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Biosíntesis fúngica de nanopartículas basadas en lantánidos para aplicaciones en sector salud: una Revisión

Fungal biosynthesis of lanthanide-based nanoparticles for healthcare applications: a Review

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Resumen

Este artículo de revisión explora el uso innovador de los hongos en la síntesis de nanomateriales basados en lantánidos para aplicaciones en nanobiotecnología. Se examina el papel crucial de los hongos en la obtención de este tipo de nanoestructuras y sus posibles aplicaciones en biotecnología, incluyendo recubrimientos antimicrobianos, agentes de etiquetado y biorecuperación de lantánidos a partir de residuos industriales y minerales. Los hallazgos destacan la importancia de métodos de síntesis ecológicos y la evaluación de la toxicidad de estos materiales para el medio ambiente y los organismos. La combinación de biogénesis fúngica y nanotecnología basada en lantánidos ofrece perspectivas prometedoras para la biomedicina y la conservación del medio ambiente. Este trabajo subraya la importancia de la investigación interdisciplinaria que integra biología fúngica y nanotecnología para un futuro sostenible, con potencial en el sector, el aprovechamiento de recursos y el progreso científico.

Palabras Clave:
Biosíntesis, síntesis verde, reciclaje elemental, bio-recuperación, nanopartículas lantánidas.

Abstract

This review article explores the innovative use of fungi in the synthesis of lanthanide-based nanomaterials for applications in nanobiotechnology. It examines the crucial role of fungi in obtaining these types of nanostructures and their potential applications in biotechnology, including antimicrobial coatings, labeling agents, and the biorecovery of lanthanides from industrial and mineral wastes. The findings highlight the importance of eco-friendly synthesis methods and the evaluation of the toxicity of these materials for the environment and organisms. The combination of fungal biogenesis and lanthanide-based nanotechnology offers promising prospects for biomedicine and environmental conservation. This work underscores the importance of interdisciplinary research that integrates fungal biology and nanotechnology for a sustainable future, with potential in the healthcare sector, resource utilization, and scientific progress.

Keywords:
Biosynthesis, green synthesis, elemental recycling, bio-recovery, lanthanide nanoparticles.

1. Introduction

Nanotechnology has arisen as a transformative field with vast potential for applications across various sectors, including biomedicine (Gutiérrez Rodelo et al., 2022; Huang et al., 2022). Among the myriad of nanomaterials, those based on lanthanides have earned attention due to their unique optical, magnetic, and chemical properties (Dhall & Self, 2018; B. Zhang et al., 2017). In particular, the synthesis of lanthanide-based nanomaterials through fungal biosynthesis represents a promising avenue in nanobiotechnology, offering both eco-friendly production and tailored functionalities for diverse biomedical applications (Khan et al., 2014; Komal et al., 2020).

By harnessing the natural capabilities of fungi, researchers have developed innovative strategies for the green synthesis of nanomaterials, circumventing the drawbacks associated with conventional synthetic methods while offering enhanced biocompatibility and sustainability (Feng et al., 2018). One of the most prominent applications of lanthanide-based nanomaterials synthesized via fungal biogenesis is in the magnetic resonance imaging (MRI) (B. Zhang et al., 2017). For example, gadolinium-based nanoparticles are widely used as contrast agents due to their

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remarkable paramagnetic properties, enabling high-resolution imaging of biological tissues. Furthermore, the utilization of fungal agents in the synthesis process ensures the production of nanoparticles with well-defined structures and sizes, essential for optimizing imaging efficiency and minimizing potential cytotoxicity.

Beyond imaging, lanthanide-based nanomaterials demonstrate multifaceted functionalities conducive to various biomedical applications. Cerium oxide nanoparticles, for instance, exhibit potent antimicrobial and antifungal properties (Rajan et al., 2019; Sharmila et al., 2019), holding promise for combating microbial infections in clinical settings. Additionally, nanoparticles incorporating terbium, gadolinium, and lanthanum have shown potential as therapeutic agents against cancers such as colon cancer and osteosarcoma, owing to their ability to selectively target malignant cells and induce apoptosis (Iram et al., 2016; Manoj Kumar et al., 2020; Nazaripour et al., 2021).

Moreover, the small size and unique physicochemical properties of lanthanide-based nanomaterials synthesized via fungal biogenesis render them suitable candidates for drug delivery systems (Khan et al., 2014). Their nanoscale dimensions facilitate efficient penetration of cellular membranes, allowing for targeted delivery of therapeutic agents to specific tissues or cells. This targeted approach minimizes off-target effects and enhances the efficacy of therapeutic interventions, thereby holding considerable promise for personalized medicine applications (Q. Zhang et al., 2017).

Apart from their biomedical applications, fungal-mediated procedures present potential solutions to environmental challenges, particularly in the recovery of expensive elements from waste materials. By harnessing the bioaccumulation capabilities of fungi, researchers have explored novel methods for extracting and recycling lanthanides from electronic waste and industrial effluents, thereby mitigating resource depletion and environmental pollution (Bahaloo-Horeh & Mousavi, 2022; Kang et al., 2022).

The purpose of this review is to highlight the versatile and sustainable approach of synthesizing lanthanide-based nanomaterials using fungi, while also extensively describing their applications in healthcare. From imaging and therapy to drug delivery and environmental remediation, these nanomaterials hold immense potential to revolutionize healthcare and address pressing environmental concerns. Further research into the optimization of fungal-mediated synthesis techniques and the exploration of new applications will undoubtedly propel the field of lanthanide-based nanobiotechnology toward unprecedented advancements in biomedicine and beyond.

