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Review article

Nanotechnology on agent identification, diseases diagnosis and therapeutic approaches

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Highlights

- Asian countries have more publications in the field of nanoparticles worldwide.
- Biological and physical nanoparticle synthesis can be produced using eco-friendly technology.
- Metallic nanoparticles have shown antimicrobial and low cytotoxicity activity.
- Raman/SERS spectroscopy emerged as a powerful alternative to diagnostic method.

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KEYWORDS
Nanotechnology;
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Abstract: Nanotechnology is the most promising technology field in the 21st century, providing benefits and scientific advances to global development. New nanotechnological devices, platforms, and production systems have shown a wide range of applicability, especially for nanoparticle applied to microorganism detection/diagnosis, treatment, and drug delivery. This review aims to point the main advances in the area through several publications involving the production and use of nanoparticles applied to the clinical sector. Nanoparticles are produced by using different physical, chemical, or biological methods. Several platforms for diagnosis have been developed, including vaccines, drug-delivery systems, and novel treatments, thus innovating the pharmacological and diagnostic areas. Immunoassay, DNA hybridization, and Raman/SERS are the most common methods used in the identification of microorganisms and diagnosis. Moreover, metallic and oxide-metallic nanoparticles have been used to inhibit the growth of filamentous fungi, yeasts, oomycetes, bacteria, viruses, and protozoans. The present review shows an increase in nanotechnology application, especially regarding nanoparticles in the biotechnology and medical fields, contributing to a revolution in this area.

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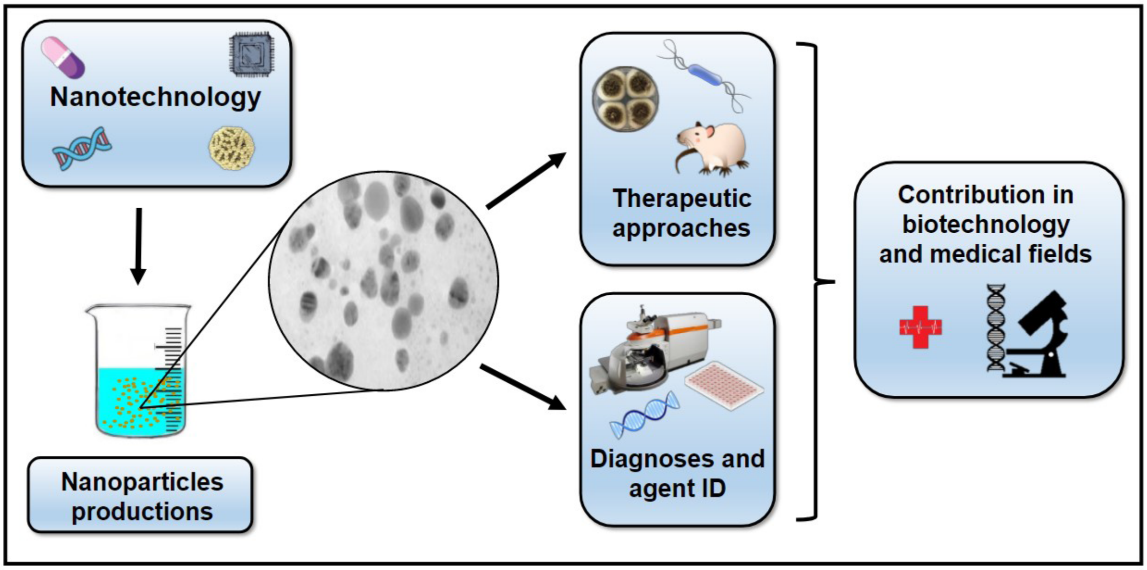
Graphical abstracts



Introduction

Nanotechnology is the most promising field of technology in the 21st century, bringing benefits to global development and scientific advances in the food industry, agriculture, medical science, and engineering (Chung et al., 2017; Thiruvengadam et al., 2018). One of the main subfields in this large area is that of is nanomaterials, which can be divided into two classes: nano-objects of natural origin and nano-objects of anthropogenic origin. Moreover, inside these classes, the nanomaterials can be divided into three types: nanoparticles, nanotubes or nanowires, and nanofilms or nanolayers (Gao et al., 2019; Schaming & Remita, 2015).

Recently, the production and application of these nanomaterials, especially nanoparticles, have attracted a growing interest due to the exceptional characteristics such as small size, multifunctionality, biocompatibility, and versatility in multidisciplinary fields. In particular, metallic, carbon, and oxide nanoparticles hold a place of great importance in a wide range of potential applications in the clinical, optical, and electronics fields (Khan et al., 2019; Venkateswarlu et al., 2018). Nanoparticle materials have a larger surface to volume ratio, which gives them increased reactivity properties on several reactions when compared with their macro metric equivalents (Guerra et al., 2018).

In the clinical field, nanoparticles cover different sectors, from diagnosis and to treatment of infectious and non-infectious diseases (Malekjahani et al., 2019; Noor et al., 2020; Sadani et al., 2020). For instance, diagnostic tools have used nanoparticles to detect specific molecules, whether they are proteins, DNA, or other markers of interest (Cinti et al., 2017; Rizzo et al., 2021; Sheffee et al., 2021; Vaquer et al., 2021) Thus, technological advances in nanoparticle production and development can lead to more efficient, low cost, and label-free based medical devices (Gahlawat & Choudhury, 2019).

