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A Review on Different Types of Nanoparticles Synthesized from *Azadirachta indica* and *Gymnema sylvestre* and their Role in Combating Various Diseases

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ABSTRACT

The core function of nanotechnology is to generate nanoparticles in a sophisticated and environmentally responsible manner. An advanced field of nanobiotechnology is developed when nanotechnology and biology are combined. Nanoparticles (NPs) exhibit distinct properties making them valuable in a wide range of life science applications. In response to the concerning levels of toxic substances in the environment, researchers have come up with green techniques that harness the properties of plants, fungi, bacteria, and algae for the production of nanoparticles. It has been determined that these environmentally friendly techniques are safer than the physical and chemical methods. Biosynthesized nanoparticles have a wide range of applications. One of the most important applications is their role in herbal medicine. This comprehensive review focuses on different types of nanoparticles green synthesized through the utilization of leaf extracts from *Azadirachta indica* and *Gymnema sylvestre* and their effect as herbal nano-medicine. Nanoparticles are known to increase the bioavailability, stability and targeted delivery of the bioactive compounds, thus improving the remedial outcomes and reducing the possible side effects. These two well-known herbs, *A. indica* and *G. sylvestre* have been widely used in nano-herbal medicines. They are used to produce nanoscale formulations which have proved enhanced bioavailability and improved pharmacological effects. Numerous diseases including diabetes and cancer are being offered novel solutions through the use of nano-herbal means extracted from these plants.

Keywords: *Azadirachta indica*; *Gymnema sylvestre*; Herbal nano-medicine; Antimicrobial activity.

1. INTRODUCTION

Nanoscience is a domain which is based on the study of materials which are of very small dimensions. Prior research highlights the use of physical and chemical methods for the synthesis of nanoparticles. These methods utilize toxic chemicals and radiations, so they can cause environmental degradation. Due to these issues, scientists are trying innovative methodologies which offer an alternative to these techniques and prioritize environmental sustainability (Mustapha *et al.* 2022). Nanotechnology includes a large section of nanomaterials but the most extensively studied category is metallic nanoparticles. The relationship between science and biology initiates the green route to synthesize such nanoparticles using microorganisms and plants. A vast majority of phytochemicals are found in plant extracts that contribute in the reduction of nanoparticles (Nilavukkarasi *et al.* 2020; Moghaddas *et al.* 2020).

Many metals have been utilized for the synthesis of metallic nanoparticles including silver, zinc, copper, selenium and titanium. The present paper provides an outline of zinc oxide and selenium nanoparticles, focussing on their methods of preparation and applications. The prospective outcomes of the research helps in insightful grasp of the likely consequences of these materials.

Gymnema sylvestre has been used in a lot of research works to synthesize a variety of nanoparticles including zinc nanoparticles (ZnO) (Gotteparthi *et al.* 2023), silver nanoparticles (Rajkumar *et al.* 2020), gold nanoparticles (Nakkala *et al.* 2015), titanium oxide nanoparticles (Bharathy *et al.* 2021) and nickel/nickel oxide nanoparticles (Bhoye *et al.* 2023). These nanoparticles exhibit many medicinal benefits because they hold antidiabetic (Chavan *et al.* 2022; Gotteparthi *et al.* 2023), antibiotic and antimicrobial (Rajkumar *et al.* 2020), antioxidant (Jangam *et al.* 2023; Bi *et al.* 2023), anti-inflammatory (Bharathy *et al.* 2021; Jangam *et al.* 2023; Bi *et al.* 2024), anticancer (Ghosh *et al.* 2023), antihyperlipidemic (Shanker *et al.* 2017), immunostimulatory (Gupta *et al.* 2010), hepatoprotective (Srividya *et al.* 2009), and wound healing activity (Kiranmai *et al.* 2011).

Numerous studies have documented the use of *Azadirachta indica* in the synthesis of nanoparticles such as ZnO NPs (Sohail *et al.* 2020; El-Beltagi *et al.* 2024; Yadeta *et al.* 2024), iron oxide nanoparticles (Zambri *et al.* 2019; Nur *et al.* 2019), selenium nanoparticles (Reddy

and Bandi, 2022; Chaurasia *et al.* 2023; Hawsah *et al.* 2023), silver nanoparticles (Verma and Mehta, 2016; Roy *et al.* 2017; Avinash *et al.* 2017; Kumari *et al.* 2022), copper nanoparticles (Gurudevi and Sirisha, 2023; Yadeta *et al.* 2024) and nickel nanoparticles (Yadeta *et al.* 2024). They hold pharmaceutical activity (Avinash *et al.* 2017; Sohail *et al.* 2020), photocatalytic activity (Yadeta *et al.* 2024), and antimicrobial activity (Roy *et al.*2017; Gurudevi and Sirisha, 2023; Hawsah *et al.* 2023).

