



## Review

## Biogenic nanomaterials: Synthesis, characterization, growth mechanism, and biomedical applications

R.M. Tripathi<sup>a,b</sup>, Sang J. Chung<sup>a,\*</sup><sup>a</sup> School of Pharmacy, Sungkyunkwan University, 2066 Seoburo, Jangan-gu, Suwon, Gyeonggido 16419, Republic of Korea<sup>b</sup> Amity Institute of Nanotechnology, Amity University, Uttar Pradesh, Sector 125, Noida 201303, India

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## ABSTRACT

The biosynthesis of nanomaterials is a huge and intensifying field of research due to their application in various areas, in particular the biomedical and pharmaceutical fields. In this review, we focused on the biosynthesis of both metallic and semiconductor nanomaterials and their application in biomedicine and pharmaceuticals. In order to meet an exponentially increasing need for nanostructured materials, the biological route for the synthesis of nanomaterials will have to be explored, offering advantages over chemical and physical methods as a simpler, more cost effective, and environmentally friendly method, and for which there is no need to use high pressure and temperatures or toxic chemicals. This review discusses in detail the potential role of bioreducing and capping/stabilizing agents in biosynthesis. This review also investigates the application of various biosynthetic nanomaterials as antimicrobial materials, in clinical detection, for drug delivery and wound-healing, and as anti-diabetic materials.

## 1. Introduction

Nanotechnology is one of the most active research fields and deals with the creation and utilization of materials with structural features of atoms and bulk materials with at least one dimension in the nanoscale (Saxena et al., 2012). Nanotechnology research and development is intensifying very rapidly because the properties of materials are different at the nanoscale. The synthesis of nanostructured materials is the backbone of nanotechnology and involves synthesizing nanoscale materials of different shapes and sizes for applicability in different fields, including electronics, chemistry, energy, and medicine. Nanoparticles (NPs) have been widely used to improve the pharmacological and therapeutic properties of anti-cancer drugs by targeted drug delivery (Prabaharan, 2015). NPs can have novel or superior properties depending on their size, shape and distribution (Song and Kim, 2009). The synthesis of nanomaterials can be broadly categorized into two approaches: top-down and bottom-up. Top-down approaches involve crushing or cutting of the bulk materials into fine particles at the nanoscale. The bottom-up approaches involves the creation of nanoscale materials by assembling them atom by atom, molecule by molecule, or cluster by cluster. A variety of methods have been developed for the synthesis of nanomaterials, including chemical reduction (Banerjee et al., 2014; Li et al., 2017a, 2017b, Xue et al., 2017), electrochemical

reduction (Liu et al., 2013), photo-chemical reactions in reverse micelles (Yi et al., 2017), and via the green chemistry route (Tripathi et al., 2012). Nanomaterials are generally synthesized by chemical methods, which involve the use of toxic chemicals such as thiophenol (Ravindran et al., 1999), mercaptoacetate (Wageh et al., 2015), and thiourea (Pattabi and Uchil, 2000). These chemicals are hazardous in nature and lead to serious environmental problems and physical method required high energy and pressure. Physical method for synthesis of silver NPs has been required tube furnace at atmospheric pressure, large space occupies by furnace, needs a huge amount of energy while raising the temperature surrounding the source material, and needs lot of time to attain thermal stability (Iravani et al., 2014). Nowadays researchers are using the biological synthesis approach to overcome the problems associated with the chemical and physical methods. Biosynthesis of nanomaterials using plant extracts is both advantageous and cost effective, as well as environment friendly, and the synthesis process does not involve neither toxic chemicals nor high energy inputs (Saxena et al., 2010). Several plants have been used for the synthesis of silver NPs, including *Ficus benghalensis* (Saxena et al., 2012), *Ficus pand* (Tripathi et al., 2013b), *Saraca india* (Tripathi et al., 2013c), among others, the details of which are listed in Table 1 (Azizi et al., 2017; Chandran et al., 2006; Huang et al., 2007; Jha and Prasad, 2010; Saxena et al., 2010; Song et al., 2009). Silver NPs have also been synthesized by using

Abbreviations: NPs, Nanoparticles; CNDs, Carbon nanodots

\* Corresponding author.

E-mail address: [sjchung@skku.edu](mailto:sjchung@skku.edu) (S.J. Chung).

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**Table 1**  
Biological source- mediated synthesis of nanomaterials.

S.No.	Nanomaterials	Biological source	References
1.		Plants <i>Ficus benghalensis</i> , <i>Allium cepa</i> , <i>Ficus panda</i> , <i>Saraca indica</i> , <i>Aloe vera</i> , <i>Cinnamomum camphora</i> , <i>Pinus desfflora</i> , <i>Diopyros kaki</i> , <i>Ginkgo biloba</i> , <i>Magnolia kobus</i> , <i>Platanus orientalis</i> , <i>Cycas</i> , <i>Citrullus colocynthis</i>	(Saxena et al., 2012, 2010; Tripathi et al., 2013b, c; Chandran et al., 2006; Huang et al., 2007; Song et al., 2009; Jha and Prasad, 2010; Azizi et al., 2017)
	Silver	Bacteria <i>Cupriavidus necator</i> , <i>Pseudomonas Antarctica Pseudomonas proteolytica</i> , <i>Pseudomonas meridiana</i> , <i>Aerobacter kerguelensis</i> , <i>Aerobacter gangotriensis</i> , <i>Bacillus indicus</i> , <i>Bacillus cecembensis</i> , <i>Klebsiella pneumoniae</i> , <i>Escherichia coli</i> and <i>Enterobacter cloacae</i> , <i>Aeromonas sp.</i> SH10	(Castro-Mayorga et al., 2018; Shivaji et al., 2011; Shahverdi et al., 2007; Mouxing et al., 2006)
2	Gold	Fungi <i>Aspergillus terreus</i> , <i>Aspergillus fumigates</i> , <i>Phanerochaete chrysosporium</i> , <i>Aspergillus flavus</i> , <i>Trichoderma longibrachiatum</i> , <i>Fusarium semitectum</i> , <i>Volvarella volvacea</i> , <i>Cladosporium cladosporioides</i> , <i>Rhizopus stolonifer</i> , <i>Raphanus sativus</i> , <i>Penicillium fellutanum</i> , <i>Metarhizium robertsii</i> , <i>Aspergillus oryzae</i> , <i>Candida albicans</i>	(Velhal et al., 2016; Rhainsa and D'Souza, 2006; Vigneshwaran et al., 2006; Vigneshwaran et al., 2007; Elamawi et al., 2018; Basavaraja et al., 2008; Philip, 2009; Balaji et al., 2009; Abdelrahim et al., 2017; Singh et al., 2017; Kathiresan et al., 2009; Rózsalska et al., 2016; Phanjom and Ahmed, 2015; Abdehghah et al., 2017)
		Plants <i>Ficus benghalensis</i> , <i>Alfalfa</i> , <i>Aloe vera</i> , <i>Pelargonium graveolens</i> , <i>Stevia rebaudiana</i> , <i>Lemongrass</i> , <i>Magnolia kobus</i> and <i>Diopyros kaki</i>	(Tripathi et al., 2012; Gardea-Torresdey et al., 2002; Chandran et al., 2006; Elia et al., 2014; Sadeghi et al., 2015; Shankar et al., 2004; Song et al., 2009)
		Bacteria <i>E. coli</i> , <i>Bacillus megaterium D01</i> , <i>Desulfivibrio desulfuricans</i> and <i>E. coli DH5α</i> , <i>Pseudomonas aeruginosa</i> and <i>Rhodopseudomonas capsulate</i>	(Du et al., 2007; Wen et al., 2009; Deplanche and Macaskie, 2008; Singh and Kundu, 2014; He et al., 2007)
		Fungi <i>Rhizopus stolonifer</i> , <i>Verticillium luteoalbum</i> , <i>Fusarium oxysporum</i> , <i>Trichoderma harzianum</i> , <i>Rhizopus oryzae</i>	(Binupriya et al., 2010; Genicke and Pinches, 2006; Thakker et al., 2012; Tripathi et al., 2014c; Das et al., 2010)
3.	Copper	Plants <i>Ficus benghalensis</i> , <i>Ocimum sanctum</i>	(Agarwal et al., 2016; Patel et al., 2016)
4.	Palladium	Plants <i>Ocimum sanctum</i> , <i>Euphorbia granulata</i> , <i>Pulicaria glutinosa</i> , <i>Origanum vulgare</i> , <i>Pevilla frutescens</i> , <i>Hippophae rhamnoides Linn</i>	(Gogoi et al., 2017; Nasrollahzadeh and Sajadi, 2016; Khan et al., 2014; Shaik et al., 2017; Basavegowda et al., 2015; Nasrollahzadeh et al., 2015)
5.	Iron	Fungi Yeast extract	(Mehrotra et al., 2017)
6	Platinum	Plants <i>Anacardium occidentale</i> , <i>D. kaki</i> , <i>O. sanctum</i> , <i>Azadirachta indica</i>	(Shery et al., 2013; Song et al., 2010; Soundarrajan et al., 2012; Thirumurugan et al., 2016)
7	Gold-silver biometallic and alloy nanoparticles	Plants <i>Cacumen platycladi</i>	(Zhan et al., 2011)
		Fungi <i>Neurospora crassa</i> , <i>F. oxysporum</i> , <i>Trichoderma harzianum</i>	(Castro-Longoria et al., 2011; Senapati et al., 2005; Tripathi et al., 2015)
8.	Cadmium sulfide	Plants <i>Linaria maroccana</i> L.	(Borovaya et al., 2014)
		Bacteria <i>Bacillus licheniformis</i> MTCC 9555	(Tripathi et al., 2014b)
9.	Titanium dioxide	Plants <i>Vitex negundo Linn</i> , <i>Vigna unguiculata</i> , <i>Curcuma longa</i> , <i>Calotropis gigantea</i> , <i>Psidium guajava</i> , <i>Trigonella foenum-graecum</i> , o	et al., 2013; Santhoshkumar et al., 2014; Subhapiya and Gomathipriya, 2018)
		Bacteria <i>Aeromonas hydrophila</i> , <i>Bacillus subtilis</i>	(Jayaseelan et al., 2013; Kirthi et al., 2011)
		Fungi <i>Fusarium oxysporum</i> , <i>Sacharomyces cerevisiae</i> , <i>Aspergillus tubingensis</i>	(Bansal et al., 2005; Jha et al., 2009; Tarafdar et al., 2013)
10.	Zinc oxide	Plants <i>Trifolium pratense</i> flower	(Dobrucka and Dugaszewska, 2016)
		Bacteria <i>Bacillus licheniformis</i> MTCC 9555	(Tripathi et al., 2014a)
11	CdSe quantum dots	Fungi <i>Fusarium oxysporum</i>	(Kumar et al., 2007)
12	Carbon nanodots	Plant <i>Musk melon</i>	(Mahajan et al., 2016)

