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Review Article

Nanoparticles from Fungi: A novel approach toward eco-friendly Drug Designing

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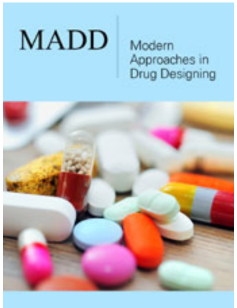

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Abstract

The present review focused on synthesis of nanoparticles using an eco-friendly approach through microorganisms, especially fungi. Various physical and chemical methods and techniques have been developed by scientists and researchers to manufacture nanoparticles. But nanoparticles synthesized in these forms are not eco-friendly and often allow toxic compounds to be released which could have adverse effects on nature and in human beings. It is therefore important to develop eco-friendly and economical techniques for nanoparticle synthesis and to respond to green approaches by using natural microorganisms such as bacteria, fungi and algae, etc. which are capable of producing nanoparticles. Today's biologist works on most of the biological material for nanoparticle synthesis but shaping all of these is focused on fungi for nanoparticles that can help to reduce time and we can obtain nanoparticles in desired size and shape. This is also the key reason for using fungal microbes for nanoparticle synthesis to grow perfect and non-toxic material production, which can help to reduce environmental impacts, increase energy efficiency and mitigate environmental pollution. The present review therefore emphasized the biological method for the synthesis of nanoparticles by fungi, the development of different types of metal nanoparticles by fungal microbe and the application of novel nanoparticles in the current emerging sector.

Keywords: Nanoparticles;Fungi;Immaculate;Toxic;Enzymes;Laser;Pyrolysis

Introduction

Nanotechnology is the most advanced branch of science and technology used to tackle the size of the material at a small nanoscale level. Quantitative and qualitative properties of nano-sized substances varied significantly from their macroscopic immensity reserves [1]. If we commonly describe nanotechnology, it is a method or technique that has the ability to design, identify, build and use nanoscale structures and systems in order to regulate shape and dimension. Owing to their small scale, nanoparticles have inimitable characteristics relative to their macroscopic form. The synthesis of nanoparticles from a variety of resources participate in the medical, biomedical and life-saving pharmaceutical industries and other essential products such as advanced materials, energy storage systems, electronic and optical displays etc. There are different types of physical and chemical methods used for the preparation of nanoparticles, but recently, green chemistry or nanobiology synthesis has attracted the scientific community to develop metal nanoparticles by using living cells such as bacteria, fungi, actinomycetes and plants as shown in Figure 1 [2-5].

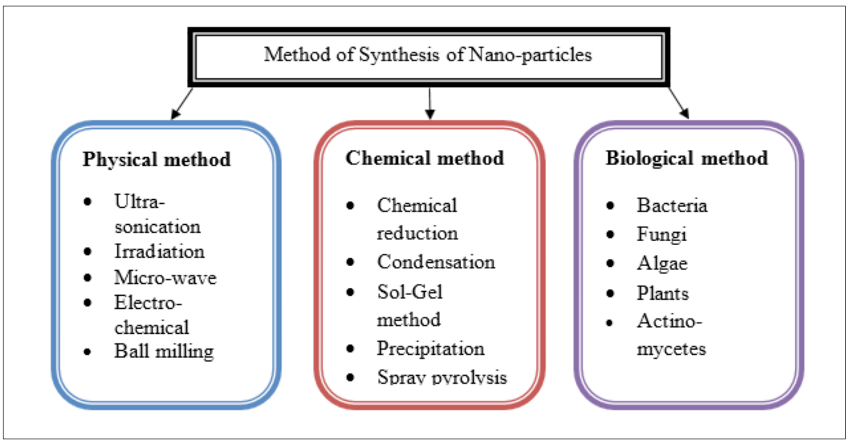

Figure 1: Different methods of nanoparticles synthesis.

