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TÍTULO: A Review on the Biosynthesis and Applications of Selenium- and Tellurium-based Chalcogenide Nanoparticles

Trabajo de integración curricular presentado como requisito para la obtención del título de Ingeniero Biomédico

Autor:

Katherine Villota Revelo

Tutor:

Ph.D. Thibault Terencio

Urcuquí, Septiembre del 2024

AUTORÍA

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Katherine Estefania Villota Revelo

CI: 1004014724

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RESUMEN

Debido a las peculiares propiedades presentes en la nanoescala, las nanopartículas han sido cada vez más estudiadas en el contexto biomédico. Estas aplicaciones abarcan la terapia fotodinámica, la administración de fármacos, la bioimagen o la actividad antimicrobiana.

La ruta de síntesis más común para estas atractivas partículas sigue siendo la química, pero en general existe una toxicidad intrínseca asociada a esta ruta. Para evitar este problema, la biosíntesis se ha demostrado como una forma más prometedora para las bioaplicaciones a pesar de sufrir menos control sobre las partículas obtenidas.

Si bien el enfoque en las nanopartículas se ha incrementado gradualmente con el tiempo, generalmente se encuentran los mismos elementos, por ejemplo, oro, plata, platino, cobre, hierro o sus óxidos. Por esta razón, en este trabajo se centrará en las nanopartículas constituidas por. elementos calcógenos que se consideran metaloides: Selenio y Telurio. A través de la revisión de la literatura científica, este trabajo resume qué especies biogénicas se encuentran como potenciales generadores de nanopartículas de Se y Te, entre ellas Hongos, levaduras, bacterias o algas.

Dado que el selenio y el telurio son elementos muy raros en la Tierra y clasificados como elementos críticos para la energía, se sabe que ambos son buenos candidatos para usos fotovoltaicos. Por otro lado, se resume información práctica sobre la caracterización de estas nanopartículas y cómo su morfología puede ser controlada mediante la biosíntesis.

Palabras clave:

Calcógenos, Selenio, Teluro, Biosíntesis, Nanopartículas, Aplicaciones, Biomédicas

ABSTRACT

Owing to the peculiar properties present at the nanoscale, nanoparticles have been more and more studied in the biomedical context. These applications encompass Photodynamic Therapy, Drug delivery, bio-imaging or antimicrobial activity.

The most common synthesis route for these attractive particles remains the chemical one but there is in general an intrinsic toxicity associated to this path. To avoid this problem, the biosynthesis has been demonstrated as a more promising way for bio-applications despite suffering from less control over the obtained particles.

While the focus on nanoparticles has gradually increased over time, the same elements are usually encountered, e.g., gold, silver, platinum, copper, iron or their oxides. The metals always provide useful properties, but the elements at the frontier with the nonmetals are profoundly less known. For this reason, this work will focus on nanoparticles constituted of chalcogenides elements which are considered as metalloids: Selenium and Tellurium. Through a review of the scientific literature, this work summarizes which biogenic species are found as potential generators of Se and Te nanoparticles, including fungi, yeasts, bacteria or algae. While various organisms can build these nanoparticles, only few different compound types are found.

Since Selenium and Tellurium are very rare elements on Earth and classified as energy critical elements, known to be both good candidates for photovoltaic uses. One of the main objectives of this work is to balance their potential for biomedical applications, and particularly for bio-imaging, in front of their scarcity. On the other hand, practical information is summarized about the characterization of these nanoparticles and how their morphology can be controlled by biosynthesis is summarized.

Keywords:

Chalcogenides, Selenium, Tellurium, Biosynthesis, Nanoparticles, Applications. Biomedical

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1. INTRODUCTION

1.1.Chalcogenides

Chalcogenides are elements belonging to the group 16, including oxygen (O), sulfur (S), selenium (Se), tellurium (Te), polonium (Po) and livermorium (Lv) (Brasted, 2017). While oxygen element has been a central part of chemistry and biology, and sulfur is well-known, the elements below have been less studied. On the other hand, Polonium and Livermorium are radioactive elements, which render them as unfit for most bio-applications. Polonium was famously discovered, along with Radium, by Marie Curie who received a Nobel prize of chemistry in 1911 for this contribution (Papoh, 2018). The heavier element of this group, Livermorium, is an element which cannot be found in nature and is made through the bombarding of curium atoms with calcium and is only used in few researches until now. Intermediate elements, namely Selenium and Tellurium, are rare but present in nature and remain relatively lesser studied (Papoh, 2018).

1.2.Tellurium

Tellurium is the semi-conductor chemical element with the atomic number 52 and was discovered in 1782. Tellurium etymology comes from the Latin "Tellus" meaning Earth. With an abundance similar to Platinum in Earth crust, Tellurium is one of the rarest stable solid elements on the planet (Royal Society of Chemistry, 2023b). Interestingly, this scarcity is not a reflection of its abundance in the universe and is thought to be potentially due to special events on earth which provoked its loss into space. Tellurium is a metalloid and thus a fascinating element, as very few atoms of the periodic table are in this category, in between nonmetals and metals (Royal Society of Chemistry, 2023b).

Traditionally, Tellurium has been used in order to make copper or steel alloys to improve the machinability (Brasted, 2023). Nowadays, the main use of Tellurium is for solar panels (CdTe) and thermoelectric devices (HgCdTe, BiTe)(Brasted, 2023). CdTe is one of the most efficient materials for solar cell electric power generation. While rare on earth, Tellurium has a special place and is considered as a technology-critical element, critical to modern and emerging technologies (National Center for Biotechnology Information, 2024). Biologically, Tellurium is thought to play almost no role in nature. It has however been found that some fungi can use it to replace sulfur or selenium in amino acids but is a rare occurrence. Since its abundance is very low, Tellurium does not seem to play a determinant role in nature (National Center for Biotechnology Information, 2024).

1.3.Selenium

Selenium is the chemical element with the atomic number 34 and was discovered by Berzelius in 1817. Noting a similarity with Tellurium, Selenium was named from the Greek goddess of moon. It is considered as a nonmetal or sometimes as a metalloid, intermediate between metals and nonmetals (Brasted, 2024).

It is also a good semi-conductor and can convert alternate current to direct current in rectifiers. Selenium has also the capability to change its conductivity with light in photovoltaic cells. The main part of applications for Selenium is still as an additive to glass, for decolorizing, colorizing or reduce the transmission of light. It is also used to make pigments for paint, plastics or ceramics (Brasted, 2024).

On biological aspects, Selenium is an essential trace element for humans and some other species: health problems can be provoked by a lack of selenium. Human bodies contain about 14 milligrams of it, while an excess of Selenium can be carcinogenic and teratogenic (Royal Society of Chemistry, 2023a).

1.4.Comparison of Selenium and Tellurium

When searching the terms "Tellurium" and "Selenium" in Scopus database (2023), it returns 53000 and 13400 scientific articles respectively. As a comparison, searching for the keyword "carbon" results in 2460000 works in total, showing less effort is dedicated to these elements in the scientific community. Nevertheless, when comparing the two, it is found that selenium has extensive scientific articles in the Scopus database than tellurium.

This tendency is even more evident when combining this search with "biological": 9400 articles for Selenium and 930 for Tellurium. The biological impact of these two elements is still not entirely known. Between both elements, Selenium has been studied much more than tellurium, probably because tellurium is rare and more difficult to obtain for laboratory experiments.

Se and Te are both used for solar cell applications due primarily to their energy bandgaps, 1.79 and 0.33 eV respectively, allowing to absorb visible and near-infrared light respectively (Fiducia et al., 2019).

It is worth to notice that Se and Te can also form an alloy and the best proportion for solar application has been predicted (Geoffrion & Guisbiers, 2021). Although a very specific work published in 2021, it is possible that this alloy could also have biological applications (Geoffrion & Guisbiers, 2021).

