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Review

Phytochemical-Mediated Selenium Nanoparticles from Moringa Oleifera: Antioxidant and Antidiabetic Perspectives

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Abstract

Background: This review examines the integration of nanotechnology and ethnopharmacology through the green synthesis of Moringa oleifera-mediated selenium nanoparticles (Moringa-SeNPs), highlighting their potential in mitigating oxidative stress-related metabolic disorders. Methods: A systematic search of Scopus, PubMed, Web of Science, ScienceDirect, and Google Scholar identified peer-reviewed English-language studies (2010-2025) focused on Moringa-SeNP synthesis, characterization, and biomedical activity. Studies lacking primary data or unrelated to green synthesis were excluded. Due to methodological heterogeneity, a qualitative narrative synthesis was used. Results: Evidence indicates that Moringa phytochemicals flavonoids, polyphenols, and saponins serve as natural reducing and stabilizing agents, yielding biocompatible, stable nanoparticles. Moringa-SeNPs demonstrate strong antioxidant effects by scavenging reactive oxygen species, enhancing endogenous antioxidant enzymes, and modulating redox-responsive signaling pathways. Antidiabetic mechanisms include a-amylase and a-glucosidase inhibition, improved insulin sensitivity via glucose transporter-4 (GLUT4) translocation, and protection of pancreatic b-cells from oxidative injury. Collectively, these actions support their promise as adjunct therapeutics for diabetes and metabolic syndrome. Conclusions: Moringa-SeNPs represent an eco-friendly nanoplatform with dual antioxidant and antidiabetic potential. However, progress is limited by inconsistent synthesis protocols, variable characterization practices, insufficient toxicity assessment, and minimal translational validation. Future efforts should prioritize standardized synthesis frameworks, robust safety evaluation, and well-designed preclinical and clinical investigations to facilitate biomedical advancement and support sustainable therapeutic innovation. Such advancements will strengthen reproducibility, enhance regulatory readiness, and clarify dose-response relationships essential for clinical translation. Ultimately, integrating phytochemistry with nanotechnology may yield safer, effective, and accessible interventions for global metabolic health challenges. This review therefore provides a foundation for future multidisciplinary research directions.

Keywords

Moringa oleifera, Moringa-SeNPs, Antioxidant activity, Antidiabetic potential, Green nanotechnology

Article History

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1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from inadequate insulin secretion, impaired insulin action, or both [1]. Globally, the prevalence of DM is rising at an alarming rate affecting approximately 537 million adults in 2021 and projected to reach 783 million by 2045 [2]. This escalating trend presents a profound challenge to public health systems worldwide. Central to the pathophysiology of diabetes is oxidative stress, which arises from an imbalance between reactive oxygen species (ROS) production and antioxidant defense [3]. Chronic hyperglycemia intensifies oxidative stress, leading to excessive ROS generation that damages pancreatic b-cells, aggravates insulin resistance, and triggers complications such as cardiovascular, renal, and retinal disorders, Chronic hyperglycemia, a hallmark of Type 2 Diabetes Mellitus (T2DM), initiates a cascade of pathophysiological events that profoundly impact cellular function and tissue integrity [4,5]. Consequently, modulating oxidative stress remains a key therapeutic target in preventing disease progression and improving patient outcomes [6].

Recent advances in nanotechnology have introduced new opportunities for addressing the multifaceted pathology of diabetes. Nanomaterials, with their unique physicochemical characteristics particularly high surface-area-to-volume ratios, tunable morphology, and enhanced reactivity offer improved drug solubility, stability, and targeted delivery [7]. These nanosystems can encapsulate bioactive compounds, protect them from degradation, and release them in a controlled manner at specific sites of metabolic dysfunction [8,9]. Such features make nanoparticles promising for managing chronic diseases like diabetes, where conventional therapies often exhibit limited efficacy and undesirable side effects [4].

Within this framework, Moringa oleifera and selenium emerge as potent candidates for nanotherapeutic development. Moringa oleifera contains a rich array of flavonoids and polyphenols that exert antioxidant, anti-inflammatory, and antihyperglycemic effects [10,11]. Selenium, an essential trace element, acts as a cofactor for redox-active enzymes such as glutathione peroxidase (GPx) and thioredoxin reductase, thereby regulating oxidative homeostasis and enhancing insulin sensitivity and glucose metabolism [12]. Selenium deficiency, conversely, has been associated with heightened oxidative stress and impaired glycemic control [12].

Integrating the phytochemical richness of Moringa oleifera with the metabolic modulatory role of selenium through green nanocarrier synthesis represents an innovative therapeutic avenue. Such hybrid systems can synergistically attenuate oxidative stress, enhance glucose uptake, and restore redox balance laying the groundwork for sustainable, biologically derived nanomedicines in diabetes management [11].

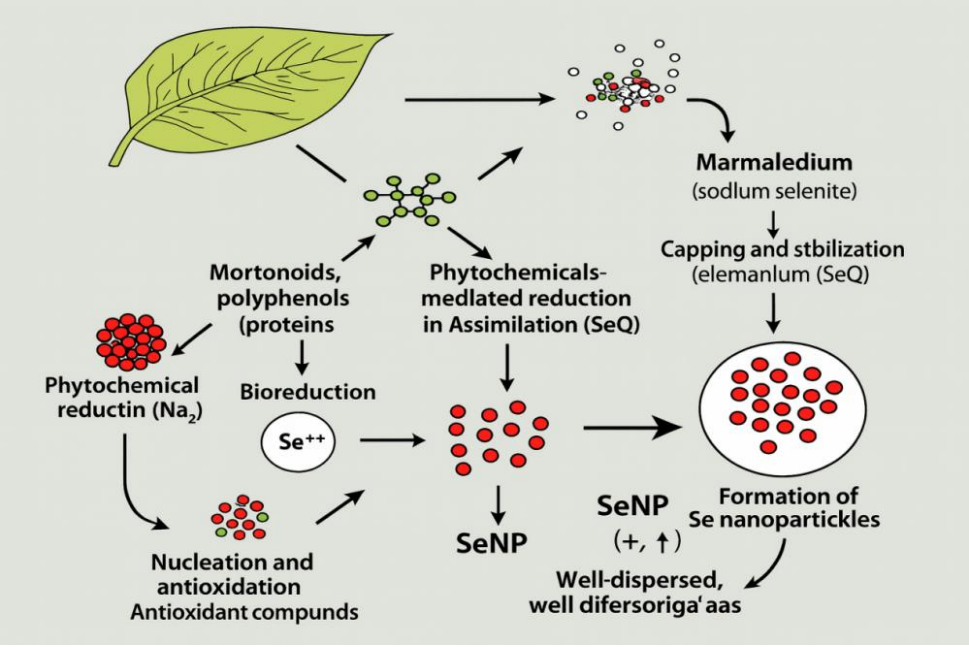

Figure 1. Moringa oleifera-mediated selenium nanoparticle synthesis and it mechanism.

Figure 1 above showed process of extraction of bioactive compounds from plant leaves, including polyphenols, flavonoids, proteins, and antioxidants. These phytochemicals interact with sodium selenite (SeO_3^{2-}), acting as both reducing and stabilizing agents. During the bioreduction step, phytochemicals donate electrons to convert Se^{4+} ions to elemental selenium (Se^0). Subsequent nucleation forms primary selenium nanoparticles (SeNP) cores, followed by nanoparticle growth, capping, and stabilization mediated by plant metabolites. The combined actions of reduction, nucleation, antioxidation, and phytochemical capping result in the formation of uniformly dispersed, stable SeNP. Figure 1 summarizes the complete green-synthesis pathway, including phytochemical interaction, reduction chemistry, and nanoparticle maturation.

