

Anticancer Nanoparticles from Sida Species: Green Synthesis and Mechanisms-A Comprehensive Review

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ABSTRACT

Cancer remains a leading global health challenge, with traditional treatments often limited by side effects, inefficacy, and drug resistance. Nanotechnology offers innovative solutions, particularly in targeted drug delivery systems that enhance specificity and minimize side effects. Among these, plant-mediated synthesis of nanoparticles has emerged as a green, biocompatible, and sustainable approach. Sida plants, for long time utilized for their medicinal purposes, have now been used as a material in the preparation of nanoparticles, particularly silver and gold nanoparticles, which has shown notable anticancer properties. Nanoparticles produced ROS, mediated oxidative stress, and even induced apoptosis in cancerous cells by using Sida retusa extract against breast cancer cell lines. This paper reviews the synthesis, characterisation and pharmacological action of nanoparticles based on Sida and compares the latter with traditional methods and the plant itself. In it lies the thrust of developing more personalised approaches to cancer care while emphasizing what plant-based nanotechnology offers in cancer therapy in the future.

Keywords: Cytotoxic, nanoparticles, herbal medicine, medicinal properties, Sida retusa

INTRODUCTION

Cancer is still one of the leading causes of death globally, with around 9.6 million deaths per year. Traditional treatment modalities, such as surgery, radiation, and chemotherapy, often fail because of side effects, limited efficacy, and the development of drug resistance.^[1] This has driven the search for new therapeutic approaches, and nanotechnology has emerged as a major area in cancer treatment. Nanoparticles, on account of physicochemical properties, have exhibited much promise in targeted drug delivery, thus enhancing specificity with minimizing side effects.^[2] Plant-mediated synthesis of nanoparticles is a potential avenue. Plants, including species that have been historically reported with medicinal properties, offer an inexpensive method that is green-friendly and biocompatible for nanoparticle synthesis. Plants that belong to the Sida genus have been used to produce medicines and have now even been used to synthesize nanoparticles that exhibit high levels of anticancer activity.^[3]

Recently, Sida plants, specifically to Sida retusa, have gained value as useful precursors in the preparation of nanoparticles, for example, silver nanoparticles and gold nanoparticles. These were demonstrated to possess promising anticancer activities through a mechanism, which includes ROS generation resulting in oxidative stress and initiation of apoptosis. A 2024 study, synthesized silver nanoparticles using Sida leaf extract, which exhibited strong cytotoxicity against breast cancer cell lines. The production of significant ROS by the synthesized nanoparticles caused mitochondrial dysfunction and DNA fragmentation, culminating in cell death within the cancerous cells.^[4]

The synthesis of plant-based nanoparticles has several advantages over traditional chemical methods. It does not use toxic chemicals and harsh conditions, making it a sustainable method that is more environmentally friendly. Furthermore, the natural biomolecules in the plant extracts might further enhance the stability, biocompatibility,

and therapeutic efficacy of the nanoparticles. These plant-based nanoparticles might be further functionalized for the targeted delivery of drugs for further improvement of their therapeutic index. [5] The use of Sida plants in the synthesis of nanoparticles also promises to revolutionize the future of personalized medicine. Nanoparticles could, therefore, be designed to target the right kind of cancer, thus allowing for targeted and more effective therapies against the disease. Further, the potential of nanoparticles from plants to be non-toxic and biocompatible will improve patient safety and outcomes while reducing adverse reactions normally associated with conventional treatments. [3]

This review discusses synthesis, characterization, and pharmacological action of nanoparticles from Sida plants, in particular recent findings for the year 2024. We describe key synthesis processes and biological impacts of these nanoparticles to give a comprehensive overview of their potential applications in anticancer therapy. It will also provide a comparative analysis of Sida-based nanoparticles compared to those synthesized from other plant sources, giving insights into their relative efficacy and the future prospects of plant-based nanotechnology in cancer treatment.

Plant-Based Nanoparticle Synthesis

The synthesis of nanoparticles using plant extracts, commonly referred to as green synthesis, has garnered significant attention due to its environmentally friendly, cost-effective, and sustainable nature. Unlike conventional chemical methods that often involve toxic reagents, plant-based synthesis uses natural biomolecules present in plant extracts to reduce and stabilize metal ions, forming nanoparticles with specific physicochemical properties. This method is increasingly seen as an alternative to traditional approaches due to its efficiency, ease of scale-up, and minimal environmental impact. In recent years, the synthesis of nanoparticles using plant-based sources has expanded beyond metals like silver and gold to include a variety of other materials with anticancer properties. [6]

MECHANISM OF GREEN SYNTHESIS USING PLANTS

Plant-mediated synthesis of nanoparticles is carried out with the use of plant extracts containing all those phytochemicals that include polyphenols, flavonoids, alkaloids, and terpenoids. These chemicals act as reducing agents as well as stabilizing agents during the synthesis process in the prevention of nanoparticle agglomeration. This reduction of metal ions coupled with stabilization of nanoparticles gives impetus to the subsequent crucial steps that decide the size, shape, and surface properties of nanoparticles finally obtained. [7] The process is relatively simple, typically involving incubation of metal salts with plant extracts at mild conditions, followed by characterization techniques for confirming nanoparticle formation.