Moreover, due to their ability to inactivate and inhibit viruses, bacteria, filamentous fungi, and yeasts, nanoparticles may offer alternative methods to classical disinfection protocols used in the clinical area and have demonstrated efficiency in limiting the advance of the microbial resistance crisis (Lee et al., 2019; Kobayashi & Nakazato, 2020). In this context, the present review highlights the recent advances in the nanotechnological field related to biotechnological development in the last decade. For this purpose, a literature review on the Scopus, PubMed, and LILACS databases were performed using the search terms “nanotechnology” and “Diagnosis or microbiology” (Figure 1). Therefore, this review focuses on the use of nanoparticles in microbiological diagnosis and treatment of infectious diseases and noninfectious diseases, recent advances and highlighting future perspectives.

Nanotechnology from the beginning and nowadays

Nanotechnology was an emerging ‘new branch of science’, when Nobel laureate Richard P. Feynman presented his 1959 lecture “There’s Plenty of Room at the Bottom”, notwithstanding, the term nanotechnology was used for the first time to describe nanosized materials in 1974 (Taniguchi, 1974). Nowadays, nanotechnology comprises the design, production, and use of nanostructured systems and the growing, assembling of such systems either mechanically, chemically, or biologically to form nanoscale architectures, systems, and devices (Pinheiro et al., 2011). In addition, nanomaterials are used to improve the characteristics of their similar larger-sized counterparts, as they can present self-healing, self-cleaning, anti-freezing, antibacterial, antifungal, anti-cancer properties and therefore can increase the durability and quality of engineering and medical devices (Jeevanandam et al., 2018; Rashidiani et al., 2018).

Some nanomaterials, as nanoparticles, can naturally occur in volcano ashes, oceans, dust and are present in plants and animals (Buzea et al., 2007). The first evidence

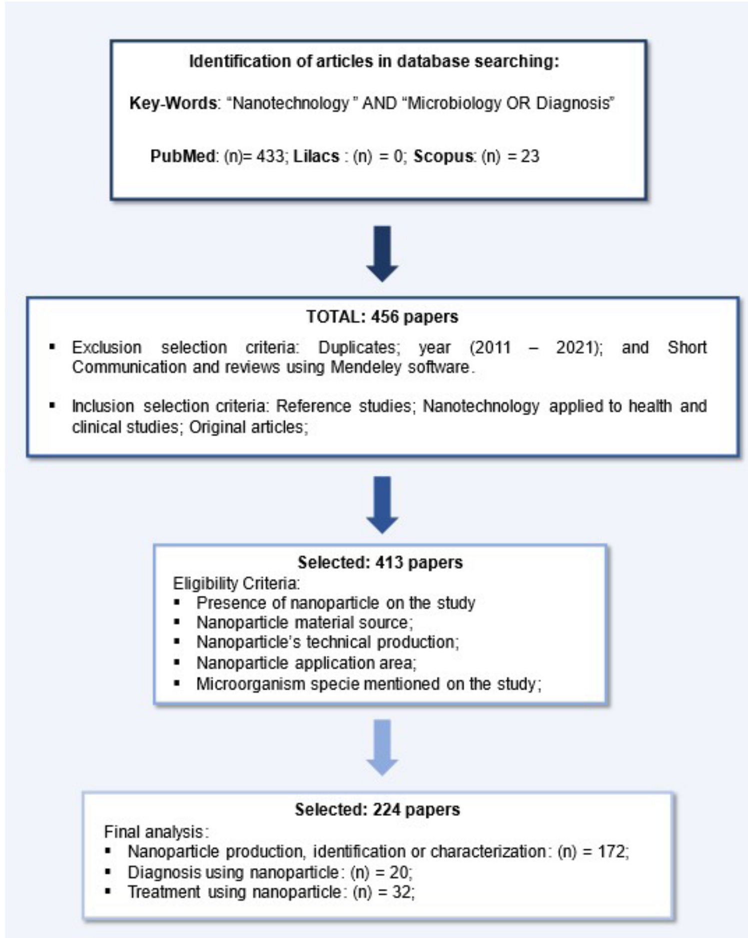


Figure 1. Workflow of the search methodology in the different databases.

of the synthesis of metallic nanoparticles (NPs) via chemical methods dates back 1500 years ago when Egyptians and Mesopotamians started making glass using metals, which was assumed as the beginning of the metallic nanoparticle era (Johnson-McDaniel et al., 2013; Schaming & Remita, 2015). The term 'nanoparticle' originated from the Greek word 'nano' that means 'dwarf or small', indicating a size of 10−9 (one billionth) of a meter (You et al., 2013). Afterward, in the 4th century, a Roman glass cup made of dichroic glass, called Lycurgus Cups, was notorious for displaying different colors: red when light beam illuminates it from the inside and green when light beam reflects from the front. This incoming light alteration leads to different scattered wavelength (Leonhardt, 2007). Later, the deep red glass was manufactured using this process worldwide, e.g., in the mid-19th century, a similar technique was used to produce the Satsuma glass in Japan (Nakai et al., 1999).

In the modern era (Figure 2), Michael Faraday reported the synthesis of a colloidal gold nanoparticle (AuNP) solution, which is the first scientific description to report NP preparation. He also revealed that the optical characteristics of gold (Au) colloids are dissimilar compared to their respective macro representants (Faraday, 1857), suggesting the colloidal vivid colors were related to the interaction between light and very small particles.

Subsequently, Mie (1908) explained, using Maxwell's electromagnetic theory of light scattering by a sphere the reason behind the colors in the metal colloids. During the 1990s, the first companies to commercialize products with nanomaterials were created, and in 2003, the first application of nanoparticles in medical devices was described (Hirsch et al., 2003).

More recently, there have been about 1814 nanotechnology-based products commercially available in 32 countries (Vance et al., 2015). Additionally, regarding nanoparticle research, there has been an increase in the number and quality in terms of publication. Asia is the most prominent, with India, China, South Korea, and Iran representing over 40% of total studies published in the last five years (Figure 3).