1.5.Nanotechnology and nanoparticles

Nanotechnology is the field of science encompassing both nanoparticles (NPs) and nanomaterials (NMs) which are defined as materials possessing at least one dimension between 1nm to 100nm (Dolez, 2015). This part of technology has been blooming over time and represents now a considerable part of scientific research (Dan, 2020).

When comparing with bulk materials, NPs displays particular properties which are linked to their size, or more precisely to the surface/volume ratio (Nagarajan, 2008). Atoms at the surface are fundamentally different from inside the material: in the bulk every atom is surrounded by other atoms in every 3D direction whereas at the surface void constitute one or more direction(Akbari, Tavandashti, & Zandrahimi, 2011; Nagarajan, 2008). In this aspect, the external surface would change with both the volume and the shape of the nano particles (Akbari et al., 2011).

Since the shape and size are always parameters difficult to control during the synthesis, the classification in the vast majority of the time is based on the chemical element nature. Among the possible sorting propositions, one interesting for biomedical applications is to divide it into four categories: metallic nanoparticles, bimetallic or alloy nanoparticles, metal oxide nanoparticles and magnetic nanoparticles (McNamara & Tofail, 2016).

The most representative nanoparticles of each category are as follow (McNamara & Tofail, 2016):

- metallic nanoparticles: gold and silver
- bimetallic particles: Fe-Co, Fe-Ni, Fe-Cu, Cu-Ni and Fe-Pt
- metal oxide nanoparticles: TiO₂, CeO₂, SiO₂ and ZnO.

• Magnetic nanoparticles: Fe₃O₄, Co–Fe₂O₄ and Mn–Fe₂O₄.

This list is not exhaustive, as almost every chemical element has been tried as nanoparticles, but, constitutes a reflection of the most used elements in biomedical applications: Fe, Cu, Ag, Au, Pt, Ni.

Until now, only few research has focused on Selenium and Tellurium nanoparticles (Tiekink, 2012) while Selenium is already present in human body and tellurium needs only few traces to find its application, rendering both as potentially interesting for applications. Moreover, both elements are slightly outside of the previous classification, because these are considered metalloids. This point is the main interest of this review: figure it out if these nanoparticles are useful for biomedical applications.

2. PROBLEM STATEMENT

Nanoparticles are very promising due to their peculiar properties linked to their intermediate size between molecules and macro materials. Their very small size brings features close to the quantum level while the shape is also a key factor of the nanoparticles. Their conduction, optical properties or toxicity are sometimes dramatically different from their bulk counterpart.

The chemical synthesis of these nanomaterials is in general well-known, can be done through a multitude of approaches, but people handling the nanomaterials may suffer from toxicity due to the reactants involved. On the other hand, biosynthesis of materials has proven recently to also be an interesting route for the construction of these materials. This manner takes advantage from the wide range of natural resources available in nature, e.g. enzymes, virus, fungus, algae, etc. However, the variety of biological sources conjugated with the complexity of each biological medium renders difficult to precisely understand every effect and thus control selectivity upon nanoparticles design.

While biosynthesis is more and more understood, studies about nanoparticles from Selenium and Tellurium elements remain scarce. As shown in the introductory part, these two bulk elements are preferred for photo applications but their properties could change at the nano scale.

3. OBJETIVES

3.1.General objective

Review the various factors governing the biosynthesis, sources and applications of selenium and tellurium nanoparticles.

3.2.Specific objectives

- Encounter the various biological systems capable to synthesize Selenium and Tellurium nano particles.
- Detail the analytical techniques most used to characterize these systems.
- Understand the key factors to control morphology and site during the biosynthesis.
- Overview of the Bioapplications of biosynthesized Se-NPs and Te NPs.

4. CONVENTIONAL METHODS-CHEMICAL SYNTHESIS OF TE AND SE NANOPARTICLES

4.1.General approaches used for nanoparticles synthesis

For nanoparticles synthesis two approaches are executed: the physical top-down approach, corresponding to start from a bigger bulk material and patterning the surface, or the chemical bottom-up approach, where particles are generated atoms per atoms (Bellah, Christensen, & Iqbal, 2012). The top-down approach involves in general six steps: lithography, oxidation, etching, ion implantation, diffusion, and deposition. These methods in very well-designed materials but two main drawbacks appear using them: costly and difficult to obtain materials smaller than 100 nm (Bellah et al., 2012). The bottom-up approach with the assembly at an atomic level allows to obtain nanomaterials at all scales, despite a harder control on the morphology of the particles obtained. In some recent occurrences, both manners can also be combined to obtain a more precise control over nanoparticles morphology (Diaz Fernandez et al., 2014).

4.2. Chemical Bottom-up approach of synthesis

A key factor influencing the utilization of nanomaterials and their applications across different domains is the process of synthesizing and growing nanostructures and nanomaterials. They are methods used to improve the regularity and uniformity of the structure of nanomaterials through the control of their morphology, particle size and elemental valence of synthetic materials, A nanostructured material that is well-suited for one application might prove to be more advantageous in another if it is synthesized using a different method or technique. Likewise, the structure and morphology of a nanomaterial are influenced by the growth and synthesis methods employed. For instance, while the plasma magnetron sputtering technique allows for the straightforward growth and synthesis of amorphous nanostructured thin films, achieving a similar structure through thermal evaporation can be challenging due to the inherent characteristics of that technique (Abid et al., 2022).

In the bottom-up approach, nanostructures are created by assembling individual atoms or molecules. This method involves the controlled arrangement of atoms or molecules to form desired nanostructures within the size range of 2 to 10 nm. Generally, there are two primary techniques that utilize this approach: gas-phase synthesis and liquid-phase formation. Various methods employed in the bottom-up approach include plasma arcing, chemical vapor deposition, metal-organic decomposition, laser pyrolysis, molecular

beam epitaxy, sol-gel processes, wet synthesis, and self-assembly techniques (S. Kumar, Bhushan, & Bhattacharya, 2018).

The main chemical methods for nanoparticles synthesis are chemical reduction, coprecipitation, hydrothermal synthesis, microemulsion, sol-gel, seeding, and sonoelectrodeposition (Nie, Zhao, & Xu, 2023). Chemical reduction is probably one of the easiest and fastest nanoparticle synthesis routes. Metal-containing salts, known as precursors, are dissolved and chemically reduced in a suitable solvent. During the initial stage of nucleation, the metal salt undergoes reduction to produce zero-valent metal atoms. While easy to execute, this method requires the use of reducing agents such as hydrazine, sodium borohydride, or N,N-dimethylformamide which can be toxic for the environment or human-health. Appart from reducing the metal properly, these agents can also provide the particles with enhanced stability (Nie et al., 2023).

One important route towards nanomaterials is the hydrothermal synthesis which is easily done as one-pot approach, with heat, solvent, and pressure, (in an autoclave) to synthesize for example porous metal-organic frameworks (Nie et al., 2023).

Another interesting method is the class of sol-gel or microemulsion family, which allows to control the size of the particles through the specific emulsion done. Through this approach, it is possible to limit physically the available space for the particle growth (Nie et al., 2023).

4.3. Other techniques

4.3.1. Chemical synthesis of Se and Te nanoparticles

The chemical synthesis of Te and Se nanoparticles follow the same technics described above for nanoparticles in general. The most common method for obtaining nanoparticles is the reduction method, involving sometimes toxic solvents (Artioli, 2017).

