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Review

Moringa oleifera Seed Cake: A Review on the Current Status of Green Nanoparticle Synthesis

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Abstract: Growing demands for sustainable and ecological nanoparticle synthesis methods have incentivized the scientific community to develop new approaches to counteract these challenges. Green synthesis resorts to biocomponents obtained from plants, bacteria, fungi, and other organisms to synthesize nanostructures, with beneficial gains in the economic and ecological cost associated with the process, simplicity of the process, and resource efficiency. *Moringa oleifera*, a native plant originally from India with immense nutritive value, has long been used by researchers in the biosynthesis of nanoparticles. Leaves, flowers, bark, and seeds are among the "miracle tree" parts that can be used in nanoparticle green synthesis. *Moringa oleifera* seed cake, a by-product obtained from defatted seeds, is often overlooked due to its apparent low commercial value. The main objective of this review is to highlight the recent findings reported in the literature on nanoparticles/nanocomposites synthesized with seed cake biocompounds acting as reducing/capping agents. Furthermore, we analyzed the methods currently employed for the extraction of bioactive compounds. *Moringa oleifera* seed for industrial applications was also addressed.

Keywords: *Moringa oleifera* seed cake; extraction methods; green chemistry; nanoparticles synthesis

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1. Introduction

Moringa (M.) oleifera is a tree widely cultivated and studied all over the world, with numerous applications in areas such as nutrition, medicine, agriculture, or cosmetics [1–3]. First described in 1785, it belongs to the *Moringaceae* family, with 14 known species. Native to the Indian subcontinent, this plant thrives in tropical or sub-tropical environments, growing swiftly and having the capacity to endure harsh conditions, such as droughts or floods [4]. It also contributes to soil fertility, and minimal water is required for its cultivation. Combining these factors with its immense nutritional value, one can understand the potential of *M. oleifera*, or "miracle tree", as it is also known, especially in impoverished countries where its medicinal and nutritive properties have been used for centuries [5]. Almost all parts of the plant are edible (for both humans and animals) and possess therapeutic effects (Figure 1) [6]. This is mainly due to its vitamins, minerals, fibers, and antioxidative and antibacterial phytochemical content [7–9].

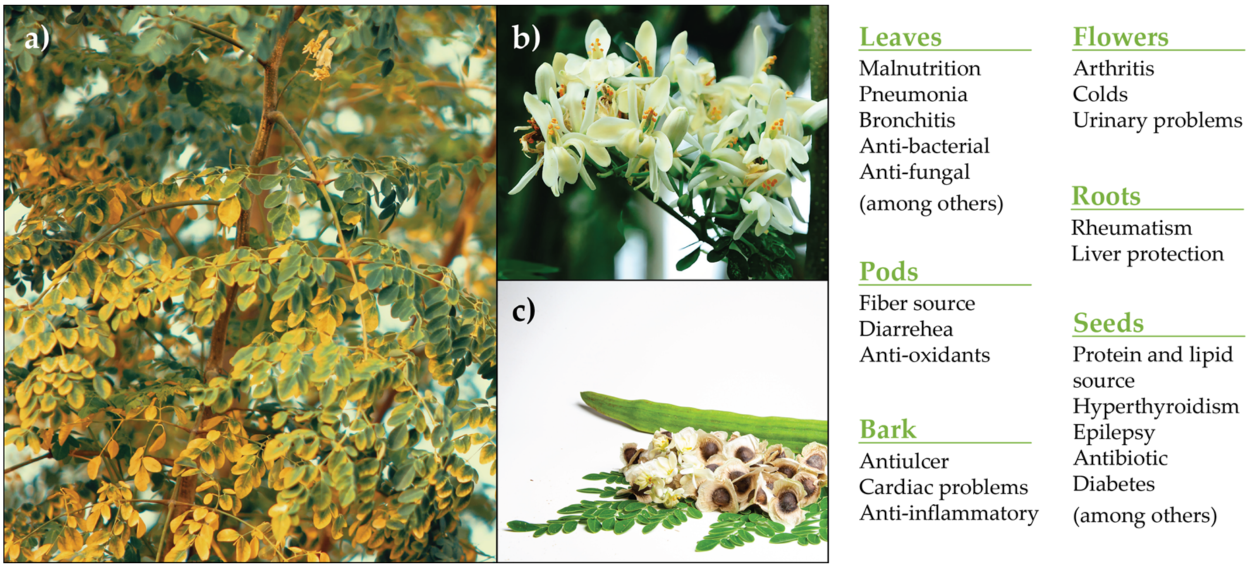

Figure 1. Nutritional and therapeutic properties of *M. oleifera*. (**a**) *M. oleifera*, also known as "miracle tree" or "drumstick tree"; (**b**) the flowers are normally used in teas and tonics, and have a subtly sweet flavor; (**c**) pods and seeds. Based on [3,9–12].