There are a variety of techniques used for characterization of nanoparticles, including Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM), Energy Dispersive X-Ray Spectroscopy (EDX), X-Ray Diffraction (XRD), zeta potential analysis and UV-Spectroscopy.

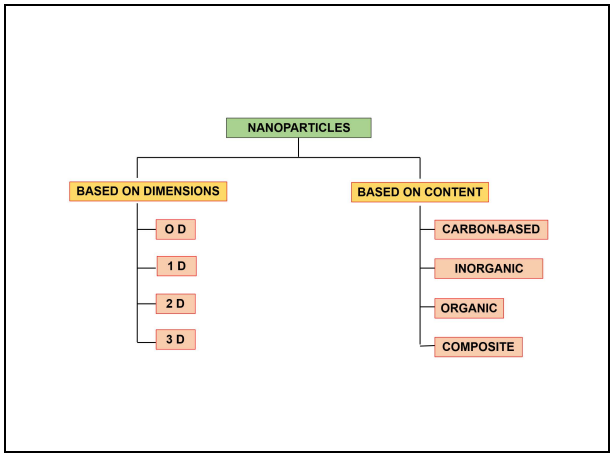


Fig. 1: Classification of nanoparticles (Abid *et al.* 2022)

2. SYNTHESIS OF NANOPARTICLES

Nanoparticle synthesis techniques can be divided into two primary categories, which are determined by the strategies employed to assemble atoms, ions, or molecules, as well as the methods for deconstructing bulk materials to produce raw materials. These classifications cover a diverse array of methodologies that are applied in the formation of nanoparticles. There are two approaches, (a)Top-Down Approach, (b) Bottom-Up Approach.

In top-down approach there is fragmentation of bulk materials into nano-structured materials. It is also known as physical approach. In bottom-up approach, small atoms are combined to form large nano-structured materials (Baig *et al.* 2021). The process of synthesizing nanoparticles requires careful attention to three critical elements: the selection of an appropriate solvent, the incorporation of a sustainable reducing agent, and the choice of a safe stabilizer. These considerations are vital for adhering to the principles of green chemistry as highlighted by Dhandapani *et al.* (2012). The synthesis of metallic nanoparticles through natural biological methods can be categorized into two distinct approaches: (a) Bioreduction - It involves a crucial oxidation-reduction reaction where the enzyme is oxidized and the metal ion is reduced, (b) Biosorption - In this, sample engages in a binding interaction with a metal ion. This step is essential for the subsequent purification and recovery of the desired materials.

3. TYPES OF NANOPARTICLES

Due to the unique properties, nanoparticles exhibit a wide range of characteristics and hence classified in many different categories, two of which are dimensions and content (Fig. 1).

3.1 Metallic Nanoparticles

Metals with dimensions in the range of 1-100 nanometers are classified as metallic nanoparticles. The presence of free surface electrons plays a crucial role in determining the physicochemical properties of these substances. Consequently, many exceptional characters are shown by them which includes high surface energies and remarkable plasmon excitation efficiencies. In addition to these, they also exhibit multiple fascinating optical behaviours (Tim *et al.* 2022). Previous literature clearly reveals the synthesis of many metallic nanoparticles in both pristine and compound form. There are multiple applications of these nanoparticles in many fields including electronics and catalysis (Hossain *et al.* 2023; Narayan *et al.* 2019). The optical properties of these nanoparticles make them highly useful in the formation of quantum dots (Kambhampati, 2021), quantum devices (Cotta, 2020), as well as in various electronic applications (Yan *et al.* 2016). It is known that metals are useful for plants because they are important for growth. The choice of metallic nanoparticles is generally done as they are ^{not} toxic to plants. Nanoparticles made from zinc, copper, iron, manganese, and their oxides fall within this group. Because of their enhanced surface-to-volume ratio, size, regulated drug delivery through endothelial cells, enhanced bio-accessibility, penetrability, and persistence, metallic nanoparticles are used in drug administration (Gnanadesigan *et al.* 2019). The stability of these nanoparticles is ensured by two different ways; one is by coating them with inorganic capping agents or organic ligands and other is by keeping them in an inactive environment. The features of these nanoparticles diverge distinguishably from their respective metals. The difference arises due to alteration in properties at nanoscale. This review is mainly based on the discussion of the nanoparticles of zinc oxide and selenium.