2. Fungus-mediated synthesis of lanthanide-based nanostructures

Lately, lanthanide-based nanoparticles (LnNPs) have gained interest in the material science community due to their unique optical and magnetic properties with promising applications in numerous fields such as medicine, bioimaging, drug delivery, sensing electronics, and catalysis (Wen & Wang, 2013). In this sense, the development and optimization of synthesis methodologies that ensure control over these nanosystems properties remains one of the main objectives of materials science. The synthesis of LnNPs can be divided into two main categories: bottom-up and top-down approaches, represented in a conceptual map in **Figure 1** (Fichtner et al., 2019; Tong et al., 2022). In the case of bottom-up approaches, the growth of the nanomaterial is achieved by promoting isotropic/anisotropic self-assembling conditions or nucleation growth mechanisms of the supplied precursor species (i.e., molecules or atoms) to obtain the nanostructured material. These growth conditions can be achieved by various physical and chemical techniques, such as chemical vapor deposition (CVD), sol-gel methods, and hydrothermal synthesis, resulting in precise control over the size and composition of the NPs. Bottom-up synthesis is advantageous for creating uniform and highly ordered nanostructures with specific properties tailored to their intended applications.

On the other hand, top-down approaches involve the miniaturization the bulk precursor materials by supplying substantial amounts of energy in short periods of time to obtain nano-sized particles. Techniques such as ball milling, laser ablation, and lithography are commonly used in top-down synthesis. This method is particularly useful for producing large quantities of nanoparticles from bulk materials, though it may result in less uniformity and control over the final particle size and distribution compared to bottom-up methods. Top-down approaches are often employed when scalability and the use of existing bulk materials are important considerations.

However, conventional synthesis methods for the obtention of LnNPs involve the use of toxic and hazardous chemicals, which can lead to environmental and health drawbacks. Therefore, there is a growing interest in developing sustainable methods for synthesizing LnNPs with controlled morphological and physicochemical surface properties (Nadeem et al., 2020). Among the bottom-up approaches, green synthesis methods are eco-friendly processes that utilize natural origin agents, such as microorganisms or extracts (e.g. plant, flowers, fruits extracts, yeast, fungi, bacteria) to obtain nanoparticles of various materials (e.g. Au, Ag, Cu, Pd, Ru, Ag, CdS, PbS, ZnS, CdTe, TiO_2, Fe_3O_4, CuO, ZnO among others) (Arumugam et al., 2015; Feng et al., 2018; Hussain et al., 2016; Nasrin et al., 2014; Nath et al., 2023). In recent years, fungal biosynthesis of metal-containing nanoparticles (for instance, *Rhizopus stolonifera*, *Trichoderma sp.*, *Fusarium oxysporum*, *Aspergillus terreus*, *Aspergillus flavus*, among other fungal species*)* is becoming a promising approach that avoids the use of toxic/hazardous reagents to produce nanoparticles (Gopinath et al., 2015; Simões et al., 2020). Additionally, biological features of these organisms, such as high biomass production, growth resilience, and ability to tolerate and accumulate metals, can contribute to scaling up the production of nanoparticles with a narrow size distribution, high purity, and cost-effectiveness. This makes them an attractive alternative to traditional chemical methods for nanoparticle synthesis.