bacterial biomass such as *Cupriavidus necator* (Castro-Mayorga et al., 2018), among other bacterial biomasses, as shown in Table 1 (Mouming et al., 2006; Shahverdi et al., 2007; Shivaji et al., 2011). *Aspergillus terreus* (Velhal et al., 2016), *Aspergillus fumigatus* (Bhainsa and D'souza, 2006), and other fungal biomasses have also been found suitable for synthesis of silver NPs, the details of which are listed in Table 1 (Abdehghah et al., 2017; Abdelrahim et al., 2017; Balaji et al., 2009; Basavaraja et al., 2008; Elamawi et al., 2018; Kathiresan et al., 2009; Phanjom and Ahmed, 2015; Philip, 2009; Rózsalska et al., 2016; Singh et al., 2017; Vigneshwaran et al., 2007; Vigneshwaran et al., 2006). The biologically synthesized silver nanoparticles have been applied in various field like biomedical application, colorimetric detection (Ismail et al., 2018), and catalysis detoxification (Tripathi et al., 2018b). *Ficus benghalensis* was used to synthesize silver nanoparticles and applied for preparation of antibacterial biodegradable nanocomposite film of poly (vinyl alcohol)-biogenic silver for food packaging materials (Tripathi et al., 2018a). Gold NPs were synthesized from plant extracts of *Ficus benghalensis*, having a narrow size distribution and a high stability (Tripathi et al., 2012). Table 1 shows other plant extracts which were also used to synthesize gold NPs (Chandran et al., 2008; Elia et al., 2014; Gardea-Torresdey et al., 2002; Song et al., 2009). Bacterial and fungal biomasses have also been used for the synthesis of gold NPs, including *E. coli* DH5a (Du et al., 2007) and *Bacillus megaterium* D01 (Wen et al., 2009), among others, as listed in Table 1 (Binupriya et al., 2010; Deplanche and Macaskie, 2008; Gericke and Pinches, 2006; He et al., 2007). Biogenic gold NPs have been extensively exploited in biomedical application like in cancer treatment (Rajeshkumar, 2016), potential mechanism for drug delivery (Tripathi et al., 2015c) and bacterial transformation (Kumari et al., 2017). Biologically synthesized gold NPs have been also used for the environmental remediation especially wastewater treatment (Tripathi et al., 2018c). Silver-gold biometallic NPs have been previously biosynthesized using filamentous fungus *Neurospora crassa* (Castro-Longoria et al., 2011). In a previous study, we have reported on the biosynthesis method for gold-silver (Au-Ag) alloy NPs using fungal biomass of *Trichoderma harzianum* (Tripathi et al., 2015b). Highly luminescent CdSe quantum dots were synthesized by the fungus *Fusarium oxysporum* at room temperature with a mixture of CdCl<sub>2</sub> and SeCl<sub>2</sub> (Kumar et al., 2007). We developed a novel eco-friendly method for the synthesis of cadmium sulfide (CdS) NPs using bacterial and fungal biomasses *Bacillus licheniformis* MTCC 9555 (Tripathi et al., 2014b) and *Trichoderma harzianum* (Bhadwal et al., 2014). Biogenic CdS quantum dots with 2–5 nm synthesized by *Camellia sinensis* have been applied for various application, like antibacterial activity, bioimaging, and apoptosis of lung cancer (Shivaji et al., 2018). We also developed a biosynthesis method for hydroxyapatite nanofibers using yeast extract (Tripathi et al., 2015a). A novel, unprecedented, and environmental friendly method for the synthesis of zinc oxide (ZnO) nanoflowers was also developed using *Bacillus licheniformis* MTCC 9555 at ambient room temperature (Tripathi et al., 2014a). As such, various biological sources (plants, bacteria, and fungi) have been used to synthesize metallic and semiconductor nanomaterials with different morphologies and sizes.

Biosynthesized nanomaterials have been applied in various fields, including antibacterial nanomaterials, nanomaterials for biosensors, drug delivery, and cancer treatment. The antibacterial activity of biologically synthesized silver NPs has been found to have highly antibacterial properties against *E. coli* and *Salmonella typhimurium* (Saxena et al., 2010). Furthermore, silver NPs obtaining using *Ficus benghalensis*, *Saraca indica* leaf extract, and *Trichoderma koningii* show excellent antibacterial activity (Saxena et al., 2012; Tripathi et al., 2013a, c). We previously reported that the antibacterial activity of gold NPs synthesized by *Trichoderma harzianum* was lower than that of silver NPs (Tripathi et al., 2018a). In addition to silver NPs, ZnO nanostructures are also used extensively for antibacterial activity, depending on their size and morphology, for a wide spectrum of bacterial species (Raghupathi et al., 2011; Ramesh et al., 2015). Gold NPs synthesized

from *Couroupita guianensis* have anticancer activity due to pharmacological properties of *Couroupita guianensis* (Geetha et al., 2013). As-synthesized gold NPs are fully capable of destroying cancer cells without the need for any doping of molecules (Geetha et al., 2013). Au-Ag alloy NPs biologically synthesized by yeast were used to fabricate a sensitive electrochemical vanillin sensor (Zheng et al., 2010). This shows that biosynthesized nanomaterials have great applicability in various biomedical and pharmaceutical fields.

This review article discusses current advances in biosynthesized metallic and semiconductor nanoscale materials, with a diagrammatic representation of their mechanisms. The biosynthetic mechanism of nanomaterials is illustrated in two respects: microbial biomasses (bacteria and fungi) and plant leaf extracts. The review also critically evaluates the existing knowledge of the biomedical and pharmaceutical applications of biogenic nanomaterials obtained using bacteria, fungi, and plant extracts.

## 2. Nanomaterials and classification

Materials with dimensions < 100 nm are defined as nanomaterials. One billionth of a meter is equal to one nanometer, which is approximately 100,000 times smaller than the diameter of a human hair. Currently, the field of nanomaterials has gained a lot of interest due to its high surface area to volume ratio. This attribute of nanostructured materials is generated by a quantum mechanical effect. The quantum size effect determines the variation of electronic properties with a reduction in material size. This effect is negligible at the micro level, but becomes useful at the nanoscale. The physical properties of materials vary with the changes from the micro to nano dimensions. Nanomaterials can have one, two, or three dimensions in the nanoscale. Nanotubes, fullerenes, nanowires, dendrimers, nanorods, nanoflowers, quantum dots, and nanofibers are some examples of nanomaterials. Nanostructured materials are classified according to the number of dimensions (Fig. 1) (Kushwaha, 2001), which are not confined to the nanoscale range (< 100 nm): three-dimensional (3-D), two-dimensional (2-D), one-dimensional (1-D), and zero-dimensional (0-D) structures.

Three-dimensional structures, or bulk materials, and do not have dimensions confined to the nanoscale. The two-dimensional structures that are not confined to the nanoscale include nanocoatings, nanoflowers, nanofilms, and nanolayers. The one-dimensional structures that are not confined to the nanoscale include nanorods, nanofibers, nanowires, and nanotubes. The nanomaterials of which all dimensions are confined to the nanoscale are called zero-dimensional structures, for example NPs. The dimensionality of a quasi-*n*-dimensional systems can be reduced by sandwiching them between two layers of higher energy gap materials (Fig. 1) (Kushwaha, 2001).

## 3. Biogenic synthesis of nanomaterials

### 3.1. Silver nanostructures

Silver NPs (AgNPs) have wide applications in various areas such as the development of antimicrobials (Saxena et al., 2012; Tripathi et al., 2013c) and antitumor (Jeyaraj et al., 2013), antibiotic (Singh et al., 2012), and nitro-aromatic compounds (Narayanan and Sakthivel, 2011), as well as sensing materials to detect the presence of pollutants, including metals (Balavigneswaran et al., 2014). Nowadays, silver NPs can be found in water purification systems, wall paints, and laundry detergents (Sun and Xia, 2002). AgNPs have significant potential in the medical field as surgical instruments, where contraceptive devices are coated with AgNPs to prevent infection (Lansdown, 2006). AgNPs have been used as optical receptors, polarizing filters, and for bio-labelling (Ghorbani et al., 2011). AgNPs are also a popular choice for redox catalysts, requiring smaller amounts of activation energy and providing a separate path for the electron transfer reaction (Mallick et al., 2006).

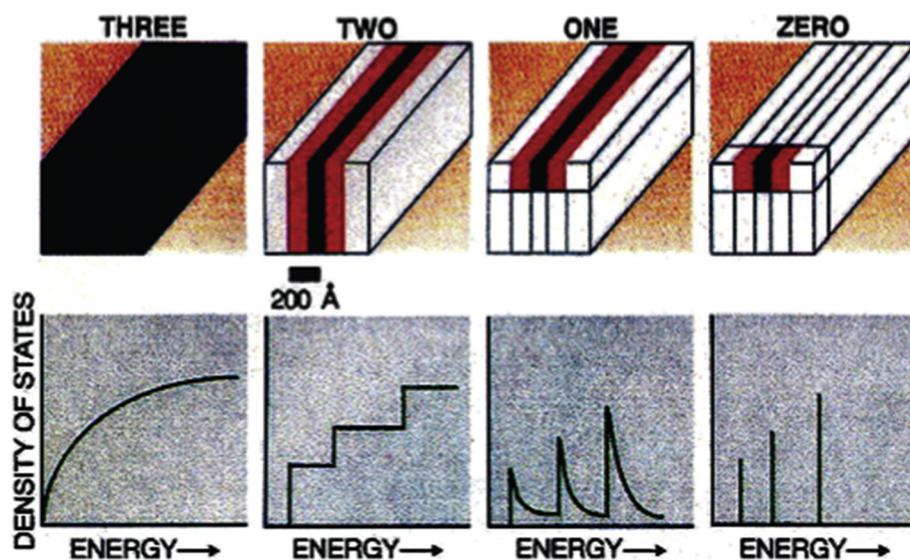


Fig. 1. Diagrammatic illustration of quantum confinement (top panel) for obtaining quasi- $n$ -dimensional systems. The bottom panel represents the alteration in the density of states (DOS) as a result of confinement. Figures were reproduced from Kushwaha, 2001, with the permission of Elsevier Science.

