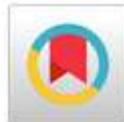


Biosynthesis of metal nanoparticles using microorganisms and its medicinal applications

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Abstract

Nanotechnology is one of the most important technologies that enter into multiple fields, as it depends on the synthesis of particles with nano scale called nanoparticles (NPs). Biosynthesis of nanoparticles can be done using plants or microorganisms; however, synthesis of NPs using microorganisms is economical and an ecofriendly method. This review article provides highlights on the latest studies on using diverse microorganisms such as; bacteria, actinobacteria, fungi and algae for the biosynthesis of some metal nanoparticles including; silver, gold, palladium, selenium, magnesium, titanium dioxide, zinc oxide.. etc, under simple manufacturing conditions and within a short period that ranges from a few minutes to several days. The resulting NPs mostly show anti-fungal potential towards several fungal species that cause important human diseases mainly; *Candida albicans* and *Aspergillus niger*. Moreover, NPs has antibacterial efficacy against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, which recently become less affected by several antibiotics like penicillin and methicillin. This review will help the researchers who work in biosynthesis of NPs and in the nano-medical application fields.

Keywords: Nanoparticles, Microorganisms, Biosynthesis, Nano-medical applications

1. Introduction

The word "nano" is derived from the Greek word "nanos" which means "dwarf", and nanometer represents a part of a billion, and therefore the nanometer (nm) is equivalent to 10^{-9} meters. To imagine the matter, 1 nanometer measures three carbon atoms aligned next to each other, and the average diameter of a human hair measures about 10,000 nm, according to [Hulkoti and Taranath, \(2014\)](#). It is known that materials are within the nanomaterials scale if one of their dimensions does not exceed 100

nm. The science that deals with the applications of using these materials is called Nanotechnology ([Madkour, 2019](#)).

A study conducted by [Rao and Gan, \(2015\)](#) highlighted that nanotechnology is one of the most important technologies that enters into multiple fields, it depends on the synthesis of nanoparticles (NPs), as these particles have properties different from the minerals from which they are formed. In recent years,

an interest has increased on the production of metallic nano-materials, due to their various uses in several fields such as; biomedical, agricultural, environmental and industrial fields ([Singh *et al.*, 2016](#)).

According to [Biglu *et al.*, \(2011\)](#), the Science Citation Index Expanded during 2001-2010 showed a steady growth in the field of nanotechnology, and the research numbers indicate an exponential increase in the published articles in the field of nanotechnology. The importance of NPs is primarily due to the high ratio of its surface area to its volume, due to its infinite smallness; and this feature increases its surface contact with the other bodies ([Gahlawat *et al.*, 2016](#)). NPs is synthesized in one of two ways; building from the bottom up, by engineering the construction of NPs starting from their ions, and this happens by chemical and biological methods, or by top to bottom way, and this happens by physical methods such as grinding ([Shedbalkar *et al.*, 2014](#)). A recent study conducted by [Irshad *et al.*, \(2020\)](#) reported that the physical and chemical methods used in the manufacture of NPs are disputed because they take longer time, use harmful and hazardous solvents that may be difficult to dispose of; their effects remain in the environment, in addition to their need for high energy sources. However, the biological method of synthesizing NPs is highly cost-efficient and simpler compared to the physical and chemical methods. The biosynthesis of NPs is carried out by using the metabolites of microorganisms (i.e. bacteria, mold fungi, yeasts and algae), or plant extracts. One of the advantages of this method is that it is ecofriendly, does not require high energy, cheap and fast. Recently, the use of microorganisms in biological methods is the commonly used source, which is highly effective for nano-synthesis ([Hari, 2020](#)).

The objectives of this study were to deal with the latest researches in the field of biosynthesis of NPs using microorganisms, and highlight its applications in the medical field.

2. Biosynthesis of metal NPs using microorganisms

Microbes are used as promising biological sources for metal NPs synthesis. However, [Roy *et al.*, \(2019\)](#) highlighted that not all the microorganisms have the ability to convert metals to nano forms. Microbial metal NPs biosynthesis can occur intra-cellularly or extracellularly, as revealed by the study of [Jain *et al.*, \(2011\)](#). Intracellular synthesis of NPs requires additional steps to release the synthesized NPs, such as ultrasound treatment or reactions with appropriate detergents ([Kalimuthu *et al.*, 2020](#)), while, extracellular biosynthesis is cheap and requires simple processing. This favors the large-scale production of NPs to explore its potential applications. Because of that, many studies have focused on extracellular methods for metal NPs biosynthesis ([Prasad *et al.*, 2016](#)).