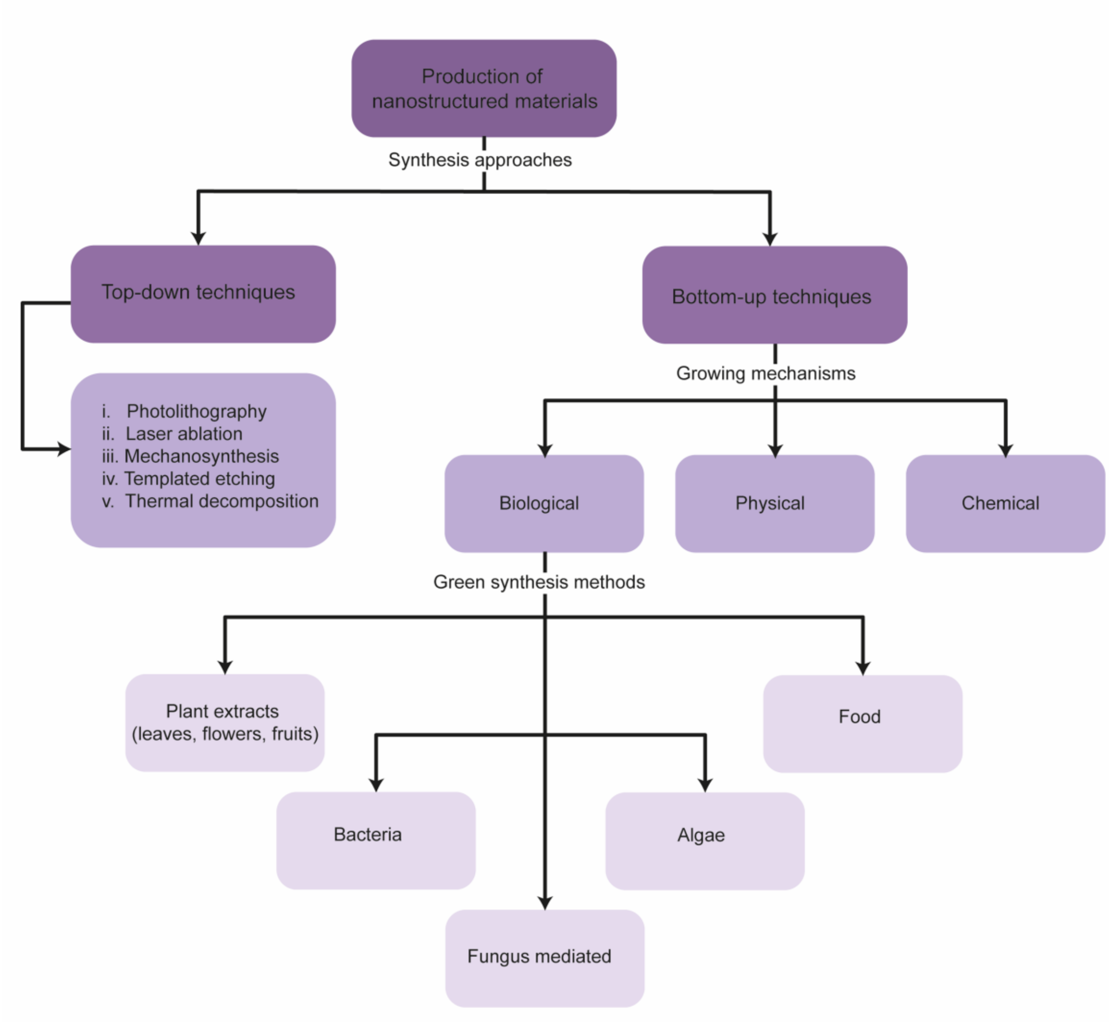

Figure 1. Conceptual map illustrating different approaches (bottom-up and top-down) for the synthesis of nanostructured materials, emphasizing the field of green synthesis mediated by fungal agents as a sustainable alternative for obtaining nanostructures.

In the case of mycogenic metal-containing NPs, the decomposing nature and metabolic process of these organisms are exploited in the synthetic process. The precise myogenic process strongly depends on the microorganism used. However, it can be summarized as follows: (i) First, the fungus mycelium is exposed to the precursor compound, which contains the desired metal to be grown as part of their composition, normally metal salts. (ii) As the salt gets dissociated (either by heat, pH changes, or an aqueous media), the presence of toxic metal ions leads the cells of the fungus to produce enzymes and metabolites that let the organism undergo harsh growing conditions. (iii) The former substances then produce oxidation-reduction reactions on the metal ions to have atoms in oxidation states that are harmless to the organism (i.e., neutral metals M^0). This process can occur both intracellularly and extracellularly. Therefore, because of their new oxidation state, these metal atoms tend to undergo an agglomeration process (i.e., formation of metal nuclei), in which the reduction of the surface Gibbs free energy of the system is considered as the main driving for the growth of 0D nanostructures. (iv) Finally, when the cumulus has reached the desired size, the use of stabling and capping agents to achieve biocompatibility and size control are also reported.

Fungal extracts contain various biomolecules such as proteins, polysaccharides, and other metabolites that can interact with the surface of nanoparticles and prevent their aggregation, therefore acting as both reducing and stabilizing agents. Proteins can bind to the surface of nanoparticles and form a protective layer. The stabilization of nanoparticles is important to prevent their agglomeration, which can lead to changes in their properties and affect their application. The growing process is schematized in (**Figure 2 (a)**). The mechanism of fungal biogenesis by which oxide nanoparticles are made is similar to that of obtaining metal nanoparticles. However, the synthesis process of metal oxide nanoparticles involves additional steps for the oxidation of metal ions to their corresponding metal oxide forms. The reader is referred to the review works on the fungal biosynthesis of noble and transition metal NPs (Patel et al., 2021; Zielonka & Klimek-Ochab, 2017).

All these considerations make fungus a suitable bio candidate for sustainable mass and large-scale production. However, their use for the obtention of lanthanide-based nanostructures is relatively new and yet to be explored as most of the publications are primarily focused on the obtention of transition and noble metal nanoparticles. Several fungal species, including *Aspergillus flavus*, *Aspergillus terreus*, *Humicola* sp, and *Fusarium solani*, have been reported to synthesize LnNPs. **Table 1** shows various publications found in the literature reporting fungal biosynthetic approaches for obtaining LnNPs. The articles were selected by performing searches in the Web of Knowledge database using fung*, *synthesis, nano* keywords, and Boolean operators, sweeping the whole lanthanide series names and chemical symbols. Concepts such as Rare Earth and Lanthanides were also used. SciFinder, Scopus, Google Scholar, and EBSCO databases were also consulted.

Table 1. Fungal biosynthesis of Lanthanide based nanoparticles

Fungi	**Material obtained**	**Precursor, Growth conditions**	**Culture medium**	**Location (Ext./Int[†])**	**Size (nm)**	**Shape**	**Key aspects**	**Ref**
Aspergillus terreus & *Talaromyces pupureogenus*	CeO_2	$Ce(NO_3)_3$, 80ºC 6 h	PDB*	Ext.	28.5	Spherical	Antifungal activity against drug resistant *Candida albicans* strains	(Komal et al., 2020)
Fusarium solani	CeO_2	$CeCl_37H_2O$, 5 h	CDB*	Ext.	20-30	Spherical	Antimicrobial activity against various G+ & G- bacteria	(Venkatesh et al., 2016)
Aspergillus niger	CeO_2	$CeCl_3$ $7H_2O$, 80oC 4-6 h	CDB	Ext./Int.	5-20	Spherical	Antimicrobial activity against various G+ & G- bacteria	(Gopinath et al., 2015)
Curvularia Lunata	CeO_2	_	_	Ext./Int.	5-20	Spherical	_	(Munusamy et al., 2014)
Humicola sp.	CeO_2	CeN_3O_9 $6H_2O$, 50ºC	MGYP*	Int.	12-20	Spherical	Strong Violet emission	(Khan & Ahmad, 2013)
Humicola sp.	Gd_2O_3	$GdCl_3$, 5h, pH 9	MGYP	Ext.	3-8	Quasi-spherical	Drug bioconjugation to improve anticancer response	(Khan et al., 2014)
Fusarium oxysporum	Nd_2Se_3	$NdCl_2$. $SeCl_4$, 25ºC	PB*	Ext	18	Spherical	In-situ hydrophilic functionalization layer	(Ansary et al., 2022)
Penidiella sp.	$DyPO_4$	$DyCl_3$ 30ºC	BSM*	Int	200	_	Dy accumulation on the cytoplasm and in the cell surface	(Horiike et al., 2016)
Aspergillus flavus	$ZnS:Gd^{3+}$	$ZnSO_4$ $7H_2O$ & $Gd(NO_3)_3$, 10 min	PDA*	Ext.	10-18	Spherical	Reliable fluorescence sensing platform of heavy metals	(Uddandarao et al., 2019)
Zygomycota & *Ascomycota fungus****	$YPO_4:Eu^{3+}$	_	Eu^{3+} doped agar solution	Int.	100-200	Irregular	Strong nanophosphor compound obtained	(Jia, 2010)

[†]Ext.: Extracellular; Int.: Intracellular.
*PDB: Potato dextrose broth; MGYP: peptone (0.5%), glucose (1%), malt extract (0.3%) and yeast extract (0.3%) mixture; CDB: Czapek-Dox-Broth medium; PDA: Potato dextrose agar medium; PB: phosphate buffer; BSM: basal salt medium.
***Specific organism employed not mentioned.