5. BIOSYNTHESIS OF SELENIUM AND TELLURIUM BASED CHALCOGENIDE NANOPARTICLES

Transition metal (TM) chalcogenides are a category of semiconductor materials that have a wide range of applications, including antibacterial particles and thin films used in energy conversion devices. (Muslih, Munir, & Khan, 2021). Notable advancements in synthetic biology, along with the advantages of low energy consumption and minimal toxic waste associated with "green synthesis," have led to increased research focus on biosynthesis (Dahoumane, Jeffryes, Mechouet, & Agathos, 2017; Zambonino et al., 2021).

In recent years, living organisms have been used for the biosynthesis of nanoparticles due to their low cost, cost-effectiveness and as a good ecological tool (Bao, Hao, Yang, & Zhao, 2010; Bharathi M., Roy, Moharana, Ghosh, & Paira, 2020; Jacob, Lens, & Balakrishnan, 2016).

Biosynthesis of Transition metal (TM) chalcogenides is indeed considered a bottom-up approach that utilizes natural bio-resources as promoters for the synthesis of various types of nanoparticles (NPs)(Abid et al., 2022; Dahoumane et al., 2017). TM chalcogenide nanoparticles (NP) can be produced by a variety of microorganisms including bacteria, fungi, algae, and yeast, and soil organisms (Feng, Marusak, You, & Zauscher, 2018).

Figure 1 Shows the general process used in the biosynthesis of selenium-based and tellurium-based nanoparticles (Se-NPs and Te-NPs). First the biological material collection, where organisms like bacterias, fungi, algae, yeas and soil organisms are cultured under suitable conditions following established procedures, and they are prepared according to the specific objectives of the research using isolated cells, cell-free extracts, or whole living cultures (Dahoumane et al., 2017; Pyrzynska & Sentkowska, 2021; Zambonino et al., 2023). Then, to be occur the biosynthesis of Se-NPs and Te-NPs is adding the metal salts solutions or precursors, occurring physical and chemical changes that is often indicated by a visible color change in the solution (Abdel-Salam, Omran, Whitehead, & Baek, 2020; Bao, Lu, et al., 2010; Prasad & Jha, 2010). Finally, the Se-NPs and Te-NPs are purified and characterized with detailed mechanisms of 2020; & synthesis(Abdel-Salam et al., Pyrzynska Sentkowska, 2021).



Figure 1. General schematization of the process for the biosynthesis of Selenium – based and Telluriumbased nanoparticles (Se-NPs and Te-NPs). Created in BioRender.com

5.1.Biosynthesis by Yeast

The budding yeast species Saccharomyces cerevisiae has demonstrated significant potential as a microorganism for the heterologous expression of biosynthetic pathways. Its effectiveness as a host organism is largely attributed to the extensive knowledge gained from over a century of rigorous scientific research. Yet many challenges are currently faced in engineering yeast strains for the biosynthesis of complex secondary metabolite production, *Saccharomyces cerevisiae* is a yeast that although it does not naturally produce hyaluronic acid, has favorable advantages for its possible scaling and production. Due to the extensive knowledge and genetic tools that exist of this microorganism is an attractive host for the production of this polymer (Siddiqui, Thodey, Trenchard, & Smolke, 2012).

The biosynthesis of cadmium selenide (CdSe) nanoparticles using yeast has been explored as a potential green synthesis method (Bharathi M. et al., 2020; Sur et al., 2019). Yeast is a simple eukaryotic microorganism that is widely used in biotechnology and can be genetically engineered to produce a variety of biomolecules, the yeast *S. cerevisiae* is an attractive host for terpene bioproduction, due to its robustness, applicability to industrial bioprocesses, and the possibility for terpene scaffold decoration by the functional expression of cytochrome P450 enzymes (Baghban et al., 2019).

In the biosynthesis of CdSe quantum dots (QDs) by yeast, it is important to know the metabolic processes involved. It has been established that Glutathione (GSH) is crucial for the production of CdSe QDs in yeast cells by deleting certain genes involved in glutathione metabolism, facilizing the inorganic substances to be metabolized within cells, triggering the in vitro creation of QDs (Shao et al., 2018). Therefore, in the biosynthesis of CdSe with *Saccharomyces cerevisiae* presented by Cui et al., 2009 and Li et al., 2013 states that yeast produce a correct balance between cadmiun and selenium reactions reducing the selenium throughout stationary phase and by the intracellular pathway(Cui et al., 2009; Y. Li et al., 2013). The biosynthesis of CdSe nanoparticles using yeast involves the reduction of cadmium and selenium ions to form CdSe. This can be achieved by growing the yeast cells in a medium containing cadmium and selenium ions. The yeast cells will then take up the ions and reduce them to form CdSe nanoparticles

(Baghban et al., 2019; Brooks & Lefebvre, 2017; Cui et al., 2009; Y. Li et al., 2013). The same results are shown in the biosynthesis of CdSe with *Candida utilis*

WSH02-08 using different precursors concentrations to regulate the fluorescence properties occurring in intracellular biosynthesis (Tian et al., 2017).

Another approach is using *Rhodotorula mucilaginosa* PA-1 yeast cells to biosynthesized CdSe NPs under aerobic conditions at exposing to Sodium selenite (Na2SeO3) and Cadmium chloride (CdCl2), showing that these QDs are formed with a narrow size in the extracellular polysaccharide exhibited a photocatalytic activity (Cao et al., 2020).

Extracellular polysaccharides are as structurally and functionally diverse as the bacteria that synthesize them. They can exist in various forms, such as cell-bound capsular polysaccharides, free "slime," and as components of lipopolysaccharide O-antigens, each serving a diverse array of biological functions. These functions include resistance to desiccation, protection against both nonspecific and specific host immunity, and adherence. Consequently, considerable effort has been devoted to documenting the vast structural complexity of extracellular polysaccharides, which arises from the numerous combinations of available monosaccharides and non-carbohydrate residues., and linkage types, and to elucidate their biosynthesis and export (Bazaka, Crawford, Nazarenko, & Ivanova, 2011)

Additionally, the obtention of CdTe QDs demonstrate a simple biosynthesis method formed by an extracellular growth pathway. This biosynthesis shows good crystallinity, optical and fluorescence properties, stability and water solubility(Bao, Hao, et al., 2010).

5.2. Biosynthesis by Bacteria

The biosynthesis of peptidoglycan in bacterial cell walls is a multifaceted process that involves a series of enzymatic reactions. These reactions arise in different cellular locations: the primary synthesis of nucleotide precursors takes place in the cytoplasm, while the production of lipid-linked intermediates occurs on the inner surface of the cytoplasmic membrane. Finally, the polymerization reactions occur on the outer side of the membrane (Barreteau et al., 2008).

Se-Te-Based NPs have been produced using bacterias. There are different methods for synthesizing CdSe nanoparticles, using bacteria offers certain advantages such as environmental friendliness and ease of scalability. Additionally, to biosynthesized QDs with bacterias it requires a process that includes, selection of bacteria , preparation of

medium culture, inoculation and growth, addition of precursors, nanoparticle synthesis, harvesting and purification (Bao, Lu, et al., 2010; Borghese et al., 2016, 2017; Kominkova et al., 2014; Monrás et al., 2012).

For example, Pseudomonas aeruginosa RB strain was used in the synthesis of CdSe nanoparticles with lactic acid as a carbon source under various conditions such as weak alkaline and acidic conditions showing high purity and antimicrobial activity due to high resistance to cadmium (Ayano, Kuroda, Soda, & Ike, 2015). One commonly used bacterium for CdSe biosynthesis is *Escherichia coli (E. coli)*. which has been genetically engineered to express specific proteins that facilitate the formation of CdSe nanoparticles.

