial properties. *Chemical communications*, (34), 4013-4015.
79. Ansari, M. A., Khan, H. M., Khan, A. A., Cameotra, S. S., Saquib, Q., & Musarrat, J. (2014). Interaction of A l2 O 3 nanoparticles with E scherichia coli and their cell envelope biomolecules. *Journal of applied microbiology*, *116*(4), 772-783.
80. Lellouche, J., Friedman, A., Gedanken, A., & Banin, E. (2012). Antibacterial and antibiofilm properties of yttrium fluoride nanoparticles. *International journal of nanomedicine*, *7*, 5611.
81. Vidic, J., Stankic, S., Haque, F., Ciric, D., Le Goffic, R., Vidy, A., ... & Delmas, B. (2013). Selective antibacterial effects of mixed ZnMgO nanoparticles. *Journal of Nanoparticle Research*, *15*(5), 1595.

82. Jin, T., & He, Y. (2011). Antibacterial activities of magnesium oxide (MgO) nanoparticles against foodborne pathogens. *Journal of Nanoparticle Research*, *13*(12), 6877-6885.
83. Hewitt, C. J., Bellara, S. R., Andreani, A., Nebe-von-Caron, G., & McFarlane, C. M. (2001). An evaluation of the anti-bacterial action of ceramic powder slurries using multi-parameter flow cytometry. *Biotechnology letters*, *23*(9), 667-675.
84. Leung, Y. H., Ng, A. M., Xu, X., Shen, Z., Gethings, L. A., Wong, M. T., ... & Leung, F. C. (2014). Mechanisms of antibacterial activity of MgO: non-ROS mediated toxicity of MgO nanoparticles towards Escherichia coli. *Small*, *10*(6), 1171-1183.
85. Sawai, J., Kojima, H., Igarashi, H., Hashimoto, A., Shoji, S., Sawaki, T., ... & Shimizu, M. (2000). Antibacterial characteristics of magnesium oxide powder. *World Journal of Microbiology and Biotechnology*, *16*(2), 187-194.
86. Yamamoto, O., Ohira, T., Alvarez, K., & Fukuda, M. (2010). Antibacterial characteristics of CaCO3–MgO composites. *Materials Science and Engineering: B*, *173*(1-3), 208-212.
87. Jeong, M. S., Park, J. S., Song, S. H., & Jang, S. B. (2007). Characterization of antibacterial nanoparticles from the scallop, Ptinopecten yessoensis. *Bioscience, biotechnology, and biochemistry*, *71*(9), 2242-2247.
88. Sawai, J. (2003). Quantitative evaluation of antibacterial activities of metallic oxide powders (ZnO, MgO and CaO) by conductimetric assay. *Journal of microbiological methods*, *54*(2), 177-182.
89. Narayanan, K. B., & Sakthivel, N. (2010). Biological synthesis of metal nanoparticles by microbes. *Advances in colloid and interface science*, *156*(1-2), 1-13.
90. Thakkar, H. P., Patel, B. V., & Thakkar, S. P. (2011). Development and characterization of nanosuspensions of olmesartan medoxomil for bioavailability enhancement. *Journal of Pharmacy and Bioallied Sciences*, *3*(3), 426.
91. Hurst, S. J., Lytton-Jean, A. K., & Mirkin, C. A. (2006). Maximizing DNA loading on a range of gold nanoparticle sizes. *Analytical chemistry*, *78*(24), 8313-8318.
92. Khandel, P., Yadaw, R. K., Soni, D. K., Kanwar, L., & Shahi, S. K. (2018). Biogenesis of metal nanoparticles and their pharmacological applications: present status and application prospects. *Journal of Nanostructure in Chemistry*, *8*(3), 217-254.
93. Egorova, E. M., & Revina, A. A. (2000). Synthesis of metallic nanoparticles in reverse micelles in the presence of quercetin. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *168*(1), 87-96.
94. Patel, P., Agarwal, P., Kanawaria, S., Kachhwaha, S., & Kothari, S. L. (2015). Plant-based synthesis of silver nanoparticles and their characterization. In *Nanotechnology and plant sciences* (pp. 271-288). Springer, Cham.
95. Mukunthan, K. S., & Balaji, S. (2012). Cashew apple juice (Anacardium occidentale L.) speeds up the synthesis of silver nanoparticles. *International Journal of Green Nanotechnology*, *4*(2), 71-79.