As a result, AgNPs support electron transfer and help in degrading dyes (Tripathi et al., 2013b).

The biosynthesis of silver NPs has attracted attention as an environmentally friendly and a cost-effective method. Several plant extracts have been used to synthesize silver NPs, including *Ficus benghalensis* (Saxena et al., 2012), *Allium cepa* (Saxena et al., 2010), *Ficus panda* (Tripathi et al., 2013b), and *Saraca indica* (Tripathi et al., 2013c), among others, as listed in Table 1. The biological synthesis of NPs with microbial biomasses is more beneficial than with plants because microbes produce more protein, which results in a higher production of NPs and provides a higher stability. AgNPs have been synthesized using various microorganisms, including *Fusarium oxysporum* (Ahmad et al., 2005), *Aspergillus fumigatus* (Bhainsa and D'Souza, 2006), and *Neurospora crassa* (Castro-Longoria et al., 2011), among others, as listed in Table 1.

The synthesis of AgNPs can be primarily identified using UV–vis spectroscopy (Fig. 2a), with an absorption range of 400–500 nm (Sastry et al., 1997). X-ray diffraction patterns consist of reflections of different intensities, which can be used to analyze crystal structures (Fig. 2b). The different biological systems have provided a variety of AgNP sizes and shapes. *Ficus panda* leaf extract is a prominent material for the synthesis of AgNPs, which results in a very narrow size distribution (12–36 nm) and a spherical morphology (Fig. 2c) (Tripathi et al., 2013b).

Generally, biological methods lead to NPs with spherical morphologies, but different morphologies have also been reported in silver NPs. Silver nanoflakes (Fig. 3) have been previously synthesized using the leaf extracts of *Crossandra infundibuliformis* (Kaviya et al., 2012). This shows that the biological synthesis method is an adaptable method for changing the morphology of metallic nanostructures.

### 3.2. Gold NPs

Gold is an exceptional metal element that exists in aqueous solution in three different complexes: gold(0), gold(I) and gold(III) (El-Brollosy et al., 2008; Yu et al., 2008). The formation of gold NPs was achieved by the reduction of gold ions. At the nanoscale, gold shows unique chemical and physical properties, as quantum size effects lead to drastic chemical changes in the transition from bulk to nanoscale (He et al., 2007; Srivastava et al., 2013). Gold NPs may have advantages over other metal NPs in terms of non-toxicity and biocompatibility (Dhar et al., 2008; Shukla et al., 2005) and can be easily conjugated to a large

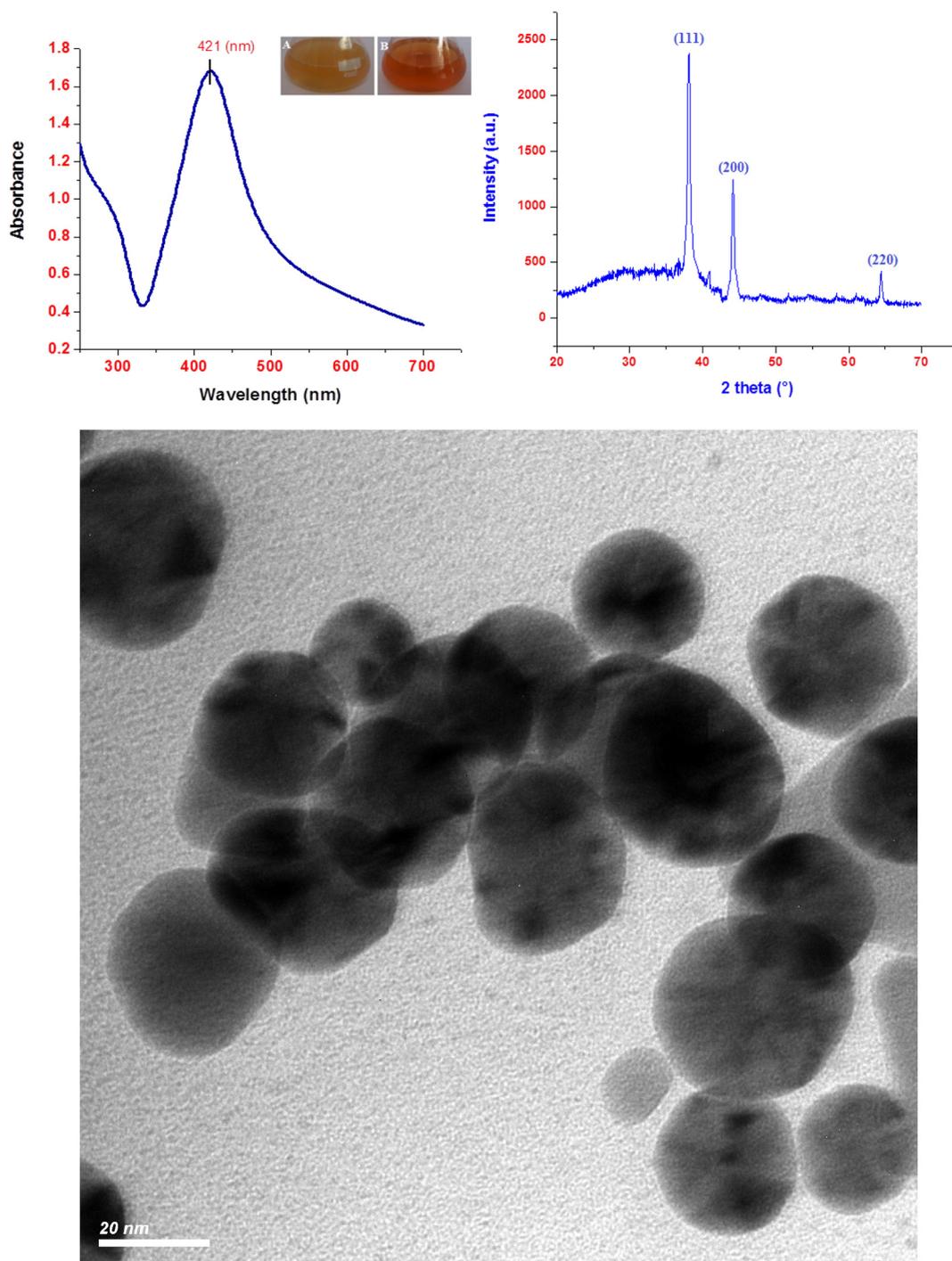
number of biomolecules, including amino acids (Selvakannan et al., 2004), proteins/enzymes (Niemeyer and Ceyhan, 2001), DNA (Alivisatos et al., 1996), and other molecular species, without changing the biological properties of the conjugated species.

Gold NPs have been synthesized using various plant extracts. *Stevia rebaudiana* leaf extract was used to synthesize very narrow size distributions of gold NPs from 5 to 20 nm with a spherical morphology (Sadeghi et al., 2015). *Ficus benghalensis* leaf extract was used as the reducing and capping agent for the synthesis of gold NPs and synthesized particles which were well dispersed and had a spherical morphology with a size ranging from 17 to 50 nm (Tripathi et al., 2012). Lemongrass extract was reported for the synthesis of triangular gold nano-prisms (Shankar et al., 2004). These and other plant-mediated synthesis methods are listed in Table 1. Extracellular gold NPs were synthesized by microbial biomasses. The bacterial biomass of *Pseudomonas aeruginosa* and *Rhodospseudomonas capsulate* were used for the synthesis of gold NPs (Singh and Kundu, 2014). Several filamentous fungi, such as *Fusarium oxysporum* (Thakker et al., 2012) and *Coriolus versicolor* (Sanghi and Verma, 2010), can also be used, but unfortunately these fungi are pathogenic (Inoue et al., 2002; Wardlaw and Geddes, 1992). In a previous study, we reported on the synthesis of gold NPs using *Trichoderma harzianum* (Tripathi et al., 2014c), a non-pathogenic and agriculturally important fungus and synthesized NPs with high stabilities and narrow size distributions, ranging from 26 to 34 nm, with spherical morphologies (Fig. 4).

The cell-free aqueous extract of *Rhizopus oryzae* was used to bio-synthesize gold NPs with various morphologies by changing the synthesis parameters, including reaction time, concentration of gold salt, and the pH of the reaction mixture (Fig. 5) (Das et al., 2010). A triangle-shaped gold nanostructure was achieved with 1000 mg/L of gold salt at pH 8 and a hexagon morphology was obtained with 1500 mg/L gold salt was used at pH 3. The reaction time is also important for achieving triangle and hexagonal shapes, which is generally of 10 h.

### 3.3. Copper nanostructures

Copper and its compounds are very important in various fields, including electronics, catalysis, and biomedical. Copper has good electrical conductivity, which plays a major role in modern electronic circuits (Schaper et al., 2004). Copper NPs are of great technological interest due to their catalytic and optoelectronic properties (Dhas et al.,



**Fig. 2.** Silver NPs synthesized by *F. panda* leaf extract. (a) UV–vis absorption spectrum, (b) XRD pattern, and (c) TEM micrograph of AgNPs. Figures were reproduced from Tripathi et al., 2013b, with the permission of Elsevier Science.

1998; Huang et al., 1997). Copper has applications in the field of nanodevices and non-linear optical devices (Flytzanis, 2005).

