



Review article

Fungi as veritable tool in current advances in nanobiotechnology

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ABSTRACT

Fungi have great prospects for synthesis, applications and developing new products in nanotechnology. In recent times, fungi use in nanotechnology is gaining more attention because of the ecological friendly state of their metabolite-mediated nanoparticles, their safety, amenability and applications in diverse fields. The diversity of the metabolites such as enzymes, polysaccharide, polypeptide, protein and other macro-molecules has made fungi a veritable tool for nanoparticles synthesis. Mechanism of fungal nano-biosynthesis from the molecular perspective has been extensively studied through various investigations on its green synthesized metal nanoparticles. Fungal nanobiotechnology has been applied in agricultural, medical and industrial sectors for goods and services improvement and delivery to mankind. Agriculturally, it has found applications in plant disease management and production of environmentally friendly, non-toxic insecticides, fungicides to enhance agricultural production in general. Medically, diagnosis and treatment of diseases, especially of microbial origin have been improved with fungal nanoparticles through more efficient drug delivery systems with great benefits to pharmaceutical industries. This review therefore explored fungal nanobiotechnology; mechanism of synthesis, characterization and potential applications in various fields of human endeavours for goods and services delivery.

1. Introduction

Generally, fungi are eukaryotic organisms which are predominately decomposers. Today, over 1.5 million species of fungi are believed to thrive and survive in various habitats on Earth; however, only 70,000 species have been well taxonomically identified. In addition, approximately 5.1 million fungal species were found when high-throughput put sequencing method was carried out. Regardless of the differences in the fungal population in the world as reported by different studies, it is worth stating that fungi are actually ubiquitous and in fact, their population might actually be more than ever reported in any study. The major cosmopolitan characteristics of the fungal kingdom reside in extracellular breakdown of substrate, secretion of important enzymes to breakdown compounds of great complexity into simpler forms and use of diverse energy sources (Blackwell, 2011). Thus, the exploration of fungi, its implication and potential in nanobiotechnology is important.

Myconanotechnology, as it is commonly called, is thus defined as the interface between nanotechnology and mycology (Hanafy, 2018; Sousa et al., 2020). The field of myconanotechnology is of great potentials, partly due to the wide range and diversity of fungi (Khande and Shahi,

2018). Mycology is the study of fungi while nanotechnology is the study involving the design, synthesis and application of technologically important particles of nano size (Sousa et al., 2020). In this light, the design and synthesis of metal nanoparticles using fungi is termed mycofabrication. In recent times, the fungal system has emerged as important bionanofactory for the synthesis of nanoparticles of gold, silver, CdS, platinum etc. Fungal bionanofactories has produced important nanoparticles of good dimensions and monodispersity (Guilger-Casagrande and Lima, 2019).

Furthermore, fungi are reported to produce proteins in large quantities, they are important in the significant large-scale production of nanoparticles. Most fungal proteins are known for hydrolyzing metal ions. More so, fungi are easily isolated and cultured. More so, fungal nanoparticles of enzymes, polysaccharides, protein and other macro-molecules are diverse in size and mostly secreted extracellularly. Therefore, fungal enzymes' extraction and purification is less complicated than synthetic processes as fungi play a critical role in preventing environmental pollution. The use of microorganisms in the synthesis of nanoparticles is an appealing green nanotechnology choice and the use of biological systems, like fungi, has recently emerged as a novel approach

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for nanoparticle synthesis (Castro et al., 2014; Dorcheh and Vahabi, 2016; Elegbede and Lateef, 2018; Elegbede et al., 2019). This review however discusses the various principles in vogue for fungal nanoparticles production and applications in different fields of human endeavours.

1.1. Outstanding properties of fungi in nanobiotechnology

It is believed that, any microorganism that would be considered for nanobiotechnological purposes must be of generally recognized as safe (GRAS) status in all fronts without any sort of controversy. Similarly, the main property of fungi in nanobiotechnology is the GRAS status and regardless of the enzyme, habitat and biology of the fungi, they must be generally safe. Interestingly, fungi producing important nanoparticles are of GRAS status. In addition, because of their tolerance and metal biological accumulation potential, fungi are of great interest in the biological development of metallic nanoparticles (Sastry et al., 2003). Metal ions can be accumulated by fungi through physical, chemical and biological mechanisms such as extracellular binding of polymers and metabolites, binding to particular polypeptides, and metabolism-dependent accumulation.

Furthermore, fungi can easily be scaled up even in thin solid substrate fermentation technique and this is an important attribute of using them in nanoparticle synthesis. Also, fungi are excellent secretors of extracellular enzymes, so large-scale processing of enzymes is possible (Castro-Longoria et al., 2012). Another benefit of using a green approach mediated by fungi to synthesize metallic nanoparticles is the ease with which biomass can be used. Since a variety of fungal species grow rapidly, culturing and maintaining them in the laboratory is very easy (Castro-Longoria et al., 2011). Since fungi are culturable in large amounts, their potential use has gotten a lot of attention. Furthermore, extracellular secretion of enzymes has a benefit in downstream biomass processing and handling. Another property of fungi that made it favoured for nanobiotechnological functions is the high wall-binding and intracellular metal uptake (Bourzama et al., 2021). Fungi can generate metal nanoparticles/meso and nanostructures by using a reducing enzyme, either intracellular or extracellular, and a biomimetic mineralization technique (Mughal et al., 2021; Siddiqi and Husen, 2016; Duran et al., 2005). In comparison to bacteria and other microorganisms, fungi are excellent protein secretors, resulting in a higher yield of nanoparticles (Mughal et al., 2021; Guilger-Casagrande and Lima, 2019). As a result of fungi's dissimilatory properties, fast and environmentally friendly solutions are possible.

1.2. Common fungi in nanobiotechnology

In the world today, fungi are the prime organism in secreting nanoparticles in a far less environmentally damaging way. Fungi diversity have been reported as valuable biological substance for the synthesis of nanoparticles. *Penicillium aurantiogriseum*, *Penicillium citrinum* and *Penicillium waksmanii* mediated synthesis of copper nanoparticles were reported by Honary et al. (2012). The synthesized nanoparticles displayed a fairly uniform with spherical shape. Proteins produced from fungi culture are capable of hydrolyzing metal precursors to form metal oxides extracellularly were supported by UV-vis and fluorescence Spectrum. *In vitro* approach for gold nanoparticles biosynthesis from the fungus *Penicillium aurantiogriseum*, *Penicillium citrinum* and *Penicillium waksmanii* have also been established. The synthesized gold nanoparticles formed showed a fairly uniform with spherical shape with the Z-average diameter of 153.3 nm, 172 nm and 160.1 nm for *Penicillium aurantiogriseum*, *Penicillium citrinum*, and *Penicillium waksmanii*, respectively.

The synthesized nanoparticles formed showed a fairly well-defined dimension and good monodispersity. The nanoparticles formed were relatively uniform with spherical shape and superiorly monodispersed with the average diameter of 60 nm. The result showed the scolical effects of the synthesized nanoparticles extremely significant for all the

four concentrations evaluated and at various exposure times in comparison to the control group ($P < 0.0001$).

This development is a great news as nanobiotechnology is already proving to be of great use in diverse fields especially in medical field where high level of purity is required of any compound (Khan et al., 2019). Fungi are now important medically in disease diagnosis and treatment; most importantly allowing for efficient drug delivery in places that have always been difficult to reach. In addition, gold nanoparticle production has been reported in *Aspergillus*, *Neurospora*, *Fusarium*, *Pleurotus* and *Verticillium* species (Wang et al., 2021; Rai et al., 2021; Kitching et al., 2015; Priyadarshini et al., 2014). At room temperature, 5–40 nmpolydispersed silver nanoparticles are produced by *Trichoderma viride*. Fungi in general have secreted diverse nanoparticle sizes.

