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Research Article

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Biological synthesis of silver nanoparticles using Biological Systems: A Systemic Review

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Summary
Nanotechnology has evolved a great deal. Biological synthesis of nanoparticles and silver nanoparticles in particular has been widely studied. The current review focuses on different studies across the globe that adopted different methods and biological system to synthesize silver nanoparticles. Special emphasis has been given to North East India as many of the studies from this part of the world tried to synthesize functional nanoparticles based on indigenous medicinal plant extract.

Keywords: Biological systems, Nano particles, North East India

Introduction
Nanotechnology is a branch of science which has provided with a vast area of researches. It encompasses the study and the understanding of the fundamentals of nano-scale objects. Researches regarding nanoparticles are important aspects of nanotechnology due to their various applications. Significant advances with nanoparticles have been seen in areas such as bio sensing, imaging, drug delivery, optical fibers and sensors, bio-labelling and so forth.

The conventional method of producing nanoparticles involves the use of chemical reducing agents which inspite of producing pure nanoparticles, have disadvantages such as hazardous effects on environment and their high expenditure. Green nanotechnology is an approach to reduce the harmful by-products in conventional ways of synthesizing nanoparticles. Green nanotechnology is derived from the field of green chemistry and its principle of green chemistry. The green chemistry concept was first started in the United States with cooperation from various scientific societies, researchers and industries [1]. The green synthesis or the biological method of producing nanoparticles utilizes the naturally occurring plants and microorganisms which is less toxic and cost-effective as compared to the chemical synthesis. On the other hand, the use of plants and microbes are suitable for large scale production of nanoparticles.

This study emphasizes on the use of plants and microorganisms extract to synthesize silver nanoparticles. Plants and microorganisms contain numerous therapeutic biomolecules and compounds that have been exploited since ancient time. Recent studies implicates that the use of medicinal plants is advantageous since it is easily available and less harmful besides being least toxic.

Sources of the Plant Parts Used
Different parts of plants have been used as the source of the extract in nano synthesis experiments.

In one of the study entitled "Rapid biological synthesis of Silver nanoparticles from *Ocimum sanctum* and their characterization" carried out by Khan et al. (2017), the leaf broth of *Ocimum sanctum*is used for the bioreduction of $AgNO_3$ [2]. The plant is traditionally known to have strong antimicrobial and antioxidant property.

In another study with the title "Synthesis of Silver nanoparticles using aqueous extract of medicinal plants' (*Impatiens balsamina* and *Lantana camara*) fresh leaves and analysis of antimicrobial activity" by Aritonang et al. (2019), the aqueous leaf extracts of the medicinal plants *Impatiens balsamina and Lantana camara* were used as bioreducing agents to synthesize silver nanoparticles [3].

In a separate study, "Green synthesis of silver nanoparticles from flower extract of *Hibiscus rosa sinensis* and its antimicrobial activity" Rajakumar et al. (2016), the flower extract of medicinal plant *Hibiscus rosa sinensis* has been used to synthesize silver nanoparticles [4].

In the study, "Synthesis of plant- mediated silver nanoparticles is using papaya fruit extract and evaluation of their antimicrobial activity" by Jain et al. (2009), the reduction of silver ions present in silver nitrate solution is done by using the cell free aqueous extract of papaya fruit [5].

Biological Method of Synthesizing Silver Nanoparticles
International Scenario
In a study entitled "Synthesis and biological characterization of silver nanoparticles derived from the cyanobacterium *Oscillatoria*

limnetica" by Hamouda et al. (2019), the aqueous extract of *Oscillatoria limnetica* fresh biomass was used for the green-synthesis of AgNPs [6]. *O. limnetica* culture was centrifuged and the resulting pellet was made into an aqueous extract. The color change (green to brown) brought about by the addition of biomass extract in the reaction substrate indicates the formation of AgNPswhich implies the biotransformation of Ag^+ to Ag^0. This study indicated the green-synthesized silver nanoparticles using *Oscillatoria limnetica* aqueousextract which act both as reducing and stabilizing agent have antibacterial property.

