MULTIDISCIPLINARY & HEALTH EDUCATION JOURNAL, Vol. 6. No. 1, 2024, Pages 944-956.
http://journalmhe.org

REVIEW ARTICLE / ARTÍCULO DE REVISIÓN

Antimicrobial Potential of Metallic Nanoparticles: Pathogens *Staphylococcus aureus* and *Klebsiella pneumoniae*

Potencial Antimicrobiano de Nanopartículas Metálicas: Patógenos *Staphylococcus aureus* y *Klebsiella pneumoniae*

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Article history:
Received November 13, 2023
Received in revised from November 15, 2023
Accepted November 19, 2023
Available online February 10, 2024

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A B S T R A C T

The increase in antimicrobial resistance has allowed biotechnology to continue evolving. In this sense, this review article focuses on the various mechanisms that both *Staphylococcus aureus* and *Klebsiella pneumoniae* have in causing infections in humans and how, through various virulence factors, they can evade the action of antibiotics. Based on this, it is also shown how nanomaterials, such as metal nanoparticles, are an excellent alternative to respond to the current problem with these two pathogens.

Keywords: biotechnology, pathogen, nanoparticles, virulence factor, antimicrobial resistance

R E S U M E N

El incremento de la resistencia antimicrobiana ha permitido que la biotecnología siga evolucionando. En este sentido el presente artículo de revisión se centra en los diversos mecanismos que posee tanto *Staphylococcus aureus* y *Klebsiella pneumoniae* en originar infecciones en el ser humano y como a través de diversos factores virulencia pueden evadir la acción de los antibióticos. Basándonos en esto se muestra también como los nanomateriales, como las nanopartículas metálicas son una excelente alternativa para da respuesta a la problemática actual con estos dos patógenos.

Palabras claves: biotecnologia, patógeno, nanoparticulas, factor de virulencia, resistencia antimicrobiana.

Antimicrobial resistance has become a health problem that affects millions of people around the world. It is caused by bacteria, viruses, fungi and parasites that change their mechanism and stop responding effectively to medications, which makes the treatment of diseases difficult, in addition to causing the spread of the disease to increase, the appearance of forms more serious and even the death of individuals. With the passage of time, it has become a challenge for health personnel who are constantly studying the causes why antibiotics are not able to eradicate different microorganisms, as well as the formation of new mechanisms with hope that they can fight those (Alós, 2015). Self-medication represents the main cause of antimicrobial resistance because excessive and improper intake of these leads to the formation of microorganisms that are capable of

circumventing the effects of antibiotics, using resistance strategies such as receptor mutation, modification of the antibiotic, impermeability of the bacteria, as well as the expulsion of the bacteria, all with the same purpose, which is to prevent the antibiotic from fulfilling its effect on the microorganism.

In 2021, the World Health Organization (WHO) highlighted that antimicrobial resistance represents one of the 10 main public health threats, emphasizing the increase in deaths among children and young adults. Infectious diseases have been one of the leading causes of morbidity and mortality in underdeveloped countries, so adequate and timely treatment of them will have a favorable impact on health indicators (Tong *et al.*, 2015). In this sense, one of the main microorganisms that cause a wide variety of infections is Staphylococcus. aureus , this being an important bacteria for humans causing a wide variety of clinical conditions (pneumonia, infective endocarditis, sepsis, soft tissue infection, among others), which can be acquired in different common environments, as well as in hospital areas, which is more frequent because it is a nosocomial bacteria. (Cuelo and Pascal, 2009). On the other hand, *Klebsiella pneumoniae* is a bacterial pathogen that is also usually associated with infections at the hospital (nosocomial) level, causing infections of the urinary tract, respiratory tract, bloodstream, causing sepsis, mainly affecting immunosuppressed people (Podschun *et al*., 2018., Martin *et al*., 2018)

Due to the previously described problem of antimicrobial resistance, new sciences such as Bionanotechnology have emerged, which have developed and evaluated nanomaterials which have exhibited great antimicrobial capacity. These nanomaterials have included metallic nanoparticles (gold, copper, iron, silver and cadmium), which have been able to observe their ability to generate significant damage to the cell wall, as well as alterations in their vital cellular processes, giving As a result, the inhibition of microbial growth produces a biocidal effect (Hajipour *et al.*, 201; Ramyadevi *et al*., 2012).