96. Azizi, S., Ahmad, M., Mahdavi, M., & Abdolmohammadi, S. (2013). Preparation, characterization, and antimicrobial activities of ZnO nanoparticles/cellulose nanocrystal nanocomposites. *BioResources*, *8*(2), 1841-1851.
97. Shankar, S. S., Rai, A., Ahmad, A., & Sastry, M. (2004). Rapid synthesis of Au, Ag, and bimetallic Au core–Ag shell nanoparticles using Neem (Azadirachta indica) leaf broth. *Journal of colloid and interface science*, *275*(2), 496-502.
98. Dhuper, S., Panda, D., & Nayak, P. L. (2012). Green synthesis and characterization of zero valent iron nanoparticles from the leaf extract of Mangifera indica. *Nano Trends: J Nanotech App*, *13*(2), 16-22.
99. Narayanan, K. B., & Sakthivel, N. (2008). Coriander leaf mediated biosynthesis of gold nanoparticles. *Materials Letters*, *62*(30), 4588-4590.
100. Singh, J., Kaur, G., Kaur, P., Bajaj, R., & Rawat, M. (2016). A review on green synthesis and characterization of silver nanoparticles and their applications: a green nanoworld. *World J Pharm Pharm Sci*, *7*, 730-762.
101. Ahmed, S., Ahmad, M., Swami, B. L., & Ikram, S. (2016). A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications: a green expertise. *Journal of advanced research*, *7*(1), 17-28.
102. Altemimi, A., Lakhssassi, N., Baharlouei, A., Watson, D. G., & Lightfoot, D. A. (2017). Phytochemicals: Extraction, isolation, and identification of bioactive compounds from plant extracts. *Plants*, *6*(4), 42.
103. Ingle, K. P., Deshmukh, A. G., Padole, D. A., Dudhare, M. S., Moharil, M. P., & Khelurkar, V. C. (2017). Phytochemicals: Extraction methods, identification and detection of bioactive compounds from plant extracts. *Journal of Pharmacognosy and Phytochemistry*, *6*(1), 32-36.
104. Vijayaraghavan, K., & Ashokkumar, T. (2017). Plant-mediated biosynthesis of metallic nanoparticles: a review of literature, factors affecting synthesis, characterization techniques and applications. *Journal of environmental chemical engineering*, *5*(5), 4866-4883.
105. Iravani, S., Thota, S., & Crans, D. C. (2018). Methods for preparation of metal nanoparticles. *Metal nanoparticles: synthesis and applications in pharmaceutical sciences*, 15-32.
106. Ahmed, S., Saifullah, Ahmad, M., Swami, B. L., & Ikram, S. (2016). Green synthesis of silver nanoparticles using Azadirachta indica aqueous leaf extract. *Journal of radiation research and applied sciences*, *9*(1), 1-7.
107. Kumar, V., & Yadav, S. K. (2009). Plant-mediated synthesis of silver and gold nanoparticles and their applications. *Journal of Chemical Technology & Biotechnology: International Research in Process, Environmental & Clean Technology*, *84*(2), 151-157.
108. Ali, K. A., Yao, R., Wu, W., Masum, M. M. I., Luo, J., Wang, Y., ... & Li, B. (2020). Biosynthesis of silver nanoparticle from pomelo (Citrus Maxima) and their antibacterial activity against acidovorax oryzae RS-2. *Materials Research Express*, *7*(1), 015097.

109. Aisida, S. O., Ugwu, K., Nwanya, A. C., Bashir, A. K. H., Nwankwo, N. U., Ahmed, I., & Ezema, F. I. (2020). Biosynthesis of silver oxide nanoparticles using leave extract of Telfairia Occidentalis and its antibacterial activity. *Materials Today: Proceedings*.
110. MOIDEEN, R. S., & PRABHA, L. (2020). Biosynthesis of Silver Nanoparticle Using Vitex negundo Leaf Extract and Its Antibacterial Activity. *IJRAR-International Journal of Research and Analytical Reviews (IJRAR)*, *7*(1), 801-809.
111. Obeizi, Z., Benbouzid, H., Ouchenane, S., Yılmaz, D., Culha, M., & Bououdina, M. (2020). Biosynthesis of Zinc oxide nanoparticles from essential oil of Eucalyptus globulus with antimicrobial and anti-biofilm activities. *Materials Today Communications*, *25*, 101553.