Another study conducted by Vahabi et al. (2011), "Biosynthesis of Silver nanoparticles by fungus *Trichoderma reesei*" was carried out [7]. This research paper reported the extracellular biosynthesis of silver nanoparticle by the use of fungus, *Trichoderma reesei.* In this process, the mycelium of the fungus is exposed to the silver nitrate solution. The fungus produces enzymes and metabolites thereby reducing the Ag^+ to AgNPs through its catalytic effects. The biosynthesis of nanoparticles by *Trichoderma reesei* has large scale production potential.

Alyousef et al. (2019) published an article "Biogenic silver nanoparticles by *Myrtus comunis* plant extract: biosynthesis, characterization and antibacterial activity" [8]. This investigation describes the use of *Myrtus communis* plant leaves to synthesize silver nanoparticles. *M. communis* leaf and bark extracts contain various active secondary metabolites. In this process, the leaf extract was prepared by boiling the cut leaves in sterile water to get an aqueous extract. The extract was filtered and further used to biosynthesize silver nanoparticles by reacting with silver nitrate solution. The characterization of the AgNPs was done by using UV-Vis spectrophotometer, FTIR, TEM and X-ray. The study shows that the process of synthesis is simple, reproducible and ecofriendly.

"Biosynthesis of silver nanoparticles from *Desmodium triflorum:* a novel approach towards weed utilization" was carried out by Ahmed (2010) where it was showed that the biomolecules found in *Desmodium triflorum*induces the reduction of silver nitrate to silver nanoparticles [9]. Nanoparticles which are stable and spherical were produced. The synthesized AgNPs showed good antibacterial property against common pathogens.

The study by Sadatsharifi et al. (2016) investigated the extracellular biosynthesis of AgNps using *A. fumigatus, A. clavatus, A. niger and A. flavus* [10]. The analysis of the nitrate reductase activity was carried out to determine the role of this enzyme in silver nanosynthesis. It was concluded that the synthesis of silver nanoparticle by the *Aspergillus* species depended on their nitrate reductase activity. The highest nitrate reductase activity was shown by *A. fumigatus* which is also the most efficient in synthesizing the AgNPs among the four *Aspergillus* species.

"Green biosynthesis of silver nanoparticles is using *Curcumalonga* tuber powder was done by Shameli et al. (2012), where it reported the role of *Curcumalonga* tuber powder in the bioreduction and stabilization of silver ions to silver nanoparticles [11]. The powder extract was used to reduce the silver ions to AgNPs which was indicated by the color change (yellow to brown). This shows the potential for forest plants for the synthesis of AgNPs.

"Silver nanoparticles: biosynthesis using an ATCC reference strain of *Pseudomonasaeruginosa* and activity as broad spectrum clinical antibacterial agents" was carried out by Quinteros et al. (2016) [12]. This work demonstrated the use of AgNPs synthesized by *Pseudomonasaeruginosa,* as a broad spectrum bactericidal agents for pathogenic bacteria such as methicillin-resistant *S. aureus*, *A. baumannii* and *E. coli*. The biosynthesized AgNPs also shows antimicrobial activity against human pathogens.

"Biosynthesis of silver nanoparticles by the fungus *Arthrodermafulvum* and its antifungal activity against genera of *Candida*, *Aspergillus* and *Fusarium*" was performed by Xue et al. (2016) [13]. This study reported the antifungal activity of biosynthesize AgNPs by soil-isolated strain of *Arthrodermafulvum.* Inhibition of growth of *Candida* strains was reported on adding AgNPs. Effects of AgNPs on Aspergillus and Fusarium were also studied. It provides a valuable resource for treatment of fungal diseases.

In another study by Sulaiman et al. (2016), silver nanoparticles synthesized by using leaf extract of *Catharanthusroseus* exhibited strong antimicrobial activity against pathogens such as *E. coli, C. koseri, K. pneumonia, P. aeruginosa and S. aureus* was recorded. It has been reported that the produced AgNPs have wound-healing capability in albino mice when treated [14]. There has been no evidence of microbial contamination or deterioration of the wound.