Bacteria are extremely convenient targets for green NPs synthesis, due to their diverse variety and ability to adapt to different environmental conditions. There are various bacterial cellular components such as; enzymes, proteins, peptides and pigments, acting as factories of NPs. A recent study conducted by [Tsekhnistrenko *et al.*, \(2020\)](#) reported that bacteria used as nanofactories can afford a new platform not only for the removal of metal or metalloid ions, but also for the production of materials with distinctive properties. Metallic NPs can be made by bacteria both intra-cellularly and extracellularly. Extracellular creation is more effective and easier for extraction of the NPs. In this case, biosynthetic metal NPs are less affected by oxidation, which makes it possible to use them in many fields, as revealed by [Gahlawat and Choudhury, \(2019\)](#). Some studies showed that not only living bacteria, but also dead forms of these bacteria can be used for NPs biosynthesis ([Tsekhnistrenko *et al.*, 2020](#)).

Actinobacteria are fungi-like bacteria, they are Gram-positive with high G-C content, and have the ability to produce metal NPs. Recently, [Omar *et al.*, \(2019\)](#) reported that actinobacteria can produce several kinds of bioactive compounds that have great beneficial values. Meanwhile, yeasts are eukaryotic, unicellular microbes classified in the kingdom of

fungi. They use organic compounds as energy sources ([Lachance, 2016](#)). An early study of [Skalickova *et al.*, \(2017\)](#) highlighted that the benefits of using yeast strains for NPs manufacture are that they are easy to control under the laboratory environments, show quick growth, in addition to being cheap to cultivate.

An early research work of [Kobayashi *et al.*, \(2012\)](#) reported that the dense outer capsid coating is an interesting feature of virus proteins, which provide a highly appropriate platform for metal ion interaction. Nevertheless, [Gahlawat and Choudhury, \(2019\)](#) recently revealed that the synthesis of NPs by viruses still faces numerous disadvantages, such as involvement of the host organism for protein expression that restricted further research. Because of their structural and biochemical stability, ease of cultivation, non-toxicity and non-pathogenicity in animals and humans; plant viruses are considered safe for nanotechnological applications. One study conducted by [Gahlawat and Choudhury, \(2019\)](#) indicated that low concentrations of tobacco mosaic virus (TMV), used as additives along with extracts of various plants such as; *Nicotiana benthamiana*, *Avena sativa* and *Musa pradisiaca*, not only led to size reduction but also substantially increased the number of NPs, compared to the non-virus control.

According to [Golhani *et al.*, \(2020\)](#), biosynthesis of NPs by fungi is known as mycosynthesis, which is a widespread way of synthesizing the NPs, due to its well-defined dimensions, different chemical structures, sizes and great production of synthesized NPs. Mycosynthesis of metal NPs takes place by different mechanisms, the most common one is through the fungal nitrate reductase enzyme. Fungi are more versatile in growth and in metal tolerance, in contrast to the bacterial population ([Sangappa and Thiagarajan, 2012](#)).

Abundance of algae, easy of discovery, cost-effectiveness, extensive synthesis of highly stable and safe NPs with better biological properties make them good sources for metal NPs biosynthesis ([Azizi *et al.*, 2014](#)). Additionally, synthesis of NPs with algae

occurs in a shorter time than the other methods of biosynthesis, as recently demonstrated by [Dağlıoğlu and Öztürk, \(2019\)](#). Algae was mediated for the biosynthesis of gold (Au), silver (Ag), palladium (Pd), platinum (Pt), iron (Fe), cadmium (Cd), titanium oxide (TiO₂) and zinc oxide (ZnO) bimetallic NPs.

3. Biosynthesis of silver nanoparticles (AgNPs)

A study conducted by [Jeyaraj *et al.*, \(2013\)](#) placed AgNPs of particular importance, due to its valued properties including; high thermal and electrical conductivity, chemical stability, high catalytic activity and antimicrobial activities. For these reasons, AgNPs has been used in several industrial fields, such as; wound dressings, clothing, cosmetics, sports shoes, etc., as indicated in the recent study of [Azarbani and Shiravand, \(2020\)](#).

Numerous studies used bacteria as residual agents for the production of AgNPs. [Gahlawat *et al.*, \(2016\)](#) successfully utilized *Ochrobactrum rhizosphaerae* for the production of spherical shaped AgNPs of around 10 nm in size, and focused on investigating its role as an antimicrobial agent against *Vibrio cholera* (the causal agent of cholera). A recent research work of [Das *et al.*, \(2017\)](#) revealed the extracellular synthesis of AgNPs within 24 h, using *Bacillus cereus* isolated from heavy metal polluted soil. Furthermore, [Ghiută *et al.*, \(2018\)](#) reported the biosynthesis AgNPs using AgNO₃ as a precursor by *Bacillus amyloliquefaciens* and *Bacillus subtilis*, with a spherical shape and of 142 nm average diameter. Later, [Allam *et al.*, \(2019\)](#) synthesized AgNPs by *Sphingomonas paucimobilis*, AgNPs was spherical to oval in shape (4-20 nm), which could be used for decontamination of wastewater from harmful dyes. Similarly, [Divya *et al.*, \(2019\)](#) used *Alcaligenes* spp. as a mediate to synthesize AgNPs (30-50 nm). In this study, AgNPs displayed antimicrobial activity against clinical microbe isolates such as; *Bacillus* spp., *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida albicans*. [Ameen *et al.*, \(2020\)](#) described the synthesis of spherical AgNPs (13 nm) by *Spirulina platensis* extract, through