For instance, the work of Khan & Ahmad, (2013) explores the synthesis of cerium oxide (CeO_2) nanoparticles using the micellar mass of *Humicola* sp. as a precursor of cerium oxide. The authors report the use of CeN_3O_9 6 H_2O at a temperature of 50 ºC to obtain nanoparticles of 16 nm in diameter. In addition, the characteristic signals of amide groups determined by X-ray Photoelectron (XPS), Fourier Transform Infrared (FTIR), and Ultraviolet-visible (UV-Vis) spectroscopies allowed corroborating the obtaining of a protein capping layer on the surface of the NPs that prevents their agglomeration and improves their dispersibility in water. The obtained systems also show an intense emission band associated with Ce *4f* and O *2p* levels when excited with a 300 nm source that could be attractive in imaging applications. Thus, the authors present a relatively simple route for the extracellular production of rare earth nanoparticles with biomedical applications such as the inhibition of reactive oxygen species (ROS).

Another report of the obtention of nanoceria (CeO_2) systems by a fungal-mediated approach is found in the work of Komal et al., (2020). In this regard, the authors employed two common strains of *Aspergillus terreus* (**Figure 2 (b)**) and *Talaromyces purpurogenus* (**Figure 2 (d)**) to treat cerium (III) nitrate to obtain 28.5 and 24.4 nm CeO_2 NPs, respectively. The resulting nanostructures can be observed in the electron microscopy images depicted in **Figure 2 (c, e),** where significant agglomeration between the synthesized NPs can be noted. Gas chromatography-mass spectroscopy (GCMS) measurements were used to determine the presence of bio solvents in the fungal filtrate that work as both capping and reducing agents. Furthermore, the synthesized CeO_2 nanostructures were used to inhibit the growth of the multidrug-resistant *Candida albicans* strain, indicating their potential as an alternative approach in antifungal therapy.

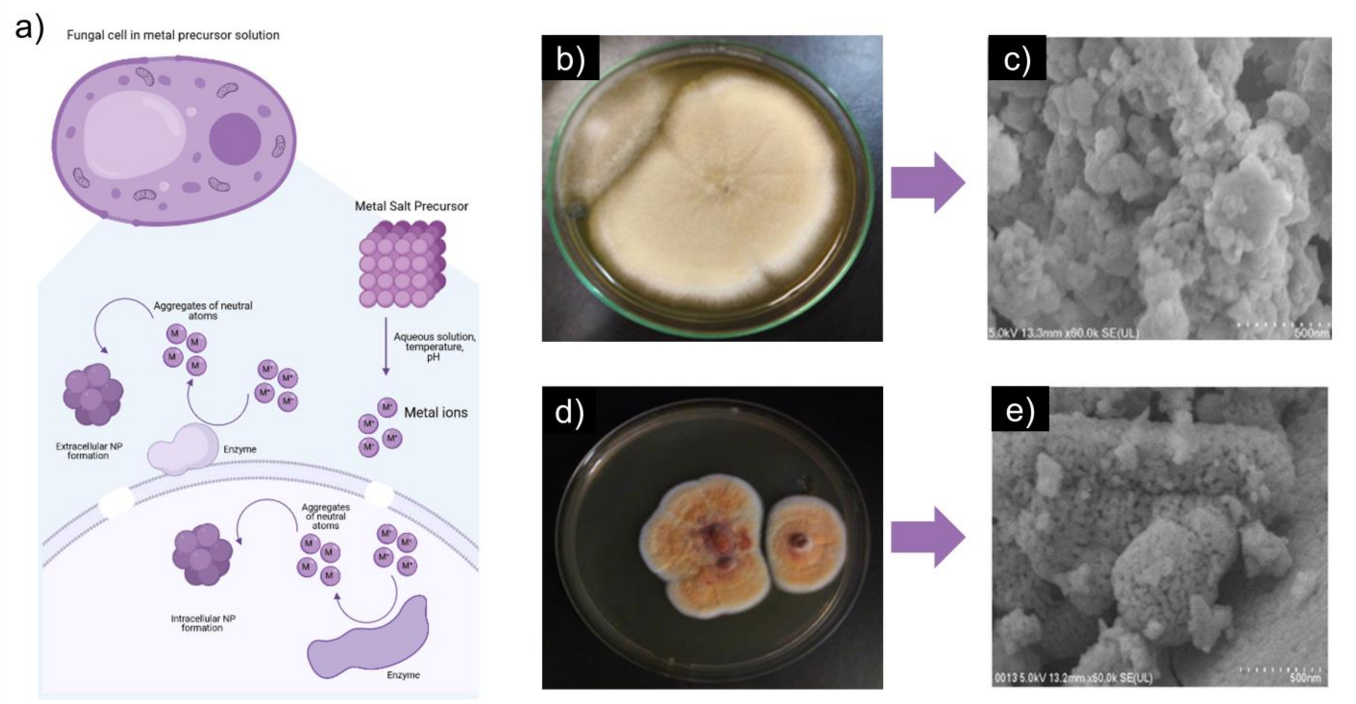

Figure 2. (a) Schematic illustrating the process of metal nanoparticle synthesis using fungal agents. Created with BioRender.com. (b-e) CeO_2 nanoparticles synthesized using (b,c) *Aspergillus terreus* and (d, e) *Talaromyces pupureogenus*. (b,d) Photographs of the cultures used and (c, e) scanning electron microscopy (SEM) images of the nanoparticles obtained(Komal et al., 2020). Copyrights IOP Publishing 2020.

