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Biological and Industrial Applications of Metallo Nanoparticles Synthesized from the Leaf Extract of *Phyllanthus niruri*: A Review

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Abstract: *Phyllanthus niruri*, commonly known as "gale of the wind," is a member of the Phyllanthus genus within the *Phyllanthaceae* family. It holds significant promise for both biological and industrial applications. Researchers have successfully synthesized nanomaterials from the leaf extract of *Phyllanthus niruri* and used them to produce metal nanoparticles using various metal ions, including silver, zinc, and iron. This review provides an overview of studies on the green synthesis of metallo-nanoparticles from *Phyllanthus niruri*, including characterization techniques. It highlights the advantages of the green synthetic approach compared to other methods and discusses factors influencing particle size, accuracy, and precision. Additionally, the review explores various applications of the synthesized nanomaterials, including their potential for photocatalytic, antiviral, antifungal, and antimicrobial activities.

Keywords: *Phyllanthus niruri*; green synthesis; metallo nanoparticle.

1. Introduction

Nanotechnology encompasses the science and technology involved in producing, characterizing, and utilizing particles within the size range of 1 to 100 nanometers [1,2]. The unique mechanical, optical, electronic, and magnetic properties of nanomaterials (NMs) arise from their small particle size. This technology enables the development of new materials with tailored properties suitable for advanced devices across various applications [3-6]. At the nanoscale, material size influences electron wave properties and atomic interactions, primarily because of the increased ratio of surface atoms, which are highly reactive and energetically favorable [7-10]. Consequently, nanomaterials exhibit a high surface-to-volume ratio, leading to significant enhancements in their chemical properties. Researchers are drawn to nanotechnology for its cost-effectiveness, scalability for bulk production with lower energy requirements, and the ability to precisely control material properties by manipulating particle size, structure, and preparation conditions [11-14].

Nanotechnology has emerged as a highly competitive field of scientific inquiry, attracting researchers and scientists due to its vast array of applications across many aspects of human life [15]. It finds utility across diverse sectors, including agriculture, optics, the petroleum industry, biomedicine, the food industry, and sensor technology, with pharmaceuticals among its most prominent domains [16,17]. Nanoparticles (NPs) have emerged as potent tools, particularly in pharmaceuticals, enabling advancements in nanomedicine. This technology opens up avenues for exploring biological processes in unprecedented ways [18-20].

Various methods can be employed to formulate nanoparticles (NPs), including physical, chemical, and biological synthesis techniques. However, the physical and chemical approaches are complex and expensive, and involve the use of toxic chemicals, as well as high energy, temperatures, and pressures [21-24]. Additionally, they generate harmful waste products, posing significant environmental risks [25]. Consequently, there is a growing demand for non-toxic, environmentally friendly, and cost-effective methods for producing metallic NPs to facilitate their potential pharmaceutical and industrial applications [26-28].

Biological synthesis methods are gaining attention for their lower cost, non-toxicity, and environmentally sustainable procedures [29]. Among these methods, the use of plant extracts, known as the green synthesis approach, offers advantages over microbial-based systems by eliminating the need for maintaining cell cultures and avoiding lengthy incubation times or high temperatures [30].

In recent times, green synthesis methods have been widely adopted by scientists due to their efficiency, cost-effectiveness, speed, and eco-friendly nature. Phyto nanofabrication is rapid owing to the presence of various chemical compounds such as amines, amides, alkaloids, flavonoids, phenols, terpenoids, proteins, and pigments in plant extracts [31]. These phytochemicals play a crucial role in stabilizing and reducing metal ions during the green synthesis of metallo-nanoparticles (MNPs) [32]. The rapid reduction of metal ions occurs because plant constituents, via their functional groups, donate electrons to them [33,34]. This review aims to consolidate research findings on the synthesis of MNPs from *Phyllanthus niruri* plant extract and highlight their potential across various fields.