Using *E. coli* cells, CdSe QDs are obtained aerobically by intracellular reactions and getting uniform size and favorable optical characteristics that can be used in a variety of applications. Also, the QDs shows at the surface a layer by proteins improving the biocompatibility (Z. Yan et al., 2014). In the case of CdTe biosynthesis by *Escherichia coli*, it has proven to be a green chemistry method with low costs. Which, metal-binding proteins and polypeptides such phytochelatin and metallothionein have increased levels of gene expression of Phytochelatin Synthase (PCS) genes, Metallothionein Genes and FtsZ and FtsQ genes (Bao Lu et al., 2010; Kominkova et al., 2014; Monrás et al., 2012).

5.3.Biosynthesis by Fungi

In recent years, the green approach of nanoparticle synthesis by biological entities has been gaining great interest over various other physico-chemical methods, which are landed with many disadvantages. Key challenges in contemporary nanotechnology involve creating dependable experimental methods for synthesizing nanoparticles with varying compositions and sizes while achieving high monodispersed. Biological systems present unique opportunities to customize nanomaterials with specific properties. Fungi are particularly favored as microorganisms because they provide numerous advantages compared to bacteria, yeast, actinomycetes, plants, and other physical or chemical techniques.

The use of microorganisms for the deliberate synthesis of nanoparticles is a fairly new and exciting area of research with considerable potential for further development (Dhillon, Brar, Kaur, & Verma, 2012). The biosynthesis of cadmium telluride, cadmium selenide and lead selenide nanoparticles by fungi has gained attention in recent years due to the unique metabolic capabilities of certain fungal species such as *Fusarium oxysporum*

(S. A. Kumar, Ansary, Abroad, & Khan, 2007; Syed & Ahmad, 2013; Yamaguchi et al., 2016), *Rhizopus Stolonifer* (Mareeswari, Brijitta, Harikrishna Etti, Meganathan, & Kaliaraj, 2016), *Trametes versicolor* (Qin et al., 2018), *Trichoderma sp.* (Diko et al., 2020), *Helminthosporum solani* (Suresh, 2014) *and Aspergillus spp.* (Mary Jacob, Balakrishnan, & Kumar, 2014).

The biosynthesis process in all these fungi species include fungal culture preparation with a suitable growth medium, adding the cadmium and tellurium salts precursors. These precursors serve as the sources of cadmium and tellurium ions for nanoparticle synthesis. Then, the fungal cells take up the cadmium and tellurium ions from the culture medium through various transport mechanisms. Fungi have the ability to accumulate and tolerate heavy metals, making them suitable for nanoparticle synthesis through biomineralization (Diko et al., 2020). The Biomineralization is mineralization that happens in biological environments in which an organic matrix or soluble biomolecules, along with biological-induced local environments, facilitate the crystallization of minerals and control their morphologies and locations of nucleation (Lowenstam & Weiner, 1989).

Once the nanoparticles are synthesized, the fungal biomass is harvested, and the nanoparticles are separated from the fungal cells and culture medium. Techniques such as centrifugation, filtration, or other separation methods can be used to isolate the nanoparticles (Diko et al., 2020; S. A. Kumar et al., 2007; Mareeswari et al., 2016; Mary Jacob et al., 2014; Qin et al., 2018; Suresh, 2014; Syed & Ahmad, 2013; Yamaguchi et al., 2016).

5.4.Biosynthesis by Algae

CdSe biosynthesis using algae refers to the process of producing these nanoparticles using certain species of microalgae, where them have been explored as potential bioreactors for the synthesis of nanoparticles due to their ability to accumulate metal ions and their high photosynthetic activity. Some common species used in nanoparticle synthesis include *Chlorella pyrenoidosa* and *Scenedesmus obliquus* microalgaes as bio-reactors.

Then, the culturing algae under controlled laboratory conditions is necessary for adding the Cadmium and selenium precursors and the algae take up these metal ions from the medium. This production involves a controlled synthesis process, often utilizing biological methods, such as culturing algae, or chemical methods like hot injection techniques of CdSe QDs that shows high crystallinity, exceptional fluorescence characteristics, and a monodispersed, uniform spherical shape. Also, this process is able to reduce the energy consumption and good environmental impact (Z. Zhang et al., 2018).

On the other hand, another biosynthesis made from algae is the Zinc selenium nanoparticles (ZnSe NPs) that were synthesized using an aqueous extract of the seaweed *Gracilaria corticate* (Mirzaei et al., 2020). The synthesis process was led with the seaweed was dried, powdered, and subjected to aqueous extraction, followed by the addition of zinc nitrate and sodium selenite to form the nanoparticles (Mirzaei et al., 2020). Characterization techniques such as UV-Vis spectroscopy, FTIR, SEM, TEM, XRD, and EDX confirmed the successful synthesis, revealing spherical NPs with sizes ranging from 50-250 nm and a crystallite size of 55.5 nm (Mirzaei et al., 2020). The ZnSe NPs exhibited an absorbance peak at 350-400 nm and demonstrated significant biological activities, including approximately 67% antioxidant activity, antibacterial effects against various strains, and biofilm inhibition on *Pseudomonas aeruginosa* and *Bacillus subtilis* (Mirzaei et al., 2020). Furthermore, they showed anticancer activity against HTB-9 and KB cell lines with IC50 values of 19.24 and 28.42 μ g/ml, respectively and this study highlights the potential of green-synthesized ZnSe NPs for therapeutic and preventive applications (Mirzaei et al., 2020).



Figure 2. Process of Biosynthesis by Algae using inorganic precursors with their applications and characterization. Taken from (Khanna, Kaur, & Goyal, 2019). Created with BioRender.com

5.5.Biosynthesis by Soil organisms

The biosynthesis of cadmium telluride (CdTe) nanoparticles using soil organisms is an emerging field of research, but it is not as extensively studied as biosynthesis using bacteria or algae. However, there have been some studies exploring the potential of soil organisms for CdTe nanoparticle synthesis. For instance, using *Lumbricus rubellus* earthworm exposed in a contaminated soil with CdCl₂ and Na₂TeO₃ salts was obtained a luminescent QDs extracted from the chloragogenous tissues surrounding the worm's gut. In order to carry heavy metals to the chloragogenous tissues (similar to liver cells), where toxins are eliminated, the earthworm *L. rubellus* can acquire excess amounts of cadmium (Stürzenbaum et al., 2013).

Other biosynthesis, is using *Eisenia fetida*, commonly known as red earthworm or compost worm, is an area of scientific research that aims to utilize the natural abilities of these organisms for nanoparticle synthesis. In the process to get QDs the soil worm is exposed to a soil growth medium that contains cadmium chloride (CdCl₂) and sodium tellurite (Na₂TeO₃) at a concentration of 50 μ g g⁻¹ of soil for both ions. *Eisenia fetida* earthworms have the ability to accumulate heavy metals, including cadmium, in their tissues occurring a biomineralization process, leading to the formation of CdTe (Kominkova et al., 2014; Neuhauser, Loehr, Milligan, & Malecki, 1985).