The different technologies applied to obtain metal nanoparticles in incredibly small sizes, generally between one and 100 nanometers, have allowed their synthesis which are very useful in different areas such as medicine, electronics, mechanics, environmental, in the textile industry, and others. The synthesis is carried out by different methods, the same being physical and chemical, which present disadvantages not only due to high costs or technological due to the need for specialized equipment, but also due to environmental damage due to the use of organic solvents that increase toxicity and other chemical compounds that are highly aggressive for the environment (Albrecht *et al*., 2006). That is why currently technological efforts are based on biological methods, which are more feasible and environmentally friendly, where the use of plants, isolated biomolecules such as flavonoids, plant extracts, cells and tissues is required, for the synthesis of NPs (Kasithevar *et al.*, 2017., Sarkar and Paul., 2017). There are investigations that demonstrate the antimicrobial capacity of CuNPs, on pathogens such as bacteria, viruses and fungi, where they become potential antimicrobials, therefore they have recently been considered as a new generation of antimicrobial agents (Rosenthal, 2010). Among the studies based on investigating the antimicrobial capacity of NPs, the one by Figueroa Calderón (2019) stands out, titled, “Synthesis of iron nanoparticles from the aqueous extract of Eucalyptus robusta Sm leaves. And evaluation of its antimicrobial activity", which found that the FeNPs exhibited antimicrobial activity against the various microorganisms tested such as: *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus* and *Bacillus subtilis*, finding a close relationship between synthesis conditions and antimicrobial activity. According to the above and taking into account drug resistance by bacterial agents, it is convenient to synthesize new nanomaterials that can be implemented to combat antimicrobial resistance and their possible uses in medical instruments.

Staphylococcus aureus

They are Gram-positive, non-sporulated cocci, found in pairs or clusters of grapes, they are a facultative anaerobic bacteria, non-motile, they do not have a capsule, although some have a slime capsule. It has a thick cell wall composed of acid teichoic acid and peptidoglycan. They can be part of the human microbiota, however, some of them are very successful pathogens, especially the case of *S. aureus*, and many live as commensals and can also be transmitted in environments such as hospital environments, community environments, and is the causal agent of many infectious diseases (Hurtado *et al.,* 2002).

Infections caused by *Staphylococcus aureus*

Skin infections, often causing abscesses, however, the bacteria can travel through the bloodstream (called bacteremia) and infect virtually any part of the body, especially heart valves (endocarditis) and bones (osteomyelitis).

Some staph infections are more likely in certain situations:

- Bloodstream infections: when a catheter inserted into a vein remains in place for a long time
- Endocarditis: when the person injects illegal drugs, has an artificial heart valve or has a catheter in the blood vessels infected
- Osteomyelitis: If *S. aureus* spreads to the bone from a bloodstream infection or from a nearby soft tissue infection, as can occur in people who suffer from deep pressure ulcers or foot ulcers due to diabetes.
- Corticosteroids or other drugs that depress the immune system (immunosuppressants) are taken, or when those affected have been hospitalized due to needing tracheal intubation and mechanical ventilation (called nosocomial pneumonia [in-hospital or contracted in the hospital]) (Bush, 2023).

Resistance mechanism

The resistance mechanisms of *S. aureus* to β-lactams are the production of β-lactamase enzymes, the presence of proteins linked to penicillin (Penicillin Binding Protein, PBP) modified (known as intrinsic resistance to methicillin) and tolerance phenomena. Penicillinase-resistant penicillins (oxacillin, methicillin, cloxacillin) have a molecular structure that protects them against the action of β-lactamases. The resistance mechanism of *S. aureus* to methicillin is based on the synthesis of a new PBP (PBP2a or PBP2´), which exhibits little affinity for methicillin and other β-lactams, blocking the arrival of the antibiotic to its target site and thus produces a resistance pattern (Figure 1).