Among these studies, it was observed the occurrence of publications focusing on the use of metal nanoparticles and metal oxide in the diagnosis and treatment of antibiotic multi-resistant microorganisms (Wang et al., 2018; Mobed et al., 2020; Goel et al., 2021; Bahari et al., 2021) and to diagnose emerging infectious diseases (Asghari-Paskiabi et al., 2019; Hassanpour et al., 2020; Zhang et al., 2021b). Moreover, these countries also invest in the nanotechnology sector as they host the main companies in the nanotechnology production area (Vance et al., 2015; Jeevanandam et al., 2018; Liu et al., 2009).

In Brazil, concerning to the therapeutic area, the research focuses on the application of metallic nanoparticles, metallic

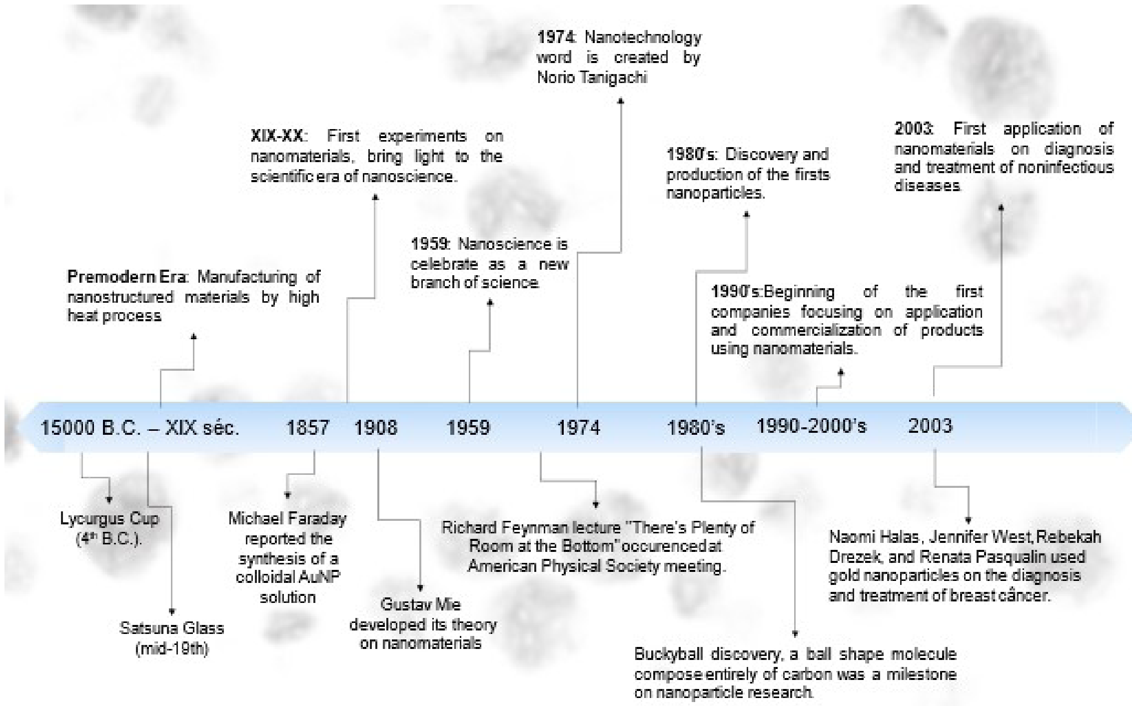


Figure 2. Chronological order of the main facts and pioneering marks of nanotechnology development.