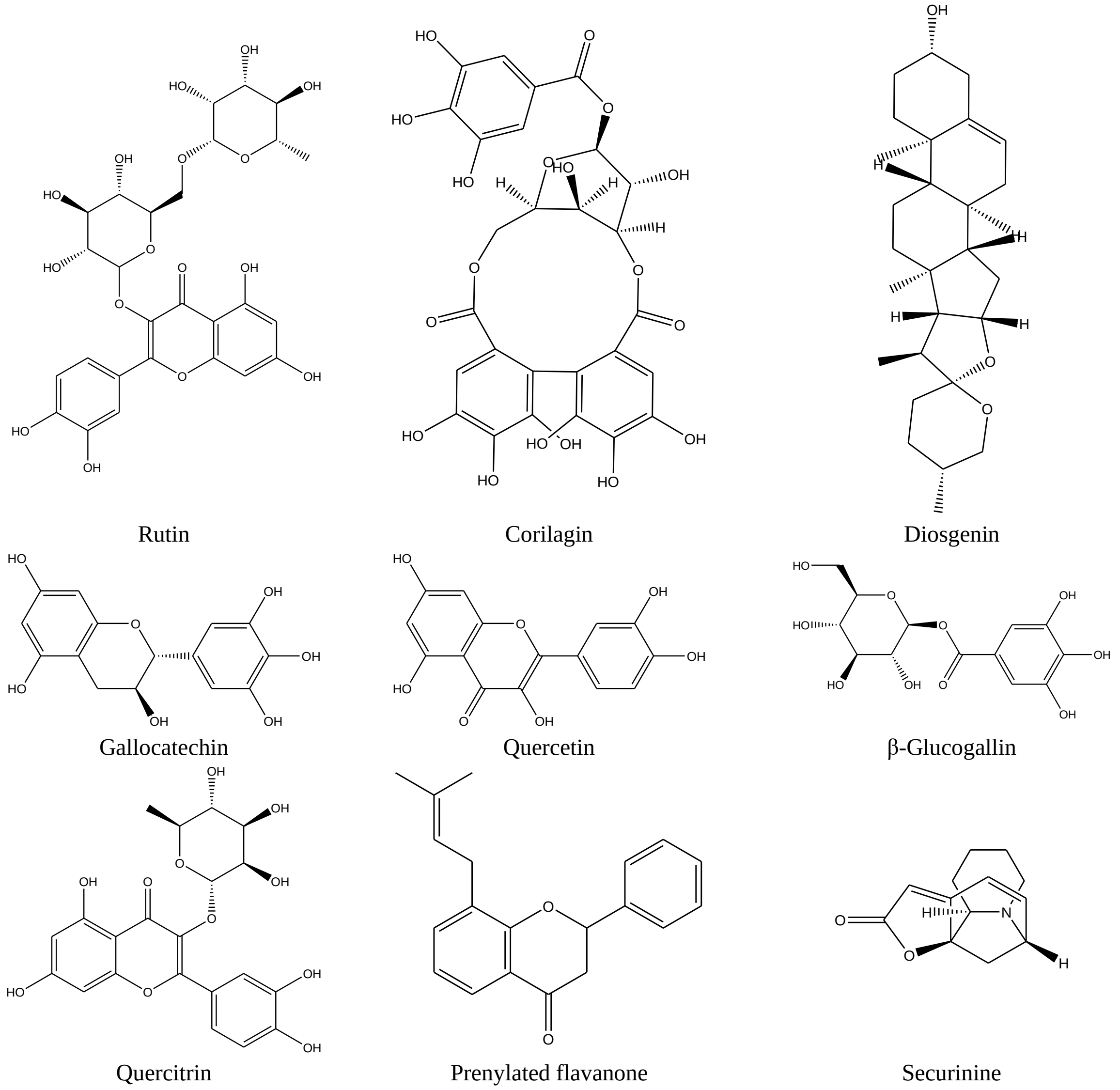
2. Therapeutic Uses of *Phyllanthus niruri*

The Phyllanthus genus, part of the *Phyllanthaceae* family, includes around 1301 species of flowering plants. These species are found across tropical and subtropical regions such as Africa, America, Asia, and Australia [35,36]. Among these, *Phyllanthus niruri* is particularly significant, especially in Indian Ayurvedic medicine, where it is highly valued for its therapeutic properties.

Phyllanthus niruri has been extensively studied, with numerous clinical studies highlighting its wide range of medicinal benefits. One of its notable therapeutic effects is its antifungal activity, which is effective against conditions like ringworm, ulcers, scabies, and jaundice. This makes it a valuable plant in traditional medicine for treating various skin infections and other related conditions [37].