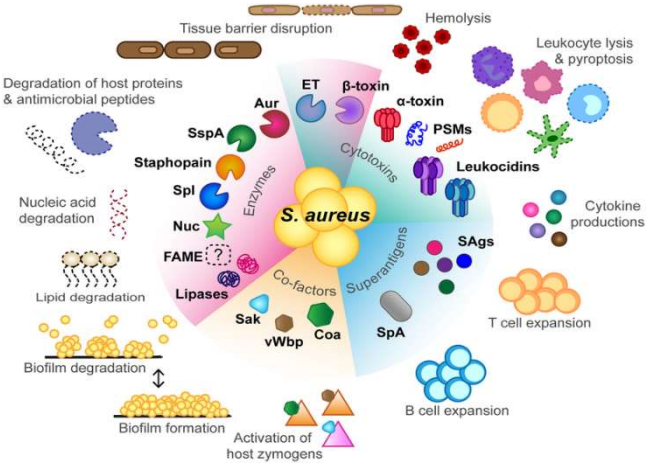

Figure 1. Virulence f *Staphylococcus aureus* actors of Staphylococcus aureus

- The chromosomal genetic element responsible for resistance is the *mecA* gene, whose expression depends on two genes, *mecR1*, which regulates transcription, and *mecI*, which encodes the repressor protein. The β-lactam antibiotic induces a catalytic process in the bacterial membrane, and the *mecA* gene is transcribed and synthesized into the membrane protein PBP2a.
- Other resistance modalities in which the presence of the *mecA* gene is not evident are borderline resistance to oxacillin (Borderline Oxacillin-Resistant *S. aureus*,

BORSA) in bacteria hyperproducing β-lactamases, and modified resistance (Modified *S. aureus*, MODSA) in those that present modifications in the affinity of PBPs 1, 3 and 4, so they exhibit weak resistance to methicillin . Other resistance genes are the blaZ gene and fem (essential factor for methicillin resistance) (García *et al*., 2019).

Klebsiella pneumoniae

It is a Gram-negative bacteria, bacillary in shape, facultatively anaerobic, non-motile, normally encapsulated, forming mucous colonies that can be associated with *Klebsiella pneumoniae*, It is isolated from upper respiratory tract, intestinal flora and skin, they are opportunistic, associated with nosocomial infections, catheters (Echeverry and Castaño, 2010; Tártara, 2013)

Virulence factors

- The capsule is a polysaccharide composed mainly of glucose, galactose, fucose, mannose, rhamnose and uronic acids . This capsule is important for the bacteria since it allows it to evade the immune system, preventing phagocytosis. The *K. pneumoniae* capsule provides high resistance to desiccation, as well as protection against phagocytosis mediated by polymorphonuclear cells and macrophages (Figure 2).
- Pili or fimbriae are non - flagellar filamentous structures that allow the bacteria to adhere to biotic and abiotic surfaces. The main pili described in *K. pneumoniae* are: the type 1 pilus, the "*Escherichia* pilus coli common pilus" (ECP) and the type 3 pilus The type 1 pilus recognizes receptors on cell surfaces that contain mannose and is involved in adhesion to the cells of the renal epithelium, being considered essential to produce urinary tract infection. The ECP pilus is present in all pathotypes and commensal strains of E. coli and is also present in *K. pneumoniae*, being expressed during biofilm formation and upon contact with HeLa epithelial cells. The type 3 pilus in K. pneumoniae plays an important role. in its pathogenicity , conferring adhesion to eukaryotic cells and during the formation of biofilms.

