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REVIEW ARTICLE

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Phyto-Nanotherapy: An Innovative Approach towards Microbial Management

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ABSTRACT

Microbes have evolved and diversified to cover everything on this plant in last three billion years. Wrong prescriptions, genetic modifications and over usage of the antibiotics enhanced resistance capabilities of microbes. There is a growing need of a combination therapy that can treat microbial infections through a safe, environmental friendly and cost-effective approach. Phyto-nanotherapy involves the biological synthesis of nanoparticles in plants or by the use of plant products as secondary metabolites with a combination of advanced nanotechnology for the therapeutic treatment of several disorders. A Herbo-metallic combination is an ancient approach of therapeutics. This review emphasizes the ancient to modren approach of phyto-nanotherapy and its future challenges.
Keywords: Phyto-nanotherapy, Secondary metabolites, Antibiotics, Microbial infections and Therapeutics.

INTRODUCTION

One can learn more and more from 'Nature'. Nature is itself a technology but is so complex that we can understand only a few percent. For all the sciences, the basic idea lies on natural principles. Like other sciences, Nanotechnology is also concerned with understanding how nature works ? Modern nanotechnology is an interdisciplinary science concerning the tiniest of particles and their special chemical, physical and mechanical properties at the meeting points of physics, chemistry, biology, medicine, electronics and information technology. In practice, the special areas of nanotechnology overlap and blur the boundaries between the natural sciences [Krukemeyer et al., 2015]. Noble metal nanoparticles as silver and gold nanoparticles are attracting huge interest from the scientific community owing to their fabulous properties and diversity of applications. Mankind has been fascinated by gold and silver since prehistoric times and applications of their nanoparticles have attracted attention for millennia, although understanding phenomena at the nanoscale is very recent. Nanoscale analogs are being explored due to their unusual functional attributes quite unlike the bulk.

Tunability of the properties by varying the size, shape, composition or local environment presents them with unusual capabilities. By manipulating the chemical composition of the materials at the nanoscale, their electrical, chemical, optical and other properties that can be manipulated precisely [Sreeprasad and Pradeep, 2013]. In general, nanoparticles can be synthesized using a variety of methods including physical, chemical, biologicaland hybrid techniques [Abada et al., 2024]. The production of nanoparticles through conventional physical and chemical methods results in toxic byproducts that are environmental hazards. Additionally, these particles cannot be used in medicine due to health-related issues, especially in clinical fields. Conventional methods can be used to produce nanoparticles in large quantities with defined sizes and shapes in a shorter period of time; however, these techniques are complicated, costly, inefficient and outdated. In recent years, there has been growing interest in the synthesis of environmentally friendly nanoparticles that do not produce toxic waste products during the manufacturing process. This can only be achieved through benign synthesis procedures of a biological nature using biotechnological tools that are considered safe and ecologically sound for nanomaterial fabrication as an alternative to conventional physical and chemical methods. This has given rise to the concept of green technology or green nanobiotechnology. In general, green nanobiotechnology means synthesizing nanoparticles or nanomaterials using biological routes such as those involving microorganisms, plants, and viruses or their byproducts, such as proteins and lipids, with the help of various biotechnological tools [Paul et al., 2015, Bailey et al., 2004]. In recent years, synthesis of metal nanoparticles is a subject of focused research interest due to its wide potential applications in biomedical, optical and electronic fields [Chavan and Ghadage, 2018]. There are several evidences that support the formation of gold and silver nanoparticles in living plants. Some researchers directly attained the biosynthesis of metal nanoparticles by plant extracts and their potential applications [Arya, 2010]. Biological approach for the synthesis of silver nanoparticles (Green synthesis) is an eco-friendly and cost-effective method as compared to the other chemical and physical methods. This has promoted research in the well known activity of silver ions and silver-based compounds, including silver nanoparticles. This effect was size and dose dependent and was more pronounced against gram-negative bacteria than gram-positive organisms [Arya et al., 2011].

Phyto-nanotherapy: A general background

Several chemical methods have been developed for the synthesis of silver nanoparticles including chemical reduction, aqueous solution chemical reduction, nonaqueous chemical reduction, the template method, electrochemical reduction, ultrasonic-assisted reduction, photo-induced or photo-catalytic reduction, microwave assisted synthesis, irradiation reduction, the microemulsion method, biochemical method etc., but these chemical methods have been reported along with various drawbacks, including the use of toxic solvents, generation of hazardous by-products, and high energy consumption, which pose potential risks to human health and to the environment [Gandhi and Khan, 2016]. As microorganisms that are exposed to pollutants in the environment such as metal ions have a remarkable ability to fight with metal stress. These metalmicrobe interactions have already found an important role in Biotechnological applications. It is only recently that microorganisms have been explored as potential biofactories for the synthesis of metallic nano particles [Uma and Shantha, 2012].