heating the mixture of cyanobacterial extract (1%) with 0.5% AgNO₃ solution at 40 °C for 7 h. In another research work, [Ahmed et al., \(2020\)](#) synthesized AgNPs using *Bacillus cereus* strain SZT1; AgNPs obtained was spherical shape, its sizes ranged from 18 to 39 nm. Also, [Ahsan, \(2020\)](#) employed *Pseudomonas fluorescens* to synthesis AgNPs by mixing 90 ml of AgNO₃ with 10 ml of *P. fluorescens* broth extract at 80 °C, the mixture was kept at pH 5 with continuous stirring for 2 h and then left for one day. Scanning electron microscope (SEM) images showed that AgNPs was spherical and irregular (10-100 nm).

Among actinobacteria, *Streptomyces* spp. are most generally used in medicinal and enzymatic applications, because out of more than 10 000 identified antibiotics; 55 % are formed by them. In a previous study, [Wypij et al., \(2018\)](#) synthesized spherical and poly-dispersed AgNPs (5-20 nm) using *Streptomyces xinghaiensis* at room temperature within 2-3 d. Recently, [Avilala and Golla, \(2019\)](#) used marine *Nocardiopsis alba* actinobacteria to synthesize spherical AgNPs (20-60 nm) in bright conditions within 24 h. These AgNPs demonstrated antiviral and antibacterial potential against several bacterial pathogens including; *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Streptococcus aureus*. Similarly, [Fouda et al., \(2019\)](#) used three endophytic actinobacteria namely; *Streptomyces capilliparalis* Ca-1, *Streptomyces zaomyceticus* Oc-5, and *Streptomyces pseudogriseolus* Acv-11 as biocatalysts for green synthesis of AgNPs. These NPs was spherical in shape with size ranging from 23.77 to 63.14 nm, 11.32 to 36.72 nm, and 11.70 to 44.73 nm, for Ca-1, Oc-5, and Acv-11, respectively. The activities of biosynthesized AgNPs were concentration dependent and the obtained results confirmed the efficacy of AgNPs as antimicrobial agents against Gram-positive and Gram-negative bacteria, as well unicellular and multicellular fungi. The minimum inhibitory concentration (MIC) for Gram-positive bacteria, Gram-negative bacteria (*E. coli*), and eukaryotic microorganisms was 0.25 mM, with clear

zone diameter ranging from 10.3 to 14.6 mm. Meanwhile, the MIC for *P. aeruginosa* was 1.0 mM for AgNPs synthesized by strain Ca-1, and 0.25 mM for NPs synthesized by strains Oc-5 and Acv-11.

In another study, [Dağlıoğlu and Öztürk, \(2019\)](#) used green microalgae *Desmodesmus* spp. as a reducing agent for manufacturing AgNPs intracellularly within 24 h without any aggregates. Further, a TEM image of the algae cells showed the presence of spherical AgNPs (15-30 nm) inside them. Recently, [Salaam et al., \(2020\)](#) successfully synthesized AgNPs using green algae *Chlorella vulgaris*, where the best biosynthesizing conditions were pH 10 and 37 °C. The AgNPs was not only spherical and sized to 10 µm, but also showed antibacterial efficacy against particular strains of *Citrobacter* spp., *Staphylococcus aureus*, *E. coli* and *P. aeruginosa*. Thus these AgNPs can be used safely as an alternative to antibiotics. Also, [El-Naggar et al., \(2020\)](#) employed *Chlorella vulgaris* for the biosynthesis AgNPs, in which the algal extract was added to 100 mM of AgNO₃ and then incubated in the dark, so that the pale green color turned brown within 24 h; indicating AgNPs formation. TEM image showed that AgNPs was spherical with size of 3.63-8.68 nm. AgNPs produced in this study had antimicrobial potency against *Bacillus* spp., *Erwinia* spp. and *Candida* spp. On the other hand, [Yilmaz Öztürk et al., \(2020\)](#) used extract of the red algae *Gelidium corneum* as a reducing agent for biosynthesis AgNPs; noticeable color change from light red to dark brown indicated AgNPs formation. Moreover, TEM image confirmed that AgNPs was spherical or angular in shape with size that ranged 20-40 nm. In this study, AgNPs presented a great antimicrobial potential at very low MIC values for both *Candida albicans* (0.51 µg/ ml), and *E. coli* (0.26 µg/ ml) (Fig. 1). Furthermore, [Hamad, \(2019\)](#) the synthesized AgNPs by using 50 ml of (5 mM) AgNO₃ solution mixed with 50 ml cell filtrate biomass of *Penicillium citreonigrum*, incubated in darkness at room temperature until color change. The color changed from wan yellow to light brown after 24 h of incubation.