3.1.1 Zinc Oxide Nanoparticles

Zinc oxide displays a wide range of promising applications. ZnO is known as II-VI semiconductor because Zn belongs to group II and O to group VI respectively (Neumark *et al.* 2007).

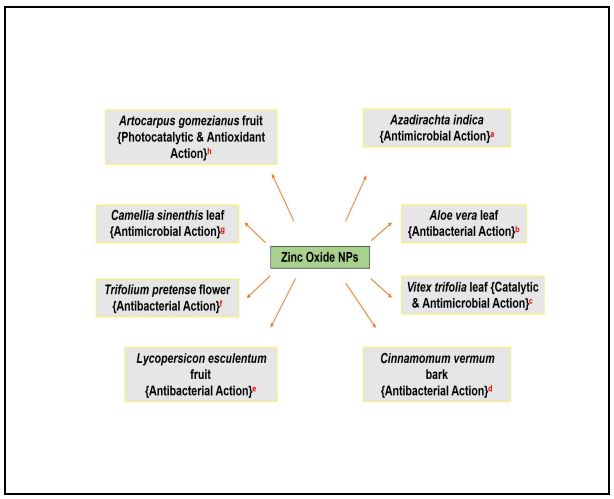


Fig. 2: Applications of different plants mediated ZnO nanoparticles ((a) Handago *et al.* 2019: (b) Rasli *et al.* 2020: (c) Elumalai and Velmurugan, 2015: (d) Ansari *et al.* 2020: (e) Ogunyemiet *et al.* 2019: (f) Dobrucka and Dlugaszewska, 2016: (g) Irshad *et al.* 2018: (h) Suresh *et al.* 2015)

The synthesis of ZnO nanoparticles can be done by physical, chemical and biological methods. Physical synthesis methods include vapour deposition, plasma and ultrasonic irradiation (Król *et al.* 2017) while chemical synthesis includes mechanochemical process (Ao *et al.* 2006), controlled precipitation (Kumar *et al.* 2013), sol–gel (Suwanboon, 2008), vapour transport (Wu, 2015), solvothermal (Segovia *et al.* 2012) and hydrothermal methods (Chen *et al.* 1999), and methods involving emulsion and micro-emulsion environments (Kołodziejczak *et al.* 2012).

By acquisition of such eco-friendly methods, non-polluting production practices are developed. It contributes in greater awareness towards environment. Green synthesis of nanoparticles is done by using microorganisms and plant extracts. Synthesis is based on the biological processes exhibited by these species, which highlights their significance in the field of nanotechnology.

The successful synthesis and applications of ZnO nanoparticles by using the plant extracts is clearly evident from the previous literature (Fig. 2).

3.2 Selenium Nanoparticles

Selenium is a scarce element, accounting for roughly 90 parts per billion of Earth's crust. Researchers are intrigued by selenium due to its dual nature of being essential for human health yet toxic at high doses. Scientists are actively studying the mechanism of action of selenium in order to minimize its toxicity while enhancing its effectiveness.

Selenium nanoparticles can be effectively achieved through physical methods, such as pulsed layer ablation (Van *et al.* 2013; Quintana *et al.* 2002; Guisbiers *et al.* 2017), microwave irradiation (Panahi *et al.* 2014), and laser irradiation (Singh *et al.* 2010). Chemical techniques have been extensively employed in various applications and have proved useful in a variety of applications, such as free radical scavenging activity (Huang *et al.* 2003), anticancer activity (Huang *et al.* 2013; Zheng *et al.* 2012; Kong *et al.* 2011), antibacterial activity (Huang *et al.* 2016; Tran and Webster, 2011), thyrotoxicity (Hassanin *et al.* 2013) and nephrotoxicity (Li *et al.* 2011). Selenium nanoparticles (SeNPs) are also produced through various biological methods, including bacteria, virus, fungi, algae, plants and other particles such as protein molecules. Plant materials rich in polyphenols, saponins, flavonoids, alkaloids, polysaccharides, and other compounds that reduce and stabilize have a higher likelihood of achieving success (Pyrzynska and Sentkowska, 2021). In addition, many plants have been utilized for synthesizing SeNPs (Table 1).