In addition to fungi mediated nanoparticles from the normal environment, important nanoparticles have been reported from extreme environments. As reported by Tiquia-Arashiro (2014), the classification of extremophiles and their ecology is the first step in creating processes and goods that will benefit mankind as extremophiles are biotechnologically interesting because they generate extremozymes, which are enzymes that work in extreme environments. Extremozymes are important in industrial manufacturing processes with great applications in research as they possess the capability to stay active in adverse conditions such as high temperature, pH, and pressure. Identifying extremophiles from natural environments has just touched the surface of research with just around 1% of the species have been described, and far fewer have had their beneficial properties sequenced. However, as many researchers have pointed out, the detection of extremophiles has opened up possibilities for commercial, biotechnological, and medical applications (Gabani and Singh, 2013; Pomaranski and Tiquia-Arashiro, 2016).

Extremozymes have a lot of potential in industrial biotechnology because they can be utilized in unusually extreme environments, which can lead to substrate transitions that aren't possible with regular enzymes. Enzyme-mediated reactions permit for more complex chemo-, regio-, and stereo-selectivity in organic synthesis than chemical catalysis (Koeller and Wong, 2001). However, enzymes' long-term viability and reusability have been cited as significant obstacles to their widespread use by Schmid et al. (2011). Diverse nanoparticles have recently been used to boost conventional enzyme immobilization methods in industrial biotechnology to improve enzyme loading, function, and stability while lowering biocatalyst costs.

2. Current advances in the principles of synthesizing fungal mediated nanoparticles

The synthesis of fungi mediated nanoparticles offers great advantages compares to other microorganisms like bacteria and actinomycetes. Some of these great advantages offer by fungi includes their easy to handle and downstream the process, economically feasible and ecologically friendly to cover a large surface (Syed and Ahmad, 2012). Enzymes in the cytoplasm and cell wall of fungi transform metal ions into nanoparticles (Chatterjee et al., 2020). In term of nanoparticles production, fungi have higher productivity and higher tolerances to metals especially in context of high cell wall binding capacity of metal ions with biomass (Singh et al., 2016). Fungi is attracted by the positive charge possessed by the metal ions and this triggers the biosynthesis. However, specific proteins are also induced by metal ions, and these hydrolyze the ions. Some of the recent studies conducted on nanoparticles synthesis using fungi are shown in Table 1.

As stated above, the presence of proteins on fungal cell surfaces, fungi are suitable for the synthesis of nanoparticles as opposed to other species of microorganisms. The synthesis of metal nanoparticles via the reduction of reductase enzymes present in the cell wall of fungal cells is the most common process of intracellular biological synthesis. As a cellular protective process against the chemical toxins present in their environments, fungi develop nanoparticles and various chemical reactions reduce toxic ions to their metal nanoparticles, with some of these

Table 1. Examples of recent studies on nanoparticle synthesis using fungi.

Nanoparticle	Fungus	Application	Intra/Extra	Reference
Platinum	<i>Fusarium oxysporum</i>	Nano medicine	Extra	(Chatterjee et al., 2020)
Iron oxide	<i>Aspergillus niger</i> BSC-1	Wastewater treatment	Extra	(Mohmed et al., 2017)
Silver	<i>Aspergillus terreus</i>	Antibacterial, anticancer	Extra	(Hulikere and Joshi, 2019)
Silver	<i>Cladosporium cladosporioides</i>	Antioxidant, antimicrobial	Extra	(Zhang et al., 2019)
Silver	<i>Ganoderma lucidum</i> <i>G. applanatum</i>	Antimicrobial	Both	(Aygün et al., 2020)
Copper	<i>Aspergillus niger</i>	Antidiabetic and Antibacterial	Extra	(Zhang et al., 2019)
Gold	<i>Cladosporium oxysporum</i>	Catalysis	Extra	(Srivastava et al., 2019)
Selenium	<i>Mariannaea</i> sp. HJ	Medicinal and electronics	Both	(Vijayanandan, and Balakrishnan, 2018)
Cobalt oxide	<i>Aspergillus nidulans</i>	Energy storage	Extra	(Joshi et al., 2017)
Gold	<i>Cladosporium cladosporioides</i>	Antioxidant, antimicrobial	Extra	(Bhargava et al., 2016)
Silver, Gold, Selenium	Mushrooms	Biomedicals	Both	(Adebayo et al., 2021)

reactions including complexation, immobilisation, precipitation and co-precipitation, biosorption, ion-form alteration and bio-coupling (Dorcheh and Vahabi, 2016). At the reductive state, fungi use their cellular enzymes, proteinaceous molecules, or cell membrane-bound molecules like electron donors, and the poisonous ions are quickly precipitated as metal nanoparticles, either intracellularly or extracellularly, depending on the biological synthesis process (Figure 1).

The formation of structures atom by atom, molecule by molecule, or by self-organization is a type of bottom-up technique in which the main reaction is dependent on reduction or oxidation of the substrate, resulting in a rise in colloidal structures and it has been established that fungal enzymes or metabolites are often responsible for a decrease in metallic composition of nanoparticles. The bottom-up approach is demonstrated by the way myco-reduced metal atoms transfer nucleation with subsequent development, resulting in the forming of nanostructures and the benefit of a bottom-up approach is the greater likelihood of creating nanostructures without significant defects, as reported in nanorods or nanosheets, with the secretion of more homogeneous chemical compositions. Furthermore, owing to the reduction of Gibb's free energy, which this technique is driven by, the bottom-up strategy means a better chance of receiving less faulty nanoparticles and a much more homogeneous chemical composition.

2.1. Extracellular fungal biosynthesis of nanoparticles

The extracellular biological synthesis of metal nanoparticles relies heavily on fungal cell membranes as they contain a significant number of differently bound compounds, such as peptides, proteins, polysaccharides, oxidoreductases, and quinones, which are involved in the reduction and precipitation of metal ions (Keat et al., 2015; Moghaddam et al., 2015). Extracellular reductase is the enzyme in control of metal nanoparticle biological synthesis and development (Vahabi and Dorcheh, 2014) with *Fusarium oxysporum* been shown to manufacture NADPH-dependent nitrate and sulfite reductases, which are used in the biological synthesis of Ag- and Au-nanoparticles, respectively.

Additionally, hydrogenases, flavin adenine dinucleotide (FAD)-dependent glutathione reductase, and nitrate reductases have also been discovered to play a role in the biological synthesis of metal nanoparticles through fungi; however, studies have indicated that metal reduction involves an electron shuttle in the reductase enzyme system. Quinones (anthraquinones and naphthoquinones), as well as their quinone counterparts, have been discovered to aid in the reduction process and furthermore, when fungal cells were exposed to heavy metal ion exposure, metalloproteins such as phytochelatin and metallothionein were found to be overexpressed, and these metalloproteins assisted in the reduction process by complexing the metal ions via their binding and reductive abilities (Park et al., 2016).

Protein molecules found in mycelial membranes can be used to facilitate extracellular fungal nanoparticle biological synthesis and it has

been suggested that surface-bound proteins in *R. oryzae* and *Corioliu versicolor* mycelia associate with gold and silver ions, resulting in the reduction and stabilization of Au-nanoparticles and Ag-nanoparticles respectively (Das et al., 2012). The electrostatic reactions between protein-free amine or cysteine residues and enzyme carboxylate groups in fungal cells are believed to be responsible for the formation of protein-metal bonds and as a result, a redox state is formed, allowing metal nanoparticles to precipitate and form (Park et al., 2016).