Copper NPs have been synthesized using plant extracts and microbial biomasses. The leaf extract of *Ocimum sanctum* is an outstanding biological source for obtaining NPs from the reduction of and encapsulating to stabilize them (Patel et al., 2016). Patel et al. synthesized copper NPs by preparing  $\text{CuSO}_4$  solution ( $1 \times 10^{-3}$  M) and mixing with methanolic leaf extract of *Ocimum sanctum*. The resulting NPs had a Z-average diameter of 122.7 nm with high stability. Analysis of their antibacterial activity yielded significant results. Agarwal et al. (2016) reported an unprecedented biological method for the synthesis of

copper nanoflowers using leaf extracts of *Ficus beghalensis* (Agarwal et al., 2016). Copper nanoflowers were synthesized using a solution of copper sulphate penta-hydrate ( $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ ) followed by stirring for 15 min at 60 °C. Thereafter, the leaf extract was added, which caused a reduction of ions and thereafter copper nanoflowers were produced. Fig. 6 shows a SEM micrograph of copper nanoflowers and the three-dimensional (3D) appearance of nanoflowers, with a size ranging from 250 nm to 2.5  $\mu\text{m}$  (Fig. 6a–c). The average mean size of nanoflowers is 500 nm (Fig. 6a), with nanopetals of 25 nm (Fig. 6e). SEM micrographs show three to four nanopetals in one nanoflower, but all are connected to each other to create a diameter of 500 nm (Fig. 6d). The nanopetals

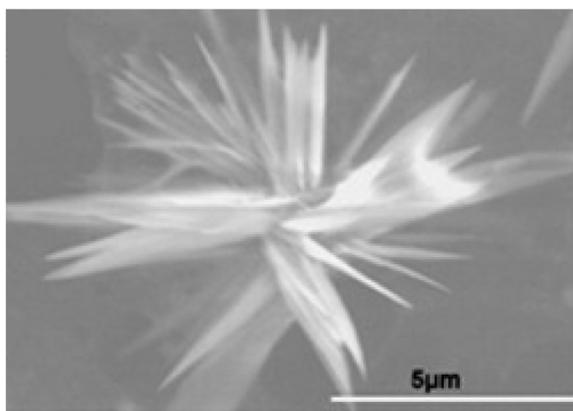


Fig. 3. FESEM micrograph of biosynthesized silver nanoflakes. The figure was reproduced from Kaviya et al., 2012, with the permission of Elsevier Science.

have a length of about 150 nm (Fig. 6e).

### 3.4. Palladium NPs

Palladium NPs have received special attention due to their applicability in various fields, including medical, catalysis, and biosensors, among others. An eco-friendly synthesis method has been applied to synthesize palladium NPs. Some plant extracts have been applied for the synthesis of palladium NPs, including *Ocimum sanctum* (Gogoi et al.,

2017) and *Euphorbia granulate*, among others, as listed in Table 1. Palladium NPs can be biosynthesized using the leaf extract of *Hippophae rhamnoides* Linn (Nasrollahzadeh et al., 2015). Nasrollahzadeh et al. used 10 mL of leaf extract of *Hippophae rhamnoides* Linn which was then added dropwise into 50 mL (0.003 M) of PdCl<sub>2</sub> solution at 80 °C with continuous stirring. The leaf extract reduced the palladium ions into neutral ions (Pd<sup>0</sup>) in 25 min. After 25 min, the color of the solution changed from transparent yellow to dark brown, indicating the formation of palladium NPs.

### 3.5. Iron NPs

Iron-based nanomaterials have widespread application in various fields, including medical biology and environmental remediation, among others. Their biomedical application includes the labelling and magnetic separation of biomolecules, MRI contrast enhancement, directed drug delivery, and treatment of hypothermia (Pankhurst et al., 2003). Iron and its oxide NPs have been also used in the field of environmental remediation of heavy metals like mercury, nickel, cadmium, lead, and chromium. Common organic pollutants such as organic solvents (trichloroethene) and organic dyes (bromophenol blue and methylene blue) have been previously degraded using iron NPs and their composites. The organochlorine insecticide Dichlorodiphenyltrichloroethane, lindane, and the organophosphorus insecticide Malathion have also been previously degraded by zero valent iron NPs (Elliott et al., 2009; Poursaberi et al., 2012; Singhal et al., 2012).

Zero valent iron NPs have been previously synthesized using plant

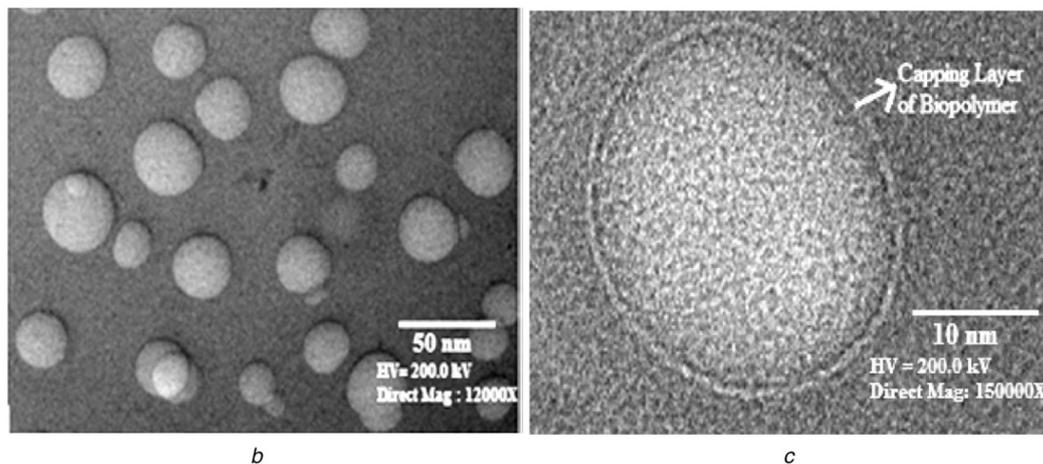
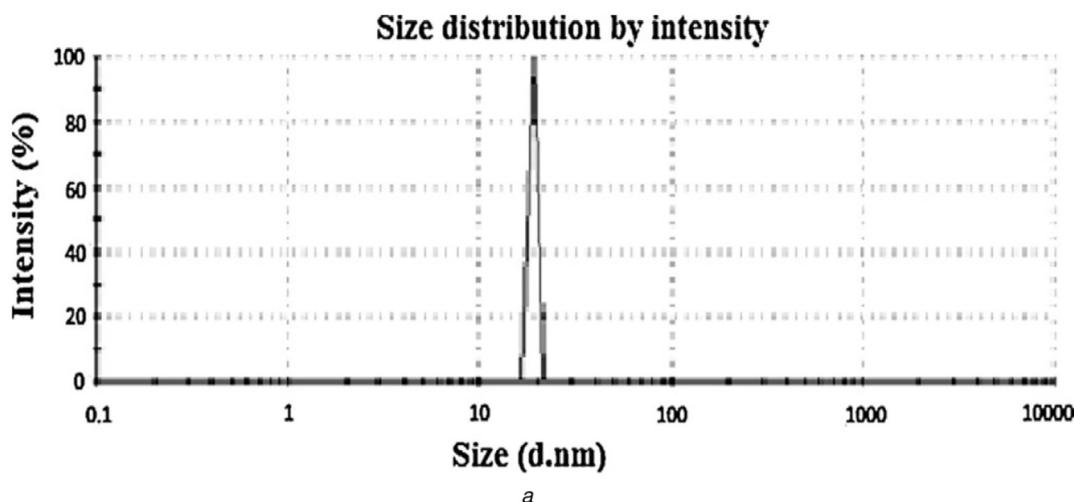


Fig. 4. Gold NPs biosynthesized by *T. harzianum* biomass. (a) Size distribution profile by DLS, (b) TEM micrograph, and (c) TEM micrograph at high-resolution. Figures were reproduced from Tripathi et al., 2014c, with the permission of Elsevier Science.

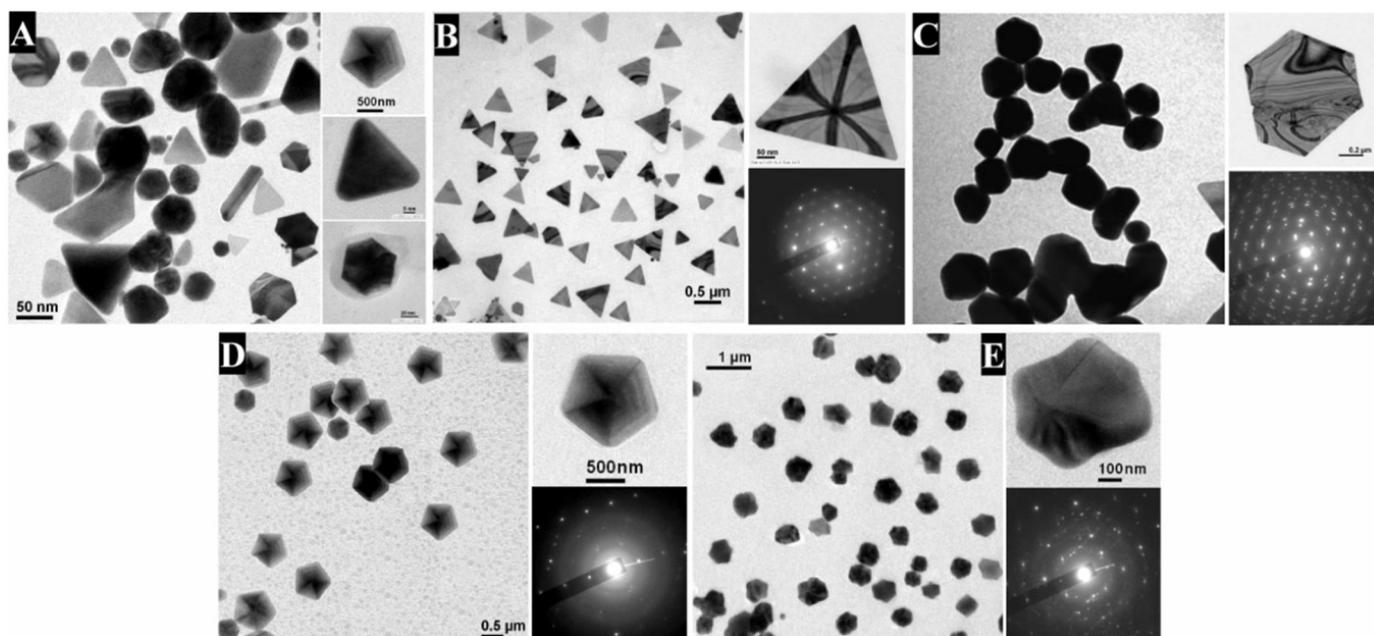


Fig. 5. TEM images of biosynthesized gold nanostructures- A) Mixed nanoplates (triangle, hexagon, pentagon, star, etc.) B) triangle, C) hexagon, D) pentagon, and E) star-shaped gold nanoplates. Figures were reproduced from Das et al., 2010, with the permission of Elsevier Science.

extracts and microbial biomasses. In a previous study, we have reported on the synthesis of zero valent iron NPs using yeast extract and a biological method (Mehrotra et al., 2017). We have prepared yeast extract solution by dissolving 1.5 g of yeast extract powder in 20 mL deionized water and boiling for 10 min.  $\text{FeCl}_3$  (1 mM) solution was prepared in 25 mL of deionized water and, after 10 min of stirring, 750  $\mu\text{L}$  of yeast extract solution was added, which reduced the  $\text{Fe}^{3+}$  ions to  $\text{Fe}^0$ . The color of the solution changed from pale yellow to golden brown, indicating the formation of zero valent iron NPs. The synthesized iron NPs had particles size in the range of 3–10 nm, with the majority particles being 5 nm, as confirmed by transmission electron microscopy (Fig. 7). All the particles were well dispersed and had spherical morphologies (Fig. 7a). Fig. 7b and c show the HRTEM of zero valent iron NPs. Fig. 7e shows the selected-area electron diffraction pattern of the iron NPs, which indicates that iron had polycrystalline rings.