Lalitha et al. (2013) published a study as "Green synthesis of silver nanoparticle using the aqueous extract of *Portulacaoleracea* (L)" [15]. The green synthesis of AgNPs was carried out by using aqueous extracts of *Portulacaoleracea* under different experimental condition- sonification, reaction at room temperature and at 75^o C. This study revealed the presence of functional group responsible for stabilizing the synthesized silver nanoparticles.

National Scenario

Elumalai et al. in 2011 reported an article "Biofabrication of Ag nanoparticles using *Moringa oleifera* leaf extract and their antimicrobial activity" which shows that the leaf extract of *Moringa oleifera* was added to silver nitrate solution and heated the reaction substrate [16]. A change in colour from brown to reddish color was observed. The characterization of the so formed silver nanoparticles was done by UV-Vis spectrophotometry and Transmission Electron Microscopy (TEM).

The study by Ankana et al. in 2010 reported the synthesis of highly dispersed silver nanoparticles using the stem bark of *Boswellia ovalifoliolata as the reducing agent* [17]. The exposure of the extract to silver nitrate solution leads to rapid reduction of silver ionto silver nanoparticles. The biological approach of nanoparticle synthesis has many advantages such as ease, large-scale production and economic viability.

In another study by Devi et al. 2014, it established the larvicidal effect of silver nanoparticles synthesized by using leaf extract of *Euphorbia hirta* [18]. Considerable mortality rate was seen after the treatment of larval instars and pupae with *Gossypium hirsutum* leaves coated with differing concentration of the synthesized Ag nanoparticles.

"Leaf extract mediated green synthesis of silver nanoparticles from widely available Indian plants: synthesis, characterization, antimicrobial property and toxicity analysis" Banerjee et al. (2014), explored the use of Indian medicinal plants in silver nanoparticle's synthesis, namely *Musabalbisiana*, *A. indica*, *O. tenuiflorum* [19]. Due to differing properties present in the three different plants, AgNPs synthesized using these plants are found to be different in size, among which the smallest AgNPs yield was from banana leaf extracts. This study also reported that the banana leaf extract was found to be better reducing agent than Neem and Tulsi leaf extracts.

In a study on "Green synthesis of silver nanoparticles using fresh water green alga *Pithophoraoedogonia* (Mont.) Wittrock and evaluation of their antibacterial activity" by Sinha et al. (2014), It was demonstrated that silver nanoparticles can be biosynthesized by using fresh water algae, *Pithophoraoedogonia* (Mont.) Wittrock extract [20]. The AgNPs produced are cubical and hexagonal in shape.

The study by Mathew et al. (2014) on "Microwave assisted biosynthesis of silver nanoparticles using the rhizome extract of *Alpiniagalanga* and evaluation of their catalytic and antimicrobial activities" [21]. It was reported that through the assistance of microwave radiation, smaller nanoparticles have been produced in lesser time period as compared to nanoparticles fabricated at room temperature. The rhizome extract of *Alpiniagalanga* proves to be a good reducing and stabilizing agent. This method is another approach of green synthesis which have great prospect for large scale production of silver nanosynthesis for the application in areas such as nanocatalysts and antimicrobial agents.

"Green synthesis and antimicrobial activity of silver nanoparticles onto cotton fabrics: an amenable option for textile industry" a study performed by Prasad et al. (2015) used *Clerodendron infortunatum* leaf extract in the fabrication of silver nanoparticle's synthesis [22]. The AgNPs was loaded on cotton fabric to analyze the antibacterial efficacy. The nanoparticles successfully inhibited the growth of bacteria and showed good antibacterial property.