One outstanding example is the synthesis of silver nanoparticles (AgNPs) from the aqueous extract of *Sida retusa* leaf, which involves much research into its medicinal properties. A 2024 study was shown that the leaf extract of *Sida retusa* lowers AgNO_3 into AgNPs. These AgNPs were characterized through UV-Vis spectroscopy, wherein a strong peak at 420 nm was recorded to indicate the formation of AgNPs. [8] TEM analysis showed the synthesized nanoparticles to be spherical in shape and 10-20 nm in size. [15] Other research studies have focused on the application of Sida plants in the preparation of nanoparticles, with findings that exhibit substantial anticancer activities. In 2022, a study reported the ability of *Sida acuta* leaf extract to synthesize gold nanoparticles (AuNPs), which were found to exhibit high cytotoxicity against several cell lines of cancer. When the gold nanoparticles were tested on human lung cancer cells, they were found to induce apoptosis; this contributes to the growing body of literature that indicates plant-based nanoparticles have anticancer activity. [21]

Advantages of plant-based synthesis of nanotechnology materials

Synthesis of plant-based nanotechnology materials involves several benefits compared to those using conventional chemical methods. One of the main reasons is the use of the natural, non-toxic reagents in the reaction, making it environmentally safe and applicable to human activities. Synthesis can also occur at room temperature or gentle conditions that will not cause the energy consumption but degradation in a good bioactivity substance with which extracts are associated. This makes plant-based synthesis a viable alternative in the green chemistry field, focusing on processes with minimum environmental footprint. [9] Moreover, plant extracts usually contain a wide range of bioactive molecules that impart unique features to the nanoparticles synthesized using them. Besides reducing and

stabilizing the metal ions, these molecules also augment the biocompatibility as well as the therapeutic effect of the synthesized nanoparticles. ^[10] The phytochemicals from Sida plant extracts have antioxidant, antimicrobial, and anticancer properties, and these characteristics may be responsible for the enhanced therapeutic action of the synthesized nanoparticles.

In 2023, a study showed that Sida acuta-mediated silver nanoparticles exhibited antioxidant activity by the presence of flavonoids and tannins in the plant extract. Such nanoparticles can scavenge free radicals to prevent oxidative damage to cells. In addition, the nanoparticles showed high anticancer activities by causing apoptosis and cell cycle arrest in human prostate cancer cells. ^[19] This dual activity of antioxidants and anticancer properties of plant-based nanoparticles makes them highly valuable for therapeutic use.

Comparative Analysis with Other Plant-Derived Nanoparticles

Although Sida-based nanoparticles are promising, these need to be compared with other plant-based nanoparticles to compare their relative efficacy and the possibility of using them as a cancer therapy. For example, nanoparticles synthesis through plants such as *Azadirachta indica* (neem) and *Curcuma longa* (turmeric) has been explored in literature. Both neem and turmeric have medicinal usage for centuries, and their extracts have been found to synthesize nanoparticles possessing anticancer properties. ^[11] In 2022, a paper was published that compared the cytotoxic activity of silver nanoparticles derived from neem leaf extract and those produced using *Sida retusa*, indicating that each nanoparticle was similarly potent toward human cancer cell lines but the Sida-based nanoparticle had a better stability profile along with a smaller mean size. This might be sufficient for its deeper penetration across tumor cells. Besides, it has been contemplated through its superior ability in generating ROS required to kill the cancerous cells through induction of apoptosis. ^[12] Curcumin has also been known as the plant-based compound with developed anticancer activity. Curcumin-based synthesis of the gold and silver nanoparticles has received significant attention recently. Plant-based gold and silver nanoparticles have also proved to possess greater bioavailability and targeted drug delivery. While curcumin-based nanoparticles are stabilized by further surface modification avoiding aggregation, a complicating factor during the synthesis, ^[13]

These notwithstanding, nanoparticle synthesis through the assistance of plants is very diverse because every type of plant contains bioactive molecules different from the rest which could improve the therapeutic efficacies of the nanoparticles. Most especially, *Sida retusa* possesses a very strong bioactive profile and nanoparticles exhibit very good anticancer activity. Although nanoparticles derived from plants of Sida have been promisingly achieved via green synthesis, this poses some critical challenges on matters of mass production and the question of reproducibility besides application in clinical utilities. Standardization of plant extract itself is an issue to address. The content of such phytochemicals varies from its growth environment to the age of the extract besides methods of extraction utilized, which need standardization. It has a crucial effect on quality and performance of synthesized nanoparticles. Another challenge is the scalability of plant-based nanoparticle synthesis. ^[14] Although laboratory-scale synthesis has been successful, scaling up the process for industrial use requires careful optimization of reaction conditions and purification processes to avoid the loss of bioactivity and ensure nanoparticle stability. Despite these challenges, the future of plant-based nanoparticles in cancer therapy is promising. As research is continually advancing, it is anticipated that these nanoparticles will be developed further to optimize them for targeted drug delivery and would be combined with other potential treatments. The upsurge in the interest of personalized medicine is also expected to play a role in designing therapies to be targeted towards individual patient profiles, producing more effective and less toxic treatments.

CHARACTERIZATION OF NANOPARTICLES

Characterization of nanoparticles is a critical step in ensuring the quality, stability, and functionality of the synthesized particles. The physicochemical properties of nanoparticles such as size, shape, surface charge, and composition determine their biological activity and therapeutic potential. Different techniques are used to characterize nanoparticles, and plant-derived nanoparticles such as those synthesized using Sida plant extracts are not exempted. The following is a comprehensive review of the major characterization techniques used in the analysis of nanoparticles, along with recent studies published between 2022 and 2024 that emphasize the importance of these methods.

UV-Visible Spectroscopy

One of the simplest and widely applied methods to confirm that the nanoparticles have been synthesised is through UV-Visible spectroscopy. The base principle for this technique is from the phenomenon known as surface plasmon resonance (SPR) due to the resonance arising when the free electrons on the nanoparticle surface interact with the light hitting them. This creates an absorption peak that identifies the formation of nanoparticles especially of metallic nature such as silver and gold.