2. Method

2.1 Study Design and Scope

This review employed a systematic and integrative design to examine recent advancements in the biosynthesis, characterization, and biomedical applications of Moringa oleifera-mediated selenium nanoparticles (Moringa-SeNPs). Emphasis was placed on evaluating their antioxidant and antidiabetic activities, elucidating underlying mechanistic pathways, and highlighting their translational potential in nanomedicine.

The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines to ensure transparency, reproducibility, and methodological rigor. A qualitative synthesis was prioritized over a quantitative meta-analysis due to the substantial heterogeneity in experimental designs, nanoparticle synthesis protocols, characterization techniques, and biological assays among the included studies. This approach facilitated a more mechanistic and contextual interpretation of findings rather than a purely statistical aggregation.

2.2 Literature Search Strategy

A systematic and comprehensive literature search was conducted across major scientific databases, including Scopus, PubMed, Web of Science, ScienceDirect, and Google Scholar, covering studies published 2020 to 2025.

The search strategy employed Boolean operators to refine and expand the retrieval of relevant studies. The following search string was used:

("Moringa oleifera" OR "moringa extract") AND ("Moringa-SeNPs" OR "Moringa-SeNPs") AND ("green synthesis" OR "biosynthesis") AND ("antioxidant" OR "antidiabetic" OR "biomedical applications")

To ensure comprehensive coverage, the reference lists of relevant review papers and primary research articles were manually screened to identify additional studies not captured in the initial database search. Duplicate records were removed using EndNote (v.21), and only peer-reviewed, English-language publications focusing on the green synthesis, characterization, or biomedical applications of Moringa-mediated Moringa-SeNPs were included.

2.3 Inclusion and Exclusion Criteria

Studies were included if they: Reported the green or phyto-mediated synthesis of Moringa-SeNPs using Moringa oleifera or comparable plant matrices. Investigated biological or pharmacological activities, such as antioxidant, antidiabetic, anti-inflammatory, or cytoprotective effects. Were original research articles, reviews, or conference papers published in peer-reviewed journals (2020-2025) and written in English

Studies were excluded if they: Employed chemically or microbially synthesized Moringa-SeNPs without plant mediation. Lacked clear experimental methodologies or biological outcome descriptions. They were non-peer-reviewed sources, such as book chapters, theses, or opinion articles.

2.4 Data Extraction and Synthesis

Extracted information included: Type and source of Moringa oleifera extract utilized. Synthesis and stabilization conditions for SeNP formation. Characterization techniques (UV-Vis, X-ray diffraction (XRD), fourier-transform infrared spectroscopy (FTIR), dynamic light scattering (DLS), zeta potential, and impedance spectroscopy). Reported biological activities and mechanistic interpretations. The extracted data were organized thematically into five analytical categories: (1) Synthesis and stabilization mechanisms; (2) Physicochemical characterization; (3)Antioxidant potential; (4) Antidiabetic and metabolic modulation effects; (5) Translational challenges and opportunities. This thematic synthesis enabled a comparative evaluation of how Moringa-derived phytochemicals mediate SeNP formation and enhance bioefficacy across studies.

2.5 Quality Assessment

The scientific quality and methodological rigor of each study were appraised using the Joanna Briggs Institute Critical Appraisal Checklist for experimental research and systematic reviews. Each study was assessed by two independent reviewers, and disagreements were resolved through discussion.

Evaluation criteria included: Clarity and reproducibility of synthesis protocols. Validity and completeness of characterization data. Adequacy of biological controls and statistical analysis. Reproducibility and transparency of reported findings. Only studies meeting the minimum Joanna Briggs Institute quality threshold were retained for final synthesis.

2.6 Data Presentation and Selection Flow

All validated data were summarized through structured tables and conceptual figures, highlighting key aspects such as biosynthetic routes, mechanistic insights, and comparative advantages of Moringa-SeNP formulations.

A PRISMA- selection process, including the number of studies:

Identified through database searches (n = 312);

After duplicate removal (n = 248);

Screened for eligibility (n = 117);

Included in the final synthesis (n = 68).

Visual schematics were developed to depict synergistic interactions between selenium and Moringa oleifera phytochemicals, aiding the mechanistic understanding of antioxidant and antidiabetic activity.

3. Application of Moringa oleifera Phytochemicals in the Preparation of Moringa-SeNPs

Nanobiotechnology has been developed as a groundbreaking science with a fast-growing pace of development. It is a combination of nanotechnology, biology, and materials engineering to produce new solutions to biomedical and environmental problems. One such promising boundary to this area is the creation of green synthesis methods, which use natural plant extracts as reducing and stabilizing agents in the synthesis of nanoparticles. The process will be safer, more sustainable, and more nature-friendly, as this method does not require harsh chemicals and other toxic agents [13,14].

What is known as the variety of medicinal plants that are being studied in the production of nanoparticles, Moringa oleifera, is the increasing research. It has a rich variety of phytochemicals that can be found in its leaves, such as polyphenols, flavonoids, tannins, vitamins, sterols, amino acids, and saponins that have intrinsic antioxidant and electron-donating abilities [15,16]. They act by reducing the selenium precursors to elemental Moringa-SeNPs (Moringa-SeNPs), capping the nanoparticles, and preventing agglomeration of the nanoparticles [10,17].

This bifunctionality makes Moringa oleiferaextracts a highly promising biogenic host in the production of Moringa-SeNPs, in line with the current trend of nanomaterials that are environmentally friendly in biomedical, pharmaceutical, and agricultural biosensors.

3.1 Reduction and Stabilization by Phytochemicals

Moringa oleifera leaves are rich in chemicals, which offer a unique benefit to the production of nanoparticles. The active roles of a wide range of phytochemicals, such as alkaloids, flavonoids, tannins, carotenoids, amino acids, glycosides, sterols, vitamins, and phenolic compounds, reduce selenium salts and stabilize the resulting nanostructures [15,16].

Of key interest to this process are the polyphenols. They donate their hydroxyl groups to selenium ions to reduce the precursor forms of selenium (e.g., to selenious acid or sodium selenite) to elemental selenium [18]. This redox conversion is accompanied by the oxidation of the polyphenolic compounds themselves to form a self-reinforcing reaction cycle. An aromatic structure of the polyphenols and flavonoids improves the stability of the nanoparticles by creating a barrier to aggregation based on steric and electrostatic interactions [19].

Another highly expressed group in Moringa oleifera, flavonoids, acts in the same way, as their hydroxyl substitutions transfer the electrons, frequently forming smaller, uniformly distributed nanoparticles. Such molecules, along with the phenolics, get adsorbed onto the nanoparticle surface, creating a natural capping layer that prevents uncontrolled growth and agglomeration [18].

Saponins and tannins (other phytochemicals) also provide additive stabilizing effects by introducing hydrophilic groups that increase solubility, but carotenoids and sterols can also adsorb to nanoparticle surfaces to alter morphology [20]. As a result, synergistic interaction of various chemical classes leads to a reduction process and ensures long-term colloidal stability of Moringa-SeNPs.