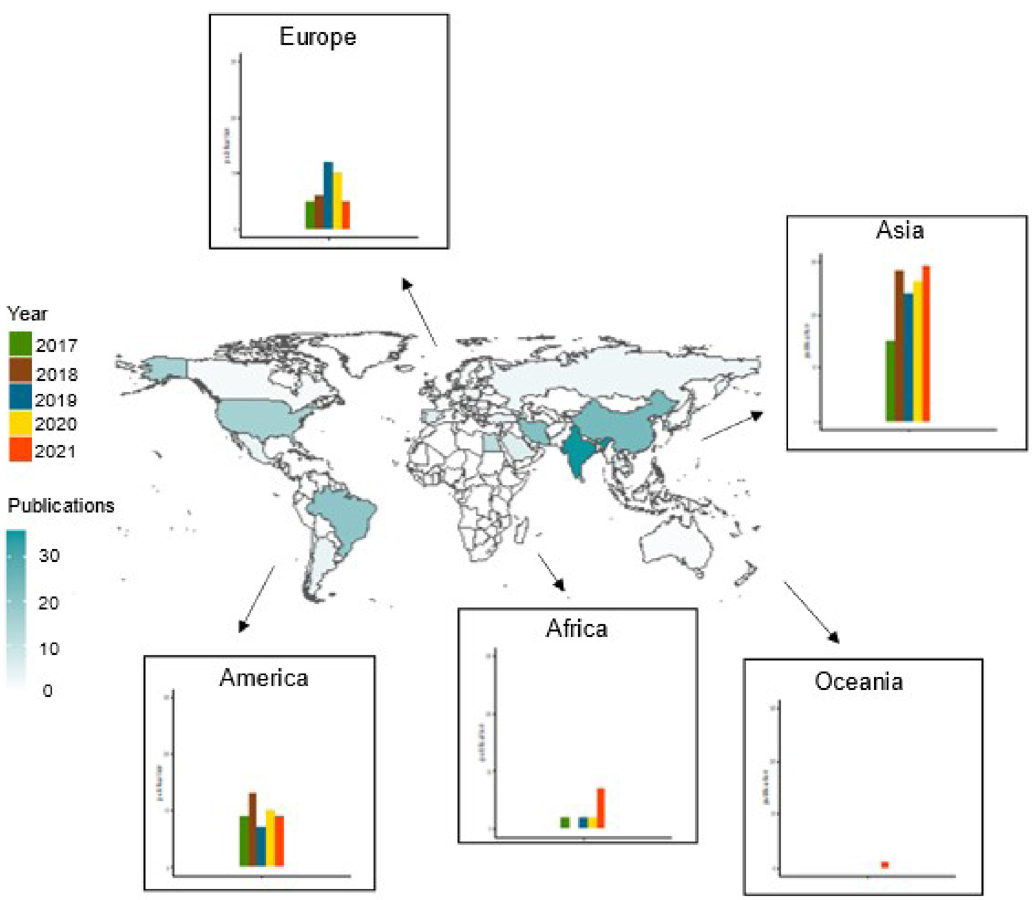


Figure 3. Number of publications related to nanoparticle production worldwide. Data were obtained from a review of 222 studies in 42 countries. Black arrow indicates the number of publications per year in each continent. The colors on the graphs represent a different year in the period analyzed. The number varies between 30 publications in 2021 in Asia and a single publication in Oceania. The colors on the map represent the total number of publications in each country from 2017 to 2021.

oxide, proteins, and carbons nanoparticles and on the development of biosensors to diagnose endemic infectious diseases such as the dengue virus (Basso et al., 2018) and *Plasmodium vivax* (Regiart et al., 2021). Moreover, there is the development of nanovaccines for the Zika virus (Favaro et al., 2021) and treatments for fungal infections using drug-delivery systems (Arias et al., 2020) and biological silver NP (Bocate et al., 2019; Valente et al. 2020; Cavali et al., 2021) in addition to the development of nanoparticles against carcinogenic cells, stimulating the apoptosis process (Andrade et al., 2020).

Nanoparticles production (physical, chemical, and biological synthesis)

Synthesis methods for nanoparticles (NPs) are typically grouped into two categories: top-down and bottom-up approaches (Figure 4). The first approach involves the breaking down of the bulk material into nano-sized structures or particles. This approach may address mechanical milling or other physical (Horikoshi et al., 2013) techniques like laser ablation, chemical methods (Al-Shawafi et al., 2017; Ghayempour et al., 2017), and volatilization of a solid followed by condensation of the volatilized components (Figure 5AB). Using this characterization, it is possible to produce metal nanoparticles usually large in size (close to 1 µm) and they have wide size distribution (Bhushan et al., 2014; Guisbiers et al., 2017; Guerra et al., 2018; Ealia & Saravanakumar, 2017).

The alternative approach, bottom-up, refers to the buildup of material from the bottom: atom-by-atom, molecule-by-molecule, or cluster-by-cluster in a gas phase or solution (Luechinger et al., 2010). The latter approach is more popular and usually less expensive in the synthesis of NPs and can be identified in two sub-categories: (1) Vapor (Gas) Phase Methods (e.g., pyrolysis, inert gas condensation); (2) Liquid Phase Methods (e.g., solvothermal reaction, sol-gel, microemulsion method). The Figure 5B represents an example of chemical reduction of nanoparticles production (Bhushan et al., 2014; Ealia & Saravanakumar, 2017; Zhou et al., 2019).

Moreover, the biosynthesis of nanoparticles as emerging bionanotechnology (the intersection of nanotechnology and biotechnology) has been explored since this technology is able to synthesize eco-friendly NPs. (Acay, 2021; Allend, et al., 2021; Gahlawat and Choudhury, 2019; Van Staden et al., 2021).

The biological methods to produce NPs in this field include microorganisms-assisted biogenesis, bio-templates-assisted biogenesis, and plant extracts-assisted biogenesis (Dhand et al., 2016).

The microorganisms can produce nanoparticles because of their metabolism (Bocate et al., 2019; Joshi et al., 2019). According to literature, there are two recognized forms: 1) metal ions first trapped on the surface or inside microbial cells and then reduced to nanoparticles in the presence of enzymes (Figure 5C); 2) A a second way is through the production of organic polymers, which can impact nucleation, favoring (or inhibiting) the stabilization of the first mineral seeds (Li et al., 2011; Acay, 2021; Allend et al., 2021; Gahlawat & Choudhury, 2019; Mohanpuria et al., 2008; Van Staden et al., 2021).

Furthermore, it is important to determine some parameters in the synthesis of NP production, and one of the consequences of these parameters is, for example, the "size effect", which implies a drastic reduction in the melting point of ultrafine particles compared to the bulk. NPs can move easier at lower temperatures, as the high surface area to volume ratio of NPs provides a large driving force for diffusion. A second size-dependent feature of NPs is the dielectric constant. The use of NPs embedded in electronic devices allows one