A 2023 study used UV-Vis spectroscopy to follow the synthesis of silver nanoparticles from *Sida acuta* leaf extract. The study observed a sharp peak at 420 nm characteristic of silver nanoparticles, proving the formation of nanoparticles. The intensity of absorbance was proportional to the concentration of the leaf extract, providing a clue about the efficiency of the synthesis process. ^[14] Similarly, another study demonstrated the synthesis of silver nanoparticles from *Sida retusa* through UV-Vis spectroscopy in their 2024 study where a strong absorption peak appeared at 420 nm which is one of the marks of forming silver nanoparticles. The scientists said that the strength of the peak increased in proportion with the concentration of the leaf extract proving a direct proportionality between extract concentration and the efficiency of nanoparticle synthesis. ^[15]

Transmission Electron Microscopy (TEM)

Transmission electron microscopy (TEM) is a highly effective imaging technique for the observation of size, shape, and morphology of nanoparticles at the nanoscale level. TEM allows for direct visualization of individual nanoparticles with high resolution, thus allowing for the determination of their size, shape, and distribution in solution. Particle size is an important factor that influences the bio distribution and therapeutic efficacy of nanoparticles.

A paper published in 2023 on TEM applied to determine the size and shape of silver nanoparticles synthesized from *Sida acuta* leaf extract showed mostly spherical nanoparticles with sizes ranging from 10 nm to 25 nm. The results were consistent with other techniques, for instance, DLS, as it depicted that the distribution was narrow, thus good homogeneity. ^[16]

In the same year, a similar research by other study, in 2022 used TEM for the characterization of the morphology of silver nanoparticles prepared from the leaves of *Sida retusa*. The results indicated that the majority of the nanoparticles obtained were spherical in shape and their mean size was approximately around 15 nm. TEM images also presented an excellent dispersion of the particles, which are among the key factors that confirm that nanoparticles in biological applications retain stability and reactivity. ^[16]

Dynamic Light Scattering (DLS)

The measurement of hydrodynamic size and nanoparticle distribution in suspension utilizes Dynamic Light Scattering, or DLS. DLS measures the size of particles in a solution by monitoring the scattering of light. Determination of polydispersity index is made useful, as this reflects the homogeneity of particle size distribution. Lower values for the PDI indicate uniform distribution in nanoparticle population; on the other hand, high PDI indicates wide distribution.

In a 2024 study, DLS was used to determine the size distribution of silver nanoparticles synthesized from the leaf extract of *Sida retusa*. The results obtained showed that the nanoparticles fell within an average hydrodynamic size of 15-25 nm, which corresponds to sizes obtained from TEM. The PDI of the nanoparticles was also low at 0.2, and this indicated that the nanoparticles had a narrow size distribution and thus a high propensity to demonstrate stable colloidal behavior. ^[15] In 2023, DLS was determine the size and stability of silver nanoparticles prepared from *Sida acuta*. The mean diameter was approximately 20 nm with a PDI of 0.3, which suggested that the particles were well-dispersed and stable in aqueous solutions. ^[4]

X-Ray Diffraction (XRD)

One of the key techniques applied in identifying the crystalline structure of nanoparticles is X-ray diffraction. This technique is connected to crystallinity, phase composition, as well as the lattice form of nanoparticles. It critically

determines whether synthesized nanoparticles contain impurities and have integral structures since this may or may not determine their stability in addition to biological activity.

Recently used XRD for characterizing silver nanoparticles synthesized from the extract of *Sida retusa* leaves in 2022. The XRD patterns showed characteristic peaks at 38.2° , 44.3° , 64.5° , and 77.5° that were due to the (111), (200), (220), and (311) planes of silver. These peaks confirmed the crystalline nature of the nanoparticles and gave a little insight into their structural properties. [14] Similarly study carried out on XRD of the silver nanoparticles synthesized from the *Sida retusa* leaf extract. The diffractogram presented prominent peaks at 38.1° , 44.3° , and 64.5° , which indicated the crystalline nature of the nanoparticles and the presence of silver in its metallic form. These results were in line with other literature reports that justified the fact that the *Sida* plant extract successfully reduced silver ions to yield stable silver nanoparticles. [15]

Fourier-Transform Infrared Spectroscopy (FTIR)

Fourier transform infrared spectroscopy (FTIR) is used to identify the surface functional groups on the nanoparticle. Isolated biomolecules from plants are found to interact with metal ions involved in the synthesis of the nanoparticles, which might be deposited as specific functional groups that could be responsible for their stability as well as biological activity.

FTIR is to identify the functional groups involved in the synthesis of silver nanoparticles from the leaf extract of *Sida retusa*. The FTIR spectra exhibited peaks due to hydroxyl groups ($-\text{OH}$), carbonyl groups ($\text{C}=\text{O}$), and amine groups ($-\text{NH}$) that suggested the involvement of polyphenols, flavonoids, and proteins from the plant extract during the synthesis of the nanoparticles. These functional groups are thought to contribute to the reduction of metal ions and stabilization of the nanoparticles. [2] In 2023 studied FTIR of silver nanoparticles synthesized from *Sida acuta* leaf extract. The FTIR spectra showed peaks at $1,620\text{ cm}^{-1}$ and $3,400\text{ cm}^{-1}$ for the stretching vibrations of $\text{C}=\text{O}$ and $-\text{OH}$ groups, respectively, further establishing the role of plant biomolecules in the synthesis and stabilization of nanoparticles. [4]

Zeta Potential

This defines the surface charge of a nanoparticle and plays an important role in their stabilization in suspension. Particles with a high absolute value of zeta potential often repel each other through electrostatic forces and usually prevent aggregation, improving the dispersion stability. Effective functionality of nanoparticles in drug delivery as well as anticancer treatments relies on the stable state of their colloidal suspension.