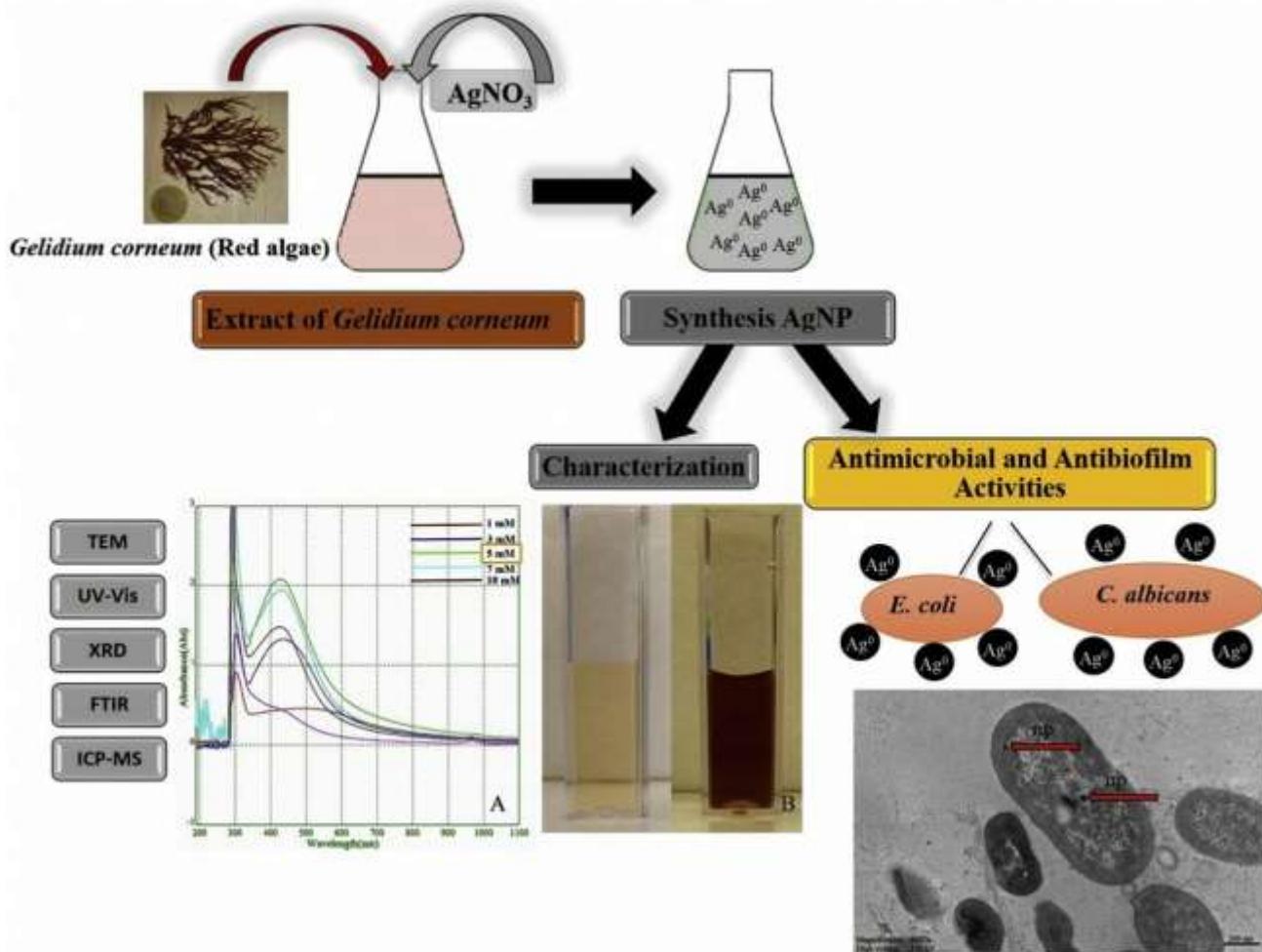


Fig. 1. Summarizes the biosynthesis of AgNPs using *Gelidium corneum*, AgNPs characterization and antibacterial potential (source: [Yilmaz Öztürk et al., 2020](#)).