The medicinal properties of *Phyllanthus niruri* are largely due to its rich phytochemical composition. The plant contains various bioactive compounds with antimicrobial and antiprotozoal properties [38]. Some key phytochemicals found in *Phyllanthus niruri* include rutin, gallocatechin, prenylated flavanone glycosides, quercetin, quercitrin, *p*-Cymene, corilagin, diosgenin, securinine, and β-glucogallin (Figure 1). Each of these compounds contributes uniquely to the overall therapeutic profile of the plant.

Figure 1. List of phytochemicals present in *Phyllanthus niruri*.



For example, rutin and quercetin are known for their antioxidant properties, which help reduce oxidative stress and inflammation [39]. Gallocatechin is a type of catechin that has strong antimicrobial properties, making it effective against a range of pathogens [40]. Prenylated flavanone glycosides have shown potential in various pharmacological activities, including anti-inflammatory and anticancer effects [41]. P-Cymene is recognized for its antiseptic properties [42], while corilagin has antiviral and antibacterial activities [43]. Diosgenin plays a role in hormone regulation and has anti-inflammatory effects [44], and securinine is noted for its neurostimulant and antimicrobial properties [45]. Lastly, *β*-glucogallin has demonstrated promise in protecting against liver damage and possesses antioxidant properties [46].

Phyllanthus niruri is highly regarded for its ability to treat a wide variety of ailments. It is traditionally used to treat conditions such as dysentery, influenza, vaginitis, tumors, diabetes, as a diuretic, and for jaundice, kidney stones, and dyspepsia. Additionally, it has demonstrated antihepatotoxic and anti-hepatitis B properties, making it beneficial for liver health [47,48]. Its antihyperglycemic effects are particularly important for managing diabetes, and its antiviral and antibacterial properties further enhance its therapeutic versatility.

The diverse phytochemical composition and extensive medicinal potential of *Phyllanthus niruri* have attracted significant interest from researchers. One area of research that has garnered attention is the synthesis of metallic nanoparticles (MNPs) using extracts from *Phyllanthus niruri*. The unique properties of these phytochemicals make them suitable for reducing metal ions, leading to the formation of nanoparticles with potential applications in medicine, environmental science, and industry. These nanoparticles have been explored for their biological activities, including antimicrobial, anticancer, and drug-delivery applications, highlighting the vast commercial and therapeutic potential of *Phyllanthus niruri*.

3. General Synthesis of MNPs from *Phyllanthus niruri*

Fresh leaves of *Phyllanthus niruri* were collected from available sites and thoroughly washed with tap water to remove surface dust particles. Subsequently, they were rinsed with distilled water. After cleaning, the leaves were air-dried for 10-15 days at room temperature before being finely powdered using a blender. Approximately 10 grams of the dried powder were then boiled with an appropriate volume (100-250 ml) of distilled water and stirred at an elevated temperature. The resulting extract was filtered using Whatman filter sheets to obtain a clear solution. This solution extract was used to synthesize various metallic nanoparticles (MNPs), in which plant phytochemicals served as reducing agents for the metals. The reduction of metals was visually observed through a change in color, initially measured using a UV-Visible spectrophotometer.

4. Physicochemical Factors Affecting Green Synthesis of MNPs

The phytochemicals in plant extracts significantly enhance dispersion and reduce agglomeration [49]. These compounds are known to play a pivotal role in imparting unique properties to synthesized materials. Along with phytochemicals, several other factors are also associated with nanoparticle synthesis. These factors have a direct bearing on the characterization and applications of nanoparticles synthesized using green methods. Table 1 outlines some of the physical factors influencing nanoparticle synthesis.

Table 1. The influence of physical factors on the synthesis of MNPs.