### 3.6. Platinum NPs

Platinum NPs possess a wide range of properties that can be exploited for many practical applications. In anti-cancer drugs, metallic platinum compounds (i.e. *cis*-Diamminedichloroplatinum) are used (Hall et al., 2007). Fuel cells and hydrogen storage materials use platinum NPs (Li and Yang, 2007; Wen et al., 2008). Platinum NPs show excellent catalytic activity in proton membrane exchange fuel cells (Schmidt et al., 1999). Ismail and Al-Radadi (2017) reported that human cancer cell lines, including colon carcinoma cells (HCT-116), hepatocellular carcinoma (HePG-2), and breast cancer cells (MCF-7), can be treated *in vitro* using platinum NPs with excellent anticancer activity (Ismail and Al-Radadi, 2017). They also found that platinum NPs show effective antibacterial activity against Gram positive bacteria, *Bacillus subtilis* (RCMB 010067), and Gram negative bacteria, *Escherichia coli* (RCMB 010052).

Platinum NPs have been synthesized from tea polyphenol, which acts as a reducing and capping agent (Sheny et al., 2013). *O. sanctum* leaf broth was used to biosynthesize platinum NPs at 100 °C in 1 h (Soundararajan et al., 2012). The leaf extract of *D. kaki* has been used for the extracellular biosynthesis of platinum NPs at 95 °C using  $\text{H}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O}$  and resulted in NPs of 2–12 nm (Song et al., 2010). Thirumurugan et al. (2016) reported on the biosynthesis of platinum

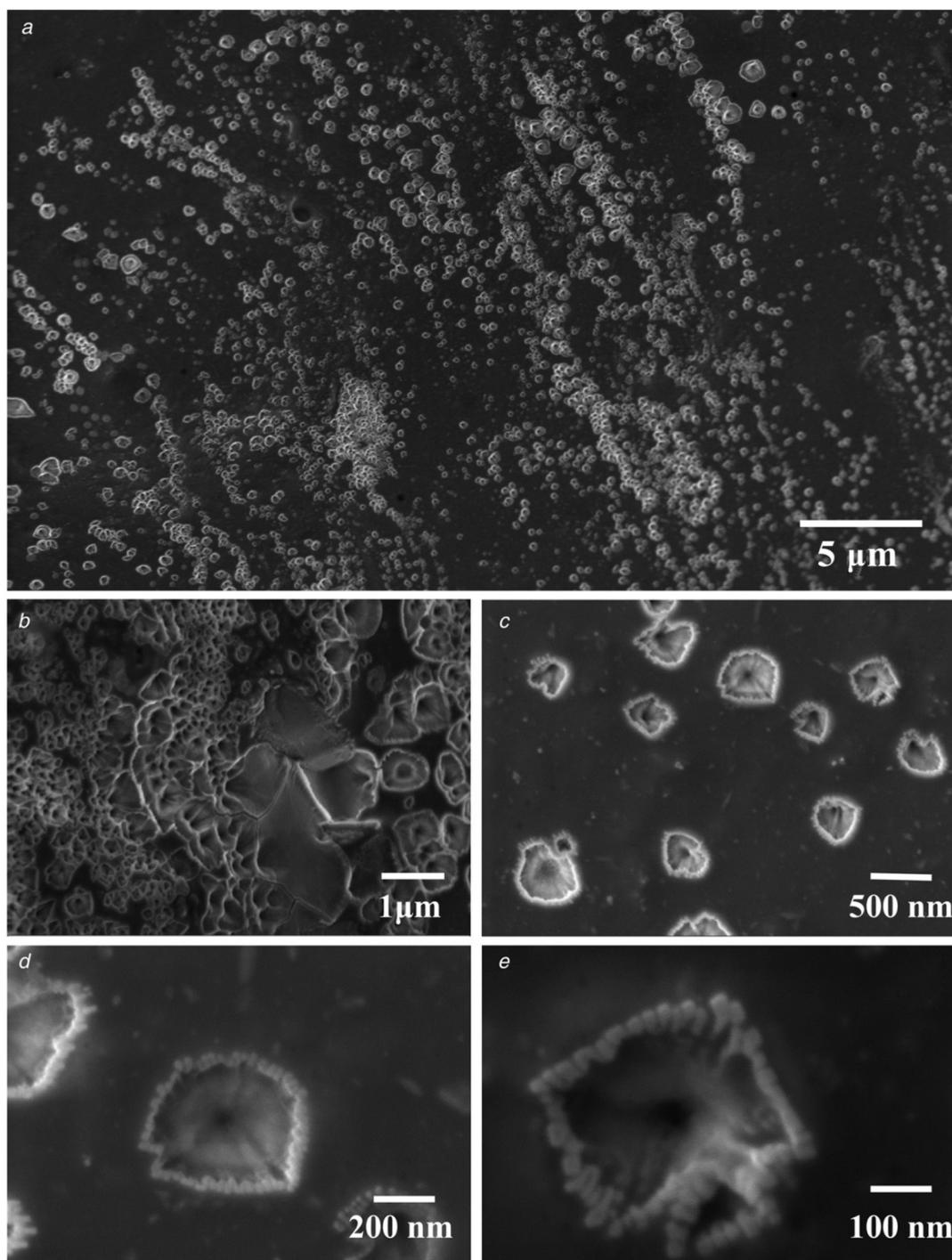
NPs from *Azadirachta indica* extract and synthesized NPs with a narrow size range of 5–50 nm with spherical morphologies (Thirumurugan et al., 2016).

### 3.7. Alloy and bimetallic NPs

Alloy and bimetallic NPs received huge interest in various fields, such as medicine, catalysis, and electronics, as optical materials and coatings, among others (Senapati et al., 2005; Tripathi et al., 2015b; Zheng et al., 2010). Au–Ag alloy NPs have been synthesized by *F. oxysporum*, where the secreted cofactor NADH plays a significant function in determining the structure of Au–Ag alloy NPs (Senapati et al., 2005). A simple and environmentally friendly method has been reported for the biosynthesis of Au–Pd bimetallic NPs (~7 nm) by the simultaneous bioreduction of Au(III) and Pd(II) precursors with *Cacumen platycladi* leaf extract in aqueous solution (Zhan et al., 2011). We developed a biosynthesis method for Au–Ag alloy NPs using the fungal biomass of *Trichoderma harzianum* (Tripathi et al., 2015b). They dispersed the *Trichoderma harzianum* biomass (5 g wet) and added  $\text{HAuCl}_4$  and  $\text{AgNO}_3$  to it. The mixture solution was incubated for 72 h at  $28 \pm 1$  °C with continuous stirring. After 72 h of incubation, the color of the solution changed, indicating the formation of alloy NPs. Fig. 8 shows a TEM micrograph which reveals that the biosynthesized Au–Ag alloy NPs had a narrow size distribution profile in the range of 1025 nm. Various shapes of alloy NPs have been previously synthesized, including triangles, spheres, rods, squares, and hexagons (Fig. 8a). A thin layer of organic polymer encapsulated the alloy NPs, which are shown in Fig. 8b. This organic layer was secreted by fungus biomass. Fig. 8c shows the HRTEM micrograph of alloy NPs, which shows that the particles are crystalline in nature and with a d-spacing of 0.24 nm.

### 3.8. Cadmium sulfide nanostructures

The biosynthesis of semiconducting NPs, such as cadmium sulfide (CdS) nanostructures, have gained attention due to the wide range of their potential applications, including as solar cells, biosensors, and fluorescent probes for medical purposes (Bhadwal et al., 2014; Du et al., 2009; Li et al., 2011; Liu et al., 2008). CdS quantum dots have been



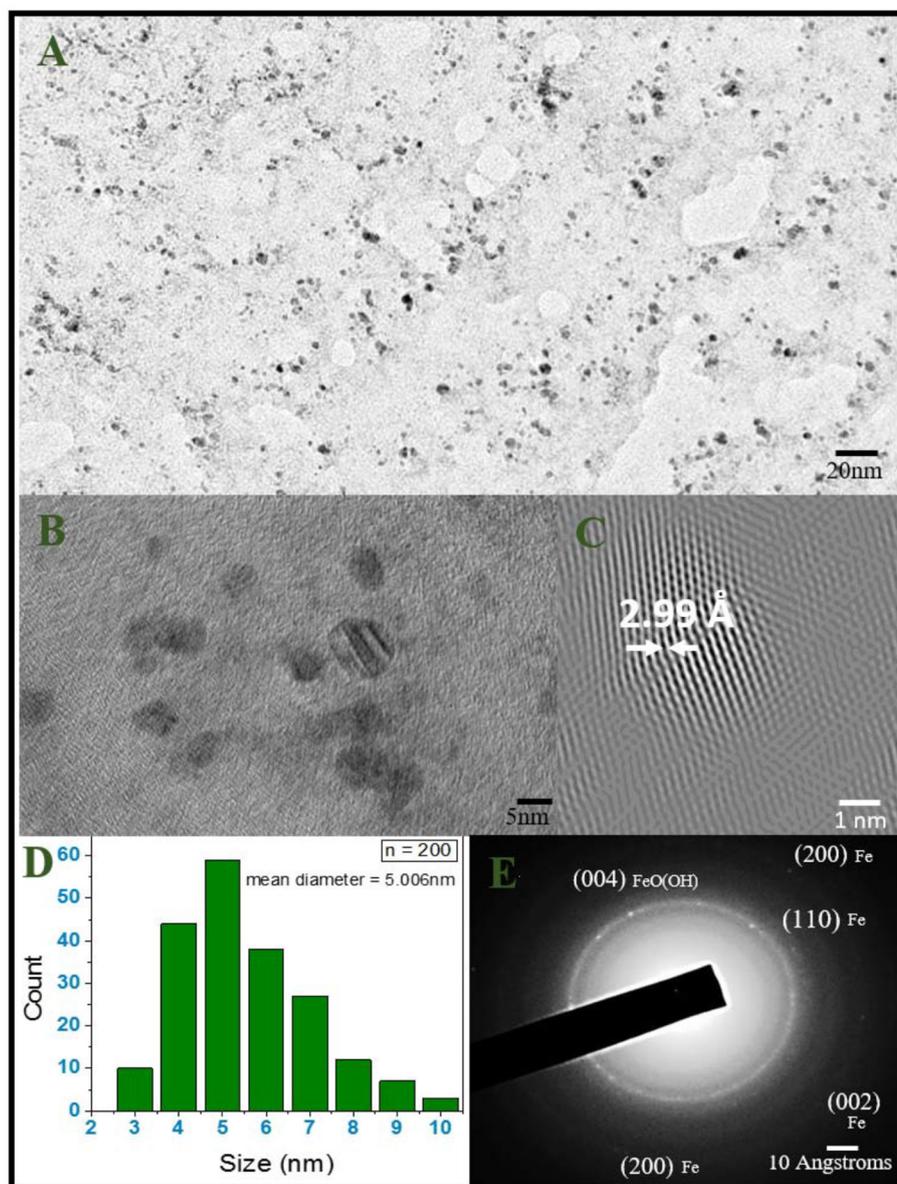
**Fig. 6.** SEM micrograph of biosynthesized copper nanoflowers. a, b) Copper nanoflowers with sizes ranging from 250 nm to 2.5  $\mu\text{m}$ . c) No agglomeration was observed. d) Length of nanopetals. e) The diameter of nanopetal base (sepal). Figures were reproduced from Agarwal et al., 2016, with the permission of IET.

