RESEARCH PAPER

Harnessing Medicinal Plants for Nanoparticle Synthesis in Antimicrobial Research

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ABSTRACT
The emergence of antimicrobial resistance has necessitated the development of innovative, effective, and sustainable antimicrobial approaches. In recent years, the application of medicinal plants in the synthesis of nanoparticles has shown promise for the development of antimicrobial agents. This approach has linked nanotechnology with natural bioresources. Plant-based synthesis involves the application of bioactive molecules like flavonoids, phenolics, alkaloids, and terpenoids, which serve as reducing agents in the synthesis of nanoparticles. This approach is eco-friendly because it does not require the application of toxic chemicals, thus being safe for the environment and human health. The review article aims to show the potential of medicinal plants as natural biofactories for the synthesis of different nanoparticles. It will cover the basics of green nanotechnology, synthesis methods, and the influencing parameters for the synthesis of nanoparticles. In addition, it will cover the basic characterization techniques used for the determination of the physical and chemical properties of nanoparticles. Moreover, the antimicrobial potential of plant-derived nanoparticles is discussed, which includes membrane disruption, the production of reactive oxygen species, and disruption of microbial metabolism. In addition, the efficacy of plant-derived nanoparticles against different types of microbes, ranging from bacteria, viruses, and fungi, is discussed, as well as the different methods used for their evaluation. Furthermore, the advantages of plant-mediated nanoparticles, which include their biocompatibility, cost-effectiveness, and increased antimicrobial efficacy, are discussed, as well as the limitations of plant-mediated nanoparticles, which include the differences in plant extracts, lack of standardization, and large-scale production problems. Overall, plant-mediated nanoparticles have immense potential for the synthesis of next-generation antimicrobial agents.

Keywords: Antimicrobial resistance, Plant-mediated nanoparticles, Natural biofactories, Antimicrobial agents
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1. INTRODUCTION:

Nanotechnology has become a major area of innovation in contemporary science with new exciting ways to solve problems in the three areas of medicine, agriculture and environmental protection through the use of nanoparticles. Nanoparticles used in the field of antimicrobial research have gained tremendous interest because of their unique physical properties which include a very high surface area to volume ratio of a particle; their enhanced reactivity; and their ability to interact with microbes at the molecular level (Rai et al., 2012; Singh et al., 2018). These physical properties of nanoparticles provide them with a unique ability to effectively kill a wide variety of pathogens, which includes bacteria, fungi, and viruses. The dramatic increase in antimicrobial resistance has become a major threat to global health, as conventional antibiotics are becoming less effective and creating a greater need for

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alternative treatment measures (World Health Organization, 2020). In light of these issues, nanoparticles have been recommended as a potential new type of antimicrobial agent due to their ability to kill bacteria through several different mechanisms of killing bacteria, thereby reducing the likelihood that the bacteria would develop resistance to treatment (Lemire et al., 2013).

Nanoparticle synthesis through conventional methods such as chemical routes or physical methods, often uses hazardous or toxic or chemical or energy; therefore, researchers have turned toward green production methods that use microbes or plant material for production (Iravani, 2011). Many researchers are focusing on using plant-mediated nanoparticle production methods because of their low cost, simplicity, and environmentally friendly nature (Ahmed et al., 2016). Medicinal plants are an extremely rich source of bioactive compounds like flavonoids, alkaloids, phenolics, terpenoids and proteins, which can be used as both reducing agents and stabilizing agents for the production of nanoparticles (Kumar & Yadav, 2009). In addition, phytochemicals found in medicinal plants can facilitate metal ions converting to nanoparticles and also help stabilize them so that they can be biologically active. In addition, most medicinal plants are also known to have antimicrobial properties which may provide synergy with the effectiveness of the nanoparticles produced (Mittal et al., 2013).

Studies have shown that nanoparticles derived from plants (particularly silver and gold) have the ability to kill many (Rai et al. 2014; Ahmed et al. 2016) different pathogens using multiple methods, including disrupting cell membranes, creating free radical species and blocking access to normal functioning processes. These therefore contribute to the death of the pathogen. As such, using medicinal plants to produce these types of particles via a green method is seen as an environmentally friendly, sustainable method for developing future types of antimicrobials. As such, this review will discuss how medicinal plants can be used in the green synthesis of nanoparticles and how they could assist in treating infections caused by microorganisms. This article also highlights the advantages, disadvantages and future direction for developing nanoparticles through medicinal plants for antimicrobial applications.

2. MEDICINAL PLANTS AS BIOFACTORIES

Due to having numerous bioactive compounds, medicinal plants have been shown to be highly effective and sustainable users of bio gas for the creation of different types of nanostructured materials. Plants contain a wide variety of phytochemical compounds that can be classified into six different classes; these are: flavonoids (flavones), alkaloids (e.g. caffeine), terpenoids (essential oils), phenolic acids (e.g. acetic acid), tannins, and proteins. The use of these phytochemical compounds will facilitate the biocatalytic reduction of metallic ions to nanoparticles, and subsequently allow for the stabilization of these metallic nanoparticles (Kumar and Yadav, 2009; Ahmed et al., 2016). The introduction of these natural products during the formation of a nanoparticle will eliminate the use of potentially hazardous chemicals as reducing and stabilising reagents; thus, providing a safe and environmentally friendly way of producing nanoparticles biocompatibly.

