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Phytosynthesized nanoparticles as an alluring step for antimicrobial drug delivery: A brief Introduction

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Abstract
Since its advent, nanotechnology has become an indispensable area of research and innovation, introducing revolutionary changes in current research areas like engineering, medical sciences, drug discovery and formulations, optoelectronics and biosensors. Various antimicrobial agents have been used to kill or inhibit the growth of microbes such as bacteria, fungi and viruses. But recently, biosynthesized nanoparticles attained great attention of researcher to use these nanoparticles as a system for delivery of antimicrobial drug. Phytosynthesized nanoparticles are widely used due to many advantages like small and controllable size, large surface area to mass ratio, and functionalizable structure. These properties make the nanoparticles, a suitable delivery system of antimicrobials. This briefly introduction explores the huge plant diversity to be utilized towards rapid and single step protocol preparatory method with green principles over the conventional ones and describes the antimicrobial of Photosynthesized nanoparticles.

Keywords: Phytosynthesis, Nanoparticles, Antimicrobial

Introduction
Microbial infections are recognized as the significant cause of morbidity and mortality in human. Population worldwide. With the introduction of innovative medicine known as antibiotics in the twentieth century has brought a melodramatic reduction in the illness and death resulting from the life-threatening diseases. Current available therapeutic strategies have been modified with the addition of a variety of antimicrobial agents to eradicate the microbial infections. With the concerning limitations in current therapeutic regimens i.e. the incompetency and deprived delivery of antimicrobial agents, it could result in consequences such as inadequate therapeutic index and having deteriorating health impacts like vomiting, irritation, nausea, scaling and microbial flora reduction in the gut. However, variations in the environment and society have largely contributed to the emergence of new infectious diseases and resurrection of the multidrug-resistant microbes [1]. The continuing presence of antibiotic resistance in pathogenic and opportunistic microorganisms forces the pharmaceutical companies and the researcher community to continuously develop novel antibacterial drug, drug targets and delivery system to improve the activity against multidrug-resistant bacteria. Different approaches were used to combat against microbes but nanotechnology attained great attention in the past few years. The domain of nanotechnology have emerged from established areas of science like physics, chemistry, biology and engineering sciences. Nanotechnology involves intervention of novel strategies with the help of which atoms and small particles are manipulated. Nanoparticles (NPs), the key product of nanotechnology, are particles having dimensions ranging from 1–100 nm [2]. The properties of NPs show immense variations to those of bulk materials due to their extremely small size [3, 4]. With the advancement in nanotechnology, size controlled synthesis of nanoparticles can be carried out to furnish NPs that possess properties suiting a particular purpose. The properties that NPs possess are due to two core reasons, novel quantum impact and increased surface to volume ratio. As compared to their bulk counterparts, the pre-eminent surface to volume proportions in NPs imitates enhanced catalytic reactivity. Likewise such small dimensions of NPs signifies the influence of quantum impact on quality and properties of material [5]. Since its dawn, NPs have dominated different areas of science. The use of NPs have been reported in areas like catalysis [6], Photonics [7, 8], gadgets [9], bio labeling [10], detection, and surface upgraded Raman Scattering [11-14], drug delivery [15].

This review climaxes the effect of biological synthesized nanoparticles against different microbial strains.

Green synthesized Nanoparticles

Nanoparticles are synthesized through many physiochemical processes which have posed numerous pressures on the environment. Plant-based synthesis of nanoparticles is a simple process, a metal salt is mixed with plant extract and the reaction completes in minutes to few hours at ordinary room temperature. The metallic salt solution is reduced into respective nanoparticles. This fashion of simplicity have got considerable attention during the last decade. Recently, different methods have been used to synthesize NPs such as physical (sonication, laser ablation and radiation), chemical (condensation, sol gel method and reduction) and biological methods as shown in (Fig 1). The conventional approaches have many challenges and encouraged researchers to find alternative approaches [16]. The biological synthesis of nanoparticles is safe, dynamic and energy efficient [17, 18]. This method uses various biological resources ranging from prokaryotes to eukaryotes for *in vivo* production of NPs [19].

