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A Review on Synthesis and Biological Evaluation of Plants Based Metallic Nanoparticles

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Abstract

Nanotechnology is a field of research and innovation concerned with building 'things'-generally, materials and devices on the scale of atoms and molecules. Nanotechnology has become very popular in the past few years. The development of synthesis of metallic nanoparticles has become a major focus of researchers. Metallic nanoparticles have become increasingly used because of their advantages including high stability and loding capacity. Nanoparticles can be synthesized chemically or biologically approaches. One of the most considered methods is the production of metal nanoparticles using organisms. Among these organisms, the plants seem to be the best candidates and are suitable for the large-scale synthesis of nanoparticles. Metallic nanoparticles that have immense application are industries of different type namely gold, silver, and copper, iron oxide and titanium magnetic, etc. the size of the nanoparticles are in the range of 1 to 100 nm. Characterization of synthesized nanoparticles is accomplished through UV spectroscopy, X-ray, FTIR, SEM, TEM, XRD, DLS and EDX. This review based on the recent scientific publications to synthesize metallic nanoparticles along with various methods for silver, copper and titanium metallic nanoparticles by using plants also the review explore the recent development in antibacterial, anticancer and biosensing application of metallic nanoparticles reported by the researchers during the last decades.

Keywords: Synthesis; Silver; Copper; Titanium oxide nanoparticles; Evaluation of biological activities

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Introduction

This review is concerned with the synthesis of metallic nanoparticles using plant extracts and their biological evaluation. Plant based synthesis is useful not only because of its reduced environmental impact compared with some of the physicochemical production methods, but also because it can be used to produce large quantities of nanoparticles that are free of contamination and have a well-defined size and morphology. Plant based synthesis can actually provide Nanoparticles (NPs) of a better defined morphology and size than some of the physicochemical methods of production [1-11].

The ability of plant extracts to reduce metal ions has been known since the early 1900s, although the nature of the reducing agents involved was not well understood. In view of its simplicity, the use of plant extract for reducing metal salts to nanoparticles has attracted considerable attention within the last few years. Plant extract mediated synthesis of metallic nanoparticles is an increasing focus of attention because of the enhanced biological properties of plant mediated nanoparticles [12-32]. Nanoparticles are already used in numerous applications including in catalysis, biosensors, antimicrobial, photo thermal therapy and pharmaceutical production.

Characterization Techniques

Several techniques are employed for the physico-chemical and morphological characterization of the produced metallic nanoparticles. A detailed overview of the determined charactersticsand attribute of each morphological and physico-chemical chracterization technique is presented in **Table 1** [33-45].

Morphological and physico-chemical chracterization technique	Determined characterstics and attribute
Ultraviolet-visible spectroscopy (UV-vis)	Concentration and shape of NPs
Fourier Transform Infrared spectroscopy (FTIR)	Nature of bonds and functional groups
X-ray diffraction (XRD	Size and crystallinity of NPs
Scanning Electron Microscopy (SEM)	Shape, size and structure of nano-formulations

Field Emission Scanning Electron Microscopy (FESEM)	Structural and morphological characteristics
Transmission Electron Microscopy (TEM)	Shape, size and structure of nano-formulations
Particle Size Analysis (PSA)	Size distribution of solid or liquid particulate materials
Malvern Zetasizer (MZS)	Size, zeta potential, and protein mobility
Energy-dispersive X-ray spectroscopy (EDX/EDS)	Composition of NPs
Nanoparticle Tracking Analysis (NTA)	Particle size, concentration, and fluorescent properties
Nanoparticle Tracking Analysis (NTA)	Particle size, concentration, and fluorescent properties
Small-angle X-ray scattering (SAXS)	Shape and size conformation
X-ray Reflectometry (XRR)	Thickness, density, and roughness
X-ray fluorescence spectroscopy (XRF)	Chemical composition and concentration
Brunauer-Emmett-Teller analysis (BET)	Specific surface area
Selected Area Electron Diffraction (SAED)	Shape, size and structure of nano-formulations
Atomic Force Microscopy (AFM)	Particle size and surface characterization
Atomic Force Microscopy (AFM)	Particle size and surface characterization
Particle size and surface characterization	Amount of metal present in metallic nano-formulations

Table 1: Determined characterstics and attribute of each morphological and physico-chemical chracterization technique [1].

Synthesis of nanoparticle

There are different physical and chemical methods for successfully synthesizing NPs. One can categorize all these methods into two main approaches that can apply to any research in the field of nanoscale science: (1) the top-bottom and (2) the bottom-top approach shown in **Figure 1.**

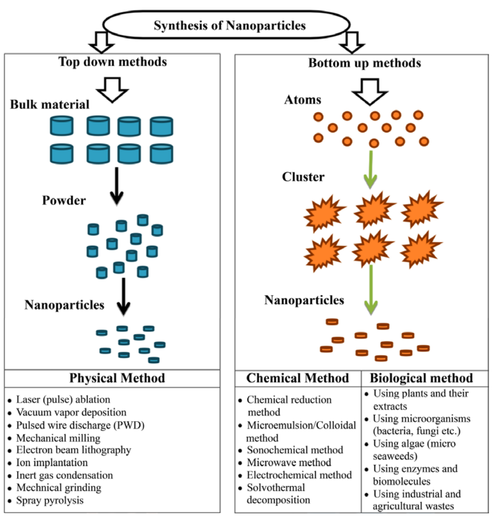

Figure 1: Different methods used for the synthesis of NPs.

Each of which has specific characterization and application. The use of environmentally benign materials like plant extract bacteria, fungi and enzymes for the synthesis of metallic nanoparticles offer numerous benefits of eco-friendliness and compatibility for pharmaceutical and other biomedical applications as they do not use toxic chemicals for the synthesis protocol. In general, metallic nanoparticles are produced by two methods, i.e. "bottom-up" (buildup of material from the bottom: atom by atom, or molecule by molecule or cluster by cluster) and "top-down" (slicing or successive cutting of bulk material to get nano-sized particle). The "bottom-up" approach is usually a superior choice for the nanoparticles preparation involving a homogeneous system wherein catalysts (for instance reducing agent and enzymes) synthesize nanostructures that are controlled by the catalyst itself [46-55]. However, the "top-down" approach generally works with the material in its bulk form, and the size reduction to the nanoscale is achieved by specialized ablations, for instance thermal decomposition, mechanical grinding, etching, cutting, and sputtering. The main demerit of the top-down approach is the surface structural defects. Such defects have a significant impact on the physical features and surface chemistry of metallic nanoparticles of the biological methods of synthesis, the methods based on microorganisms have been widely reported [56-61]. Microbial synthesis is of course readily scalable, environmentally benign and compatible with the use of the product for medical applications, but production of microorganisms is often more expensive than the production of plant extracts. Plant mediated nanoparticle synthesis using whole plant extract or by living plant were also reported in literature has been studied [62-69].

Use of plant extracts in nanoparticle synthesis

In these days, the emphasis has been shifting toward the synthesis of NPs by using plants and plant extracts to gain the advantages of this method shown in **Figure 2.** Many scientists used different plant extracts to prepare different type of NPs in **Figure 3** with different sizes and shapes depending upon the synthesis conditions.

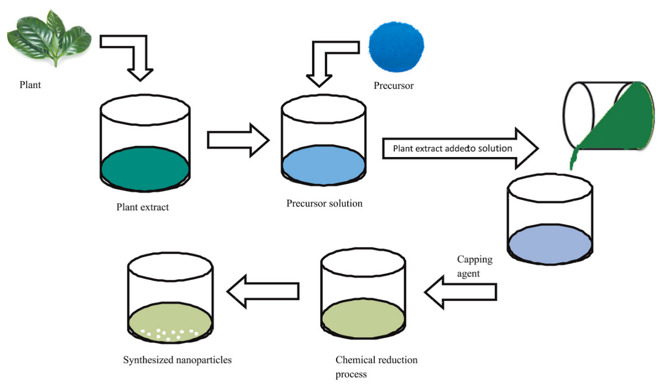

Figure 2: Biological synthesis of NPs From plants extract.