S. No.	Factor	Mode of influence	Ref.
1	Adopted method	MNPs can be synthesized via physical, chemical, or biological methods. Biological methods are preferred because they are non-toxic and environmentally friendly.	[50,51]
2	Temperature	The choice of synthesis method determines the required temperature. Physical methods need temperatures above 350°C, chemical methods below 350°C, and green synthesis methods below 100°C to avoid phytoconstituent decomposition.	[52,53]
3	Pressure	The reduction rate of metal ions is influenced by the pressure of the medium. Green synthesis methods are faster under ambient pressure, and the applied pressure affects the shape and size of MNPs.	[54,55]
4	Concentration of metal ion	A low concentration of metal ions (around 0.1 mmol/L) is typically sufficient. The agitation time of the reaction mixture also influences the synthesis process.	[56]
5	pH	The pH of a solution affects the morphology, size, and texture of MNPs. Lower pH (≤ 3) stabilizes MNPs by hindering electrostatic integration, while neutral pH deprotonates aggregated molecules.	[57,58]

S. No.	Factor	Mode of influence	Ref.
7	Particle size	Smaller MNPs have a lower melting point. Particle size is critical in determining the properties of MNPs.	[59,60]
8	Stirring time	The duration of stirring affects the interaction between metal ions and phytochemicals. It is influenced by pH and temperature, reducing the power of the extract, radiation wavelength, enzyme presence, and plant extract metabolites.	[61]
9	Environment	MNPs can transform into core-shell structures by absorbing or reacting with surrounding materials, through oxidation or corrosion, thereby altering their physical structure and chemical composition.	[62,63]

To optimize the green synthesis of MNPs using *Phyllanthus niruri* for industrial-scale production, several challenges must be addressed. Standardizing the phytochemical composition of plant extracts is crucial, as variations in bioactive compounds can affect nanoparticle synthesis. Additionally, scaling up the process requires optimizing key reaction parameters, such as pH, temperature, and extract concentration, to ensure uniform nanoparticle size and morphology. Achieving cost-efficient and high-yield production while controlling waste generation and managing biomass byproducts is essential for environmental sustainability. Purification techniques must be refined to remove contaminants, and stabilizing nanoparticles for long-term storage poses another challenge. Moreover, ensuring compliance with regulatory standards and assessing toxicity and environmental impact are critical to safety. Integrating green synthesis into existing industrial processes, coupled with automation and continuous-flow technology, can enhance scalability. Finally, economic feasibility and market demand need to be considered to ensure that the green synthesis of MNPs is both commercially viable and competitive with conventional methods.

5. Characterization of MNPs Synthesized from *Phyllanthus niruri*

Various characterization techniques have been employed to characterize MNPs synthesized from the *Phyllanthus niruri* plant at both the molecular and material levels. These analytical methods include UV–Visible spectroscopy (UV–Vis), Fourier-transform infrared (FTIR) spectroscopy, field-emission transmission electron microscopy (FE-TEM), selected area electron diffraction (SAED), scanning electron microscopy (SEM), dynamic light scattering (DLS), X-ray diffraction (XRD), and energy dispersive X-ray spectroscopy (EDX) (Table 2).

Table 2. The characterization techniques and their applications in studying MNPs.

Technique used	Purpose	Reference
UV–Vis	Used to identify, characterize, and study the optical properties of MNPs, which are influenced by size, shape, concentration, agglomeration, and refractive index near the surface.	[64]
FTIR	Determines the structure and bonding characteristics of MNPs, verifying surface chemical composition or functionalization, and confirming metal-oxygen bonds by comparing spectra to free ligands.	[65]
FE-TEM	Provides high-resolution images of the surface morphology of MNPs, revealing crystal orientation, aggregation state, electron structure, lattice spacing, and phase shifts, as well as shape and diameter.	[66]
SAED	Utilizes microdiffraction patterns in TEM to determine lattice symmetry and interplanar distances, confirming phase identification based on literature and chemical analyses.	[67]
SEM	Uses electron beams to generate signals from MNPs, providing insights into surface topography, composition, and electrical conductivity. Nonconductive samples require a conductive coating.	[68]

Technique used	Purpose	Reference
DLS	Analyzes the size distribution of particles in a solution through their diffusive motion, with larger particles scattering more light. Also measures the binding affinity between the metal and the starting material.	[69]
XRD	Analyzes phase and crystallinity of nanoparticles using the Scherrer equation by measuring X-ray scattering angles and intensities. Determines crystallinity percentage and unit cell dimensions from peak sharpness.	[70]
EDX	Analyzes the chemical composition of nanomaterials based on X-rays produced by electron transitions following inner shell electron ejection, typically used with SEM or TEM.	[71]