Nowadays, there is a growing need to develop eco-friendly processes, which do not use toxic chemicals in the synthesis protocols. Green synthesis approaches include mixed-valence polyoxometalates, polysaccharides, Tollens, biological, and irradiation method which have advantages over conventional methods involving chemical agents associated with environmental toxicity [Rodrigues et al., 2024]. Selection of solvent medium and selection of eco-friendly nontoxic reducing and stabilizing agents are the most important issues which must be considered in green synthesis of NPs.

In plants, the real focal point of utilising plant concentrates for silver nanoparticle combination is that they are effortlessly accessible, safe and nontoxic much of the time and that they have an expansive mixed bag of metabolites that can help in the reduction of silver ions. Compared with bacteria, fungi have the capacity to produce larger amounts of nanoparticles because they are regarded as the organisms that produce nanoparticles extracellularly due to extensive secretory components, which is included in the reduction and capping of nanoparticles [Ahmad et al., 2003, Gudikandula and Maringanti, 2016]. The advancement of green syntheses over chemical and physical methods is: environment friendly, cost effective and easily scaled up for large scale syntheses of nanoparticles, furthermore there is no need to use high temperature, pressure, energy and toxic chemicals [Ahmed et al., 2016].

Silver NPs are of interest because of the unique properties which can be incorporated into antimicrobial applications, biosensor materials, composite fibers, cryogenic super-conducting materials, cosmetic products, and electronic components. Several physical and chemical methods have been used for synthesizing and stabilizing silver NPs [Iravani et al., 2014]. Of all the nanoparticles developed and characterized thus far, Ag NPs assume a significant position owing to their inherent characteristic of acting as an antimicrobial agent even in solid state. Although, its significance was recognized much earlier, it was not well exploited except for its use in oriental medicine and in coins. It is estimated that nearly 320 tons of Ag NPs are manufactured every year and used in nanomedical imaging, biosensing and food products [Siddiqi et al., 2018]. Although; among the various biological methods of silver nanoparticle synthesis, microbe mediated synthesis is not of industrial feasibility due to the requirements of highly aseptic conditions and their maintenance. Therefore; the use of plant extracts for this purpose is potentially advantageous over microorganisms due to the ease of improvement, the less biohazard and elaborate process of maintaining cell cultures [Ahmed et al., 2016].

So, Phyto-nanotherapy involves the production and therapeutic application of cost-effective and environmental benign nanoparticles synthesized from the biological route i.e. from plants.

Nanotherapy: Ancient to Modern approach

Since ancient days, natural products, including plants, have been the basis of treatment of human diseases. The basis of concept of modern medicine development remains rooted in traditional medicine and therapies [Anarkali, 2012, Anitha et al., 2016] In different parts of the world like ancient China, Egypt, Africa, America, and India, plants had been used for medicinal purposes long before recorded history. Chemical analysis first became available in the early 19th century which started the extraction and modification of herbal ingredients [Ansari et al., 2012].

The Ayurvedic system of medicine has great antiquity, dating back to about 5000 years B.C. Its Materia Medica contain resources in the form of drugs derived from plant, animal, metal and mineral sources, the uses of which have been advocated in various different pathological manifestations. During the medieval period, with the advent of *Rasashastra*, use of certain heavy metals and minerals in Ayurvedic therapeutics increased. *Rasashastra*, an integral part of Ayurveda, deals with the drugs of mineral origin, and details their varieties, characteristics, processing techniques, properties, therapeutic uses, possibilities of developing adverse effects and their management etc. in a comprehensive way. Although the roots of this science (Rasa Shastra) exist in the ancient texts of Indian civilization, its development as an independent system of therapy started around the 8th century A.D. Ayurvedic classics written before that time, like *Charaka Samhita and Sushruta Samhita* etc. contain descriptions of metals and minerals, their processing techniques and their utilization in therapeutics etc. The classic *Charaka Samhita* described that metals like Gold, Silver, Iron, Copper, Lead, Tin etc. as well as some alloys were used to treat a wide range of diseases. Fine powders of these metals were prescribed for both internal and external applications [Galib et al., 2011]. Use of metallic herbal preparations (bhasma or calcination) in which bhasma is prepared through a process termed bhasmikarana (mixing metal with sulfur and herbal preparations and then controlled intermittent heating so that metal is converted to its sulfide form) is something unique to Ayurveda. Converting a metal to its sulfide form or calcination of a metal is regarded in Ayurveda as removing toxic properties of the metal, especially mercury [Rahmatullah et al., 2014]. In general, there are two types of Ayurvedic herbal formulations: Kasthoushadhies (pure herbal preparations) and Rasaushadhies (herbo-bio-mineral metallic preparation), in which the latter contains minerals added for their therapeutic effect [Parasuraman et al., 2014]. In Siddha system also, the herbals, metals, minerals and animal products has been used to prepare the medicines for treating various illness. Siddha medicines are divided into internal medicines and external medicines [Sivakkumar et al., 2018].