The leaves are the most nutritious part of the plant and are commonly used to treat malnutrition, hypertension, and bronchitis, among other health conditions [10,13,14]. Apart from the seeds, leaves have the highest protein content of the plant and are also rich in minerals such as iron, potassium, zinc, and calcium [15]. Consumption of flowers can alleviate the symptoms of common colds or arthritis [11]. The bark is known for its antiulcer and cardiac stimulant properties [11,16]. Immature pods, also known as "drumsticks", possess a high content of protein and fiber and are utilized to treat diarrhea or vitamin C deficiency [17,18]. Stems are appropriate for animal feeding, whereas roots help with rheumatism [19,20]. The seeds, the focus of this review, are a great protein and lipid source and can act as antimicrobial and/or anti-inflammatory agents in the treatment of diseases such as hyperthyroidism, diabetes, and fatty livers, among others [15,21–23]. Phenolic acids and flavonoids are also present in high quantities, contributing to their anti-oxidative properties. The oil extracted from the seeds corresponds to about 40% of its weight, making it highly valuable, not only as a viable substitute for olive oil but also for its advantageous effects on aging, cholesterol, and cardiovascular diseases [24,25]. It is a natural source of behenic acid, from which it gets its commercial name, "Ben oil" or "Behen oil". The residue of the seeds after defatting is a by-product named seed cake or seed meal, with proteins constituting approximately 50% (on average) of its weight [3,22,25]. Singh et al. [26] reported a staggering 85% protein extraction at optimal conditions. This allows the cake to be used in animal feeding as a valuable source of plant-based protein. A summary of *M. oleifera* nutritional composition can be found in Table 1.

Table 1. Nutritional composition (in %) of different *M. oleifera* tree parts [3,7,9,22,25,27].

Nutrient	Leaves	Flowers	Bark	Pods	Stem	Seeds	Cake	Roots
Protein	26.1	4.9	2.5	1.4	18.7	33.7	50.8	16.9
Lipids/Fats	4.9	0.2	0.6	0.7	12.2	40.8	3.1	10.8
Carbohydrate	38.7	–	90	89	20.4	9.6	18.2	14.9
Fiber	9.1	1.0	2.2	3.3	41.6	4.5	13.0	45.4
Others	21.2	–	4.7	5.6	7.1	11.4	14.9	12.0

Over the past few years, an increasing number of studies have shifted their attention from *M. oleifera* leaves to its seeds. This is mainly due to the "Behen oil" obtained after the defatting process, but also to the seed cake, a defatting by-product initially thought to have no commercial value but that now has several industrial purposes, such as water purification, livestock feeding, insecticides, and fertilizers [28–31]. These applications are especially valuable to rural economies in developing countries. To obtain the cake, or meal, the seeds (with an average size of 1 cm) are removed from the mature pods, deshelled, and dried; then the kernels are crushed and defatted to obtain the oil; finally, the remaining powder is dried and stored (Figure 2) [32]. Despite being a lesser-known component, commonly minimized when compared to its oil counterpart, the seed cake possesses a rich macro- and micro-nutritive composition, with all the essential minerals present, namely calcium, sodium, or potassium, as well as some non-essential ones such as iron and zinc [2,33]. Amino acids like leucine, phenylalanine, and arginine are also present in large amounts; likewise, the seed cake retains high levels of vitamins A, C, and E. These properties can vary based on the seed quality and processing conditions. In addition to anti-inflammatory and antimicrobial attributes, some studies suggest that the press cake also has anticancer properties, although further research is needed to understand and confirm the mechanisms involved [34,35].

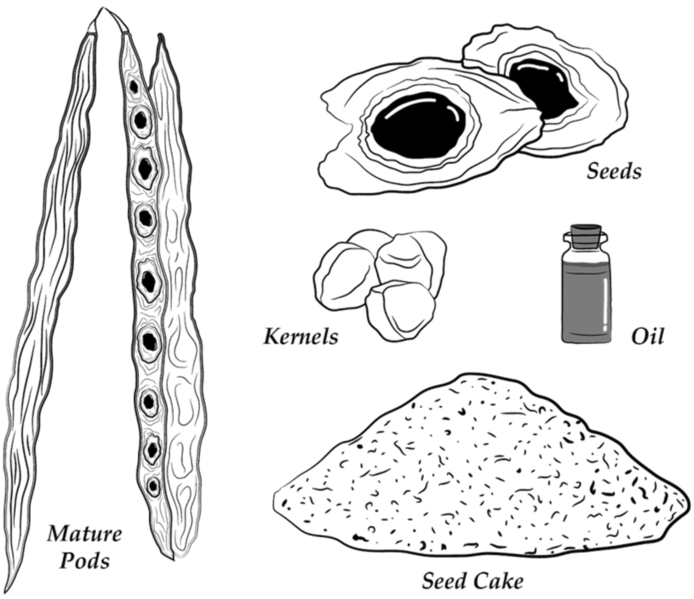

Figure 2. *M. oleifera* seeds anatomical fractions. Seed cake, a by-product of Behen oil extraction, can be obtained by various extraction methods (see Section 2).