Table 1. Green synthesis of selenium nanoparticles using plant-based extracts

Plant Used	Part Used	Application	References
Citrus limon and *Citrus paradise*	Fruit	Antibacterial	(Alvi *et al.* 2021)
Melia azedarach	Leaves	Antifungal	(Shahbaz *et al.* 2023)
Cinnamon cassia and *Gymnema sylvestre*	Leaves	Non-Cytotoxic, Antioxidant, Anti-inflammatory	(Bi *et al.* 2024)
Vaccinium Arctostaphylos (L.)	Fruit	Antibacterial	(Khudier *et al.* 2023)
Malphigia emarginata, *Allium cepa* and *Gymnanthenum amygdalinum*	Pulp, Bulb and leaves respectively	Antibacterial	(Souza *et al.* 2022)

4. GREEN SYNTHESIS OF NANOPARTICLES

The method of employing plant extracts for the fabrication of nanoparticles is commonly known as green synthesis. This environmentally friendly technique involves the reduction of metal ions through the action of plant extracts, which serve as both reducing and stabilizing agents. Previously, most of the nanoparticles were synthesized using microbes and plants (Table 2). But the present research in this field is more focussed on using plants, thus shifting the trend. The non-virulent nature of plants is highly beneficial as it ensures overall safety during synthesis and later potency of the product (Khan, 2020). The nanoparticles synthesized using plants are more stable as compared to others, thus creating a higher interest of researchers in this method (Abuzeid *et al.* 2023).

Table 2. Microbes-mediated synthesis of nanoparticles

Name of Organism	Type of Organism	Application	Nanoparticle	References
Staphylococcus aureus	Bacteria	Antibacterial	ZnO	(Rauf *et al.* 2017)
Pseudomonas aeruginosa	Bacteria	Antioxidant	ZnO	(Singh *et al.* 2014)
Bacillus megaterium	Bacteria	Antifungal	Se	(Hashem *et al.* 2021)
Alternaria tenuissima	Fungi	Antimicrobial, Anticancer, Antioxidant, Photocatalytic	ZnO	(Abdelhakim *et al.* 2020)
Aureobasidium pullulans	Fungi	Anti-infection potential	Se	(Liang *et al.* 2022)
Unnaria pinnatifida	Algae	Chemotherapeutic agent	ZnO	(Chen *et al.* 2008)

The use of medicinal plants for synthesizing nanoparticles has a sustainable impact in the field of green chemistry. Different plant parts including roots, leaves and stems ensure overall efficacy of the product and contribute to ecological benefits. The eco-friendly nature of this technique is advantageous as it eliminates pollution, uses non-toxic materials, reduces reaction time and makes large-scale synthesis easy. Many researchers are focussing their attention towards this procedure as it avoids high pressure, high temperature, high energy consumption and toxic substances. (Xulu *et al.* 2022).

The basic steps involved in the synthesis process are the choice of plant, selection of the desired plant part and then preparation of the extract. Later, a suitable salt solution is chosen and the prepared extract is added into it. Finally, the mixture is subjected to stirring, which promotes the synthesis of nanoparticles (Demissie *et al.* 2020; Naseer *et al.* 2020; Iqbal *et al.* 2021).

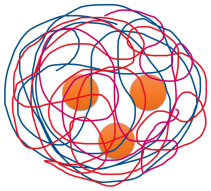
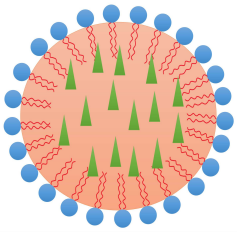
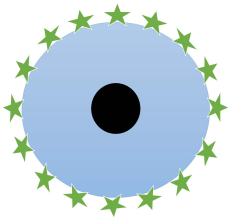
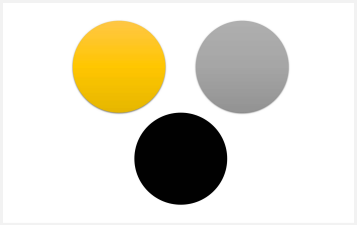
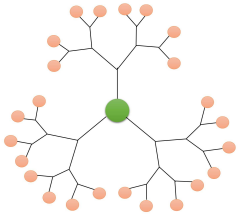
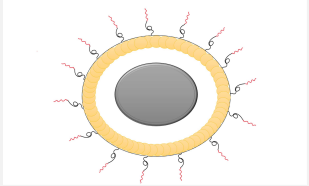
5. HERBAL NANOMEDICINE