The People’s Republic of China has had a great deal of experience in the use of herbal medicines against various bacteria for over 2,000 years. Before the advent of antibiotics, many people with infectious diseases could be saved by numerous antibacterial herbal decoctions. From a modern medicine perspective, these herbal agents contained mainly polyphenols, flavones, and polysaccharides, and the reducing and antimicrobial properties of these compounds are fully understood from previous reports. However, the complexity of component analysis and identification posed a real challenge in the modernization of traditional Chinese medicine (TCM). This was in part because the active ingredients in these decoctions were so complicated that precise quantification of the active substance seemed difficult, resulting in uncertainty with regard to their use in antimicrobial [Sun et al., 2014].In traditional Chinese medicine, heavy metals have been used for numerous health complaints. For example, Hg is part of certain preparations under the terminology of ‘cinnabaris’ (mercury sulfide), ‘calomel’ (mercury chloride) or ‘hydrargyrioxydumrubrum’ (mercury oxide). At present, a lot of research is going on the combination application of TCM and nanotechnology for the advancement of the therapeutic measures. Heavy metals have also been detected in African traditional remedies like hexavalent chromium (Cr (VI), a class 1 carcinogen, is commonly used in South African traditional medicines and known locally as ndonya [Street, 2012].

Epidemicity of Anti-microbial resistant infections

Antimicrobial resistance allows infections to progress in many people and to kill some of them, but it is not a disorder of people. It is a disorder of bacterial populations. Bacteria have evolved and diversified over three billion years to cover everything on this planet, including the surfaces of our skins; mouths, and guts. While we are alive, we manage for the most part to exclude bacteria from our tissues, but those tissues also become bacteria thereafter [Zehra et al., 2025]. The new problem is that many of the antimicrobial agents no longer kill many strains of bacteria. Those resistant strains make proteins that nullify the effects of the agents in various ways. Each such protein is expressed by a gene that the strain's susceptible ancestors lacked. The rise of the prevalence of such resistance genes in the bacterial populations that always cover and sometimes infect us is the problem. It can be seen as two processes: emergence and dissemination [O'Brien, 1997]. In February 2017, the World Health Organisation (WHO) published it's first-ever list of antibiotic-resistant pathogens for which new anti-microbials are needed u-rgently. Out of the 12 resistant pathogens listed, seven were noted to possess resistance to beta-lactam antibiotics. The three pathogens categorised as "Critical" are resistant to carbapenems, imipenem for example, and four others are resistant to fluoroquinolones, such as ciprofloxacin which are also widely used in clinical practice. This is an alarming fact as in the future this will not only challenge prescribing practices but will also increase the difficulty in obtaining suitable antibiotics to treat patients [Kumar et al., 2018]. A century ago when antibiotics came into use were considered as 'miracle drugs' and their popularity rapidly led to overuse. Due to uninsured quality and irrational use of antibiotics pathogens are losing their effectiveness against them 3. Accumulation of resistance genes on plasmids that are replicated and passed between microbial cells is main reason behind rapid rise in drug resistant pathogens. Such multi-drug resistant (MDR) microbes are termed as 'superbugs'. Almost 70% of current day infections are suspected to be due to drug resistance 5, alone U.S ranked 4th for death caused by bacterial infections. Reports shows over 50% of hospital bloodstream infections are incurred by Vancomycin Resistant Enterococci (VRE) and Methicillin Resistant Staphylococcus aureus (MRSA). Among the Escherichia coli (E. coli) isolates from India and China, less than 50% are susceptible to commonly used antibiotics (e.g., Cephalosporins and Ciprofloxacin [Gupta et al., 2013].

