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REVIEW

Copper Nanoparticles: A Review on Synthesis, Characterization and Applications

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Abstract

An emerging field of science "Nanotechnology" which is involved in manipulation of atoms and molecules has shown great potential in all fields of sciences. Nanotechnology deals with nanoparticles ranging from size 1 to 100 nm in diameter, due to small size and high surface area eventually increases the state of activity. This review focuses on metal and metal oxide nanoparticles and mainly on green synthesis, characterization and application of copper nanoparticles. Green synthesis of copper and copper oxide (Cu and CuO) is economically beneficial and ecofriendly. Copper nanoparticles are used in diverse fields such as biomedicine, pharmaceuticals, bioremediation, molecular biology, bioengineering, genetic engineering, dye degradation, catalysis, cosmetics and textiles. Structural properties and biological effects of copper nanoparticles have promising effectivity in field of life sciences.

Keywords: Economically beneficial- copper nanoparticles- Green synthesis- antimicrobial- anti-cancerous

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Introduction

Nanotechnology is an emerging field of science which involves change in matter at atomic or molecular level. Production of matters at a nanoscale is developed using Nanotechnology [1].This is a field of science which involves manipulation of atoms and molecules. A nanoparticle (NPs) is an ultrafine particle, a matter that ranges between 1 to 100 nm in diameter and with length of 1 to 1000 nm in one dimension [2]. The size of nanoparticles depends on the method of reduction and its surrounding environment.

Nanoparticles are applicable in varied fields of biomedical and pharmaceutical like diagnostics, biomarkers, bio-imaging, cosmetics, antibacterial, anticancer, immunology, cardiology, genetic engineering, drug delivery for treating cancer and other infectious diseases, bioremediation (environmental applications), water treatments and energy production [3], [4], [5]. Metal nanoparticles such as gold, copper, etc. have shown great approach in improving living standards and their need to be synthesized biologically has increased tremendously. Various metal and metal oxide as titanium dioxide (TiO_2) and silicon dioxide are mostly used NPs in paints, to provide antifungal, anti-algal and antibacterial property to paints. AZO NANO also tell about Nano silver NPs showing antimicrobial property by binding to bacterial cell proteins, with deodorizing, hydrophobicity property and less toxic effect [6]. These NPs have immense role in cosmeceuticals which gives therapeutically effect on skin, hairs also for treatment of photo aging, wrinkles, dark spots, etc. Various Nano carriers which encapsulate

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the drug to be targeted is formulated in cosmetics to show its effects [7]. More specifically copper NPs are also used in making buildings, as reduces the roughness of steel which will give resistance to corrosion, great thermal conductivity, and heat transfer property, polymer-coated CuNPs shows antibacterial property, and also gives hydrophobicity property [8] .Recently there is development in synthesis of inorganic NPs includes all metal and metal oxide NPs (such as silver, gold, zinc oxide, copper oxide etc) which have shown wide range of application in all fields. Synthesis of NPs basically happens by two main methods Top down and Bottom up, in which green synthesis method of Bottom up approach is widely taken into consideration as synthesis method is ecofriendly, cost effective, and nontoxic way of developing nanoparticles [9]. These NPs have wide range of application with all the field of sciences. So, this review will focus more on metal nanoparticles, with its green synthesis, characterization methods and applications.

There are various classifications of nanoparticles depending upon characteristics of material, dimensions, and origin [2], [10],[4],[11].

1. Classification based on characteristics of material:

i. Carbon nanomaterials- It includes carbon nanotubes (CNTs), carbon nanofibers, fullerenes (C60) etc.

ii. Inorganic nanomaterials- It includes metal and magnetic nanoparticles like silver, gold, also metal oxides/ semi-channel NPs such as TiO_2, ZnO, and CuO etc.

iii. Organic nanomaterials- It includes nanomaterials made from organic matter having weak interactions e.g. liposomes, dendrimers, micelles etc.

iv. Composite nanomaterials- These NPs are multiphase NPs which complicated structure of metal-organic frameworks. It may be combination of carbon, metal or organic with other metal or polymer.