At present, attention has been paid to the development of nanoparticles, in particular through the use of fungal mycoflora and the large-scale biosynthesis of nanoparticles from these microbes in this area, due to their tolerance capacity against metal accumulation high binding affinity and the majority of intracellular absorption of metal ions compared to other microbes [6-10]. Biosynthesis of nanoparticles by fungi is a very easy and rational approach because of its ability to synthesize nanoparticles by extracellular and intercellular mode of action. For the synthesis of nanoparticles from fungal microbes, first it grows in a suitable broth medium for a sufficient incubation period and, after completion of the incubation period, washes mycelia using sterilised distilled water to remove the medium from the fungal met and then transfers mycelia to the deionized water flask and incubates for a period of 24, 48, 72h. After this, the biomass filter again using Whatman filter paper and cell-free culture filtrate (CFCF) will be collected and mixed with aqueous metal solution and incubated for an acceptable time or until the visual color has improved (Figure 2). During nanoparticles biosynthesis, different metals show changes in the color of the CFCF as white yellow to yellow show the production of manganese and zinc nanoparticles, pale yellow to pinkish color display synthesis of gold nanoparticles and pale yellow to brownish color is developed during the formation of silver nanoparticles [11-15].

Figure 2: Intracellular method for synthesis of nanoparticles by fungi.

Unique Properties of Nanoparticles synthesized by Fungi

The green synthesis of nanoparticles using microorganisms, in particular fungi, has specific chemical, electrical, magnetic, mechanical and electromagnetic properties. Since the nanoparticles are synthesized by fungi due to the reduction of metal ion dimensions that influence the properties of the material, such as increasing large surface area, surface density, reducing imperfection and spatial conformation which are variable from their original form size material. Nanoparticles formed by fungi have substantial thermal properties due to a lower transition temperature and melting point compared to their bulk form [16]. These particles also showed different optical properties which help to make them suitable sensors depending on their shape, size and surrounding medium and also vary in the visible region due to the interaction of electron clouds present on the surface of nanoparticles with electromagnetic radiation. The other important properties of nanoparticles are magnetic properties, which play a significant role in the medical sciences, especially in the different diagnostic techniques [17]. Some other biosynthesized iron-based nanoparticles, such as Feridex, are commonly used to monitor the movement of stem cell inserts into the wound site [18] and also utilized as magnetic memory storage devices, magnetic resonance image enhancement and magnetic refrigeration etc. [19]. Nanoparticles also exhibit surface plasmon properties useful for studying the various physical and chemical properties of molecules such as adsorption and chemosorption [20] (Figure 3).

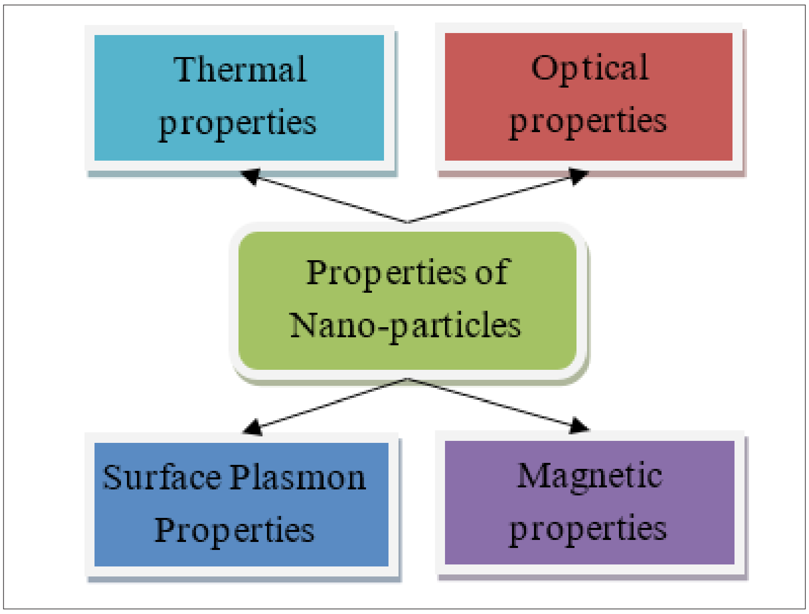

Figure 3: Unique Properties of Nanoparticles synthesized by fungi.

