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Review Article

Nanoparticles from Tulsi (*Ocimum Sanctum*) in Immune Enhancement against COVID-19 Situation

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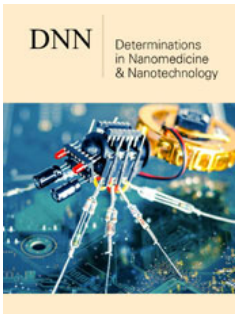

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Abstract

The world is witnessing the outbreak of COVID-19, a disease caused by a novel corona virus, SARS-CoV-2. It has largely affected people throughout the world and has weakened their immune systems to a great extent. To get rid of suffering and curing ailments and to enhance our immune system humans have been using plants from prehistoric times. Nanoparticles in plants are referred to as building blocks of nanotechnology. Plants produce stable nanoparticles and also the rate of synthesis is faster than that of the microorganisms. *Ocimum sanctum* commonly known as tulsi is considered as "The Queen of Herbs". It has a significant role to play in traditional medicine. Several scientific studies have been conducted to reveal the efficient use of the whole plant or its parts for the treatment of different diseases. Nanoparticles in Tulsi can help to fight against various diseases and improves the immune system. Using leaf broth of medicinal herb *Ocimum sanctum* (Tulsi), the synthesis of antibacterial silver nanoparticles (AgNPs) is reported. Silver nanoparticles (AgNPs) are microbicidal agents. It could be potentially used as an alternative to antivirals to treat human infectious diseases generally where the other antivirals have generally proven unsuccessful, especially in the case of influenza virus infections [1-5]. It has been reported as one type of potent therapeutic nanoparticles which boost the immune system to a greater extent especially in the COVID-19 situation.

Keywords: Nanotechnology; Nanoparticles; *Ocimum sanctum*; Immune system; Silver nanoparticles; Corona virus; COVID-19

Abbreviations: CoV: Coronaviruses; MERS: Middle East Respiratory Syndrome; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2

Introduction

The outbreak of COVID-19 caused a huge effect on people and greatly affected their immune systems. The immune system of our body fights against various viruses, bacteria, and infectious diseases [6,7]. Anti-viral, anti-bacterial, and anti-oxidant properties of plants act as an immune booster especially during the time of COVID-19 situation. Nanoparticles are the building blocks for nanotechnology and the nanoparticles from plants are known for stability and faster rate of synthesis. *Ocimum sanctum* has also known as Tulsi is reported as the best herb with various properties to fight against infectious diseases. Nanoparticles in tulsi help fight against diseases and improve the immune system [8].

Corona virus

Coronaviruses (CoV) is a family of viruses that can cause illnesses ranging from the common cold to more severe diseases like severe pneumonia, acute respiratory distress syndrome, sepsis, and septic shock occur, all potentially leading to death [9-11]. Alpha, beta, gamma, and delta are four subtypes of coronavirus used by scientists to categorize the various species. Among all the types of coronaviruses, seven have affected humans out of which four most common are 229E, NL63, OC43, and HKU1. They cause mild illnesses in the upper and

lower airways, nose, sinuses, throat, and lungs while the remaining three i.e., SARS-CoV, MERS-CoV, SARS-CoV-2 can cause more severe illness. SARS-CoV virus causes severe acute respiratory syndrome or SARS, and its symptoms include fever, tiredness, chills, muscle aches, cough, difficulty breathing, diarrhea [12]. In severe cases, SARS can cause a lack of oxygen in the blood, leading to death in 10% of people. While MERS-CoV is a type of coronavirus that causes Middle East Respiratory Syndrome, or MERS causing fever, cough, shortness of breath. Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), the virus responsible for the COVID-19 pandemic [13]. It was first identified in Wuhan, China, in December 2019 and has since spread globally that is mainly transmitted through droplets generated when an infected person coughs, sneezes, or exhales.