Nanoparticle synthesis, mediated by and/or involving the plant life cycle, can be divided into three main stages. Firstly, during the reduction stage, phytochemicals donate electrons to their corresponding metallic ions (e.g. Ag^+, Au^{3+}) in the reduction of the ions to their corresponding metallic nanoparticle states (Iravani, 2011). Following the reduction phase, the reduced atoms aggregate together to start to form stable nanoparticle cores, this is known as the nucleation stage of nanoparticle synthesis. The final stage of the nanoparticle synthesis considers the role of the various plant metabolites as stabilising or capping agents to provide resistance of the formed nanoparticles to aggregation as well as increasing the particle stability and functionality of the nanoparticles produced (Mittal et al., 2013).

The use of various parts taken from different types of medicinal plants i.e. leaf, root, stem, bark, flower and seed will allow synthesis of nanoparticles. The extracts from leaves are generally preferred because they contain higher concentrations of active metabolites, which makes them easier to process than any other part of the plant (Singh et al., 2018). The physical attributes associated with the synthesized nanoparticles, such as size, shape and biological activity, will also depend on the type and concentration of phytochemicals found in the original extracts from which these nanoparticles were synthesized.

There are a number of benefits associated with the use of medicinal plants for the production of nanoparticles, one of which is that they have natural antibacterial properties; thus, they can increase the antibacterial activity of the nanoparticles in synergy. For example, silver nanoparticles produced from plant materials are generally superior to their chemically synthesized equivalent in terms of antibacterial activity because of the synergistic effect provided by the metal ions and the various phytochemical constituents derived from the plant (Rai et al., 2014). The use of medicinal plants also has an added benefit of being cost effective, easy to scale up and can be conducted using non-complex equipment and without requiring sterile conditions.

The major concern with using medicinal plants for the production of nanoparticles is that the variability in the composition of phytochemicals found in each of the plant will affect reproducibility and consistency of the synthesized nanoparticles; this is common due to factors such as geographical location of the plant, plant species and methods used to extract phytochemicals (Ahmed et al., 2016). Regardless of these concerns, the use of medicinal plants remains a valuable option for green nanotechnology and the creation of green antimicrobial nanomaterials.

3. GREEN SYNTHESIS OF NANOPARTICLES

The use of green approaches for the creation of nanoparticles has become very popular due to their environmentally-friendly nature in comparison to standard physical as well as chemical methods of nanoparticle creation. Traditional methods of nanoparticle creation typically involve utilizing bad chemicals that generate hazardous by-products, use excess energy, and cause harm to human beings and the ecology. However, the green approach to making nanoparticles uses naturally occurring biological systems (including, but not limited to, plants, bacteria, fungi as well algae) to create nanoparticles safely and with less harm to the environment than the standard methods to produce nanoparticles. Green nanotechnology is performed by utilizing the basic principles of green chemistry, which include the ideas of using less hazardous materials in a material's design and creation process. The use of plants to aid in creating nanoparticles is currently emerging as an efficient and cost-effective method to create nanoparticles due to the speed of the process and the simplicity of the use of plants in this way. Plants contain many different types of chemicals that can aid in reducing, capping, and stabilizing nanoparticle structures, which allows for the production of nanoparticles without needing to use any additional materials.

The method by which bio-synthesized nanoparticles are made usually involves a blend of a plant extract and a solution of a metal salts like silver nitrates ($AgNO_3$) or chloroauric acids ($HAuCl_4$). The phytochemicals contained in the extract reduce the metal ions (i.e., Ag^+, Au^{3+}) from the solutions to their analogous bacteriophage specific sizes (i.e., nano size). This reduction of metal ions from solution is frequently indicated by an outward change of color resulting from the phenomenon of surface plasmon resonance (SPR) which provides proof of the occurrence of nanoparticle manufacturing (Mittal et al., 2013). The resultant nanoparticles which have been bio-synthesized are also stabilized by the same metabolites of the plant(s), thus avoiding of any aggregation of the nanoparticles and increasing their biological activity.

Numerous parameters affect the production and characteristics of bio-synthesized nanoparticles. Such parameters include (but are not limited to): pH levels; temperature; length of reaction time; concentration of the plant extract; and concentration of the metal ions being utilized in the synthesis process. For example, higher temperatures and optimized pH conditions will increase rates of reduction and ultimately affect the size and morphology of the nanoparticles produced (Singh et al., 2018). Control over parameters is required to produce nanoparticles which meet specific desired attributes for use in various applications.

In addition to offering the advantages of eliminating sterile conditions, easier to scale up, and quicker time to produce than microbial synthesis, the use of plants in green synthesis also provides greater functionality for nanoparticles due to the presence of bioactive compounds with antimicrobial properties found in medicinal plants (Iravani, 2011). While these benefits exist, there are also challenges associated with green synthesis, such as: variation in phytochemical composition from one extract to the next; standardizing large-scale production processes that work consistently; and limitations of our current understanding of biochemistry regarding how nanoparticles form; (Ahmed et al., 2016). Currently, research continues to focus on optimizing synthetic conditions and improving reproducibility so that green-synthesized nanoparticles may become widely used in both antimicrobial and biomedicine applications.