The isolation and characterization of specific proteins from the cake were first reported in 1995, by Gassenschmidt et al. [36]. At the time, three flocculating proteins were described and named MO1, MO2, and MO3, although the corresponding family of proteins was not identified at the time. Pereira et al. purified and characterized a chitin-binding protein from the seeds in 2011, named Mo-cBP4 [37]. With a molecular mass of 11.78 kDa, this glycoprotein showed strong antidermatophytic activity against *T. mentagrophytes*, as studied by Lopes et al. [38]. A year later, in 2012, J.M. Gifoni characterized a highly thermostable and antifungal protein named Mo-CBP3 [39]. Composed of two chains linked by disulfide bonds, the protein has a molecular mass of 14 kDa. Another similar protein was studied by J.X.S. Neto in 2017, exhibiting powerful anticandidal activity [40]. Mo-CBP2 constituted 0.2% of the total seed protein, with as high as two times the carbohydrate content of Mo-CBP3 and Mo-CBP4. All these proteins belong to the 2S albumin family, one of the three major groups of seed storage proteins, together with prolamins and globulins [41]. 2S albumin proteins are cationic, have secondary α-helix structures, and are essential to the plant's seeds. We highlight the extended review on the extraction, preparation, and applications of *M. oleifera* seed proteins made by Kumar et al. [42].

The biological and chemical constituents of *M. oleifera* parts vary considerably according to the region and soil where it grows, as well as the fertilizers/treatments applied [43,44]. In addition, extractions and purification methods greatly impact the type and quantity of bioactive compounds extracted from the plant, so choosing the proper method for your work is a crucial step [45]. Despite not being the main topic for this review, we will briefly mention some extraction techniques (particularly the ones regarding the seeds), their principles, vital factors, advantages, and drawbacks. Furthermore, current uses and applications of *M. oleifera* seeds will be presented, with an emphasis on those resorting to the green synthesis of nanoparticles (NPs) and/or nanocomposites. Finally, we intend to fill the current void of reviews comprising the latest works on nanoparticle synthesis with *M. oleifera* seed cake extracts as a reducing/capping agent.

2. Extraction and Purification Methods

Plants such as *M. oleifera* are natural sources of polysaccharides, proteins, and vitamins. Depending on the specific bioactive compound or application, a proper extraction method must be selected to achieve a high yield and quality of the isolated components [46]. Conventional techniques such as aqueous or ethanolic extraction have been employed for centuries now, with the past few decades seeing the development of modern methods such as microwave-assisted extraction or supercritical fluid extraction [47,48]. Figure 3 presents a summary of the techniques employed to isolate bioactive compounds from *M. oleifera*.

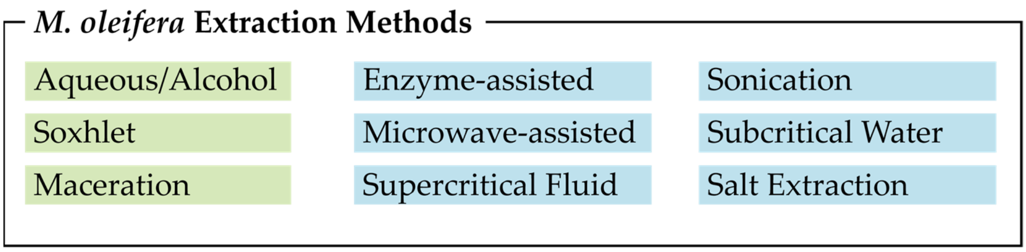

Figure 3. Different extraction methodologies applied to obtain bioactive compounds from *M. oleifera*. These techniques can be conventional (green) or non-conventional (blue). Factors such as temperature, extraction time, pH, solvents used, cost, and environmental concerns influence the quality and quantity of the biocomponents retrieved. Prior to the extraction, pre-processing is usually required.

Extraction methods can be divided into two main categories: conventional and non-conventional. Maceration, Soxhlet, and aqueous extractions fall into the first category, whereas the already mentioned microwave-assisted extraction and supercritical fluid extraction, sonication, and enzyme-assisted extractions are considered non-conventional [45,49]. Every approach has its own advantages and disadvantages and can even be combined for optimal results.

The most commonly used extraction methods are water and alcohol extraction, mainly due to their simplicity and reduced cost. Bichi et al. divided the *M. oleifera* seeds into two portions, with both aqueous and salt extractions being used [50]. Soxhlet extraction was employed on yet another portion, and it is the most common method used for oil removal, although microwave-assisted extraction has been more widely used, since it requires smaller volumes of solvent and is faster [51]. X. Gu et al. compared the biocompounds extracted from *M. oleifera* seeds using water, ethanol, petroleum ether, and two other solvents [52]. Simple aqueous extraction led to the highest saponin content, whereas the highest total flavonoid content was extracted with butanol. A seed ethanol extract obtained by maceration presented sedative and hypnotic effects, potentially useful for insomnia treatment [53]. The enzyme-assisted method is highly selective and environmentally friendly; however, there is an elevated cost and complexity associated with the process. Five different enzyme mixtures were used for simultaneous oil and protein extraction by Latif et al., with improved results when compared to hexane extraction [54]. A high-yield purified protein extract from *M. oleifera* seeds was obtained by ultrasound-assisted extraction, in which ultrasound power and pH were the two most influential experimental parameters impacting protein yield and quality [55]. Other factors such as temperature, time, and cost also impact the biocomponents extracted from *M. oleifera* and should be carefully optimized, depending on the specific requirements of the intended application [56].