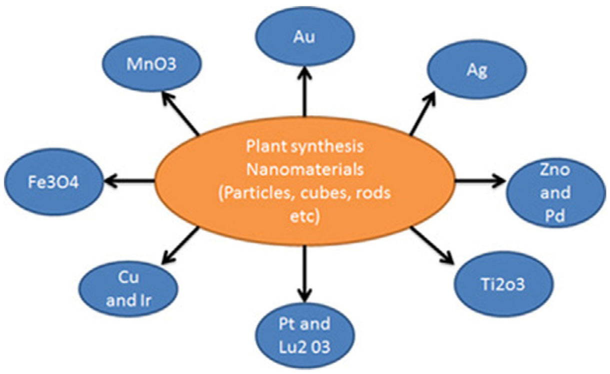

Figure 3: Different types of nanoparticle synthesis from plants resources.

Synthesis of Ag-NPs from plant extract

Illustrated that the first approach of using plants for the synthesis of metallic NPs was done by using Alfalfa sprouts, which was the first description about the synthesis of Ag-NPs using living plant system. A plant mediated nanoparticles synthesis using whole plant extract or by the living plants were also studies in the literature studied that Acorus calamus extract can be used as capping agent for the synthesis of Ag-NPs to evaluate its oxidation state, anticancer, and antibacterial effect. The spherical Ag-NPs have been synthesized using the extract of *Abutilon indicum* and also studied their high antimicrobial activity against *S. typhi*, *E. coli*, *S. aureus*, and *B. subtilis* microorganism by illustrated that Ag-NPs are synthesized by peanut shell extract and their characteristics and antifungal activity is compared with commercial Ag-NPs. UV-Vis spectra, XRD peaks, and FTIR confirmed that synthesized and commercial NPs are similar and HRTEM results indicate that NPs were mostly spherical and oval in shape with an average diameter up to 10-50 nm. In another method, spherical Ag-NPs were also synthesized by using the fruit extract of *Malus domestica* as capping agent with an average diameter of 20 nm. The formation of NPs is analyzed by UV–Vis spectroscopy, distinctive phases and morphology are confirmed by using XRD and TEM, and FTIR is used to identify the biomolecules which are responsible for reduction and stabilization of NPs reported that Ag-NPs are synthesized using the extracts of *Boerhaavia diffusa*, XRD and TEM results showed an average size 25 nm having face-centered cubic geometry with spherical shape. These NPs were used for antibacterial action against three fish bacteria, namely *Pseudomonas fluorescens, Aeromonas hydrophila, and Flavobacterium* reprted Ag-NPs with an average size of 15-22 nm by using reishi mushroom (*Ganoderma lucidum*) extract reported that *Origanum vulgare L.* plant extract can be used as capping agents for the synthesis of AgNPs to evaluate its oxidation state. Synthesized Ag-NPs characterized by various microscopic and spectroscopic techniques and results indicated the formation of crystalline face-centered cubic. It is found that green synthesis using plant and plant extracts appears to be faster than other microorganisms, such as bacteria and fungi [70-85]. The use of plant and plant extracts in green synthesis has drawn attention because of its rapid growth, providing single step technique, economical protocol, non-pathogenic, and eco-friendly for nanoparticles synthesis. The different parts of plant such as stem, root, fruit, seed, callus, peel, leaves and flower are used to syntheses of metallic nanoparticles in various shapes and sizes by biological approaches **Figure 4**

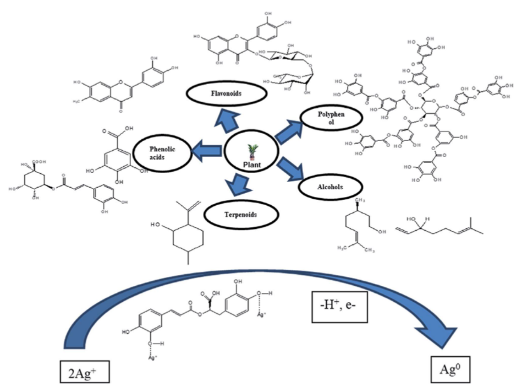

Figure 4: Mechanism for the synthesis of AgNPs from plant sources.

Different sizes and shapes of silver, copper and titanium oxide nanoparticles derived from plants resources. Biosynthesis reaction can be altered by wide range of metal concentration and amount of plant extract in the reaction medium; it may transform the shape and size of the nanoparticles [86-88]. Other plant species which has been used for the synthesis of Ag-NPs shown in **Table 2**

Plant name	Plant part	Size (n.m.)	Shape	Reference
Tephrosia tinctonia	Stem	73	Spherical	[7]
Grewia flavis cences	Leaf	50-70	Hexagonal	[8]
Skimmia laureola	Leaf	46	Spherical	[9]
Clerodendrum serratum	Leaf	35	Spherical	[10]
Averrhoa carambola	Leaf	14	spherical	[11]
Crataegus microphylla	Fruit	30-50	Spherical	[12]
Reishi mushroom	Plant extract	15-22	Spherical	[13]
Gymnema sylvestre	Leaf	20-30	Spherical	[14]
Cucurbita pepo	Leaves	5-100	Spherical	[15]
Tragopogon collinus	Leaf	7	Nano crystals	[16]
Musa paradisicia	Leaf	20-30	Spherical	[18]
Tribulus terristris	Fruit	16-28	Spherical	[19]
Ziziphus jujube	Leaf	20-30	Crystalline	[20]

Allium ampeloprasum	Leaf	2 and 43	Quasi-spherical, spherical, ellipsoidal, hexagonal and irregular.	[21]
Enhydra fluctuans	Plant extract	100-400	Spherical	[22]
Gliricidia sepium	Plant extract	Oct-50	Spherical	[23]
Eucalyptus citriodora	Plant extract	-20	Spherical	[24]
Gliricidia sepium	Plant extract	Oct-50	Spherical	[25]
Ficus benghalensis	Leaf	-16	Spherical	[26]
Pistacia atlantica	Seed	Oct-50	Spherical	[27]
Ocimum tenuiflorum,	Plant extract	28	Irregular	[28]
Solanum tricobatum,	Plant extract	26.5	Irregular	[29]
Ziziphora tenuior	Extract	38	Cubic	[30]
Fiscus carica	Leaves	13	Spherical	[31]
Cymbopogan citratus	Leaves	32	Spherical	[32]
Acalpia indica	Leaves	0.5	Spherical	[33]
Premnna herbacea	Leaves	0-30	Spherical	[34]
Calotropus procera	Plant	19-45	Spherical	[35]
Centella asiatica	Leaves	30-50	Spherical	[36]
Argyreia nervosa	Seed	20-50	Spherical	[37]
Psorelia corylilifolia	Seeds	100-110	Spherical	[38]
Brassica lappa	Leaves	16.4	Spherical	[39]
Melia dubia	Leaves	35	Spherical	[40]
Memeceylon edule	Leaves	20-25	Triangular, circular, hexagonal	[41]
Datura metal	Leaves	16-40	Quasi linear	[42]

Table 2: Plant mediated synthesis of silver nanoparticles.