A number of extracellular fungal products have been discovered to contribute to the biological synthesis of metal nanoparticles, under which these nanoparticles were synthesized to mitigate the toxic actions of metal ions, which were then precipitated as nanoparticles and in response to the toxicity of Cu(II), Pb(II), and Zn(II), *Curvularia lunata* was found to contain extracellular mucilage materials. Furthermore, toxicity of Ni(II) and Cd(II) were reported to allow *Aureobasidium pullulans* to develop pullulans, and glomalin glycoprotein was found to sequester Cu(II) in *Glomus* cultures (Cornejo et al., 2008).

2.2. Intracellular fungal biosynthesis of nanoparticles

Metal nanoparticle intracellular biological synthesis in fungal cells is primarily due to cellular ATPases and hydrogenases while *Fusarium oxysporum* was discovered to generate Au-nanoparticles intracellularly in cytoplasmic vacuoles, with plasma membrane-ATPase, 3-glucan binding enzyme, and glyceraldehyde-3-phosphate dehydrogenase playing a vital role in the reaction (Vahabi and Dorcheh, 2014). Hydrogenases generate cytoplasmic hydrogen, which is needed for metal nanoparticle precipitation (Riddin et al., 2009) and in detoxification, yeast cells utilize intracellular glutathione as well as two metal-binding proteins (phytochelatin and metallothionein). This was due to the fact that these compounds have significant redox and nucleophilic properties, allowing them to participate in metal ion biological reduction and furthermore, it has been documented that fungal cell use their antioxidative systems to detoxify metal ions in order to shield themselves from the oxidative power of these metal ions (Jha and Prasad, 2016).

As cells are exposed to heavy metals, oxygen is depleted intracellularly, resulting in the formation of reactive oxygen species (ROS), such as hydrogen peroxide, which can then generate highly active and harmful free hydrogen radicals; however, to avoid these reactions, the fungal cellular machinery employs a variety of enzymatic systems, including antioxidative systems (Morano et al., 2012). Catalases and superoxide dismutase, methionine sulfoxide reductase, thioredoxins, peroxiredoxins, glutathione and glutathione peroxidases and transferases are all antioxidative systems contained in fungi and to transport required substrates (C- and N-sources), micronutrients, and ions inside fungal cells, different membrane channels and transporter proteins are employed (Ujam et al., 2021; Ibrahim et al., 2021; Vitale et al., 2020). Toxic metals, on the other hand, may use these channel structures to access the cytoplasmic space and to prevent poisonous metal ions from entering the

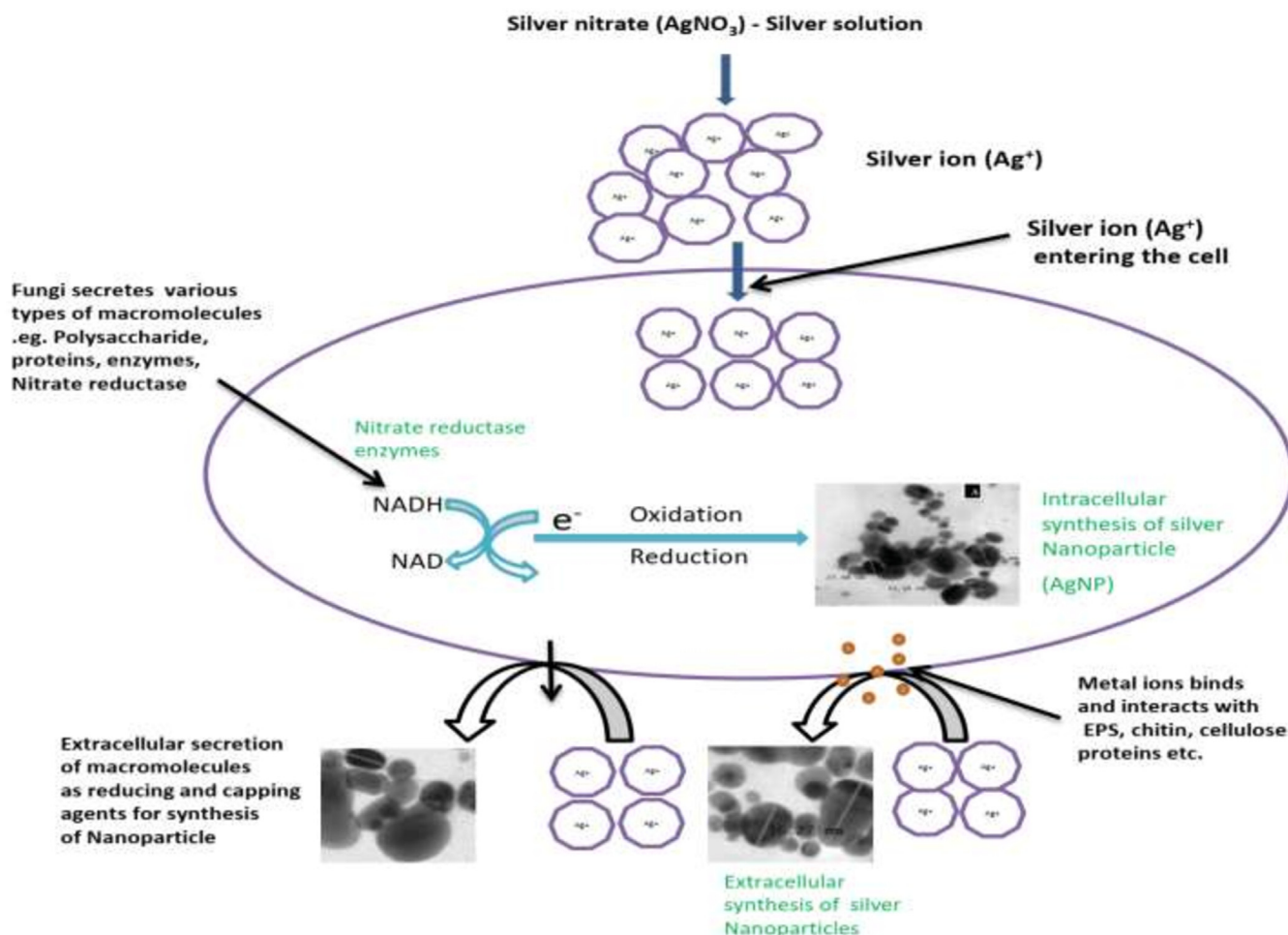


Figure 1. Mechanism of Fungi mediated silver nanoparticles (AgNPs).

cytoplasm, cells may obstruct or even remove certain transport systems. However, this has the potential to disrupt cellular machinery, and certain metal ions can reach cells through several routes while cellular enzymes can react with metal ions and precipitate nanomaterials in such situations (Gahlawat and Choudhury, 2019).

The same enzymes and proteins that are involved in the extracellular biosynthesis of nanoparticles are often involved in the intracellular biological synthesis of metal nanoparticles as growth conditions change. As *Trichothecium* sp. cells grow in static cultures, extracellular nanoparticles were synthesized while biological synthesis was transferred to intracellular pathways during development in submerged culture and different intracellular pathways were used to biosynthesize metal nanoparticles to accomplish this turn. This shift in biological synthesis was due to the observation that static cultures enable fungal cells to excrete their enzymes and proteins extracellularly, while in a submerged culture environment, these enzymes were not released.

2.3. Synthesis of some fungal mediated nanoparticles of different sizes

One of the well-established researches on the biological synthesis of metal nanoparticle via fungi is the production of silver nanoparticles extracellularly by the filamentous fungal cells of *Verticillium* sp. documented by Mukherjee et al. (2001a, b). In the biosynthesis of nanoparticles, the filamentous cells of *Fusarium oxysporum* has also been extensively used among the thousands of fungi documented for this purpose. Mostly, the production of extracellular nanoparticles is reported in exposing biomass to metallic ion solutions in a study by Ahmad et al. (2002). Many fungi are reported to secrete CdS, MoS₂, ZnS and PbS

nanoparticles with a feasible sulfate diminishing enzyme-based process for nanoparticles production linked to the presence of proteins in the aqueous solution and by using fungi; leading to separate and easy recovery of silver nanoparticles. Fungal nanoparticles produced have diverse morphologies with sizes ranging from 5 to 50 nm as reported by Ahmad et al. (2003).