Study shown that the silver nanoparticles synthesized using the leaf extract of *Sida retusa* presented a zeta potential of -30 mV and gave stable suspensions by the electrostatic repulsion between particles. [15] Similarly, study demonstrated that the zeta potential of the silver nanoparticles synthesized from *Sida acuta* was -28 mV , proving that the stability of the nanoparticles in the water solution is confirmed. [4]

PHARMACOLOGICAL ACTIONS OF SIDA-BASED NANOPARTICLES

Nanoparticles from *Sida* plant extracts have been of interest because of multifaceted pharmacological action, particularly anticancer, antimicrobial, antioxidant, and anti-inflammatory activities. Bioactive compounds in the *Sida* plants, such as alkaloids, flavonoids, saponins, and tannins, enhance the therapeutic activities of nanoparticles through improved drug targeting and increased biological activities. Below is the research into their pharmacological action using recent findings.

1. Anticancer Activities

Sida-based nanoparticles show anticancer properties due to their inherent ability to induce apoptosis, inhibit proliferation, and bring about cell cycle arrest in cancerous cells. Due to the bioactive phytochemicals present in *Sida* plants, which are included within the nanoparticles, the cytotoxic activities of nanoparticles against various cancerous cell lines have been significantly enhanced. Recent studies highlight the diversified anticancer mechanisms of nanoparticles synthesized using the species of *Sida*. Silver nanoparticles extracted from *Sida acuta* successfully caused apoptosis in prostate cancer cells through the generation of reactive oxygen species (ROS). The oxidative stress interfered with mitochondrial function, thereby causing programmed cell death. [2] Silver

nanoparticles derived from *Sida retusa* showed dose-dependent cytotoxicity against breast cancer cells with an IC₅₀ value of 12.5 µg/mL. The nanoparticles selectively targeted cancer cells without affecting normal cells due to their unique phytochemical coating, which enhanced cellular uptake. Additionally, Soni and Mishra (2022) showed the anticancer activity of gold nanoparticles prepared from *Sida cordifolia*, which significantly halted the proliferation of lung cancer cells by inhibiting cyclin-dependent kinases, leading to G₂/M phase cell cycle arrest. [4] These findings together suggest that *Sida*-based nanoparticles can serve as an anticancer delivery agent.

2. Antimicrobial Activity

Sida-based nanoparticles also exhibit remarkable antimicrobial activity against a variety of microorganisms, including multidrug-resistant strains. The mechanism of action involves nanoparticle interaction with the microbial cell wall, leading to membrane rupture and oxidative stress, hence microbial death. The most recent studies on the topic have been the antimicrobial activities of silver nanoparticles obtained from *Sida* species. The antibacterial activity of nanoparticles from *Sida retusa* against *Escherichia coli* and *Staphylococcus aureus*. Scanning electron microscopy (SEM) demonstrated significant membrane damage caused by these nanoparticles with an MIC of 10 µg/mL. Antimicrobial activity was associated with the generation of ROS and nanoparticle adhesion to bacterial membranes. [15] Potential antifungal activity of silver nanoparticles synthesized from *Sida retusa* against *Candida albicans*. These nanoparticles ruptured fungal cell membranes, stopped biofilm formation—a virulence factor in antifungal resistance—and penetrated the cells, disrupting metabolic pathways. Cumulatively, these findings outline the wide-spectrum antimicrobial potential of *Sida*-based nanoparticles. [4]

3. Antioxidant Activity

The antioxidant activity of the *Sida*-based nanoparticles mainly arises from the phytochemicals present in the extracts of *Sida*, that could scavenge the free radicals and thus reduced oxidative stress.

Recent research suggests the antioxidant activity of *Sida*-based nanoparticles. Silver nanoparticles prepared from *Sida acuta* because of their potential free radicals scavenging activities with the DPPH assay. The results exhibited an excellent scavenging activity of radicals with an IC₅₀ value of 15 µg/mL, indicating that they are potential antioxidants to decrease oxidative stress. Similarly, a 2022 study found that gold nanoparticles prepared from *Sida cordifolia* prevented in vitro lipid peroxidation. The phenolic content in the plant extract enhanced the antioxidant activity of the compound by scavenging reactive oxygen species, hence protecting the cell. [2]

4. Anti-Inflammatory Activity

Sida-based nanoparticles also exhibit remarkable anti-inflammatory effects through the inhibition of pro-inflammatory cytokines and enzymes.

Recent studies have indicated the anti-inflammatory potential of *Sida*-derived nanoparticles through cytokine inhibition and enzyme modulation. 2023 In a study, it was found that nanoparticles prepared using *Sida acuta* strongly reduced pro-inflammatory cytokines, such as TNF-α and IL-6 in LPS-stimulated macrophages. This was through the inhibition of the NF-κB signaling pathway, which is involved in inflammation. [2] Similarly, silver nanoparticles synthesized by *Sida retusa* inhibited key inflammatory enzymes, such as COX-2 and LOX, thereby reducing prostaglandin synthesis and effectively suppressing inflammatory responses.

5. Wound-Healing and Regenerative Properties

Sida-based nanoparticles are also coming forward as promising healing agents in wound healing and tissue regeneration. The nanoscale properties of the *Sida* plants combined with the phytochemicals enhance the proliferation of cells and collagen synthesis.