Synthesis of Cu-NPs from plants extract

Plant-based polyphenols are considered to be the largest groups of natural antioxidants with extraordinary potential as drugs, nutraceuticals, and food additives. The underlying principle in the green synthesis approaches is that the phytochemicals present in the plant parts serve the twin role of a natural reductant besides being a nanoparticle stabilizer (**Figure** 5). According to reports, highly stabilized NPs may be quickly synthesized from plant extracts rather than microbebased synthesis. Therefore, the plant extract could be an efficient approach for reducing NPs early material plus stabilized that. For example, an interesting study by *S. Renganathan* and his coworkers studied that Cu-NPs were synthesized using leaf extract from *Capparis zeylanica* as a reducing agent in aqueous $CuSO_4$ solution. The NPs were fabricated for 12 h which were cubical in shape with size range 50-100 nm. The antimicrobial study of the Cu-NPs was established using both gram positive and gram negative pathogens (as *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*) reported the green approach of CuO-NPs synthesis using *Calotropis procera* which belongs to the asclepiadaceous family. These NPs are widely used in many applications such as catalysis because of their narrow band gap, used in photo catalytic properties (**Figure** 6). In another study, reported the green synthesis of copper NPs using *Punica granatum* peels extract. *Punica granatum* fresh peels are obtained and washed for several times. After peels dried, they turned into powder and mixed with sterile distilled water and boiled until the color of solution change to yellow. To synthesize CuO-NPs, copper acetate powder was dissolved in the water and stirred with magnetic stirrer. After that, P. granatum extract was added to the solution at the first step, the color of solution turned to green and then it turned to brown which shows the formation of monodispersed Cu-NPs. and reported the green synthesis of copper NPs from fresh leaves of *Abutilon indicum*. The fresh leaves of Abutilon indicum were collected and washed gently to remove dust particles as well as dried and shaded parts. Next, the leaves were pulverized and seived using a 200 nm mesh sieve to be used as fuel. To synthesize CuO NPs, Copper (II) nitrate trihydrate was mixed with *Abutilon indicum* extract in double-distilled water. The solution was homogenized for 2-5 min with constant stirring using a magnetic stirrer. Next, combustion reaction was performed on the mixture using a pre-heated muffle furnace at the temperature 400 ± 5 C to produce CuO-NPs. The resultant mixture was filtered to remove the ash contents of the plant extracts. The solution was washed with distilled water, followed by methanol to remove impurities. In another methods M. M. S. R. Subbaiya studied that *Hibicus rosa-sinensis* leaf extract can be used to reduce the CuNO3 solution, then the solution was placed in a dark room for 48 h and spherical Cu-NPs were prepared. Cu-NPs showed good antimicrobial activity against clinically important pathogens like *Bacillus subtilis* and *E. coli*. It is also illustrated that the synthesized Cu-NPs were acting as an effective. Haneefa and co-authors synthesized Cu-NPs using lemon solution as a reducer and curcumin as an additive under certain conditions. Experimental outcomes revealed that size of Cu-NPs was observed in the range of 60-100 nm with nearly spherical shape. Antimicrobial activity of Cu-NPs is more excellent as compared to standard drug against both bacterial and fungus species like *S. aureus*, *B. subtilis* and *Candida albicans*. Similar inhibition response was practically noted against *E. coli*, S. bacillus (bacterial species) and *Cochliobolus lunata*, *Aspergillus niger* (fungus species). From this discussion it can be summarized that the synthesized Cu-NPs are prominent in antibacterial and antifungal studies which may be found in various applications of medicine used papaya extract to synthesize Cu-NPs at 50-60° C under constant stirring for 1 h. It has been concluded that the green synthesized Cu-NPs are nearly spherical and crystalline. The average particles size of Cu-NPs is around 20 nm. Shende and his coworkers reported Cu-NPs synthesis with an average size of 20 nm by using Citron juice (*Citrus medica Linn*.). The synthesized Cu-NPs showed a significant inhibitory response against *E. coli* followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, Propioni bacterium acnes and *Salmonella typhi*. Regarding pathogenic fungi testes, *Fusarium culmorum* was observed to be the most responsive followed by *Fusarium oxysporum* and *Fusarium graminearum*. Suresh studied the green synthesis of tea decoction stabilized Cu-NPs at room temperature which are stable in air with respect to oxidation for about 25 days because of the thin layer of tea decoction molecules surrounded by the NPs. The average particle size is found to be around 11 nm. Further Subhankari and Nayak reported the production of Cu-NPs using aqueous extract of *Syzygium aromaticum* (Cloves). Copper sulfate was reduced with aqueous solution of clove extracts in 1 h and 5–40 nm spherical Cu-NPs were obtained. Kulkarni studied that the leaf extract of Ocimum sanctum can make a reduction of Cu cations into Cu-NPs within 8–10 min. So this technique can be applied for rapid and eco-friendly synthesis of Cu-NPs. Sampath and his fellows synthesized bud-shaped Cu-NPs using a green reduction method where polyvinyl pyrrolidone (PVP), L-Ascorbic Acid (AA) and isonicotinic acid hydrazide (INH) are used as a capping agent, antioxidant agent and reducing agent, respectively and water as a solvent at 60-700 C (pH-7) in the presence of air and the average particle size was observed as 6.95 nm. Antibacterial study of these Cu-NPs was analyzed by measuring response against Gram negative (*E. coli*) and Gram positive (*S. aureus*) bacteria. In another study by it was observed that datura meta leaf extract can reduce $CuSO_4$ solution into Cu-NPs with size 5 nm in 8-10 min. These NPs have excellent antimicrobial response compared to standard Chloramphenicol, hence used as antimicrobial agent. Kundu studied the synthesis of Cu-NPs using *Citrus sinensis* (orange) extract in $CuSO_4$. The mixture was then incubated in a rotary shaker at 55 C for about 3 h. Manikandan and Sathiyabama synthesized Cu-NPs by adding acidic chitosan solution to $CuSO_4$ solution with stirring for 12 h at 70 C. Transmission Electron Microscopy (TEM) showed the homogenous spherical size of NPs in the range of 20-30 nm and showed the antibacterial response against gram negative as well as gram positive bacteria. However, antibacterial response was more prominent against the gram negative bacteria which may be based on the variation in composition of cell wall. Recently biological synthesis of Copper oxide nanoparticles (CuO-NPs) was performed using S. acuta leaf extract CuO-NPs were synthesized and characterized using UV-vis, FTIR, SEM and TEM analyses. Synthesized CuO-NPs was tested against Gram negative (*Escherichia coli* and *Proteus vulgaris*) and Gram positive (*Staphylococcus aureus*) pathogens, which showed zones of inhibition at different concentrations. It is also investigated that these CuO-NPs showed effective photocatalytic activity against commercial dyes. The synthesis of spherical copper nanoparticles using zingiber officinale, piper nigrum and piper longum extract has been studied [89-110]. The synthesized copper nanoparticles were characterized using UV-Visible spectroscopy, Fourier transform infrared spectroscopy (FTIR), x-ray diffraction (XRD), field emission gun scanning electron microscopy (FEG-SEM) with EDS and high-resolution transmission electron microscopy (HR-TEM). The size of these synthesized nanoparticles was found 15-30 nm. These nanoparticles show antimicrobial activity against micro organisms like against *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 737), *Pseudomonas aeruginosa* (MTCC 1681) and *Escherichia coli* (MTCC 1687). In another methods Developed copper nanoparticles Cu-NPs from copper salt (CuCl) solution by using *Camelia sinensis* leaf extract. These synthesized nanoparticles characterized by using FTIR, SEM, TEM, EDX analysis and average size of syntesized nanoparticles 60 ± 6 nm. CuO-NPs was evaluated by using bromophenol blue (BPB) dye under sunlight irradiation. The maximum photo degradation of BPB dye was up to 83.7%. Uv-vis spectral analysis of Cu-NPs proved them as an efficient photo catalyst in dye degradation reported that face-centered cubic and spherical copper nanoparticle were synthesize by using *Uncaria gambir Roxb*. Leaves extract. These nanoparticles were characterized by UV-Visible Spectrophotometry, X-ray Diffraction, Fourier transform, Infrared, and Transmission Electron Microscopy analysis. X-ray Diffraction pattern performed three sharp peaks specifically referred to face-centered cubic structured of metallic copper. Transmission Electron Microscopy revelated that the size of nanaoparticles in diameter of 2.5-15 nm. The formation of copper oxide nanoparticles (CuO-NPs) by *Ailanthus altissima* leaf aqueous extract was reported these synthesized copper oxide nanoparticles were characterized by UV-vis, SEM, TEM, FT-IR analysis tools. CuO-NPs nanoparticles were well crystalline in nature with particle shape spherical and average particle size 20 nm and antimicrobial activity of these nanoparticles was determined by disk diffusion method against some selected species of bacteria, demonstrated a significant inhibitory activity against *S. aureus* followed by *E. coli* [111-123].