Effects of Covid-19

COVID-19 has caused respiratory and intestinal infections in humans as well as animals. It can cause fever, dry cough, tiredness aches and pains, sore throat, diarrhea, conjunctivitis, headache, loss of taste or smell and a rash on the skin, or discoloration of fingers or toes [14-20]. The symptoms differ in severity, some people who have no symptoms up to those with fever, cough, sore throat, general weakness, and fatigue, and muscular pain while in very serious cases, severe pneumonia, acute respiratory distress syndrome, sepsis, and septic shock occur, potentially leading to death. Thus, it has largely affected the human immune system and reduced resistance against viruses and bacteria's [21].

Immune enhancement in covid-19

Immune system is the fighter that protects our body against viruses and diseases and produces antibodies to kill pathogens [22,23]. They play a very significant role in fighting against infectious diseases and keep us healthy. It is important to enhance our immune system to fight against viruses like covid-19. Nanoparticles in plants that contain various properties and applications act as the best agents in fighting against various diseases and enhancing our immune system. Nutritional compounds like vitamin C, antioxidants, and zinc do work with your immune system while Vitamin C, Zinc, anti-viral and anti-bacterial properties of plants act as an immune booster thus keeping infection at bay [24].

Tulsi & its Nanoparticles

Tulsi scientifically known as *Ocimum Scantum* is considered as Queen of Herbs and described as a sacred and medicinal plant in ancient literature. It is derived from 'Sanskrit', which means "the incomparable one". Tulsi in ayurvedic medicine is being used in various clinical conditions like anxiety, chronic cough, bronchitis, fever, snake, and scorpion bites [25]. It has various properties like Anti-stress, Antioxidant, Hepatoprotective, Immunomodulating, Anti-inflammatory, Anti-bacterial, Antiviral, anti-fungal, Antipyretic, Antidiuretic, Antidiabetic, Hypoglycemic, Hypolipidemic, Antimalarial, etc. Synthesis of antibacterial silver nanoparticles (AgNPs) is reported using leaf broth of medicinal herb *Ocimum sanctum* (Tulsi) [26,27].

Nanoparticles in Tulsi

Nanoparticles in plants are widely used due to their stability and faster synthesis and play a significant role in traditional medicine [28]. Tulsi nanoparticles (AgNPs) have great potential in a broad range of applications as antimicrobial agents, biomedical device coatings, drug-delivery carriers, imaging probes, and diagnostic and optoelectronic platforms biochemical functionality tailored by diverse size- and shape-controlled AgNPs [29]. They are considered as one of the most significant nanoparticles due to their exceptional broad-spectrum bactericidal properties, relatively low cost of manufacturing AgNPs, unique properties, and ability to form diverse nanostructures. Silver nanoparticles (AgNPs) are one of the most fascinating nanomaterials among several metallic nanoparticles as they are involved in biomedical applications. AgNPs have a significant role in nanoscience and nanotechnology, particularly in nanomedicine.

AgNPs biological and biomedical applications are antibacterial, antifungal, antiviral, anti-inflammatory, anti-cancer, anti-angiogenic, Bio-sensing, drug carrier, anti-tumor, anti-oxidative, imaging, and human health care [30,31]. Silver nanoparticles (AgNPs) are found in various shapes like spherical shape AgNPs, oval shape AgNPs, rod shape AgNPs, Flower shape AgNPs, and Precursors. AgNPs are microbicidal agents which could be potentially used as an alternative to antivirals to treat human infectious diseases, especially influenza virus infections where antivirals have generally proven unsuccessful. Its antibacterial effects of silver nanoparticles have been used to control bacterial growth also produce reactive oxygen species and free radicals which cause apoptosis leading to cell death preventing their replication. It is reported as one type of potent therapeutic nanoparticle which boosts the immune system to a greater extent especially in the COVID-19 situation [32,33].

Synthesis of AgNPs

Silver nanoparticles (AgNPs) have proved to be most effective because of its good antimicrobial efficacy against bacteria and viruses [34,35]. They are undoubtedly the most widely used nanomaterials among all and it has been reported through the studies about the successful biosynthesis of silver nanoparticles by plants such like *ocimum scantum*. They can be potentially used as an alternative to antivirals to treat human infectious diseases. There are three main categories for silver nanoparticle (AgNPs) mainly known as physical method, chemical method, biological method [36] (Figure 1).