In a study by Duran et al. (2005), spherical silver nanoparticles have sizes ranging from 20 to 50 nm using *F. oxysporum*. The differences in sizes of fungal silver nanoparticles have been heavily linked to different culturing temperature (Riddin et al., 2006). The most often created nanoparticles are quasi-spherical as reported by several authors, different morphologies of nanoparticles are recovered in the metallic ion solution of fungi. With *F. oxysporum*, the production of nanoparticles of diverse metals has been reported (Duran et al., 2005). Technique of nanoparticle synthesis is mainly extracellularly, producing different forms and sizes of the particle. The metallic ion reduction in *F. oxysporum*, has been linked to a NADH-based reductases and a shuttle Quinone extracellular procedure by Mukherjee et al. (2001a, b).

Furthermore, it was documented that various concentrations of NADH had an effect on the production of Au–Ag alloy nanoparticles with a number of compounds (MubarakAli et al., 2012). Furthermore, phytochelatin and purified -NADPH-dependent nitrate reductase produced by *R. stolonifer* were used to successfully manufacture silver nanoparticles in the 10–25 nm size range (Binupriya et al., 2010). Govender et al. (2009) proposed a method using a purified hydrogenase enzyme from *F. oxysporum* to biologically reduce H₂PtCl₆ and PtCl₂ into platinum nanoparticles while metal nanoparticles of varying shapes and sizes were synthesised using fungal biomass and/or cell-free extract (Shankar et al., 2013).

Generally, diverse fungal species can be utilized to produce diverse nanoparticles under similar experimental condition and for example, while *Verticillium* sp. nanoparticles had a cubo-octahedral shape with a size range of 100–400 nm magnetite, *F. oxysporum* nanoparticles had an irregular structure with a complete quasi-spherical morphology with a size range of 20–50 nm as reported by [Bharde et al. \(2006\)](#). The differences in the nanoparticles produced can be due to the condensation of biomolecules, incubation conditions, precursor etc. Also, the use of *Rhizopus oryzae* in synthesizing metal nanoparticles is well established for controlling the form of gold nanoparticles at room temperature by regulating growth factors like gold ion concentration, solution pH, and response time ([Das et al., 2010](#)).

3. Current advances in fungal nanobiotechnology applications

Fungal nanobiotechnology has found applications in diverse areas of human lives. Nanoparticles from fungi have been employed for several purposes; ranging from human health management, through agriculture, food production to several other industrial processes.

3.1. Medical application of fungal nanobiotechnology

In recent times, there is an increase in acceptability level of nanotechnology in biomedicine and this has triggered the huge development observed in fungal nanobiotechnology in biomedical sciences. From diagnosis to treatment and drug delivery, studies in the field of nanomedicine have progressed steadily and significantly. Fungal nanobiotechnology has found applications in biologically labeling fluorescent, gene and drug delivery factors and in biological detection of pathogens, tissue engineering, tumor demolition through heating (hyperthermia), MRI contrast enhancement, phagokinetic investigations etc ([Table 2](#)). Magnetic nanoparticles are good for targeted drug delivery and hyperthermia use with discrete nanoparticles often applied in nanobiomedicine. The availability of several journals and articles on the applications of fungal nanoparticles in biomedicine has greatly contributed to the advancement over the years.

Due to the fact that biosynthesized nanoparticles are a relatively recent field, researchers have already begun to examine their possible applications in fields such as drug delivery, cancer therapy, gene

treatment and DNA analysis, antibacterial, biological sensors, separation science, and MRI. [Mishra et al. \(2011\)](#) studied the biosynthesis of AuNP in the fungus *Penicillium brevicompactum* using the supernatant, live cell filtrate, and biomass while [Jeyaraj et al. \(2013\)](#) looked at the effects of Ag-NP on cancer cell lines in another study. More specifically, using the fungus *Trichoderma viride*, silver nanoparticles with sizes ranging from 5 to 40 nm were biologically synthesized ([Fayaz et al., 2010b](#)).

Nanoparticles have also been studied for their ability to enhance the antimicrobial activity of a number of antibiotics against Gram-positive and Gram-negative bacteria. Ampicillin, kanamycin, erythromycin, and chloramphenicol's antibacterial properties were improved with Ag-NP against pathogenic species with the highest effect recorded in ampicillin in combination with the nanoparticles. This finding indicated that combining antibiotics with Ag-NP improved antimicrobial activity. [Duhan et al. \(2007\)](#) reported antagonistic effect of extracellularly formed silver nanoparticles of *Fusarium oxysporum* against *Staphylococcus aureus* and thus, suggested this application into textile industry in addition to the biomedical application.

[Gajbhiye et al. \(2009\)](#) reported the antifungal property of biosynthesized nanoparticles in combination with fluconazol (a triazole antifungal drug) against *Phoma glomerata*, *P. herbarum*, *Fusarium semitectum*, *Trichoderma* sp. and *Candida albicans*. Fluconazole's antifungal efficacy was improved by AgNPs generated by *Alternaria alternata*, against all tested strains except *P. herbarum* and *F. semitectum*. In a separate research, mycelia-free water extracts of the fungal strain *Amylomyces rouxii* were found to be high in AgNPs and effective against *Shigella dysenteriae* type I, *Staphylococcus aureus*, *Citrobacter* sp., *E. coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Candida albicans* and *Fusarium oxysporum* ([Musarrat et al., 2010](#)). [Das et al. \(2009\)](#) produced AuNPs on *Rhizopus oryzae* surface and inhibited the growth of G^- and G^+ bacterial species.

Trichoderma viride filtrate mediated AgNPs demonstrated significant importance in labeling and imaging with laser excitation and photoluminescence measurements emission at the range of 320–520 nm ([Sarkar et al., 2010](#)). A major problem in contemporary laser medicine has been the intensive interaction of sensitive tissues outside of the operating realm. On the contrary, this problem can be solved by locating dyes which allows the redirection of the radiation blurs to the surface of irradiated tissues in limiting optical radiation ([Podgaetsky et al., 2004](#)).

Table 2. Fungi and properties of fungi-mediated nanoparticles used for medical application.