On the other hand, Venkatesh et al., (2016) presents the fungal biosynthesis of CeO_2 NPs using the plant infective fungus *Fusarium solani*. In this work, the authors present a detailed FTIR analysis (**Figure 3 (a)**) of the fungal filtrate used in the synthesis (curve 1), the NPs as obtained from the green synthesis (curve 2), and the NPs calcined at 400 ºC (curve 3). With these results, the study corroborates the participation of organic biomolecules such as proteins, heterocyclic compounds, and amines in obtaining ceria nanostructures. The synthesized NPs were observed by TEM micrographs in which a spherical morphology with sizes between 20-30 nm is observed (**Figure 3 (b)**). **Figure 3 (c)** shows the electron diffraction pattern composed of rings, which evidences the polycrystalline nature of the obtained NPs, presenting a fluorite-type cubic structure. These results were also corroborated by X-ray diffraction (XRD) and Raman spectroscopy measurements. In addition, the study also demonstrates the antibacterial effects of CeO_2 nanomaterials against *P. aeruginosa*, *K. pnemoniae*, *E. coli*, and *S. aureus* at a concentration of 1 mg NPs, indicating strong inhibition of bacterial growth. These findings indicate that this method could offer an economically viable and environmentally sustainable approach to producing nanoparticles with promising biomedical uses.

Furthermore, the use of bioreducting agents extracted from the fungus *Fusarium oxysporum* to obtain Nd_2Se_3 NPs is addressed in the work of Ansary et al., (2022). In this study, the authors report the use of nitrate reductase as a reducing agent starting from $NdCl_2$ and $SeCl_4$ as chalcogenide precursors. The proposed synthesis mechanism is presented in **Figure 3 (d)**. In addition, a synthesized peptide sequence (Glu-Cys) n-Gly was used as a capping agent to obtain spherical Nd_2Se_3 nanostructures of 18 nm in size, without considerable agglomeration effects (**Figure 3 (e)**). The functionalization layer also displayed hydrophilic properties that allow the NPs dispersibility in water. Thus, the results of this study propose an alternative strategy for obtaining nano-chalcogenides adaptable to biomedical applications without the need for subsequent functionalization.

Finally, Khan et al., (2014) present another relevant study regarding the biosynthesis of gadolinium oxide (Gd_2O_3) nanoparticles using a *Humicola* sp. mediated approach. The researchers found that the synthesized nanoparticles had potential applications in cancer therapy as they could be bioconjugated with the chemically modified anticancer drug taxol. The study also investigated the biodistribution of the nanoparticles *in vivo* and found that they accumulated in various organs, including the liver and heart. Therefore, the results could be used to enhance drug delivery systems for cancer treatment.