Antimicrobial resistance is mainly driven by inappropriate use. Global antibiotic consumption in humans has increased by 36% between 2000 and 2010. Half of this increased use is regarded as unnecessary, e.g. when antibiotics are used to treat illnesses like common colds that are caused by viruses, where antibiotics have no effect. In many countries, antibiotics can be bought without prescription or do not have underlying standard treatment guidelines. These factors increase antibiotic resistance because of a lack of knowledge of proper antibiotic use [WTO, 2016]. WHO adopted the Global Action Plan on Antimicrobial Resistance (GAP-AMR) in 2015. The plan focuses on a comprehensive approach meaning that actions in all relevant sectors should be implemented synergistically. To tackle antimicrobial resistance, the global action plan sets out five strategic objectives:

- to improve awareness and understanding of antimicrobial resistance;
- to strengthen knowledge through surveillance and research;
- to reduce the incidence of infection;

- to optimize the use of antimicrobial agents; and
- to develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions.

Nanoparticles as an eco-friendly anti-microbial agent

Resistance in human pathogens is a big challenge in fields like pharmaceutical and biomedicine. Antibiotic resistance profiles lead to fear about the emergence and re-emergence of multidrug-resistant (MDR) pathogens and parasites [Tenover, 2006]. Once an individual is infected with MDR bacteria, it is not possible to cure easily and he/she has to spend more time in the hospital and requires a multiple treatment of broad-spectrum antibiotics, which are less effective, more toxic and more expensive [Webb et al., 2005]. Therefore, development of or modification in antimicrobial compounds to improve bactericidal potential is a priority area of research in this modern era [Rai et al., 2012]. Several metals, metal oxides, metal halides and bimetals in nanoparticulate form have been documented for antimicrobial activity as the bacteria are less likely to develop resistance to nanomaterials. These comprise NPs containing Ag, Au, Zn, Cu, Ti, Mg, Ni, Ce, Se, Al, Cd, Y, Pd and super-paramagnetic Fe. Zerovalent bismuth-containing NPs have shown promise in treating infections due to drug-resistant bacteria in combination with X-rays [Mohanta et al., 2023].

The primary reason why NPs are being considered as an alternative to antibiotics is that NPs can effectively prevent microbial drug resistance in certain cases. The rampant use of antibiotics has led to the emergence of numerous hazards to public health, such as superbugs that do not respond to any existing drug and epidemics against which medicine has no defense. The search for new, effective bactericidal materials is significant for combatting drug resistance, and NPs have been established as a promising approach to solve this problem. However, NPs can also promote the emergence of bacterial resistance in certain cases. Nanoparticles works on the anti-microbial resistant microbes by the following ways [Wang et al., 2017].

1. Overcoming the existing antibiotic resistance mechanisms
2. Combatting microbes using multiple mechanisms simultaneously
3. Acting as good carriers of antibiotics
4. The ultra-small and controllable size of NPs is suitable for conducting antimicrobial operations and combating intracellular bacteria
5. NP carriers can help to increase the serum levels of antibiotics and protect the drugs from resistance by target bacteria.
6. Precision and security
7. Sustained and controllable release of antibiotics can be achieved flexibly by using nanoparticles.
8. Multiple drugs or antimicrobials can be packaged within the same NP.

The production of metallic silver nanoparticles with different morphologies and sizes has been realized during the last decade using different routes [Rai and Posten, 2013]. Among these, biological approach is cheap and eco-friendly. In physical methods, nanoparticles are synthesized as results of aggregation, lithography etc.

The chemical method follows electrochemical, thermal laser, microwave, polyol and various other techniques, however, these approaches adds advantage of large-scale production. Hazardous reducing agents used for chemical procedure mounts a bias for eco-friendly and feasible approach for synthesis of nanoparticles. In such procedures, traces of unreacted reagents or unwanted by products remain in the silver colloidal solution rendering the Silver nanoparticles inappropriate for biological application [Das et al., 2010]. These synthetic methods involve the reduction of an ionic form of silver and gold in an appropriate medium using various reducing agents. In addition, typical synthetic methodologies involve complex physical and chemical processes that use high temperature and high pressure, large amounts of energy and many toxic substances producing pollution to the environment. The most environmentally benign method uses plant extract as reducing agent. This biological approach to silver nanoparticles synthesis is ideal in terms of green chemistry [Arya, 2015]. A lot of literature is available for the biological synthesis of nanoparticles in plants and their extracts. Some of them are given in Table 1.