Fungus species	Nanoparticles	Localization	Size (nm)	Shape	Application	Reference
<i>Aspergillus fumigatus</i>	ZnO	Extracellular	1.2–6.8	Spherical and hexagonal	Bio medical	Raliya and Tarafdar (2013)
<i>Aspergillus oryzae</i>	FeCl ₃	-	10–24.6	Spherical	Biomedical	Raliya (2013)
<i>Aspergillus tubingensis</i>	Ca ₃ P ₂ O ₈	Extracellular	28.2	Spherical	Biomedical	Tarafdar et al. (2012)
<i>Helminthosporium solani</i>	Au	Extracellular	2–70	Polydispersed	Anti-cancer drug	Kumar et al. (2008)
<i>Penicillium brevicompactum</i>	Au	-	10–50	Spherical	To target cancer cells	Mishra et al. (2011)
<i>Volvariella volvacea</i>	Au	-	20–150	Spherical	Therapeutic	Philip (2009)
<i>Candida albicans</i>	Au	-	20–40, 60–80	Spherical & nonspherical	Detection of liver cancer	Chuhan et al. (2011)
<i>Fusarium oxysporum</i>	Ag	Extracellular	20–50	Spherical	Antibacterial	Duran et al. (2005)
<i>Aspergillus niger</i>	Ag	Extracellular	3–30	Spherical	Antibacterial and antifungal activity	Jaidev and Narasimha (2010)
<i>Aspergillus fumigatus</i>	Ag	-	15–45	Mostly spherical	Antiviral against HIV-1	Alani et al. (2012)
<i>Pleurotus sajor caju</i>	Ag	Extracellular	30.5	Spherical	Antibacterial activity	Vigneshwaran and Kathé (2007)
<i>Aspergillus niger</i>	Ag	-	5–35	Spherical	Antimicrobial	Kathiresan et al. (2010)
<i>Volvariella volvacea</i>	Ag	-	15	Spherical	Medical applications	Thakkar et al. (2010)
<i>Phoma glomerata</i>	Ag	-	60–80	Spherical	Antibiotic	Birla et al. (2009)
<i>Trichoderma viride</i>	Ag	-	5–40	Spherical, rod-like	Antibacterial activity	Fayaz et al. (2009a)
<i>Trichoderma viride</i>	Ag	Extracellular	5–40	Spherical, rod-like	synergistic effect with antibiotics	Fayaz et al. (2010b)
<i>Amylomyces rouxii</i> KSU-09	Ag	-	5–27	Spherical	Antimicrobial	Musarrat et al. (2010)
<i>Aspergillus clavatus</i>	Ag	Extracellular	550–650	-	Antimicrobial	Saravanan and Nanda (2010)
<i>Aspergillus terreus</i> CZR-1	Ag	Extracellular	2.5	Spherical	Biomedical	Raliya and Tarafdar (2012)
<i>Volvariella volvacea</i>	Au–Ag	Extracellular	20–150	Triangular	Medical application	Thakkar et al. (2010)
<i>Aspergillus flavus</i>	TiO ₂	-	62–74	Spherical	Antimicrobial	Rajakumar et al. (2012)

In addition, there are other studies that reported the cadmium telluride quantum dots (CdTe QDs) fabrication by extracellular synthesis of nanoparticles by *Saccharomyces cerevisiae* (Bao et al., 2010) and *Escherichia coli*. The nanoparticles were of great optical features of tiny size, protein cover and great ability in water as analyzed using UV-visible spectroscopy and spectrofluorimetry with photoluminescence emission at 488–551 nm. The CdTe QDs associated with folic acid has been reported in the imaging of cancer cells, and they were shown to have biological compatibility in a cytotoxicity assay (Bao et al., 2010).

Furthermore, nanotechnology and its impact on pharmaceutical improvement alongside with metallic nanoparticles and their wide range of potentials in pharmaceutical applications such as anti-cancer, anti-parasite, bactericidal, fungicidal, etc. had been reported by several researchers. A systematically review of the efficacy of these nanoparticles (NPs) against lung cancer through *in vitro* models was reported by Barabadi et al. (2019). The ability of the biosynthesized nanoparticles (NPs) from *Penicillium* species has been considered as a potential approach for combating vectors of malaria and also as a treatment for malaria (Barabadi et al., 2019). Khatua et al. (2020), reported the fungicidal potential of emerging gold nanoparticles using *Pongamia pinnata* leave extract as a novel approach in nanoparticle synthesis. The results showed a strong inhibition potential against plant pathogen and can be suggested as potential antifungal agent for plant pathogens. Mushroom fruiting bodies mediated metallic nanoparticles with different biomedical applications have been reported (Adebayo et al., 2021).

3.2. Agricultural application of fungal nanobiotechnology

Fungal nanobiotechnology has greater potential application for growth of diverse agricultural sectors and allied part, which will likely produce a myriad of nanostructured materials (Goel, 2015; Rai and Ingle, 2012; Rai et al., 2015; Prasad, 2014). Diverse agricultural applications of the myconanofabrications are nanofungicides, nanopesticides, nano-insecticides and nanofertilizers and so on in conjunction with the ability to serve as the antimicrobial agents has been reported by several authors (Prasad et al., 2014, 2017; Bhattacharyya et al., 2016). Fungal nanobiotechnology can be used for the development of nanobiosensors which is referred to as a new class of biosensors. Nanobiosensor is a means of detecting biological agents such as antibodies, nucleic acids, pathogens, and metabolites. Nanobiosensors can be successfully used for sensing a vast variety of fertilizers, herbicide, pesticide, pathogens, moisture, and soil pH (Prasad et al., 2014, 2017). These systems allow farmers to know the best time for planting and harvesting. Some of the prominent applications of fungal nanobiotechnology in several agriculture sectors are previously reported. The effect of the synthesized silver nanoparticles mediated by fungus *Aspergillus versicolor* against *Sclerotinia sclerotiorum* and *Botrytis cinerea* in strawberry plants was observed by Elgorban et al. (2016). The obtained result showed a dose dependent activity towards pest with highest observation effect against of *B. cinerea*. The effect of the biological synthesized nanoparticles from the fungus *Epicoccum nigrum* was observed against isolates of the pathogenic fungi *C. albicans*, *Fusarium solani*, *Sporothrix schenckii*, *Cryptococcus neoformans*, *Aspergillus flavus*, and *Aspergillus fumigatus* Qian et al. (2013). Nanoparticles synthesized from the fungus *Guignardia mangiferae* showed a potential ability to control the phytopathogenic fungi *Colletotrichum* sp., *Rhizoctonia solani*, and *Curvularia lunata* Balakumaran et al. (2015). In other work, the mycofabrication of the nanoparticles using the phytopathogenic fungus *Fusarium solani* (isolated from wheat) have a potential for the treatment of wheat, barley, and maize seeds contaminated by different species of phytopathogenic fungi (Abd El-Aziz et al., 2015).

Many authors have documented the combination of biogenic nanoparticles and conventional biocides. The potential evaluation of the nanoparticle's synthesis mediated by the fungus *Alternaria alternata*, in combination with the antifungal compound fluconazole against the fungi *Phoma glomerata*, *Phoma herbarum*, *Fusarium semitectum*, alongside with biological control agent *Trichoderma* sp. and the human pathogenic

fungus *Candida albicans* were established by Gajbhiye et al. (2009). The efficacy of the combined nanoparticles and fluconazole, with *C. albicans* displayed highest sensitivity after exposure, followed by *Trichoderma* sp. and *P. glomerata*. Other authors have documented the agricultural importance of the biogenic synthesis of the nanoparticles from *Trichoderma harzianum* with mortality when they were tested against the larvae and pupae of the dengue vector mosquito *Aedes aegypti* (Sundaravadivelan and Padmanabhan, 2014).

Nanobiotechnology has been applied in agricultural practices to boost production of food in terms of nutrients, security, quantity and quality. The most effective approaches to increase production of food are to apply fertilizers, pesticides, herbicides, and plant growth factors/regulators efficiently, via nanocarriers for regulated release. Poly (epsilon-caprolactone) nanocapsules, for example, have recently been developed as herbicide carrier for atrazine (Oliveira et al., 2015). When mustard plants (*Brassica juncea*) were treated with atrazine-loaded poly (epsilon-caprolactone) nanocapsules, the herbicidal effect was significantly increased relative to commercial atrazine, with a substantial decline in net photosynthetic rates and stomatal conductance, a significant increase in oxidative stress, and consequently weight loss and growth restriction of the tested plants (Cao et al., 2018). Polymeric nanoparticles (Kumar et al., 2017), silica nanoparticles (Cao et al., 2018) and other nanocarriers have also been developed as adapted release systems to transport pesticides in a regulated approach.

Nanoscale carriers are used to efficiently transport and unleash these organisms over time. Precision farming is a method of farming that increases crop yields while minimizing soil and water damage (Duhan et al., 2017). Most interestingly, nanoencapsulation will reduce herbicide dosage without sacrificing efficacy, which is good for the environment. Insect-resistant varieties are produced using nanoparticle-mediated gene or DNA transfer in plants, in addition to nanocarriers (Sekhon, 2014).