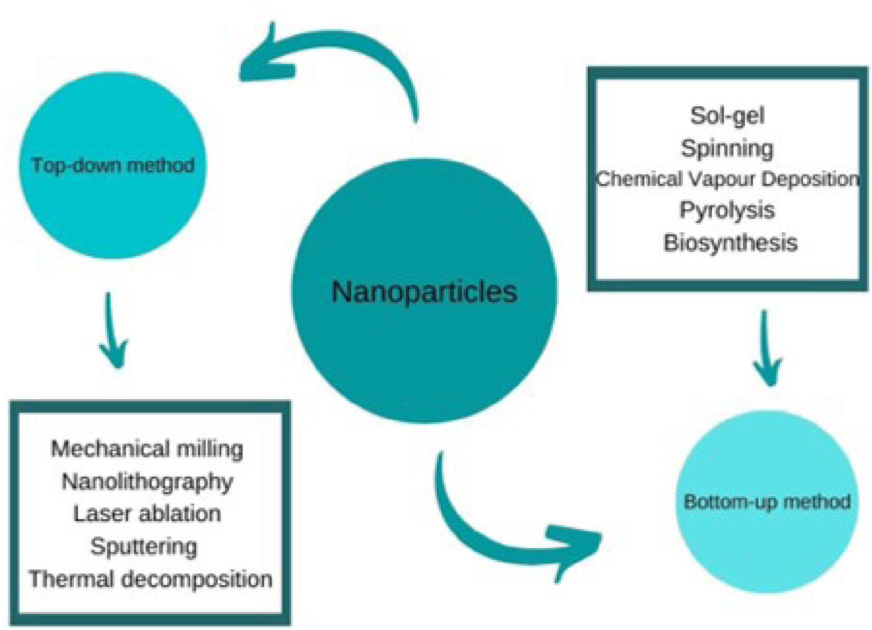


Figure 4. Nanoparticles production schematic diagram. Nanoparticles have two categories of production (Bottom-up method and Top-down method).

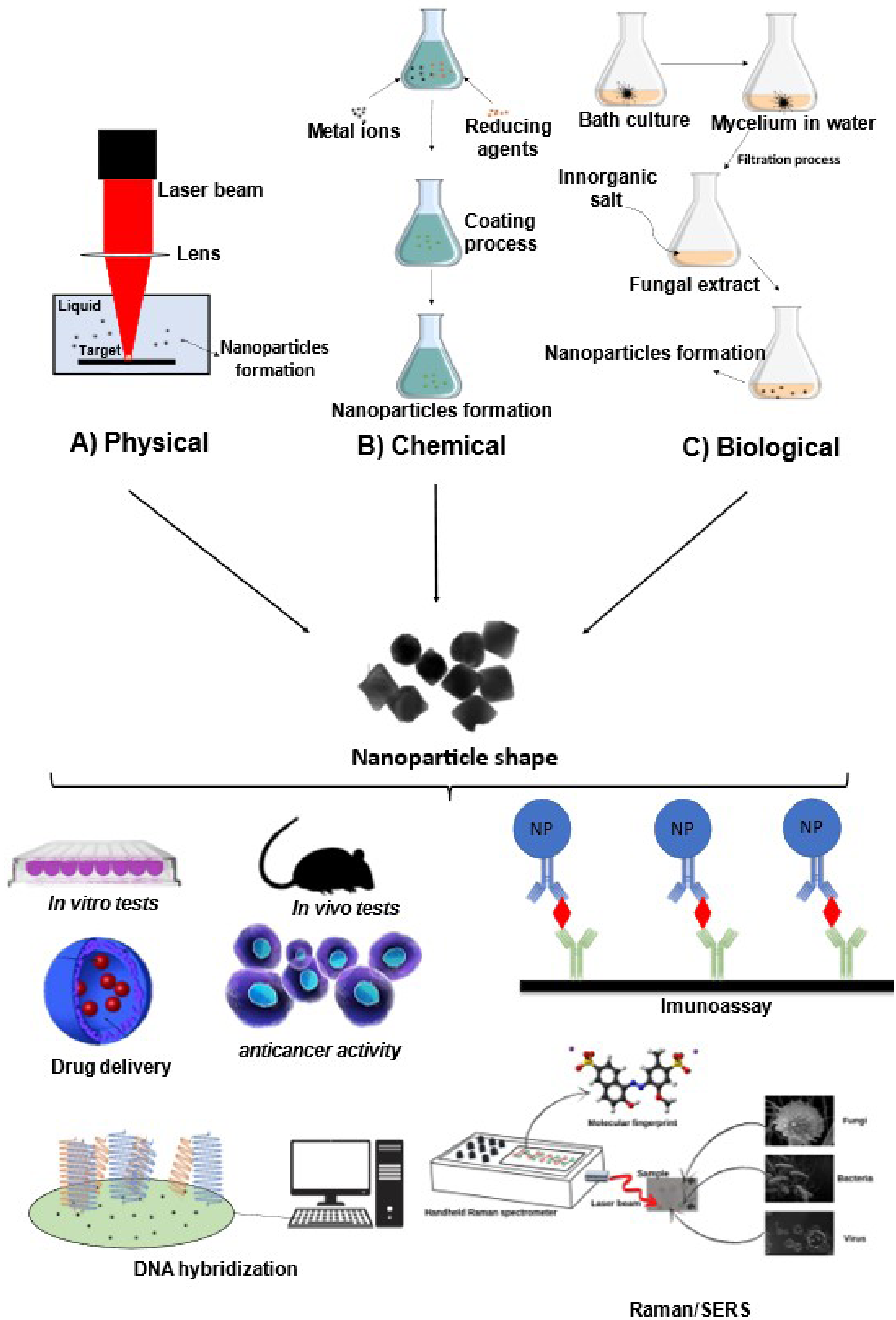


Figure 5. Production and application of nanoparticles (NPs) in the biotechnological and health area. There are three forms of NPs production: A) Example of physical production by ablation using laser beam; B) Example of chemical production by salt reduction; C) Example of biological production using biotransformation by fungal strains. Nanoparticles can be employed in the Treatment and Diagnosis/Detection of infectious and noninfectious diseases.

to improve product performance by making smaller devices with high dielectric constants (Bhushan et al., 2014).

The interaction between with the optical electromagnetic field and the NPs can lead to a coherent oscillation of the conduction band electrons. This happens when they are small enough to absorb the light with a specific wavelength. The physical properties are feature size-dependent, and Surface Plasmon Resonance (SPR) is the concept of interaction with light with different wavelengths according to the metal and size. Nanocomposites and nanocrystalline materials show differences in their physical properties compared with microstructures. Some of these differences are caused by SPR. (Bhushan et al., 2014).