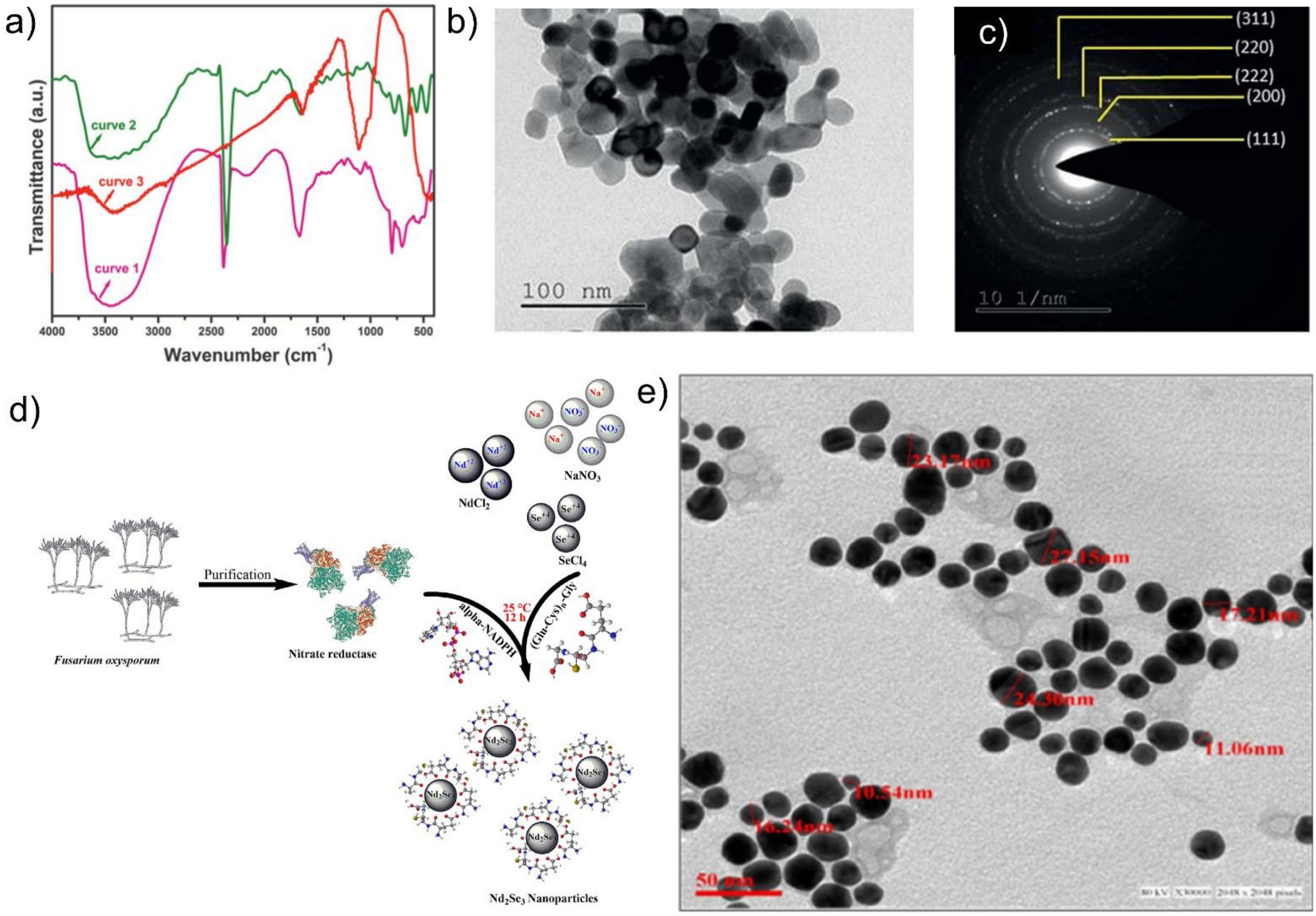

Figure 3. Characterization results and proposed synthesis mechanism for lanthanide-based NPs synthesized through a mycogenic process. (a) FTIR spectra of (curve 1) fungal filtrate of *Fusarium solani*, (curve 2) CeO_2 NPs, (curve 3) CeO_2 NPs calcined at 400ºC. (b) Transmission electron micrographs (TEM) of synthesized CeO_2 NPs. (c) Electron diffraction pattern showing the polycrystalline character of the obtained NPs (Venkatesh et al., 2016). Copyrights Royal Society of Chemistry 2016. (d) Scheme showing the synthesis mechanism for obtaining Nd_2Se_3 NPs using *Fusarium oxysporum* filtrate. (e) TEM micrograph of synthesized hydrophilic Nd_2Se_3 NPs(Ansary et al., 2022). Copyrights MDPI 2022.

Overall, the studies provided in this paper illustrate the potential use of fungi as biofactories for producing nanoparticles with various biomedical applications such as drug delivery, imaging, theragnostic, antifungal properties, and antibacterial effects. Fungi offer advantages due to their capacity to secrete enzymes and proteins that can convert metal ions into nanoparticles, their cost-effectiveness, and environmentally friendly characteristics. However, additional research is necessary to comprehensively grasp the processes involved in synthesizing nanoparticles using fungi and evaluate their potential risks and benefits for biomedical purposes.

3. Applications of lanthanide-based nanomaterials synthesized by green routes.

Although this review delves into the synthesis of lanthanide-based nanomaterials utilizing fungal agents, it is also noteworthy to mention the potential impact of these nanomaterials on biological entities such as cells, bacteria, or fungi. This section aims to present key findings in toxicological assessment, biocompatibility, nanoparticle-cell interactions, and biomedical applications of lanthanide-based nanomaterials, emphasizing sustainable green synthesis approaches. **Figure 4 (a)** schematically illustrates some of the applications of nanoparticles obtained through environmentally friendly synthesis methods.

For instance, Nazaripour et al., (2021) conducted a study on the production of cerium oxide nanoparticles using extract from *Prosopis fracta* fruit. Through various characterization methods such as FTIR, XRD, UV–Vis, SEM, and TEM analyses, they verified the crystalline structure and morphology of the nanoparticles with sizes ranging from 15–20 nm. Cytotoxicity tests conducted on colon cancer cell lines (HT-29) revealed non-toxicity at concentrations below 62.5 µg/mL for CeO_2, suggesting at potential biomedical applications pending further research.

In another research by Manoj Kumar et al., (2020), the biogenic synthesis and characteristics of lanthanum nanoparticles utilizing *Mutingia calabura* leaf extract were reported alongside their biological activity. Characterization techniques, including

FTIR, SEM, and energy-dispersive X-ray spectroscopy (EDAX) confirmed nanoparticle synthesis and traits. The findings revealed moderate antibacterial properties coupled with antioxidant activities along with hemolytic, anticoagulant, thrombolytic activities, and dye degradation efficiency, suggesting promising prospects for both biological and environmental applications.

Furthermore, Iram et al., (2016) presented a study on terbium oxide (Tb_2O_3) NPs produced using the fungus *Fusarium oxysporum*. These nanoparticles showed significant inhibition of osteosarcoma cell lines (MG-63 and Saos-2) while remaining non-toxic to primary osteoblasts. Concentration-dependent cell toxicity, changes in cell morphology, increased oxidative stress, and induction of apoptosis were observed, highlighting the biocompatibility of nanoparticles and potential for combating osteosarcoma. The research highlights important factors in synthesizing inner transition metal nanoparticles and proposes that the method is suitable for a wide range of biological applications, thus creating opportunities for various uses.

Furthermore, gadolinium-based nanomaterials have been widely used as magnetic resonance imaging contrast agents. For instance, B. Zhang et al., (2017) presents a significant advancement in the synthesis of ultrafine GdNPs measuring sub-10 nm in size, obtained by green synthesis process. These nanoparticles demonstrate notable biocompatibility, stability, and enhanced relaxivity in comparison to conventional Gd-DTPA solutions (magnevist). Through in vivo experimentation in tumor-bearing mice, discernible accumulation of GdNP within the kidneys and tumor is evidenced, facilitating precise demarcation of tumor boundaries and peripheral angiogenesis (**Figure 4 (b)**).

Moreover, Khan et al., (2014) reports the extracellular growth of gadolinium oxide (Gd_2O_3) NPs using the thermophilic fungus *Humicola* sp. These nanoparticles, known for their stability, were radiolabeled with Tc-99m to assess biodistribution in rats. The gamma camera imaging technique was utilized to track the dispersion of Tc-99m labeled Gd_2O_3 nanoparticles in a rat's body over a period. Results revealed the presence of Tc-99m–GdNPs in the kidneys, heart, and liver initially (**Figure 4 (c)**), followed by their elimination via urine within 45 min. Also, the aurthors bioconjugated the nanoparticles with modified taxol, an anticancer drug, to explore its potential in cancer therapy. This study provides valuable insights into a biological approach for synthesizing gadolinium oxide nanoparticles and their potential application in enhancing the efficacy of taxol against cancer cells, paving the way for promising nanoscale drug delivery strategies in cancer treatment.