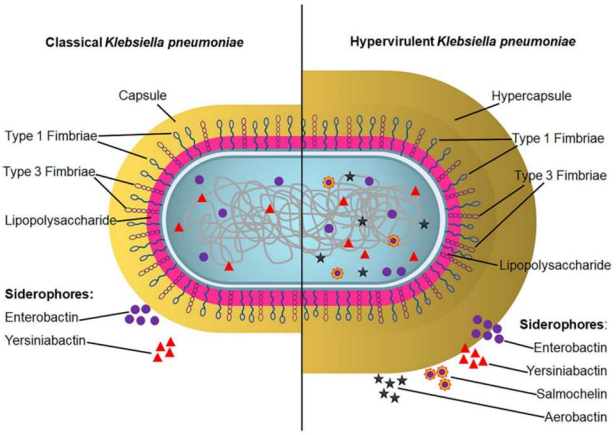

Figure 2. Important virulence determinants in classical and hypervirulent *K. pneumoniae* strains responsible for establishing infection and successful survival inside the host

- Lipopolysaccharide: It has endotoxic activity due to lipid A, which causes the activation of macrophages and induces an inflammatory response with a pyrogenic effect. On the other hand, the polysaccharide chains of the "O" antigen facilitate the initial adhesion process and confer resistance to the microorganism against the bactericidal activity of the serum.
- Siderophores constitute another virulence factor in *K. pneumoniae* since they are molecules that allow it to capture iron under limiting conditions of said metal in the host, iron being an essential factor for bacterial growth, functioning mainly as a catalyst for oxidation reactions. Reduction

of proteins that participate in electron and oxygen transport.

- *K. pneumoniae* presents three main outer membrane proteins (EPS): OmpA, OmpK35 and OmpK36. The OmpA protein is one of the major PMEs in Gram-negative bacteria and in K. pneumoniae it helps with resistance against cationic antimicrobial peptides and evasion of phagocytosis mediated by alveolar macrophages. The OmpK35 and OmpK36 proteins constitute the most important porins in *K. pneumoniae* through which hydrophilic molecules, such as nutrients, diffuse into the bacteria and molecules harmful to the bacteria, such as antibiotics, are expelled to the outside. It has been shown that the absence of these porins remodels the surface of *K. pneumoniae* and increases the adherence of the bacteria to macrophages, which causes greater susceptibility to phagocytosis (De la Cruz *et al*., 2020).
- Urease: This enzyme contributes to the formation and growth of bacteria, which grow in the urinary tract and form infection stones. The hydrolysis of urea will cause a precipitation of inorganic salts (and increase in pH) that leads to incrustation, mainly in catheters, impaired urine flow and biofilm formation that can inhibit antibiotic treatment.
- Biofilm formation: Biofilm formation by *K.pneumoniae* promotes resistance to host killing and antimicrobials. Furthermore, the biofilm community is more resistant to the action of many antibiotics. The biofilm matrix, a dense matrix of proteins, polysaccharides and DNA, prevents the effective diffusion of antibiotics. Biofilms formed by *Klebsiella pneumoniae*, according to the most current studies , present resistance to beta- lactams or ciprofloxacin.
- Antibiotic resistance: in this section we highlight two mechanisms of action. The production of beta-lactamase enzymes (against cephalosporins and penicillins) and carbapenem enzymes (against all beta-lactams, including carbapenems, cephalosporins, penicillins and monobactams) (Galiana, 2022; De la Cruz *et al*., 2020).

Resistance mechanism

In the vast majority of cases *K. pneumoniae* is resistant to ampicillin through the presence of SHV-1 β- lactamase, encoded in the chromosome of the bacteria. The modifications of the enzymes SHV-1 and TEM-1 (responsible for resistance to ampicillin in *E. coli* and other bacteria), and subsequently the emergence of a new family of ESBL, which due to its predilection to hydrolyze cefotaxime was named CTX-M, caused the appearance of numerous types of ESBL. As the genes that encode these β lactamases are carried by plasmids, their transmission to other bacterial species and genera occurred rapidly and their geographical expansion did not wait long. These enzymes, included in group A of the Ambler classification of beta-lactamases, confer resistance to penicillins, cephalosporins (with the exception of cefamyxins: cefoxitin and cefotetan) and monobactams; β- lactamase inhibitors (sulbactam, tazobactam and clavulanic acid) block their activity. The clinical consequences of resistance caused by infections whose etiological agent is this type of bacteria are reflected in the increase in hospital stay, mortality and medical care costs. Many of the ESBL-producing strains are also resistant to other antibiotics by different mechanisms, and the majority of severe infections, although sensitive in vitro to them, respond only to antimicrobials from the carbapenem group, with the consequences that this brings, in terms of costs and selective pressure of the microbial flora.