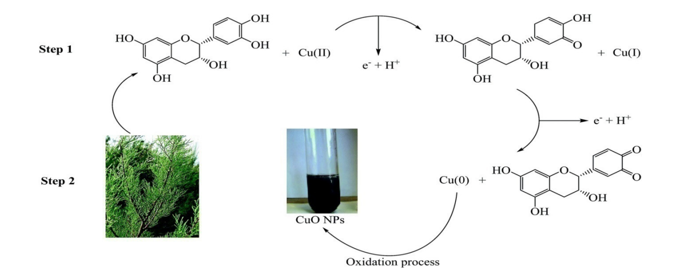

Figure 5: Mechanism for the synthesis of CuO-NPs from plant source.

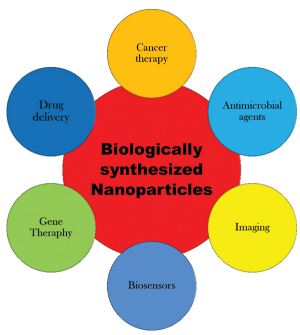

Figure 6: Application of biologically synthesized metallic nanoparticles.

Many researcher has been reported the usage of different plant extracts to prepare copper and copper oxide nanoparticles such as *Nerium oleander* Leaf aqueous extract, peel extract of Punica granatum, fruit extract of *Ziziphus spina-christi, Rosa canina* fruit extract, fruit extract of *Syzygium alternifolium* (Wt.) Walp and *Asparagus adscendens Roxb*. root and leaf extract, some of which might be not cost effective or not easily available and other plants which has been used for the synthesis of copper nanoparticles shown in **Table 3**.

Synthesis of titanium dioxide nanoparticles from plant extract

Nowadays the biosynthesis of nanoparticles has been used in a wide range by a synthetic route using plants. Plant based of Metallic Nanoparticles (MNPs) titanium dioxide nanoparticles (Tio2-NPs) synthesis is cost effective, eco-friendly and energy efficient. Researchers have exploited the potential of biological resources for the synthesis of Tio2-NP a simple precursor salt is mixed with biological extract; the metabolites present in the extract can then reduce and stabilize the bulk metal into elemental form following various mechanical steps. This biosynthetic approach offers many advantages and has emerged as a simple, safe and feasible substitute to chemical and physical methods apart from these, biological approach can effectively catalyze the synthesis process at any scale and condition. Moreover, NPs with controlled size and shape can also be produced. Owing to these benefits, numerous researchers have intended to explore diverse species for their potential to synthesize Tio2-NPs).

In the biological species, plants are considered as one of the most suitable candidates for the synthesis of NPs as they are cost effective, safe and easily available. A diverse array of compounds in plants (phenolic acids, alkaloids, proteins and among them enzymes, as well as carbohydrates) regulate through reduction and stabilization processes the synthesis of NPs. Numerous plants species have been used for synthesis of various shapes of Tio2-NPs show in **Table 4**. The reaction mixtures start vigorously when a precursor Tio2 salt is adul terated with plant extract; color change indicates the first sign of synthesis that can then be confirmed after wards by spectroscopic techniques. Several color indicators have been reported ranging from light green to dark green in the formation of Tio2-NPs Dobrucka. Majority of green synthesis studies have been conducted on leaves extracts, as it is a rich source of metabolites. Spherical Tio2-NPs resulted when Annona squamosa L. was added to the aqueous solution of Tio2 salt at room temperature.

Plant name	Plant part	Size (n.m.)	Shape	Reference
Calotropis procera L.	Latex	15+1.7	Polydispers and spherical	[56]
Psidiumguajava L.	Leaves	13.13-0.19	Spherical	[57]
Aloe vera F.	Fruit	40	Spherical	[58]
Capparis zylanica	Leaves	50-100	Cubical	[59]
O. sanctum	Leaves	77	FCC	[60]
Datura metal	Leaves	15-20	Spherical, hexagonal etc.	[61]
Citrus reticulata	Peel	Oct-40	Spherical	[62]
Citrus medica	Extract	Oct-60	FCC	[63]
Eclipta prostrata	Leaf	23-57	FCC	[64]
Punica grantatum	Plant extract	56-59	Spherical	[65]
Tilia	Aqueous extract	4.7-17.4	Hemispherical	[66]
Uncaria gambis ROXB	Leaf	2.5-15	Spherical	[67]
Lemon grass	Leaf	5.67-9.10	Spherical	[68]
Ginger officinale	Mixing leaf extract	15-30	Crystalline	[69]
Piper longer				
Piper nigrum				
Solanum lycopersicum	Extract	40-70	Crystalline	[70]
Rhuscoriaria L.	Fruit	22-27	Crystalline	[71]
Curcuma langa	Extract	May-20	Crystalline	[72]
Catharanthus roseus	Leaf	___	Crystalline	[73]
Ailanthus altissima	Leaf	20	Crystalline	[74]
Eringium caucasicum	Aqueous extract	40	Crystalline	[75]
Enicostemma axillary (Lim.)	Leaf	30	Crystalline	[76]
Gloriosa superb L.	Leaf	05-Oct	Monoclinic	[77]
Arevalanata	Leaves	40-100	Spherical	[78]
Saraca indica	Leaf	40-70	Spherical	[79]
Carica papaya	Leaves	140	Rod shape	[80]
Osmium basilicum	Plant extract	70	Spherical	[81]
Euphorbia esula L.	Leaves	40	Face centered cubic	[82]
Cassia fistula	Fruit	20-000	Amorphous	[83]
Aqueous ginkgo biloba	Leaf extract	15-20	Spherical	[84]

Aqueous broccoli	Extract	4.8	Spherical	[85]
Punica granatum	Seed extract	40-80	Spherical	[86]
Plantago asiatica	Leaf extract	Jul-35	Spherical	[87]
Ixora coccinea	Leaf	167.1	Spherical	[88]
Tridax procumbens	Leaf	85-118	Spherical and monodispersed	[89]
Pineapple	Leaf extract	30-50	Cubic	[90]
Tridax procumbens	Leaves	87	Spherical	[91]
Triumfettarotundifolia	Plant extract	12.46	Like triangle	[92]
Syzygium aromaticum	Bud	12	Spherical	[93]
Acanthophyllum Laxiusculum schiman-czeika	Roots	20-25	Spherical	[94]
Ageratina altissima[L.]R.M.king and H.Rob.	Leaves	60-100	Spherical	[95]
Annona squamosa L.	Peel	23	Polydispersed	[96]
Calotropis gigintae L. Dryand	Flower	10	Spherical	[97]
Catharanthus	Leaves	25	Cluster	[98]
Senna auriculata (L.) roxb.	Leaves	38	Spherical	[99]
Cicer aerentium L.	Seed	14	Spherical	[100]
Cinamomum tamla (Buch-Ham.) T.Nees	Leaves	Aug-20	Tetragonal	[101]
Citrus sinensis (L.) osbeck	Peel	19	Tetragonal	[101]
Curcuma longa L.	Wp	120	Polydisperse	[102]
Cynodon dactylon (L.) pers.	Leaves	13-34	Hexagonal	[103]
Eclipta prostrate (L.) L.	Leaves	36-68	Spherical	[104]
Ephorbia prostrate aition	Leaves	83.22	Polydisperse	[105]
Hibiscus rosasinensis	Flower extract	24.89	Crystalline	[106]
Jatropha curcas L.	Latex	20-100	Spherical	[107]
Morinda citrifolia L.	Leaves	15-19	Spherical	[108]
Moringa olifera lam.	Leaves	100	Spherical	[109]
Nyctanthes arbor – tristis L.	Leaves	100	Spherical	[111]
Ocimum basilicum L.	Leaves	50	Hexagonal	[101]
Piper betle	Leaves	7	Spherical	[112]
Psidium juajava L.	Leaves	32.58	Spherical	[113]
Dandelion	Pollen	___	Rod	[114]
Trigonella foenum –graecum L.	Leaves	20-90	Spherical	[115]

Table 3: Plant mediated synthesis of copper oxide nanoparticles..