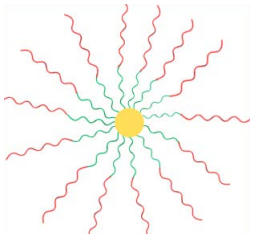
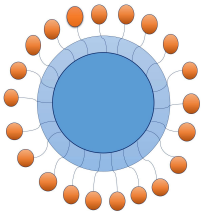
Herbal medicines are characterized by the World Health Organization as therapeutic agents that include “herbs, herbal materials, herbal preparations, and finished herbal products that contain as active components parts of plants, other plant materials, or combinations.” Medicinal plants are composed of a diverse array of compounds, such as flavonoids, alkaloids, terpenoids, fatty oils, tannins and triterpenes. Herbal medicines have thousands of elements that all work together to combat ailments, unlike the commonly utilized allopathic method (Yadav and Agarwala, 2011).

Extraction techniques include maceration, percolation, decoction, Soxhlet extraction, pulse electric field extraction, enzyme assisted extraction, microwave assisted extraction, etc (Zhang *et al.* 2018).

Recently, the term "nanomedicine" has been used to describe the use of nanotechnology in biological systems for tracking, diagnosis, treatment, and control. There are many different types of nano-pharmaceuticals as shown in Table 3.

Table 3. Different types of nanopharmaceuticals

Nanopharmaceuticals	Representation	References
Polymeric Nanoparticles		(Elmowafy *et al.* 2023)
Solid Lipid Nanoparticles		(Fayaz *et al.* 2023)
Quantum Dots		(Probst *et al.* 2013)
Metal and Inorganic Nanoparticles		(Patel *et al.* 2024)
Dendrimers		(An *et al.* 2023)
Magnetic Nanoparticles		(Marszall, 2011)

Polymeric Micelles		(Sun *et al.* 2022)
Colloidal Nanoliposomes		(Su *et al.* 2018)

These nano-based drug delivery systems have been adopted for the following reasons: Because of their special size and large loading capabilities, they seem to be able to deliver significant concentrations of drugs to disease locations, maintain required concentration of the drug at the target for a prolonged period, improve penetration through biological barriers and reduce dosage (Deepak *et al.* 2011). Fig. 3 illustrates the loading of herbal drug in nanoparticles.

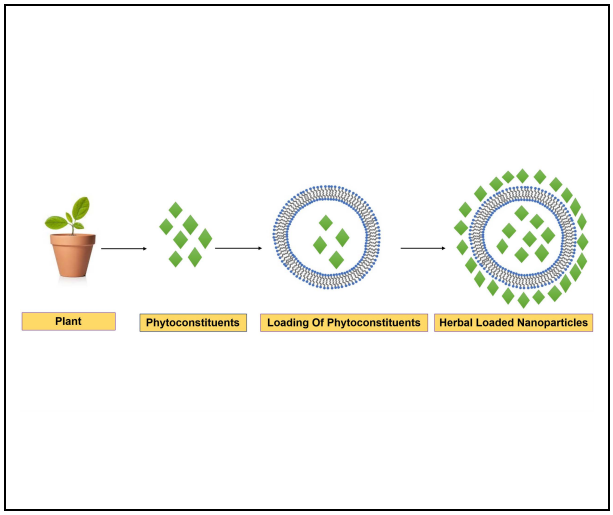


Fig. 3: Herbal loading of nanoparticles

There has been a significant rise in the production of nanoparticles derived from medicinal plants, which play an essential role in the development of nanomedicines (Shah *et al.* 2015; Bharadwaj *et al.* 2021). Many researchers have synthesized nanoparticles of different metals utilizing a variety of plants, such as *Carica papaya*, *Jatropha curcas*, *Malva parviflora*, *Allium sativum*, and many more (Chandra *et al.* 2020). These synthesized nanomedicines hold numerous applications as depicted in Fig. 4.