In another study, [Hulikere and Joshi, \(2019\)](#) employed for the first time an endophytic fungus of *Cladosporium cladosporioides* that was isolated from brown algae to synthesize AgNPs. The color of the reaction mixture (AgNO_3 with aqueous fungal extract) progressively changed from colorless to dark brown, which confirmed AgNPs formation. The scanning electron microscope (SEM) images showed that AgNPs was spherical, its sizes ranged from 30 to 60 nm. Interestingly, no aggregation or precipitation happened after two to three weeks of AgNPs incubation. According to [Noshad et al., \(2020\)](#), AgNPs

was produced by mix 1:1 fungal extracts of *Trichoderma harzianum* and *Aspergillus fumigatus* separately with AgNO_3 and then heated to 29 °C for 24 h. The change of mixture color from yellowish to dark brown confirmed the formation of AgNPs. Similarly, the study of [Khaddam et al., \(2019\)](#) used *Aspergillus* sp. and *Rhizopus* sp. for AgNPs biosynthesis. Fig. (2) demonstrates the formation of AgNPs by change in the color of the cell-free extract from yellow to dark brown for *Aspergillus* sp., whereas *Rhizopus* sp. showed a color change from colorless to dark yellow after 24 h of incubation, as clear in Fig. (3).

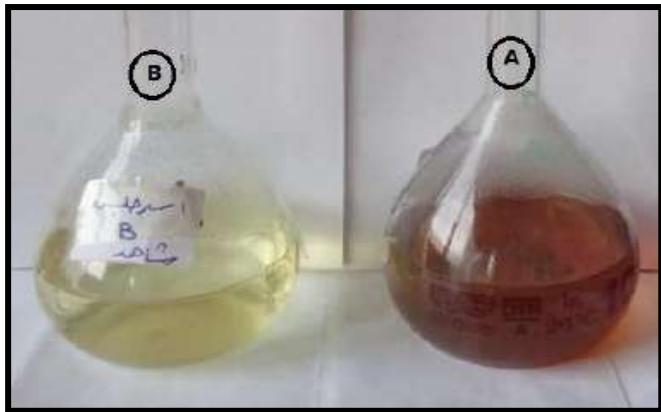


Fig. 2. Color change after 24 h of incubation, using culture filtrate of *Aspergillus* sp. (A) Culture contain AgNPs, (B) Control. (source: [Khaddam et al., 2019](#))



Fig. 3. Color change after 24 h of incubation, using culture filtrate of *Rhizopus* sp. (A) Culture contain AgNPs, (B) Control. (source: [Khaddam et al., 2019](#))

[Jalal et al., \(2018\)](#) used supernatant of *C. glabrata* for extracellular biosynthesis of spherical AgNPs (2-15 nm). The minimum bactericidal concentration (MBC) and minimum fungicidal concentration (MFC) were found in the range of 62.5-250 g/ ml and 125-500 g/ ml; respectively, which revealed that bacterial strains were more susceptible to AgNPs than the fungal ones. These differences in MBC and MFC values of the AgNPs were related to the differences in the structure of the bacteria and the fungal cells. By analyzing the interaction of AgNPs with *C. albicans*, TEM showed the penetration of AgNPs inside the *Candida* cells, which led to the formation of “pits” and “pores” that result from the rupturing of both the cell wall and the cell membrane. Moreover, the TEM image showed that *Candida* cells treated with AgNPs were highly deformed. This might be attributed to the interaction of AgNPs with the yeast cell wall and membrane, which disrupted the structure of the cell membrane due to the formation of pores, and inhibited the normal budding process that finally caused cell death, as demonstrated in Fig. (4). Recently, [Salah et al., \(2020\)](#) employed *P. chrysogenum* extract to synthesize AgNPs; SEM

images demonstrated that AgNPs was spherical, while Atomic Force Microscopy (AFM) showed that the particles size was 18.83 nm. An early research work conducted by [Verma et al., \(2010\)](#) used *A. clavatus* to synthesize AgNPs by extracellular way; the produced AgNPs was spherical to hexagonal ranging from 10 to 25 nm in size. These NPs presented antibacterial activity against *P. fluorescens* and *E. coli*, with an average MIC of 5.83 µg/ ml, and had potent antifungal efficacy against *C. albicans* with MFC of 9.7 µg/ ml.

4. Biosynthesis of gold nanoparticles (AuNPs)

A research work of [Stozhko et al., \(2019\)](#) highlighted that biosynthesis of AuNPs is of great importance, as it has important applications in the field of nanomedicine, and this is due to its effectiveness as an antibacterial, fungal, anti-cancer, and anti-oxidant. Previously, [Huang et al., \(2007\)](#); [Khlebtsov and Dykman, \(2011\)](#) demonstrated that AuNPs has also been used to detect tumors, diagnose genetic diseases and genetic disorders, in addition to its use in optical imaging and phototherapy.