	NPs	Organism	T(°C)	NPS (nm)	Shape	Synthesis	Ref.	
YEAST	CdTe	Saccharomyces cerevisiae	25–35 °C	Monodisperse 2–3.6nm, QDs	Cubic	Extracellular	(Bao, Hao, et al., 2010)	
		Rhodotorula mucilaginosa PA-1	30 ℃	3.2 nm, QDs	Spherical	Extracellular	(Cao et al., 2020)	
	CdSe	Saccharomyces cerevisiae		2.8 nm QDs		Intracellular	(Brooks & Lefebvre, 2017)	
		Saccharomyces cerevisiae BY4742		well-dispersed 3 nm QDs		Intracellular	(Shao et al., 2018)	
		Candida utilis WSH02-08	30 ℃	4.38 nm QDs	Spherical	Intracellular	(Tian et al., 2017)	
		Saccharomyces cerevisiae	30 °C	2.69 nm QDs	Spherical	Intracellular	(Cui et al., 2009) (R. Zhang et al., 2017)	
		Saccharomyces cerevisiae	30 °C	7 nm QDs		Intracellular	(Sur et al., 2019)	
BACTERIA	CdTe	Escherichia coli	37 °C	5.98 – 4.8 nm	crystal- shaped.	Intracellular	(Monrás et al., 2012) (Kominkova et al., 2014)	
		Escherichia coli	30 °C	Monodisperse 2–3nm, QDs	cubic zincblende structure	Extracellular	(Bao, Lu, et al., 2010)	
		Pseudomonas, Psychrobacter, Shewanella	15–28 °C		Spherical	Intracellular	(Plaza, Gallardo, Straub, Bravo, & Pérez-Donoso, 2016)	
	CdSe	Providencia vermicola	37 °C	2-4 nm QDs	cubic	Intracellular	(Rawan, Bahig, Abdullah, & Nasser, 2019)	
		Escherichia coli	30 ℃				(Z. Yan et al., 2014)	
		Pseudomonas aeruginosa	30 °C	25-40			(Ayano et al., 2015)	
		Bacillus licheniformis	10 °C		Spherical		(Z. Y. Yan et al., 2017)	
		Bacillus amyloliquefaciens	13 °C	6-8 nm QDs			(Z. Y. Yan et al., 2018)	
	CdSe	Helminthosporum solani	10 °C	10-15 nm QDs		Extracellular	(Suresh, 2014)	
		Fusarium oxysporum	15 °C	Monodisperse 2–7nm, QDs	Spherical	Extracellular	(S. A. Kumar et al., 2007) (Yamaguchi et al., 2016)	
		Rhizopus Stolonifer	25 °C				(Mareeswari et al., 2016)	
FUNGI	FUNGI	CdTe	Fusarium oxysporum	30 °C	Polydisperse 15–20nm, QDs		Intracellular	(Syed & Ahmad, 2013)
		Trametes versicolor	20 °C		Spherical		(Qin et al., 2018)	
		PbSe	Aspergillus terreus	15 °C	Polydisperse 20–50nm diameter, QDs		Extracellular	(Jacob et al., 2014)
		Trichoderma sp.	25 °C			Intracellular	(Diko et al., 2020)	
ALGAE	CdSe	C. pyrenoidosa and S. obliquus	33 °C	6nm	spherical	Intracellular	(Zhang et al., 2018a)	
	ZnSe	Gracilaria corticata	25 -35 °C	55.5 nm	Spherical	Intracellular	(Mirzaei et al., 2020)	
SOIL ORGANISMS	CdTe	Lumbricus rubellus earthworm	25 °C	Monodisperse 2.33+0.59nm, QDs	Spherical	Intracellular	(Stürzenbaum et al., 2013)	
		Eisenia fétida earthworm	25 °C	Monodisperse 2.33+0.59nm, QDs	Spherical	Intracellular	(Kominkova et al., 2014)	

Table 1. Summary of the biosynthesis of Se-Te-based Chalcogenides Nanoparticles with yeast, bacteria,fungi, fungi, algae and soil organisms.

T=temperature; NPS=nanoparticle size; NPs=Nanoparticles

6. CONTROL SIZE AND MORPHOLOGY OF NANOPARTICLES

Controlling the size and shape of selenium-tellurium (Se-Te) based nanoparticles during biosynthesis follows similar principles to other nanoparticle systems. There are some strategies that can be considered for achieving size and shape control specifically for Se-Te nanoparticles.

The ratio of selenium (Se) to tellurium (Te) precursors can influence the composition and resulting properties of Se/Te nanoparticles. Adjusting the molar ratio of Se and Te precursors can impact the size and morphology of its respective nanoparticles. Different ratios can lead to the formation of distinct crystal structures and affect the growth kinetics, thereby influencing the size and shape of the nanoparticles (Manna, Scher, & A. Paul, 2000; Peng et al., 2000). Even, parameters such as temperature, pH, and reaction time play a critical role in Se-Te nanoparticle biosynthesis. Optimizing these parameters can enable control over the growth kinetics and nucleation processes, leading to the formation of nanoparticles with specific sizes and shapes. Higher temperatures and longer reaction times may result in larger nanoparticles, while the temperature is less than 50°C and shorter reaction times can favor the formation of smaller nanoparticles. Calcination can remove the organic residues, increase the porosity, and change the phase of your nanoparticles. Etching can reduce the size, change the shape, and create hollow or porous structures of your nanoparticles. Coating can improve the dispersion, stability, and biocompatibility of your nanoparticles (Manna, Milliron, Meisel, Scher, & Alivisatos, 2003; Manna et al., 2000; Peng et al., 2000; Qu & Peng, 2002; S. M. Wu et al., 2015).

The use of additives or surfactants can help control the growth and aggregation of Se-Te nanoparticles during biosynthesis. These compounds can stabilize the nanoparticle surface, prevent uncontrolled growth or aggregation, and influence the resulting size and shape. Surfactants can also act as capping agents, affecting the surface energy and morphology of the nanoparticles (Manna et al., 2003).

Seed-mediated growth is a sophisticated synthesis technique that employs preformed nanoparticles as seeds or templates for the controlled growth of desired nanoparticles, such as Selenium (Se) and Tellurium (Te) chalcogenides. This method involves two main stages: nucleation and growth (Y. Li et al., 2013; S. M. Wu et al., 2015; R. Zhang et al., 2017) . Initially, small nanoparticles (seeds) with diameters typically less than 20 nm are synthesized, which serve as nucleation sites for the subsequent growth phase. During the growth stage, additional precursor materials are introduced, and the reaction conditions, including temperature, precursor concentration, and the presence of shape-directing agents, are carefully controlled to dictate the size and morphology of the resulting nanoparticles (Y. Li et al., 2013; S. M. Wu et al., 2015; R. Zhang et al., 2017) .

. The use of templates or confined environments further enhances the control over the growth process, allowing for the creation of complex shapes and structures. By manipulating the size and shape of the seed nanoparticles and precisely adjusting the reaction parameters, researchers can achieve a high degree of control over the size and morphology of the final Se/Te nanoparticles, tailoring their properties for various applications in fields such as electronics, optics, and catalysis (Y. Li et al., 2013; S. M. Wu et al., 2015; R. Zhang et al., 2017).

For example, using porous materials, emulsion droplets, or other confined spaces as reaction environments can influence the growth and shape of the nanoparticles. Templating methods involve the use of organic or inorganic templates that guide the growth of Se-Te nanoparticles into specific shapes (Manna et al., 2003, 2000; Peng et al., 2000; Qu & Peng, 2002; S. M. Wu et al., 2015).

Genetic engineering of microorganisms involved in Se-Te nanoparticle biosynthesis can offer control over the synthesis process. Modifying the genetic makeup of the organism can enhance the expression of enzymes or proteins that regulate nanoparticle growth, leading to desired size and shape characteristics.

It is important to note that the specific strategies and parameters for size and shape control may vary depending on the synthesis approach and the properties of the Se-Te system under investigation. Optimization and systematic exploration of these factors are necessary to achieve precise control over the size and shape of Se-Te nanoparticles during biosynthesis (Dahoumane et al., 2017; Manna et al., 2003)

7. CHARACTERIZATION METHODS

Characterization techniques of the nanoparticles allow to obtain detailed physicochemical properties of the nanoparticles like their size, shape, stability, crystallinity, surface chemistry, and optical properties among others. The suitable analytical techniques including X-ray diffraction (XRD), transmission electron microscopy (TEM), scanning electron microscopy (SEM), ultraviolet-visible spectrophotometry (UV-Vis) and color change.

