# CHAPTER-2

# LITERATURE SURVEY

## 2.1 Methods for Synthesis of Nanoparticles

The nanotechnology is built upon materials at nano size. Preparation of many nanostructured materials and devices depend solely on nanoparticles. For rapid development of nanoscience and engineering, the production of nanoparticles and their research is important. Broadly the techniques of nanoparticles production is classified under two categories namely 'bottom-up' and 'top-down' approach. The bottom-up approach is a nano-architectural phenomenon of self assembly of materials from cluster-to-cluster, molecule-to-molecule or atom-to-atom. Nanolithography and nanomanipulation techniques also fall under bottom-up approach. For the formation of composite nano substances these techniques are extensively employed. Top-down approach consists of starting with a block bulk material and crafting, engineering or milling it down to required shape. For more homogeneous chemical compositions having fewer defects the approach of 'bottom-up' has a definite advantage since the reduction is carried out in the Gibb's free energy [1]. Quite the reverse, top-down approach almost certainly leads to internal stress as well as surface defects. Bottom-up methods for the synthesis of nanoparticles are available under the following categories: i) Chemical precipitation [2] ii) interfacial polymerization (**Fig. 2.1**) [3-5]

iii) hydrothermal method [6, 7], pyrolysis [8] iv) solventless synthesis [9] v) chemical vapor deposition (CVD) [10] vi) laser abbrasion [11].

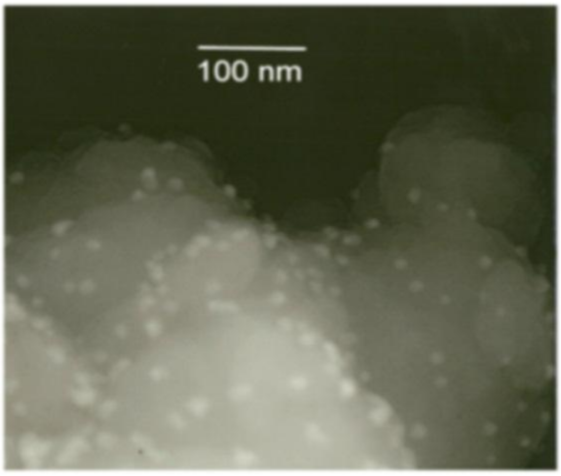


**Fig. 2.1** TEM image of polypyrrole silver synthesized by interfacial polymerization technique

## 2.2 Properties of nanomaterials

The reduction of materials' dimension to nano level has marked effect on physical properties than bulk material it self. The nanomaterials display these special physical properties because of (i) large surface energy, (ii) large surface area, (iii) spatial confinement, and (iv) reduced imperfections. Few properties of nanomaterials are noted as follows: i) Optical property: [12] ii) magnetic property [13] iii) mechanical property [14] iv) thermal property [15].

## 2.3 Application of Nanomaterials

Nanotechnology offers extremely wide-ranging latent applications in optical communications, electronics and smart materials in biological systems [16]. The wide range of applications shown by nanostructures and nanomaterials are due to i) the unusual physical properties exhibited by nanosized materials, e.g. gold nanoparticles used as an inorganic dye for coloring the glass, ii) the large surface area, such as gold nanoparticles supported on metal oxide are used as low temperature catalyst and iii) as sensors. For many applications, new materials and new properties are introduced. For example, various organic molecules are incorporated into electronic devices. Some of the applications of nanostructures and nanomaterials are listed as; i) Molecular electronic and Nanoelectronics [17] ii) nanorobots [18]. iii) catalytic application [19] iv) biological application [20].

## 2.4 Synthesis of Nanoparticles using Bio-based Protocol

Nanoparticle synthesis and their assembly have exciting possibilities of development in the area of nanotechnology. So obtained bio-constituents from micro-organisms and plants reduce the toxicity by reduction of the metal ions or by formation of insoluble complexes with metal ions in the form of stable colloidal nanoparticles [21]. This has created interest among material scientists for the utilization of different bio-moieties in the synthesis of nanomaterials [22]. Inorganic nanomaterials can be synthesized using both uni and multicellular microorganisms either extracellularly or intracellularly [23, 24]. A few noted examples are diatoms (siliceous materials) [25–27], S-layer bacteria (which produce gypsum and calcium carbonate layers) [28, 29] and magnetotactic bacteria (magnetite nanoparticles) [30–32]. In 1999, Klaus et al., synthesized well defined AgNP of hexagonal shape in the range of 200 nm using the strains of *Pseudomonas stutzeri* AG259. Very recently, our seniors have developed silver nanoparticles using the marshland fungus, *fusarium semitactum* [33]. They have also emphasized on the stability and the size control by making the variation in the parameters (like temperature, pH, and the optimal concentration etc. in the reaction mixture of the synthesis) which can help to produce monodispersed nanoparticles of required size that can be used for various pharmaceutical applications like drug delivery systems.