Furthermore, nanomaterials function as pesticides with increased sensitivity and toxicity, and metal oxide nanomaterials such as ZnO, TiO₂, and CuO are being investigated for their intrinsic toxicity to protect plants from pathogenic infections. ZnO nanoparticles, for example, have been shown to effectively inhibit the growth of microorganisms including *Fusarium graminearum* (Dimkpa et al., 2013), *Aspergillus flavus* (Rajiv et al., 2013), *A. niger*, *A. fumigatus*, *F. culmorum* and *F. oxysporium* (Rajiv et al., 2013).

Poor nutrient absorption efficiencies and high losses plague traditional mineral fertilisers, but the production of nanofertilizers has provided an innovative alternative to such economic loss. Nanofertilizers can help crops and soil microorganisms consume more nutrients by reducing nutrient depletion and increasing nutrient incorporation (Dimkpa and Bindraban, 2018). At the nanoscale, commercialised nanofertilizers are mostly micronutrients like Mn, Cu, Fe, Zn, Mo, N, B). Other nanomaterials, like carbon nano-onions (Tripathi et al., 2017) and chitosan nanoparticles (Khalifa and Hasaneen, 2018), may be used instead of traditional crop fertilizers to improve crop quality and growth, and in the next decade, novel nanofertilizers are predicted to inspire and turn existing fertiliser processing industries.

Nanosensors, especially wireless nanosensors, have been developed to track crop diseases and development, nutrient production, and environmental conditions in the field due to the many beneficial aspects of nanomaterials. Engineered nanosensors, for example, can detect chemicals like pesticides and herbicides, in addition to pathogens in food and agricultural environments at a trace level and along with the proper use of nanofertilizer, nanopesticide, and nanoherbicides, an in situ and real-time monitoring device will help to mitigate possible crop losses and increase crop yield. According to a recent review, copper doped montmorillonite can be used for on-line testing of propineb fungicide in aquatic habitats (both fresh and salt water) with a detection limit of about 1 µm (Abbacia et al., 2014).

Food protection has increased as a result of the recognition of fungal nanobiotechnology in food production and storage. Many traditional chemicals used as food additives or wrapping materials have been

discovered to occur in part at the nanometer scale and food-grade TiO₂ nanoparticles, for example, have been discovered in the nanometer scale up to 40% (Dudefoi et al., 2017). Nanomaterials, like animal feed ingredients, are well engineered as colour or flavour additives, preservatives, or carriers for food supplements via nanoencapsulation and nanoemulsion. The specific properties of engineered nanomaterials have significant benefits for food production as additives or supplements, and nanoclay is one of the most commonly used and researched novel nanomaterials for food packaging due to its mechanical, thermal, and barrier properties, as well as its low cost.

Edible nanomaterial-encoded coatings have also shown their ability for food preservation and storage, with coated fresh food items like vegetables and fruits staying active during storage and transportation. As transportation and storage time increases, active respiration processes can cause major postharvest losses and low cosmetic and nutritional quality in products, but controlling such nutrition and weight loss is critical to extending the shelf life of fresh food products. The effects of relative humidity and temperature on fresh food respiration and microbial activity in goods are of the great importance. A thin coating of hybrid nano-edible films usually less than 100 nm thick, can be used as a gas and moisture barrier to enhance mechanical properties and sensory senses, avoid microbial spoilage, and prolong the shelf life of fresh foods (Flor-es-López et al., 2016).

Pesticides detection (Sahoo et al., 2018), pathogens detection (Sun et al., 2018a, b; Kearns et al., 2017; Percin et al., 2017), and toxins detection (Sun et al., 2018a, b; Zhang et al., 2017) are among the other applications in food packaging that are currently under active research and development due to the ultra-sensitive properties of nanomaterials as reported in Table 3 and according to a recent study by Sahoo et al. (2018), ZnO quantum dots (QD) can be used to identify a variety of pesticides, such as aldrin, tetradifon, glyphosate, and atrazine, since pesticides with heavy halogen groups (e.g. -Cl) react with QD easily and with a large binding affinity of 10⁷ M⁻¹. Moreover, during the interaction, ZnO QD can photocatalyze pesticides and other nanomaterials such as copper nanoparticles (Geszeke-Mortiz et al., 2012), carbon nanotubes, gold nanoparticles (Lin et al., 2011), and silver nanoparticles (Jokar et al., 2016) have also been developed as nanosensors for real-time monitoring of food safety.

3.3. Industrial application of fungal nanobiotechnology

Several fungi mediated nanoparticles are found useful in several industrial processes. In addition to the importance of fungi mediated nanoparticles to industries, such nanoparticles are secreted extracellularly in abundant amount in fungi. In addition to the suitability and attractiveness of fungal nanoparticles for industrial applications, fungi may live in harsh environments because they contain special enzymes capable of conducting chemically challenging reactions as reported by Viswanath et al. (2008). The leading fungi mediated nanoparticle applied in several industrial processes is the laccase. Although, laccase can be found in plants (Shraddha et al., 2011), insects (Kramer et al., 2001) and bacteria (Abdel-Hamid et al., 2013), laccase main source remain the fungi and several biological functions have been suggested for laccases in fungi, including spore tolerance and pigmentation (Williamson et al., 1998), lignification of plant cell walls (Malley et al., 1993), humus turnover, lignin biodegradation and detoxification processes (Baldrian, 2006), virulence factors, and copper and iron homeostasis (Stoj and Kosman, 2003).

Surprisingly, the majority of biotechnologically beneficial laccases (those with high redox potentials) are fungal, with laccase activity found in over 60 fungal strains of the Ascomycetes, Basidiomycetes, and Deuteromycetes families. Laccase production is strongest in lignin-degrading white-rot fungi (Shraddha et al., 2011), but litter-decomposing and ectomycorrhizal fungi also secrete laccases, and laccase provides a wide variety of oxidations, including non-phenolic substrates, in the presence of small redox mediators. As a result, fungal laccases are seen as ideal

green catalysts with significant biotechnological effects since they need little resources to produce bioelectrocatalysis and only produce water as a byproduct (Kunamneni et al., 2008).

Laccase's biotechnological utility, on the other hand, can be enhanced by the use of a laccase-mediator device (LMS). Laccase and LMS have potential applications in delignification (Virk et al., 2012) and bio-bleaching of pulp (Weirick et al., 2014); enzymatic dye-bleaching and fibre modification in the textile and dye industries (Kunamneni et al., 2008); enzymatic removal of phenolic compounds in beverages—wine and beer stabilization, fruit juice processing (Minussi et al., 2002); and enzymatic cross linking of lignin-based materials in producing medium density fiberboards (Widsten et al., 2004); bioremediating and detoxifying of aromatic pollutants (Khambhaty et al., 2015); detoxifying of lignocellulose hydrolysates in producing ethanol via yeast (Larsson et al., 1999); treating of industrial wastewater (Viswanath et al., 2014); and constructing of biofuel cells and biosensors (Viswanath et al., 2014; Shraddha et al., 2011). Laccase has drawn a lot of attention because of its catalytic ability and possible biotechnological applications (Abdel-Hamid et al., 2013).

Laccase can also oxidize a diverse organic and inorganic compound, including mono, di, polyphenols, aminophenols, methoxyphenols, and metal complexes, which is why it is so useful in a variety of biotechnological processes. Laccases have recently sparked renewed interest due to their possible applications in pollutant detoxifying and phenolic compound bioremediating (Singh et al., 2011). With constant application in pulp and paper processing and the synthesis of fine chemicals, fungal enzymes can turn jet fuel (Viswanath et al., 2014), paint, plastic, and wood, among other materials, into nutrients (Viswanath et al., 2008).