3.1 CONCEPT OF GREEN NANOTECHNOLOGY

"Green nanotechnology" is an emergent field that represents a combination of concepts from both nanotechnology and green chemistry to create nanomaterials in an environmentally safe and non-toxic manner. The overall goal of this approach is to reduce the quantities of hazardous materials used, minimize the amount of waste generated from production processes, and increase the safety and efficiency of how nanoparticles are manufactured (Anastas & Warner, 1998; Iravani, 2011).

The idea of applying green nanotechnology to the synthesis of nanoparticles has its basis upon the twelve original principles of green chemistry that support the ability to synthesize chemicals in a safer manner, be more energy efficient, use renewable materials and reduce the amount of by-products generated from the synthesis of any chemicals. Through this synergy, green nanotechnology seeks to implement the use of biological systems (e.g., plants, microorganisms and/or enzymes) as environmentally friendly alternatives to conventional chemical and/or physical techniques used for the synthesis of nanoparticles (Ahmed, et al., 2016). Biological systems function as naturally occurring reducing and stabilizing agents, which eliminates the necessity for toxic chemical reagents and/or high energy.

Renewable biological resources, especially plant extracts, can be utilized in green nanotechnology for the synthesis of nanoparticles. The use of medicinal plants for nanotechnology is significant because they contain a high quantity of phytochemicals (flavonoids, phenolics, etc.) that can reduce metal ions to form nanoparticles and stabilize those nanoparticles (Kumar & Yadav, 2009). This can simplify the process of synthesizing nanoparticles while improving the biocompability and functional properties of nanoparticles.

Along with consideration of using renewable biological resources for synthesis, the green method focuses on reducing the amount of energy required to synthesize nanoparticles. The majority of nanoparticles synthesized using green methods are produced under ambient temperature and pressure conditions, resulting in a decrease in energy consumption compared to traditional methods (Iravani, 2011). Additionally, fewer toxic by-products are generated through green methods of nanoparticle synthesis, thereby improving the health and safety of researchers and the environment.

A key aspect of green nanotechnology is focusing on evaluating the entire life cycle of the nanomaterial and ensuring the nanomaterials are safe to produce, use and dispose of. This is especially important in biomedical and antimicrobial applications where a safe nanoparticle is of utmost importance (Singh et al., 2018). The field of green nanotechnology is facing obstacles to advancement in the field. These include the inconsistency of biological materials; challenges in producing large volumes of product; and limited understanding of biogenic synthesis pathways (Ahmed et al., 2016). Continued advancements in research are anticipated to help to overcome these obstacles, and will further enhance the role of green nanotechnology in achieving sustainable development. Thus, green nanotechnology can be viewed as a fundamental shift in how we approach the synthesis of nanoparticles, shifting toward safer, cleaner and more sustainable methods, and has tremendous potential in antimicrobial studies and other biomedical applications.

3.2 METHODS OF NANOPARTICLE SYNTHESIS

Nanoparticles are produced by three main methods: physical, chemical, and biological (green), each of which has unique principles, efficiency, and impact on the environment. The physical method is breaking down bulk material into nanoscale particles using an external energy source such as heat, light or mechanical force. Some common techniques that are used to produce nanoparticles from metals through physical means include evaporation - condensation, laser ablation, ball milling, and thermal decomposition. The main characteristic of the physical method is that it produces highly pure nanoparticle products with very little, if any, chemical contamination. However, all the physical methods are very energy intensive, the equipment used to produce the nanoparticles are expensive, and most of the physical methods cannot be scaled up to produce large quantities of nanoparticles. (Iravani, 2011).

When it comes to controlling nanoparticle size, shape, and distribution, chemical methods come out on top as they are the most commonly used techniques. There are several types of chemical methods including chemical reduction, sol-gel processing, coprecipitation, and microemulsion. In chemical reduction, a chemical reduction agent such as sodium borohydride or citrate is used to convert metal ions (Ag^+ or Au^{3+}) into nanoparticles with the aid of a stabilizing agent to avoid aggregation (Mittal et al., 2013). In addition to being an effective way to produce nanoparticles at large scale, due to the use of toxic chemicals and byproducts, there are environmental safety and biomedical applicability concerns with chemical methods.

Alternatively, biological or "green" synthesis methods include using natural biological systems (plants, bacteria, fungi, algae) to create nanoparticles. For example, plant-mediated synthesis has several significant advantages over other forms because it is a relatively straightforward method, has a rapid reaction time, and does not require the use of sterile conditions (Ahmed et al. 2016). Another significant benefit of using plant extracts is that they contain many phytochemicals, which can act as both reducing agents and stabilizing agents, allowing for the creation of nanoparticles in an environmentally friendly manner. Although there are still challenges to using green synthesis due to the biological composition variability associated with plants and the limited ability to control the characteristics of the particles produced by each plant, this synthesis method has emerged as a very viable alternative for creating sustainable nanoparticles, especially in the area of antimicrobial research where biocompatibility and lower toxicity are required (Iravani 2011; Ahmed et al. 2016).