In an interesting study, Yacaman and coworkers have demonstrated the growth of gold and silver nanoparticles from sprouts, roots and stems of live alfalfa plants [34]. As an alternative to physical and chemical methods, biosynthetic method employing plant extracts are proved to be more viable and simple. Reports are available for bio-reduction of Au and Ag ions yield metal nanoparticles using part of the plant like *Cinnamomum camphora* [35], geranium leaf broth [36], lemongrass extract [37], tamarind leaf extract [38] and *aloe vera* plant extracts [39]. One more work which inspired our research is 'neem extract based biosynthesis of noble metals' published from Prof. Murali Sastry et al. This paper proves that bio-based protocols have edge over advantages to physical and chemical methods of synthesis [40].

Unlike nanoparticle synthesis done using different microbes and other plant extracts, the current method of nanoparticle synthesis with different plant extract and reducible bio-excretories is advantageous because it is simple and highly reproducible, and can be processed in room temperature. Rate of nanoparticles synthesized with this modus is comparable to chemical and physical methods, and has an excellent time related advantage over benign and conventional methods using microorganisms and plants. Microwave-assisted guava leaf mediated synthesis of gold nanoparticles carries an advantageous time related benefit since it is observed that the reaction of reduction process in the synthesis completes within few minutes.

## 2.5 Bio-functionalization of noble metal nanoparticles

Considering the fact that nanoparticles exist in the same size domain as bio-markers like protein makes nonmaterials suitable for bio tagging or labeling [41]. To make these nanoparticles interact with biological target or receptor, a bio-coating like proteins, antibodies, hormones, biopolymers or any other suitable bio-moiety which can act as bioinorganic interface will be attached to the surface of nanoparticles [42]. This process makes nanoparticles safe and biocompatible for further pharmaceutical and medical applications. Nanoparticle synthesized with bio-route usually forms core of the biomaterial [43]. The bio-functionalized (bio-shell-metal-core nanoparticles) are finding widespread applications. These core-shell nanoparticles are self-assembled nano structures that commonly have a metal core covered with a biological layer on them [44]. The size of the nanoparticles is found to be in 10- 100 nm range. The core-shell nano bio structure enhances the thermal and chemical stability of the nanoparticles, improves solubility, makes them less cytotoxic and allows conjugation of other molecules to these particles. The shell covering or capping can also avoid the oxidation of the central core material [45]. **Fig. 2.2** shows the processed picture of functionalized AgNP and its application as an antibacterial agent. In the present research, we describe the synthesis and characterization of bio-functionalized noble metal nanoparticles like silver and gold and also screened for their possible pharmacological activities with their toxicology studies.

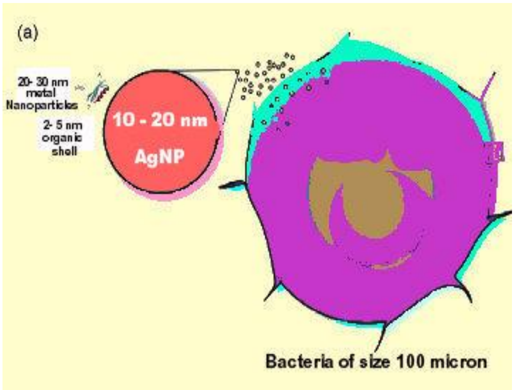


**Fig. 2.2** Pictogram of functionalized AgNP antibacterial action

## 2.6 Characterization of Silver and Gold nanoparticles

We understand that the multi-disciplinary approaches of nanobiotechnology concepts are based on fundamentals of chemistry, biochemistry, biotechnology and materials science. For the synthesis and characterization of these nanoparticles (size dependent active materials) research community of nanotechnology has developed over the past three decades into today's powerful discipline like nanobiotechnology which allows the understanding of advanced technical devices like SEM, TEM and AFM. **Fig. 2.3** shows the TEM image of functionalized AuNP synthesis using fungus *F. semitectum.*

On the other hand, they help to decide the applicability of thus screened nanoparticles for pharmaceutical and biomedical applications [46]. Using these analytical techniques is necessary part of bio-adsorbed novel metal nanoparticle biosynthesis and gives very essential information on the size, shape, texture, despersivity, bio adsorption, biocompatibility and further direction for their usefulness [47].