Resistance to carbapenems can occur through three mechanisms. First, hyperproduction of *AmpC* in association with the loss of outer membrane porins can produce resistance to

carbapenems. The second mechanism corresponds to changes in the affinity of the "target enzymes" (proteins to which penicillins bind) for carbapenems. The production of a β-lactamase that is capable of hydrolyzing carbapenems is the third mechanism. In the case of K. pneumoniae, the first cases of resistance were described through the production of metallobetalactamases (MLBs). These enzymes (type IMP, VIM, SMP and GIM), dependent on zinc for their activity and classified in Ambler's group B , They are not inhibited by clavulanic acid, tazobactam or sulbactam , they are susceptible to the chelator EDTA and capable of degrading virtually all β-lactams, with the exception of aztreonam (López and Echeverry, 2010).

Scientific evidence of the antimicrobial potential of metal nanoparticles

Below, a series of previous works related to the synthesis of nanoparticles by different methods are presented, emphasizing those carried out through the use of plant extracts, or also called biological synthesis.

Logroño *et al.* (2022): the type of research that was carried out was experimental with a quantitative approach, its objective was to develop a membrane from Furcraea Andina, covered with silver nanoparticles using reticulated Citrus peel as a reducing agent and analyze the antimicrobial activity on *Staphylococcus aureus* and *S. pyogenes*. The methodology used was the wet chemistry method in which mandarin peel extracts (common and King varieties) were used as a reducing agent; evaluating the concentration levels, temperature and immersion times of the rope fibers. UV-visible spectroscopy was used for characterization, obtaining a wavelength range between 430 to 450 nm. Regarding the determination of the surface, it was carried out by scanning electron microscope (SEM), energy dispersive X-ray spectroscopy EDX and Fourier transform infrared spectroscopy FT-IR. Based on what was studied by the authors. It was concluded that these processes allowed the obtaining of a material with nanoparticles in which its antimicrobial activity against *Staphylococcus aereus* could be verified and *S. pyogenes*.

Espinosa *et al.* (2021): the objective of this work was the biosynthesis of silver nanoparticles (NPsAg) using the aqueous extract of Geranium (*Pelargonium* spp). It was carried out by means of HPLC-MS with which the organic compounds found in the extract were obtained, the highest proportion being Quercetin-3-glucosyl-ramonosyl-glucoside, to which the synthesis of the nanoparticles is attributed. . To demonstrate the formation of the AgNPs, XRD was carried out where peaks were obtained at the 2θ angle at 38.11, 44.29, 64.44, 77.39°, and characteristic of silver. Likewise, the UV-visible method generated the result of the surface plasmon resonance which had a range of 340-400 nm. The size of the nanoparticles was obtained by means of scanning electron microscopy (SEM) with which they resulted in an average size of 36.55 nm. Regarding FTIR, the functional groups present in the Geranium extract (*Pelargonium* spp), with quercetin being the main compound.

Flowers. (2022): the objective of the study was to synthesize copper oxide NPs (CuONPs) using an eco-friendly method and determine their antimicrobial properties, using the aqueous extract and the supernatant of the liquid culture of the *Ganoderma sessile* fungus as reducing agents. Ultraviolet visible (UV-vis) spectrometry was used for this. Likewise, the morphology and size were determined by transmission electron microscopy (TEM), obtaining quasi-spherical nanoparticles with a size of 4.5 nm ±1.9 with the supernatant and 5.2 nm ±2.1 with the extract *Aqueous*. CuONPs showed antimicrobial activity against *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. The minimum inhibitory concentration (MIC) for *E. coli* was 192.5 µg/ mL for CuONPs -EA and 186 µg/ mL for CuONPs -SN. For *P. aeruginosa* and *S. aureus*, a MIC of 165 µg/ mL was obtained with the CuONPs-EA, and 159.5 µg/mL with the

CuONPs-SN. Likewise, it was shown that low concentrations (< 15 µg/ mL) of CuONPs -EA are not toxic to kidney cells or macrophages. While the CuONPs-SN showed cytotoxicity at concentrations equal to or greater than 0.91 µg/ mL in liver and macrophage cell lines. Based on the results obtained, it is concluded that the CuONPs synthesized with the *G. sessile* mushroom extract could be used in the treatment of superficial infectious diseases, however, more biosafety evaluations are required to show that they have low absorption into the circulation and a low concentration during the renal excretion process.