Again a study by Mathew et al. (2018) on "*Indigoferatinctoria* leaf extract mediated green synthesis of silver and gold nanoparticles and assessment of their anticancer, antimicrobial and catalytic properties" illustrated the synthesis of gold and silver nanoparticles using the leaf extract of medicinal plant *I. tinctoria*. The AgNPs and AuNPs synthesized showed good anticancer properties against lung cancer cell lines 4549 [23].

The study by Venkatachalam et al. (2017) entitled "Enhanced antibacterial and cytotoxic activity of phytochemical loaded-silver nanoparticles using *Curculigo orchioides* leaf extracts with different extraction techniques" demonstrated that AgNPs were fabricated using different type of broths prepared from the leaf of *C. orchioides*. The AgNPs produced were spherical and it has potential anticancer activity at low concentration [24].

Sharma et al. (2019) recently published a work on "Green synthesis and antibacterial activity studies of silver nanoparticles from the aqueous extracts of *Wrightiatinctoria*" where the silver nanoparticles were synthesized using the leaf extract of Wrightia tinctoria [25]. The antibacterial property was tested on *Pseudomonas aeruginosa* and *Bacillussubtilis* and it was found to be effective and considerably interfere with the motility of the microorganisms.

Khan et al. (2016) published an interesting piece of work where biological synthesis of silver nanoparticles and was carried out using by E. coli and it was found to inhibit the growth of different microbes [26].

Northeast India Scenario

The group of researcher's leads by Phanjom et al. (2012) published a work entitled "Green synthesis of silver nanoparticles using leaf extract of *Myricaesculenta*" [27]. This study demonstrated the successful bio-reduction of silver ion to silver nanoparticles by using the leaf extract of *Myricaesculenta*. The so formed AgNPs were almost spherical in shape. The so formed AgNPs were almost spherical in shape. The use of plant such as Myrica esculenta has desirable quality since it is a low-cost method and convenient way of producing nanoparticles.

More recently Barman et al. (2020) worked on "Biosynthesized silver nanoparticles are using *Zinziber officinale* rhizome extract as efficient catalyst for the degradation of environmental pollutants" [28]. In this study, AgNPs synthesized by using the rhizome extract of *Zinziberofficinale* was analyzed. The AgNPs was used to degrade harmful dyes such as methylene blue (MB), safranin O. and methyl red. Due to the addition of AgNPs, the reduction of the dyes was found to be much faster than reduction reaction carried out in the absence of AgNPs.

Dutta et al. in 2019 worked on "Green synthesis of silver nanoparticles from *Rhynchostylisretusa* (L.) Blume leaf extract under sunlight" [29]. The Silver nanoparticles were synthesized by adding the leaf extract of Rhynchostylis retusa (L.) Blume to silver nitrate solution and subjected to direct sunlight. The produced AgNPs are effective against Gram positive and Gram negative bacteria.

Wangkheirakpam et al. (2014) in his work on "Green synthesis of silver nanoparticle using *Strobilanthes flaccidifolius* Nees leaf extract and its antibacterial activity" confirmed that the leaf extract of *S. flaccidifolius* was found to reduce the silver ions to silver nanoparticle and also stabilizes the nanoparticles [30]. The AgNPs show potential antimicrobial activity against clinically isolated pathogens.