3. Seed Cake Industrial Applications

As a sustainable and eco-friendly resource, *M. oleifera* seed cake is a valuable by-product with various industrial applications (Figure 4). One of its first and most common uses is in agriculture as an organic fertilizer, since the nutritional and chemical composition of the cake provides the soil with much-needed elements such as potassium and nitrogen, increasing soil fertility and enhancing crop yields [57]. The application of seed cake as a fertilizer is more advantageous (eco-friendly) than the synthetic ones that usually lead to soil degradation and environmental contamination. With proven insecticide and fungicide properties, *M. oleifera* seeds can also act as a pest control agent [58]. Plant and soil pathogens can be tackled with purified extracts from *M. oleifera* seeds, as demonstrated by Sousa et al. [59]. The development and growth of *Meloidogyne incognita*, a common soil-borne pathogen, are strongly affected by the activity of exuded seed proteins, leading to the nematode cell's death. Purified lectins from the cake showed insecticidal effects on larvae, eggs, and the oviposition of *Aedes aegypti*, also known as the yellow fever mosquito, associated with the spreading of diseases like dengue, zika, and yellow fever [60].

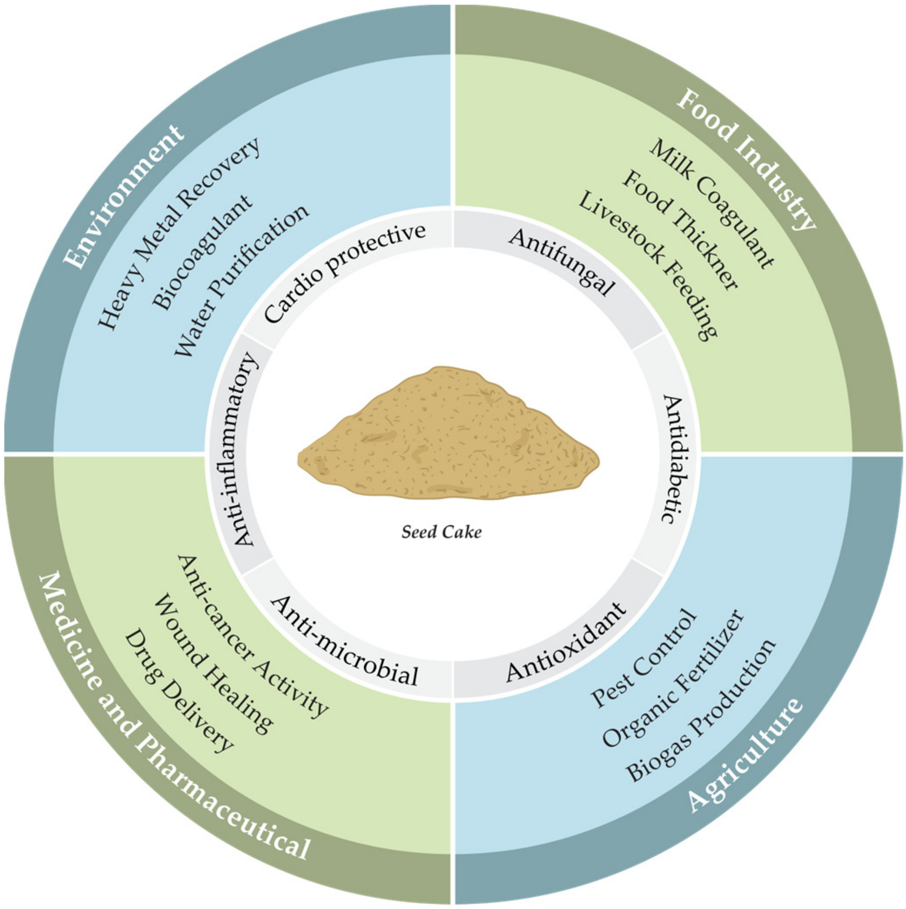

Figure 4. *M. oleifera* seed cake has beneficial properties and industrial applications in various areas. Current patents for industrial applications can be consulted in Table S1 (Supplementary Materials).

Physical parameters, namely humidity, ash content, and calorific value, define a component's biomass energy potential. The seed cake was proven to be a viable renewable fuel for biogas production by anaerobic digestion [61]. Another area of interest is medicine, where the antibacterial, anti-inflammatory, and antioxidant capacities of the seed cake can be highly valuable. Biocomponents isolated from extracts of *M. oleifera* seeds showed substantial inhibitory activity against carcinogens [62]. In another study, Maiyo et al. found that specific isolated compounds exhibited significant cytotoxicity against Caco-2 cell lines (originally derived from a colon carcinoma) [63]. Methanol extracts of *M. oleifera* seeds also showed in vitro cytotoxicity against different human cancer cell lines [64]. Polysaccharides isolated from the seeds were mixed with $AgNO_3$ to form a composite that promoted wound contraction and healing in animals [65]. Proteins present in the seeds were utilized to enhance the longevity and stability of amorphous magnesium-calcium phosphates, increasing the drug delivery capacity of these components. In the food industry, the high protein, fiber, and carbohydrate contents present in the cake allow the enrichment of food products, improving their nutritional value in both human and livestock nutrition. In two separate studies, Wang et al. isolated the protease aspartic-type endopeptidase to be potentially used as a milk coagulant [66,67]. Seed extracts can also be used as a food thickener agent [68].