112. Vijilvani, C., Bindhu, M. R., Frincy, F. C., AlSalhi, M. S., Sabitha, S., Saravanakumar, K., ... & Atif, M. (2020). Antimicrobial and catalytic activities of biosynthesized gold, silver and palladium nanoparticles from Solanum nigurum leaves. *Journal of Photochemistry and Photobiology B: Biology*, *202*, 111713.
113. Zayed, M. F., Mahfoze, R. A., El-kousy, S. M., & Al-Ashkar, E. A. (2020). In-vitro antioxidant and antimicrobial activities of metal nanoparticles biosynthesized using optimized Pimpinella anisum extract. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, *585*, 124167.
114. Küp, F. Ö., Çoşkunçay, S., & Duman, F. (2020). Biosynthesis of silver nanoparticles using leaf extract of Aesculus hippocastanum (horse chestnut): Evaluation of their antibacterial, antioxidant and drug release system activities. *Materials Science and Engineering: C*, *107*, 110207.
115. Renuka, R., Devi, K. R., Sivakami, M., Thilagavathi, T., Uthrakumar, R., & Kaviyarasu, K. (2020). Biosynthesis of silver nanoparticles using phyllanthus emblica fruit extract for antimicrobial application. *Biocatalysis and Agricultural Biotechnology*, 101567.
116. Zhang, C., Liu, J., Ahmeda, A., Liu, Y., Feng, J., Guan, H., ... & Almasi, M. (2020). Biosynthesis of zinc nanoparticles using Allium saralicum RM Fritsch leaf extract; Chemical characterization and analysis of their cytotoxicity, antioxidant, antibacterial, antifungal, and cutaneous wound healing properties. *Applied Organometallic Chemistry*, e5564.
117. Rahayu, E., Wonoputri, V., & Samadhi, T. W. (2020, April). Plant extract-assisted biosynthesis of zinc oxide nanoparticles and their antibacterial application. In *IOP Conference Series: Materials Science and Engineering* (Vol. 823, No. 1, p. 012036). IOP Publishing.
118. Maghimaa, M., & Alharbi, S. A. (2020). Green synthesis of silver nanoparticles from Curcuma longa L. and coating on the cotton fabrics for antimicrobial applications and wound healing activity. *Journal of Photochemistry and Photobiology B: Biology*, *204*, 111806.
119. Velsankar, K., Sudhahar, S., Parvathy, G., & Kaliammal, R. (2020). Effect of cytotoxicity and aAntibacterial activity of biosynthesis of ZnO hexagonal shaped nanoparticles by Echinochloa frumentacea grains extract as a reducing agent. *Materials Chemistry and Physics*, *239*, 121976.
120. Dulta, K., Ağçeli, G. K., Chauhan, P., Jasrotia, R., & Chauhan, P. K. (2020). A novel approach of synthesis zinc oxide nanoparticles by bergenia ciliata rhizome extract: antibacterial and anticancer potential. *Journal of Inorganic and Organometallic Polymers and Materials*, 1-11.
121. Rathinavel, T., Ammashi, S., & Marimuthu, S. (2020). Optimization of zinc oxide nanoparticles biosynthesis from Crateva adansonii using Box-Behnken design and its antimicrobial activity. *Chemical Data Collections*, *30*, 100581.
122. Singh, A., Gaud, B., & Jaybhaye, S. (2020). Optimization of synthesis parameters of silver nanoparticles and its antimicrobial activity. *Materials Science for Energy Technologies*, *3*, 232-236.
123. Hekmati, M., Hasanirad, S., Khaledi, A., & Esmaeili, D. (2020). Green synthesis of silver nanoparticles using extracts of Allium rotundum l, Falcaria vulgaris Bernh, and Ferulago angulate Boiss, and their antimicrobial effects in vitro. *Gene Reports*, *19*, 100589.
124. Devi, M., Devi, S., Sharma, V., Rana, N., Bhatia, R. K., & Bhatt, A. K. (2020). Green synthesis of silver nanoparticles using methanolic fruit extract of Aegle marmelos and their antimicrobial potential against human bacterial pathogens. *Journal of traditional and complementary medicine*, *10*(2), 158-165.
125. Archana, Sharma, S. N., & Srivastava, R. (2020). Silver oxide nanoparticles synthesized by green method from Artocarpus Hetrophyllus for antibacterial and antimicrobial applications. *Materials Today: Proceedings*.