NPs are generally characterized in particle size distribution, morphology, charge determination, and surface hydrophobicity. More specific characterizations depend on the properties of NPs synthesized such as magnetic characterizations for NPs featuring magnetic properties (e.g., Fe, Fe3O4) and electric characterizations for conductive or dielectric NPs such as Ag, Cu, Au, SiO2, BaTiO3, etc. (Bhushan et al., 2014). Magnetic NPs containing pure transition metals – or some mixture of their oxides – are one of the most studied nanomaterials in view of the potential, ubiquitous applications in quite different areas, the most notable being biomedicine, sensor technology, and magnetic recording (Bhushan et al., 2014).

Nanoparticles for biosensor constructions in the diagnosis and detection of infectious and noninfectious diseases

Recent studies bring light to an extensive application of nanoparticles in the health area, mainly to detect pathogenic microorganisms (viruses, bacteria, and fungi) or molecules (proteins and genetic material) using biosensors (Barroso et al., 2018; Jangpatarapongsa et al., 2021; Jijie et al., 2018; Kalita et al., 2017; Lopreside et al., 2019). Biosensors are devices for the chemical detection of biological structures (enzymes or cells), which are coupled with an electrochemical transducer and a detector that makes it possible to reveal the target material without the need for the application of substances (Cinti et al., 2017; Basso et al., 2018; Ganganboina et al., 2020).

The equipment used for detection is based on optical phenomenon surface plasmon resonance as they use colorimetric metal nanoparticles, such as gold, silver, and copper produced by physical, chemical, and biological methods (Figure 5). These nanoparticles are applied to increase the sensitivity and effectiveness in detecting microorganisms, reducing time, costs, and the need for advanced laboratory structures to perform the diagnosis (Jain et al., 2020; Landry et al., 2017; Li et al., 2018; Safarpour et al., 2021). Immunoagglutination using gold (AuNP) and DNA probes immobilization on surfaces coated with metallic nanoparticles (AuNPs and MNPs) where the DNA probe on the surface of AuNPs was a signal reporter by fluorescence are some examples of this application (Raji et al., 2021).

The immunoassay test from the association of metallic nanoparticles was reported with monoclonal antibodies that bind conjugately to epitopes (molecules, DNA, cells) of the microorganism on a surface with an affinity to the antibody (Basu et al., 2004; Basso et al., 2018; Mikaelyan et al., 2017). This surface contains antibodies specific for the antibody associated with the nanoparticle, which retains them and allows visualization by colorimetric change (Raji et al., 2021). This association has shown to be a promising platform for outbreak elucidation and diagnosis of various agents (Bhattarakosol, et al., 2018; Chen et al., 2018; Chen et al., 2019; Elahi et al., 2019; Vedova-Costa et al., 2021), as well as monitoring the evolution of neurodegenerative diseases such as Alzheimer's and diabetes (Popli et al., 2018).

DNA probe hybridization tests have proven to be an alternative to diagnose microorganisms (Mobed et al., 2020; Nagraik et al., 2020; Zopf et al., 2019). This technique functions by annealing the ssDNA (single-stranded DNA) to a probe designed for a specific microorganism attached to a metal nanoparticle (Figure 5). The annealing between the DNA sample and the probe generates an electrochemical interaction detected by a microchip serving to identify and quantify the pathogen in certain substrates (Ling et al., 2019; Hassanpour et al., 2020).

In response to the demand for a non-destructive, label-free, versatile, non-invasive technique for biochemical analysis, Raman spectroscopy has been explored (Tahir et al., 2021; Rajan et al., 2019). Raman spectroscopy is used to determines the molecular composition of samples in a variety of states, but there are limitations due to the amount of analyte required and the signal to ratio intensity for this technique (Tahir et al., 2021). To solve the problem, surface-enhanced Raman spectroscopy (SERS) has emerged as a fast-growing research area with high sensitivity that, in some cases, can even allow a single molecule detection (Moisoiu et al., 2019; Nie et al. 1997). The SERS effect was first reported by Fleischmann et al., working with pyridine adsorbed onto Ag electrodes in 1974 (Aoki et al., 2012).

Some of the most fundamental characteristics of SERS effects to effective analytical techniques are: 1. narrow spectral bands, easier to identify as vibrational fingerprints of determined molecules; 2. non-destructive analysis; 3. minimum sample required quantities; 4. the possibility of carrying out measurements in biological fluids; 5. simultaneous detection of different molecules (multiplexing); 6. possibility of carrying out on-site analysis with portable instruments (Etchegoin & Le Ru, 2008; Zrimsek et al., 2016). Those characteristics are evidence of an effective analytical technique that has excellent potential in bioanalysis and diagnosis, including some applications *in vivo*, biological sensing, drug delivery, and live-cell imaging assays (Tahir et al., 2021; Etchegoin & Le Ru, 2008; Zrimsek et al., 2016). Thus, the Raman/SERS shows a promising field when combined to or used in biotechnology.

Metallic and oxide-metallic nanoparticles in the infectious diseases' therapeutic application

The application of nanotechnology for the treatment of infectious diseases has increased in recent years, mainly regarding the antimicrobial effect of these nanoparticles (Table 1). Considering the number of works applying metallic

Table 1. Metallic nanoparticles and metal oxide applied against bacteria, fungi, virus e protozoans.