Proteins from *M. oleifera* seeds, namely globulins and albumins, have high coagulation/flocculation potential and have been used for decades for water turbidity and impurity treatment, especially in developing countries [69,70]. The seed cake can also replace traditional coagulant and flocculating agents', such as aluminum sulfate and synthetic polymers, since the biocoagulants do not present many of the drawbacks associated with traditional chemical agents [71]. The coal beneficiation industry generates pollutant effluents with fine particles and impurities that can be removed with defatted seed cake [51]. Sera et al. studied the ability of seed cake to remove heavy metals, with promising results toward arsenic, cadmium, and lead [72]. Due to its antimicrobial effects, seed cake can also be used as a disinfectant for drinking water, although the number of studies in this area is still low. Mateus et al. combined iron oxide nanoparticles with proteins extracted from the seeds to produce a functionalized composite with significant removal efficiencies in waters with high turbidity [73]. Using *M. oleifera* seed cake in nanotechnology can definitely expand the range of applications of this multifunctional by-product, increasingly attracting the scientific community.

A comprehensive list of tested applications has been identified above. We should now focus on the most promising industrial applications with potential short-term impact, where patent applications are particularly significant. At the moment of writing this manuscript, several patent applications exploring the use of *M. oleifera* seed cake can be found. Seven of these are listed in Table S1 (Supplementary Materials), with five covering cosmetic, health, and nutrition applications. One patent explores the use of *M. oleifera* seed cake in a water treatment system for hydroponic cultivation, suggesting broader applications in sustainable agriculture. Quite interestingly, another patent explores the application of *M. oleifera* seed cake to the development of a cigarette filter stick. In this case, both special fragrance and good absorption properties were considered important for high-quality cigarette manufacture with reduced harm.

4. *M. oleifera* in Green Synthesis

It was in the 1980s that nanotechnology truly emerged as a revolutionary field with enormous potential in multiple scientific areas. Currently, the impact of nanotechnology is striking in distinct fields, such as electronics, materials, or medicine, with the development of devices like nanotransistors, carbon nanotubes, and nanomaterials for controlled drug delivery in our organisms [74–79]. Understandably, such progress raises concerns, mainly about the toxicity and environmental impact of nanoparticles [80]. In recent years, the paradigm for developing new materials has been shifting towards a greener approach, where sustainability, efficiency, and environmental cost play a major part. Eco-friendly nanoparticle synthesis methods resort to bioactive agents obtained from plants, microorganisms, bacteria, fungi, and even fruit and agricultural wastes [81–83]. The use of harmful solvents and substances is minimized or eliminated entirely, the processes are frequently easily scalable, and by-products are either degraded to inoffensive substances or reutilized for further use. In consequence, the biosynthesis of nanostructures has drawn increasing interest over the last two decades, at the expense of conventional physical and chemical methods. Additional information regarding the advantages and drawbacks of green chemistry can be found in Table S2 (Supplementary Materials). Although the exact mechanism of nanoparticle biosynthesis is not yet fully known, it is believed that plant-based extracts provide biomolecules that assist in the reduction of metal ions, as well as in the consequent steps of nucleation, growth, and stabilization of nanoparticles (Figure 5) [84,85]. The size and shape of the particles are dependent on the reaction conditions, namely the type of plant used or the metal salt concentration. Further insight on the mechanisms and the different organisms used in the biosynthesis of NPs can be found in the review by H.R. El-Seedi et al. [82].