3.3 PLANT-MEDIATED SYNTHESIS

Nanoparticle synthesis by using plants is a promising sustainable method in green nanotechnology and is based on using plant materials (extracts) as natural reducing agents and stabilizers. Plant extracts are characterized by their high variability and large number of secondary metabolite classes (phytochemicals), e.g., flavonoids, phenolic compounds, terpenes, sugars, and proteins, which play an active role in converting metallic ions into metallic nanoparticles, (Shankar et al. 2004, 2009 Jha et al.;). Synthesis via plants eliminates many of the toxic chemicals and complicated processes associated with conventional synthesis and is therefore a good candidate for use in applications related to biomedical and antimicrobial materials.

The process of synthesizing nanoparticles is usually not difficult; one starts with an extract from a plant in water, adds some metal salt solution (for example, silver nitrate or chloroauric acid) to it and lets them go together. There are naturally occurring chemicals in the plant which will reduce the metals (silver, gold) and create the nanoparticles through electron transfer from the extract to the metal ions (Ag^+ and Au^{3+}). You can see the reduction of the metal ions to the metal nanoparticles because of the change in color associated with the formation of the nanoparticles - you can see this as a color change occurs due to the surface of the nanoparticles creating new plasmons (Song & Kim 2009). At the same time as the plant extracts chemically react and produce the nanoparticles, some of the biomolecules will attach onto the surface of the nanoparticles to provide additional stabilization and to prevent them from aggregating.

Nanoparticles can be created from many different parts of plants, including leaf, root, bark, flower, and seed material. However, leaf extracts are most often used because they contain a high concentration of metabolites and are abundant in the environment. The size, shape, and dispersity of nanoparticles produced using leaf extracts may depend on many different parameters, including the pH, temperature, time of reaction, and concentration of plant extract and metal ion, all of which have been previously reported

(Noruzi, 2015). In order to optimize nanoparticles for use as antimicrobial agents, these parameters must be adjusted to provide nanoparticles that are appropriate for a given application.

A significant advantage of synthesizing nanoparticles using plants is the synergistic relationship between plant-based phytochemicals and the nanoparticle, resulting in enhanced antimicrobial function. The bio-functionalized nanoparticles have a greater capacity to interact with the microbial cell resulting in a broader range of activity against a variety of pathogens (Iravani et al., 2014). Additionally, plant-mediated synthesis is a cost effective, scalable and does not require stringent aseptic conditions thereby facilitating its feasibility for use.

Currently, issues remain including variation in phytochemical composition, non-standardization and limited mechanistic knowledge of how they work. However, plant-mediated synthesis has the potential to continue as a rapidly developing, eco-friendly platform to create antimicrobial nanomaterials.

4. TYPES OF NANOPARTICLES SYNTHESIZED USING MEDICINAL PLANTS

Medicinal plants have been extensively employed in the green synthesis of numerous metal and metal oxide nanoparticles. The phytochemical diversity and reducing potential of the plants are the main reasons for the synthesis of nanoparticles. Among the plant-mediated synthesized nanoparticles, silver nanoparticles (AgNPs) have been extensively researched due to their significant antimicrobial activity. The plant-mediated synthesized AgNPs have been observed to possess significant antimicrobial activity against a broad range of pathogenic microorganisms, including multidrug-resistant bacteria. The antimicrobial activity of plant-mediated synthesized AgNPs has been attributed to the disruption of the cell membrane and the production of reactive oxygen species (ROS) in the target organisms. The plant extracts of Azadirachta indica, Ocimum sanctum, and Aloe vera have been successfully employed in the synthesis of AgNPs.

Gold nanoparticles (AuNPs) synthesized by using medicinal plants have also been found to be of considerable interest, especially in biomedical fields. AuNPs have been found to possess less antimicrobial activity compared to silver nanoparticles. However, AuNPs have been found to be of considerable interest in the field of drug delivery. Stable AuNPs have been synthesized using the extracts of Terminalia chebula and Camellia sinensis (Huang et al., 2007).

Zinc oxide nanoparticles (ZnO NPs) synthesized using plant extracts have gained importance because of their excellent antimicrobial and photocatalytic properties. These nanoparticles have been found effective against both Gram-positive and Gram-negative bacteria. These nanoparticles have been successfully used in applications like wound healing, coating, and food packaging. The antimicrobial activity of ZnO nanoparticles is based on the production of ROS and the release of Zn^{2+} ions (Raghupathi et al., 2011).

Copper nanoparticles (CuNPs) and copper oxide nanoparticles (CuO NPs) synthesized by plant-mediated approaches have been found to possess excellent antimicrobial activity. These nanoparticles have been used as substitutes for silver and gold nanoparticles because of their excellent bactericidal activity, which is based on the production of oxidative stress in microbial cell membranes (Ren et al., 2009)

Another form of nanoparticles, namely Titanium dioxide nanoparticles (TiO2 NPs), has also been synthesized from medicinal plants. They have photocatalytic and antimicrobial properties. In the presence of UV light, TiO2 nanoparticles produce ROS, which are responsible for the antimicrobial potential of these nanoparticles. They have potential applications in water purification and self-cleaning technology (Fujishima et al., 2008).

Besides the above nanoparticles, some other nanoparticles like Iron oxide nanoparticles (Fe3O4 NPs), Nickel oxide nanoparticles (NiO NPs), and Magnesium oxide nanoparticles (MgO NPs) have also been synthesized from plant extracts. This has increased the scope of green nanotechnology. From the above discussion, it is evident that medicinal plants have shown great promise in synthesizing different nanoparticles with enhanced antimicrobial potential, which makes them highly valuable for nanomedicine.