Nanoparticles synthesis by fungi

Synthesis nanoparticles by fungi have a wide variety of uses in the medicinal, chemical, electrical, agricultural and cosmic industries [16]. The biosynthesis of gold nanoparticles through the use of fungi is an innovative way to ensure a healthy, cost-effective and environmentally sound nanotechnology process [21]. Fungal strain *Penicillium chrysogenum* from the Ahar mine in North West Iran was also capable of reducing aqueous gold ions to nanoparticles, and confirmation of nanoparticles was performed by UV-visible spectrum, XRD spectrum and electron microscopy transmission [22]. The gold nanoparticles from *Aspergillus niger* were biosynthesized and tested for insecticidal activity against the larvae of *Anopheles stephensi*, *Culex quinquefasciatus*, and *Aedes aegypti* and measured by probit analysis at six different concentrations over a time span of 24, 48, 72h and observed that the gold nanoparticles synthesised by fungus can be a rapid and eco-friendly development and it has been observed that gold nanoparticles synthesised by fungi can be a fast and eco-friendly advance for mosquito control than current approaches [23]. Fungi *Fusarium oxysproum* isolated from a wilt-infected banana plant also found synthesis of nanoparticles of auric chloride solution containing 22nm sized particles and capped by protein [24]. Stable gold nanoparticles of variable size and shape were formed from 7-13nm and 15-18nm in the case of a lower molar concentration of 0.3 to 0.5mm of gold chloride solution.

Now a day's silver nanopartilces synthesized by fungi and other microbes are widely used as anti-bacterial agents, fruit preservation, for labeling and sensing, in textile and pharmaceutical industries [25,26]. Endphtytic fungi *Aspergillus fumigatus* isolated from *Canabis sativa* fromed silver nanoparticles that were validated by surface resonance Plasmon as UV-Visible spectrum checked [27]. Nanoparticles synthesised by endophytic fungi demonstrated good antibacterial activity against *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus sp.* and the *Staphylococcus albus* [28]. Fungal strain *Trichoderma viride* was also observed for silver nanoparticle synthesis ranging in size from 1-50nm and antibacterial activity of synthesised nanoparticles was also observed by agar well diffusion method against human pathogenic bacteria Methicillin-resistant *Staphylococcus aureus*, *S. boydii*, *A. baumannii*, *S. sonnei* and *S. typhimurium* [29]. Nitrate reductase (NADPH dependant enzyme) plays a major role in the synthesis of silver nanoparticles [30]. Nitrate reductase reduces Ag+ ions from AgNO3 and results in the formation of silver nanoparticles as observed under XRD, TEM and UV-Visible absorption.

Copper nanoparticles synthesized by fungi are very cost-effective as opposed to silver and non-toxic as silver nanoparticles and have many applications in conductive film, lubrication, nanofluids, catalysis and have demonstrated nano-scale antimicrobial activity [31]. Cuevas et al. [32] has been shown to be capable of producing synthesis of copper nano-parts by fungal strain *Stereum hirsutum*, which has been incubated under various pH conditions. Confirmation of the size of the nanoparticles synthesised by the fungal strain was observed using UV-visible spectroscopy, electron microscopy (TEM), X-ray diffraction analysis (XRD) and Fourier transforms and found that the white rot *S. hirstum* was found to be potential for the synthesis of copper nanoparticles. Fungal species isolated from Egyptian soil were observed for copper nanoparticle synthesis and fungal strain *Aspergillus fumigates* was reported for improved biosynthesis of copper nanoparticles. The highest yield of nanoparticles could be produced when mycelium was contacted with 1 mM of copper nitrate solution adjusted to pH 6 and incubated in the dark at 30°C for 60h under submerged conditions [33] (Figure 4).

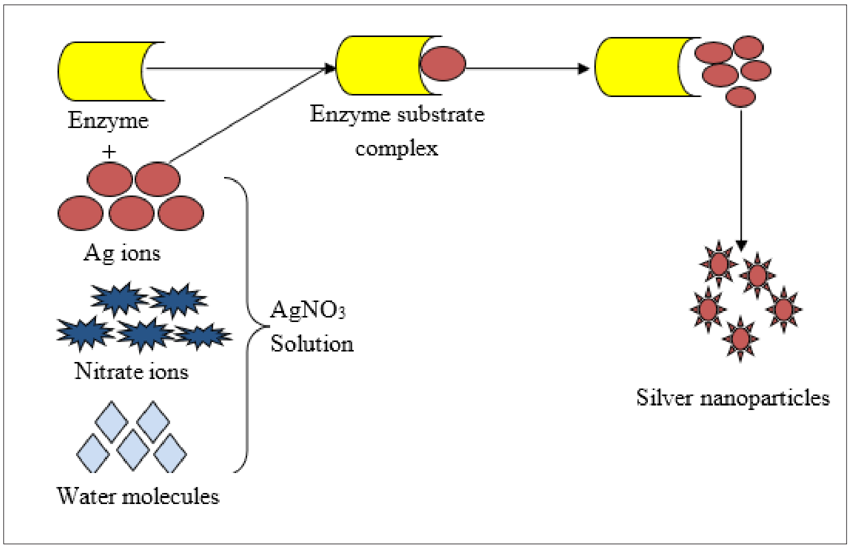

Figure 4: Synthesis of silver nanoparticles by enzymes.