Investigating the interactions between plant phytochemicals and metal ions during the green synthesis of MNPs is essential for optimizing the process and ensuring nanoparticle quality. Phytochemicals, which act as natural reducing and stabilizing agents, play a critical role in determining the size, shape, and stability of the MNPs. A clear understanding of these interactions enables better control over nanoparticle formation, thereby influencing their functional properties across applications such as drug delivery and environmental remediation. Moreover, different phytochemicals interact with metal ions in distinct ways, affecting the efficiency of nanoparticle synthesis and overall yield. By elucidating these mechanisms, researchers can standardize and scale up the process for industrial production, ensuring consistent nanoparticle characteristics while maintaining the eco-friendly, sustainable nature of the green synthesis approach.

6. Applications of MNPs Synthesized from *Phyllanthus niruri*

MNPs synthesized from Phyllanthus niruri plant extract have diverse applications across multiple fields, including healthcare, environmental science, catalysis, and nanotechnology. Table 3 outlines some of the reported applications.

Table 3. Applications of MNPs synthesized from *Phyllanthus niruri***.**

Sl No	Metal used	The characterization technique used	Particle size (nm)	Shape	Application	Ref.
1	Ag	UV–Vis, SEM,EDX, FTIR, TEM,XRD	~ 20	Spherical	Antibacterial activity against *P. aeruginosa*, *Bacillus cereus*, *E. coli*, and *S. aureus*	[72]
2	Ag	UV–Vis, FE-TEM, SAED, XRD, DLS, FT-IR, LC-MS	N. S	Spherical, triangular, and polygonal	Antibacterial activity against *Eggerthella lenta* and *Escherichia coli*	[73]
3	Ag	UV–Vis, TEM, XRD, DLS	N. S	N.S	Antibacterial activity against *X. axonopodis* pv.	[74]
4	-	XRD FT-IR FESEM with EDX	N.S	Spherical	Antioxident	[75]
5	Zn	UV–Vis, DLS	125.4	Spherical	Antibacterial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Aspergillus niger*	[76]
6	Ag	XRD, FT-IR SEM	N S		Antibacterial activity and anticorrosive against *Pseudomonas aeruginosa* and *Escherichia coli*	[77]
7	Ti	XRD, SEM	20	Spherical	Adsorbent for dye adsorption	[78]
8	Fe	UV–Vis, SEM, TEM	42 ± 08	Spherical	Antibacterial activity against *E. coli*	[79]

Sl No	Metal used	The characterization technique used	Particle size (nm)	Shape	Application	Ref.
9	Ag	N. S	N. S	chikungunya	Antiviral activity against chikungunya virus- CHIKV	[80]
10	Ag	N S	90	Spherical	Antifungal, antibacterial, and Antioxidant activity against Lactobacillus, *S. mutans*, and *C. albicans* DPPH radical-scavenging activity	[81]
11	Ag	N. S	N S	Spherical	Anticancer activity against oral pathogens such as *Staphylococcus aureus*, *Streptococcus mutans*, *Pseudomonas* species, and *Enterococcus* species.	[82]
12	-	UV–Vis, SEM, XRD	150 - 250	Spherical	Anticancer activity against prostate cancer	[83]
13	Ti	FTIR, UV Vis XRD FESEM with EDX	8 -11	Spherical	Anticancer activity against oral cancer cell lines	[84]
14	Ti	FTIR, UV Vis XRD FESEM with EDX	23	Spherical and semi-spherical	Catalyst: photocatalytic dye degradation water remediation activities	[85]
15	Ag	FTIR, UV Vis XRD SEM	63.45	Spherical	Against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas spp*, *Proteus vulgaris*, and *Salmonella typhi*	[86]
16	Fe	IR, UV-Vis, TEM, SEM, XRD	60-500	Square	Antimicrobial against *P. aeroginosa* and *E. coli*.	[87]
17	Ti	FT-IR, UV-Vis, TEM, DRS	30-50	Spherical	Catalyst: degradation of organic molecules	[88]