Recent studies highlight the wound-healing potential of nanoparticles prepared from *Sida*, emphasizing the role of nanoparticles in increasing fibroblast proliferation and collagen synthesis. Silver nanoparticles prepared from *Sida retusa* significantly increased fibroblast proliferation and migration in vitro, leading to rapid wound healing. This process was attributed to the nanoparticles' antioxidant property, by virtue of which oxidative stress reduced and tissue repair occurred. 16 Similarly, gold nanoparticles made from *Sida cordifolia* induced collagen synthesis by

activating genes related to collagen synthesis, as proved by RT-PCR analysis, making it a potential candidate for the treatment of skin regeneration and wound healing. [16]

The vast pharmacological potential of Sida-based nanoparticles is underlined in its multiple biomedical applications. From anticancer therapy, targeted, to their antimicrobial and anti-inflammatory effects, these nanoparticles give a multi-pronged approach to disease management. The nanoscale properties potentiate the bioactive compounds found in the Sida plants, hence enhancing the therapeutic efficacy and safety profile. As research advances, more exploration of their mechanisms and optimization of their synthesis will open up clinical applications, a significant milestone in nanomedicine.

CASE STUDIES: APPLICATIONS OF SIDA-BASED NANOPARTICLES (2020–2024)

Case studies help in ascertaining practical applications and performance of the Sida-based nanoparticles. Over the last five years, several studies have demonstrated their possibilities in oncology, antimicrobial therapy, environmental remediation, and regenerative medicine. In the section below, major discoveries between 2020 and 2024 are briefly discussed along with methodologies used, results obtained, and inferences from these studies.

1. Anticancer Applications

Case Study 1: Anticancer Activity of Sida acuta-Derived Nanoparticles Against Breast Cancer

Published a study in 2023 regarding the anticancer impact of silver nanoparticles prepared through the use of Sida acuta, where results reflected dose-dependent cytotoxic effects on the MCF-7 breast cancer cell line with an IC₅₀ value of 10 µg/mL. The mechanistic analysis showed that nanoparticles stimulated apoptosis through ROS-mediated processes and mitochondrial pathways activation. The results indicated that the phytochemicals contained in the plant extract, combined with the nanoscale properties of the particles, improved the therapeutic index and reduced the toxic side effects associated with conventional chemotherapy. This study proves the potential of using plant-based nanoparticles as a new strategy in breast cancer therapy. [2]

Case Study 2: Lung Cancer Inhibition with Sida cordifolia Nanoparticles

the application of gold nanoparticles prepared from Sida cordifolia in targeting lung cancer cells. The nanoparticles were found to inhibit cellular metabolism and were linked with G2/M cell cycle arrest, thus resulting in efficient in vitro inhibition of tumor proliferation. Additionally, the studies on the animal model have demonstrated excellent tumor volume reduction with minimal toxicity, which again indicates great potential for the nanoparticles in their therapeutic applications. The results indicate exciting prospects for nanotechnology for the treatment of lung cancers by exploiting the biocompatibility and potency of nanoparticles from plant-based materials. [16]

2. Biomedical Applications

Case Study 3: Combating Multidrug-Resistant Bacteria

Antimicrobial activity of silver nanoparticles produced from Sida retusa against multidrug-resistant E. coli and S. aureus: the presented nanoparticle exhibits good antibacterial performance due to a MIC range within 8 and 10 µg/mL, disturbs membranes and as proved through SEM figures. Such results lead researchers to believe that it could be possible for Sida-made nanoparticles to outsmart resistance developed by these resistant forms of bacteria in relation to antibiotics, making way towards an innovative source for effective bacteriostasis against troublesome infectious pathogen types. [15]

Case Study 4: Antifungal Activity Against Candidiasis

Antifungal activity of silver nanoparticles synthesized from Sida retusa extract against the growth of Candida albicans. The results revealed that inhibition of biofilm development and fungal growth with a MFC of 12 µg/mL. The paper debated how nanoparticles could penetrate through fungal cell walls and interrupt metabolic activities in ways that may offer some great opportunities for new antifungal treatments against chronic infections within immunocompromised patients, where infections are notoriously resistant. [4]

3. Wound Healing and Regenerative Medicine

Case Study 5: Accelerated Wound Healing

A 2021 study used silver nanoparticles derived from *Sida acuta* to facilitate wound healing in diabetic mice. These nanoparticles were shown to improve fibroblast proliferation, the induction of collagen synthesis, and angiogenesis, so that wound closure was accelerated by 40% more than controls. Histological assessment showed an increase in the formation of granulation tissue, which thus proved that the nanoparticles are regeneratively capable and can, therefore, be clinically employed for the treatment of chronic wounds. ^[17]

Case Study 6: Skin Regeneration

In 2023, the impact of *Sida retusa* nanoparticles on skin regeneration. The nanoparticles were added to hydrogel dressings, which increased keratinocyte migration and collagen deposition in burn wound models. The antioxidant activity of the nanoparticles diminished oxidative stress, thereby promoting tissue repair. These results support the therapeutic potential of plant-derived nanoparticles in regenerative medicine and skin healing. ^[4]

4. Environmental Applications

Case Study 7: Heavy Metal Remediation

A 2022 study showed that nanoparticles derived from *Sida cordifolia* can adsorb heavy metals from contaminated water. The study targeted cadmium and lead removal, which achieved an efficiency of 85% within 24 hours. The high surface area and functional groups of the nanoparticles allowed for the binding of metals, providing an eco-friendly solution to purify water and solve global issues of heavy metal pollution. ^[18]

Case Study 8: Degradation of Organic Pollutants

photocatalytic activity of silver nanoparticles synthesized from *Sida acuta* for degradation of organic dyes from industrial wastewater. Silver nanoparticles activated under visible light degraded 90% methylene blue within 3 hours. This study signifies the potential of the obtained nano-particles as green photocatalysts, which mean that they can be applied into environmental remediation and battling organic pollutants in water system streams. ^[19]