When *Fusarium oxysporum* has been incubated with hexachloroplatinic acid solution (H_2PtCl_6) in ambient conditions, it decreases the precursor and helps to form platinum nanoparticles [34]. *Streptomyces* isolated from the sediment sample collected from the coastal region of Chennai, India, were capable of synthesising platinum nanoparticles when the strain was put in hexahydrate chloroplatinic acid. Nanoplatium was also derived from the fungal strain *Alternaria alternata* and characterised by different spectroscopic approaches [35]. At present, iron nanoparticles are commonly used in a number of applications such as water treatment, food processing, textile industries and potential antimicrobial agents [36-38]. The biosynthesize iron nanoparticles using fungal species *Alternaria alternata*, which reduce the aqueous Fe^{3+} ions in the dark reaction. The structure of the synthesised nanoparticles was cubic in shape having arrange of 9±03nm in size [39]. The iron nanoparticles synthesized by *Pleurotus sp.* was also confirmed by UV-spectra analysis, FTIR and SEM [40]. In another study Pavani et al. [41] isolated the fungal strain *Apsergillus sp.* from the soil sample collected from Hyderabad. The isolated fungal strain was grown in fungal culture media containing different concentration of $FeSO_4.5H_2O$. *Aspergillus sp.* is grown in 1mM ferrous sulphate for 48h and after that medium was centrifuged and fungal pellet was collected and observed by TEM. Bhargava et al. [42] also developed iron oxide nanoparticles by using *Aspergillus japonicas* that hydrolyze the salt solution to favorable condition which released ferric and ferrous ions undergoing protein mediated co-precipitation and nucleation. Magnetic iron and magnetite nanoparticles have been developed using fugnal strain *Aspergillus niger* in crystal sizes of 8-9nm and the magnetic properties of the synthesised nanoparticles have also been observed and exhibit superparamagnetic and ferromagnetic-like behaviours for Fe and Fe^3O_4 nanoparticles, respectively [43].

Zinc oxides also have an important engineering value due to their relatively higher heat capacity, thermal conductivity, and low thermal expansion co-efficient and high melting temperature. The zinc nanoparticles synthesized by microorganisms have widely used in the field of catalysis, photodetectors, light emitting diodes, sensors, medicine, cosmetics [44]. Raliya and Tarafdar [45] were synthesized the nanoparticles of zinc, magnesium, and titanium by using the fungi identified as *Aspergillus flavus*, *Aspergillus terreus*, *Aspergillus tubingensis*, *Aspergillus niger*, *Rhizoctonia bataticola*, *Aspergillus fumigates* and *Aspergillus oryzae* isolated from the soil. The fungal strain *Candida diverse* strain JA1 isolated from the waste water of milk processing unit was used to synthesized silver and zinc nanoparticles which are characterized by using various analytical technique including UV-visible spectrophotometer, X-ray diffraction pattern analysis (XRD), FE-Scanning electron microscope (SEM) with EDX-analysis (EDXA) [46].

Factor affecting the synthesis of nanoparticles by fungi

There are many environmental factors influencing the synthesis of nanoparticles as well as the growth of fungi, such as temperature, concentration of metal ion, pH, concentration of extracts, concentration of raw materials, incubation time and reaction mixture, which play an important role in nanoparticle synthesis. Therefore, the optimization condition is not only essential help good growth but also enhances product yields.

Application of nanoparticles synthesis by fungi

Biosynthesized fungal nanoparticles have a wide variety of uses in pharmaceutical science, medicine and research. A number of microbial synthesised nanoparticles recorded to offer novel anti-bacterial, anti-fungal, anti-viral, anti-inflammatory and anti-tumor insecticide and antioxidant properties.