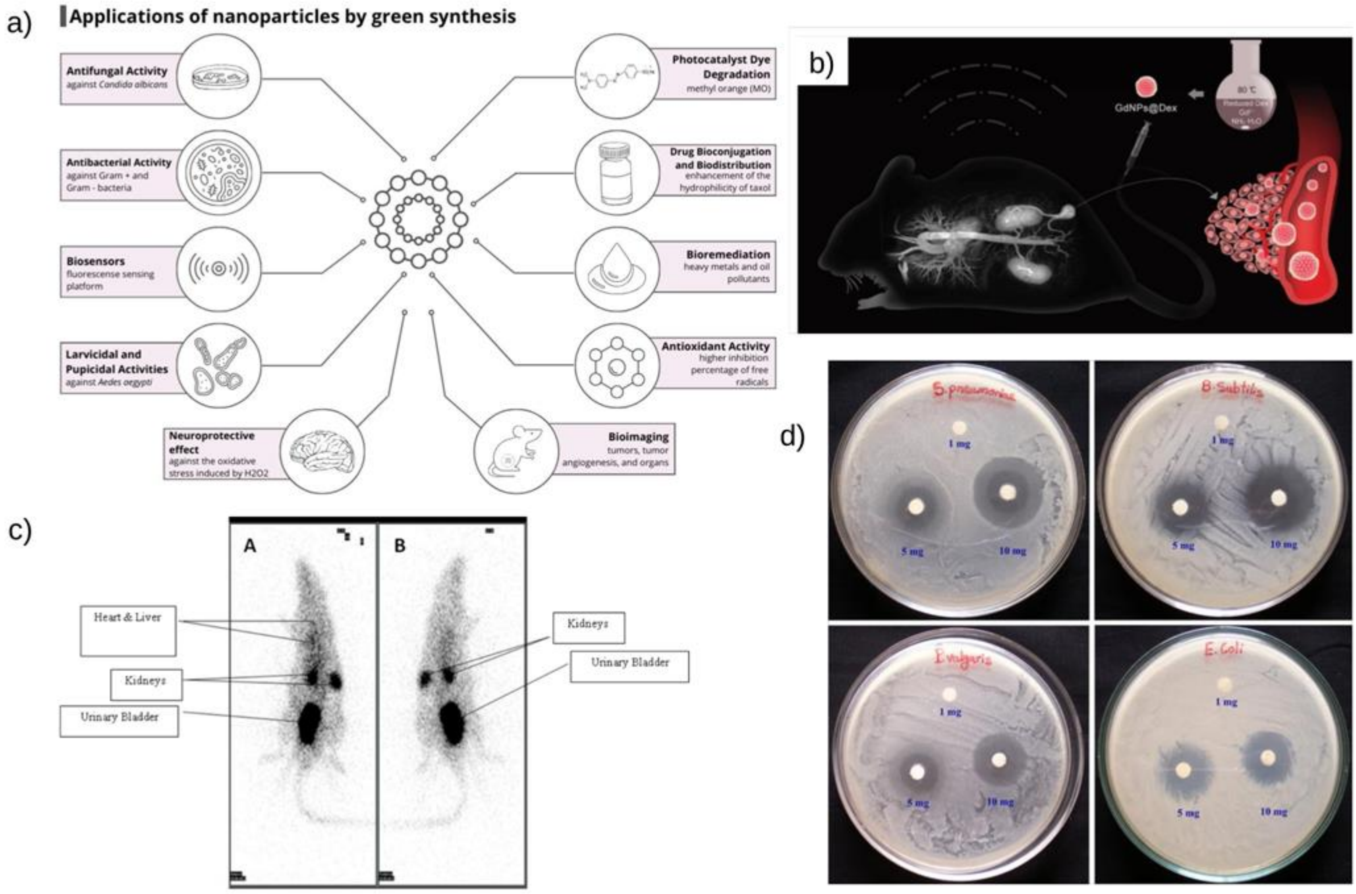

Figure 4. (a) Nanoparticle applications obtained through environmentally friendly synthesis methods. Made with CANVA software. (b) GdNPs magnetic resonance imaging efficacy for whole-body imaging, as well as tumor and tumor angiogenesis assessment (B. Zhang et al., 2017), Copyrigths Wiley 2017. c) Gamma scintigraphy image illustrating the dispersion of Tc-99m–Gd_2O_3 nanoparticles in a rat, presenting dorsal (A) and ventral (B) perspectives (Khan et al., 2014). Copyrights Beilstein J. Nanotechnol. 2014. (d) Antibacterial properties of Ln-NPs against both Gram-positive and Gram-negative bacteria (Gopinath et al., 2015). Copyrights Springer 2015.

Meanwhile, the antimicrobial potential of green-synthesized CeO_2 NPs from *Olea europaea* leaf extract is investigated by (Maqbool et al., 2016) The investigation details the process of employing *O. europaea* leaf extract as a chelating agent to reduce cerium nitrate. The resultant CeO_2 NPs display a consistent spherical shape and a pure single-face cubic structure, with an average diameter of 24 nm, as observed through TEM/SEM analysis. UV-visible spectroscopy confirms the characteristic absorption peak of CeO_2 nanoparticles at 315 nm, while FTIR analysis suggests the participation of natural components in the nanoparticle synthesis. Thermogravimetric analysis (TGA) predicts the successful encapsulation of CeO_2 nanoparticles by bioactive molecules derived from the plant extract. Antimicrobial studies reveal significant inhibition zones against bacterial and fungal strains, suggesting the potential biomedical applications of these nanoparticles. The antibacterial activity is attributed to electrostatic attraction between negatively charged bacterial cell surfaces and positively charged nanoparticles, leading to ROS generation and subsequent bactericidal effects, as depicted in **Figure 4 (d)**, showing a decrease in culture growth with increasing concentrations of CeO_2 NPs.