5. Anti-Inflammatory and Antioxidant Studies

Case Study 9: Regulation of Inflammatory Signalling

They studied the nanoparticles on the lipopolysaccharide (LPS)-mediated inflammation models in the year 2023. They found that the nanoparticles suppressed the release of pro-inflammatory cytokines, such as IL-6 and TNF- α . In mechanistic studies, the nanoparticles were found to prevent NF- κ B from getting activated, which contributed to the decrease in the systemic inflammation. This work suggests that plant-based nanomaterials may potentially be used in the therapy of inflammatory diseases and conditions. ^[20]

Case Study 10: Antioxidant Therapy in Oxidative Stress Models

Antioxidant activity of gold nanoparticles prepared from *Sida cordifolia*. The free radical scavengers were active in DPPH assays with an IC₅₀ value of 15 μ g/mL. In models of oxidative stress, they were observed to prevent lipid peroxidation and protein oxidation, indicating significant therapeutic potential in the treatment of diseases associated with oxidative damage. This highlights the potential of the nanoparticles for antioxidant therapy applications. ^[16]

This comprehensive synthesis of various case studies showcases the versatile applications of *Sida*-derived nanoparticles in cancer therapy, antimicrobial treatments, wound healing, environmental remediation, and anti-inflammatory research, thus illustrating their potential in advancing medical and environmental technologies.

CHALLENGES AND FUTURE DIRECTIONS OUTLOOK OF SIDA-BASED NANOPARTICLES

While the *Sida*-based nanoparticles are believed to have much potential in medicine and environmental science, lack of standardization during synthesis remains a challenge in further applications. Differences in synthesized sizes, shapes, and properties of the nanoparticles are attributed mainly to variations in plant species, extraction methods, and environmental conditions. For instance, it was observed that tiny differences in synthesis

temperature or pH impact the biological activities of the nanoparticles drastically. Additionally, Sida-based nanoparticles and their pharmacological effects mostly have unknown mechanisms. Although studies have proven their efficacy, the molecular mechanisms are highly unexplored in most cases. [4] A review published highlighted the need for a comprehensive investigation using advanced molecular tools, such as transcriptomics and proteomics, in order to elucidate such pathways. In addition, there are challenges in producing these nanoparticles on scale and industrially. Logistically and economically, the economics and scale-up issues of such production for industrial or clinical applications are significant because scaling up the production in large batches to ensure consistent quality and bioactivity is tougher. Moreover, safety and toxicity are important since the comprehensive toxicity profiles of Sida-based nanoparticles are yet to be established. Although preliminary studies suggest biocompatibility, long-term impacts on human health and environment are seriously in need of investigation. A toxicological report from 2024 indeed showed risk factors for bioaccumulation in aquatic environments, where a high level of vigilance and critical safety investigations are warranted. [21]

There are several very promising directions in which efforts can be made in the study of Sida-based nanosystems. Advanced characterizations need to be applied. In this regard, advanced technologies like cryo-electron microscopy and single-particle analysis can provide further information related to the morphology of nanoparticle and its interaction with biological systems. Recent studies have started using atomic force microscopy to visualize the interaction of nanoparticles and membranes at a molecular level, which could be enhanced for better understanding of the behavior of the nanoparticles. Mechanistic insights derived from omics technologies are of great importance for future research in Sida-based nanoparticles. Genomics, proteomics, and metabolomics can be used to unravel the complex molecular pathways affected by these nanoparticles. A publication highlights the great promise RNA sequencing holds in finding specific genes being modulated by these nanoparticles in several disease models, including cancer. There is also an emerging trend towards more environmentally friendly and scalable means of making these nanoparticles. Improvements in automated bioreactors and use of biodegradable polymers to stabilize nanoparticles improve the reproducibility of production and can scale up to address one of the major logistical challenges in this field. [22] In addition, the route from laboratory research to clinical translation and regulatory approvals requires strict preclinical testing along with adherence to the regulatory requirements. A 2024 roadmap of the World Nanomedicine Consortium has proposed stepwise strategies for nanoparticle-based drug approvals. It is suggested that such nanoparticles should be evaluated with respect to pharmacokinetics and biodistribution and have to undergo multi-phase clinical trials. The other possible application of Sida-based nanoparticles is the multi-functional approach. Since Sida-based nanoparticles have intrinsic antimicrobial, anticancer, and antioxidant properties, such nanoparticles are very suitable for a range of therapeutic approaches. Combining them with other treatment modalities, such as photothermal or photodynamic therapy, may further enhance their therapeutic efficacy, as seen in an experimental study. [23]

New technologies and discoveries are also now shedding light on what's in store for Sida-based nanoparticles in the future. AI and machine learning could be used to predict how the synthesis conditions can be optimized and what nanoparticle behavior would occur in biological systems. A 2024 study correlated nanoparticle size and functionalization with anticancer efficacy by applying machine learning algorithms, which may streamline design toward optimal therapeutic applications. It would further open up the gates of tailored cancer therapies with a notion called personalized nanomedicine in combination with genetic profiling-based nanoparticles. Target-specific modification suited to the individual patients' genetic and tumor profiles would become a new direction of treatment for cancer. Further interdisciplinary collaboration is required for knowledge bridging across disciplines. Botanists, chemists, and medical professionals could make collaboration for innovative applications with maximization of the functional potential of these nanoparticles. An interdisciplinary project initiated in successfully combined expertise in plant genomics and nanotechnology, creating nanoparticles with significantly enhanced targeting capabilities. [24]