In the reduction process, phytochemicals such as flavonoids and phenolic acids donate electrons to convert selenite (Se^{4+}) into elemental selenium (Se^{0}). Concurrently, other bioactive compounds cap and stabilize the nanoparticles, preventing agglomeration and ensuring colloidal stability. This dual function of reduction and stabilization underlies the success of Moringa-based SeNP synthesis.

3.2 Mechanistic Understandings of Biosynthesis Pathways

The Moringa-SeNPs biosynthesis with the help of Moringa oleifera extracts can be schematized as a redox process consisting of several steps. The process usually starts by adding a selenium precursor, like sodium selenite (Na_2SeO_3), in an aqueous solution of the plant extract. When they interact, the hydroxyl and carbonyl groups of flavonoids and polyphenols lose electrons to the selenium ions and turn them into elemental selenium [15].

This reduction is coupled with the oxidation of the phytochemicals, resulting in intermediate compounds that may further interact with selenium species. The reduced selenium atoms undergo nucleation, forming small clusters that act

as seeds for nanoparticle growth. The growth phase is then regulated by the surrounding phytochemicals, which adsorb onto the nanoparticle surface and impose steric hindrance as well as electrostatic repulsion. This prevents particle aggregation and ensures uniform dispersion [21].

The biosynthetic process has a strong impact caused by environmental variables. The changes in pH change the ionization of phytochemical functional groups, which in turn change the reduction potentials and particle sizes. Temperature has a bifurcated influence: on the one hand, the increased temperatures increase the reaction kinetics but can affect the phytochemical integrity, whereas on the other hand, moderate temperatures usually produce well-dispersed nanoparticles [22]. In this way, careful optimization of these parameters is essential to the generation of nanoparticles of preferred size, structure, and stability [18].

Complementary spectroscopic studies and gas chromatography-mass spectrometry are used to support the abundance of phytochemical activity in the phytonanotechno-reduction cofactor of Moringa oleifera and passivation. The data shows how resilient organic shells form around Moringa-SeNPs, which not only provide the particles with stabilization but also give the nanomaterials antioxidant and bioactive properties [13].

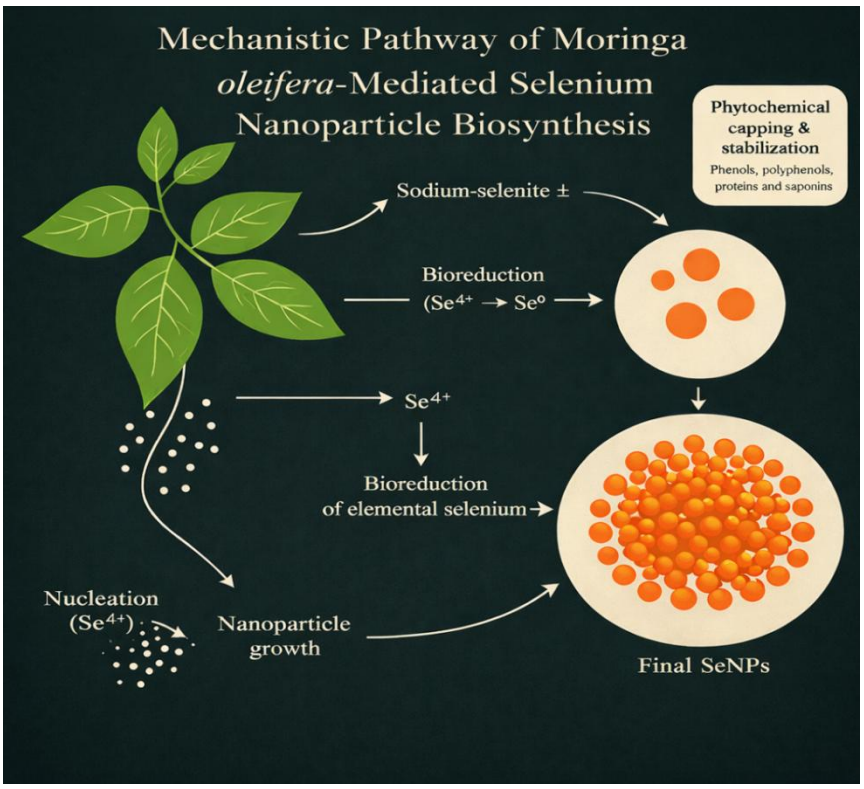

Figure 2. Mechanistic pathways of Moringa oleifera-mediated selenium nanoparticle biosynthesis.

Figure 2 above illustrates the green synthesis process through which bioactive phytochemicals from Moringa oleifera leaf extract facilitate the formation of SeNP. The leaf extract contains flavonoids, polyphenols, proteins, and antioxidants that act as electron donors and stabilizing agents. Sodium selenite (Se^{4+}) enters the system and undergoes phytochemical-mediated bioreduction to elemental selenium (Se^{0}). Initial nucleation occurs as Se^{0} atoms aggregate into small clusters, followed by nanoparticle growth through controlled assembly. Phytochemicals simultaneously cap and stabilize the forming nanoparticles, preventing agglomeration and enabling uniform size development. The pathway concludes with the production of well-dispersed, stable SeNPs. Figure 2 summarizes the complete sequence from precursor introduction to final nanoparticle stabilization.

3.3 Potential Comparative Advantages of Phyto-mediated Moringa-SeNPs

The green synthesis of Moringa-SeNPs using Moringa oleifera exhibits significant advantages over traditional chemical pathways. Classical reagents can often be based on toxic reducing agents, such as hydrazine or sodium borohydride, which leave dangerous by-products and require extensive purification [15]. On the other hand, plant-based production simultaneously performs reduction and stabilization in the same extract, thereby simplifying the process and reducing waste [14].

Another advantage is in the biocompatibility. NPs of Moringa-SeNPs of extracts of Moringa oleifera are capped by phytochemical agents, which increases their ability to be used in biological environments, reduces cytotoxicity, and increases therapeutic potential [23]. These nanoparticles are therefore very appropriate in the biomedical field, such as in antioxidant therapy, drug delivery, and antimicrobial interventions.

Moreover, phyto-mediated Moringa-SeNPs are often more stable in comparison with chemically synthesized ones. Phytochemical coating can be used as a natural surfactant, which lengthens shelf life and reduces aggregation tendency. This eliminates the need for synthetic stabilizers, which increases the environmental sustainability of the methodology even more [15].

The growing prominence of green synthesis in nanotechnology reflects a broader shift toward sustainable and biocompatible materials. Using Moringa oleifera as a bio-reductant and stabilizing agent exemplifies this transition, as its polyphenols, flavonoids, and ascorbic acid derivatives facilitate the eco-friendly reduction of selenium ions while minimizing chemical waste and toxicity. This approach aligns with the principles of green chemistry and supports the development of scalable, environmentally benign nanotechnologies.

The overall example of using phytochemicals of Moringa oleifera in the preparation of nanoparticles is representative of a circular bio-economy paradigm, where large volumes of biodegradable materials can be used to create high-tech materials with an insignificant environmental impact. This approach supports global sustainability and provides a larger scale of nanoparticle manufacturing in the regions where Moringa is extensively grown.

3.4 Implications

The evidence underlines the promise of using Moringa oleifera to make Moringa-SeNPs through a bioreactor. Not only does its unique phytochemical makeup facilitate the depletion of selenium precursors, but it also gives necessary stability and bioactivity to the resultant nanomaterials. Nevertheless, there are some important avenues that should be explored further.