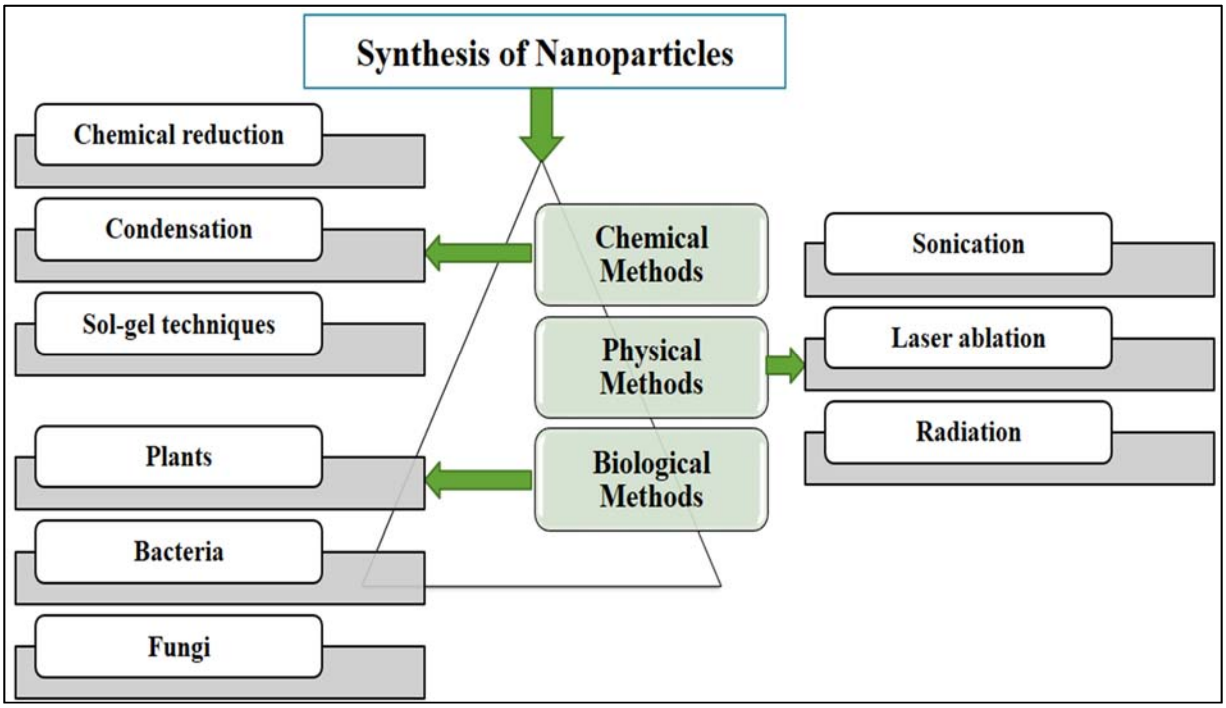

Fig 1: Various methods for making nanoparticles.

Advantages of Nanoparticles

The advantages of using nanoparticles for the drug delivery result from their two main basic properties. First nanoparticles, because of their small size, nanoparticles can penetrate through smaller capillaries and are taken up by cells, which allow efficient drug accumulation at the target sites. Second, the use of biodegradable materials for nanoparticle preparation allows sustained drug release within the target site over the period of days or even weeks [20]. But not only for drugs are nanoparticles very important. Nanotechnology can actually revolutionize a lot of electronic products, procedures, and applications. The areas that benefit by the continued development of nanotechnology when it comes to electronic products include nano diodes, nano transistors, OLED, plasma displays, quantum computers, and many more. Nanotechnology can also benefit the energy sector. Such items like batteries, fuel cells, and solar cells can be built smaller but can be made to be more effective with this technology. Another industry that can benefit from nanotechnology is the manufacturing sector that will need materials like aerogels, nanotubes, nano particles, and other similar items to produce their products with. These materials are often more durable, stronger and lighter than those that are not produced with the help of nanotechnology [21]. There are some more advantages of nanoparticles over their production and their drug delivery process. Nanoparticles are fairly easy to prepare that's why they are used in drug after targeting the area. Due to their small size Nanoparticles penetrate small capillary and are taken up by the cell which allows for efficient drug accumulation at the target sites in the body. Using Nanoparticles in drug delivery give good control over size and give good protection of the encapsulated drug. Retention of the drug at the active site has longer clearance time. Nanoparticles increased the therapeutic efficiency as well as bioavailability. They reduced fed/fasted variability that increased drug stability. Stable dosage forms of drug which are either unstable or have unacceptably low bioavailability in non-nanoparticulate dosage form. While carrying drug with nanoparticles have no biotoxicity of the carrier. Nanoparticles are do not show any problem in large scale production and sterilization but they only avoid organic solvent [22].