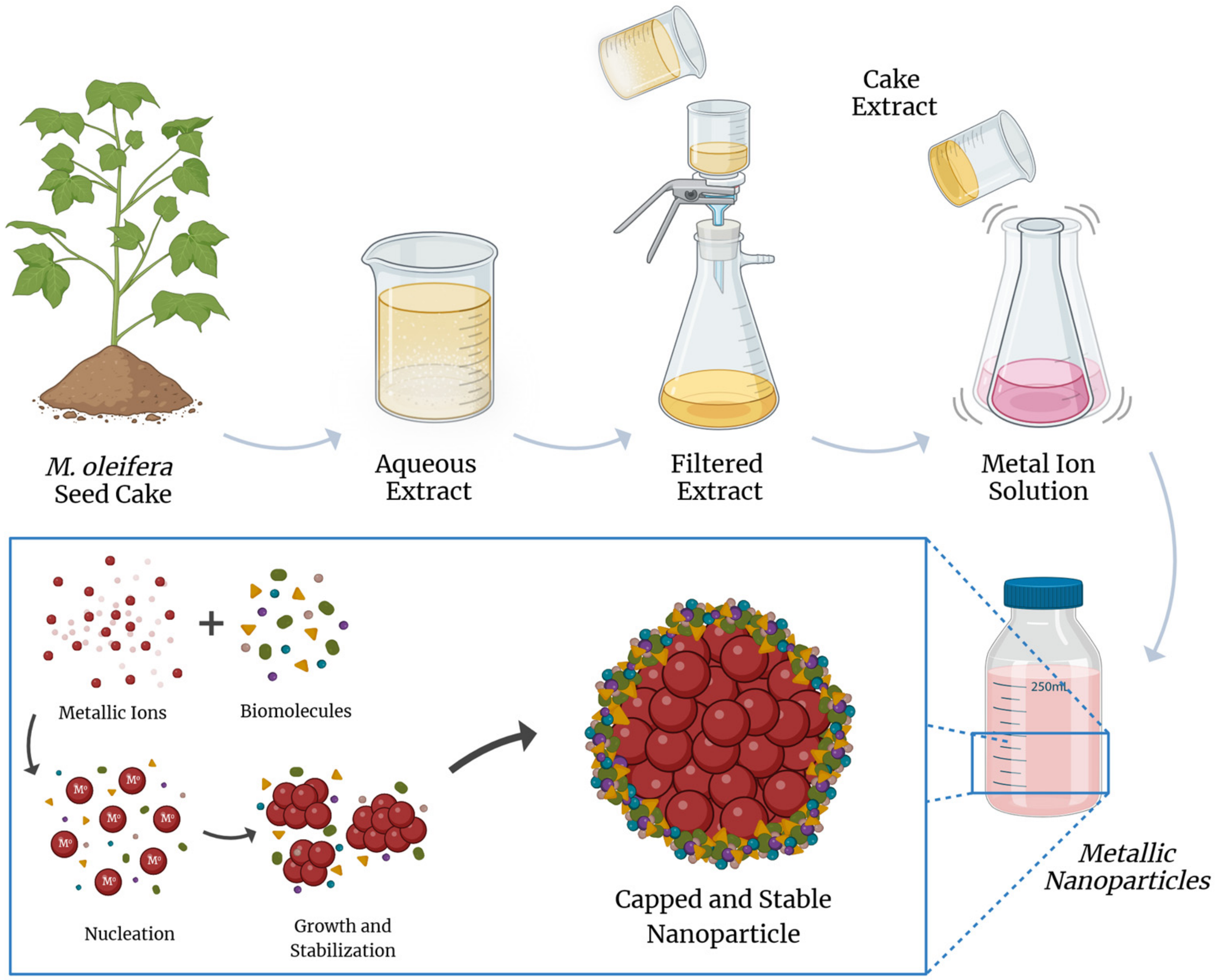

Figure 5. A sustainable route to NP synthesis using *M. oleifera* seed cake biocomponents as the reducing and stabilizing agents. Components such as alkaloids, flavonoids, phenolic acids, and proteins mediate the reaction and prevent the subsequent agglomeration and aggregation of nanoparticles. Created with BioRender.com.

Nanoparticle Synthesis Using M. oleifera Extracts

Among the benefits of NPs obtained through green synthesis methods is their biocompatibility and increased bioavailability, which allow their use in the biomedical and pharmaceutical sectors. *M. oleifera* has been widely utilized to synthesize metallic and non-metallic NPs for some years now, and no part has raised such interest as the leaves. Silver nanoparticles (AgNPs) obtained using *M. oleifera* leaf extracts have shown strong antimicrobial activity against a wide range of pathogenic microorganisms, including *Staphylococcus aureus*, *Candida glabrata*, and *Klebsiella pneumoniae* [86]. Magnesium oxide (MgO) NPs synthesized from leaf aqueous extract also exhibited antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* [87]. Tarmizi et al. studied the antioxidant and antidiabetic properties of selenium NPs, whereas zinc oxide (ZnO) NPs were also successfully synthesized from leaves and proved to have anti-acne and anti-bacterial properties [88,89]. Despite their limited industrial applications, *M. oleifera* flowers (MOF) have recently been employed as reducing agents in the synthesis of nanoparticles, as per Bindhu et al. [90]. An aqueous extract of MOF was mixed with a 1 mM solution of $AgNO_3$ to produce spheric NPs with an average diameter of 8 nm. Ngom et al. compared the structural properties of nickel oxide (NiO) NPs obtained from three separate aqueous extracts of *M. oleifera*: flowers, leaves, and seeds [91]. Surprisingly, the NPs synthesized via flower extract presented the smallest size (with a crystallite diameter of 18 nm), with a band gap of 3.24 V obtained for all NPs. Bark-mediated synthesis of metallic nanoparticles includes silver and MgO NPs, with applications in biomedicine and the biofuel industry [92,93]. Silver and ZnO nanoparticles synthesized with *M. oleifera* gum presented antibacterial potential against Gram-positive, Gram-negative, and MDR (multidrug-resistant) bacterial strains [94]. Vijayakumar et al. reported the synthesis of magnesium oxide (MgO) NPs using an aqueous gum extract (on a 9:1 ratio), producing polydisperse nanoparticles with diameters ranging from 100 to 200 nm [95].