2. Classification based on dimensions:

i. Zero-dimension nanoparticles- It includes quantum dots or quantum boxes.

ii. One-dimension nanoparticles- Polyethylene oxide nanofibers, Ag nanorods etc.

iii. Two-dimension nanoparticles- Carbon nanotubes, graphene nanosheets etc.

iv. Three-dimension nanoparticles- Dendrimers, fullerenes (C60), ZnO nanowires etc.

3. Classification based on origin:

i. Natural nanomaterials- NPs produced naturally by biological species or naturally occurring on earth spheres.

ii. Synthetic nanomaterials- NPs which produced by reduction using various physical, chemical, biological or hybrid methodologies.

2. Metal & Metal Oxide Nanoparticles

There is increase in interest of metal nanoparticles due to their physical and chemical properties and wide area of application. There is increase in demand of metal, metal oxides, polymer nanoparticles etc. due to their small size and high surface area for interaction which has several uses in material science. Properties of nanoparticles depend on the surrounding medium and required properties could be introduced by altering the environment [11].Green syntheses of ZnO NPs shows varying morphologies and have more antimicrobial activity then chemically synthesized NPs [12]. It has shown efficient inhibitory activity against *E. coli*, *S. aureus*, *P. aeruginosa*, *S. thalpophilum*, *B. subtilis*, *K. Pneumoniae* and efficient hydroxyl radical scavenging antioxidant activity [13]. Bovine serum albumin coated iron oxide nanoparticles carriers of curcumin were used for cytotoxic assay on HFF2 and MCF-7 breast cancer cell line showing positive results [14]. Green synthesis of gold nanoparticles have proven to show antidiabetic activity by showing antioxidant activity which lead to anti-apoptotic property with decrease in level of Bcl-2 protein and increased level of Bax indicating cell survival induced by NF-κB in RIN-5F diabetic cell line [15]. With significant inhibition in denaturation of BSA protein silver NPs shows anti-inflammatory activity [16].

There are several infectious microorganisms responsible for formation of Microbial biofilms that are sticky exopolymeric substances (EPS) causing adherence of microorganism to biotic surfaces such as host cells or abiotic surfaces such as medical devices cause antimicrobial resistance [17].Metal oxide nanoparticles are effective in fighting against multidrug resistance biofilm producing pathogenic bacteria, where CuO nanoparticles are found more effective than iron oxide and nickel nanoparticles [18],[19]. Antibacterial activity by copper and copper oxide NPs against biofilm producing organism *Bacillus subtilis*, *Staphylococcus aureus*, *E. coli* and *Pseudomonas aeruginosa* is shown [20],[21]. Effectivity of copper nanoparticles is found in varied applications such as Antifungal, Antiviral, Antibiotics, Anticancer, Photocatalytic, in biomedical, agriculture fields etc. and is cost effective [9].