5. CHARACTERIZATION OF SYNTHESIZED NANOPARTICLES

Characterization of the synthesized nanoparticles is an important step for identifying their physicochemical properties, which impact both their anti-microbial activity and performance. Various types of analytical techniques are utilized to measure things like size, shape, surface structure, crystal structure, chemical composition, and stability of the synthesized nanoparticles. These characterization methods enable essential determination of the successful synthesis and properties of the functionalized plant-mediated nanoparticles (Bhattacharjee, 2016; Khan et al., 2019).

One primary characterization method is UV-Visible spectroscopy, which provides preliminary confirmation of synthesis by illustrating the formation of nanoparticles through surface plasmon resonance (SPR). The development of certain absorption peaks at particular wavelengths indicates that metal ions have been reduced into a synthesized form of the nanoparticle. As an example, silver nanoparticles have an absorption peak located at approximately 400-450 nm (Link & El-Sayed, 1999).

FTIR is used to detect the various functional groups that are located on the surface of nanomaterials, as well as how phytochemicals are used in reducing and stabilising nanomaterials. Using FTIR allows for the verification of biomolecules such as proteins, phenols, and flavonoids that will act as stabilising agents or capping agents (Stuart, 2004).

Morphological analyses are frequently conducted via SEM and TEM. SEM gives users information pertaining to the morphology and distribution of the surface of the particles, with TEM providing high-resolution images that can assist in determining the dimensions, shape, and nanostructures of the particles at the nanoscale level (Goldstein et al., 2003). These are essential tools for being able to validate the presence of spherical or rod-like or irregularly shaped nanoparticles.

The crystallinity and phase make-up of nanoparticles can be investigated via X-ray Diffraction (XRD) analysis. Diffraction patterns are used to ascertain the average particle size via use of the Debye–Scherrer equation (as identified by Cullity & Stock, 2001) and to confirm whether the nanoparticles in question are purely metallic or metal oxide in nature (Bowen et al., 2015).

Dynamic Light Scattering (DLS) allows for both measurement of the hydrodynamic size-distribution and the stability of nanoparticles in colloidal solutions; information regarding the uniformity of size & angular distribution of the nanoparticles and data on the aggregation potential of particles can also be obtained from DLS measurements. Normally, DLS is performed in conjunction with zeta potential analysis to determine the surface charge and therefore, stability, of nanoparticles. Larger absolute zeta potential numbers indicate a higher likelihood of achieving improved dispersion & stability of nanoparticles (as shown by Bhattacharjee, 2016).

Other support characterisation techniques that may be employed include: EnergyDispersive X-ray Analysis (EDX) for determining elemental composition; Atomic Force Microscopy (AFM) to establish three-dimensional topography of the sample surfaces; and, when combined, these characterisation methods combine to provide a complete understanding of the physical / chemical characteristics of nanoparticles. This is essential for optimising the antimicrobial efficacy and applications of nanoparticles in biomedicine.

6. ANTIMICROBIAL MECHANISMS OF PLANT-DERIVED NANOPARTICLES

The plant-based nanoparticles have really shown that they are very good at fighting off microbes. This is because the plant-based nanoparticles work together in a way. One of the ways that the plant-based nanoparticles fight off microbes is by disrupting the cell membrane of the microbes. The plant-based nanoparticles can do this because they have a surface area. This means that the plant-based nanoparticles can interact with the cell membrane and cell wall of the microbes. When this happens the cell membrane gets. The cell content is lost. This is what kills the microbes.

The plant-based nanoparticles also fight off microbes in another way. The plant-based nanoparticles make something called ROS. This includes things like superoxide radicals and hydroxyl radicals and hydrogen peroxide. These ROS cause problems, for the microbes by making them undergo something called stress. This oxidative stress damages the cell membrane and other parts of the microbe like the lipids and proteins and DNA. In the end this causes the microbes to die, either by something called apoptosis or something called necrosis.

Plant-mediated nanoparticles get in the way of things inside cells, DNA and proteins. They can go into the cell. Stick to DNA, which changes its shape and stops it from working right. This stops the cell from making copies of itself and from dividing. Plant-mediated nanoparticles can also get to the parts of the cell where proteins are made and mess with the enzymes which're like helpers that make things happen in the cell. This stops proteins from working. Also stops the cell from doing the things it needs to do to stay alive (Rai et al., 2012).

Another way that plant-mediated nanoparticles fight off cells is by releasing tiny particles of metal like silver and zinc. These tiny particles make it even harder for bad cells to survive. They can stick to parts of proteins and enzymes which are like helpers, in the cell and stop them from working right. This causes the cell to not work properly and can even kill it (Lemire et al. 2013). The best part is that these tiny particles keep coming out. The plant-mediated nanoparticles can keep fighting off bad cells for a long time.