Limitations of Nanoparticles

In spite of these advantages, nanoparticles do have limitations.

For example, their small size and large surface area can lead to particle-particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms.

In addition, small particles size and large surface area readily result in limited drug loading and burst release [22].

Parameters for characterization of nanoparticles

The instrument uses for different parameters of nanoparticles are characterized as under:

Table 1: Different parameters for characterization of nanoparticles

Parameters	Instrument used
Particle size & size distribution	Zetasizer, Photon correlation spectroscopy, Mercury porosimetry, Laser diffractometry
Particle Morphology	Scanning electron microscopy (SEM), Transmission electron microscopy (TEM), Atomic force microscopy (AFM)
Charge determination	Laser droplet anemometry, Zeta potentiometer
Metallic nature	X-ray diffraction (XRD) Analysis
Identification of Functional groups	Fourier Transform Infrared (FTIR) Spectroscopy
Chemical analysis of surface	Static secondary ion mass spectrometry
Release profile	In-vitro release characteristic under physiologic & sink condition

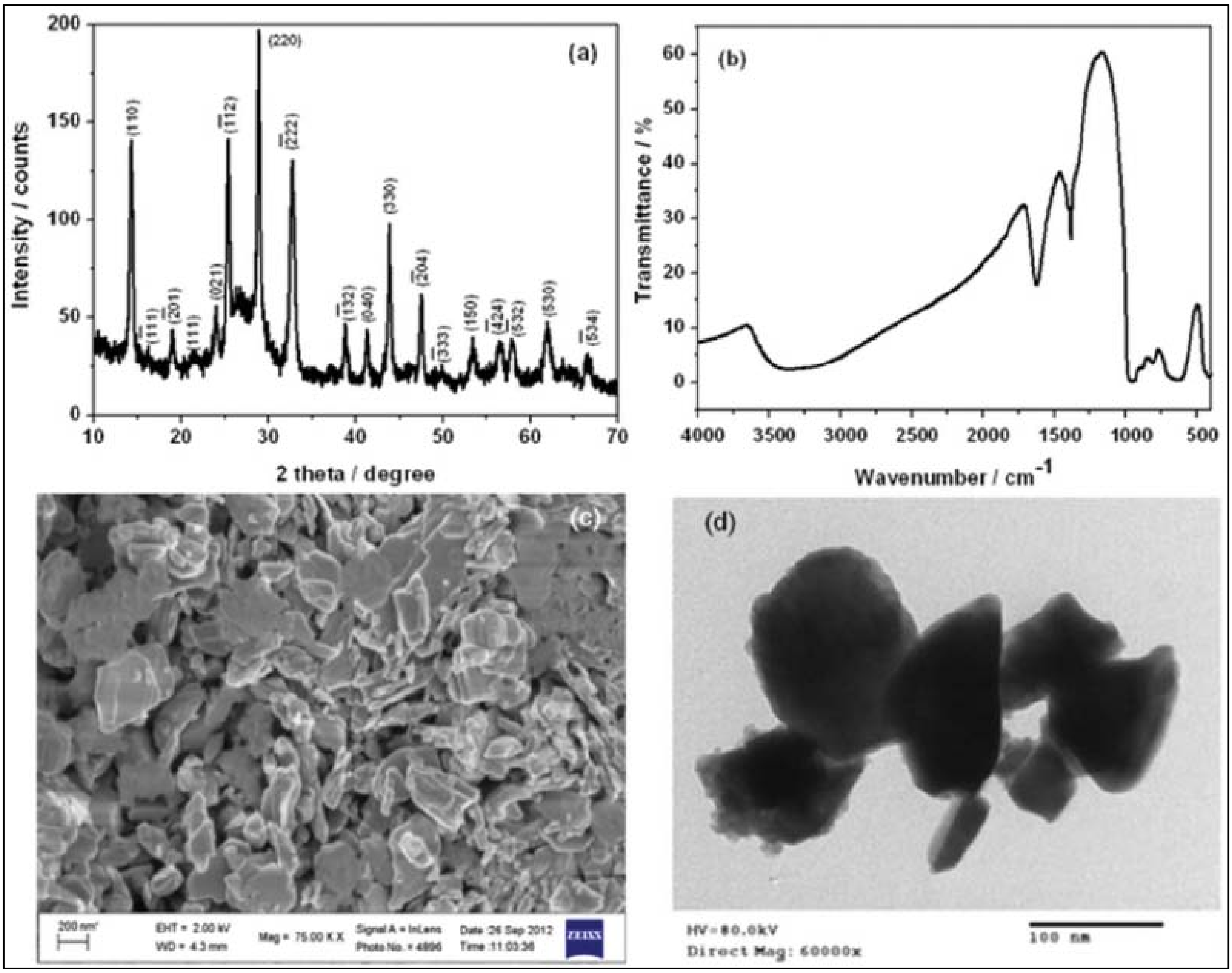

Fig 2: Images XRD, FTIR, SEM and TEM Analysis

Antimicrobial activity of biosynthesized nanoparticles

In medical world, nanotechnology has a potential to save more lives. The drugs which are formed by nanotechnology are called "smart drugs". These smart drugs have lesser side effect compared to traditional one. These "smart drugs" can help in the treatment of Cancer, Parkinson's, Alzheimer's and even to inhibit or kill the growth of microbes. The main focus is here on biological synthesized nanoparticles against different strains of microbes. Various Metals like copper, zinc, titanium, magnesium, gold [23] and metal oxides have been widely studied for their antimicrobial activities. Metal oxide nanoparticles, recognized due to its highly potent antibacterial effect, include iron oxide (Fe2O3), titanium oxide (TiO2), copper oxide (CuO), and zinc oxide (ZnO).