To begin with, the systematic optimization of synthesis parameters, such as solvent systems, extract concentration, pH, and temperature, is always required to adjust the nanoparticle size and morphology [18,24]. Second, thorough mechanistic investigations are also needed to define the exact molecular mechanisms by which certain phytochemicals affect the reduction and stabilization of selenium and, thus, allow manipulation of the properties of nanoparticles selectively. Third, the scale-out of laboratory-scale synthesis has not been demonstrated yet, but it will be a requirement for industrial and clinical translations to scale up to a cost-effective and reproducible production process [22].

The inherent bioactivity of the capped Moringa-SeNPs produced by Moringa oleifera provides promising therapeutic opportunities, especially in diseases related to oxidative stress, like diabetes, cancer, and cardiovascular disease. The inherent biological functions of selenium might be combined with a natural antioxidant shell around such nanoparticles to provide a beneficial set of therapeutic effects [15,23].

The example of the synthesis of Moringa-SeNPs with the help of the leaf extracts of Moringa oleifera provides a good example of the merits of green nanotechnology: simplicity, sustainability, and biocompatibility. The phytochemicals of the plant also perform a dual role as reducing agents, which transform selenium precursors into elemental nanoparticles, and as stabilizing agents, which prohibit aggregation and assure colloidal stability. These two functions, supported by the structural and functional diversity of the phytochemical matrix, predispose Moringa oleifera as the best host to SeNP biosynthesis.

This phyto-mediated route is safer than traditional chemical procedures, more environmentally friendly, and produces nanoparticles that are more stable and bioactive. Through the utilization of antioxidant and electron-donating properties of natural compounds, scientists will be able to produce selenium nanomaterials that are not only effective but also implicitly eco-friendly and biomedical (as dictated by ecological and biomedical needs).

In the future, more optimization and mechanistic explanation will enhance the usefulness of mediated Moringa-SeNPs by using Moringa oleifera, hence making it easy to scale the processes to medicine, agriculture, and environmental remediation. Ethnomedicine and nanobiotechnology therefore merge, bringing forth great potential for sustainable innovation in nanoscience.

Despite the improvement, the synthesis parameters, including the pH, concentration of the precursors, and reaction temperature, have to be optimized to enhance the reproducibility, yield, and control of the nanoparticles' size and morphology. The particular mechanism of interaction of the molecules that are in the process of reduction with the help of Moringa will also be elucidated in further mechanistic studies, which will enhance the translational power of Moringa-SeNPs in biomedical intervention.

The synthesized Moringa-SeNPs were characterized as predominantly spherical and nearly colorless, displaying chemical stability that suggests weak or non-covalent interactions between the nanoparticle surface and the phytochemical capping agents.

4. Characterization of Moringa-SeNPs

4.1 Structural, Morphological, and Elemental Analysis

A detailed characterization of Moringa-SeNPs produced by the Moringa oleifera will be essential to confirm the biosynthetic efficiency, physicochemical stability, and reproducibility. All the analysis methods give complementary

data about particle structure, morphology, and purity, which make up the basis of comprehending nanoparticle functioning in biomedical systems.

It is confirmed that the crystalline phase of biosynthesized Moringa-SeNPs has been reached by the X-ray Diffraction (XRD) analysis, which confirms the transformation of selenium precursors into stable nanostructures with well-defined lattice planes [18,24]. Typical diffraction peaks that are associated with hexagonal or trigonal selenium are indicative of high crystallinity and effective biomineralization. Scanning electron microscopy (SEM) with energy-dispersive X-ray spectroscopy (EDX) is used to give a detailed enlightenment on the surface topology and distribution of the elements to ascertain the deposit of selenium uniformly and the absence of any plant or metallic impurities [25]. Such findings support the hypothesis that biosynthetic strategy synthesizes uniform nanomaterials in a consistent fashion as opposed to chemically reduced Moringa-SeNPs, which tend to be aggregated and possess irregular shapes.

Transmission electron microscopy (TEM) also provides the distribution of particle size and structure organization, often showing narrow polydispersity of spherical or quasi-spherical Moringa-SeNPs. The efficiency of Moringa-derived biomolecules as capping agents is facilitated by the observation of smooth and well-dispersed nanoparticles. Complementary UV-visible spectrophotometry gives evidence of the formation of nanoparticles by showing the surface plasmon resonance peak with a range of 260-280 nm, which is typical of selenium nanostructures [10,23]. DLS verifies hydrodynamic size and polydispersity index, which is an important indicator of colloidal stability and FTIR identifies functional groups involved in reducing and stabilizing nanoparticles [26,27]. Hydroxyl (-OH), carboxyl (-COOH), and amine (-NH_2) are present, which suggests that the nucleation and growth of Moringa-SeNPs are controlled by Moringa phytochemicals, including quercetin, kaempferol, and ascorbic acid.

Combined, these studies confirm that the Moringa-functionalized Moringa-SeNPs have homogeneous crystalline characteristics, surface passivation, and stability, which are not only necessary conditions but also necessary steps towards reproducible performance in antimicrobial, antioxidant, and anticancer applications [28]. The capacity of Moringa oleifera to control the nanoparticle morphology using a variety of secondary metabolites is a unique biosynthetic benefit of other plant systems, which offers sustainable, low-toxicity nanomaterials.

4.2 Surface Chemistry and Interaction with Phytoconstituents

The surface chemistry of Moringa-SeNPs produced through Moringa oleifera is mostly influenced by the complex reactions of the nucleus of selenium with plant-based phytoconstituents. According to Fourier Transform Infrared Spectroscopy (FTIR) spectra, hydroxyl and carbonyl vibrations indicate the involvement of the functional groups of phenolic and flavonoid and the electron-giving activity of the reduction of selenium ions [15,29]. The biomolecules are also able to cap the nanoparticle surface, which suppresses uncontrolled aggregation and also gives the nanoparticles antioxidant potential.

Zeta potential analysis measures the electrostatic interactions and the surface charge of particles and provides an understanding of colloidal stability. Nanoparticles that possess a zeta potential rate of more than ±25 mV can be said to be very stable in suspension because of the intense repulsion among the particles [22]. This is especially beneficial to biological systems, as stable dispersions enhance cellular uptake and minimize cytotoxic agglomeration.

X-ray photoelectron spectroscopy (XPS) is used to gain a better understanding of selenium oxidation state and the interactions between selenium and Moringa metabolites [15,22]. The presence of peaks at Se 3d and C 1s is consistent with the partial reduction of selenium to its zero-valent state (Se^0), whereas the presence of carbon-oxygen and carbon-nitrogen bonds is a sign of organic passivation of the extract [30]. These results are further validated by TEM analysis, where thin organic layers are found to cover the nanoparticles, which are indicative of a core-shell structure as a result of phytochemical adsorption [31].

Taken altogether, these findings prove that the biomolecules obtained out of Moringa have dual action as reducing and stabilizing agents, thus improving the biofunctionality, solubility, and biocompatibility of Moringa-SeNPs. This crosstalk is what makes the Moringa-SeNPs superior to other nanoparticles, as they can be used in pharmacological and environmental practices, unlike the traditional, chemically synthesized nanoparticles, which cannot be regarded as sustainable.

The stability and reproducibility of nanoparticle biosynthesis depend on the nature of the substrate materials employed, the method applied, and the specific microenvironmental condition surrounding the bioreceptor during nanoparticle formation.