3. Synthesis of Copper Nanoparticles

3.1. Physical and Chemical synthesis

Preparation of metal nanoparticles should be done using appropriate method to obtain a particular size of nanoparticle, as with use of particular method it reduces the size of particle and stabilizes it. Copper nanomaterials are greatly in attention due its profuse amount, availability and low cost in comparison to gold and silver, so large scale productions of copper nanoparticles are using various physical and chemical method [8]. The major methods used for large scale production of nanoparticles is done through physical methods (Mechanical milling, laser ablation and sputtering) and chemical methods (Solid state, liquid state, gas phase, biological methods and other methods), terming them as Top down and Bottom up methods respectively [22]. Top-down method for synthesis of nanoparticles is a method where bulk material is the initial material which is catabolized to reduce particle size, even though this methods are easy to perform but not suitable for preparing uniform size of particles and due to this it can affect the surface chemistry of NP's [23],[22]. The mechanochemical method for synthesis of nanoparticles requires precursor for copper, salts for dilution and as starting material which are ball milled at ambient temperature, resulting into copper oxide (II) nanoparticles enclosed into salt matrix further which were washed by distilled water in ultrasonic bath. These particles showed antimicrobial activity against S. aureus and E. coli [24]. In one of the work iron metal as reducing agent with precursors, chalcocite (Cu2S) and covellite (CuS) were milled at different timings resulting into approx. 16 nm sizes of copper NPs proving to be a scalable method [25]. Technique such as laser ablation targeting bulk copper with high power pulsed laser, with 20 mJ energy, 532 nm wavelength, 4 ns pulse width and power density of 5.24×10^{12} W cm^{-2} showing synthesis of copper oxide nanoparticles enhancing the growth of rice seedlings by hydroponics [26]. Bottom-up approach for synthesis of nanoparticle is obtained through assembling of atoms, molecules or small particles giving Nano size dimension [27]. Sol-gel method of using polymers are of great interest for green synthesis of nanoparticles, using *Lantana camara* extract, it was added to mixture of copper chloride and sodium hydroxide giving average particle size of 17 nm showing photocatalytic activity [28]. Chemical reduction of copper ions with sodium borohydride and stabilization by polyvinylpyrrolidone (PVP) using copper chloride as precursor giving 7 nm size of NP's by TEM and SEM analysis [29]. Copper nanoparticles of range 38 to 50 nm were prepared using solvothermal reduction method with glycerol (reducing agent) and various surfactants for stabilizing the particles [30]. The synthesis of NPs by thermal decomposition in liquid phase has achieved attention due to production of stable nanoparticle with easy method and also has shown antibacterial activity against E. coli [31],[32]. Microwave assisted green synthesis of CuO NPs was done using fruit extract of *Myristica fragrans* at 800 W and 2450 MHz frequency for 5 min with temperature below 100 °C with color change from blue to green was observed. The size of CuO NPs with TEM, SEM and XRD was found to be 4 nm, 13 nm and 15.7 nm respectively and showing antimicrobial and catalytic applications [33]. Flame spray pyrolysis, a scalable method is flame assisted pyrolysis converting aerosol to vapor to producing fine and pure copper oxide (CuO) nanoparticles whose size can be managed with flame temperature, residence time and liquid precursor concentration for various applications [34], [35].

3.2. Green synthesis

An alternative method for synthesis of nanoparticles is "Green Synthesis" which is simple, cost effective, and reproducible, and gives stable product. This method does not require high energy, pressure, temperature, or toxic chemicals [36]. Bottoms up approach for green synthesis is similar to that of chemical reduction of NPs, the difference is chemical reducing agent are replaced with extracts of plants, fruits, flower, and algae [37],[38].

3.2.1. Plant and Fruit Extract mediated Synthesis

This process of synthesis begins by mixing the natural extracts with a metal solution; with biochemical reduction of salt color change is observed in the solution indicating synthesis of nanoparticles [39]. Biosynthesis of copper nanoparticle using aqueous extract of *Tilia* and was added to copper sulfate pentahydrate solution with 4:1 (V/V), with continuous heating at 80 °C for 25 min; further precipitation and drying by putting into oven for 2 h at 100 °C was done. Hemispherical shaped with different diameter in range of 4.7-17.4 nm was observed by TEM studies. These NPs show antimicrobial and anticancer activities against human hepatic cancer (HepG2 cells) and breast cancer (Mcf-7 cells) [40].

Peppermint extract mediated synthesis of Cu NPs was coated with rifampicin (0.2 mg/mL) with constant stirring at 700 rpm for 5 hr maintaining; 6.5 pH & temperature between 25 and 45 °C, this enhanced the antimicrobial activity against Staphylococcus aureus, monitored using atomic force microscopy (AFM) and confocal laser scanning microscopy (CLSM) assessing DNA cleavage by agarose gel electrophoresis [41]. Copper oxide nanoparticle synthesis using *Annona muricata* leaf extract into copper (II) sulphate with continuous stiring at 80°C for 12 hr followed by drying at 24 hr; further XRD, SEM and BIO-TEM analysis showed 30-40 nm size of CuO NPs, which shows photocatalytic and cytotoxic property [42]. Fruit extract of *Syzygium alternifolium* was titrated with copper sulphate precursor (5 mM) at 50 °C for 2 hr, further precipitating at 10,000 RPM resulting into 17.5 nm average copper oxide particle size exhibiting antiviral activity against Newcastle Disease Virus (NDV) [43].