Nanoparticle type	Nanoparticle production	Microorganism				References
		Bacteria	Fungi and Oomycetes	Virus	Protozoa	
Metallic	Biological	*Klebsiella* sp., *Escherichia* sp., *Staphylococcus* sp., *Micrococcus* sp., *Pseudomonas* sp., *Acinetobacter* sp., *Cutibacterium* sp., *Streptococcus* sp., *Acinetobacter* sp.	*Pyricularia* sp., *Colletotrichum* sp., *Alternaria* sp., *Fusarium* sp., *Phytophthora* sp., *Aspergillus* sp., *Microsporum* sp., *Candida* sp., *Pythium* sp.	-	*Allovahlkampfia* sp., *Leishmania* sp.	Allend et al. (2021), Ammar et al. (2019), Asghari-Paskiabi et al., 2019, Bagirova et al. (2020), Bocate et al. (2019), Van Staden et al. (2021), Souza et al. (2019), Farrag et al. (2020), Godon-Falconí et al. (2020), Jalab et al. (2021), Joshi et al., 2019, Mohammadyari et al. (2020), Neethu et al. (2020), Nogueira et al. (2019), Noor et al. (2020), Valente et al. (2020).
(Silver or Gold)	Chemical	*Klebsiella* sp., *Pseudomonas* sp., *Salmonella* sp., *Escherichia* sp., *Staphylococcus* sp., *Prevotella* sp., *Parabacteroides* sp.	*Candida* sp.	-	-	Baker et al. (2020), Begum et al. (2021), Emam et al. (2017), Mohammadyari et al. (2020), Nogueira et al. (2019), Nikolopoulou et al. (2020), Shruthi et al. (2019), Wysocka-Król et al. (2018), Zawisza et al. (2020), Zhang et al. (2018), Zhang et al., (2021a).
	Physical	-	*Candida* sp.	HSV-1	-	Guisbiers et al. (2017), Halder et al. (2018).
Oxide-Metallic	Biological	*Klebsiella* sp., *Escherichia* sp., *Staphylococcus* sp.	-	-	-	Potbhare et al., (2019a), Potbhare et al., (2019b).
(Cooper, Iron or Zinc)	Chemical	*Staphylococcus* sp., *Escherichia* sp., *Pseudomonas* sp.	*Candida* sp.	-	-	Namasivayam et al. (2021), Shi et al. (2020).

and metal oxide nanoparticles for the treatment of infectious and noninfectious disease, it is important to consider the attractive physicochemical properties of the nanoparticles, the extension of antimicrobial effects, the capacity of the nanoparticle to access the target, and even their cytotoxicity to the host (Vallet-Regi et al., 2007).

The use of metallic and metal oxide nanoparticles in the last five years has been investigating the sensitivity of species of bacteria, fungi, oomycetes, and protozoa, as shown in the Table 1. There are different action mechanisms of metallic and metal oxide nanoparticles to inhibit microorganisms (Figure 6).

The wide application of these nanoparticles for the treatment of diseases demonstrates their potential for possible use in the clinical area for a promising antimicrobial agent, especially action against bacteria and fungi. Concerning Figure 6, it is evident that the entry of nanoparticles in a cell occurs through three main pathways (endocytosis, diffusion, and channel proteins). The release and concentration of metals (constituents of nanoparticles) induce the formation of reactive oxygen species (ROS), and these react with different cellular components (DNA, mRNA, tRNA, proteins, cell membrane). Consequently, a series of structural and physiological changes are observed in the microbial cell, such as loss of cell signaling, ATP and protein synthesis, damage to replication, transcription, and translation, in addition to the disruption of the plasma membrane, causing cell death of the infectious agent. Therefore, with the application of