G. Caroling *et al,* synthesized Copper oxide (CuO) nanoparticles with 15-30nm size using plant extract. The prepared nanoparticles showed good antimicrobial activity against *Escherichia coli, Staphylococcus aureus* [24]. Au NPs synthesized using mint (Mentha piperita) leaf extract were documented to have antimicrobial activity against gram-positive and gramnegative strains [25]. Green synthesized silver nanoparticles, using Vasaka leaf extract, showed a potential to inhibit the growth of bacteria [26]. Another study showed excellent antimicrobial activity using green synthesized ZnO-NPs [27]. Au NPs were synthesized using Citrus reticulata, Citrus aurantium, Citrus sinensis and Citrus grandi fruit extracts possessed considerable antimicrobial activity [28]. Several other plants extract from different parts have been used for the synthesis of NPs as shown in Table (2and 3)

Table 2: Metallic nanoparticles and their antimicrobial activities

Metallic NPs	Plant Specie	Targeted Microbes	Method used	References
(Au-NPs) Gold Nanoparticles	*Areca catechu*	*E. coli, K. pneumonia, P. auroginosa, Enterobacter sp. (species) and S. aureus, respectively*	Agar well diffusion	[29]
(Au-NPs) Gold Nanoparticles	*Galaxaura elongata*	*Staphylococcus aureus, S. aureus, Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa*	Agar well diffusion	[30]
(Au-NPs) Gold Nanoparticles	*Pistacia integerrima*	*Klebsiella pneumonia, Bacillus subtillis and Staphylococcus aureus, Alternaria solani, Aspergillus niger and Aspergillus flavus.*	Agar well diffusion	[31]
(Au-NPs) Gold Nanoparticles	*Euphorbia hirta L.*	*E. coli, Pseudomonas aeruginosa and K. pneumonia*	Broth dilution	[32]
(Au-NPs) Gold Nanoparticles	*Mentha piperita*	*Staphylococcus aureus and Escherichia coli.*	Broth culture	[25]
(Ag-NPs) Silver Nanoparticles	*Argemone mexicana*	*Escherichia coli and Pseudomonas aeruginosa*	Disc diffusion	[33]
(Ag-NPs) Silver Nanoparticles	*papaya fruit*	*Escherichia coli and Pseudomonas aeruginosa*	Disc diffusion	[34]
(Ag-NPs) Silver Nanoparticles	*Artocarpus heterophyllus Lam*	*B. cereus, B. subtilis and S. aureus*	Agar well diffusion	[35]
(Ag-NPs) Silver Nanoparticles	*Garcinia mangostana*	*Escherichia coli and Staphylococcus aureus*	Disc diffusion	[36]
(Ag-NPs) Silver Nanoparticles	*Ceratonia siliqua*	*E. coli*	Disc diffusion	[37]