3.2.2. Bacterial and Fungal Mediated Synthesis

Microbial mediated synthesis of nanoparticles an evolving field of nanobiotechnology, involves certain mechanisms by which microorganisms thrive to grow with toxic metals which may lead to synthesis of nanoparticles as byproduct of reduction mechanism. As these microbes tend to produce enzymes which reduce the toxic metal resulting into formation of nanoparticles [44]. CuO NPs biosynthesis using *actinomycetes*, a cell free supernatant was collected and added to 25 ml of CuSO4. $5H_2O$ (10 mM) with heating at 100 °C for 15 min color change was observed. Further characteristics using XRD and TEM found 61.7 nm average size of NP which has potential antimicrobial property [45]. Fungal mediated, cell free extract of *Trichoderma asperellum* was used to synthesize 10-190 nm range of copper oxide nanoparticles where in amide and aromatic groups of secondary metabolite was found to be as encapsulating or reducing agent determined by IR spectroscopy. This nanoparticle was also studied in vitro photothermal induced therapy of human lung carcinoma- A549 cancer cells [46]. *Agaricus bisporus* (fungus) mediated green synthesis of copper NPs of size range 2- 10 nm which showed antimicrobial, antioxidant and cytotoxic activity against SW 620 colon cancer cells (Table 1) [47].

3.2.3. Algal Mediated Synthesis

Phyconanotechnology, a study of algal mediated extracellular formation of nanoparticles is economical, ecofriendly, energy efficient and less-toxic method to reduce down the metal nanoparticles [48]. Anabaena

Table 1. List of Extracts Used for Green Synthesis of Nanoparticles with Different Precursors and There Applications

Precursor	Reducing/ Oxidizing Agent	Size	Application	Reference
Copper sulphate	*Ginger Lily* leaf extract	40 nm Approx.	Antibacterial activity	[50]
Copper Acetate Monohydrate	*Psidium guajava* leaf Extract	11.07 nm	Photocatalytic Dye Degradation	[51]
Cupric Sulphate	*Centella asiatica* leaf extract	20-30 nm	Dye Degradation	[52]
Cupric acetate	*Camellia Sinensis* leaf extract	22.44 nm Approx.	Antibacterial, cytotoxicity activity	[53]
Copper Sulphate	*Punica granatum* leaf extract	20.33 nm	Dye Degradation	[54]
Copper Sulphate	*Sida acuta* leaf extract	50 nm	Antibacterial, Dye degradation, Textile	[55]
Copper Chloride	*Tinospora cordifolia* leaf extract	50-130 nm	Catalytic textile dye degradation	[56]
Copper Acetate	*Cissus quadrangularis* leaf extract	30.08 nm	Antifungal activity	[57]
Cupric Nitrate	*Gloriosa superba L.* leaf extract	5-10 nm	Antibacterial activity	[58]
Copper nitrate trihydrate	*Tinospora cordifolia* leaf extract	6-8 nm	Photocatalytic, Antioxidant, Antibacterial activity	[59]
Copper nitrate	*Aloe vera* leaf extract	22 nm	Antibacterial activity against fish pathogens	[60]
Copper Sulphate	*Tabernaemontana divaricate* leaf extract	48 nm Approx.	Antibacterial activity against urinary tract pathogen	[61]
Copper Sulphate	*Strawberry* Fruit extract (Stabilizing Agent- L ascorbic acid)	10-30 nm	Antioxidant, Antifungal, Antibacterial, Anticancer, cutaneous wound healing activity	[62]
Copper sulphate	*Terminalia bellirica* fruit extract	2-7 nm	Antimicrobial activity	[63]
Copper Sulphate	*Citrus medica Linn.* Fruit extract	10-60 nm	Antimicrobial activity	[64]
Copper (II) nitrate trihydrate	*Cordia sebestena* flower extract	20-35 nm	Photo degradation of Dyes, Antibacterial activity	[65]
Copper Sulphate	*Streptomyces spp.* (microbes)	78 nm and 80 nm	Antimicrobial, Antifungal, Antioxidant activity, Larvicidal activity	[66]
Copper (II) chloride	*Shewanella loihica PV-4* (microbes)	10-16 nm	Antibacterial activity	[67]
Copper sulphate	*Eichhornia crassipes* leaf extract	28 nm Approx.	Antifungal activity against plant fungal pathogen	[68]
Copper (II) sulphate	*Bifurcaria bifurcate* brown alga extract	18.34 nm	Antimicrobial activity	[69]