Antibacterial activity

The antibacterial study of biosynthesized nanoparticles by fungi was previously reported by various researchers against microorganisms [47]. In silver nanoparticles obtained by using encapsulated biomass bead of *Phoma exigua* fungal strain were observed for antibacterial activity against the pathogenic bacteria *Escherichia coli* and *Staphylococcus aureus* [48]. Gold nanoparticles synthesised using endophytic fungi have also been observed for their strong antibacterial activity against a variety of human pathogenic bacteria [49]. The endophytic fungus *Talaromyces purpureogenus* is isolated from *Pinus densiflora S.* was also used for the production of silver nanoparticles and observed significant antibacterial, anticancer and cell wound healing properties [50]. The endophytic fungi *Trichoderma spp.* isolated from *Bertholletia excelsa* (Brazil-nut) seeds was capable for green synthesis silver nanoparticles and observed their antibacterial activity against many Gram-negative bacteria [51].

Anticancer activity

The biosynthesized *Agaricus bisporus* silver nanoparticles have a range of 8-20nm and tested their dose-dependent cytotoxicity against MCF7 breast cancer cells. Similarly, silver nanoparticles synthesised by *Penicillium brevicompactum* also showed anticancer activity against the MCF-7 breast cancer cell line [52]. The endophytic fungi *Botryosphaeria rhodina*, identified on the basis of ITS sequences, was capable of producing silver nanoparticles and displayed a wide range of cytotoxic activity against the cancer cell line [53]. Similarly, the gold nanoparticles synthesis by the Fusarium solani islated from *Chonemorpha fragrans* showed activity against the human breast and cervical cancer cell line by inducing the apoptosis in the cancer cell line [54].

Antiviral activity

Viral infection creates the significant global problem due their resistant against a number of antiviral therapies. The nanoparticles bio-synthesized by the fungi have great interaction due to their potential antiviral activity against the viral particles and bacterio-phage [55]. The fungal strain *Aspergillus niger* formed silver nanoparticles in the 3-10mm range observed for excellent antiviral activity and the colloidal solution of these nanoparticles inhibited the growth of the virus in *E. coli* host strain [56]. The nanoparticle synthesized by *Scedosporium* fungi was also observed for antimicrobial anticancer activity. Gaikwad et al. [57] also study the antiviral activity of silver nano-particles against simplex virus type 1 and 2 and human para-influenza virus type 3 and observed that nanoparticles have ability to control the viral infection by inhibiting the interaction of the virus with the cell which is depend upon the zeta potential and size of the silver nanoparticles.

Insecticidal activity

The nanoparticles synthesized by fungi also play an important role in the field of agriculture because these nanoaprticles not only inhibit or kill the harmful insects but also degrade the toxic pesticide like the sliver nanoparticles made from *Penicillium pinophilum* potential for degradation of chlorpyrifos pesticide at different pH. Gold and silver nanoparticles formed by entomogenous fungi *Chrysosporium tropicum* were also detected against *Culex quinquefasciatus* and *Anopheles stephensi* larvae, and both *Culex quinquefasciatus* larvae were found to be more susceptible to silver nanoparticles and *Anopheles stephensi* larvae were found to be more susceptible to gold nanoparticles [58]. In further study, Kamalakannan et al. [59] observed the larvicidal activity of silver nanoparticles synthesized from *Penecillium verucosum* against filarial causing organism *Culex quinquefasciatus* by using a range of concentration from 25-250 ppm against I, II, III, and IV instar larvae and pupae of *Culex quinquefasciatus*.

Antifungal activity

Biological synthesis of fungi nanoparticles may improve stability or better antifungal activity against pathogenic fungi. The silver nanoparticles of *Penicilium fallutanum* displayed antifungal activity against pathogenic fungi *Candida albicans* and *Candida glabrata*. Roy et al. [60] synthesized the nanoparticles by using the extracellular filtrate of the fungal species *Aspergillus foetidus* MTCC8876 tested against the Aspergillus species like *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus foetidus*, *Aspergillus oryzae*, *Aspergillus parasiticus* and *Fusarium oxysporum* by agar well diffusion method that displayed higher zone of antifungal activity against the fungi. The extracellular synthesis of silver nanoparticles by *Trichoderma longibrachiatum* has also resulted in a substantial reduction in the tested fungal colonies such as *Fusarium verticillioides*, *Fusarium moniliforme*, *Penicillium brevicompactum*, *Helminthosporium oryzae* and Pyricularia grisea [61]. Xue et al. [62] isolated the 17 fungi from the soil sample collected from the Nahu Park China and found that soil fungi *Arthroderma fulvum* had the ability to synthesize the silver nanoparticles which better antifungal activity against ten fungal pathogens, including *Candida spp.*, *Aspergillus spp.*, and *Fusarium spp.* (Table 1).