previously biosynthesized by hairy root culturing of *Linaria maroccana* L., with the resulting quantum dots being 5–7 nm in size with spherical morphologies (Borovaya et al., 2014). We previously reported on the biosynthesis of CdS NPs using *Bacillus licheniformis* MTCC 9555 (Tripathi et al., 2014b). We used 0.5 g biomass of bacteria dispersed in 45 mL of deionized water and stirred at 200 rpm for 30 min. Thereafter, 0.1 mM cadmium chloride was added. Then, 0.01 mM sodium sulfide ( $\text{Na}_2\text{S}$ ) solution was added dropwise into the solution with a pH of  $8 \pm 1$ , before continuous stirring for 48 h at  $37 \pm 1$  °C. The TEM micrograph reveals the average size was of  $5.1 \pm 0.5$  nm with spherical morphology. X-ray diffraction analysis shows strong peaks at

$2\theta = 26.7^\circ, 36.6^\circ, 54.9^\circ,$  and  $67.2^\circ$ , corresponding to (002), (102), (004), and (203) lattice planes, respectively. These sets of lattice planes depict the hexagonal structure of CdS NPs.

### 3.9. Titanium dioxide nanostructures

Titanium is corrosion-resistant, strong, and shiny. Its most common compound is titanium di-oxide ( $\text{TiO}_2$ ).  $\text{TiO}_2$  used in the manufacture of paints, plastics, paper, ink, rubber, textile, cosmetics, leather, and ceramics (Anpo and Kamat, 2010).  $\text{TiO}_2$  NPs have been biosynthesized using fungi, including *Fusarium oxysporum* (Bansal et al., 2005),

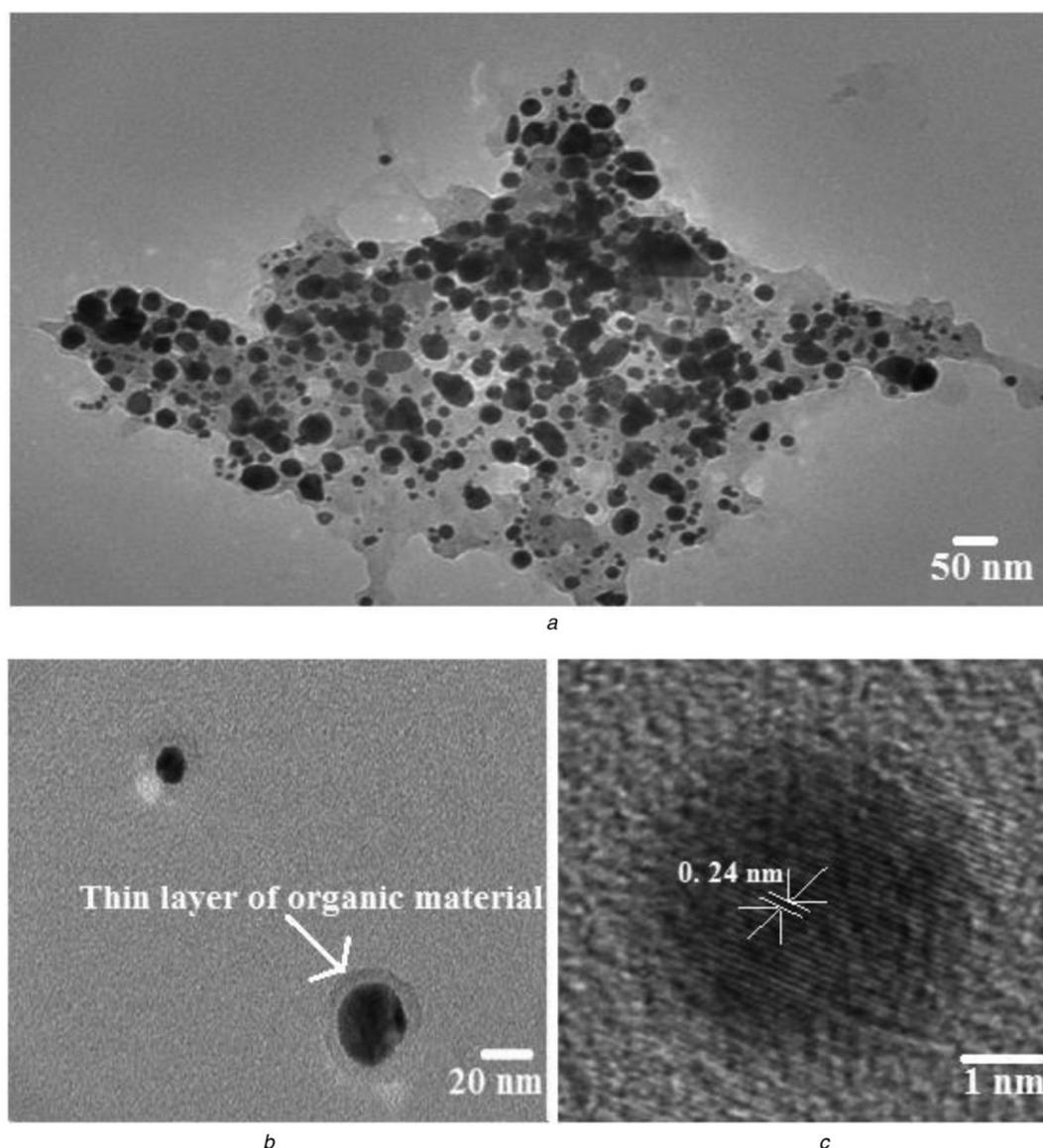


**Fig. 7.** (a) TEM micrographs of iron NPs, (b) HR-TEM (c) corresponding planar fringes, (d) size distribution, and (e) SAD pattern. Figures were reproduced from Mehrotra et al., 2017, with the permission of IEEE.

*Sachharomyces cerevisiae* (Jha et al., 2009), and *Aspergillus tubingensis* (Tarafdar et al., 2013), but also bacterial biomasses, such as *Bacillus subtilis* (Kirthi et al., 2011), *Lactobacillus* sp. (Jha et al., 2009), and *Aeromonas hydrophila* (Jayaseelan et al., 2013), and several plant materials, including *Vigna unguiculata* (Chatterjee et al., 2017), *Psidium guajava* (Santhoshkumar et al., 2014). These and other examples are listed in Table 1 (Ambika and Sundrarajan, 2016; Jalill et al., 2016; Marimuthu et al., 2013; Subhapiya and Gomathipriya, 2018). The biosynthesis of TiO<sub>2</sub> NPs has been previously carried out using plant leaf extract of *Jatropha curcas* L. (Goutam et al., 2018). Goutam et al. have used a 1:1 ratio (v/v) of TiCl<sub>4</sub> and leaf extract with continuous stirring at room temperature. After 20 min, the color of the solution changed from transparent to whitish-brown. Thereafter, 15 mL ammonia was added to obtain precipitates of the NPs. The precipitate was washed with ethyl alcohol to remove any impurities. Finally, the precipitate was calcinated at 450 °C for 3 h before grinding into a fine powder.

### 3.10. Zinc oxide nanostructures

Zinc oxide (ZnO) nanostructures have also gained attention due to their wide band gap (3.37 eV) and large electron–hole binding energy (60 meV) (Mitra et al., 2012). ZnO NPs have been used in various application, such as biosensors (Hwa and Subramani, 2014), optical devices (Yude et al., 2006), solar cells (Al-Kahlout, 2015), and photocatalysis devices (Tripathi et al., 2014a). Biosynthesized ZnO NPs have good antibacterial activity against various bacterial strains (Dobrucka and Długaszewska, 2016). For their synthesis, 30 mL extract of *Trifolium pretense* flowers was added into 0.5 M ZnO with continuous stirring at 90 °C for 4 h. After 4 h, the temperature was decreased and maintained at 30 °C for 24 h before obtaining a powder at 400 °C for 1 h. The white powder obtained was characterized using UV–Vis absorption spectroscopy, X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FT-IR), and scanning electron microscopy (SEM) with energy dispersive X-ray (EDX) analysis. The resulting ZnO NPs were found to have a size ranging from 100 to 190 nm. Several plant extracts and microbial biomasses have been used to synthesize ZnO NPs. We reported have for



**Fig. 8.** TEM images of biosynthesised Au–Ag alloy NPs using *Trichoderma harzianum*. (a) Micrograph of Au–Ag alloy NPs. (b) NPs capped by organic material secreted by *Trichoderma harzianum*. (c) HR-TEM. Figures were reproduced from Tripathi et al., 2015b, with the permission of IET.

the first time on the biosynthesis of ZnO nanoflowers using bacterial biomasses (Tripathi et al., 2014a). We prepared a 0.2 M solution of zinc acetate which was heated at 60 °C for 15 min, followed by the addition of 0.6 M sodium bicarbonate. Thereafter, 5 g of bacterial biomass of *Bacillus licheniformis* was dispersed into the mixture. The mixture solution was incubated for 48 h at 37 °C. After 48 h, a white precipitate had deposited at the bottom of flask, which was separated and characterized. Fig. 9 shows the TEM micrograph of ZnO nanoflowers which have flower-like morphology with a size ranging from 200 nm to 1 μm, where the nanopetals have a width of 40–400 nm.