* N.S-Not Specified

6.1. Clinical applications.

In contrast to chemical methods, green synthesis offers an eco-friendly approach to producing MNPs with diverse applications. Phytochemicals in the plant extract act as natural reducing agents, resulting in nanomaterials with improved biomedical compatibility [38]. MNPs synthesized from *Phyllanthus niruri* extract have demonstrated enhanced biological applications due to their smaller size and uniformity. Studies indicate that nanomaterials derived from *Phyllanthus niruri* exhibit significant clinical benefits, including antioxidant, antiviral, antifungal, and antibacterial properties. Their nanoscale size allows them to easily penetrate the intestinal wall and cells, effectively inhibiting pathogen growth. Silver is the metal of choice for synthesizing NPs, as they kill microbes more effectively. Phytochemicals reduce the toxicity of NMs during their production. The bio-reduction compounds of lignin, saponins, and flavonoids provide the chemical-free zero-valent atom and facilitate stabilization. In addition, these bio compounds increase microbial resistance and are highly effective in treating liver-related diseases [81,82,86]. Titanium NPs of Phyllanthus niruri exhibited great anticancer activity at various concentrations. Flow cytometry analysis confirmed the presence of p53 protein in the synthesized MNPs, which is responsible for the anticancer nature of these MNPs. It is also reported that the MNPs induced significant cytotoxicity in the cancer cell line of choice [83,84].

6.2. Industrial applications.

The light absorption capability of MNPs directly affects their photocatalytic activity. Nanoparticles can efficiently degrade organic molecules through photocatalysis. Green-synthesized nanoparticles are widely used for this purpose due to their wide bandgap, smaller crystallite size, large surface area, and electron-hole pair restriction properties. Studies have shown that TiO_2 nanoparticles derived from *Phyllanthus niruri* exhibit enhanced degradation efficiency of organic molecules [85-88]. Light irradiation increases the degradation rate at the reactive sites of the catalyst, and the presence of OH radicals facilitates the oxidation of dye molecules.

7. Scope for Future Study

The scope for future research on the use of *Phyllanthus niruri* in green synthesis methods is vast and promising. Firstly, standardized protocols are needed to ensure consistency and reproducibility in the synthesis of MNPs using *Phyllanthus niruri* extract. This would involve systematic studies to understand how various factors, such as extraction methods, plant growth conditions, and phytochemical composition, influence the characteristics of the synthesized MNPs. Further research is needed to optimize the roles of phytochemicals in controlling nanoparticle size, shape, and yield, and to address scalability, stability, and environmental impact in green synthesis of MNPs. Enhancing efficiency also requires studying the kinetics, cost-effective sourcing, and regulatory standards for industrial applications. Moreover, comprehensive studies evaluating the long-term environmental impact and biodegradability of green-synthesized MNPs are essential to ensure their sustainability and safety for widespread application. Overall, future research in this area holds significant potential to advance green synthesis methodologies and facilitate their broader acceptance and integration into MNP production.

8. Conclusions

This review provides in-depth information about the eco-friendly approach towards the synthesis of MNPs. Specific authors focused on summarizing the utilization of *Phyllanthus niruri* plant extract for the synthesis of NPs. Based on the literature survey, it was observed that various metal ions, such as Ag, Ti, Zn, and Ni, were used to synthesize MNPs from *Phyllanthus niruri* plant extract. In addition, this review highlights the advantages of the green synthesis method over conventional techniques such as physical and chemical methods. The size and shape of NPs depend primarily on various experimental parameters, such as time, concentration, pH, temperature, and pressure. In this review, the authors tried to describe the effect of all these factors on synthesis. Various characterization techniques, including UV-Vis, FTIR, XRD, SEM, TEM, and EDX, have been used to determine the shape, size, and morphology of the new NPs. The principles underlying these techniques were tabulated. In addition, this review article also provides the collective contributions of various researchers to the study of numerous applications of MNPs. Based on the above literature, it is evident that the *Phyllanthus niruri* plant extract has shown very promising benefits in both biomedical and industrial fields. Therefore, this review article will provide an opportunity to synthesize MNPs from the extract of Phyllanthus niruri and to identify their advantages and potential applications.

Author Contributions

Conceptualization, S.S. and K.D.; validation, K.D. and S.S.; writing—original draft preparation, S.S.; writing—review and editing, S.S.; supervision, K.D. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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