126. Sachdeva, A., Singh, S., & Singh, P. K. (2020). Synthesis, characterisation and synergistic effect of ZnO nanoparticles to antimicrobial activity of silver nanoparticle. *Materials Today: Proceedings*.
127. Fatimah, I., Hidayat, H., Nugroho, B. H., & Husein, S. (2020). Ultrasound-assisted biosynthesis of silver and gold nanoparticles using Clitoria ternatea flower. *South African Journal of Chemical Engineering*, *34*, 97-106.
128. Mirzahosseinipour, M., Khorsandi, K., Hosseinzadeh, R., Ghazaeian, M., & Shahidi, F. K. (2020). Antimicrobial photodynamic and wound healing activity of curcumin encapsulated in silica nanoparticles. *Photodiagnosis and Photodynamic Therapy*, *29*, 101639.
129. Mathew, S., Victório, C. P., Sidhi, J., & BH, B. T. (2020). Biosynthesis of silver nanoparticle using flowers of Calotropis gigantea (L.) WT Aiton and activity against pathogenic bacteria. *Arabian Journal of Chemistry*, *13*(12), 9139-9144.
130. Akhter, S. M. H., Mohammad, F., & Ahmad, S. (2019). Terminalia belerica mediated green synthesis of nanoparticles of copper, iron and zinc metal oxides as the alternate antibacterial agents against some common pathogens. *BioNanoScience*, *9*(2), 365-372.
131. Alyousef, A. A., Arshad, M., AlAkeel, R., & Alqasim, A. (2019). Biogenic silver nanoparticles by Myrtus communis plant extract: biosynthesis, characterization and antibacterial activity. *Biotechnology & Biotechnological Equipment*, *33*(1), 931-936.

132. Chums-ard, W., Fawcett, D., Fung, C. C., & Poinern, G. E. J. (2019). Biogenic synthesis of gold nanoparticles from waste watermelon and their antibacterial activity against Escherichia coli and Staphylococcus epidermidis. *International Journal of Research in Medical sciences*, *7*(7), 2499-2505.
133. Madivoli, E. S., Kareru, P. G., Maina, E. G., Nyabola, A. O., Wanakai, S. I., & Nyang'au, J. O. (2019). Biosynthesis of iron nanoparticles using Ageratum conyzoides extracts, their antimicrobial and photocatalytic activity. *SN Applied Sciences*, *1*(5), 500.
134. Ajmal, N., Saraswat, K., Bakht, M. A., Riadi, Y., Ahsan, M. J., & Noushad, M. (2019). Cost-effective and eco-friendly synthesis of titanium dioxide (TiO2) nanoparticles using fruit's peel agro-waste extracts: characterization, in vitro antibacterial, antioxidant activities. *Green Chemistry Letters and Reviews*, *12*(3), 244-254.
135. Salari, S., Bahabadi, S. E., Samzadeh-Kermani, A., & Yosefzaei, F. (2019). In-vitro Evaluation of Antioxidant and Antibacterial Potential of GreenSynthesized Silver Nanoparticles Using Prosopis farcta Fruit Extract. *Iranian journal of pharmaceutical research: IJPR*, *18*(1), 430.
136. Onitsuka, S., Hamada, T., & Okamura, H. (2019). Preparation of antimicrobial gold and silver nanoparticles from tea leaf extracts. *Colloids and Surfaces B: Biointerfaces*, *173*, 242-248.
137. Nayak, S., Sajankila, S. P., Rao, C. V., Hegde, A. R., & Mutalik, S. (2019). Biogenic synthesis of silver nanoparticles using Jatropha curcas seed cake extract and characterization: evaluation of its antibacterial activity. *Energy Sources, Part A: Recovery, Utilization, and Environmental Effects*, 1-9.
138. Nasar, S., Murtaza, G., Mehmood, A., Bhatti, T. M., & Raffi, M. (2019). Environmentally benign and economical phytofabrication of silver nanoparticles using juglans regia leaf extract for antibacterial study. *Journal of Electronic Materials*, *48*(6), 3562-3569.
139. Manikandan, D., Prakash, D. G., Arun, J., Gandhi, N. N., Mani, U., & Kathirvan, K. (2019). Antibacterial and anticancer activities of silver nanoparticles biosynthesized using Embelia ribes Burm. f. berries extract.
140. Nithya, K., & Kalyanasundharam, S. (2019). Effect of chemically synthesis compared to biosynthesized ZnO nanoparticles using aqueous extract of C. halicacabum and their antibacterial activity. *OpenNano*, *4*, 100024.