Another fungal enzyme of great biotechnological importance is the xylanase and extracellular xylanases generated by microorganisms are extremely significant in industry, with cellulase, pectinase, and xylanase responsible for roughly 20% of world enzyme market (Polizeli et al., 2005). The world demand for industrial enzymes is said to have risen rapidly in recent years, from a projected \$1 million in 1970 to a reported 4.5 billion dollars in 2012, with projections of about 7.1 billion dollars in 2018 (Kalim et al., 2015). Microbial enzymes, such as xylanases, are important in a variety of industries, ranging from food manufacturing to the paper and pulp industries (Azin et al., 2007). It plays an important role in a variety of biotechnological processes, including the clarity of fruit juice, the bleaching of beer and wine, the improvement of poultry feed digestibility, and the pulp, paper, leather, and baking industries (Uday et al., 2016). They're used to harvest extracellular polymeric substances (EPS) and plant oils, as well as to improve the nutritional value of silage, coffee, green feed, and starch (Lakshmi et al., 2009). Furthermore, xylanase has been shown to be effective in the production of biofuel from lignocelluloses (Uday et al., 2016). The latest interest in green nanoparticle synthesis for important biomedical applications (Elegbede et al., 2018; 2019) has pushed the boundaries of enzyme technology in nanobiotechnology even further (Lateef and Adeeyo, 2015; Lateef et al., 2015; Adelere and Lateef, 2016) and different forms of fungi and bacteria are known to synthesize xylanases under various production processes, but filamentous fungi are the most successful producers of xylanase, as previously mentioned, since they secrete higher levels of enzymes than other microorganisms (Rani et al., 2014). *Aspergillus* and *Trichoderma* spp. are the main sources of xylanases on a commercial scale (Shahi et al., 2011).

In general, *Aspergillus* species have the ability to synthesize a wide variety of enzymes responsible for weakening plant cell walls, while *Trichoderma* spp., which are the primary agents responsible for the degradation and decomposition of agricultural wastes, have a wide range of enzymes and are thus regarded as outstanding lignocellulolytic enzyme producers (Azin et al., 2007). Xylanase activities of *Aspergillus niger*, *A. flavus*, *Trichoderma longibrachiatum*, *A. fumigatus*, *F. solani*, and *Botryodiplodia* sp. isolates were recently identified and used in dough raising and juice confirmation activities (Elegbede and Lateef, 2018).

Table 3. Fungi and properties of fungi-mediated nanoparticles used for application in agriculture, industries and others areas.

Fungus species	Nanoparticles	Localization	Size (nm)	Shape	Application	Reference
<i>Botrytis cinerea</i>	Au	Extracellular	1–100	Spherical, triangular, hexagonal, decahedral, pyramidal	-	Castro et al. (2014)
<i>Aspergillus fumigatus</i>	ZnO	Extracellular	1.2–6.8	Spherical and hexagonal	Industrial and agricultural sectors	Raliya et al. (2013)
<i>Hormoconis resinae</i>	Ag	Extracellular	20–80	Cubic	-	Varshney et al. (2009)
<i>Aspergillus oryzae</i>	FeCl ₃	-	10–24.6	Spherical	Agricultural and engineering sectors	Raliya (2013)
<i>Aspergillus tubingensis</i>	Ca ₃ P ₂ O ₈	Extracellular	28.2	Spherical	Agricultural and engineering sectors	Tarafdar et al. (2012)
<i>Rhizopus oryzae</i>	Au	Cell surface	10	Nanocrystalline	Pesticides	Das et al. (2009)
<i>Rhizopus stolonifer</i>	Au	-	1–5	Irregularly (uniform)	-	Sarkar et al. (2012)
<i>Aspergillus niger</i>	Au	Extracellular	10–20	Polydispersed	-	Xie et al. (2007)
<i>Aspergillus niger</i>	Au	Extracellular	12.79 ± 5.61	Spherical	-	Bhambure et al. (2009)
<i>Aureobasidium pullulans</i>	Au	Intracellular	29 ± 6	Spherical	-	Zhang et al. (2011)
<i>Colletotrichum</i> sp.	Au	-	20–40	Decahedral and icosahedral	-	Shankar et al. (2013)
<i>Fusarium semitectum</i>	Au	-	25	Spherical	Optoelectronics	Sawle et al. (2008)
<i>Fusarium oxysporum</i>	Au	-	2–50	Spherical, monodispersity	-	Zhang et al. (2011)
<i>Fusarium oxysporum</i>	Au	Intracellular	128 ± 70 ^a	Aggregates	-	Mandal et al. (2006)
<i>Neurospora crassa</i>	Au	-	32	Spherical	-	Castro-Longoria et al. (2011)
<i>Verticillium</i> sp.	Au	Cell wall	20 ± 8	Spherical	-	Mukherjee et al. (2001a, b)
<i>Verticillium</i> sp.	Au	Cytoplasmicmembran	20 ± 8	Quasihexagonal	-	Mukherjee et al. (2001a, b)
<i>Verticillium luteoalbum</i>	Au	Intracellular	<10	Spheres and rods	-	Gericke and Pinches (2006)
<i>Cylindrocladium floricolum</i>	Au	Extracellular	19.5	Spherical	-	Narayanan and Sakthivel (2013)
<i>Phanerochaete chrysosporium</i>	Au	Extracellular	10–100	Spherical	-	Sanghi et al. (2011)
<i>Sclerotium rolfsii</i>	Au	Extracellular	25	Triangles, decahedral, hexagonal and rods	-	Narayanan and Sakthivel (2011)
<i>Fusarium oxyporum</i>	Au	Extracellular	8–40	Spherical and triangular	-	Mukherjee et al. (2002)
<i>Fusarium oxyporum</i>	Au	Extracellular	46.21	Spherical, triangular	-	Shankar et al. (2004)
<i>Colletotrichum</i> sp.	Au	Extracellular	8–40	Spherical	-	Shankar et al. (2013)
<i>Rhizopus stolonifer</i>	Au	-	1–5	Irregularly	-	Binupriya et al. (2010)
<i>Verticillium luteoalbum</i>	Au	Intracellular	Various	Various	-	Gericke and Pinches (2006)
<i>Coriolis versicolor</i>	Au	Extra- and intracellular	20–100, 100–300	Spherical and ellipsoidal	-	Sanghi and Verma (2010)
<i>Rhizopus oryzae</i>	Au	-	Various	Triangular, hexagonal, pentagonal, spheroidal, sea urchin like, 2D nanowires, nanorods	-	Das et al. (2010)
<i>Aspergillus niger</i>	Au	-	Various	Plates, aggregates, spherical	-	Xie et al. (2007)
<i>Aspergillus niger</i>	Au	-	Various	Nanowalls, spiral plates, spherical	-	Xie et al. (2007)
<i>Aspergillus niger</i>	Au	-	50–500	Nanoplates	-	Xie et al. (2007)
<i>Verticillium</i> sp.	Ag	Intracellular	25	Spherical	-	Mukherjee et al. (2001a, b)
<i>Fusarium oxyporum</i>	Ag	Extracellular	5–15	Highly variable	-	Ahmad et al. (2003)
<i>Fusarium oxyporum</i>	Ag	-	10–25	Aggregates	-	Kumar et al. (2007a, b)
<i>Aspergillus fumigatus</i>	Ag	-	5–25	Mostly spherical, some triangular	-	Bhainsa and D'Souza (2006)
<i>Aspergillus flavus</i>	Ag	On cell wall surface	8.92	Spherical	-	Vigneshwaran et al. (2007)
<i>Trichoderma asperellum</i>	Ag	-	13–18	Nanocrystalline	Agriculture	Mukherjee et al. (2002)
<i>Penicillium fellutanum</i>	Ag	Extracellular	5–25	Mostly spherical	-	Kathiresan et al. (2009)
<i>Penicillium</i> strain J3	Ag	-	10–100	Mostly spherical	-	Maliszewska et al. (2009)
<i>Cladosporium cladosporioides</i>	Ag	-	10–100	Mostly spherical	-	Balaji et al. (2009)
<i>Coriolis versicolor</i>	Ag	Extra- and intracellular	25–75, 444–491	Spherical	-	Sanghi and Verma (2009)
<i>Trichoderma viride</i>	Ag	-	2–4, 10–40, 80–100	Spherical	-	Fayaz et al. (2009b)
<i>Trichoderma viride</i>	Ag	-	2–4	Mostly spherical	Biosensor and bio imaging	Fayaz et al. (2010a)
<i>Trichoderma reesei</i>	Ag	Extracellular	5–50	Spherical	-	Vahabi et al. (2011)
<i>Aspergillus flavus</i> NJP08	Ag	-	17	Spherical	-	Jain et al. (2011)
<i>Rhizopus stolonifer</i>	Ag	-	25–30	Quasi-spherical	-	Binupriya et al. (2010)