Leal *et al.* (2021): The objective of the research is the production of silver nanoparticles with the *Hibiscus rosa*- sinensis flower extract, through the reaction of a reducing agent and a precursor, using the green synthesis methodology. The reducing agent used is the extract and this was mixed with silver nitrate at different concentrations. 3 different extracts of the *H. rosa* flower were obtained: synthesis: ethanolic, aqueous (1) and (2) being responsible for the ionic reduction for the formation of the nanoparticles . The AgNPs were identified by UV-VIS and LD-LASER spectrophotometry following the LD-ISO 13320 standard, resulting in spherical silver nanoparticles of 40-60 nm. Likewise, the evaluation of antimicrobial activity in gram positive bacteria (*Staphylococcus aureus*), Gram-negative (*Escherichia coli*) and a fungus (*Aspergillius niger*), using the agar dilution methodology. With the studies carried out, positive results were obtained for the bacteria and their anti-ulcer effect was enhanced by the formation of silver nanoparticle, since they were able to treat damage to the cell membrane and presented effective results in relieving gastric ulcers.

Villa *et al*. (2021). The research carried out aims at the green synthesis of silver nanoparticles (AgNPs) using garlic (*Allium sativum* L) exploring its antimicrobial and catalytic activity. To do this, the presence of the AgNPs in solution was identified by means of a UV-VIS spectrophotometer. In addition, its size and morphology were evaluated, resulting in spherical nanoparticles of 40-60nm, which were confirmed by DSL-ISO 13321. Likewise, the optimization was carried out by applying variable volumes of the *Allium* bulb extract *savitum* L, silver nitrate concentrations, pH, temperature and reaction time. Now, the method used to measure its antimicrobial capacity was the agar diffusion method, these were tested on 3 bacterial strains, which are *Escherichia coli*, *Staphylococcus aureus* and *Aspergillum niger*, exhibiting antimicrobial properties against them

Zavaleta *et al.* (2019): a experimental research. The objective of the research is to demonstrate the antibacterial effect of ZnO nanoparticles , obtained by the modified sol-gel method, on *Staphylococcus aureus* ATCC 25923 and *Salmonella* Typhi. For them, the modified Kirby - Bauer insertion was used with 7mm diameter holes using sterile punches instead of discs. An experimental design was carried out in randomized blocks with four treatments and a negative control (PEG 6000) with 5 repetitions. The value of the nanoparticle concentrations (0.4, 0.8, 1.2, 1.6, 2.0 mg/ml) were prepared in aqueous solutions of PEG 6000 at a concentration of 100 mg/ml. As results, it was obtained that there is a relationship between the increase in the concentration of nanoparticles and the antibacterial effect, presenting a greater halo of growth inhibition (14.78 mm) for *S. aureus* at a concentration of 2.0 mg/ml, contrary In the case of *S.* Typhi, which presented a smaller inhibition diameter (11.01mm) at the same concentration. These results are probably attributable to the ability of nanoparticles to generate free radicals, which interact with the bacterial cell wall causing an extrusion of the intracellular content caused by the oxidative damage of proteins and lipids, causing the antibacterial effect. Due to the previously

described, these could be an alternative in the future to combat bacterial diseases.

D solis *et al.* (2019): the objective of the following work was to carry out a comparative analysis of the antimicrobial capacity of AgNPs biogenics synthesized using the aqueous extract of *Annona muricata* and AgNPs synthesized by the chemical method. The formation of the silver nanoparticle could be identified by the color change in the solutions and was verified by spectrophotometry. Transmission electron microscopy (TEM) was used to observe its morphology and size, obtaining quasi-spherical AgNPs , with an average size of 18.6 and a range of 5 to 46 nm . To evaluate the antimicrobial properties, the disk diffusion test of the AgNPs was carried out. Biogenic tests on different strains of clinical importance such as *Candida albicans, Escherichia coli, Pseudomonas aeruginosa* and *S. aureus*, proving to be capable of inhibiting these strains.