141. Owaid, M. N., Zaidan, T. A., Muslim, R. F., & Hammood, M. A. (2019). Biosynthesis, characterization and cytotoxicity of zinc nanoparticles using Panax ginseng roots, Araliaceae. *ACTA Pharmaceutica Sciencia*, *57*(1).
142. Kumar, H. N., Mohana, N. C., Nuthan, B. R., Ramesha, K. P., Rakshith, D., Geetha, N., & Satish, S. (2019). Phyto-mediated synthesis of zinc oxide nanoparticles using aqueous plant extract of Ocimum americanum and evaluation of its bioactivity. *SN Applied Sciences*, *1*(6), 651.
143. Dudhane, A. A., Waghmode, S. R., Dama, L. B., Mhaindarkar, V. P., Sonawane, A., & Katariya, S. (2019). Synthesis and Characterization of Gold Nanoparticles using Plant Extract of Terminalia arjuna with Antibacterial Activity. *International Journal of Nanoscience and Nanotechnology*, *15*(2), 75-82.
144. Behravan, M., Panahi, A. H., Naghizadeh, A., Ziaee, M., Mahdavi, R., & Mirzapour, A. (2019). Facile green synthesis of silver nanoparticles using Berberis vulgaris leaf and root aqueous extract and its antibacterial activity. *International journal of biological macromolecules*, *124*, 148-154.
145. Balasubramanian, S., Kala, S. M. J., Pushparaj, T. L., & Kumar, P. V. (2019). Biofabrication of gold nanoparticles using Cressa cretica leaf extract and evaluation of catalytic and antibacterial efficacy. *Nano Biomedicine and Engineering*, *11*(1), 58-66.
146. Chauhan, P. S., Shrivastava, V., & Tomar, R. S. (2019). Biosynthesis of zinc oxide nanoparticles using Cassia siamea leaves extracts and their efficacy evaluation as potential antimicrobial agent. *Journal of Pharmacognosy and Phytochemistry*, *8*(3), 162-166.
147. Anwar, A., Masri, A., Rao, K., Rajendran, K., Khan, N. A., Shah, M. R., & Siddiqui, R. (2019). Antimicrobial activities of green synthesized gums-stabilized nanoparticles loaded with flavonoids. *Scientific Reports*, *9*(1), 1-12.
148. Abed, A. S., Abed, M. S., & Othman, F. M. (2019). Green synthesis of silver nanoparticles from natural compounds: glucose, eugenol and thymol. *Journal of Advanced Research in Fluid Mechanics and Thermal Sciences*, *60*(1), 95-111.
149. Gebremedhn, K., Kahsay, M. H., & Aklilu, M. (2019). Green synthesis of CuO nanoparticles using leaf extract of catha edulis and its antibacterial activity. *J. Pharm. Pharmacol*, *7*, 327-342.
150. Zhang, H., Jacob, J. A., Jiang, Z., Xu, S., Sun, K., Zhong, Z., ... & Shanmugam, A. (2019). Hepatoprotective effect of silver nanoparticles synthesized using aqueous leaf extract of Rhizophora apiculata. *International journal of nanomedicine*, *14*, 3517.
151. Parthiban, E., Manivannan, N., Ramanibai, R., & Mathivanan, N. (2019). Green synthesis of silver-nanoparticles from Annona reticulata leaves aqueous extract and its mosquito larvicidal and anti-microbial activity on human pathogens. *Biotechnology Reports*, *21*, e00297.
152. Lakshmanan, G., Sathiyaseelan, A., Kalaichelvan, P. T., & Murugesan, K. (2018). Plant-mediated synthesis of silver nanoparticles using fruit extract of Cleome viscosa L.: Assessment of their antibacterial and anticancer activity. *Karbala International Journal of Modern Science*, *4*(1), 61-68.
153. Joshi, N., Jain, N., Pathak, A., Singh, J., Prasad, R., & Upadhyaya, C. P. (2018). Biosynthesis of silver nanoparticles using Carissa carandas berries and its potential antibacterial activities. *Journal of Sol-Gel Science and Technology*, *86*(3), 682-689.
154. Jamdagni, P., Khatri, P., & Rana, J. S. (2018). Green synthesis of zinc oxide nanoparticles using flower extract of Nyctanthes arbor-tristis and their antifungal activity. *Journal of King Saud University-Science*, *30*(2), 168-175.