It should be noted that aqueous solutions, either pure water or water–ethanol mixtures, are commonly used to extract biocomponents from seed cake. The resulting extract typically contains a complex mixture of biological compounds, including plant albumins (the most abundant proteins), lesser amounts of globulins (whose solubility depends on the solvent's pH), flavonoids, and phenolic acids, among other small compounds [41]. The overall success of the synthesis process for seed cake nanoparticles is significantly influenced by several key experimental parameters [49]:

(i) Solvent composition. The choice between pure water and a water–ethanol mixture can significantly impact the extracted biomolecules;
(ii) pH. The acidity or alkalinity of the extraction solution affects the solubility of various components, particularly proteins;
(iii) Temperature. Temperature can influence extraction efficiency and potentially impact the properties of the extracted biocomponents;
(iv) Extraction time. Extraction duration significantly impacts both the quantity and the specific types of compounds extracted.

While the existing literature has demonstrated that nanoparticle size and heterogeneity are influenced by the parameters mentioned above, establishing a clear and formal correlation between these experimental conditions and the final particle quality remains challenging. This highlights the need for further research to develop more standardized and optimized extraction protocols for consistent and high-quality seed cake nanoparticle production.

Seed Cake

One of the main advantages of nanoparticles is their immense surface area when compared to macrosized particles, with increased interface reactiveness with the surrounding environment. This characteristic allows for specific applications that were simply not possible before the development of nanotechnology [96].

Industrial waste discharged into surface waters constitutes an ecological problem. Green synthesized nanoparticles (metallic and non-metallic) can be used to alleviate this problem. Seed cake obtained after oil extraction was ground using a precision mill to achieve particle sizes inferior to 100 nm [97]. These novel seed cake nanoparticles were then evaluated for the remediation of the pesticide chlorpyrifos from wastewater. In a study carried out by Kalaiyarasi et al., *M. oleifera* seed cake extract was used to synthesize ZnO NPs, and the catalytic activity towards the degradation of crystal violet (a common histological stain) in industrial effluents was investigated [98]. The results obtained under solar light irradiation confirmed the stability and efficiency of ZnO NPs in dye degradation. The synthesized NPs have also proven to be a suitable pant fertilizer as well as a significant antimicrobial agent against several bacteria and fungi. Water treatment was also the focus of research by Mewish et al. that studied the utilization of green synthesized AgNPs in textile industrial wastewater treatment [99]. The ideal conditions for NP synthesis, using seed cake biocomponents as reducing and capping agents, were established to be a 0.5 mM silver nitrate ($AgNO_3$) aqueous solution with a pH = 11 and 60 °C. The AgNPs exhibited significant antimicrobial activity against both Gram-positive and Gram-negative bacteria. In addition, photocatalytic activity towards the removal of three synthetic dyes was reported, as well as the potential removal of lead (Pb) from waste waters without producing any toxic or hazardous chemicals. Katata-Seru et al. investigated the efficiency of iron nanoparticles (FeNPs) prepared with *M. oleifera* leaves and seed extracts on nitrate removal from aqueous solutions [100]. A coagulant and antibacterial dual effect was detected, suggesting that green synthesized FeNPs can be used to treat contaminated industrial waters. A different study focused on the use of magnetic iron oxide NPs modified with *M. oleifera* seed proteins for selective recovery of precious metal ions from industrial wastes and electronic products, namely gold, palladium, and platinum [101]. The modified NPs adsorbed more ions than unmodified magnetite iron NPs, with optimal recoveries of 99.8% for gold, 72.2% for palladium, and 87.7% for platinum, although the exact mechanism for the removal of these ions was not specified.

The green synthesis of ZnO NPs with the characteristic wurtzite hexagonal structure was synthesized using *M. oleifera* seed [102]. Such NPs can be used in the textile area, in sensors, or in the cosmetics field. Coelho et al. utilized an aqueous ethanolic extract of seed cake to synthesize AgNPs with an average diameter of 127 ± 24 nm [103]. A total of 10 mL of the extract was added to 40 mL of 1 mM aqueous $AgNO_3$ solution under magnetic stirring at a flow rate of 1 mL/min and an 80 °C temperature. The color change from yellow to bronze-brown in the reaction mixture confirmed the formation of the nanoparticles, which remained stable for weeks at room temperature. Antimicrobial activity against Gram-negative *E. coli* BL21 (DE3) cultures was also reported. A novel biodegradable molluscicidal agent was tested by Ibrahim et al. [104]. A nanocomposite of cerium oxide/*M. oleifera* extract with an average particle size of 30 nm was investigated. The composite showed a significant lethal effect against *Biomphalaria alexandrina* snails, with a noticeable reduction in survival and hatchability rates of the snails. *M. oleifera* seed cake can also be used to produce multicomposite extracts for electrospun nanofiber synthesis [105]. Polyacrylonitrile (PAN) polymer was mixed with seed cake extract and doped with FeNPs to produce nanofibers by electrospinning. The adsorption capability of these nanofibers was then investigated against lead ions in aqueous solutions. Nallaselvam et al. studied the photocatalytic reduction of Cr(VI) under visible light via a TiO_2 and seed cake composite, with promising results concerning cost and efficiency [106].