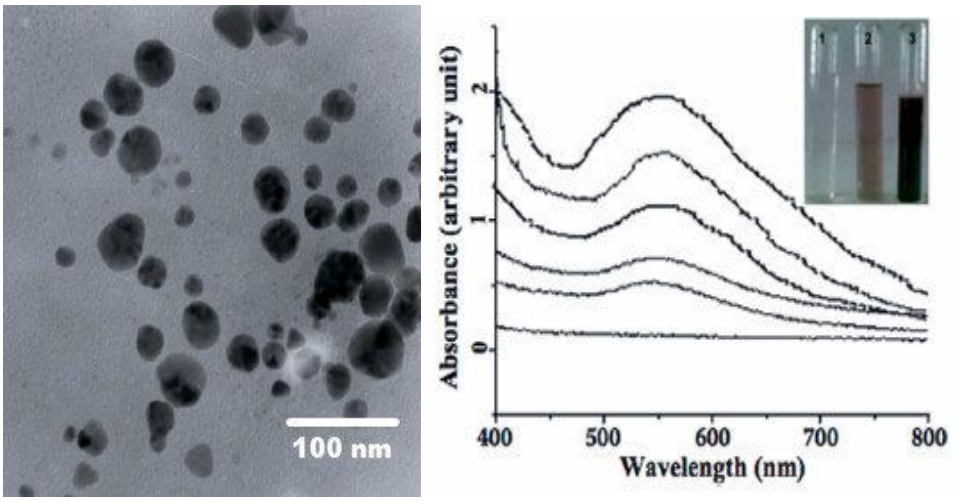


**Fig. 2.3** UV-vis spectra (down) and picture of the test tubes containing the filtrate of the *F. semitectum* biomass in an aqueous solution of $10^{-3}$ M $HAuCl_4$ at the beginning of the reaction (test tube 1) and after 4 and 24 h of the reaction (test tubes 2 & 3, respectively) and TEM images of AuNP (Left side).

The different techniques used for the characterization of bio-nanoparticles are as follows i) Visual Inspection and Intensity Characterization [48] ii) Spectroscopy techniques like UV-vis to understand the formation of metallic nanoparticles on the formation of surface plasmon resonance and fourier transform infrared spectroscopy [49] (FTIR): to understand the probable pathway of biosynthesis [50]. EDAX and XRD data are used in getting the conformation on the chemical composition, crystalline nature and elemental analysis of a sample [51]. For characterization of nanomaterials and nanostructures, field emission scanning electron microscopy (FESEM) is widely used technique [52]. This technique provides not only topographical information like optical microscopes do, but also information of chemical composition near the surface.

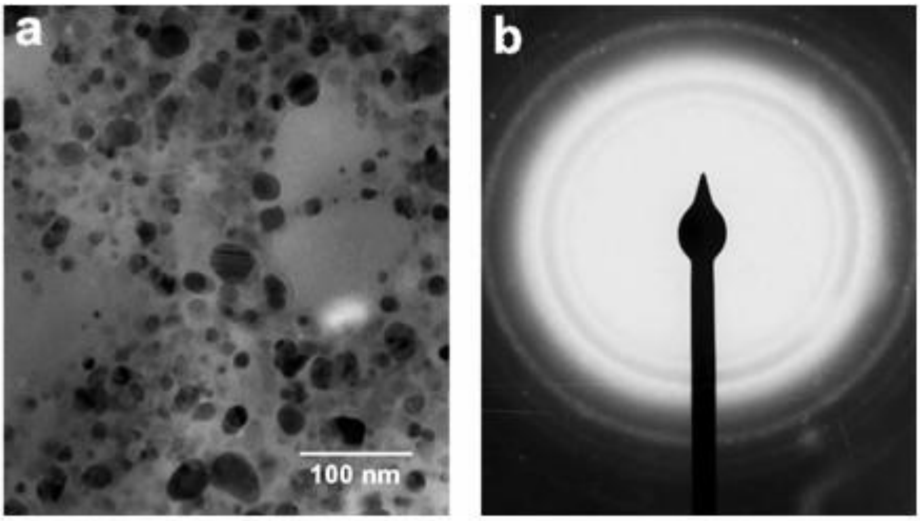


**Fig. 2.4 a** TEM images of AgNP. **b** ED pattern images of AgNP synthesized using fungus, *Cladosporium cladosporioides*