155. Bagherzade, G., Tavakoli, M. M., & Namaei, M. H. (2017). Green synthesis of silver nanoparticles using aqueous extract of saffron (Crocus sativus L.) wastages and its antibacterial activity against six bacteria. *Asian Pacific Journal of Tropical Biomedicine*, *7*(3), 227-233.

156. Jain, S., & Mehata, M. S. (2017). Medicinal plant leaf extract and pure flavonoid mediated green synthesis of silver nanoparticles and their enhanced antibacterial property. *Scientific reports*, *7*(1), 1-13.
157. Markus, J., Wang, D., Kim, Y. J., Ahn, S., Mathiyalagan, R., Wang, C., & Yang, D. C. (2017). Biosynthesis, characterization, and bioactivities evaluation of silver and gold nanoparticles mediated by the roots of Chinese herbal Angelica pubescens Maxim. *Nanoscale research letters*, *12*(1), 46.
158. Ovais, M., Raza, A., Naz, S., Islam, N. U., Khalil, A. T., Ali, S., ... & Shinwari, Z. K. (2017). Current state and prospects of the phytosynthesized colloidal gold nanoparticles and their applications in cancer theranostics. *Applied microbiology and biotechnology*, *101*(9), 3551-3565.
159. Thakkar, K. N., Mhatre, S. S., & Parikh, R. Y. (2010). Biological synthesis of metallic nanoparticles. *Nanomedicine: nanotechnology, biology and medicine*, *6*(2), 257-262.
160. Reddy, N. J., Vali, D. N., Rani, M., & Rani, S. S. (2014). Evaluation of antioxidant, antibacterial and cytotoxic effects of green synthesized silver nanoparticles by Piper longum fruit. *Materials Science and Engineering: C*, *34*, 115-122.
161. Rehana, D., Mahendiran, D., Kumar, R. S., & Rahiman, A. K. (2017). Evaluation of antioxidant and anticancer activity of copper oxide nanoparticles synthesized using medicinally important plant extracts. *Biomedicine & Pharmacotherapy*, *89*, 1067-1077.
162. Fahimirad, S., Ajalloueian, F., & Ghorbanpour, M. (2019). Synthesis and therapeutic potential of silver nanomaterials derived from plant extracts. *Ecotoxicology and environmental safety*, *168*, 260-278.
163. Rao, N. H., Lakshmidevi, N., Pammi, S. V. N., Kollu, P., Ganapaty, S., & Lakshmi, P. (2016). Green synthesis of silver nanoparticles using methanolic root extracts of Diospyros paniculata and their antimicrobial activities. *Materials science and engineering: C*, *62*, 553-557.
164. Khodadadi, B., Bordbar, M., & Nasrollahzadeh, M. (2017). Achillea millefolium L. extract mediated green synthesis of waste peach kernel shell supported silver nanoparticles: Application of the nanoparticles for catalytic reduction of a variety of dyes in water. *Journal of colloid and interface science*, *493*, 85-93.
165. Jayaprakash, N., Vijaya, J. J., Kaviyarasu, K., Kombaiah, K., Kennedy, L. J., Ramalingam, R. J., ... & Al-Lohedan, H. A. (2017). Green synthesis of Ag nanoparticles using Tamarind fruit extract for the antibacterial studies. *Journal of Photochemistry and Photobiology B: Biology*, *169*, 178-185.
166. Sathishkumar, P., Preethi, J., Vijayan, R., Yusoff, A. R. M., Ameen, F., Suresh, S., ... & Palvannan, T. (2016). Anti-acne, anti-dandruff and anti-breast cancer efficacy of green synthesised silver nanoparticles using Coriandrum sativum leaf extract. *Journal of Photochemistry and Photobiology B: Biology*, *163*, 69-76.
167. Sathishkumar, P., Vennila, K., Jayakumar, R., Yusoff, A. R. M., Hadibarata, T., & Palvannan, T. (2016). Phyto-synthesis of silver nanoparticles using Alternanthera tenella leaf extract: An effective inhibitor for the migration of human breast adenocarcinoma (MCF-7) cells. *Bioprocess and biosystems engineering*, *39*(4), 651-659.
168. Marslin, G., Siram, K., Maqbool, Q., Selvakesavan, R. K., Kruszka, D., Kachlicki, P., & Franklin, G. (2018). Secondary metabolites in the green synthesis of metallic nanoparticles. *Materials*, *11*(6), 940.

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