Plant name	Part	Size (n. m.)	Shape	Reference
Acanthophyllum Laxiusculum schiman-czeika	Roots	20-25	Spherical	[94]
Ageratina altissima[L.] R.M.king and H.Rob.	Leaves	60-100	Spherical	[95]
Annona squamosa L.	Peel	23	Polydispersed	[96]
Calotropis gigintae L. Dryand	Flower	10	Spherical	[97]
Catharanthus	Leaves	25	Cluster	[98]
Senna auriculata (L.) roxb.	Leaves	38	Spherical	[99]
Cicer aerentium L.	Seed	14	Spherical	[100]
Cinamomum tamla (Buch-Ham.) T.Nees	Leaves	Aug-20	Tetragonal	[101]
Citrus sinensis (L.) osbeck	Peel	19	Tetragonal	[101]
Curcuma longa L.	Wp	120	Polydisperse	[102]
Cynodon dactylon (L.) pers.	Leaves	13-34	Hexagonal	[103]
Eclipta prostrate (L.) L.	Leaves	36-68	Spherical	[104]
Ephorbia prostrate aition	Leaves	83.22	Polydisperse	[105]
Hibiscus rosasinensis	Flower	24.89	Crystalline	[106]

Jatropha curcas L.				
Morinda citrifolia L.	Leaves	15-19	Spherical	[108]
Moringa olifera lam.	Leaves	100	Spherical	[109]
Nyctanthes arbor – tristis L.	Leaves	100	Spherical	[111]
Ocimum basilicum L.	Leaves	50	Hexagonal	[101]
Piper betle	Leaves	7	Spherical	[112]
Psidium juajava L.	Leaves	32.58	Spherical	[113]
Dandelion	Pollen	¬¬¬¬___	Rod	[114]
Trigonella foenum –graecum L.	Leaves	20-90	Spherical	[115]

Table 4: Detailed view of plant names, parts and their size in nm.

Furthermore, a wide propitious plant extracts are left to be explored for the synthesis of Tio2-NPs. Subhapriya and Gomathi has been studied the biosynthesis of Tio2 nanoparticles (Tio2-NPs) was attained by a chemical and bio-synthesized method by using the aqueous leaf extract of *Trigonella foenum-graecum* (TF-Tio2-NPs). FTIR, UV, XRD, HR-TEM, and HR-SEM methods was used for characterization of Tio2-NPs. The X-ray diffraction displayed the existence of TF-Tio2-NPs which is confirmed by the incidence of peaks at 25-28 corresponds to anatase form. HR-SEM perceptions revealed that synthesized Tio2-NPs were spherical in shape and the size of individual nanoparticles as well as a few aggregates was found to be 20-90 nm antimicrobial activities of biosynthesized nanoparticles (TF-Tio2-NPs) were examined using Kirby-Bauer method. The TF-Tio2 nanoparticles showed significant antimicrobial activity against all the tested microorganisms. In another methods studied that Tio2-NPs were synthesized by using a plant extract of *H. the lbiecea* and *Ananos seneglensi* and characterization studied was done by UV-vis spectroscopy, Scanning Electron Microscopy (SEM), X-Ray diffraction (XRD) and Fourier Transmission infrared spectroscopy (FTIR). SEM revealed that the synthesized Tio2-NPs are spherical and crystalline in nature with average sizes of 40 and 50 nm for *H. thelbiecea* and *Ananos* respectively. Both two plants showed good antimicrobial activity against clinically important pathogens. Antimicrobial study of Tio2-NPs shows that 20 µg/ml Tio2-NPs is effective for complete inactivation of Gram positive, Gram negative as well as fungal cultures [124-133]. Studied that herbal plant extract of *Cassica fistula* can be used as a capping agent for the synthesis of titanium doxide nanoparticles (Tio2-NPs). Spherical synthesized titanium doxide nanoparticles were characterized by SEM, TEM, FTIR, AFM, TGA. These nanoparticles showed antibacterial activity against *Escherichia coli* and *staphylococcus aureus*.

Evaluation of Biological Activity of Silver, Copper and Titanium Dioxide Nanoparticles

It has been reported that materials properties influenced by the structure of the materials. Metallic nanoparticles have the most favorable antibacterial properties because of their large surface area to volume ratio, and it is the foremost interest of researchers because of microbial resistance, which is growing against metal ion, resistant strains development and antibiotics. Amongst all noble metal nanoparticles, silver nanoparticles attained a lot of interests because of its best conductivity, chemical stability, anti-viral, antifungal and antibacterial activities which can be consolidated in the form of complex fibers, superconducting materials, electronic components, and cosmetic products. The scientific community has much interest in the synthesis of silver nanoparticles because of multiple types of applications. Silver nanoparticles are efficiently used in cancer diagnostics and treatment. It is the best way to synthesize nanoparticles as it avoids hazardous chemicals and gives natural agents for capping of silver nanoparticles to reduce the cost of microorganisms. Hence, this review compiled literature about the production of silver, copper and titanium oxide nanoparticles having the best biological activities. The biomedical application of synthesized NPs is significantly becoming more important due to their antibacterial, antifungal, anti-cancer, and biosensor.

Evaluation of antimicrobial activity

Antimicrobials are typically liquids. Antimicrobial liquids kill or inhibit the growth of microorganisms such as bacteria, fungi and protozoans. Antimicrobial drugs (e.g. penicillin) are selective and kill microbes (microbiocidal) or prevent their growth (microbiostatic). Disinfectants are non-selective antimicrobial substances (e.g. bleach) and are used on non living objects or the outside of the body. With the emergence and increase of microbial organisms resistant to multiple antibiotics and the continuing emphasis on health-care costs, many researchers have tried to develop new effective antimicrobial reagents free of resistance and cost. The most important problem caused by the chemical antimicrobial agents is multidrug resistance. According to *in vitro* antimicrobial studies, the metallic nanoparticles effectively obstruct the several microbial species. The antimicrobial effectiveness of the metallic nanoparticles depends upon two important parameters: (a) material employed for the synthesis of the nanoparticles and (b) their particle size. Over the time, microbial resistance to antimicrobial drugs has become gradually raised and is therefore a considerable threat to public health. For instance, antimicrobial drug resistant bacteria contain methicillin-resistant, sulfonamide-resistant, penicillin-resistant, and vancomycin-resistant properties. Antibiotics face many current challenges such as combatting multidrug-resistant mutants and biofilms. The effectiveness of antibiotic is likely to decrease rapidly because of the drug resistance capabilities of microbes. Hence, even when bacteria aretreated with large doses of antibiotics, diseases will persist in living beings. Biofilms are also an important way of providing multidrug resistance against heavy doses of antibiotics. Drug resistance occurs mainly in infectious diseases such as lung infection and gingivitis.