7.1.X-ray Diffraction

X-ray diffraction, or XRD, is one of the most used characterization methods for determining crystallographic structures throughout the intensities of the X-rays and scattering angles that emerge from the material (Artioli, 2017; Stanjek, 2004). For example, the crystal structure of CdSe, CdTe, ZnSe, and PbSe exhibits distinctive diffraction peaks that are indexed to a variety of planes, including single crystal, cubic, amorphous, crystalline, monoclinic, and spherical, among others. Also, it is possible to predict the morphology and particle size determining the crystallinity phase (Ayano et al., 2015; Borghese et al., 2016, 2017; Jacob et al., 2016; Kamaraj, Venkatachalam, Arumugam, & Berchmans, 2014; Kominkova et al., 2014; Z. Y. Yan et al., 2017; Z. Zhang et al., 2018).

7.2. Transmission electron microscopy and Scanning Electron Microscopy

Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) are powerful technique used to analyze the morphology and structural properties of semiconductor nanocrystals such as CdSe, CdTe, PbSe, and ZnSe, providing crucial insights into their size, morphology, and structural properties, which are vital for their application in various fields such as electronics and photonics (Cumberland et al., 2002; Monaheng, Parani, Gulumian, & Oluwafemi, 2019).

TEM images show CdSe nanocrystals with a diameter of approximately 4.5 nm shown in **figure 3**. These nanocrystals can exhibit quantum confinement effects, which are significant due to their small size (Ayano et al., 2015; Bao, Hao, et al., 2010; Borghese et al., 2016; Yamaguchi et al., 2016; Z. Yan et al., 2014; Z. Zhang et al., 2018)..

ZnSe nanocrystals are observed to be around 2.8 nm in size shown in **figure 3**. The TEM images reveal distinct structural characteristics that are essential for understanding their electronic properties and potential applications in optoelectronics (Ayano et al., 2015; Bao, Hao, et al., 2010; Borghese et al., 2016; Yamaguchi et al., 2016; Z. Yan et al., 2014; Z. Zhang et al., 2018).

The synthesis of glutathione-capped CdTe/CdSe/ZnSe quantum dots has been reported, with TEM revealing spherical morphology and an average size of about 5.2 nm shown in **figure 3**. These quantum dots have shown promising properties for biological applications due to their eco-friendly synthesis method (Cumberland et al., 2002).



Figure 3. (a) CdSe Nanocrystals: The images reveal CdSe nanocrystals with an average diameter of 4.5 nm, showcasing their distinct structural characteristics. (b) ZnSe Nanocrystals: The ZnSe nanocrystals are observed to be approximately 2.8 nm in size, highlighting their unique morphology. (c) CdSe/ZnS
Core/Shell Nanocrystals: These nanocrystals feature a core size of 3.7 nm, resulting in a final diameter of 5.4 nm. The images display the core/shell structure, which is critical for enhancing optical properties. Taken from (Cumberland et al., 2002).

SEM images of ZnSe/ZnS quantum dots demonstrate their core-shell structure and morphology. These images indicate a spheroidal shape and provide insights into their dispersion on substrates, critical for applications in devices (Sun et al., 2018).

7.3.UV-Vis spectrophotometry

UV-Vis spectrophotometry is a commonly used technique for characterizing the biosynthesis of selenium-tellurium (Se-Te) nanoparticles. It provides valuable information about the optical properties of the nanoparticles, including their absorption and bandgap energy. Here's how UV-Vis spectroscopy is utilized in the biosynthesis of Se-Te nanoparticles:

Monitoring nanoparticle formation: UV-Vis spectroscopy can be used to track the formation of Se-Te nanoparticles during the biosynthesis process. As the nanoparticles are synthesized, they exhibit characteristic absorption peaks in the UV-Vis spectrum. By taking UV-Vis measurements at different time intervals during the reaction, the formation and growth of the nanoparticles can be monitored. The appearance and intensity of absorption peaks can provide insights into the kinetics and progress of nanoparticle formation (Ayano et al., 2015; Sur et al., 2019; Suresh, 2014; Suresh et al., 2011; Yamaguchi et al., 2016; Z. Yan et al., 2014; Z. Y. Yan et al., 2017; Z. Zhang et al., 2018).

Determination of nanoparticle size and shape: The absorption spectra of Se-Te nanoparticles can provide information about their size and shape. Nanoparticles with

smaller sizes typically exhibit blue-shifted absorption peaks compared to larger particles. By analyzing the position and intensity of the absorption peaks, it is possible to estimate the average size of the nanoparticles. This information can help in assessing the effectiveness of size control strategies during biosynthesis (Ayano et al., 2015; Bao, Hao, et al., 2010).

Optical bandgap determination: The UV-Vis spectra of Se-Te nanoparticles can also provide insights into their optical bandgap energy. The absorption onset or edge in the spectrum corresponds to the energy required for electronic transitions in the nanoparticles. The bandgap energy can be calculated from the absorption edge using appropriate models or method of estimating the band gap energy of amorphous semiconductors using optical absorption spectra. The optical bandgap information is crucial for understanding the electronic properties and potential applications of the nanoparticles.(Ayano et al., 2015; Bao, Hao, et al., 2010; Yamaguchi et al., 2016; Z. Yan et al., 2017; Z. Zhang et al., 2018)..

Stability and aggregation analysis: UV-Vis spectroscopy can be used to assess the stability of Se-Te nanoparticles over time. Changes in the absorption spectrum can indicate the occurrence of aggregation or agglomeration of the nanoparticles. An increase in the broadening or redshift of absorption peaks may suggest nanoparticle aggregation, while a stable and consistent spectrum indicates good stability of the nanoparticles(Ayano et al., 2015; Bao, Hao, et al., 2010; Qin et al., 2018; Z. Yan et al., 2014; Z. Zhang et al., 2018).

7.4.Dynamic Light Scattering

Dynamic Light Scattering (DLS) is a key technique for characterizing the size distribution of selenium (Se) and tellurium (Te) based chalcogenide nanoparticles in suspension. DLS measurements have shown that Se based NPs tend to be monodisperse, while Te based NPs often exhibit a polydisperse distribution (Ansary et al., 2022; Nwoko et al., 2021). DLS can detect sizes down to 2 nm with high sensitivity, making it suitable for precisely measuring nanoparticle dimensions (Covered, 2005; Jacob et al., 2016). However, DLS may struggle with polydisperse samples, as larger particles can dominate the scattering signal and mask contributions from smaller particles (Covered, 2005; Jacob et al., 2016). Overall, DLS provides essential data on the size distribution of Se-Te chalcogenide nanoparticles, which is critical for understanding their properties and applications in fields like electronics and biomedicine (Ansary et al., 2022; Covered, 2005; Jacob et al., 2016; Nwoko et al., 2021).

7.5. Atomic Force Microscopy

Atomic Force Microscopy (AFM) is a critical technique for characterizing CdSe and CdTe nanoparticles, providing high-resolution three-dimensional imaging at the subnanometer level (AFM Workshop, 2021). AFM allows researchers to analyze the morphology, size, and surface features of these nanoparticles, which are essential for understanding their properties and potential applications (Capitán et al., 2019). For instance, studies have shown that AFM can effectively complement other characterization methods such as X-ray diffraction (XRD) and transmission electron microscopy (TEM) to provide a comprehensive view of the nanoparticles' structural characteristics (Mourdikoudis, Pallares, & Thanh, 2018). In the case of CdSe, AFM has been utilized to investigate the formation of nanodots as shown in figure 3., while for CdTe, it aids in examining surface roughness and particle distribution (Capitán et al., 2019; Mourdikoudis et al., 2018). The combination of AFM with other techniques enhances the reliability of the results and facilitates a deeper understanding of the nanoparticles' behavior in various environments (Capitán et al., 2019; Mourdikoudis et al., 2019; Mourdikoudis et al., 2018).