### 3.11. Carbon nanodots (CNDs)

The development of fluorescent CNDs has steadily gained attention in different research fields in recent years. CNDs have a wide range of applications in the areas of bioimaging, biosensing, drug delivery, and photo- or electro-catalysis (Lim et al., 2015; Wang and Hu, 2014). Physical and chemical methods have been previously used to synthesize CNDs, such as the arc-discharge technique, laser ablation of graphite, electrochemical oxidation, thermal decomposition, and microwave-assisted synthesis (Liu et al., 2007; Tang et al., 2012; Zhao et al., 2008;

Zong et al., 2011). We developed a simple, eco-friendly, and cost effective biosynthesis method for CNDs using *Musk melon* extract (Mahajan et al., 2016). For this, 50 g blended *Musk melon* fruit was filtered to obtain the extract. Then, 15 mL of the extract was diluted with 25 mL water, after which 30 mL of ethanol was added. This mixture was then heated at 200 °C until the solution turned a brownish color. The resultant was further diluted and centrifuged at 5000 rpm to remove the impurities associated with CNDs. We found that the CNDs were stable even after two months of synthesis (Fig. 10a). The CNDs were obtained in sizes ranging from 5 to 10 nm, which shows that very fine dots can be synthesized using this method (Fig. 10b).

## 4. Biosynthesis mechanism

The biological synthesis of nanomaterials varies according to the type of biomaterials and biosystems used in their synthesis. All micro-organism-mediated syntheses of nanomaterials use similar mechanisms, but synthesis using plant extracts use different mechanisms. We reported on the possible biosynthesis mechanism of Au–Ag alloy NPs synthesized using *Trichoderma harzianum* fungal biomass, which acts as a reducing and capping agent (Tripathi et al., 2015b). The salts of the

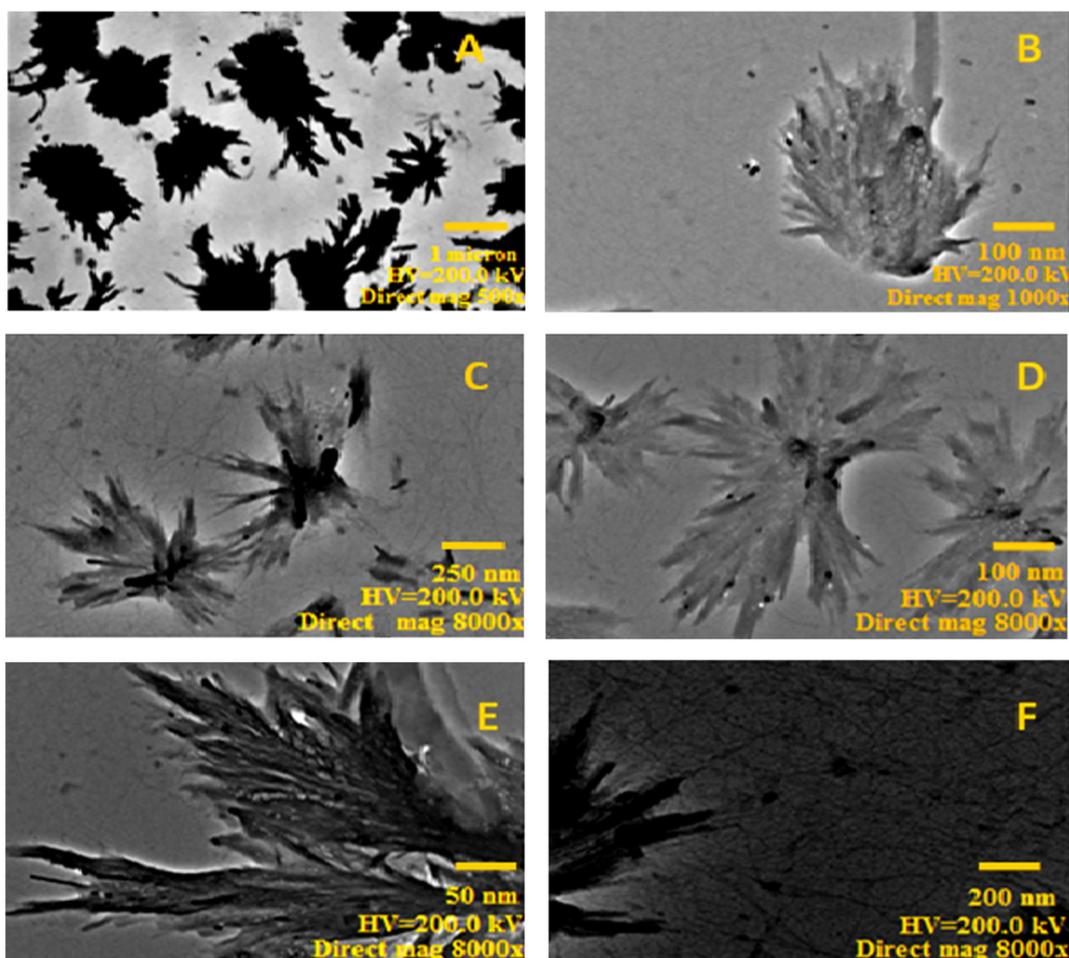


Fig. 9. TEM images biosynthesized ZnO nanoflowers. (a) ZnO nanoflowers with sizes ranging from 200 nm to 1 μm. (b) A single nanoflower having 300 nm. (c, d, e) ZnO nanoflowers showing nanopetals. (F) Fiber-like structures after sonication of ZnO nanoflowers. Figures were reproduced from Tripathi et al., 2014a, with the permission of Elsevier Science.

target alloy nanoparticle were dissociated into their respective ions in the solution. However, metals ions are toxic in many biological systems even at relatively low concentrations (Nägeli, 1893). The fungal biomass released an NADH-dependent enzyme, which oxidised into NAD<sup>+</sup> and neutralized the ions by reduction (Prusty, 2011). The neutralized ions underwent nucleation, which led to the synthesis of Au–Ag alloy NPs. Then, the fungal biomass liberated sulfur-containing proteins, which encapsulated the NPs and provided stability (Elechiguerra et al., 2005). Fourier transform infrared analysis confirmed the presence of

C–SH stretching at 713.66 and 825.53 cm<sup>-1</sup> (Nandy et al., 1973). Fig. 11 shows a diagrammatic representation of the complete biosynthesis mechanism. The potential mechanism behind plant-mediated biosynthesis of silver NPs synthesized by *Saraca indica* a medicinal plant from the ancient time was reported (Tripathi et al., 2013c). The aqueous extract of it has alkaloids, saponins, tannins, flavonoids, and glycosides. Tannins and flavonoids have the high antioxidative properties which interact with surrounding ions in the medium and neutralized them. Subsequently, nucleation is started which convert the neutral

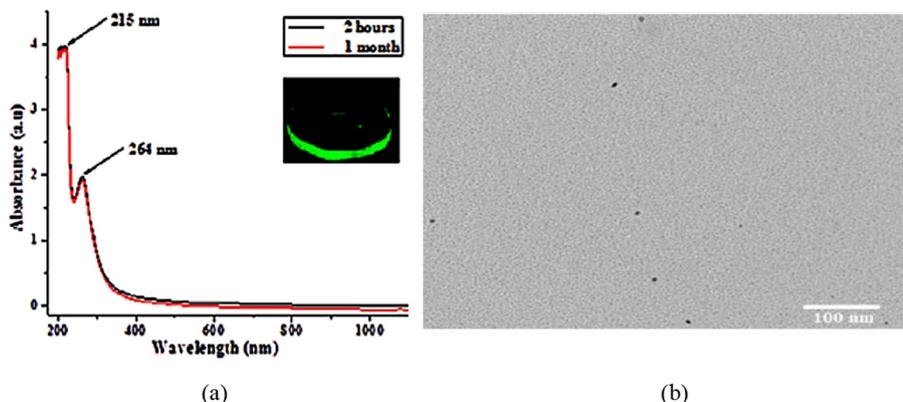


Fig. 10. (a) UV–vis absorption of CNDS biosynthesised by *Musk melon* and the inset fluorescent CNDS under UV light. (b) TEM showing size distribution and morphology of CNDS. Figures were reproduced from Mahajan et al., 2016, with the permission of IET.

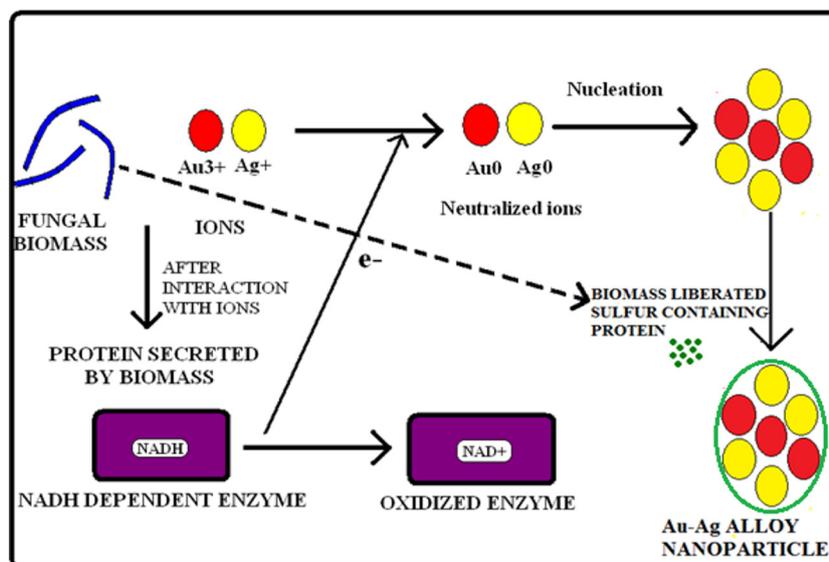


Fig. 11. Representation of biosynthesis mechanism of Au–Ag alloy NPs by *Trichoderma harzianum*. The figure was reproduced from Tripathi et al., 2015b, with the permission of IET.

ions into nanoparticles. However, further experimental analysis would be required to understand the precise biosynthesis mechanism.