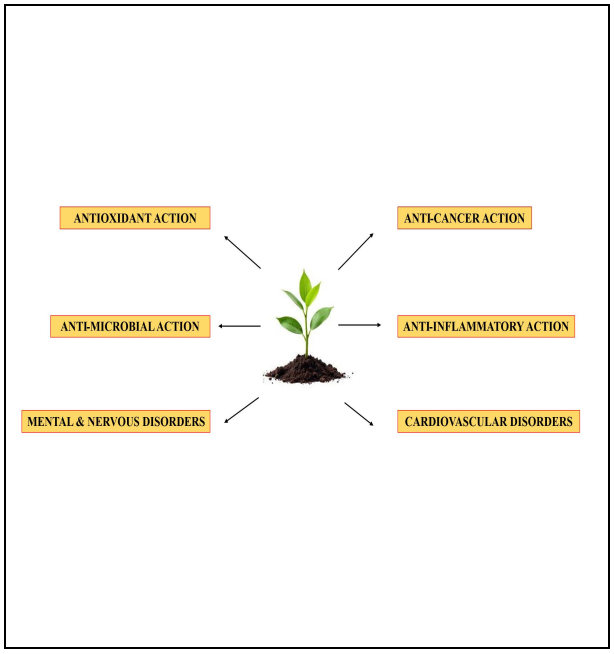


Fig. 4: Applications of nano herbal medicines

5.1 *Azadirachta indica*

Azadirachta indica, commonly known as neem, belongs to the Meliaceae family and is primarily distributed throughout various African nations and the Indian subcontinent. This versatile tree is well-regarded for its numerous applications in traditional medicine and agriculture (Alzohairy *et al.* 2016). Brahmachari, (2004) stated that all parts of the plant have been incorporated into the Indian Ayurvedic and Unani systems of medicine, and they have emerged as focal points in modern medical practices. The primary active component is azadirachtin, accompanied by other constituents including nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, and quercetin (Gokhale *et al.* 2008).

5.1.1 Ayurvedic Background of *A. indica*

Throughout history, the neem tree has been recognized as a vital element in Ayurvedic medicine in India. Each and every part of it possesses medicinal properties *viz*., bark, leaves, seeds, flowers, fruit pulp, etc (Subapriya and Nagini, 2005). It is known for a long time that green twigs of this plant are used as toothbrushes for cleaning teeth as a preventive measure against oral and dental issues. Applications of different parts of neem are given in Table 4.

Table 4. Applications of *A. indica* in ayurveda

Part	Ayurvedic Name	Action	References
Root	Nimba Mula	Antiparasitic, Analgesic, Antibacterial, Skin disorders.	(Charaka, 1981); Sushruta, 1907)
Leaf	Nimba Patra	Antimicrobial, Antitumor, Anti-inflammatory.	(Govindachari *et al.* 1998; Paul *et al.* 2011; Ebong *et al.* 2008)
Bark	Nimba Tvak	Antiparasitic, Antipyretic, Blood purifier.	(Charaka, 1981; Sushruta, 1907)
Seed	Nimba Beeja	Spermatogenic, Uterine Cleaner, Antipyretic	(Charaka, 1981; Sushruta, 1907)
Flower	Nimba Pushpa	Anti-ulcerative	(Reddy and Neelima, 2022)

5.2 *Gymnema sylvestre*

Gymnema sylvestre is a member of Apocynaceae family and is identified as a perennial and woody climbing plant. The tropical forests of central and southern India have a prosperous amount of these species. A variety of biologically active compounds are present in the leaves of this plant which include triterpene saponins, anthraquinones, flavones, hentriacontane, pentatriacontane, phytin, lupeol, β-amyrin-related glycosides, stigmasterol and calcium oxalate. Few acids such as tartaric, formic and butyric acids are also present. Many secondary metabolites are present in this plant that comprises of nine inter-related glycosides. The most common compounds are gymnemic acids A to D (Foster *et al.* 2002).

5.21 Ayurvedic Background of *G. sylvestre*

In Ayurveda, *G. sylvestre* is a well-reputed herb. It is commonly called gurmar because of its immense sugar destruction property. Sweet suppression capability of this plant is due to the presence of bioactive compounds like triterpene saponins, commonly called gymnemic acids and gymnemasaponins, along with a polypeptide called gurmarin (Tiwari *et al.* 2014). Different parts of this plant have been used in a variety of applications (Table 5).

Table 5. Applications of *G. sylvestre* in ayurveda

Part	Ayurvedic Name	Applications	References
Leaf	Meshashringi Patra	Diabetes, Obesity	(Charaka,1981)
Stem	Meshashringi Tvak	Skin Disease, Blood Disorders	(Charaka, 1981; Sushruta, 1907)
Fruit	Meshashringi Phala	Bleeding Disorders	(Sushruta,1907)