Figure 3. A) 2D view of CdSe NPs. B) 3D view of CdSe NPs. Taken from (AFM Workshop, 2021).

7.6.Color Changes

During the biosynthesis of CdSe, CdTe, PbSe and ZnSe, distinct color changes are observed, which are indicative of the formation and growth of these nanoparticles.

In CdTe Nanoparticles, the solution color transitions from greenish-yellow to light orange and eventually to red as the nanoparticles form. This progression is associated with changes in size and concentration, with the red color indicating larger particle sizes and potential aggregation(Kolny-Olesiak, Kloper, Osovsky, Sashchiuk, & Lifshitz, 2007).

Similar to CdTe, CdSe nanoparticles exhibit color changes during synthesis, often shifting from yellow to orange and then to red as they grow in size. The absorption peaks in UV-Vis spectra also reflect these changes, indicating size-dependent optical properties (Hosnedlova et al., 2020).

While specific studies on color changes in PbSe are less common, ZnSe nanoparticles have been reported to show a color change from yellow to green, which is related to their size and the formation of quantum dots. The optical properties of ZnSe are also influenced by the synthesis conditions, leading to variations in color (Mary Jacob et al., 2014; Mirzaei et al., 2020).

In general, the color changes observed across these nanoparticles are linked to their size, shape, and aggregation state. Smaller nanoparticles typically exhibit blue shifts in their absorption spectra, leading to lighter colors, while larger aggregates can result in red shifts and darker colors (Hosnedlova et al., 2020; Kolny-Olesiak et al., 2007; Mary Jacob et al., 2014; Mirzaei et al., 2020).

8. **BIOMEDICAL APPLICATIONS**

Chalcogenides, which are materials containing chalcogen elements such as sulfur, selenium, and tellurium, have several potential biomedical applications due to their unique optical, electrical, and thermal properties (Ahluwalia, 2016; Ferro, Florindo, & Santos, 2021). There are several reports describing the use of Te-Se-based nanoparticles for specific bioapplications, with many of these nanoparticles being classified as quantum dots (Abdel-Salam et al., 2020). Some of the QDs have a wide range of biomedical applications due to their unique physicochemical properties, including their small size, large surface area to volume ratio, and high reactivity to treat or diagnose some diseases (Ventola, 2017; Wang, Tang, & Kotov, 2005). Some of the fields where Se-Te-based chalcogenides nanoparticles have shown results are in bioimaging (Ballou, Lagerholm, Ernst, Bruchez, & Waggoner, 2004; X. Wu et al., 2003), biosensors (Andreadou et al., 2016), and drug delivery (Badıllı, Mollarasouli, Bakirhan, Ozkan, & Ozkan, 2020; Matea et al., 2017)

Successful implementation of Te-Se chalcogenide nanoparticles in biomedicine requires consideration of several aspects including biocompatibility of the nanoparticles, stability

of the molecules, size and shape, surface chemistry, toxicity and optoelectronic properties.



Figure 4. Biomedical fields of Selenium and Tellurium based chalcogenides Nanoparticles. Created with BioRender.com

8.1.Bioimaging

Bioimaging refers to techniques that allow for the non-invasive visualization of biological activities in real time. The goal of bioimaging is to minimize any disruption to living processes. Moreover, it is often used to gain information on the 3-D structure of the observed specimen from the outside, i.e. without physical interference. In a broader sense, Bioimaging also includes methods visualizing biological material that has been fixed for observation (Lahoti & Jogdand, 2022; X. Zhang & Booker, 2024).

QDs have a narrow and symmetric spectral line profile that makes them perfect for simultaneous detection of several fluorophores using a single light source showing photoluminescence properties (Wang et al., 2005). Therefore, Se/Te based chalcogenides nanoparticles have shown promising results in bioimaging due to their strong near-infrared (NIR) absorption and emission of light. NIR light can penetrate deep into biological tissues, allowing for non-invasive imaging of biological structures and processes. Se-Te-based nanoparticles can also be functionalized with targeting ligands or biomolecules, allowing for their specific binding to biological targets. For example, Sentinel lymph node mapping in small and large animals may be accomplished successfully without the need of a radioactive tracer by using NIR CdTe(CdSe) core(shell) type II QDs with a polydentate phosphine coating. This method also provides picture guidance during the procedure. Additionally, it can focus attention on the specific area of the Sentinel lymph node that is most likely to have cancerous cells shown in Figure 3(Kim et al., 2004; Wang et al., 2005).



Figure 5. (a) The images depict a mouse that received an intradermal injection of 10 pmol of NIR QDs in its left paw. The left image shows the pre-injection NIR autofluorescence, the middle image is a color video captured 5 minutes post-injection, and the right image displays the NIR fluorescence image taken at the same time. An arrow highlights the presumed axillary sentinel lymph node. All fluorescence images maintain consistent exposure times and normalization. (b) After a reinjection with 1% isosulfan blue, the sentinel lymph node was examined 5 minutes later. The left image shows a color video, while the right image displays NIR fluorescence images. Both isosulfan blue and NIR QDs were localized in the same lymph node, as indicated by arrows. Taken from (Kim et al., 2004)

On the other hand, some reports show the CdSe QDs are used as biological imaging agents recognizing specific antibodies or antigens (Bruchez et al., 1998; Wang et al., 2005; X. Wu et al., 2003). For example, to identify tumors it is used an immunofluorescent labeling using QDs conjugated (CdSe/ZnS core-shell Nanocrystals) linked to immunoglobulin G (IgG) and streptavidin to label the breast cancer marker Her2, on the surface identifying nuclear antigens inside the nucleus proving that QDs-based offers an efficiency and advantages over organic dyes used to label cancer cells (Wang et al., 2005; X. Wu et al., 2003).

On the other hand, it is created a class of bioconjugated and polymer-encapsulated QDs (ZnS-capped CdSe) probes in prostate cancer imaging and targeting being suitable for conjugation to both therapeutic and diagnostic substances since they are brilliant, stable, and have a flexible triblock copolymer structure, targeting to tumor areas using both passive and active mechanisms (Gao et al., 2004; Wang et al., 2005).

Also, the use of Core-shell CdSe-ZnS QDs with methoxy-poly(ethylene glycol) surface coating has been successful as a marker for fluorescence imaging obtained in any type of tissue sections and in living animals. Long-term tests have shown that these QDs continue to glow in vivo for at least four months (Ballou et al., 2004). Fluorescence imaging depends on illuminating fluorescently labeled proteins or other intracellular molecules using a specific wavelength of light, ideally close to the peak of the fluorophore's excitation spectrum, and detection of light emitted at a longer wavelength (Ettinger & Wittmann, 2014).

8.2.Biosensors

In recent years, novel approaches for the identification and quantification of biologically significant compounds have been proposed and developing, utilizing the special features of QDs. Some of the biosensors are designed for the detection of antigens. For example, a visual fluorescence sensor method for the identification of the Carcinoembryonic Antigen biomarker (CAE), which for the signal readout, CdTe/CdSe QDs and Glucose oxidase (GOD) impregnated on paper, oxidizing the glucose to create gluconic acid and hydrogen peroxide, which dampened the CdTe/CdSe QDs fluorescence (Qiu et al., 2017; Wagner et al., 2019). An immunosensor able to detect low levels of CA-125 serum biomarker in patients with ovarian cancer using an acid-modified gold electrode functionalized with silica-coated gold nanoparticles, CdSe QDs, and antiCA-125 monoclonal antibody (Johari-Ahar et al., 2015; Matea et al., 2017). There has also been created a technique for the detection of Leishmania-specific surface antigens that makes use of magnetic beads to separate the analytes from the solutions and CdSe QDs for detection and the method has proved to have a low limit of detection for Leishmania DNA (Andreadou et al., 2016).