4.3 Stability and Reproducibility in Nanoparticle Biosynthesis

In addition to the synthesis, the stability and reproducibility of Moringa-SeNPs are key factors to determine whether they can be translated in the future. The aggregation tendencies are assessed by colloidal stability tests in different pH, temperature, and ionic conditions. It is possible to track the changes in hydrodynamic size and zeta potential with time to gain knowledge concerning environmental resilience [22]. Moringa-SeNPs made using moringa are generally characterized by a strong resistance to flocculation, which is owed to constant electrostatic and steric stabilization by surface-bound biomolecules.

To guarantee reproducibility, several batches of synthesis samples are compared in terms of consistency in size, shape, and surface charge under the same conditions of the experiment [24]. A small variation in these parameters indicates reliability of the process a requirement of industrial or clinical scale-up. More sophisticated analytical techniques, including small-angle X-ray scattering and atomic force microscopy, expand the description to reveal the surface roughness at a nanoscale, packing density, and interparticle arrangement [17]. Moreover, the induced aging experiments can mimic the long-term storage environment, which contains predictive information about the shelf life and the breakdown pathway of SeNP suspensions.

These studies are able to continuously indicate that Moringa phytoconstituents do not only enable the development of stable nanoparticles but also are essential in the preservation of dispersion in the long run as well as in preventing oxidation or aggregation. This bi-fold capability emphasizes the innate benefit of phytochemical-assisted synthesis; the natural compounds are used as catalysts and stabilizers, which results in increased reproducibility and stability.

Moringa-SeNPs possess high structural integrity, reproducibility, and biostability, thus making them a new type of environmentally friendly nanomaterial. They have scalable synthesis and multifunctional nature and have applications with potential in biomedical, environmental, and catalytic fields and the paradigm of sustainable nanotechnology.

5. Antioxidant Activity of Moringa-SeNPs

Moringa oleifera extracts biosynthesized to produce Moringa-SeNPs are one such potent and eco-friendly technology that combines the therapeutic effects of selenium with a rich phytochemical matrix of the plant. The reducing and stabilizing agents, which are mostly flavonoids, phenolics, and alkaloids, serve in two aspects: to reduce selenium precursors and to cap the resultant nanoparticles, increasing structural stability and biocompatibility [10,15]. Green synthesis generates Moringa-SeNPs of much higher colloidal stability, less toxicity, and increased redox activity than conventional chemical synthesis [32].

Moringa-SeNPs have the potential to enhance the antioxidant action in DM, in which chronic oxidative stress is a contributing factor to β-cell dysfunction and insulin resistance. High concentrations of and nitrogen species (RNS) impair metabolic homeostasis by means of lipid peroxidation, protein denaturation, and DNA damage. The interaction between the enzymatic redox activity of selenium and the strong phytochemical antioxidants of Moringa generates a dual-action nanoplatform that prevents the oxidative stress at both molecular and cellular scales [9,33].

5.1 Removal of Reactive Oxygen and Nitrogen Species

Moringa-SeNPs have great free radical-scavenging capacity both directly and by catalysis. The phytochemical coating does not only inhibit aggregation of the particles but also gives electrons or hydrogen atoms to neutralize the ROS and RNS [15,23]. Phenolic -OH and methoxy (-OCH_3) groups in flavonoids like quercetin and kaempferol are the donors of electrons, and radical intermediates can be stabilized by resonance delocalization. This redox interaction takes place on the surface of the SeNP, whereby the selenium atoms enable the uninterrupted cycling of electrons, which resembles the enzymatic antioxidant systems.

Characteristic shifts at 3400 cm^{-1} and 1620 cm^{-1}, which are associated with O-H and C=O interactions, have been detected through spectroscopic analysis, especially at 3400 cm^{-1} and 1620 cm^{-1}, to confirm that phytochemical ligands and ROS are directly interacting and are undergoing a charge-transfer reaction [33]. Moringa-SeNPs are capable of stopping oxidative chain reactions effectively through these reactions and protect cellular macromolecules against structural degradation. The defense is especially important in pancreatic β-cells that have minimal intrinsic antioxidant mechanisms [12].

5.2 Cellular Redox Signalling-Modulation

In addition to direct radical scavenging, Moringa-SeNPs also exert control over intracellular redox-sensitive signalling pathways that control endogenous antioxidant enzyme expression. At the mechanistic level, the nanoparticles stimulate the Nrf2/Keap1 pathway and induce expression of antioxidant response elements that regulate catalase (CAT), superoxide dismutase (SOD), and GPx expression [9]. Simultaneously inhibiting NF-κB signaling suppresses the expression of the pro-inflammatory cytokines TNF-a and IL-6, alleviating oxidative and inflammatory stress.

This two-fold regulatory system restores the redox homeostasis, maintains mitochondrial integrity, and minimizes apoptosis in strained cells. Oxidative imbalance backgrounds in diabetic models, such as insulin secretion and receptor sensitivity, are regained by Moringa-SeNPs, leading to enhanced glucose consumption and cellular adaptability [33].

5.3 Synergistic Amplification of Moringa Bioactives

The interaction of selenium and Moringa phytochemicals is a synergistic interplay, a distinct biochemical amplification mechanism. Selenium acts as an enzyme-mimetic redox cycling agent, and Moringa bioactives, which are rich in polyphenols, flavonoids, and isothiocyanates, act as radical stabilizers and redox donors [15]. The combination of them gives rise to a greater and lasting antioxidant effect as compared to their individual constituents.

Such synergy is not limited to the biochemical effect but can also impact the stability and bioavailability of nanoparticles. Phytochemical shells increase solubility and offer a sustained release profile, which is vital in chronic oxidative diseases like diabetes [33]. Interestingly, the phytochemicals involved in stress resistance to abiotic conditions in Moringa plants, including increased biosynthesis of flavonoid compounds and ROS-neutralizing enzymes, also bring redox stability to human cellular conditions. The cross-kingdom defense analogies are indicative of an evolutionarily conserved redox regulation pathway, which can be exploited to realize nanomedical innovation [7].

5.4 Crystal Size Effect on the Antioxidant and Antidiabetic Activities

In addition to the biochemical composition, the antioxidant activity of Moringa-SeNPs is significantly influenced by the size of their crystallites. As the dimension of particles goes down, the surface volume ratio goes up, revealing more reactive surface atoms and consequently, more electron-donating capacity [34]. This is a refinement of the structure that increases the concentration of catalytic sites that can undergo redox-coupled biochemical reactions.

Smaller Moringa-SeNPs have better radical-scavenging dynamics and kinetics of electron transfer that result in effective ROS and RNS neutralization and intracellular redox balance restoration [35,36]. Also, nanoscale particles exhibit high bioavailability due to enhanced permeability of the membrane and intracellular localization [37].

Metabolically, the crystal size modulation, too, affects the insulin-mimetic behaviour of Moringa-SeNPs. The nanosized selenium atoms are able to react with the insulin receptors and regulate glucose-metabolizingbehavior enzymes like alpha-amylase and alpha-glucosidase to slow down postprandial hyperglycemia [38]. Thus, size control over crystallites does offer a way to customize antioxidant and antidiabetic functions, matching nanostructural engineering with therapeutic specificity, This approach leverages nanostructural engineering to precisely tune the biological activity of materials, offering a sophisticated avenue for developing next-generation therapeutic agents [39].