## 5. Applications

### 5.1. Antibacterial activity of biogenic nanomaterials

The threat posed by bacterial infection on human health is relevant on a worldwide scale due to the economic and social burden associated with it. Furthermore, the emergence of clinically important bacteria which are increasingly resistant to antibiotics means that soon new bactericide agents need to be developed (Andersson and Hughes, 2010; Chen and Schluesener, 2008; Fischbach and Walsh, 2009; Huh and Kwon, 2011; Kim et al., 2007). Various metallic and metal oxide nanostructures have been previously employed for their antibacterial activity. Biologically synthesized nanostructures of silver (Saravanakumar et al., 2017; Saxena et al., 2012), copper (Lv et al., 2017), platinum (Tahir et al., 2017), palladium (Surendra et al., 2016a, 2016b), zinc oxide (Vijayakumar et al., 2018), and iron oxide (Arokiyaraj et al., 2013), among others, have been used as antibacterial agents. Of these metals, silver and its nanocomposites are the most extensively used. We previously reported on the antibacterial activity of biosynthesized silver NPs using *Ficus beghalensis* and found that 45 µg/mL of silver NPs had effective antibacterial activity, with a minimum inhibitory concentration of 25 µg/mL (Saxena et al., 2012). Copper NPs (CuNPs) biosynthesized using *Shewanella liihica* PV-4 were evaluated for antibacterial activity, wherein 100 µg/mL CuNPs were found to have an antibacterial efficiency of  $86.3 \pm 0.2\%$  against a  $10^5$  CFU/mL *E. coli* suspension within 12 h (Lv et al., 2017). Biosynthesized palladium NPs with a size of  $27 \pm 2$  nm and a spherical shape exhibit good antibacterial activity against *Staphylococcus aureus* and *E. coli* (Surendra et al., 2016a, 2016b). Silver NPs have excellent antibacterial activity against bacteria resistant to common antibiotics or even multi-resistant bacteria such as *P. aeruginosa* (Salomoni et al., 2017). Biogenic silver NPs were used to developed antibacterial biodegradable nanocomposite film of poly (vinyl alcohol) for food packaging materials (Tripathi et al., 2018a). Table 2 shows the biomedical application of biologically synthesized nanoparticles. This demonstrates that the biosynthesized nanomaterials could be a potential substitute for antibiotics.

### 5.2. Biosynthesized nanomaterials for clinical detection

Currently, researchers are applying biosynthesized NPs for a variety of biomedical detection purposes. Biologically synthesized gold NPs have been used to detect HCG hormone in pregnant women urine sample (Kuppusamy et al., 2014). Biogenic gold NPs (AuNPs) have been functionalized with glutaraldehyde to improve their biosensing applications, as transducer or electroactive labels, in particular for nanoparticle-based electrochemical DNA detection (Torres-Chavolla et al., 2010). Biosynthesized AuNPs show a six-fold greater adhesion force to breast cancer cells than normal breast cells (Hampp et al., 2012). In addition, the adhesion forces between chemically and biologically synthesized AuNPs have been compared and the biologically synthesized counterparts were found to have a three-fold greater adhesion force than the chemically synthesized AuNPs. Biosynthesized palladium NPs anchored with graphene oxide and conjugated with lipase and glycerol dehydrogenase (LIP-GLDH) enzymes were used to develop an electrochemical detection platform for triglycerides (Singh et al., 2016). Biologically synthesized NPs are widely applicable for the colorimetric detection of pesticides, heavy metals, and other toxic pollutants; however, this review mainly focuses on their biomedical and pharmaceutical applications.

### 5.3. Drug delivery by biogenic nanomaterials

NPs have been most recently used as nanocarriers for targeted delivery of drugs. The mechanism behind this allows for the drug and gene-loaded NPs to effortlessly cross epithelial cell barriers and circulate into the blood stream prior to reaching the targeted site. Cancers have their own angiogenesis system, which is a complex process resulting in the formation of new blood vessel. Normal (healthy) tissues have a continuous vascular endothelium (gap 2–6 nm) whereas disease tissues have much larger gaps of 100 nm to 2 µm. This gap enhances drug penetration into the tissues which accumulates in the diseased tissues, popularly known as “enhanced permeation and retention effect” (Adisheshaiah et al., 2010; Gaumet et al., 2008; Maeda et al., 2000). Silver NPs biosynthesized using the seed extract of *Setaria verticillata* were loaded with hydrophilic anticancer drugs, doxorubicin and daunorubicin, to develop a novel drug delivery vector (Naz et al., 2017). Naz et al. found that NPs had an excellent adsorption capacity and were effective for use during leukemia chemotherapy. Zinc oxide NPs were biosynthesized by actinobacteria *Rhodococcus pyridinivorans* NT2 in

**Table 2**  
Biomedical application of biogenic nanoparticles.

Nano-materials	Shape	Size (nm)	Bio-temple	Applications	Reference
AgNPs	Spherical	16–48	Onion ( <i>Allium cepa</i> )	Antibacterial	(Saxena et al., 2010)
AgNPs	Spherical	16	<i>Ficus benghalensis</i>	Antibacterial	(Saxena et al., 2012)
PdNPs	Spherical	27 ± 2	<i>M. oleifera</i>	Antibacterial	(Surendra et al., 2016a, 2016b)
AuNPs	–	30–60	<i>Thermomonospora curvata</i> , <i>T. fusca</i> , and <i>T. chromogena</i>	Biosensing	(Torres-Chavolla et al., 2010)
PdNPs	Three dimensional	3.5	Fenugreek seeds	Lipid detection	(Singh et al., 2016)
AgNPs	–	–	Seed extract ( <i>Setaria verticillata</i> )	Drug delivery	(Naz et al., 2017)
AgNPs	Spherical	20–30	<i>Euphorbia milii</i> leaf extract	Wound healing	(Gong et al., 2018)
AuNPs	Spherical	6–13	<i>Enterococcus</i> sp	Anti- cancer for lung and liver cancer cells	(Rajeshkumar, 2016)
CdS	Quantum Dots	2–5	<i>Camellia sinensis</i>	Antibacterial activity, bioimaging, and apoptosis of lung cancer	(Shivaji et al., 2018)
AuNPs	Spherical	37	<i>S. swartzii</i>	Decrease fasting blood glucose levels	(Dhas et al., 2016)
Platinum NPs	Spherical	12	<i>Whitania somnifera</i> leaves	Anti-diabetic treatment	(Li et al., 2017c)

sizes of 100–120 nm and were found to preferentially destroy HT-29 cancerous cells over healthy peripheral blood mononuclear cells (Kundu et al., 2014). Biosynthesized gold NPs using the leaf extract of *Peltophorum pterocarpum* were used to deliver the *in vitro* and *in vivo* doxorubicin for cancer treatment (Mukherjee et al., 2016). Hence biosynthesized nanomaterials could be potential candidates for targeted drug delivery in cancer therapy.

#### 5.4. Biogenic nanomaterials for wound healing

The anti-inflammatory process is an important mechanism for wound healing and creates immune responsive compounds including interleukins and cytokines. These immune responsive compounds then produce keratinocytes as well as T-cells, B-cells, and macrophages. Copper is commonly used to reduce microbial infection at the site of wounds and increases the rate of healing. Copper also helps to induce the expression of vascular endothelial growth factor, which stimulates angiogenesis (Sen et al., 2002). Overall, the activation of angiogenesis, the anti-inflammatory response, and immunity enhances wound healing (Borkow et al., 2010). Biosynthesized copper NPs using *Pseudomonas aeruginosa* were found to enhance the speed of wound healing (Tiwari et al., 2014). Tiwari et al. found that biosynthesized copper NPs showed rapid wound healing activity in comparison to copper in its native form. Biosynthesized silver NPs using *Penicillium chrysogenum* showed effective antibacterial activity against *Staphylococcus aureus*, followed by *E. coli*, *Pseudomonas aeruginosa*, and *Bacillus cereus* (Akila and Nanda, 2014). Silver NPs biosynthesized with the size range of 20 to 30 nm by *Euphorbia milii* leaf extract show good wound healing property (treated with 10% Ointment base with biosynthesized AgNPs) in Albino rats (Gong et al., 2018). Table 2 listed the biomedical application of biogenic nanoparticles. Biosynthesized silver NPs were also found to have better wound healing activity than other standard wound healing drugs. Therefore, biosynthesized NPs have a potential application in wound healing.

#### 5.5. Anti-diabetic biogenic nanomaterials

Diabetes mellitus is a chronic disease in which the blood sugar level is high due to the abnormal functioning of the pancreas, which produces less insulin than normal or no insulin at all. Diabetes can be treated to an extent by controlling the diet or taking synthetic insulin, but an absolute cure for diabetes is not available. Biologically synthesized silver NPs have proven to be excellent agents for the effective treatment of diabetes mellitus (Prabhu et al., 2017). Biosynthesized gold NPs using *Sargassum swartzii* were found to be effective anti-diabetic materials (Dhas et al., 2016). Diabetic male albino Wistar rats were treated with biogenic gold NPs, a treatment which was found to significantly decrease fasting blood glucose levels, serum insulin,

hemoglobin, and glycosylated hemoglobin levels compared to the controls. Recently, biogenic platinum NPs were synthesized by *Whitania somnifera* leaves with a size of 12 nm and a spherical morphology (Li et al., 2017c). These NPs were injected into streptozotocin-induced diabetic rats for anti-diabetic treatment and were found to significantly decrease the plasma glucose levels. These studies support the applicability of biosynthesized NPs as anti-diabetic materials.

## 6. Conclusion

The biogenic synthesis of nanomaterials is of great research interest due to growing needs for new materials in various fields, especially in biomedical and pharmaceutical applications. This review focused on the biosynthesis of nanomaterials (metallic and semiconductor) with regards to their synthesis mechanistic approach. The biosynthesis methods of metallic (silver, gold, platinum, palladium, copper, iron, and alloy nanostructures) and semiconductor (cadmium sulfide, zinc oxide, titanium dioxide, and carbon nanodots) nanomaterials were discussed. Bacteria, fungi and plant extracts are commonly used for the biosynthesis of nanomaterials is a simpler, more environmentally friendly, and more cost effective method than physical and chemical methods. This review explores the biomedical and pharmaceutical application of nanomaterials for antimicrobials, clinical detection, drug delivery, wound-healing, and anti-diabetic materials.

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