Figueroa (2019): the following research aims to synthesize iron nanoparticles (FeNPs) from the aqueous extract of *E. robusto* Sm leaves and evaluate their antimicrobial activity on different microorganisms. To carry out the tests, adjustments were made to the parameters used in the synthesis of the nanoparticles, using different synthesis concentrations and varying the iron precursor proportion, obtaining the 1:1 ratio as the best proportion. The size distribution of the particles was evaluated with equipment designed in the laser spectroscopy laboratory which is based on the dynamic light scattering technique, yielding a maximum absorption at 280nm. Likewise, atomic force microscopy was used to determine the size and morphology of the FeNPs, obtaining spherical nanoparticles with a size of approximately 8 nm high and 70 nm wide. Likewise, to determine the antimicrobial capacity of the nanoparticles, the agar dilution method was used against *Pseudomonas* microorganisms. *P. aeruginosa, Escherichia coli, S. aureus* and *Bacillus subtilis*, finding an intimate relationship between the synthesis conditions and the antimicrobial activity, in which the conditions used presented positive results in terms of the antimicrobial activity of the metal nanoparticles.

Melendez *et al*. (2018): the research aimed to synthesize silver nanoparticles using peppermint (Mentha piperite) as a reducing agent. For them, silver nitrate (AgNO3) was used, varying the proportions with a constant volume of peppermint extract. The synthesis process of the AgNPs was verified by analyzing the color change of the solution, using atomic force microscopy (AFM) and UV-visible spectrophotometry. Obtaining as a result a color change in all solutions to an intense gold, thus evidencing that the possible formation of nanoparticles occurred, those that presented more intense colors are solutions 4 and 5. Likewise, the measurements carried out by using the UV-vis method, peaks between 400 and 470 were observed in 3 of the solutions. The morphology of the nanoparticles which were carried out with AFM, taking into account solution 5, showed sizes of 100 nm and relatively high monodispesity. From what has been previously presented, it can be concluded that the synthesis of nanoparticles using this method is viable, reduces costs and the negative impact on the environment; however, their antimicrobial capacity could be evaluated in subsequent research, as well as the parameters optimized to obtain nanoparticles of a smaller size.

Freight (2016): the research described below aimed to synthesize silver nanoparticles (AgNPs) via green chemistry using aqueous extract of *Valeriana officinalis* and *Passiflora incamata* plants, as reducing agents and silver nitrate (AgNO3) as a precursor. To measure the bioreduction reaction of silver ions Ag+ to Ag0, different concentrations of AgNO and the plant extract were used. Regarding the structure of the nanoparticles, it was carried out using the techniques of UV-VIS spectrophotometry, transmission electron microscopy (TEM),

scanning electron microscopy (SEM), X-ray diffraction (XRD) and infrared spectroscopy (IR); thus allowing to confirm the formation of the AgNPs, observing that, the higher the concentration of silver nitrate, the greater the formation of the nanoparticles . Now, the average size of the AgNPs using *Valeriana officinalis* was approximately 22 nm , with a bimodal trend with nanoparticles in the range of 10-22 nm and 45-60 nm; the case of *Passiflorina incarnata* the same behavior was observed, however it presented a better reduction speed. Likewise, the analysis of the bactericidal effectiveness of the AgNPs against a strain of *Escherichia* was carried out. *E. coli*, using the disk diffusion method, in which the results showed that as the concentration of the AgNPs increases, a greater halo of inhibition of the growth of the bacteria is obtained, therefore the antimicrobial capacity could be evidenced.

CONCLUSIONS

We are in the presence of the present and the future when it comes to antimicrobials. However, we may have the best alternatives, but without a good policy for the use of antimicrobials, what scientists develop against these pathogens will be worth very little.

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