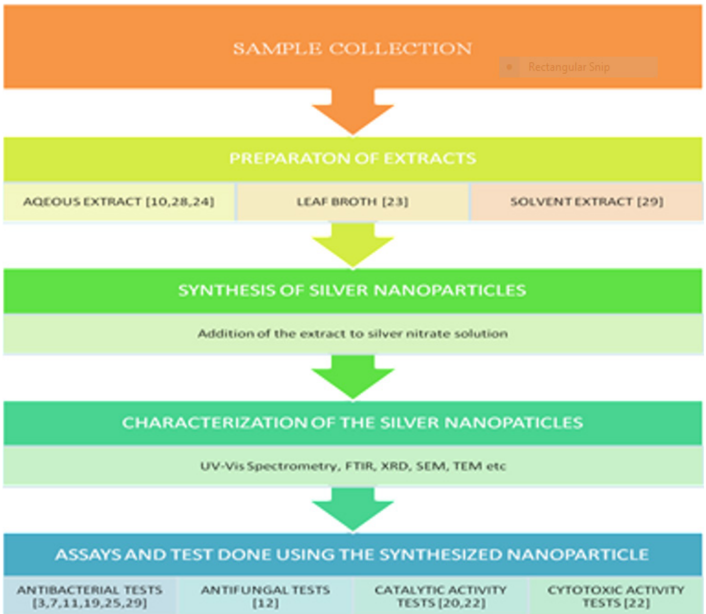
Gogoi et al. in 2013 through their work on "Green synthesis of silver nanoparticles from leaves extract of ethnomedicinal plants-*Pogostemon benghalensis* (B) O. Ktz." has shown that the leaf extract of medicinal plant *Pogostemon benghalensis* can synthesize silver nanoparticles [31]. The extract act both as a reducing agent and stabilizer. It is a low cost and ecofriendly way of synthesizing silver nanoparticles. The fabricated AgNPs were spherical.

In the study conducted by Sarma et al. (2014) on "Biological synthesis of silver nanoparticles by *Neptunia oleraceae*", a nitrogen fixing aquatic plant, *Neptunia oleraceae* was used to synthesize silver nanoparticles. The plant has great efficiency in producing AgNPs [32]. The formation of nanoparticles was found to be influenced by application of heat, which was indicated by the color change. The nanoparticles were formed in clusters and have spherical shape.

In another study by Sarma et al. in 2007 worked on the study "Biological synthesis of silver nanoparticles by *Pleurotus* species" where the efficacy of edible mushroom, *Pleurotus* sps. In synthesizing silver nanoparticle was shown [33]. The use of easily available fungus for producing AgNPs is rapid and ecofriendly.

Sarma et al. in 2017 through his review on "Nanobiotechnology in understanding cancer biology" have discussed the prospect of nanopmaterials in treatment of cancer. Nanopmaterials helps in early detection of precancerous lesions, allowing the timely release of anticancer drugs and reversing the changes [34,35].

Methodlogy



Recent Advances

Nanotechnology has made its significant place in modern sciences. The researches regarding greener way of fabricating nanoparticles has enabled an understanding towards its application in various fields. Many such applications are imparting antimicrobial property on textile fabrics [36], disease control in field [37], degradation of harmful substances which post a threat to environment[38]. One of the studies indicated that AgNPs have antiproliferative activity on MDA-MB-231 breast cancer cell line, suggesting its potential as a treatment agent in cancer therapy [39]. The broad spectrum antimicrobial properties of AgNPs have lead to its use as sterilizing agent in medical devices. In another study, hydrogel coated nanoparticles was developed for wound healing and drug delivery [40].

Many studies and researches have successfully shown that nanosynthesis can be synthesized by using naturally occurring plants [1-4, 7, 8, 10, 13-17, 29, 30], algae [19] and microorganisms such as bacteria [5, 11], fungi [6, 9, 12], yeast [31]. The green synthesis approach is environmental friendly, rapid and cost effective way of fabricating silver nanoparticles. The synthesized silver nanoparticles have varying shapes. Most of the nanoparticles synthesized were almost spherical and crystalline in nature. The AgNPs when tested for various properties was found to exhibit broad spectrum antibacterial activity [3,7,11,19,25,29], antifungal activity [12], cytotoxicity [22], catalytic activity [20,22], wound healing capacity [13], larvicidal effects [17]. Furthermore, AgNPs can degrade harmful dye such as methylene blue, safranin, methyl red [27] and have great advantage for textile industries [21]. Studies have shown that forest plants and weeds can also be utilized to synthesize nanoparticles efficiently in a cost-effective manner. The use of plants and microbes enables higher reproducibility of the techniques and process leading to increase production of nanoparticles and higher stability. Therefore, biologically fabrication of nanoparticles is suitable for large-scale production and it is safe for human therapeutic use [15].

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