Transmission Electron Microscopy (TEM) is typically used for high resolution imaging of thin films of a solid sample for nanostructural and compositional analysis [53]. Atomic Force Microscopy (AFM) operates with a highly sensitive cantilever which has a sharp tip over a surface and record deflections of the tip. The image developed using this will give useful information about the surface morphology [54]. **Fig. 2.5** shows the AFM image of functionalized AgNP using fungal strains. Zeta potential is a scientific term for electrokinetic potential in bio-nano colloidal systems. The zeta-potential value gives the important useful information about the stability of colloidal systems (e.g. multivitamin syrup). Higher the value of zeta potential, higher will be the stability i.e. the solution or dispersion will resist coagulation. Likewise lesser the value lesser will be the stability. The particles in colloidal particles suspensions tend to flocculate or coagulate when the potentiality becomes less and the attraction becomes more than the repulsion. Hence the flocculation or coagulation is seen at lower value of zeta potential while at the higher zeta potential value (+ve or -ve) the system will be in a stable condition. Thermo gravimetric analysis and Differential conductivity thermo gravimetric analyzer (TGA) measures the weight loss of materials with increase in temperature to determine the composition, thermal stability and associated phenomena [55].

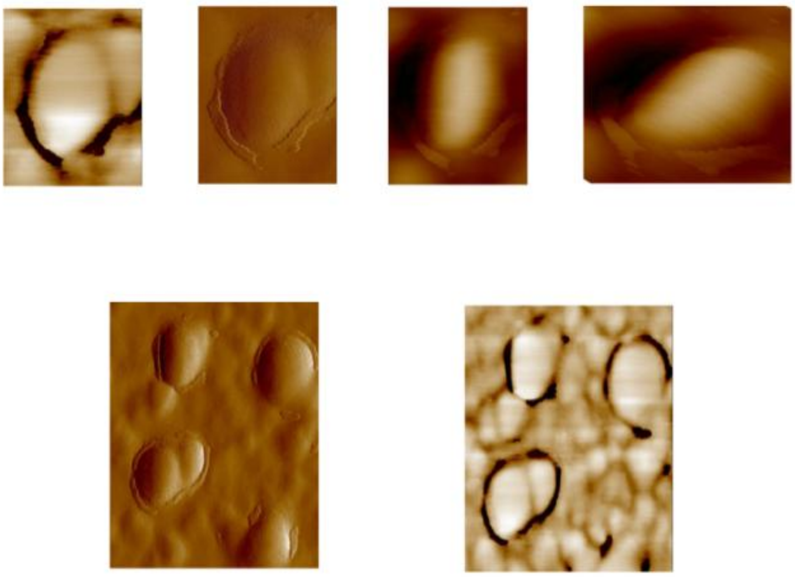

**Fig. 2.5** AFM images of Functionalized AgNP

## 2.7 Scope and objective of the thesis

Aim to develop 'bottom-up' archetype based on the properties of self-assembled nanostructures from atomic to macroscopic size is a need of the day for the researchers. The theme of our study is mainly based on biological routes for synthesis of nanomaterials with an accurate control over composition and dimension. Comprehensive knowledge of properties of bio-active nanomaterials helps for the improvement of innovative-device-technology for assembling these nanostructures on a common platform with excellent spatial arrangement. In nanobiotherapeutics [56], nanobiodiagnostics [57], nanobio-pharmaceuticals [58], nanobiopharmacuetical compositions [59]. The nanoparticles are prepared in an aqueous medium through reduction of an ionic moiety by a reducing agent. Mainly different chemical and electrochemical behaviors of the AuNP are elaborately studied for their application in different diseased conditions, predominantly, in malignancy as anti-neoplastic agent. AgNP synthesized with the biological route are studied for anti-bacterial, anti-oxidant and wound healing activity [60]. With physical and chemical synthesis processes of noble metal nanoparticles, stabilization, quantification and appropriate utilization is still a challenge.

The success in extracellular *fusarium semitactum* fungal extract mediated biosynthesis of nanoparticles, different part of the plant extracts with guava and clove, and using bio-excretory like cow urine and milk have made to keep a step ahead to synthesize, optimize, quantities, stabilize, characterize and study the chemical, electrochemical, optical, thermal and other physicochemical add-on sensory characteristics applied in imaging, managing, modifying, disturbing and destroying the cancer cells without altering the normal environment of surrounding tissues.

## 2.8 Outline of the Thesis

The essence of the work is to synthesize the noble metal nanoparticles from reported anti-malignant and wound healing plants. In this research work, we have achieved successfully the production of bio-functionalized AgNP and AuNP using micro-organisms, plant extracts, mushrooms, different bio-excretory and exposed to molecular, spectroscopic, and pathological tests for anti-bacterial, wound healing, anti-oxidant and anti-neoplastic (Anti-cancer) screening. The future idea is to detect manifestation of cancer in its premature stage itself and destroy them. Our team; we are working hard to build a concept to develop an user friendly, compact, economical method or a device to have a regular, prophylactic check in the malignant abnormalities of the blood.

## 2.9 References


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