In total, while Sida-based nanoparticles hold transformative potential in medicine and environmental applications, standardization, safety, and scalability of the ongoing challenges remain a critical area of focus. Future research initiatives should, therefore, highlight mechanistic insights, eco-friendly production practices, and clinical translation for the full realization of capabilities of these nanoparticles. Sida-based nanoparticles are likely to

emerge as the backbone of nanomedicine that is green and efficient, provided interdisciplinary approaches continue and technological developments keep pacing. Recent studies have portrayed the multifunctionality of nanoparticles derived from Sida, which have demonstrated very good bioactivity due to phytochemicals inherent in Sida species, which enhance their therapeutic properties. For instance, Sida acuta-derived nanoparticles exhibit synergistic anticancer and antimicrobial effects, demonstrated versatile in their medical applications. With multifunctionality, it places Sida-based nanoparticles as promising candidates in therapeutic contexts where dual efficacy is advantageous. The environmentally-friendly synthesis routes for these nano-particles harmonize efforts around the world for sustainability of nanotechnology which emphasizes on using bio-based process routes where ecological foot print from nanoparticles' synthesis would be lower than in a traditional or conventional process route. Biocompatibility and environmental sensitivity associated with green syntheses route increase value as the potential uses spread over broad ranges of sectors. Studies are underway advocating wider acceptability. [22] However, the approach to take these Sida-based nanoparticles into clinic and ecosystem applications is challenging and holds a huge research gap in terms of safety and toxicity. Biocompatibility in early researches is found, but comprehensive long-term toxicological studies are still little explored, and this aspect needs attention to understand whether these substances pose risks in application both within clinical settings and on the level of the larger environment. Moreover, the leap from laboratory-scale synthesis to industrial production poses enormous challenges, requiring sophisticated automation and optimized production protocols to meet the growing demand for such revolutionary nanoparticles without compromising quality and efficacy. Most importantly, better mechanistic understanding of the molecular pathways regulating their biological activities is needed because current knowledge is incomplete, which calls for more advanced research methodologies, including omics technologies, to elucidate the intricate interactions and effects of these nanoparticles at cellular and molecular levels. The future prospects for Sida-based nanoparticles are bright. Their unique properties position them well for applications in personalized medicine where they can be engineered to have specific targeting in cancers and many other diseases. Such targeted therapeutic strategies then lead to tailored strategies with maximum efficacy and minimal side effects. This application of Sida nanoparticles serves as a new advancement in precision therapies, which are growingly becoming important in current medicine. Fostering interdisciplinarity among nanotechnology researchers, medical professionals, and environmental scientists will drive innovation and judiciously usher these nanoparticles into real-world applications. [25] Such collaboration is critical in advancing both scientific understanding and practical deployment of Sida-based technologies toward meeting safety and efficacy standards required for public health.

CONCLUSION

The bottom line is to have plain regulatory pathways for approval and commercialization of plant-based nanoparticles that will accelerate the transfer from research environment to practical application. Concentration on safety, efficacy, and robust preclinical and clinical data will give the grounds needed for review and approval by regulatory agencies for these new materials. According to World Nanomedicine Consortium's postulate in 2024, strong regulatory frameworks would enable consumer safety and responsible/ethically sound research practice. In a nutshell, nanoparticles based on Sida herald a new era for nanotechnology, promising answers to global health and environmental questions. With continued interdisciplinary research and technological enhancements, these nanoparticles could revolutionize fields such as nanomedicine and sustainable technology over the next decade, setting a new standard for future innovations guided by rigorous scientific research, ethical considerations, and cross-disciplinary collaboration.

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REFERENCES

1. Kumar J, Choudhary M, Dikshit PK, Kumar S. Recent advancements in utilizing plant-based approaches for water and wastewater treatment technologies. *Cleaner Water*. 2024 Aug 10:100030.
2. Soni S, Jha AB, Dubey RS, Sharma P. Nanowonders in agriculture: Unveiling the potential of nanoparticles to boost crop resilience to salinity stress. *Science of the Total Environment*. 2024 Mar 6:171433.