cylindrical (microalgae) extract was used for biosynthesis of CuO NPs with constant stirring at 60 °C with 500-1000 rpm rotational speed, resulted into particle size of 3.6 nm and this had a potential use in disinfection of drinking water [49].

4. Characterization

The range of wavelength at which it reveals the synthesis of copper nanoparticle is of 200-800 nm by Surface Plasmon Analysis (SPR). UV-visible spectroscopy, SEM and TEM is used for determining shape, size and bandwidth, the crystal lattice structure is determined by XRD and presence of functional group on surface of nanoparticles can be determined by FTIR analysis [9]. These are the majorly used characterization techniques for analysis of nanoparticles. Characterization of nanoparticles reveals about the different shapes, size and biological activity of nanoparticles changes with its structure. The particle size of nanoparticle plays an important role in many applications such as drug delivery and smaller the particle size larger the surface which could be targeted for drug release [4].

4.1 UV- Visible Spectrophotometry

This spectrophotometric technique is widely used for quantification of various transparent fluids. According to different absorption feature of an analyte UV-vis spectrometer analyses the concentration of the absorbing components. Due to various interaction of analyte with the surrounding solution with respect to time it can change the absorption spectra [70] this is observed in case of NPs. UV-vis spec. works on basic principle of Beer-Lambert Law of absorption and transmission of light to determine concentration of NPs. This technique is sensitive to change in concentration, size, and refractive index of NPs, as its varies due to change in pH and time of interaction with the solvent [70].

Optic and colloidal property of copper NPs was characterized by UV 3000+ LABINDIA double beam spectrophotometer with spectral range of 200 to 800 nm. Formation of CuNPs using Azadirachta indica leaves was observed with gradual color change of solution with different time, which was recorded by UV-vis spec. resulting in increase of SPR peak showing continuous reduction of copper ions to CuNPs [71]. Bacillus cereus-mediated CuNPs synthesis was confirmed by SPR with size recorded between 570 and 620 nm further analysis showed presence of spherical shaped NPs [72].

3.3. XRD (X ray diffraction)

This method is used to determine crystal lattice structure, which resolves molecule at atomic level using constructive and destructive interference caused by the atom in lattice. The diffracted pattern of constructive interference by the crystal structure would be would be determined by d (spacing between planes of atoms) and reflection angle, θ which gives Bragg's equation:

$$n\lambda=2d \sin\theta$$

As XRD gives average of all crystal volume, peak broadening is seen which can be due to fine crystal structure, so the crystalline size D, can be found using Debye-Scherrer equation [73].

$D=K\lambda/\cos\theta$

D8 Advance Bruker X-ray diffractometer with Cu Kα was used to study crystal lattice of CuNPs synthesized from Garcinia mangosteen leaf extract which resulted into 26.51 nm average particle size of NP which was calculated using Debye-Scherrer formula [74].

3.4. SEM Analysis

This method of characterization of NPs does surface analysis, which will enable us to know morphology, shape, size, chemical composition and orientation of materials. During SEM characterization the solution from of NPs is converted to dry powder form which is mounted on a sample holder, and fine beam of electron is passed on sample resulting in release of secondary electrons/ back scattered electrons which will determine surface of the sample [4]. The release of electron from the nanomaterial varies according to its surface, due to which depression and elevation of surface can be analyzed enabling us to know the morphology of NPs.

The SEM analysis of CuNPs using different surfactants and precursor with varying reaction time was done using ZEISS EVO Series, Model EVO 18 microscope showing different shapes and size of crystal mainly focused, which concluded which increase in concentration of the reducing agent, the rate of reduction reaction increases [75].