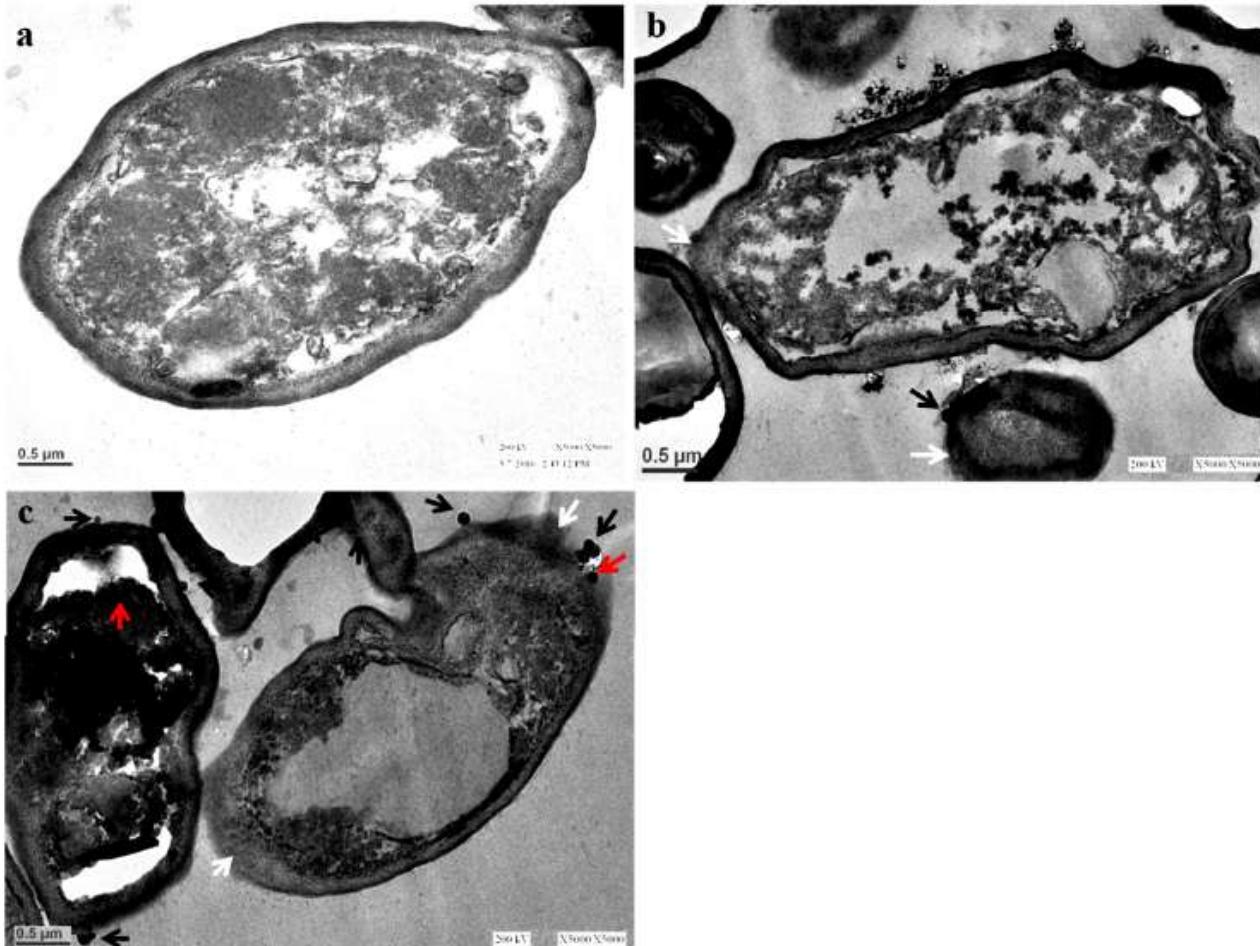


Fig. 4. TEM images of *C. albicans* cells; (a) Untreated control cells; (b, c) Cells treated with 250 g/ ml and 500 g/ ml of AgNPs showing the attachment (black arrows) and penetration of AgNPs inside the cells (red arrows), degradation; destruction, and separation of the outer-most layers of the cell wall and cytoplasmic membrane (white arrows). (source: [Jalal et al., 2018](#))