Evaluation of antimicrobial activity of silver nanoparticles

The fight against infections is as old as civilization. Silver, for instance had already been recognized in ancient Greece and Rome for its infection-fighting properties and it has a long and intriguing history as an antibiotic in human health care. Modern day pharmaceutical companies developed powerful antibiotics which also happen to be much more profitable than just plain old silver. Silver nanoparticles are the most admired inorganic nanoparticles, and they are utilized as efficient antimicrobial, antifungal, antiviral, and antiinflammatory agents. According to a literature survey, the antimicrobial potential of silver nanoparticles can be described in the following ways: (1) denaturation of the bacterial outer membrane (2) generation of pits/gaps in the bacterial cell membrane leading to fragmentation of the cell membrane, and interactions between Ag NPs and disulfide or sulfhydryl groups of enzymes disrupt metabolic processes; this step leads to cell death. The shape-dependent antimicrobial activity was also examined. According to truncated triangular nanoparticles are highly reactive in nature because their high-atom-density surfaces have enhanced antimicrobial activity explained the antibacterial activity of In situ synthesis of nanosilver on cotton using Tollen's reagent. Two bacteria, *Staphylococcus aureus*, and *Escherichia coli* were used to test the antibacterial activity of silver nanoparticles. *Acalypha indica* (*Euphorbiaceae*) leaf extracts have produced silver nanoparticles (20-30 nm) within 30 min. These nanoparticles had excellent antimicrobial activity against water borne pathogens *E. coli* and *V. cholera* (minimum inhibitory concentration (MIC)=10 mg ml-1). Furthermore, spherical silver nanoparticles (40-50 nm) were produced using leaf extract of *Euphorbia hirta* (*E. K. Elumalai*). These nanoparticles had potential and effective antibacterial property against *Bacillus cereus* and *S. aureus*. In another study, silver nanoparticles (with an average size of 57 nm) were produced when 10 ml of *Moringa oleifera* leaf extract was mixed to 90 ml of 1 m Maqueous of $AgNO_3$ and was heated at 60-80°C for 20 min. The formed nanoparticles had considerable antimicrobial activity against pathogenic microorganisms, including *S. aureus*, *Candida tropicalis*, *K. pneumoniae*, and *C. krusei*. It has been reported that cotton fibers loaded with biosynthesized silver nanoparticles (~20 nm) using natural extracts of *Eucalyptus citriodora* (neelagiri) and *Ficus bengalensis* (marri) had excellent antibacterial activity against gram-negative *E. coli* bacteria. These fibers have potential for utilizatio ninburn/wound dressings as well as in the fabrication of antibacterial textiles and finishings. *Raundra Garcinia mangostana* (mangosteen) leaf extract could be used as reducing agent in order to synthesize silver nanoparticles. The aqueous silver ions when exposed to leaf extract were reduced and resulted in silver nanoparticles with an average size of 35 nm.These nanoparticles had high effective antimicrobial activity against *E. coli* and *S. aureus*, Veerasamy). It was reported that *Ocimum sanctum* (tulsi) leaf extract could reduce silver ions into crystalline silver nanoparticles (4-30 nm) with in 8 min of reaction time. These nanoparticles were stable due to the presence of proteins which may act as capping agent. *Ocimum sanctum* leaves contain ascorbic acid which may play a role in bio-reduction of silver ions into metallic nanoparticles. Bio-synthesized silver nanoparticles have shown strong antimicrobial activity against both gram-negative (E.coli) and gram-positive (*S. aureus*) microorganisms. Singhal Furthermore, biosynthesis of silver nanoparticles by *Cacumen platycladi* extract was investigated. Reducing sugars and flavonoids in the extract were mainly responsible for the bioreduction of the silver ions and their reductive capability promoted at 90°C, leading to the formation of silver nanoparticles (18.4 ± 4.6 nm) with narrow size distribution. The nanoparticles had significant antibacterial activity against *E. coli* and *S. aureus* elucidated that Ag-NPs exhibited destabilization of the outer membrane and rupture of the plasma membrane, thereby causing depletion of intracellular ATP. Silver has a greater affinity to react with sulfur or phosphorus-containing biomolecules in the cell. Thus, sulfur-containing proteins in the membrane or inside the cells and phosphorus-containing elements like DNA are likely to be the preferential sites for silver Nanoparticle binding. In another *Jasmine Kaur* and Kulbhushan reported that Ag-NPs control bacterial growth in a variety of applications including dental work, catheters and burn wounds and anti-microbial activity of silver nanoparticles was evaluated against *E.coli* and *S.typhii* by colony counting method. Metabolic activity was also determined by MTT assay utilized aqueous *Raphanus sativus* root extract as a reducing and capping agent for the synthesis of silver nanomaterials for the first time and utilized the supernatant of the fungus strain *Penicillium aculeatum* Su1 to synthesize extracellular Ag-NPs and Jalal et al. studied the extracellular green synthesis of Ag-NPs using the supernatant of *Candida glabrata* isolated from oropharyngeal mucosa of human immuno deficiency virus (HIV) patients and evaluated them for antibacterial and antifungal potential against human pathogenic bacteria and fungi reported the biosynthesis of Ag-NPs using yeast strains synthesized Ag-NPs utilizing the culture supernatant of phenol degraded broth as the reducing agent and Ishida et al. studied the synthesis and antifungal activity of Ag-NPs synthesized utilizing the aqueous extract of the fungus *Fusarium oxysporum*. In another investigated antibacterial activity of copper nanoparticles was studied against micro organisms like against *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 737), *Pseudomonas aeruginosa* (MTCC 1681) and *Escherichia coli* (MTCC 1687) Kamrun and Shahin reported antimicrobial activity using cinamomum tamla leaf extract and its antimicrobial activity. Potential antimicrobial application against clinically isolated multidrug-resistant bacterial strains was reported by das.

Evaluation of antimicrobial activity copper oxide nanoparticles

Copper has broad-spectrum antimicrobial properties. This could be exploited for therapeutic benefit but, equally, exposures could yield undesirable activity against symbiotic bacteria in the environment, the skin or the intestine (i.e. the microbiome). So understanding copper-bacteria interaction is important. How much the nanostructuring of copper based materials governs their antimicrobial properties is not fully understood. Certainly this nanostructuring strategy may be used to tailor ‘slow release’ properties for copper ions or to allow stable aqueous formulations of copper at high concentrations without issues with hydrolysis and precipitation. However, this does not address whether particles themselves have a microbial impact beyond or in addition to released soluble copper. On the one hand, by comparison to silver, one might assume that it is only soluble copper, not particles, that are antimicrobial. On the other hand, increased activities of copper-based nanoparticles, above and beyond just copper ion content, have been indicated. Indeed, the issue of whether nanoparticles have specific activity against bacteria, remains unclear but important. For example, the European Food Safety Authority (EFSA) requests that, for new oral nanoparticles that are relevant to food, tests are carried out in terms of microbiome effects for safety assessment (EFSA, 2018).