Table 1: Applications of different nanoparticles synthesized by fungi.

Fungi	Location	NPS	Size (nm)	Shape	Application	Reference
Epicoccum nigrum	Extracellular	AuNPs	5–50	Spherical and Rod Shapes	-	[63]
Botrytis cinerea	Extracellular	AuNPs	1-100	Triangular, Hexagonal, Spherical, and Pyramidal	-	[64]
Penicillium crustosum	Extracellular	AuNPs	10	-	Antifungal	[65]
Phanerochaete Chrysosporium	Extracellular	AuNPs	10-100	Spherical	-	[66]
Rhizopus stolonifer	Extracellular	AuNPs	01-May	Irregular	Bioreducer	[67]

Cylindrocladium floridanum	Outer surface of the cell wall	AuNPs	May-35	Spherical	Toxic organic pollutant reducer	[68]
Fusarium oxysporum	Extracellular	AuNPs	-	Spherical and Hexagonal	Antibacterial	[69]
Arthroderma fulvum	Intracellular	AgNPs	20.56	Spherical	Antifungal	[62]
Aspergillus niger	Extracellular	AgNPs	Jan-20	Spherical	Antimicro-bial	[70]
Fusarium semitectum	Extracellular	AgNPs	Jan-50	Spherical and Ellipsoid	Antibacterial	[71]
Fusarium oxysporum	Intracellular	AgNPs	25–50	Spherical	-	[72]
Duddingtonia flagans	Extracellular	AgNPs	30-409	Spherical	Antimicrobi-al, Antiviral, and Antican-cer	[73]
Sclerotinia sclerotiorum	Extracellular	AgNPs	10–15	Spherical	Antibacterial	[74]
Fusarium oxysporum	Extracellular	AgNPs	24	Spherical	Antibacterial	[75]
Penicillium oxalicum GRS-1	Extracellular	AgNPs	10–40	Spherical	Antimicro-bial	[76]
Trichoderma longibrachiatum	Extracellular	AgNPs	24.43	Spherical	Antifungal	[61]
Aspergillus umigates BTCB10	Extracellular	AgNPs	322.8	Spherical	Antibacterial and Cytotox-icity	[77]
Beauveria bassiana	Extracellular	AgNPs	Oct-50	Triangular, Circular, Hexagonal	Antimicro-bial	[78]
Aspergillus niger STA9	Extracellular	CuNPs	480	-	Anticancer, Antidiabetic, and Antibac-terial	[79]
Hypocrea lixii	Extracellular	CuNPs	24.5	Spherical	Bioreme-diation of Wastewater	[80]
Stereum hirsutum	Extracellular	CuNPs	May-25	Spherical	-	[15]
Trichoderma asperellum	Extracellular	CuNPs	10-190	Spherical	Anticancer	[81]
Fusarium oxysporum	Extracellular	PtNPs	25	-	Antioxidant and Antimi-crobial	[82]
Fusarium oxysporum	Extracellular	PtNPs	May-30	Spherical	-	[34]
Fusarium oxysporum	-	PtNPs	70-180	Spherical, Triangular, Aggregates	Bio-reduc-tion	[83]
Trichoderma asperellum, Phialemoniopsis ocularis and Fusarium incarnatum	Extracellular	FeNPs	25±3.94, 13.13±4.32, 30.56±8.68	Spherical	Bio-reduc-tion	[84]
Alternaria alternata	Extracellular	FeNPs	9±3	Cubic	Antibacterial	[39]
Aspergillus species	Extracellular	PbNPs	5–20	-	-	[41]
Aspergillus niger	Extracellular	ZnNPs	40	Hexagonal	Antibacterial	[85]
Aspergillus niger	Extracellular	ZnNPs	84-91	Spherical	Antimicro-bial	[86]
Aspergillus flavus	Extracellular	TiNPs	62-74	Aggrigratte	Antimicro-bial	[87]

Conclusion

The fungi have a vast potential for production of nanoparticles which have wide application in the different fields of science and technology. The biological syntheses of nanoparticles are in developing stage. Therefore, further research in the field of nanoparticles synthesis by living cell is needed for understanding the better biological and molecular mechanisms of reaction chemical composition, shape, size etc. which can show great potential in the field of biotechnology. The future research in the field of synthesis of nanoparticles from microorganisms especially of fungi play an important role in the field of chemistry, medicine, agriculture, and electronic related industries etc.

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