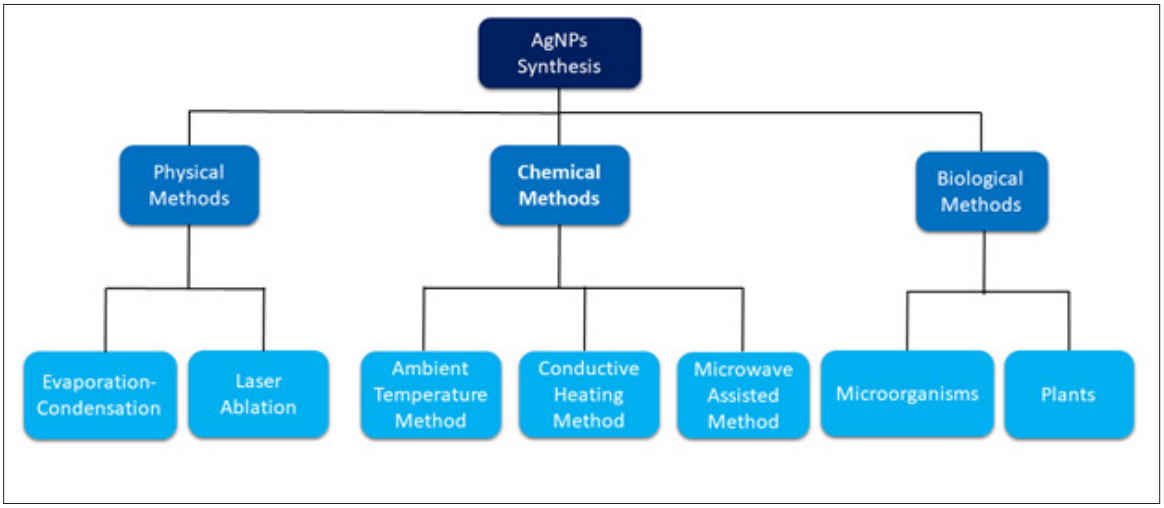

Figure 1: Synthesis of AgNPs.

Physical methods: The two approaches of physical methods are evaporation-condensation and laser ablation. Physical synthesis methods using evaporation-condensation have an advantage over chemical methods due to the absence of solvent contamination in the prepared thin films and the uniformity of NPs distribution [37]. The evaporation-condensation method is very useful since nanoparticle generator for long-term experiments for inhalation toxicity studies. Silver nanoparticles (AgNPs) can also be synthesized using the laser ablation method of metallic bulk materials in solution. The absence of chemical reagents in solutions is the main advantage of the laser ablation technique for the production of metal colloids.

Chemical methods: The chemical method has three approaches i.e., ambient temperature methods, conductive heating methods, and microwave-assisted methods. Synthesis of silver nanoparticles (AgNPs) can also be done using chemical reduction by organic and inorganic reducing agents. Silver nanoparticles can be prepared by mixing the corresponding metal ions with reduced polyoxometalates which serve as reducing and stabilizing agents at room temperature. They can also be synthesized using microemulsion techniques as they are uniform and size controllable. The presence of citrate, polyvinylpyrrolidone, poly (acrylic acid), and collagen synthesis of silver nanoparticles (AgNPs) has been reported using UV-initiated photoreduction which is a simple and effective method. Synthesis of AgNPs using the photochemical method is also a clean process that has a high spatial resolution, convenience of use, and great versatility. The most promising one is the microwave-assisted method since microwave heating has shorter reaction times, reduced energy consumption, and better product yields. Thus, preventing the agglomeration of the particles formed. In order for consistently yielding nanostructures with smaller sizes, narrower size distributions, and a higher degree of crystallization microwave heating is better than a conventional oil bath. It was reported that by employing carboxymethyl cellulose sodium as a reducing and stabilizing agent synthesis of silver nanoparticles (AgNPs) can be done using the microwave-assisted method. Synthesis of AgNPs can also be done using the simple tollens method with controlled size [38].