Table 3: Metallic oxide nanoparticles and their antimicrobial activities

Metallic Oxide NPs	Plant Specie	Targeted Microbes	Method used	References
(MgO-NPs) Magnesium oxide Nanoparticles	*Betel*	*Pseudomonas aeruginosa, Bacillus subtilis*	Agar well diffusion	[38]
(ZnO-NPs) Zinc oxide Nannoparticles	*Camellia sinensis*	*Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia colli, Staphylococcus aureus, Aspergillus fumigatus, Aspergillus flavus, Penicillium sp. and Aspergillus niger*	Agar well diffusion	[39]
(ZnO-NPs) Zinc oxide Nannoparticles	*Trifolium pratense*	*S. aureus, E. coli, P. aeruginosa, S. aureus and P. aeruginosa*	Agar well diffusion	[40]
(CuO-NPs) Copper oxide Nanoparticles	*Garcinia mangostana*	*Escherichia coli and Staphylococcus aureus*	Disc diffusion	[41]
(CuO-NPs) Copper oxide Nanoparticles	*Gloriosa superba L.*	*Klebsiella aerogenes, Pseudomonas desmolyticum, and Escherichia coli, Staphylococcus aureus*	Agar well diffusion	[13]
(CuO-NPs) Copper oxide Nanoparticles	*Bifurcaria bifurcata*	*Enterobacter aerogenes, Staphylococcus aureus*	Agar disc diffusion	[42]
(Co3O4) Cobalt oxide Nanoparticles	*Sageretia thea*	*Pseudomonas aeruginosa, Klebsiella pneumonia, and Escherichia coli, Staphylococcus epidermis, Staphylococcus aureus and Bacillus subtilis*	Disc diffusion	[43]
(NiO-NPs) Nickel oxide Nanoparticles	*Sageretia thea*	*B. subtilis, K. pneumonia, P. aeruginosa, E. coli, M. racemosus and R. solani*	Disc diffusion and Linear mycelial growth inhibition assay	[44]
(Fe2O3) Iron oxide Nanoparticles	*Sageretia thea*	*Escherichia coli, Bacillus subtilis, Staphylococcus epidermidis, Klebsiella pneumoniae, P. aeruginosa, Aspergillus niger, Aspergillus flavus, Aspergillus fumigatus, Mucor racemosus and Rhizopus Solanai*	Disc diffusion assay and linear mycelial growth inhibition	[45]

Techniques to Determine Antibacterial Activity of Nanoparticles

Various experimental methods and assays are available for measuring the antibacterial efficacy of nanoparticles. Each methods are unique and having their advantage and disadvantage. These methods/assays are [46]:

- Optical density measurement
- Spread-plate (colony counts on agar)
- Cell counting devices
- Live/dead fluorescent stain MTS/MTT/XTT assays
- Crystal violet staining

Conclusion

Green synthesis of nanoparticles, once considered as an emerging field is a well-established domain of research in nanotechnology with surplus applications in various fields of science. This route of synthesis is simple, inexpensive, eco-friendly and sustainable alternative to other processes in practice that threatens the ecosystem in one way or the other. Due to such diversified range of applications, Biosynthesized nanoparticles can prove as suitable and inexpensive alternatives to costly nanoparticles. In summary, it can be concluded that nanotechnology developed as a new approach in pharmaceutical sciences and research grasps great promise for overcoming complications related to delivery of antimicrobial and infection curing approaches.

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