Many studies were performed towards the synthesizing AuNPs using bacteria. Recent work of [Kunoh et al., \(2018\)](#) used *P. stutzeri* for biosynthesis AuNPs, through reducing gold salt in an aqueous medium. In this study, spherical AuNPs (5 nm diameter) was obtained simply by adding guanine to chloroauric acid (HAuCl_4) solution at room temperature. [San Diego et al., \(2020\)](#) utilized *Lysinibacillus* spp. and *P. stutzeri* for the extracellular synthesis of AuNPs through reduction of HAuCl_4 at pH 9. The produced AuNPs was spherical and

irregular in shapes; it showed no toxicity against *P. aeruginosa*; however, it expressed an increasing inhibition of pyocyanin production with increasing volumes of these AuNPs. In a previous study, [Ahiwale et al., \(2017\)](#) synthesized AuNPs using bacteriophages at different physiological parameters, and the recovered AuNPs was in the range of 20-100 nm. *P. aeruginosa* biofilm formation was inhibited by about 80 % at 0.2 mM of these AuNPs ([Ahiwale et al., 2017](#)). On the other hand; [Le et al., \(2017\)](#) employed Potato virus X for synthesizing elongated filament of

NPs, these NPs had more penetration capability compared to the spherical ones. [Abu-Tahon et al., \(2020\)](#) studied biosynthesis of AuNPs using *A. flavus*, the biosynthesize was carried out by adding 10 ml of HAuCl₄ to 90 ml of *A. flavus* culture supernatant adjusted at pH = 7, and heated to 30°C with shaking for 2 h. AuNPs was produced within 2 min. TEM images indicated that the mycosynthesized AuNPs was spherical in shape and had an average size of 12 nm. [Vairavel et al., \(2020\)](#) synthesized spherical AuNPs intracellularly using *Enterococcus* sp.; such AuNPs induced apoptotic cell death in human colorectal cancer cell line (HT-29).

5. Biosynthesis of different metal NPs

For synthesis of metal NPs, [Arsiya et al., \(2017\)](#) used for the first time *Chlorella vulgaris* aqueous extract to synthesis palladium NPs (PdNPs) within 10 min. TEM images indicated that PdNPs was spherical and 5 to 20 nm in size. Also, [Sriramulu and Sumathi, \(2018\)](#) used *Saccharomyces cerevisiae* aqueous extract as a reducing agent to biosynthesize PdNPs with an average size of 32 nm. In this study, SEM images showed hexagonal-shaped PdNPs, while AFM images demonstrated highly variable shapes with a rough surface. Recently, [Mishra et al., \(2020\)](#) employed green algae *Chlorella vulgaris* extract to synthesis PdNPs; the solutions of palladium chloride (PdCl₂) with algal aqueous extract were adjusted at pH 6-7, and then stirred at 60 °C for 2 h. The solutions turned from yellow to dark brown color, which indicated the formation of NPs. SEM images demonstrated the spherical and triangular shape of PdNPs, with an average size of 70 nm. On the other hand, [Ranjitha and Ravishankar, \(2018\)](#) synthesized selenium NPs SeNPs (100-250 nm) by adding 5 ml of culture extract *Streptomyces griseoruber* to 5 ml of 1mM Sodium Selenite (Na₂SeO₃), and then incubated the mixture at 37 °C for 72 h. Also, [Faramarzi et al., \(2020\)](#) synthesized SeNPs using *S. cerevisiae* within 4 d, in which the size of SeNPs ranged from 75-709 nm. Another study of [Wadhwani et al., \(2017\)](#) depicted the importance of SeNPs as an antioxidant, anti-inflammatory, antimicrobial and anticancer properties,

which has gained more attention in the medical field. Meanwhile, [da Silva Ferreira et al., \(2017\)](#) employed *Chlorella vulgaris* for the biosynthesis of spherical silver chloride NPs (AgClNPs) with the size of 9.8± 5.7 nm, with a recorded activity as an antibacterial agent against *Staphylococcus aureus* and *K. pneumonia*. In other recent study, [Rajeshkumar, \(2018\)](#) employed two brown seaweeds such as *Padina tetrastromatica* and *Turbinaria conoid* algal formulations for biosynthesis of Zinc nanoparticles (ZnONPs), and assessed its antimicrobial potency against fish pathogens.

[Mahanty et al., \(2019\)](#) biosynthesized iron oxide NPs using three fungi namely; *T. asperellum*, *Fusarium incarnatum* and *Phialemoniopsis ocularis*. The color of the reaction mixture composed of individual aqueous extract of the three fungi mixed at 1: 2 ratios of FeCl₂ and FeCl₃; respectively, changed within 5 min. as clear in Fig. (5). Imaging of NPs using both of SEM and TEM showed that FeNPs was spherical in shape with an average size ranging between 25± 3.94 nm for *T. asperellum*, 30.56± 8.68 nm for *F. incarnatum*, and 13.13± 4.32 nm for *Phialemoniopsis ocularis*.