Biological methods: The biological method has two effective approaches i.e., using microorganisms and plants. It has been reported that the synthesis of nanoparticles by chemical approaches is not eco-friendly and expensive. Thus, there is a need for developing eco-friendly processes that do not use toxic chemicals in the synthesis. During the research, it was observed that the potential of organisms in nanoparticle synthesis ranges from simple prokaryotic bacterial cells to eukaryotic fungi, and plants [39].

Biological methods can be used for the synthesis of highly stable and well-characterized nanoparticles. Synthesis of silver nanoparticles can be done by bioreduction of aqueous silver ions with culture supernatant of nonpathogenic bacterium, bacillus licheniformis. Using fusarium oxysporum silver nanoparticles AgNPs (5-50nm) could be synthesized extracellularly with no evidence of flocculation of the particles even a month after the reaction. The bioreduction of the silver ions occurred on the surface of the cells and proteins can have a critical role in the formation and stabilization of the synthesized silver nanoparticles (AgNPs). *Chaetoceros Calcitrans, Chlorella Salina*, *Isochrysis Galbana*, and *Tetraselmis Gracilis* are some of the marine algae that can be used for the reduction of silver ions and thereby the synthesis of silver nanoparticles (AgNPs). Synthesis of nanoparticles (NPs) using plants is a very cost-effective, economic, and valuable alternative, thus can be used for the large-scale production of NPs. Biosynthesis of silver nanoparticles (AgNPs) can be done using the extract of *Camellia sinensis* (green tea) as it acts as a reducing and stabilizing agent. In silver nanoparticle (AgNPs) synthesis plant extracts from

alfalfa (*Medicago Sativa*), lemongrass (*Cymbopogon Flexuosus*), and geranium (*Pelargonium Graveolens*) have served as green reactants. For green synthesizing of silver nanoparticles (AgNPs), the capsicum annuum can also be used. It was observed and reported that *Ocimum Sanctum* (Tulsi) leaf extract can reduce silver ions into crystalline silver NPs (4-30nm) within 8 min of reaction time and were stable due to the presence of proteins which may act as capping agents. Tulsi leaves contain ascorbic acid which may play a significant role in the reduction of silver ions into metallic silver nanoparticles (AgNPs).

AgNPs in immune enhancement against Covid-19

Silver nanoparticles (AgNPs) have gained considerable interest due to their unique properties like antimicrobial, antiviral, anti-inflammatory, etc. Covid-19 has adversely affected human health and reduced immune system to a great extent. Silver nanoparticles being microbicidal agents, reducing agent, stabilizer, flexibility, and other medicinal properties have significant inhibitory effects against microbial pathogens, and are widely used as antimicrobial in a diverse range of products. Antibacterial effects of silver nanoparticles have been used to control bacterial growth during covid-19 situation and helped improve human immune system. It also produces reactive oxygen species and free radicals which cause apoptosis leading to cell death preventing their replication. Thus, AgNPs acts as the best agents in fighting against various diseases and enhancing our immune system [40].

Application of AgNPs

Nanoparticles in tulsi have tremendous prospects for the improvement of the diagnosis and treatment of human diseases. They have gained considerable interest because of their medicinal as well as other properties and proven applicability in diverse areas. Their flexibility and incorporation into various media have encouraged researchers to further study the mechanistic aspects of antimicrobial, antiviral, and anti-inflammatory effects. AgNPs produce reactive oxygen species and free radicals and being one type of potent therapeutic nanoparticles, it is used to boost the immune system to a greater extent especially in the COVID-19 situation. Thus, they have huge applications in medicine and helps in the potential improvement of the immune system.

Conclusion

Tulsi nanoparticles being microbicidal agents and their incredible properties, have become significant in many fields in recent years such as health care, environment, agriculture, etc. Tulsi and its nanoparticles have highly medicinal applications and are used to improve the immune system, especially during the covid-19 situation. Viruses like covid-19 have highly affected human health and due to the medicinal effects of nanoparticles, they have served as an alternative to antivirals to treat human infectious diseases, control bacterial growth, and are proven as the best agents in fighting against various diseases and enhancing our immune system.

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