Furthermore nanoparticles made from plants are known to fight biofilms, which's important in treating long-lasting infections. They stop biofilms from forming. Can also break up existing ones by getting inside the biofilm and killing the bacteria inside. This is especially useful against bacteria that're resistant to antibiotics. The good stuff on the surface of these plant-made nanoparticles helps them work better against microbes. These natural compounds can add powers to fight microbes and help the nanoparticles work better with the bacteria. Overall plant-made nanoparticles have ways of working that make it less likely for bacteria to become resistant making them a promising option to replace traditional medicines that fight microbes in modern medicine. They are good for fighting infections. Might be used more in the future.Plant-derived nanoparticles are helpful, in treating infections.

7. ANTIMICROBIAL ACTIVITY STUDIES

7.1 AGAINST BACTERIA

Plant derived nanoparticles have been looked at a lot to see how well they work against bacteria. These nanoparticles work well because they are very small and have a surface area. They also have things in them called bioactive phytochemicals that help them work with bacterial cells. Many studies have shown that nanoparticles made from plants that are used for medicine can stop bad bacteria like Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa and Bacillus subtilis from growing (Rai et al., 2012; Franci et al., 2015).

The way plant derived nanoparticles work against bacteria is usually tested using ways of looking at tiny living things. These tests include putting a gel with tiny holes in it and seeing how far the nanoparticles can stop bacteria from growing. They also include putting a disk with nanoparticles on it in a petri dish and seeing how much of the nanoparticles it takes to stop bacteria from growing (Balouiri et al., 2016). When these tests are done they often show that the nanoparticles are good at stopping bacteria from growing. Among all the kinds of nanoparticles silver nanoparticles made from plant extracts are especially good at killing bacteria. This is because they can break through the outside of cells make special kinds of oxygen that are bad for bacteria and release silver ions that are toxic to bacteria. Plant derived nanoparticles, silver nanoparticles are very good, at stopping bacteria from growing (Franci et al., 2015)..

Nanoparticles affect Gram- Gram-negative bacteria in different ways because of the differences in their cell wall structure. Gram-negative bacteria have a layer and an outer membrane so they are more likely to be affected by nanoparticles than Gram-positive bacteria, which have a thicker layer that protects them (Slavin et al., 2017). However nanoparticles that come from plants can fight against both types of bacteria which shows they can work against a range of bacteria.

Plant-derived nanoparticles are also good at fighting bacteria that form groups and are hard to kill with antibiotics. These nanoparticles can get into the group of bacteria break it up and kill the bacteria inside which helps stop infections that will not go away. This makes them very useful for things like helping wounds heal and coating things that are put inside the body (Kalishwaralal et al., 2010). The fact that plant-derived nanoparticles can fight bacteria is important because it shows they can be used as ways to fight infections especially when bacteria are resistant to antibiotics. Plant-derived nanoparticles can do things to fight bacteria and they work well because of the way the chemicals in plants work together which makes them good choices for future treatments, against bacteria.

7.2 AGAINST FUNGI

Plant derived nanoparticles are really good at fighting off fungi. They work against a lot of kinds of fungi that can make people sick. Fungi like Candida albicans, Aspergillus niger, Aspergillus fumigatus and Fusarium spp can cause health problems. This is especially true for people who have immune systems (Kim et al., 2009; Wani & Shah, 2012).

Plant derived nanoparticles are an alternative to the usual antifungal agents we use. The problem is that fungi are getting resistant to the drugs we have now. So we need to find ways to fight off fungi. Plant derived nanoparticles can help us do that.

The reason plant derived nanoparticles are good at fighting fungi is that they can damage the fungis cell membranes and cell walls. When plant derived nanoparticles touch the fungi they cause damage to the fungis surface. This makes the cell membrane more permeable. Causes important things to leak out of the cell. Plant derived nanoparticles also make the fungi produce things that can harm the cell (Kim et al., 2009). This can damage the cells parts, proteins and even its nucleic acids. Plant derived nanoparticles are really good at fighting off fungi, like Candida albicans, Aspergillus niger, Aspergillus fumigatus and Fusarium spp.

Plant synthesized nanoparticles, silver and zinc oxide nanoparticles have a big impact on stopping fungus from growing and spreading. These tiny particles can get inside fungus cells. Mess with important processes that the cells need to work properly which ultimately stops the fungus from growing. The fact that these nanoparticles have plant chemicals on their surface makes them even better at fighting fungus by working together (Wani & Shah, 2012).

To see how well these nanoparticles fight fungus people usually do tests like putting them in a jelly like substance called agar and checking how much they stop the fungus from growing. They also check the minimum amount of nanoparticles needed to stop the fungus from growing. Lots of studies have shown that plant made nanoparticles are really good at stopping fungus from growing and can even stop fungus from forming groups that are hard to kill (CLSI, 2012). This is a deal because these strong groups of fungus are a major reason why infections can be hard to get rid of.

Even though these nanoparticles are really good at fighting fungus there are still some problems to solve. For example it can be hard to make sure the nanoparticles are all the same and we need to make sure they are not harmful, to people or animals.. Overall using plants to make nanoparticles is a great way to fight fungus in both medicine and farming.

7.3 AGAINST VIRUSES

Plant derived nanoparticles are getting a lot of attention because they can fight off viruses. This is a deal because some viruses do not respond to the usual treatments. Some studies have shown that these nanoparticles work well against many kinds of viruses like the flu, herpes, HIV and coronaviruses (Galdiero et al., 2011; Sportelli et al., 2020). The small size of these nanoparticles and the fact that they have plant chemicals makes them very good at stopping viruses from infecting and replicating.