A recent study conducted by [Noman et al., \(2020\)](#) proved the ability of *Escherichia* sp. to synthesize copper NPs (CuNPs), which was spherical shape with size ranging from 22.3 to 39 nm. Moreover, [Sidkey et al., \(2020\)](#) employed *P. stutzeri* that was isolated from soil and wastewater samples to biosynthesize magnesium NPs (MgNPs) through both extracellular and intracellular routes. The recovered intracellular MgNPs was spherical in shape, its size ranged from 229.3-553.2 nm. Similarly, [Fatemi et al., \(2018\)](#) successfully used the extracellular route to synthesize spherical iron oxide NPs (29.3 nm) using *B. cereus*, which was isolated from soil. The magnetic iron oxide NPs was obtained quickly at room temperature using FeCl₃.6H₂O after 5 min., and using FeCl₂•4H₂O after 30 min. This study also depicted that these NPs had anticancer effects against some factors of breast cancer cells.

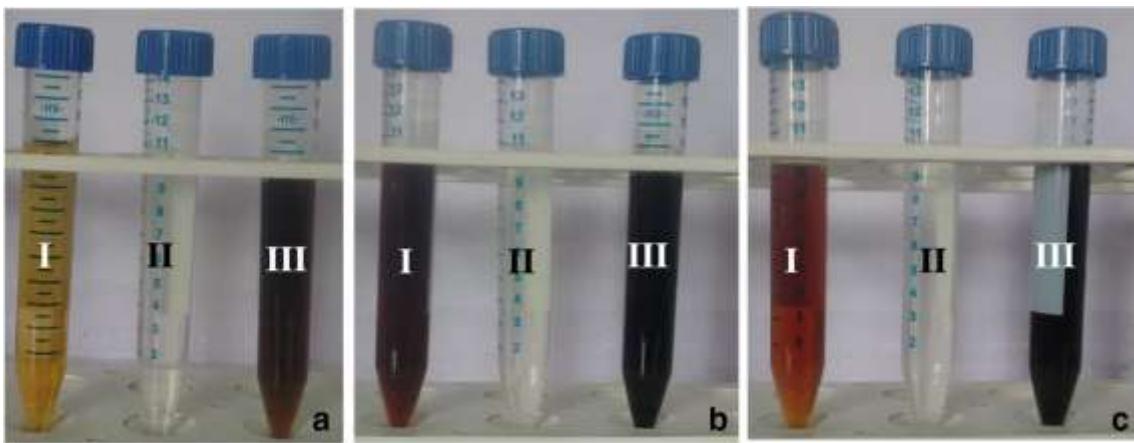


Fig. 5. Fungal isolates of (a) *T. asperellum*, (b) *Phialemoniopsis ocularis* (c) *F. incarnatum* showing mixture color change during reaction with iron precursor salts. I = (Positive control), II = Iron precursor salt (negative control), III = Appearance of black coloration due to addition of fungal extract to 1:2 ratio of FeCl_2 and FeCl_3 solution, after 5 min. of incubation. (source: [Mahanty et al., 2019](#))

In a recent research work conducted by [Ağçeli et al., \(2020\)](#), *Streptomyces* spp. was used to synthesis titanium dioxide NPs (TiO_2 NPs), these NPs was spherical (30-70 nm) and demonstrated antimicrobial efficacy against *Staphylococcus aureus*, *E. coli*, *C. albicans* and *A. niger*. On the other hand, [El-Sayyad et al., \(2020\)](#) used *Streptomyces cyaneus* for biosynthesis of tellurium dioxide NPs (TeO_2 NPs) at room temperature. The produced TeO_2 NPs was spherical of 75 nm in size. Moreover, TeO_2 NPs showed antifungal potential towards *A. fumigatus*, *A. niger* and *A. flavus*; presenting inhibition zone diameters of 19, 20 and 30 mm, and had antibacterial potency against *K. pneumonia*, *Staphylococcus aureus* and *P. aeruginosa* (15, 18, and 25 mm inhibition zone diameters, respectively). [Hassan et al., \(2019\)](#) proved the ability of two actinobacteria strains of *Streptomyces* (*S. zaomyceticus* Oc-5Hinuma) and (*S. pseudogriseolus* Acv-11) to synthesize copper oxide NPs (CuONPs) of 78 and 80 nm sizes, respectively.

Conclusion

The ability of microorganisms to manufacture NPs varies. Fungi are the most important microorganisms

used in the biological construction of NPs, due to their great diversity, are relatively easy to isolate and grow in large quantities in the laboratory. Moreover, they are able to excrete large quantities of extracellular enzymes necessary for final preparation of NPs, and thus they are superior to many other microorganisms such as bacteria. On the other hand, the biosynthesized NPs expresses one of the most promising applications in the medical field, since these NPs demonstrated antibacterial potential towards some multidrug resistant bacteria such as; *Staphylococcus aureus* and *P. aeruginosa*, which no longer respond to treatment with antibiotics.

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Conflict of interest

The authors declare no conflict of interests.

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Ethical approval

Non-applicable.

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