6. THERAPEUTIC POTENTIAL OF NANOPARTICLES SYNTHESIZED USING NEEM

Neem has been used in Ayurvedic medicine for a long time attributed to the fact that it possesses a large number of phytochemicals, required to treat numerous ailments (Alzohairy *et al.* 2016; Hawsah *et al.* 2023; Sharma *et al.* 2018). A variety of nanoparticles have been synthesized using A. indica leaves (Yadeta *et al.* 2024), flowers (Duangiai *et al.* 2019), seeds (Naz *et al.* 2017), and fruits (Alharbi and Alsubhi, 2023). The extract derived from neem leaves is known to encompass various functional substances, which include ascorbic acid, citric acid, cyclic peptides, ellagic acid, gallic acid, phenolic compounds, polyhydroxy limonoids, retinoic acid and tannins. These components are believed to significantly

contribute to the bio-reduction and stabilization processes of nanoparticles (Narde *et al.* 2023). Some of the biomedical applications of the nanoparticles synthesized using *A. indica* are listed in Table 6.

Table 6. Therapeutic applications of *A. indica* mediated nanoparticles

Nanoparticle	Activity	Results	References
AgNPs	Anti-biofilm Activity	The NPs formed show anti-biofilm efficacy against *Candida tropicalis*	(Al-Aboody *et al.* 2019)
AgNPs	Cytotoxic Activity	Demonstrated high toxicity against HepG2, LoVo, and MDA-MB231	(Algebaly *et al.* 2020)
AgNPs	Wound Healing Activity	Nano-formulation of these NPs resulted in fast wound healing in *in vivo* mice excision wound model	(Lakkim *et al.* 2020)
AgNPs	Antilarvicidal Activity	The NPs were highly effective against the larvae of *Aedes aegypti*	(Rasool *et al.* 2020)
AgNPs	Antidiabetic Activity	Show strong anti-diabetic efficacy, high potential for pancreatic and liver cell regeneration	(Rehman *et al.* 2023)
AgNPs	Angiogenic Activity	High angiogenic activity seen in the chorio-allantoic membrane of chick	(Kitimu *et al.* 2022)
AgNPs	Antiplasmodial Activity	Highly effective against 3D7 and RKL9 *Plasmodium falciparum* strains	(Hawadak *et al.* 2022)
ZnO NPs	Antibacterial Activity	Showed significant inhibition against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *B. subtilis*, *Proteus mirabilis*, *E. coli* in a dose dependent manner	(Elumalai and Velmurugan, 2015)
ZnO NPs	Antibacterial Activity	Showed significant antibacterial activity against *K. aerogenes* and *S. aureus*	(Madan *et al.* 2016)
ZnO NPs	Antifungal Activity	Showed significant inhibition against *Candida albicans* and *Candida tropicalis*	(Elumalai and Velmurugan, 2015)
ZnO NPs	Antioxidant Activity	Exhibited inhibiting DPPH free radical scavenging activity	(Madan *et al.* 2016)
Z)nO NPs	Antidiabetic Activity	Showed the inhibition of higher α-amylase and α-glucosidase	(Rehana *et al.* 2017)
ZnO NPs	Photocatalytic Activity	Exhibited more than 80% degradation efficiency	(Madan *et al.* 2016)
SeNPs	Antibacterial Activity	Polyphenols and flavonoids isolated from the plant leaf exhibits high antibacterial potential	(Marslin *et al.* 2018)
SeNPs	Antioxidant and Anti-helminthic Activity	Inhibit oxidative stress and exhibits dose-dependent response The paralysis and death time of earthworms was found to be less, thus proved to be anti-helminthic in nature	(Hawsah *et al.* 2023)
ZnO NPs	Antibacterial Activity	Showed significant antibacterial activity against *Xanthomonas oryzae*	(Mankad *et al.* 2016)

AgNPs	Anticytotoxic Activity	Exhibited high cytotoxic character against cancareous cells	(Narde *et al.* 2023)
AgNPs	Anticancer Activity	Showed anticancer activity against breast and lung cancer cell lines. It is also accompanied by cell shrinkage and necrosis	(Alharbi and Alsubhi, 2023)

6.1 Therapeutic Potential of *G. sylvestre* Nanoparticles

The term sugar destroyersuggests that *Gymenm a sylvestre* has the unusual capacity to numb the taste of sweetness. There are a variety of phytochemicals that this plant contains, which include anthraquinones, alkaloids, butyric acid, β-amyrin, flavones, formic acid, gymnemic acids, related glycosides, stigmasterol and tartaric acid (Kanetkar *et al.*2007). The nanoparticles of ZnO (Karthikeyan *et al.* 2019; Gotteparthi *et al.* 2023), silver (Rajkumar *et al.* 2020), gold (Nakkala *et al.* 2015), palladium (Kadam *et al.* 2020) and nickel (Bhoye *et al.* 2023) have been synthesized using *G. sylvestre* for evaluating their antibacterial, anticancer, antidiabetic, antioxidant, catalytic and antifungal potential (Table 7).