One of the ways that plant derived nanoparticles fight off viruses is by sticking to the proteins on the surface of the virus. This stops the virus from attaching to and getting into our cells. For example silver nanoparticles can bind to the proteins on the surface of a virus, which blocks the virus from recognizing and fusing with our cells (Galdiero et al., 2011). This stops the virus from starting to replicate of us. Plant derived nanoparticles like these are really good at fighting off viruses, like the flu and coronaviruses by stopping them from replicating.

Plant derived things are really good at fighting off viruses. People are paying attention to them because they can help control viruses that do not respond to regular treatments. Some studies have shown that these tiny particles can fight off lots of viruses like the flu, herpes, HIV and coronaviruses Sportelli et al., 2020).

Plant derived nanoparticles are good at stopping viruses because they are very small and have properties that come from plants. This helps them stop viruses from infecting and reproducing. One way that plant derived nanoparticles fight off viruses is by sticking to the outside of the virus. This stops the virus from attaching to and getting into cells. For example tiny silver particles can bind to the viruss layer, which stops the virus from recognizing and merging with healthy cells. This stops the virus from starting to make more of itself inside the body. Plant derived nanoparticles are really good at this which is why people think they can help fight off viruses, like the flu and coronaviruses.

Nanoparticles can fight off viruses. To see how well they work people use tests like plaque reduction assays and viral inhibition assays. They also do cytotoxicity tests to make sure the nanoparticles do not hurt the cells in our body. They only want the nanoparticles to hurt the viruses.

Some studies have found that nanoparticles that come from plants can be very good at fighting off viruses. Silver and gold nanoparticles are two examples of this. They can fight off viruses even when they are used in amounts.. They do not seem to hurt the cells in our body. This was shown in a study, by Elechiguerra and others in 2005 (Elechiguerra et al., 2005).

People are still learning about nanoparticles. How they can be used to fight off viruses.. Using nanoparticles that come from plants is a new and exciting idea. We need to do studies to understand how they work and to make sure they are safe to use.

7.4 METHODS OF EVALUATION

The antimicrobial power of nanoparticles that come from plants is tested using methods that check how well they can stop or kill tiny living things. These methods give us numbers and details about how nanoparticles work against bacteria, fungi and viruses. We use techniques to test nanoparticles, including diffusion-based assays, dilution methods and viability tests each of which has its own advantages when it comes to checking how well nanoparticles fight off tiny living things (Balouiri et al., 2016).

One way to test nanoparticles that's easy to understand is the agar well diffusion and disk diffusion assay. This is where nanoparticles are put into wells or added to disks that are placed on plates with a gel called agar. These plates have living things like bacteria or fungi on them. If a clear area forms around the well or disk it means the nanoparticles are working to fight off the living things. The size of this area shows how strong the nanoparticles are. These methods are simple. Do not cost a lot but they are mostly used to get a general idea of how well nanoparticles work. They can also be affected by things, like how the nanoparticles move and how well they mix with other things (Balouiri et al., 2016).

People usually figure out how good nanoparticles are at stopping microbes from growing by using the inhibitory concentration assay. This test finds out what is the amount of nanoparticles needed to stop microbes from growing. They do this test by using broth dilution methods. This means they try amounts of nanoparticles on microbes to see what happens. The minimum bactericidal concentration and the minimum fungicidal concentration are tests. These tests find out what is the amount of nanoparticles that can kill microbes completely rather than just stop them from growing as researchers like Wiegand and others found out in 2008 (Wiegand et al., 2008).

People also use something called time-kill assays to see how fast nanoparticles can kill microbes over a period of time. These tests give us information about how fast microbes are killed. Another way to measure how well nanoparticles work is, by counting the number of microbes that're still alive after being treated with nanoparticles. This is called colony-forming unit counting. It gives us an accurate measurement of how well nanoparticles can stop microbes from growing.

For studies on biofilms special methods are used. These include crystal violet staining, biofilm inhibition assays and confocal laser scanning microscopy. They help evaluate how well nanoparticles can prevent or disrupt biofilm formation. Biofilms make bacteria more resistant to agents (Stepanović et al., 2007).

In studies methods like plaque reduction assays, viral load quantification and cytotoxicity assays are used. They check if nanoparticles can stop viruses from replicating without harming host cells.

Overall using these methods together gives an understanding of how effective plant-derived nanoparticles are against microbes. This helps make them better for use, in medicine and the environment.

8.ADVANTAGES AND CHALLENGES OF PLANT-MEDIATED NANOPARTICLES

Plant-mediated nanoparticles have various advantages, which make their application very attractive, but some challenges are still hindering their widespread use. One major advantage is the eco-friendly and green approach to their synthesis, where the use of toxic chemicals is eliminated by the use of plant extracts, thus reducing the environmental toxicity and embracing the green chemistry approach (Iravani, 2011; Ahmed et al., 2016). This approach is cost-effective and easy to execute since it does not require sophisticated and costly equipment, high energy requirements, and complex procedures, making it suitable for large-scale production, especially in resource-limited situations (Kumar & Yadav, 2009).