5.5 Impact of Nanoparticle Shape on Antioxidant and Antidiabetic Activity

The shape of the Moringa-SeNPs is a crucial determinant of physicochemical reactivity and biological functioning. Other geometries, such as the spherical nanoparticles, exhibit good biocompatibility, thermodynamic stability, and distributions of surface energies, leading to high cellular interactions and metabolic regulation [40].

Surface effects, which are dependent on shape, dominate the kinetics of molecular adsorption, radical neutralization, and enzyme inhibition. The contact surface-to-volume ratio of spherical Moringa-SeNPs is maximized by a high surface-to-volume ratio, maximizing contact with biologically interesting surfaces like ROS, glucose, and redox-sensitive enzymes [41,42]. The uniformity of the electrostatic interaction with cell membranes is facilitated by the symmetrical curvature, which simplifies internalization and biodistribution [43].

On the other hand, the irregular or anisotropic type of Moringa-SeNPs have uneven charge densities and aggregation behavior, which causes irregular therapeutic effects. Thus, manipulation of nanoparticle morphology during the synthesis process is the key to reproducible pharmacokinetic profiles and reproducible biological efficacy [43]. Morphological characteristics that promote antioxidant activity, such as surface uniformity and reactivity through curvature, are valuable to catalytic and biosensing applications, highlighting the universal utility of morphology optimization in functional application [44,45].

5.6 Integrative Perspective

The antioxidant and antidiabetic activity of the Moringa-SeNPs is characterized by both biochemical and structural parameters. Electron-donating functionality and biological targeting are provided by the phytochemical matrix, and reactivity, bioavailability, and kinetic efficiency depend on nanostructural features such as crystallite size and morphology. The overlap of the two dimensions forms an exact nanonutraceutical framework, where the green-synthesized Moringa-SeNPs serve as redox-modulating nanosensors to treat chronic metabolic diseases.

In order to build up the translational framework, future research should determine the correlates of structure-activity through a combination of computational modelling with spectroscopic confirmation so as to predictively optimize the properties of Moringa-SeNPs to be used in particular biomedical applications.

Table 1 summarizes a range of experimental, computational, and review-based investigations demonstrating how Moringa-SeNPs exert antidiabetic effects across different biological systems. In diabetic rat models, orally administered, phytocapped SeNPs enhanced endogenous antioxidant enzymes, preserved β-cell architecture, and improved insulin secretion, collectively normalizing blood glucose. Complementary *in vitro* enzyme assays showed that green-synthesized Moringa-SeNPs strongly inhibited α-amylase and α-glucosidase, thereby limiting post-prandial glucose release. Reviews of polyphenol-mediated synthesis further highlighted that Moringa phytochemicals stabilize SeNPs and modulate glucose-handling enzymes through redox mechanisms. Molecular docking analyses supported these findings, revealing strong interactions between Moringa-derived metabolites and digestive enzymes, consistent with non-competitive inhibition. Broader SeNP therapeutic literature indicated that these nanoparticles also restore insulin-signaling pathways (IRS-1/Akt) while protecting β-cells from oxidative stress. Finally, in plant callus models, Moringa-

SeNP exposure up-regulated antioxidant and glucose-metabolism genes, suggesting that SeNP-phytochemical synergy enhances metabolic regulation across biological systems.

Table 1. Experimental highlights and antidiabetic mechanisms of Moringa-SeNPs.

Model (Species / Paradigm)	Experimental Highlights	Antidiabetic Mechanisms	Interpretation / Outcome	Ref.
Streptozotocin (STZ) -induced diabetic rats	Polyvinylpyrrolidone-capped Moringa-SeNPs (5 mg/kg bw) administered orally for 21 days; comparison with diabetic control and standard drug	Enhanced GPx, catalase, and SOD; improved pancreatic β-cell histology and insulin secretion	Demonstrated insulin-mimetic and antioxidant effects leading to glucose normalization	[33]
In-vitro α-amylase / α-glucosidase inhibition	Green-synthesized Moringa-SeNPs (25- 200 µg/mL) incubated with carbohydrate-hydrolyzing enzymes	Strong inhibition of α-amylase and α-glucosidase; suppression of post-prandial glucose release	Validated dual enzymatic blockade and oxidative stress attenuation	[10]
Review of polyphenol-mediated SeNP synthesis	Compilation of studies describing Moringa polyphenols as reducing and capping agents for SeNP formation	Polyphenols improve nanoparticle stability and modulate glucose-handling enzymes via redox signaling	Highlighted synergistic contribution of phytochemicals to SeNP bioefficacy	[34]
Computational / enzyme interaction modeling	Docking of Moringa phytoconstituents (flavonoids, phenolics, alkaloids) with digestive enzymes	Active-site hydrogen bonding and non-competitive inhibition of α-amylase / α-glucosidase	Confirmed molecular basis for enzyme inhibition and glycemic control	[35]
Comprehensive SeNP therapeutic review	Summary of selenium-based nanomedicine in oxidative and metabolic disorders	Moringa-SeNPs activate insulin receptor substrates (IRS-1/Akt) and enhance antioxidant enzyme systems	Showed redox-regulated insulin-signaling restoration and β-cell protection	[32]
Plant callus culture model (Caralluma tuberculata)	Phytomediated Moringa-SeNPs (50-100 µg/mL) under light stress for 14 days	Up-regulated antioxidant genes and glucose-metabolism pathways; increased secondary metabolite yield	Demonstrated that SeNP-plant synergy boosts metabolic regulation	[36]

6. Antidiabetic Activity of Moringa-SeNPs

DM is among the metabolic diseases that are mostly prevalent around the world that have been characterized by the persistence of hyperglycemia, insulin signaling impairment, and b-cell dysfunction in the pancreas. The recent data points at the emerging evidence suggesting that Moringa-SeNPs (Moringa-SeNPs) produced with the support of Moringa oleifera extracts are a next-generation therapeutic modality able to tackle several pathological targets at once [10,33]. Environmentally benign nanoparticles are formed by using the reduced and capped properties of morphine and flavonoids, phenolics, alkaloids, and glucosinolates as reducing and capping agents, respectively, to form bioactive and stable nanoparticles, utilizing both types of phytochemical constituents [34,35]. Green synthesis has an advantage over the traditional method of chemical synthesis: not only is it much less toxic, but the nanoparticles formed by it are even more biocompatible and targeted. Such Moringa-SeNPs can therefore be used as all-purpose therapeutic vessels that enhance glucose homeostasis and alleviate oxidative stress and inflammation, thereby dealing with the symptoms and pathophysiology of DM [32,36].

6.1 Glucose Uptake and Insulin Sensitivity Regulation

Another primary pathway in which the Moringa-SeNPs can stimulate the antidiabetic effect is through increased glucose uptake and normal levels of insulin sensitivity in peripheral tissues like muscle, fat, and liver tissues. Moringa-SeNPs stimulate the downstream phosphatidylinositol 3-kinase (PI3K)/Akt cascade, which occurs because of the ultrasmall size and high surface-to-volume ratio of Moringa-SeNPs, which allow them to interact with insulin receptor pathways. This activation causes the translocation of glucose transporter-4 (GLUT4) vesicles to the plasma membrane and results in the increased intracellular glucose uptake effectively identical to the effects of metformin and thiazolidinediones [37].