Combinatorial Nanomedicines: Herbal-Nano Formulations

In recent year, the nanonization of herbal medicines has attracted much attention. Nanonized herbal drugs are also bioactive molecules or biodegradable nanoparticles which has high bioavailability, solubility, retention time, efficacy, specificity, tolerability and therapeutic index of corresponding drugs. At the same timenanonized drugs reduce the patient's expenses, risks of toxicity and have many advantages such as the protection of premature degradation, enhancement of intracellular penetration and interaction with the biological environment. Nanosizing led to increased solubility of components, reduction in the dose via improved absorption of active ingredient [Gupta et al., 2013].

Table 1. Antimicrobial efficacy of silver nanoparticles synthesized from plants.

Botanical Name	Size of Nanopartilces	Effective against Microbes	References
Allium Cepa	33.6 nm	*Pseudomonas aeruginosa*	[15]
Azadira chtaindica	200 nm	*E. coli*	[14]
Carica Papaya	2-5 nm	*Pseudomonas Aeruginosa, Enterococcus*	[29]
Ceratonia siliqua	5-40 nm	*E. coli*	[11]
Eichhornia crassipes	18–30 nm	*Staphylococcus aureus, Bacillus subtilis, Escherichia hermanii, and Pseudomonas aeruginoss*	[42]
Mollugo nudicaulis	8.3-10.2 nm	*Staphylococcus aureus, Vibrio cholera*	[4]
Musa balbisiana	200 nm	*E. coli, Bacillus sp.*	[14]
Ocimum tenuiflorum	200 nm	*E. coli*	[14]
Olea europaea	440–458 nm	*Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli*	[27]

Phaseolus vulgaris	4-30 nm	*E. coli, Candida albicans*	[39]
Securinega leucopyrus	11-20 nm	*Pseudomonas aeruginosa, Klebsiella pneumonia*	[18]
Solanum torvum	434 nm	*Pseudomonas aeruginosa, Staphylococcus aureus, Aspergillus flavus, Aspergillus niger.*	[21]
Syzygium cumini	20 to 60 nm	*Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Azotobacter chroococcum, Bacillus lichen iformis*	[40]
Eclipta alba	400–440 nm	*Escherichia coli, Staphylococcusaureus, Pseudomonas aeruginosa*	[41]
Azadirachta indica	436–446 nm	*Staphylococcus aureus, Escherichia coli*	[3]
Prunus persica	40-98 nm	*E. coli and V. cholera*	[33]
Coriandrum sativum	6.45 nm	-	[28]
Origanum vulgare	2-25 nm	*Shigella sonnei, Micrococcus luteus, Escherichia coli, Aspergillus flavus, Alternaria alternate, Paecilomyces variotii, Phialophora alba*	[47]
Sesbania grandiflora	10-50 nm	*Escherichia coli, Pseudomonas spp., and gram-positive Bacillus spp., Staphylococcus spp*	[34]

The intervention of phytochemicals from herbs, plants, fruits and various herbal roots is expected to create a new paradigm in integrative medicine which combines holistic approaches of herbal medicine to make the overall combination therapy more effective, less toxic and ultimately bringing down health care costs globally.

A lot of research is going on the phytochemical based or guided combinatorial nanomedicines. Recently, in the form of liposomal formulations, nanostructured lipids and metallic nanoparticles from plants, phytochemicals are guided to treat lung cancer. Aside from being the active treatment agent for lung cancer studies, phytochemicals in liposomal systems may also act as permeating agents for other liposomal formulations utilized against lung cancer. For instance, cineole-loaded liposomes created via thin film hydration (TFH) have been implicated in an increased effect in combination with nanoliposomes containing antisense oligonucleotide (ODN) which was significantly stronger than single ODN nanoliposome agent ($p<0.05$). The use of nanostructured lipid as carriers of phytochemicals has been scarce in lung cancer, with prominent applications in delivering gene therapy and chemotherapeutic drugs. It is to be noted that this system has been successfully demonstrated in vitro and in vivo for its applications in other types of cancers, such as pancreatic and prostate cancers.