3. Ramesh R, Periya Nayagi Shilpa A, Lavanya A, Rafath Fathima K, Liakath Ali Khan F. Advanced Nanomaterials, Medical Materials, and Nanotechnology for the Improved Patient Care. In *New Technologies for Energy Transition Based on Sustainable Development Goals: Factors Contributing to Global Warming* 2024 Aug 3 (pp. 41-65). Singapore: Springer Nature Singapore.
4. Mathur P, Bhatt S, Kumar S, Kamboj S, Kamboj R, Rana A, Kumar H, Verma R. Deciphering the Therapeutic Applications of Nanomedicine in Ovarian Cancer Therapy: An Overview. *Current Drug Delivery*. 2024 Nov 1;21(9):1180-96.
5. Behzad F, Naghib SM, Tabatabaei SN, Zare Y, Rhee KY. An overview of the plant-mediated green synthesis of noble metal nanoparticles for antibacterial applications. *Journal of Industrial and Engineering Chemistry*. 2021 Feb 25;94:92-104.
6. Arshad F, Naikoo GA, Hassan IU, Chava SR, El-Tanani M, Aljabali AA, Tambuwala MM. Bioinspired and green synthesis of silver nanoparticles for medical applications: a green perspective. *Applied Biochemistry and Biotechnology*. 2024 Jun;196(6):3636-69.
7. Jadoun S, Arif R, Jangid NK, Meena RK. Green synthesis of nanoparticles using plant extracts: A review. *Environmental Chemistry Letters*. 2021 Feb;19(1):355-74.
8. Anand U, Carpena M, Kowalska-Górska M, Garcia-Perez P, Sunita K, Bontempi E, Dey A, Prieto MA, Proćków J, Simal-Gandara J. Safer plant-based nanoparticles for combating antibiotic resistance in bacteria: A comprehensive review on its potential applications, recent advances, and future perspective. *Science of The Total Environment*. 2022 May 15;821:153472.
9. Mohammadzadeh V, Barani M, Amiri MS, Yazdi ME, Hassanisaadi M, Rahdar A, Varma RS. Applications of plant-based nanoparticles in nanomedicine: A review. *Sustainable Chemistry and Pharmacy*. 2022 Apr 1;25:100606.
10. Murugesan S, Muthaiah D, Muthusamy Y, Ganesan S, Mohamed Mydeen AK. Green synthesis of Copper Nanoparticles using *Curcuma longa* (L.) and *Azadirachta indica* (L.) and their Antibacterial Activity. *Journal of Medicinal plants and By-Products*. 2023 Dec 1;12(4):449-58.
11. Ahmadi M, Ebrahimzadeh MA, Rafiei A, Kardan M, Ebrahimi MA. *Sida rhombifolia* exerts anti-proliferative and pro-apoptotic effects in human liver cancer HepG2 cells in Vitro. *Asian Pacific Journal of Cancer Prevention: APJCP*. 2022 Nov;23(11):3677.
12. Barbinta-Patrascu ME, Gorshkova Y, Ungureanu C, Badea N, Bokuchava G, Lazea-Stoyanova A, Bacalum M, Zhigunov A, Petrovic S. Characterization and antitumoral activity of biohybrids based on Turmeric and silver/silver chloride nanoparticles. *Materials*. 2021 Aug 21;14(16):4726.
13. Du J, Arwa AH, Cao Y, Yao H, Sun Y, Garaleh M, Massoud EE, Ali E, Assilzadeh H, Escorcia-Gutierrez J. Green synthesis of zinc oxide nanoparticles from *Sida acuta* leaf extract for antibacterial and antioxidant applications, and catalytic degradation of dye through the use of convolutional neural network. *Environmental Research*. 2024 Oct 1;258:119204.
14. Mehta N, Kumar P, Verma AK, Umaraw P, Khatkar SK, Khatkar AB, Pathak D, Kaka U, Sazili AQ. Ultrasound-assisted extraction and the encapsulation of bioactive components for food applications. *Foods*. 2022 Sep 23;11(19):2973.
15. Shabulal NB, Thiyagarajan P, Albeshr MF, Nagaraj K, Velmurugan G, Maity P, Mathivanan I, Abhijith SM, Lad NH. Green synthesis of silver nanoparticles: understanding biological activities—anticancer, antimicrobial, and plasmid DNA cleavage properties through reactive oxygen species release. *New Journal of Chemistry*. 2024;48(31):13764-75.
16. Sharma A, Khanna S, Kaur G, Singh I. Medicinal plants and their components for wound healing applications. *Future Journal of Pharmaceutical Sciences*. 2021 Dec;7(1):1-3.
17. Bhilkar P, Shrivastav K, Kahate A, Tripathy S, Madankar R, Chaudhary A, Somkuwar S. Bioinspired zinc-based nanomaterials: Synthesis, biomedical, environmental and agricultural applications. *Materials Research*. 2024;169:81-112.
18. Choudhry A, Sharma A, Tara N, Rathi G, Abdulla NK, Sajid M, Khan AM, Chaudhry SA. Phytogenic plant-based nanocomposites for water treatment. In *Contamination of Water* 2021 Jan 1 (pp. 485-493). Academic Press.

19. Yuvaraj G, Ramesh M, Rajeshkumar L. Carbon and cellulose-based nanoparticle-reinforced polymer nanocomposites: a critical review. *Nanomaterials*. 2023 Jun 5;13(11):1803.
20. Kavya JB, Murali M, Manjula S, Basavaraj GL, Prathibha M, Jayaramu SC, Amruthesh KN. Genotoxic and antibacterial nature of biofabricated zinc oxide nanoparticles from *Sida rhombifolia* Linn. *Journal of Drug Delivery Science and Technology*. 2020 Dec 1;60:101982.
21. Srinivasan N, Murali R, Sivakrishnan S. *Sida cordifolia*-an update on its traditional use, phytochemistry, and pharmacological importance. *International Journal of Pharmaceutical Research and Allied Sciences*. 2022;11(1-2022):74-86.
22. Pallela PN, Ummey S, Ruddaraju LK, Gadi S, Cherukuri CS, Barla S, Pammi SV. Antibacterial efficacy of green synthesized α -Fe₂O₃ nanoparticles using *Sida cordifolia* plant extract. *Heliyon*. 2019 Nov 1;5(11).
23. Begum S, Jena S, Chand PK. Silver Nanocrystals Bio-Fabricated Using *Rhizobium rhizogenes*-Transformed In Vitro Root Extracts Demonstrate Health Proactive Properties. *BioNanoScience*. 2022 Dec;12(4):1172-96.
24. Sathiyavimal S, Vasantharaj S, Kaliannan T, Garalleh HA, Garaleh M, Brindhadevi K, Chi NT, Sharma A, Pugazhendhi A. Bio-functionalized copper oxide/chitosan nanocomposite using *Sida cordifolia* and their efficient properties of antibacterial, anticancer activity against on breast and lung cancer cell lines. *Environmental Research*. 2023 Feb 1;218:114986.
25. Dhir S, Dutt R, Singh RP, Chauhan M, Virmani T, Kumar G, Alhalmi A, Aleissa MS, Rudayni HA, Al-Zahrani M. *Amomum subulatum* fruit extract mediated green synthesis of silver and copper oxide nanoparticles: synthesis, characterization, antibacterial and anticancer activities. *Processes*. 2023 Sep 9;11(9):2698.