In trying to determine whether copper-based particles, or the copper ions that they release in an aqueous environment, are responsible for antimicrobial activity, a number of aspects must be carefully considered. Firstly, in standard bacterial assays, total exposure to particulate or soluble (solubilised) copper will be determined by an interaction between time and rates of particle dissolution. Secondly, the chemistry of copper is complicated. At typical biological (near–neutral) pHs, particles may form when 'soluble' salts are added to a solution phase, due to oxo-hydroxide formation, polymerisation, cross linking and precipitation. Finally, particles, whether inadvertently formed or specifically added to a fluid phase, may agglomerate and/or aggregate. As such, studies investigating exactly what bacteria experience in terms of exposure to copper-based particles, and thus what chemical form is active, are lacking Synthesized CuNPs demonstrated a significant inhibitory activity by Kirby-Bauer disk diffusion method against *Escherichia coli* followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, Propioni bacterium acnes and *Salmonella typhi*. In another study by Yoon reported that Cu-NPs showed efficient antibacterial activity as compared to the silver NPs by utilizing single representative strains of *E. coli* and *B. subtilis* for Ag and Cu-NPs. Scientists have also suggested the utilization of silver and copper particles as efficient disinfectants for wastewater produced from clinics containing infectious microorganisms.Y.S.and Zain reported that when Cu and Ag-NPs were fused together to make bi-metallic NPs, their antibacterial effects were improved where size played a key role in bactericidal effect (N.M.) CuO-NPs showed excellent antimicrobial activity against various bacterial strains (*Escherichiacoli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Enterococcus faecalis*, *Shigella flexneri*, *Salmonella typhimurium*, *Proteusvulgaris*, and *Staphylococcusaureus*). Moreover, *E.coli* and *E.faecalis* exhibited the highest ensitivity to CuO-NPs while *K. pneumonia* was the least sensitive and reported that the antibacterial activity of CuO nanoparticles was tested against bacterial strains *K. pneumonia*, *S. Typhimurium*, and *E. aerogenes* using the agar diffusion method. The minimum inhibitory concentration of these three gram-negative bacterial strains *K. pneumonia*, *S. Typhimurium*, and E. aero genes were found to be 0.55, 0.15, and 0.30 µg/ml, respectively. Further antimicrobial properties of copper nanoparticles were investigated Radhakrishnan et al. using *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Staphylococcus aureus*. The bactericidal effects of copper nanoparticles were studied based on the diameter of the inhibition zone in disk diffusion tests of nanoparticles dispersed in batch cultures. The copper nanoparticles showed excellent activity against *Escherichia coli* and *Staphylococcus aureus*, with excellent inhibition zones of 14 mm and 10 mm, respectively. Bacterial sensitivity to nanoparticles was found to vary depending on the microbial species and synthesized copper oxide nanoparticles (CuO-NPs) using Ailanthus alissima leaf aqueous extract were studied for antimicrobial activity against pathogenic bacteria by disc diffusion method. Chloromphenical was used as a control antimicrobial agent. These copper oxide nanoparticles showed inhibition zone against Gram negative *Escerichia coli* and Gram positive Staphyococcus aureus bacteria. It was observed that an increase in CuO-NPs concentration increases the MZI of *E. coli* and *S. aureus* bacteria. CuO NPs showed excellent antimicrobial activity against various bacterial strains (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Enterococcus faecalis*, Shigella fexneri, *Salmonella typhimurium*, *Proteus vulgaris*, and *Staphylococcus aureus*). Moreover, *E. coli* and E. faecalis exhibited the highest sensitivity to CuO NPs while *K. pneumonia* was the least sensitive. CuO NPs showed excellent antimicrobial activity against various bacterial strains (*Escherichia coli*. *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Enterococcus faecalis*, *Shigella Salmonella typhimurium*, *Proteus vulgaris*, and *Staphylococcus aureus*). Moreover, *E. coli* and E. faecalis exhibited the highest sensitivity to CuO NPs while *K. pneumonia* was the least sensitive. CuO NPs showed excellent antimicrobial activity against various bacterial strains (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Enterococcus faecalis*, *Shigella flexneri*, *Salmonella typhimurium*, *Proteus vulgaris*, and *Staphylococcus aureus*). Moreover, *E. coli* and E. faecalis exhibited the highest sensitivity to CuO NPs while *K. pneumonia* was the least sensitive.

Evaluation of antimicrobial activity of titanium dioxide nanoparticles

In literature, different metallic NPs have been used against various strains of bacteria. Tio2-NPs also exhibited a value-added property of antimicrobial function. In previous studies, researchers reported that Tio2-NPs exhibited significant toxicity effects against both Gram-positive and Gram-negative bacteria, as well as algae, zebrafish, and mice. The usefulness of the antibacterial effect of Tio2-NPs was used in the disinfection of water contaminated with *Escherichia coli*. The already published studies on bacterial activity have demonstrated that Tio2-NPs can kill bacteria even at low concentrations, in which the photocatalytic process of Tio2-NPs causes fatal damage to microorganisms. Only a few studies on the antifungal effect of NPs were found in scientific publications. Nevertheless, researchers only focused on the silver (Ag) and zinc (Zn) NPs and their antifungal activity against fungal species, *Candida albicans* (*C. albicans*). Both NPs exhibited a strong antifungal effect toward the *C. albicans* in a concentration-dependent manner. By comparison, zinc is less potent than silver NPs in reducing *C. albicans* growth with a dose of 0.1 mg/mL and a dose of 0.4,3.3, respectively. To date, access to the antifungal activity of most manufactured NPs remains extremely limited. Hence, in this paper, the antifungal activity of Tio2-NPs against *C. albicans*, a prevalent human pathogen, was investigated using a trypan blue exclusion as say, which is a simple quantification method. The study covers the effect of different forms (anatase versus rutile) of Tio2, their exposure times, and dosage concentrations on *C. albicans* culture. Nadeem and colleagues. Similarly, Tio2-NPs also exhibit eco-friendly biocidal properties, which are attributed to their strong oxidizing potential. These NPs have been used against a wide range of infectious microbes including various bacterial strains, endospores, fungi, algae, protozoa, viruses, microbial toxins and prions. Tio2-NPs trigger the onset of Reactive Oxygen Species (ROS) when confronted with microbial cells Jayaseelan and colleagues (2013). These ROS kill microbes by disrupting cell wall's integrity mainly by phospholipids oxidation, which results in reduced adhesion and distorted ionic balance. Inside the cytosol, it inhibits the respiratory cytosolic enzymes and modifying macromolecules structures, producing substantial effects on cellular integrityand gene expression. Furthermore, it also decreases the phosphate uptake and cellular communication across the cell Jayaseelan and colleagues (2013). A possible mechanism of action is described in **Figure** 7. Both green synthesized and chemically derived Tio2-NPs kill microbes in same fashion but the biologically derived NPs show better antibacterial activity. Their excellent antimicrobial potential is attributed to the capping agents provided by the plant extracts Kumar and colleagues (2014). Morphology of NPs, membrane biochemistry and type of bacteria significantly affect antibacterial activity.

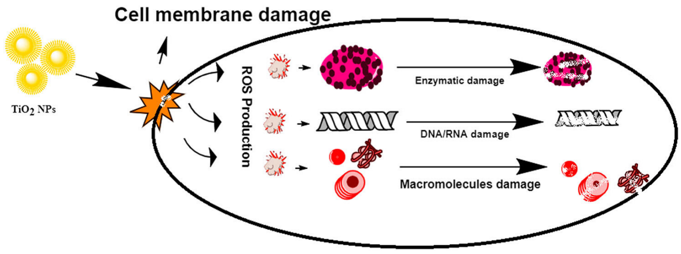

Figure 7: Evaluation antimicrobial activity of titanium dioxide.

Green synthesized Tio2-NPs can efficiently inhibit both gram-positive and gram-negative bacteria, but due to comparative structural complexity of gram-negative bacterial cell wall, it is more reactiveagainst gram-positive bacteria Marimuthu and colleagues. The antimicrobial activity of biomediated Tio2-NPs can be enhanced if irradiated with UV and fluorescent light Jayaseelan and colleagues ,Roopan and colleagues. Tio2-NPs Nano composites also exhibit enhanced antileshmanial activity, when green synthesized Tio2-NPs were applied to Leishmanial cultures; lower cell viability, stunted growth and DNA fragmentation was observed Kubacka and colleagues. When compared to standard antibiotic disk Tio2-NPs showed better antimicrobial activity Santhoshkumar and colleagues. Thus with such improved antimicrobial activity it considerably diminishes the occurrences for the development of antibiotic confrontation of pathogenic stains. Jesline. John reported antimicrobial activity of zinc and titanium discovers antibacterial activity and UV protection of the in situ synthesized tiatanium oxide nanoparticles on cotton fabrics.