The study emphasizes the eco-friendly synthesis of CeO_2 nanoparticles and their promising antimicrobial properties, highlighting their potential for future therapeutic applications. Future research will focus on investigating the size-dependent anticancer and antimicrobial properties of these nanoparticles, particularly their cytotoxic behavior towards healthy and cancer cells.

Furthermore, other authors (Divya et al., 2024; Gopinath et al., 2017; Jan et al., 2020; Sharmila et al., 2019) have reported the use of plant extracts (*Aquilegia pubiflora*, *Syzygium travancoricum*, *Pisonia alba*) for the synthesis of rare earth oxides with antimicrobial applications (against *Salmonella typhi*, *Escherichia coli*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus vulgaris*) and antifungal properties (against *Fusarium solani*, *Aspergillus flavus*, *Candida albicans*, *Aspergillus niger*, and *Mucor racemosus*). These studies have demonstrated inhibitory responses, making them potential candidates for sustainable biological applications.

Finally, another relevant application in the field of rare earth applications with biological agents is the use of fungal metabolites for the recycling and biorecovery of rare earths from industrial waste or for the extraction of ions from minerals. An example of the potential of these approaches is demonstrated in the work of Bahaloo-Horeh & Mousavi, (2022), where a novel green approach for recovering valuable metals from spent automotive catalytic converters (SACCs) using fungal metabolites is presented. With increasing concerns over the environmental impact of SACCs, this innovative strategy harnesses the power of *Aspergillus niger*-derived oxalic acid-enriched spent culture medium to efficiently treat SACCs. Through the application of Central Composite Design (CCD), optimal conditions for oxalic acid production were identified, resulting in a remarkable 15.3 g/L yield. The subsequent bioleaching process using fungal metabolites demonstrated exceptional metal recovery rates, with up to 99.5% extraction of various metals, including Fe, Zn, Mn, Sr, Al, and rare earth elements (REEs). Notably, the enrichment of REEs in the residual powder reached an impressive 81%, highlighting the efficacy of this green approach.

Further characterization of bioleaching residues through XRD, FTIR, and SEM analyses elucidated the underlying mechanisms, revealing the significant role of carboxyl groups in metal leaching. Notably, the study emphasizes the sustainability of fungal-generated oxalic acid as a benign lixiviant for metal leaching processes, paving the way for eco-friendly strategies in metals recovery from automotive catalysts. The findings also suggest potential applications in other fields, with the bioleaching residue demonstrating safe disposal or reusability, thus offering a promising solution to mitigate the environmental impact of spent automotive catalysts.

Kang et al., (2022) explored a method for harnessing *Aspergillus niger*'s ability to solubilize natural struvite and recover cerium from the resulting leachate. By incubating struvite with *A. niger*, complete solubilization is achieved within two weeks, facilitated by the fungal production of oxalic acid. Electron microscopy reveals the formation of distinctive crystal morphologies in the leachate upon mixing with Ce^{3+}. Subsequent analyses confirm the formation of cerium oxalate decahydrate ($Ce_2(C_2O_4)_3 \cdot 10H_2O$) and cerium phosphate hydrate ($Ce(PO_4) \cdot H_2O$) at high Ce concentrations (20 mM $CeCl_3$). These biogenic Ce minerals efficiently remove more than 99% of the Ce from the solution. These biogenic Ce phosphates can also be converted into cerium phosphate ($CePO_4$) and cerium oxide (CeO_2) (cerianite) after annealing at 1000 °C. Moreover, FTIR spectroscopy identifies functional groups in the amorphous minerals, shedding light on their composition. The findings offer new insights into fungal-mediated biomineralization processes and highlight the potential for nanomaterial biosynthesis, bioremediation, and metal. Kang's study presents a promising avenue for sustainable resource recovery and environmental remediation through fungal-mediated biotransformation of soluble REE species using struvite leachat.

In summary, nanostructured systems based on rare earths synthesized through green techniques present a wide range of potential applications, from combating pathogenic microorganisms to enhancing medical imaging techniques and elemental recovery. However, it is important to consider possible limitations, such as the scalability of production and the long-term stability of these materials. Despite these challenges, the outlook is promising, and ongoing research and development in this field are likely to lead to significant advances in the near future.

4. Conclusions and perspectives

In conclusion, the combination of fungal biogenesis and lanthanide-based nanotechnology presents promising prospects for advancement in the fields of biomedicine and environmental conservation. Utilizing fungi for the synthesis of nanomaterials holds potential for sustainable healthcare, resource utilization, and scientific progress. It is crucial to further investigate this interdisciplinary area to optimize the advantages of lanthanide-based nanobiotechnology while reducing its impact on the environment.

The versatility of lanthanide-based nanomaterials synthesized via fungal biogenesis is evident in their applications as contrast agents for MRI, antimicrobial agents, therapeutic agents against cancer, and drug delivery systems. These nanomaterials exhibit tailored functionalities that address specific biomedical needs, offering targeted and efficient solutions for diagnostics, treatment, and drug delivery.

Looking ahead, as nanostructured lanthanides increasingly find applications in optoelectronic, biomedical, and energy technologies, their release into the environment raises concerns about potential ecological impacts. Therefore, comprehensive studies are needed to evaluate the environmental fate and effects of lanthanide nanoparticles on terrestrial and aquatic ecosystems. Furthermore, the recovery of lanthanides from waste or mineral resources using fungal organisms warrants further investigation to develop sustainable and efficient recycling strategies.

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Conflict of Interest

The authors declare that there are no conflicts of interest.

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