3.5. TEM Analysis

This technique is used for analysis of physical properties such as size, morphology, and shape of NPs along with chemical compositions; it provides spatial resolution range of 1 to 100 nm resulting into 2D images. The resolution of microscopy depends on the accelerating voltage of primary electrons of range 100-300 kV. This method analyses 2D of a particle by estimating perpendicular electron beam but cannot estimate parallel beam, but 3rd dimension of particle could be analyzed using energy-filtered TEM and transmission electron tomography. The sample preparation of nano-material for analysis should be done precisely, for physicochemical analysis of NPs. With bright field imaging of TEM, the transmitted electrons from the specimen are analyzed whereas dark-filed imagining is due to diffracted electron. The image is recorded by CCD camera and fluorescent screen is used to view image [76].

The dry form of copper oxide NPs synthesized by Asamoah et.al., was re-suspended in proportionate water. This was further sonicated to avoid agglomeration of particles, and immobilizing the suspension on carbon grid and was analyzed after drying. Analysis resulted into formation of nanorods with average length and width of 100 nm and 14 nm respectively [77] showing antibacterial activity. TEM images taken by JEOL JEM-1200EX microscope at 120kV using energy dispersive spectrometer (EDS) showed spherical shaped CuNPs and average size of NPs was found to be 15-20 nm detection using quasi elastic light scattering data (QELS) [78].

3.6. FTIR Analysis

This spectroscopy method enables us to know functional groups present on surface of NPs by measuring vibrational frequency of the bonding present in the functional group. The molecules responds to range of 10^{13}-10^{14} Hz infrared radiation [79], which allows us to analyze the functional group such as carboxylate group, amino groups, phenolic group etc. So the extract used for reduction of CuNPs, the chemical components of those extracts which interacts with Cu ions this will result in attachment of functional groups on surface of NPs. This could be detected by FTIR analysis. Copper oxide synthesis using White-Rot Fungus (*Stereum hirsutum*) showing plasmon resonance between 590 to 650 nm with highest peak at 620 nm was observed, FTIR analysis done by CARY 630 FTIR Agilent Technologies resulted in band regions of 3280 cm^{-1} and 2924 cm^{-1} show presence of primary and secondary amines [80]. The average size of copper NPs formed using *Calotropis procera L.* latex extract was found to be 20 nm using XRD and FTIR results showed role of free amino groups or carboxylate group in reduction and stabilization of CuNPs. This NPs possessed cytotoxicity activity against tumorous cells [81] . Seedless dates extract for synthesis of copper and copper oxide NPs revealed 8 peaks by FTIR analysis which represented presence of phenolic compound which may be acting as capping agent providing more stability [82]

5. Applications

Nanoparticles have potent applications in biomedical and pharmaceutical fields due to nano-size and high surface area. Major Fields of sciences which are benefited with CuNPs are covered below:

A) Biological Applications

Copper NPs shows antimicrobial activity towards Bacillus subtilis, E. coli, S. aureus, Micrococcus luteus, Pseudomonas aeruginosa, Salmonella enterica, and Enterobactor aerogenes [83],[84],[85] and also antifungal activity against Fusarium oxysporum and Phytophthora capsici [86]. The copper ions are capable of damaging cell membrane, DNA, RNA and other molecules, thus Cu NPs have shown profound effect against viruses such as human influenza A (H1N1), avian influenza (H9N2), and many more including COVID-19 virus reducing its viability, and half-life [87].

Nanoparticles tend to elicit intrinsic and extrinsic apoptotic pathway for death of cancerous cells, and copper has found promising against cancer [23]. Copper and copper oxide nanoparticles exhibit anticancerous activity against HeLa cells, MD A-MB-231 (human breast cancer cell lines), Caco-2 (human colon cancer cells), and HepG2 cells (Hepatic cancer cells) and Mcf-7 breast cancer cells [90],[91], [40],[92].

Wound healing property of CuNPs with significant increase in concentration of fibrocytes eventually forming collagen for repairing and wound contraction was seen with in vivo study on mouse [93]. Cutaneous wound healing was also studied in vivo by synthesis of copper NPs by Falcaria vulgaris leaf extract and also showed potent cytotoxicity, antioxidant, antifungal, antibacterial activities [94].