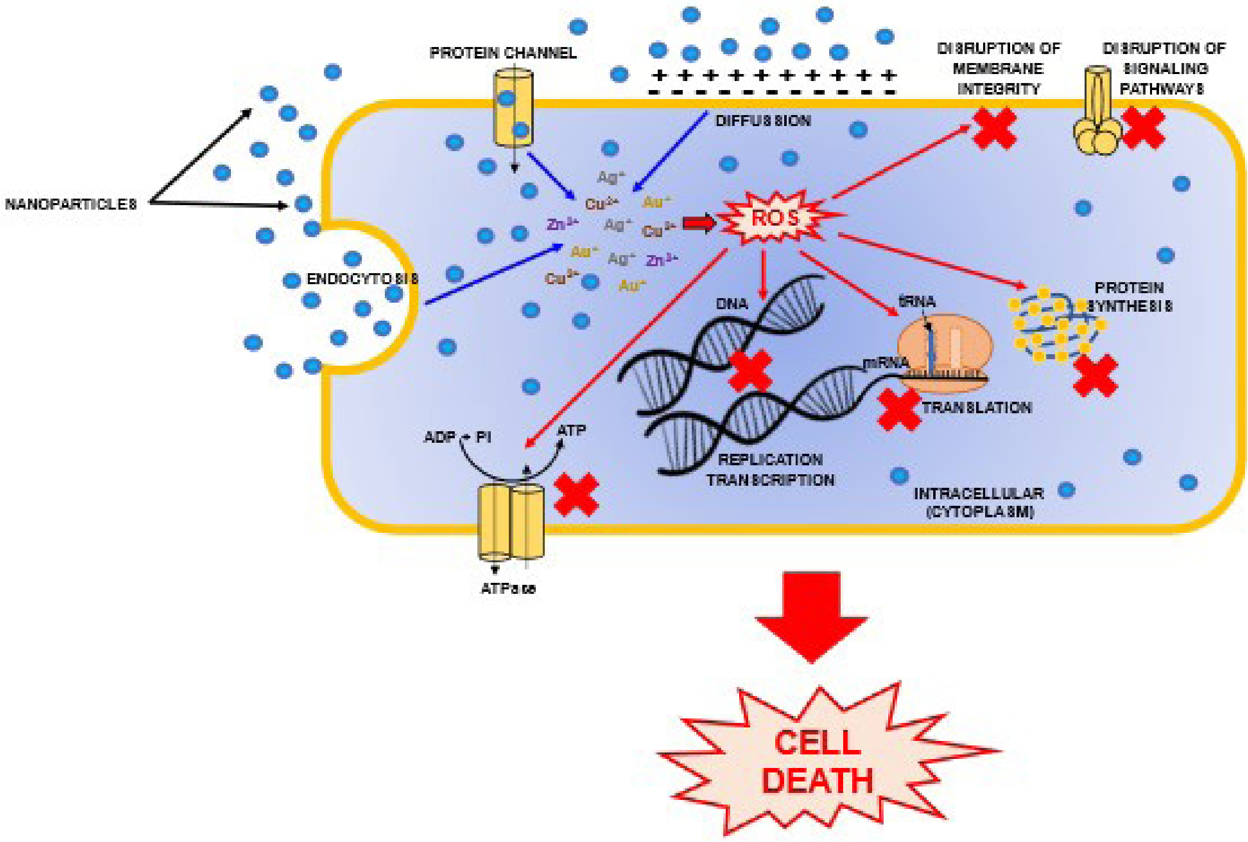


Figure 6. Mechanisms of action of metallic and oxide-metallic nanoparticles with antimicrobial effect. It is observed that these nanoparticles enter (blue arrows) through endocytosis, protein channel and diffusion (by the change in the electrical charge of the plasma membrane indicated by + and -), causing different damage (red arrows) to cellular components: deoxyribonucleic acid (DNA), messenger ribonucleic acid (mRNA), transporter ribonucleic acid (tRNA) and ATPase, through the formation of reactive oxygen species (ROS) induced by the metal concentration as Au+ (gold), Ag+ (silver), Cu2+ (copper) and Zn2+ (zinc), consequently, cell death is evidenced for the inhibition of the cell functions (indicated by the red X), as the adenosine triphosphate (ATP) synthesis from adenosine diphosphate(ADP) and inorganic phosphate (Pi) (Figure adapted from Mba & Nweze, 2021).

these nanoparticles and considering their mechanisms of action, it is possible to improve, and infectious diseases treatment caused by drug-resistant microorganisms more effectively (Mba & Nweze, 2021).

To study the antimicrobial effects, different methodologies are performed in vitro and in vivo (Figure 5). The main in vitro methods are the disk diffusion and microdilution tests in broth to show a minimum inhibitory concentration (MIC). In addition, minimal fungicidal and minimal bactericidal concentration analyses evaluate whether the nanoparticles are lethal at certain concentrations and the reduction in biofilm production in bacteria and fungi (Guisbiers et al., 2017; Bocate et al., 2019). Furthermore, the use of metallic nanoparticles and metal oxide in association with antimicrobials enhances the effects and reduces the concentrations used. In *in vivo* tests using New Zealand's rabbits, metallic nanoparticles have the potential to fungal subcutaneous lesions treatment (Valente et al., 2020).

The use of nanoparticles in the therapeutic area has been increasing due to the demand for rigorous evaluation about toxicity to regulate the safe use of different nanoparticles. The nanoparticles show this effect applied in human and other animal tissues due to the organ-dependent toxicity effect, specifically the target cell (Kong et al., 2011). Considering that metal nanoparticles are extensively produced in different methods, some of them can be applied as potential carrier agents for substances (Dobson, 2006; Wilczewska et al., 2012). Several types of nanoparticles can be used in a drug delivery system; the review shows more than 13 types of nanoparticles indicated (Shinde et al., 2012). The most widely applied nanocarriers being polymeric nanoparticles, liposomes, nanopores, and quantum dots (Desai et al., 1996; Allen, 1997; Cherian et al., 2000; Smeets et al., 2006). Liposomes have been used more extensively due to their efficiency in reducing toxicity and the possibility of early degradation of the system after introduction into the target organism (Shinde et al., 2012). Toxicity effects may have differences, even in nanoparticles consisting of the same material, as size and shape also directly influence this aspect (Kong et al., 2011).

The delivery of systemic therapy has been evidenced by different nanoparticles administered in the targeting, such as silica, crystals, chitosan, protein (Figure 5). Drug delivery to target cells has been reported for diseases such as ovarian cancer (Roberts et al., 2017), Parkinson, depression and anxiety, from inhibition of monoamine oxidase B (Wu et al., 2021); biofilms of pathogenic fungi such as *C. albicans* (Arias et al., 2020); eye treatments (Buosi et al., 2020); HIV viral infections (Mukadam et al., 2020) or vaccines for viral infections (Favaro et al., 2021).

Currently, novel applications of nanoparticles have shown remarkable advances in the diagnosis and treatment of infectious and non-infectious diseases, as they show to be one of the most efficient, low-cost, and dynamic forms to elucidate outbreaks and epidemics, which reduces costs and speeds up the correct diagnosis by health professionals, either in the detection of possible environmental sources, as in the use of Raman spectroscopy or the diagnosis of difficult-to-elucidate diseases, like endemic mycoses, or multi-resistant bacteria. Moreover, the pre-clinical analysis of metal nanoparticles toxicity and antimicrobial activity indicate that the nanoparticles could be applied to treatment of infection diseases associated to microorganisms. This review is not intended to be a definitive study on the application of nanoparticles in clinical settings; the results point that this technology is a promising field of research and new drugs using nanoparticles in their composition are expected in the coming years, which may be a solution for solving several emerging diseases whose clinical demands are imperative.

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