Additionally, the Moringa-SeNPs mimic the insulin effect since they have the ability to phosphorylate key insulin signaling pathway proteins, such as Akt and p70 S6 kinase, targeting insulin-resistant states with improved glucose utilization [32,38]. At the same time, bioactives derived from Moringa, like quercetin, kaempferol, and chlorogenic acid, work in synergy to promote insulin sensitivity by inhibiting oxidative and inflammatory signals, especially by inhibiting the activity of TNF-α and NF-κB [11]. The two-fold activity, i.e., insulin mimicry and oxidative control, makes Moringa-SeNPs a versatile nanoplastic platform between redox control and metabolic control.

6.2 Carbohydrate-Hydrolyzing Enzyme (α-Amylase and α-Glucosidase) Inhibition

Moringa-SeNPs are also effective carbohydrate-digesting enzyme inhibitors like α-amylase and α-glucosidase that destroy polysaccharides and disaccharides in the diet to form glucose. The nanoparticles semi-stifle these enzymatic

pathways, thereby decreasing the absorption of glucose into the intestines and preventing postprandial hyperglycemia [33]. This move is similar to the pharmacodynamics of commercial inhibitors such as acarbose but with a possible reduced number of gastrointestinal side effects because it is composed of natural and biocompatible components [39].

Competitively, phytochemicals in Moringa extracts, i.e., polyphenols and alkaloids, occupy active sites of the enzyme, decreasing the affinity of substrate and catalytic turnover [35]. Combined with Moringa-SeNPs, they amplify to create a sustained-release framework that ensures the enzyme inhibition during the digestion, leading to excellent glycemic regulation [36]. Moreover, the surface chemistry of Moringa-SeNPs enables reversible binding with enzymes that can be dynamically used to modulate glucose metabolism as required by physiological requirements something that traditional inhibitors cannot do.

6.3 Pancreatic β-Cell Protection and Regeneration

In addition to their metabolic control, the Moringa-SeNPs also provide cytoprotective and regenerative properties to the pancreatic b-cells. The B-cells are major targets of the oxidative stress and chronic inflammation because of their minimal inherent antioxidant defense mechanisms. Moringa-SeNPs remove this stress through redox reactions to neutralize (ROS) and through preservation of mitochondrial membrane potential [12]. These effects are further increased by the presence of the Moringa phytochemicals with antioxidant and anti-inflammatory effects to inhibit cytokine-mediated B-cell damage.

Recent reports have indicated that B-cell neogenesis and insulin biosynthesis can be stimulated by Moringa-SeNPs, thus restoring pancreatic activities even in diabetic models [38,40]. This regenerative capacity is possible due to the Se-mediated expression of transcription factors, including Pdx1 and MafA, that are essential in insulin gene expression as well as b-cell maturation. All these properties allow Moringa-SeNPs to not only protect the existing b-cells but also trigger the restoration of the pancreatic insulin-producing functionality something that many existing antidiabetic medications do not do.

6.4 Gut Microbiota Regulation and Systems-Level Interaction

The development of evidence indicates that the gut-pancreas axis, which is a major regulator of glucose metabolism, can be controlled by nanomaterials. Moringa-SeNPs can alter the gut microbiota composition by favoring the increase in the abundance of beneficial bacteria, like Lactobacillus and Bifidobacterium, and inhibiting pro-inflammatory species that can cause insulin resistance [41]. This intestinal microbiota regulation helps to improve the intestinal barrier integrity and endotoxemia in the system, which indirectly leads to better insulin sensitivity and metabolic homeostasis.

Additionally, the systemic influence of redox-active Moringa-SeNPs in reprogramming host metabolism occurs. Moringa-SeNPs preserve the redox homeostasis of various organ systems, which is essential to prevent secondary diabetic complications like neuropathy and nephropathy by regulating selenoprotein activities, especially that of GPx and thioredoxin reductase [42]. This type of system-level integration underscores the promise of Moringa-SeNPs as a multi-organ regulatory nanomedicine.

6.5 Comparative and Translational Perspectives

Compared to traditional oral antidiabetic drugs like metformin, sulfonylureas, or DPP-4 inhibitors, Moringa-SeNPs have a number of different advantages. Their multimodal action that includes antioxidant, insulin-like, enzymatic, and regenerative pathways allows multifaceted action without the use of glucose-lowering activities only. Also, they can be biogenically synthesized to increase the biocompatibility and reduce the hepatic toxicity characteristic of synthetic drugs.

Nonetheless, there are still issues of translation. The long-term safety, biodistribution, and possible accumulation of selenium are to be investigated in a systematic manner. To make sure that biosynthetic procedures can be used by regulating bodies, dose optimization and chronic toxicity tests should be standardized [43]. The combination of computational pharmacokinetics and organ-on-chip modelling may assist in predicting the behavior of SeNP in complex biological systems, improving the level of precision in the dosing process and reducing off-target effects [44].

6.6 Integrative Potential of Personalized and Lifestyle Medicine

Lastly, integrating Moringa-SeNPs into precision nutrition and lifestyle medicine models is a new opportunity. Their high bioavailability and ability to alter redox conditions are the factors that make them good choice factors in functional food fortification and genetic and metabolic-based micronutrient therapies. Moringa-SeNPs may be used as the component of integrative strategies to prevent or manage diabetes by sustainable and individualized methods in combination with dietary and behavioral interventions [45,46].

Together, Moringa-SeNPs can have a convergence of antioxidant, enzymatic, signalling, and regenerative signalling, providing a systems-level solution to the metabolic dysfunction in DM. The redox effect of selenium and the phytochemical diversity in Moringa create a prototype of eco-sustainable nanomedicine such that interventions based

on traditional herbal therapy combined with the nanotechnology of the next generation can be initiated to combat diabetes.

7. Advantages at the System-Level and Synergy

Metabolic syndrome is a global health problem, which is characterised by a combination of abnormalities related to each other, such as dyslipidaemia, insulin resistance, hypertension, and abdominal obesity. The comorbidity of conditions is closely related to the risk of the development of type 2 diabetes and cardiovascular disease, and the interventions that need to be developed should not be targeted at specific conditions [41,42]. There is no single treatment adequate to cure the syndrome complexity thus the increasing trend in more effective treatment options that are built up and work on different pathways [43,47].

7.1 Antioxidant x antidiabetic pathways Crosstalk

The two common characteristics of metabolic syndrome are oxidative stress and compelling glucose metabolism, which serves as a factor both individually and in gradual degrees. High levels of ROS disrupts insulin signalling, modulate the activity of glucose transporters, and leads to the activation of proinflammatory signalling [6,48]. Prolonged hyperglycaemia, conversely, promotes the oxidative injury by forming advanced glycation end-products, mitochondrial dysfunction, and lipid peroxidation, which results in an unremitting metabolic imbalance [49].

It is a two-way relationship that underscores the clinical advantages of the therapy directed towards the oxidative stress and glycaemic control simultaneously. The attenuation of ROS can augment the insulin sensitivity, and other oxidative damage can be reduced through the improvement of glycaemic control. The antihyperglycaemic and antioxidant effects are both concomitant to reestablish metabolic balance, as well as relieve the inflammation and vascular dysfunction that are the most common traits of metabolic syndrome [47,48].

Table 2. Antioxidant and antidiabetic pathways modulated by Moringa-SeNPs.