Copper nanoparticles have improved antioxidant enzymes with decline of pro-inflammatory markers in CFA (complete Freund's adjuvant- which mimics human arthritis outcome) stimulated arthritis in rats proving anti-inflammatory and anti-arthritic potentials [104].

B) Textile

UK manufacturer Promethane Particles along with textile companies and research institutes are developing Personal Protective Equipment (PPE) and are designing fabrics having Nano-copper into polymer fibers such as nylon, by melt extrusion process and developing antimicrobial fabrics which is under examination [88]. Copper nanoparticles are incorporated in cotton fibers and antimicrobial evaluation is done against *E. coli*, *S. aureus*, *Proteus vulgaris* and *K. pneumoniae* [56], [89], [55]which can be used in textiles to produce PPE.

C) Biocatalyst and Bioremediation

Copper being low cost metal, less toxicity and copper based catalyst can be recycled and reused again [95]. Bioremediation of pollutant such as dyes has become important to treat the polluted water which can lead to alterations in aquatic life and can lead to dangerous outcome. So the properties of CuNPs are discussed for remediating polluted water bodies due to textile effluents, industrial disposal etc. Copper Oxide NPs for waste water purification [96] and the catalytic property of CuNPs was observed in reduction activity of Xanthene dye along with strong reducing agents which act as precursor of Cu2+ ions in formation of CuNPs which causes fluorescence quenching. These could also be applicable in biological sensing and bio-labelling [97]. Degradation activity of CuO NPs was higer than Ni@Fe_3O_4 against organic dyes such as congo red, methylene blue and Rhodamine B [98] and also showed reduction of 4-nitrophenol [99] to treat Textile Wastewater. Aspergillus species responsible to produce aflatoxins (AFs) which is found to be carcinogenic, mutagenic etc., the adsorbent capacity of Cu-NPs for aflatoxin B1 was found to be more than Ag-NPs but less than Fe-NPs [100].

D) Therapeutics

According to US NIH as: 'Nanomedicine refers to highly specified medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve' [4]. Nanoparticles provide site specific drug delivering system, due to its small size, large absorptive surface for drug to carry and also shows improved therapeutic efficacy with less toxicity. Brest Cancer was targeted using chitosan coated copper nanoparticles at different pH for drug doxorubicin, on MCF-7 cell line by studying apoptotic activity of cells [101]. Antimicrobial activity using biopolymer chitosan micro particles conjugated with copper NPs which shows greater synergic effect for antibacterial activity of tetracycline against Gram positive and Gram Negative bacteria [102] also core-shell Nano carriers were used to enhance activity of tetracycline, where copper oxide NPs was used as core and hyper-branched polyglycerol as shell [103].

E) Other Applications

Copper NPs have also shown profound applications in Food Packaging [105] and agriculture for crop improvement [106]. Thus Copper nanoparticle shows wide range of application in field of biological, physical and chemical sciences.

In Conclusion, nanoparticle production from natural extracts is emerging widely in field of nanotechnology as greener the process better the outcome without any toxic effects. The main reason to use natural extracts is it becomes eco-friendly and free of chemical contaminants which has applications in major fields of sciences. A proper method, time, precursor, pH, temperature, incubation time must be taken into consideration to optimize the synthesis process. These methods are scalable, and more safe and stable then produced through physical and chemical procedures. Major synthesis of metal nanoparticles is observed due to their effective application.

Efforts are made to obtain secondary metabolites from the natural extracts at different concentrations, which act as reducing and stabilizing agent useful for capping. Also polymeric based nanoparticles are also emerging with development of nanoscience. This green synthesis methods are effective to reduce down the size of nanoparticle and extract itself stabilizes the NPs, thus this method is completely eco-friendly having considerable effects in showing antimicrobial, antifungal, anti-cancer, catalytic, textile, cosmetics, water remediation etc. and many more applications which opens door for many therapeutics and treatments. Due to the nature of biological entities with varied concentrations along with other organic agents will influence the size, shape and effectivity of NPs.

Various researches are being carried out to scale up green synthesis methods. This can fulfill the future aspects of demand for welfare of human.

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