The study of the properties of the QDs is important to know its potential for possible bioapplications. In the case of Te-based chalcogenides nanoparticle applications, it is reported that by employing the electrostatic layer-by-layer (LBL) self-assembly technique, a blood glucose sensor has been created using multilayer films containing glucose oxidase (GOD) and CdTe quantum dots (QDs). The photoluminescence property of CdTe QDs allows the high sensivity of the glucose sensor. It is achieved through the adjusting of the layers of QDs and GOD to get the linear range and sensitivity for glucose testing. It is not necessary the sample pretreatment, showing a complete successfully

employed to measure the blood glucose concentration in serum samples, and it demonstrated acceptable repeatability and accuracy (X. Li et al., 2009). Another application is the immunomagnetic separation technique for rapid enumeration of E. coli, throughout magnetic nanoparticles Fe3O4@Au to separate bacterias and CdTe QDs are used for labeling, getting a high sensitivity and specificity (Dogan et al., 2016).

8.3.Drug Delivery

Due to their distinct physicochemical properties, quantum dots (QDs) are regarded as effective fluorescent markers utilized in drug delivery systems for tracking the metabolism of pharmaceuticals in the body (Badıllı et al., 2020). It is reported the use of CdSe/ZnS QDs functionalized with matrix metalloproteinase-9 (MMP-9) detachable, PEG, cathepsin B cleavable GEM and targeting ligand CycloRGD for targeted pancreatic cancer therapy through Gemcitabine (GEM)-programed nanovectors (Matea et al., 2017). It was obtained by cellular internalization process potencieted by the acumulation of QDs in the tumor when the CycloRGD is exposed and PEG corona is removed by MMP-9 promoving the release GEM (Han et al., 2017; Matea et al., 2017).

In order to have a theranostic approach in cancer therapy, paclitaxel (PTX) is active pharmacentical ingredient(API) co-loaded in nanostructured lipid carriers along with CdTe, CdS, ZnS QDs showing at 80% of encapsulation efficacy with a tumor growth supression rate of 77.85% (Matea et al., 2017; Olerile et al., 2017).

On the other hand, it was proposed an hybrid silica nanocapsules containing ZnSe:Mn/ZnS core–shell and the anticancer drug PTX demostrating improved solubility and sustained released of drug in 12 hours (Matea et al., 2017; Zhao et al., 2017).

8.4.Bioremediation

The application of Se -Te based nanoparticles in bioremediation is an emerging area of research that focuses on utilizing these nanoparticles for the detoxification and recovery of hazardous materials from the environment due to their unique properties, including their ability to act as efficient agents in bioremediation processes (X. Liang et al., 2019; Sabuda et al., 2020). These nanoparticles can protect living organisms from oxidative damage and exhibit antimicrobial properties, making them valuable in environmental cleanup efforts(X. Liang et al., 2019).

Both Se and Te nanoparticles can be synthesized biologically through microbial processes. This method not only helps in detoxifying Se and Te oxyanions but also facilitates the recovery of these elements in a less toxic nanoparticle form. For instance, microorganisms can reduce toxic selenite (Se(IV)) and tellurite (Te(IV)) to their elemental forms, which can then be harvested as nanoparticles (X. Liang et al., 2019; Piacenza et al., 2018).

This approach combines nanotechnology with bioremediation techniques. Nanoparticles enhance the degradation of pollutants by increasing the surface area for reactions and improving the bioavailability of contaminants. They can facilitate the breakdown of organic pollutants and heavy metals in contaminated soils and water(X. Liang et al., 2019; Sabuda et al., 2020).

Some investigations examined the use of the Se-Te-based chalcogenides NPs in other fields than the prior bio-applications. Some Se-Te-based NPs are excellent electrochemical-based sensors applied on agricultural fields for detection of organophosphate pesticides (H. Liang, Song, & Gong, 2014; Xue et al., 2016). For instance, the detection of organophosphorus pesticides (OPs) utilizing CdTe QDs and bi-enzyme-immobilized eggshell membranes has been developed showing at excellent stability with a long shell-life at least 2 months. This method has shown promise in determining the concentration of pesticides in alimentary industry (H. Liang et al., 2014; Xue et al., 2016).

8.5.Antimicrobial

Cadmium selenide (CdSe) and cadmium telluride (CdTe) nanoparticles have gained attention for their antimicrobial applications due to their unique properties and effectiveness against various pathogens.

CdSe nanoparticles exhibit notable antimicrobial activity, particularly against multidrugresistant bacteria. Research has demonstrated that CdSe nanoparticles can enhance the antibacterial properties of antimicrobial peptides (APs). For instance, AP-loaded CdSe nanoparticles (AP-CdSe NPs) have shown strong antibacterial effects against Escherichia coli and Staphylococcus aureus, achieving high rates of bacterial cell death (98.76% and 99.13%, respectively) in both in vitro and in vivo studies. The mechanism of action involves the generation of reactive oxygen species (ROS) and disruption of bacterial cellular functions, which leads to cell lysis and death (Deshpande, Garg, Patel, Bhatt, & Keharia, 2013; W. Li et al., 2021).

The incorporation of CdSe nanoparticles into therapeutic strategies not only improves the efficacy of existing antimicrobial agents but also enhances their stability and bioavailability. This makes CdSe nanoparticles a promising candidate for developing new antibacterial treatments, especially in the context of rising antibiotic resistance (Deshpande et al., 2013; W. Li et al., 2021)..

While specific studies on CdTe nanoparticles are less prevalent compared to CdSe, CdTe is also recognized for its potential antimicrobial properties. CdTe nanoparticles can similarly disrupt bacterial cell membranes and interfere with metabolic processes, contributing to their bactericidal effects. Their application in antimicrobial coatings and drug delivery systems is being explored, as they can provide a dual function of targeting bacteria while delivering therapeutic agents effectively (Ali, Ovais, Cui, Rui, & Chen, 2020; Sánchez-López et al., 2020).

9. CONCLUSIONS

In conclusion, the biosynthesis of selenium-tellurium (Se-Te) based chalcogenide nanoparticles offers a promising approach for the production of these materials with unique properties. The biosynthesis of Se-Te chalcogenide nanoparticles holds great potential for a wide range of applications in fields such as optoelectronics, catalysis, sensors, and biomedicine.

Through the utilization of microorganisms or biological systems, Se-Te nanoparticles can be synthesized in a more environmentally, friendly and sustainable manner compared to traditional chemical synthesis methods.

Various crucial factors influence the biosynthesis process and the resulting nanoparticles. The selection of microorganisms, optimization of growth medium composition, control of precursor concentration and ratio, and the manipulation of reaction conditions play pivotal roles in achieving desired nanoparticle properties such as size, shape, and composition.

Furthermore, the biosynthesis approach offers the possibility of tailoring nanoparticle properties through genetic engineering and manipulation of microorganisms, providing

additional avenues for optimizing and customizing the synthesis process. Additionally, the use of reducing agents, stabilizers, and proper bioreactor design further aids in controlling the synthesis process and nanoparticle characteristics.

Characterization techniques like UV-Vis spectrophotometry provide valuable insights into the biosynthesis process. UV-Vis allows for real-time monitoring of nanoparticle formation, determination of size and shape based on absorption peaks, assessment of optical bandgap energy, and evaluation of nanoparticle stability and aggregation.

Overall, the biosynthesis of Se-Te based chalcogenide nanoparticles represents a promising and sustainable route for the production of these advanced materials, with potential for significant advancements in various technological and scientific domains. Further research and development in this field will contribute to expanding our understanding and utilization of these nanoparticles for practical applications.

10. REFERENCES

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