Also, polymeric NPs are often chosen as carrier systems of drugs in the field of cancer research due to its stability in storage. Despite this, only a handful of research has been done on potential lung cancer therapeutics utilizing this nanocarrier system. For instance, a PEG-PLGA-Rg3 formulation of ginsenoside has also been shown b to decrease the protein expression levels of metallomatrixproteinase-9 (MMP-9), HIF-1, and vascular endothelial growth factor (VEGF) [Aw-Yong et al., 2018]. Similarly, combinatorial nanomedicine is also successfully used for the colon cancer [Anitha et al, 2016].

Among the novel drug delivery systems, nanoparticles are considered to be an important one. Nanoparticle can be used to target the herbal medicine to individual organ which improves the selectivity, drug delivery, effectiveness and safety and thereby reduces dose and increases patient compliance. The requirement of an ideal nanoparticulate system is that it should be capable of circulating in blood stream and should be small enough to reach target cells and tissues. Herbal medicines can be targeted to various organs such as brain, lung, liver, kidney, gastrointestinal tract, etc. Most of the herbal actives are poorly water soluble because of their hydrophobic nature. This property leads to decreased bioavailability and increased systemic clearance thus necessitating repeated administration or increased dose, and thus limits the clinical use of herbal medicines. Therefore, nanoparticles can be utilized to increase the herbal drug solubility and help to localize the drug in a specific site thus resulting in better efficacy and improved patient compliance [Kumar et al., 2013].

Despite that, numerous studies in the past have also reported a list of limitations that the nanotechnology-based therapeutics are facing. For instance, safety and toxicity issues are the most discussed limitation of the nanoparticle-based drug delivery. NPs are well known for their ability to deliver various drugs or compounds to the targeted tissue in human body. This is due to their very small size as well as other unique properties. However, their unique properties were also the main reason which causes a variety of toxicity effects [Aw-Yong et al., 2018]. Nano-sized delivery system was selected because of the following reasons [Ansari et al., 2012]:

• They appear to be able to deliver high concentrations of drugs to disease sites because of their unique size and high loading capacities.

• Deliver the drug in the small particle size that enhances the entire surface area of the drugs allocating quicker dissolution in the blood.

• The concentration seems to persist at the sites for the longer periods.

Current status and Future Approach

Although nanotechnology based approaches are beneficial for medicinal areas, it is necessary to emphasize some of the disadvantages. Clinical researchers have revealed some negative factors, such as high cost, difficulty of calling up processes, and the easy inhalability of nanomedicines, which can result in dangerous lung disorders, and they often lead to other fatal diseases that can lead to changes in homeostasis, or even can cause death [Jain et al., 2015, Singh et al., 2013]. Nanotechnology based drug delivery system for phytochemicals overcomes the limitations of solubility, pharmacokinetic and toxicity problems to normal tissues. Further, these nanomedicines result in selective release of phytochemical in diseased tissue and can be engineered with targeting ligands to achieve site specific tumor targeted delivery. Recently, combinatorial nanomediciness based on co-encapsulation of phytochemical and chemotherapeutic agents have gained much interest.

It is anticipated that ongoing research efforts in the area of combinatorial nanomedicines will be commercialized as a new chemotherapeutic regimen for the disease [Rizwanullah et al., 2017].

In case of phtonanoparticles synthesis, it is essential to synthesize nanoparticles of uniform size, shape and characteristics, which is still a challenge. In general, A concentration of 1 mM silver nitrate, ambient temperature, and neutral pH represent the best conditions for AgNP synthesis in optimum time. However, this condition as pH and temperature also varies among different plants. A definitive mechanism of actionof AgNPs for the cancer cells or other infected cells has not yet been discovered. Possible mechanisms may be ROS production, and in some cases, the binding of silver ions to the cell membrane, leading to cell death. One undesirable result of a reaction between AgNPs and cells or tissues, which needs to be prevented, is the leakage from theAgNPs of silver ions that are sequestered by the cells or tissues. These silver ions are toxic for normal as well as diseased cells. If we compare what is known about plants and their ability to synthesize AgNPs by other means, it is clear that much more research is needed on the ability of AgNP synthesis by plants. The cost of silver nitrate in the quantities needed versus the cost of antibiotics in effective doses signifies their medicinal applications. In order for silver nanoparticles to be considered for use as a drug in treatment of disease, extensive in vivo testing in animals and clinical testing is legally required, in addition to in vitro testing [Mashwani et al., 2015].

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