Evaluation of anticancer activity

At well over 500,000 lives lost per year, cancer is the second most common cause of death in the United States. Most patients diagnosed with cancer undergo chemotherapy treatment; however, some cancer cells are known for their high resistance against chemotherapy drugs, so called Multi-Drug Resistance (MDR) 2,3. MDR often leads to relapse in cancer patients that have undergone chemotherapy treatment. In addition to the complications associated with MDR, chemotherapy treatments lead to mild to severe side effects in over 80% of patients, including nausea, hair loss, fatigue, increased risk of infection and anemia. These side effects limit the dosages at which chemotherapy drugs may be used a higher dose would more effectively kill chemotherapy drug-resistant cancer cells, but at the cost of greater unintended damages to the body. A strategy to overcome this dose limiting issue is localized high-concentration delivery of chemotherapy drugs to sites of cancerous growth.

Evaluation of anticancer activity of silver nanoparticles

In a work done by synthesized chitosan-coated silver nano-triangles (ChitAg-NPs) were used as a photothermal agents against a line of human nonsmall lung cancer cells (NCI-H460). In another work, AgNPs (10 nm) were synthesized using Sargassum vulgare and its ability to kill cancerous human myeloblastic leukemic cells HL60 and cervical cancer cells HeLa was tested and have been found to be active against plasmodial pathogens and cancer cells. Biosynthesized AgNPs have also been found to inhibit the brain cancer cell line HNGC2. These spherical AgNPs ranged in size from 20-80 nm, and the IC50 values were dose-dependent. Biosynthesized AgNPs have also shown notable inhibitory activity against the cervical cancer cell lines Siha and HeLa. Growth of the Siha cancer cell line was inhibited by 2-18 nm triangular and hexagonal AgNPs, with an IC50 of ≤ 4.25 µg/mL. In contrast, spherically shaped Ag-NPs, with sizes ranging between 5-120 nm, achieved inhibitory effects on HeLa cancer cell lines. The IC50 values varied depending on the preparation method of the AgNPs and also depended upon the plant extracts used. The bio synthesized AgNPs, inhibited four colon cancer cell lines (e.g., COLO 205, HCT 15, HCT-116 and HT29 cells), with IC50 values ranging from 5.5-100 µg/mL. The particles were substantially spherical in shape, with sizes ranging from 7.39-80 nm. Available data regarding these Ag-NPs in the context of brain, cervical and colon cancers. Cuboidal and spherical bio Ag-NPs with sizes ranging from 59-94 nm, prepared from different plant extracts, inhibited the A431 cell line, an epidermoid carcinoma, with IC50 values ranging from 78.580-83.57 µg/mL. Inhibition by bio-extract-derived spherical Ag-NPs with sizes ranging from 5-50 nm was also observed against the AGS cell line, a gastric carcinoma, with an IC50 of 21.05 µg/mL. The H1299 and HL-60 leukemia cell lines were inhibited by 22 nm spherical bio-Ag-NPs with an IC50 value of 5.33 µg/mL and in a dose-dependent manner, respectively. The data related to epidermoid carcinoma, laryngeal carcinoma, gastronomic carcinoma, hepatic cancer, intestinal cancer and kidney cancer.

According to a literature review, bio-extracts have been successfully used as reducing agents to prepare Ag-NPs that can block the activities of the A549 lung cancer cell line. The size of those spherically shaped NPs ranged from 13–136 nm, and the inhibitory actions were observed to follow a dose-dependent relationship, with various IC50 and LD50 values as mentioned below. The B16F10 melanoma cell line was inhibited by the 20-228 nm spherical bio-Ag-NPs, with an IC50 value of 7.6 ± 0.8 µg/mL, following a dose-dependent relationship. The 100-120 nm flower-shaped AgNPs exhibited notable repressive actions against the KB oral cancer cell line, where the IC50 was 0.6 µg/mL. The 15-32 nm spherical bio-Ag-NPs impeded the PA1 ovarian cancer cell line, with an IC50 value of 7.5 µg/mL an dina dose-dependent manner. In hibitory activities were observed against the Bx PC3 pancreatic cancer cellline by spherical bio-AgNPs with sizes ranging from 8-22 nm, and the IC50 was 38.9 µg/mL.

Evaluation of anticancer activity of copper oxide nanoparticles

Studies report that the biosynthesis of copper oxide nanoparticles from different plant extracts, such as that of *ficus religiosa* or *acalipha indica*. These NPs showed cytotoxic effects on A 549 human lung cancer cells and MCF-7 breast cancer cells, respectively. The mechanism of cytotoxicity was demonstrated to be through the induction of apoptosis with inhanced ROS generation. The green synthesis of these NPs has been proposed as realible, simple, nontoxic and ecofriendly method. Copper oxide nanoparticles from have many industrial applications, but recent studies have reported the antifungal and bacteriostatic properties of copper NPs polymer composites *in vitro* studies demonstrated that cuprous oxide NPS selectivily induce that apoptosis of tumor cells *in vitro*. Recent studies on the anticancer potential and cytotoxic activity of "plant based'' synthesized copper NPs from Sargassum polycystum brown seaweed, utilizing copper sulfate ($CuSO_4$) as the precursor, indicated that NP concentrations of 100 µg. ml^{-1} can efficiently provoke inhibition of the growth of MCF-7 breast cancer cells at percentages higher than 93% and with an IC50 value of 61.25 µg. Ml-1 Studies on the biosynthesis of copper NPs utilizing plants including Nerium oleander and Magnolia Kobus, have previously been reported.

Evaluation of biosensing activity

A biosensor is a device that combines a sensitive biological recognition component and a physical transducer to detect analytes of interest. Analysis results are displayed through transforming the biological reaction into a measurable signal, which can be used for qualitative and quantitative determinations. The biological recognition component part of biosensors usually includes nucleic acids, enzymes, antibodies, receptors, microorganisms, cells, tissues, and even some biomimetic structures. Physical transducers vary significantly with the source of the quantifiable signal, and utilize mostly optical and electrochemical systems.

Evaluation of biosensing activity of copper nanoparticles

The dispersion of metal nanoparticles displays intense colors due to the Surface Plasmon Resonance (SPR) absorption. The surface of metals like Cu can be treated as free electron systems called plasma, containing equal numbers of positive ions (fixed in position) and conduction electrons (free and highly mobile). Under the irradiation of an electromagnetic wave, the free electrons are driven by the electric field to oscillate coherently at a plasma frequency relative to positive ions. The metals rich in free electrons revealed this property so, it mostly used as a plasmonic material and a number of metals are supporting SPR for at least part of the UV-Vis-NIR region. These free electrons provide the negative real permittivity that is an essential property of any plasmonic material. However, metals are suffering from large losses, especially in the Uv-Vis. spectral ranges, arising in part from inter-band electronic transitions.

Evaluation of biosensing activity of titanium dioxide nanoparticlesn

Titanium dioxide was used as the substrate on the sensing surface, because Tio2-based semiconductor metal-oxide material has attracted substantial interest due to their low cost and production flexibility. The bio-compatibility of Tio2 nanoparticles in the development of biosensor promises better sensing performance and enhancing the electron-transfer kinetics. To increase the surface-to-volumeratio and enhance sensitivity, enabling the semiconducting conductance to be easily modulated by the target DNA for metal-oxide nanostructures have been proposed.

Conclusion

Biosynthesis of metal nanoparticles using plant derivatives is extremely studied in the last two decades. The plant metabolites induce the production of metallic nanoparticles in eco friendly manner. The use of plant extracts for making metallic nanoparticles is simple, convenient, and inexpensive, easily scaled up, less energy-intensive, eco-friendly, minimize the usage of unsafe materials and maximize the efficiency of the process.

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