Summarized information regarding the synthesis of nanoparticles with *M. oleifera* seed cake extracts and their applications can be found in Table 2.

Table 2. Nanoparticle green synthesis by *M. oleifera* seed extracts and possible applications.

Metal Solution	Synthesis Conditions	Application	Ref.
Zinc sulfate ($ZnSO_4 \cdot 7H_2O$)	1–5 mM to 1–5 mL several seed extract additions under sunlight	Dye degradation Organic fertilizer Antimicrobial agent	[98]
Silver nitrate ($AgNO_3$)	10 mL extract added to 90 mL of 0.5 mM silver nitrate solution, pH = 11.0, 60 °C	Textile dye degradation Antimicrobial agent Lead water removal	[99]
Iron chloride ($FeCl_3 \cdot 6H_2O$)	Extract added to 0.1 M $FeCl_3$, (1:2) stirred for 30 min	Nitrate water removal Coagulant and antimicrobial agent	[100]
Zinc nitrate ($Zn(NO_3)_2$)	5 g of $Zn(NO_3)_2$ added to 150 mL aqueous extract at 60 °C	Production of sensors Food processing Cosmetics	[102]
Silver nitrate ($AgNO_3$)	$AgNO_3$ added to aqueous extract (1:5) at 1 mL/min flow rate, 80 °C	Antimicrobial agent Bio-sensing Water purification	[103]
Cerium(III) oxide (Ce_2O_3)	30 mL extract added to 50 mL of 1 mM Ce_2O_3 and stirred for 3 h at 80 °C	Molluscicidal agent	[104]

5. Conclusions and Future Prospects

The way the scientific community approaches chemical processes and the fabrication of novel materials has seen a paradigm shift with the introduction of green chemistry, represented by a set of environmentally sustainable methods with minimal or inexistent waste associated. In 1998, Paul Anastas and John Warner established the twelve principles of green chemistry, a process framework supported by ideas such as atom economy, renewable feedstocks, and energy efficiency design [107]. The green synthesis of nanoparticles is based on the use of bioactive compounds (extracted from plants or microorganisms, for example) as agents in the reduction, nucleation, and stabilization of metallic and non-metallic nanoparticles. The utilization of natural resources like plants allows for a cost-effective and sustainable alternative to traditional methods. *Moringa oleifera* is a native plant from India with numerous applications. Used worldwide (especially in developing countries), it is regarded as a bioresource with incredibly high potential. This "miracle tree", as it is also known, possesses immense nutritional and therapeutic value and is used to treat health conditions such as malnutrition, rheumatism, bronchitis, or diabetes. In recent years, practically all parts of *Moringa oleifera* have been employed in the synthesis of nanoparticles. Biocompounds extracted from the plant, namely alkaloids, flavonoids, phenolic acids, or proteins, mediate the reaction and prevent the agglomeration and aggregation of the synthesized nanoparticles, although further research is needed to clarify those mechanisms. The leaves of *Moringa oleifera* are by far the tree part most investigated concerning green chemistry. Nonetheless, the seeds have emerged as a promising material for the synthesis of nanoparticles, especially the seed cake, a by-product of oil production. Numerous seed cake extracts have been employed in the synthesis of metallic and non-metallic nanoparticles, such as silver, iron, zinc, and cerium. This is attributed to its unique characteristics, including its abundance, low cost, and high content of biologically active compounds, which offer several advantages over conventional methods. For example, AgNPs synthesized using seed cake extracts exhibited strong antibacterial activity against a wide range of microorganisms, rendering them potential candidates for antimicrobial coatings and dressings suitable for various applications in medicine.

M. oleifera seed cake proves to be a sustainable solution for nanoparticle synthesis due to its various advantages. Firstly, it promotes a circular bioeconomy. *M. oleifera* seed cake, a byproduct generated during oil extraction from the seeds, finds new life as a valuable resource for nanoparticle production. This approach minimizes waste generation and exemplifies a closed-loop system where waste streams become inputs for new products. Secondly, *M. oleifera* itself is a highly renewable resource. Cultivated across four continents in tropical and subtropical regions, this fast-growing and drought-resistant tree ensures a readily available supply of raw material for nanoparticle production [4]. Finally, *M. oleifera* seed cake offers resource efficiency compared to some conventional methods. Water usage for nanoparticle synthesis has the potential to be lower when using seed cake, and the process avoids generating additional waste products often associated with harsh chemicals used in conventional methods. In essence, these factors contribute significantly to the sustainability of using *M. oleifera* seed cake for nanoparticle synthesis. It effectively transforms potential waste residue into a valuable byproduct.

In summary, *Moringa oleifera* seed cake is a promising material for the environmentally friendly synthesis of nanoparticles. Its environmental compatibility, versatility, and ability to produce high-quality nanoparticles with adjustable properties make it an attractive alternative to chemical reagents. As research continues to explore its unique properties, it is very likely that new innovative applications will be found in various fields, from medicine to agriculture and remediation.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/applbiosci3020013/s1, Table S1: *Moringa oleifera* seed cake industrial applications patents; Table S2: Green chemistry of nanoparticles: advantages and drawbacks [108–112].

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