Table 7. Therapeutic applications of *G. sylvestre* mediated nanoparticles

Nanoparticles	Activity	Results	References
AgNPs	Antibacterial Activity	Exhibit strong inhibitory action against Gram-positive and Gram-negative bacteria	(Supraja *et al.* 2017)
AuNPs	Antidiabetic Activity	Prompt the restoration of pancreatic islet cells in diabetic rats	(Seetharaman *et al.* 2023)
SeNPs	Non-cytotoxic, Antioxidant and Anti-inflammatory Activity	High anti-inflammatory, antioxidant and non-cytotoxic activities make them a good target for nanoherbal medicine	(Bi *et al.* 2024)
ZnO NPs	Anticancer and Antibacterial Activity	These nanoparticles after doping with rare earth metals showed the enhancement of antibacterial and anticancer properties	(Karthikeyan *et al.* 2019)
ZnO NPs	Antidiabetic Activity	These nanoparticles showed increased serum insulin levels and shows increased expression of mRNA gene	(Gotteparthi *et al.* 2023)
SeNPs	Anticancer Activity	Biofunctionalized nanoparticles synthesized against HT29 human adenocarcinoma cells and proves to be anti-cancareous against these cells	(Arunachalam *et al.* 2015
AgNPs	Photocatalytic Activity	The NPs formed exhibit degradation of methyl orange solution in the presence of sunlight	(Pingale *et al.*2018
Ni/NiO NPs	Antifungal Activity	Peak efficacy of the nanoparticles against *Candida albicans* and *Aspergillus niger*	(Bhoye *et al.* 2023

7. TOXICITY EVALUATION

The innovative capabilities of nano-pharmaceuticals in enhancing therapeutic efficacy and precision in medical applications are indeed promising; however, the implications for safety must be thoroughly considered (Narang *et al.* 2011). Investigations conducted over recent decades have highlighted the challenges linked to the substandard quality of herbal medicinal products present in the market. A number of these concerns stem from the substitution of species and the practice of adulteration (Newmaster *et al.* 2013). Such issues not only undermine the trust in herbal remedies but also pose risks to public health. The protection of consumers necessitates a thorough authentication process for the herbal ingredients used, as well as for the finished products available for purchase.

8. CONCLUSION

Studies found that the superior antimicrobial efficacy of biogenic nanoparticles, which is approximately twenty-fold higher than that of their chemically synthesized counterparts, can be attributed to their favourable interactions with biomolecules (Rezazadeh *et al.*2020). They tend to reduce and stabilize the metal ions. The nanoparticles of various metals have been synthesized but zinc oxide nanoparticles have gained significant interest, primarily due to their distinctive characteristics. By adjusting their size and shape, their characteristics are simply adjustable (Jadoun *et al.* 2022). They have a variety of biomedical applications such as drug delivery, gene delivery, nanomedicines, bioimaging, etc (Basnet *et al.* 2018). Selenium nanoparticles are easy to produce and they integrate with other biological or chemical agents to improve biological characterisation because of their low toxicity, biocompatibility, and surface modification (Devi *et al.*2023). They possess numerous therapeutic applications like antibacterial activity (Shoebi and Mashreghi, 2017), antiviral activity (Men *et al.* 2009), antioxidant activity (Wang *et al.* 2007), anticancer activity (Ramamurthy *et al.* 2013), protective effect (Ungvári *et al.* 2014) and many more (Hosnedlova *et al.* 2018).

Studies found that both *A. indica* and *G. sylvestre* possess significant applications to use them as a nano-herbal component. They encapsulate the nanoparticles and are successfully targeted to the site of action for promising results. *Azadirachta indica* is a multipurpose medicinal tree and contains many bioactive compounds, and nanoparticles made using it enhances bioavailability of the phytochemicals. To ensure targeted delivery of these nanoparticles, they can be engineered. The nanoparticles which have been synthesized from *A. indica* possess lower toxicity and biocompatibility, thus impeding their use in nano-herbal medicine (Kumar *et al.* 2024). The use of *G. sylvestre* in herbal medicines is due to the fact that it reduces blood sugar level and improves the sensitivity of insulin.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper.

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