(continued on next page)

Table 3 (continued)

Fungus species	Nanoparticles	Localization	Size (nm)	Shape	Application	Reference
<i>Aspergillus terreus</i> CZR-1	Ag	Extracellular	2.5	Spherical	Agriculture and engineering sector	(Raliya and Tarafdar, 2012) and Tarafdar et al., 2012
<i>Fusarium oxysporum</i>	Au–Ag	Extracellular	8–14	Quasi-spherical	-	Senapati et al. (2005)
<i>Fusarium oxysporum</i>	Fe ₃ O ₄	Extracellular	20–50	Irregular, quasi-spherical	-	Bharde et al. (2006)
<i>Verticillium</i> sp.	Fe ₃ O ₄	Extracellular	100–400, 20–50	Cubo-octahedral, quasi-spherical	-	Bharde et al. (2006)
<i>Aspergillus flavus</i> TFR7	TiO ₂	-	12–15	Extracellular	Plant nutrient	Raliya et al. (2015)
<i>Fusarium oxysporum</i>	BT	Extracellular	4–5	Quasi-spherical	-	Bansal et al. (2006)
<i>Fusarium oxysporum</i>	Cd	Extracellular	9–15	Spherical	-	Kumar et al. (2007a, b)
<i>Fusarium oxysporum</i>	Pt	-	70–180	Rectangular, triangular, spherical and aggregates	-	Govender et al. (2009)
<i>Fusarium oxysporum</i> , <i>F. sp. lycopersici</i>	Pt	Extra-and intracellular	10–100	Hexagonal, pentagonal, circular, squares, rectangles	-	Riddin et al. (2006)
<i>Fusarium</i> sp.	Zn	Intracellular	100–200	Irregular, some spherical	-	Velmurugan et al. (2010)
<i>Aspergillus versicolor</i> mycelia	Hg	Surface of mycelia	20.5 ± 1.82	Alteration	-	Das et al. (2008)
Fungi isolated from the soil	Zn, Mg and Ti	extracellular	Various	-	-	Raliya et al. (2013)

Other industrial uses of fungi mediated nanoparticles are reported in Table 3.

4. Challenges and way forward in fungal nanobiotechnology

Like every other aspect of nanobiotechnology, some challenges are facing the use of fungi and its metabolites to render goods and services to humankind. Some of these challenges are discussed below with some recommendations to improve the technology.

4.1. Existing challenges and recommended solutions in fungal nanobiotechnology

The major problem facing fungal nanobiotechnology is under exploration of fungi. As stated earlier in this chapter, only few fungi are well documented for their nanoparticles production potential and biology at large. This has somehow limited the full exploration of this great kingdom. Some fungi are not even culturable in the laboratory as the incubation conditions and media requirements are not fully understood or just cannot be met. Furthermore, optimization of fungal growth and nanoparticle production has remained a major challenge in this option of microbial nanobiotechnology.

Generally, nanobiotechnology faces the challenges of public acceptance; limited clinical research on long term exposure to nanoparticles and little or no legislation guiding nanoparticles application in most countries. Microbial nanobiotechnology tends to solve some of these problems but sadly the problems still abound in a way even with fungal nanobiotechnology. Beside titanium dioxide and iron oxide that are applied in food pigments and coloration, respectively, no other nanomaterials are included in human food (McClements and Xiao, 2017) and the main factor for this is that there are few constitutions or laws guiding nanofood and nanotechnology as a whole, for nanotechnology is complex and there is no in-depth legislation (Kavitha et al., 2018; Xiao et al., 2018). A stronger reason for the lack of regulation is a lack of understanding of the toxicity and danger that novel nanomaterials may pose (Deng et al., 2018; Dasari et al., 2014). Several researches on nanomaterial toxicity are *in vitro*, but there are very little data on *in vivo* toxicity, let alone chronic effects of nanomaterials (Duncan, 2011). At least a few holes must be filled: effects of nanomaterial exposure to mammalian cells, tissues/organs, and chronic effects on the human body; nanomaterial migration to food; nanomaterial depletion or environmental fate; nanomaterial bioaccumulation and ecological influence. Definitely, more investigations and adequate funding are going to be needed in this all-encompassing field.

Another critical factor is public acceptability which is mostly overlooked by scientists, producers, and government agencies (Arnaldi and Muratorio, 2013). It decides whether nanotechnology can be implemented and/or approved by customers in the long run and regardless of who accepts these novel nanomaterials, the waste will eventually be disposed into the atmosphere, causing unique effects on plants, animals and habitats. In making matters worse, neither researchers, nano-industries nor governmental agencies have extensively discussed the proper disposal technique, resulting in a lack of *in vivo* toxicity data for nanomaterials, including the possible chronic impact on man organs.

More clinical research on the safety of fungi nanoparticles is important in making fungal nanobiotechnology widely acceptable to humans. Researches on fungal nanobiotechnology needs to be moved to the advanced stages of evaluating nanoparticles safety *in vivo*, possibly in volunteered human population. Furthermore, education of humans on the safety and benefits of nanoparticles is essential. Nanobiotechnology in general, should be embraced as the field may lead to prospects in some areas of human endeavor that looked like a dead-end in past years. More so, every country should provide strong legislation to guide and support nanoparticles usage in her economy.

5. Concluding remarks

Biological synthesis of nanoparticles is safe and relatively inexpensive. The synthesis of metallic nanoparticles using microbes had been shown to possess a strong potential with various applications. The utilization of fungi to fabricate nanoparticles has been greatly considered sequel to several advantages including easy handling and downstream processing. However, the interest of several researchers had been captivated of a recent towards the myconanofabrications of nanoparticles. Myconanofabrications of nanoparticles has been considered to be a structured and satisfactory method for the synthesis of various types of nanoparticles with a vast potential and remarkable applications in diverse fields such as agriculture, food, textile, medicine, cosmetics, optical and electronics. In the world today, several species of fungi are of great importance in nanobiotechnology due to the safe, ecofriendly, amenable and important nanoparticles they produced. Furthermore, the extracellular abundant production of the nanoparticles favours fungal nanobiotechnology among all microbial nanobiotechnology as it saves the cost of downstream process. Several researches in the field have further helped in the development of more novel principles and broader application of this nanobiotechnology in various human lives.

In this light, fungal nanobiotechnology has been applied in agriculture, medicine and in various industrial processes. Presently, fungal

nanobiotechnology is integral in the management and control of fungal diseases in man, animals and plants. More so, food product formulation, shelf-life improvement and packaging have employed fungal nanobiotechnology greatly. Medically, fungi nanoparticles are important in drug delivery systems, diagnosis and treatment of resistant infections and cancer. Fungi-produced metal nanoparticles possess a lot of promise for use as sensors and electronic devices in biomedical imaging. Laccase and xylanase from fungi have found applications in diverse industries as important enzymes suggesting the usefulness of this technology in the improvement of quality of goods and services to humanity.

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