Another notable advantage associated with the nanoparticles synthesized by this method lies in the biocompatibility and low toxicity levels. The phytochemicals on the surface of the nanoparticles provide them with high biocompatibility and low toxicity levels. This makes them highly suitable for medical applications such as the delivery of medicine and wound healing (Mittal et al., 2013). Furthermore, the nanoparticles synthesized by the method exhibit a synergistic effect in antimicrobial activity. This means the nanoparticles have the capability to exhibit high antimicrobial activity against a wide range of microbes, including those resistant to antibiotics (Rai et al., 2014). The method also ensures the stability of the nanoparticles. This is because the phytochemicals act as a natural capping agent to the nanoparticles.

However, the method also has a number of challenges associated with it. The main limitation associated with the method lies in the fact that the nanoparticles synthesized by the method have a high tendency to be inconsistent. This is because the plant extracts used in the synthesis process have a high tendency to vary in composition. For instance, the extracts vary according to the species, geographical location, and season (Ahmed et al., 2016).

Furthermore, there are challenges in scale-up and commercialization processes owing to variations in raw materials used and requirements for optimization of processes. There is a need for thorough toxicity and safety studies, especially for long-term use in biomedical applications, as the interaction between nanoparticles and living organisms is complex and not fully understood (Iravani, 2011). Moreover, there is a lack of understanding regarding the mechanistic aspects of plant-mediated synthesis, which is necessary for optimization of the process.

Thus, in conclusion, though there are many advantages in using plant-mediated nanoparticles as a sustainable and cost-effective approach compared to conventional methods for producing nanoparticles, there are challenges to be faced for standardization and successful integration into advanced applications for antimicrobial purposes.

9. APPLICATIONS IN ANTIMICROBIAL RESEARCH

Plant-mediated nanoparticles have shown immense applications in antimicrobial studies with increased efficiency, biocompatibility, and multi-functionality. One of the Primary applications of plant-mediated nanoparticles is in the field of medical therapeutics, wherein these nanoparticles are employed for treating various microbial infections, especially those caused by resistant pathogens. For example, silver and zinc oxide nanoparticles synthesized from various medicinal plants were employed for developing wound-healing agents to facilitate faster healing and inhibit infection (Rai et al., 2014; Singh et al., 2018).

The second most important application of plant-mediated nanoparticles is in coating medical devices such as catheters, implants, and surgical instruments. Microbial growth on such devices is often responsible for various hospital-acquired infections. Plant-mediated nanoparticles can be employed for coating such devices to inhibit microbial growth and thereby extend their useful life (Hajipour et al., 2012).

In terms of drug delivery systems, plant-mediated nanoparticles have shown significant potential in improving the delivery of antimicrobial agents. Due to their small size, they can easily interact with microbial agents and improve the efficiency of drugs by delivering them directly to the affected area, thus minimizing adverse effects (Singh et al., 2018).

Plant-derived nanoparticles have shown significant potential in water purification systems. Due to their antimicrobial potential, they can be used for water purification. They have shown significant antimicrobial potential against various pathogens in water, thus improving the quality of water (Qu et al., 2013).

The plant-derived nanoparticles have shown significant potential in the food industry. They have been used in packaging materials for foods in order to improve the quality of foods by inhibiting the growth of pathogens in foods. They have shown significant potential in improving the quality of foods by inhibiting the growth of pathogens in foods (Espitia et al., 2012).

Moreover, plant-mediated nanoparticles have the potential to be used in the textile industry to create antimicrobial textiles. These textiles will be instrumental in the healthcare industry in the prevention of the spread of infections. These nanoparticles will offer antimicrobial properties without affecting the quality of the fabric (Dastjerdi & Montazer, 2010).

From the above-mentioned applications, it is evident that plant-mediated nanoparticles have the potential to be used in the field of antimicrobial research. Their application in the field will be a step in the right direction in the prevention and control of microbial infections.

10. CONCLUSION

The use of plants to make nanoparticles is a great way to do things in a way that is good for the environment and helps us find new ways to fight germs. Medicinal plants can help us make nanoparticles in a way that's easy on the earth because they have natural chemicals that can help us make and stabilize nanoparticles. This way of making nanoparticles is not easy but it also makes the nanoparticles work better with the natural chemicals from the plants.

Medicinal plants can help us make kinds of nanoparticles like silver and gold and zinc oxide and copper nanoparticles. These nanoparticles are really good at fighting germs like bacteria and fungi and viruses. They work in ways like breaking down the germs outer layer and making bad things that hurt the germs and stopping the germs from being able to do what they need to do to survive.

Medicinal plants nanoparticles are also very useful in areas like medicine and delivering drugs and making things that can kill germs and cleaning water and keeping food fresh. They are good for the earth. Do not cost too much and they work well with living things so they are great, for both medical and industrial uses.

However we still have to deal with some problems when we use plant extracts to make nanoparticles. The biggest issues are that the composition of these plant extracts can vary a lot we do not have ways of doing things and we cannot make a lot of nanoparticles at the same time. We need to do research to figure out the best way to make these nanoparticles understand how they really work and see if they are safe and effective by doing tests on living things and in clinical studies.

In conclusion using plants to make nanoparticles is a new and effective way to fight off infections and deal with the growing problem of microbes becoming resistant to antibiotics. If we keep making progress in this area we can develop nanoparticles that're safe work well and are good, for the environment, which can be used in the future to help people.

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