Mechanistic Target / Pathway	Experimental or Conceptual Evidence	Antioxidant Modulation	Antidiabetic Effect	Integrated Interpretation	Ref.
Oxidative stress - Insulin resistance axis	Chronic hyperglycemia induces ROS, impairing insulin receptor signaling (IRS-1/Akt pathway)	Moringa-SeNPs scavenge ROS and upregulate antioxidant enzymes (GPx, SOD, CAT)	Restores insulin receptor sensitivity and glucose uptake	Reduction in oxidative burden breaks the feedback loop of insulin resistance	[3,6]
Redox-sensitive transcription factors (Nrf2/Keap1 and NF-κB)	Nrf2 activation promotes antioxidant defense, while NF-κB triggers inflammatory cytokine expression	Moringa polyphenols activate Nrf2 and suppress NF-κB translocation	Decreased proinflammatory signaling enhances insulin sensitivity	Balanced redox signaling regulates inflammation- insulin interplay	[32,48]
Mitochondrial dysfunction in β-cells	Excess ROS damages mitochondrial membranes and reduces ATP-linked insulin secretion	Moringa-SeNPs stabilize mitochondrial membranes and enhance ATP generation	Improves β-cell survival and insulin secretion capacity	Antioxidant protection directly supports pancreatic function	[12,33]
Advanced Glycation End-Products (AGEs) formation	Glycation of proteins and lipids induces oxidative stress and inflammation	Moringa-SeNPs and Moringa flavonoids inhibit AGE formation and neutralize free radicals	Reduces oxidative inflammation and vascular complications	Dual inhibition of AGEs and ROS preserves vascular and metabolic integrity	[46,50]
AMP-activated protein kinase (AMPK) pathway	AMPK regulates energy homeostasis, glucose transport, and fatty acid oxidation	Moringa-SeNPs activate AMPK via redox modulation; Moringa compounds enhance phosphorylation	Promotes GLUT4 translocation and cellular glucose uptake	Redox-linked AMPK activation integrates antioxidant and glucose-regulatory responses	[4,11]
Inflammatory cytokine-oxidative stress cycle	TNF-α and IL-6 elevate ROS production and block insulin signaling	Moringa-SeNPs suppress cytokine generation and ROS accumulation	Prevents cytokine-mediated insulin resistance	Combined antioxidant and anti-inflammatory actions restore metabolic homeostasis	[42,51]

Table 2 summarizes how Moringa-SeNPs exert coordinated antioxidant and antidiabetic effects by targeting multiple interconnected biochemical pathways involved in diabetes. Chronic hyperglycemia generates excessive (ROS), which disrupt insulin receptor signaling and mitochondrial function; Moringa-SeNPs counter this by scavenging ROS and boosting antioxidant enzymes such as GPx, SOD, and CAT, thereby restoring insulin sensitivity. They also modulate redox-regulated transcription factors, activating the protective Nrf2 pathway while suppressing pro-inflammatory NF-

κB, which reduces cytokine-driven insulin resistance. Their antioxidant properties protect pancreatic b-cell mitochondria, enhancing ATP production and improving insulin secretion. Additionally, Moringa-SeNPs inhibit the formation of advanced glycation end-products (AGEs), helping prevent oxidative inflammation and vascular complications. Through redox-linked activation of AMPK, they further promote GLUT4 translocation and glucose uptake. By simultaneously suppressing inflammatory cytokines (TNF-a, IL-6) and oxidative stress, Moringa-SeNPs create a synergistic environment that restores metabolic balance and strengthens both antioxidant defenses and glucose regulatory mechanisms.

7.2 Indirect Mechanism of Gut Microbial Modulation

Besides oxidative and glycaemic events, current evidence proposes that the gut microbiota is an important controller of metabolic health. Inflammatory responses of low grade result in dysbiosis and a close association with the distortion of lipid metabolism and insulin resistance [50,51]. GIT-liver and gut-pancreas interactions have been exemplified to show that the microbial imbalance has a direct effect on hyperglycemia and hepatic steatosis.

The effects of restoring the microbial population are indirect since the microbial community has been observed to enhance short-chain fatty acid production and glucose absorption and reduce systemic inflammation [6]. Consequently, antioxidant- and antidiabetic-based approaches using microbiota modulation have the capacity to induce broader systemic outcomes and enable metabolic homeostasis.

7.3 Translational Potential of Management of Metabolic Syndrome

Both an overlap of oxidative stress, inflammation, and metabolic dysfunction in metabolic syndrome and the urgent need to consider therapeutic solutions on the systems level are proved [44,51]. The conventional therapies have been known to be effective on risk factors in isolation, yet the reductionist therapies will seldom have long-term benefits. Quite the contrary, it is not so with synergistic interventions (i.e., a combination comprising antioxidant capacity, insulin sensitization, and microbiome regulation) that intervene in the activation of several pathological loops simultaneously.

This single paradigm can reduce the cardiovascular risk due to the metabolic syndrome. Oxidative stress facilitates endothelial dysfunction and hypertension, and insulin resistance accelerates dyslipidemia, which all contribute to cardiovascular morbidity [8,52]. By targeting these interconnected pathways, an opportunity to counter metabolic syndrome and its effects will have a more lasting defense [53,54].

The antioxidant and antidiabetic processes facilitated by the indirect management of gut microbiota are a plan for overall control of the metabolic syndrome. The suggested means of intervention through cross-stress overcoming between oxidative stress, glucose metabolism, and inflammation have potential in extending interventions on symptoms beyond patient management to restoration of the systemic metabolic integrity.

8. Challenges and Opportunities

8.1 Toxicity and Dosage Safety Problems

The narrow therapeutic index of Moringa-SeNPs is one of the most urgent issues associated with biomedical use of the latter since upon mildly increased concentration, antioxidant properties may be replaced by oxidative toxicity [38]. This dual redox action, known commonly as a hormetic effect, is caused by the dual redox behavior of selenium, where it functions as an antioxidant at lower doses and a pro-oxidant at higher doses. Mechanistically, overload Moringa-SeNPs may prompt the developing of (ROS) and selenol radicals, resulting in mitochondrial malfunction, fragmentation of DNA, and apoptosis in non-target cells [55].

Physicochemical properties particle size, morphology, and surface charge are major influences on biodistribution and toxicity. As an example, smaller Moringa-SeNPs (smaller than 50 nm) have improved cellular absorption but may lead to cytotoxicity or oxidative damage during prolonged exposure due to accumulation in the liver, kidney, and spleen [56]. Research has shown that surface capping agents (e.g., plant polyphenols of Moringa oleifera) have the potential to alleviate such effects by improving biocompatibility and alleviating aggregation. However, little has been done on systematic dose optimization and chronic toxicity, which explains the necessity to use standardized preclinical procedures that could determine dose-dependent toxicity, organ distribution, and clearance kinetics to offer a safety margin prior to clinical application [32].

8.2 Pharmacokinetics and Biodistribution Problems

Although the bioavailability and pharmacokinetic behavior of Moringa-SeNPs have shown promising preclinical data, these two aspects are important bottlenecks to therapeutic translation. They are frequently colloidally unstable, which causes aggregation in physiological fluids and changes absorption, half-life, and tissue retention profiles [56]. The differences in particle size, route of synthesis, and modification of the surface also increase the pharmacokinetic variability by affecting opsonization, renal clearance, and immune recognition [57].

New approaches, e.g., surface functionalization with biocompatible polymers (e.g., PEGylation, chitosan coating), and encapsulation in lipid or protein nanocarriers have already been demonstrated as having the potential to increase stability, solubility, and systemic circulation time. These alterations have the benefit of decreasing the immune clearance, as well as enhancing targeted delivery and localized release to pathological sites. Recent in vivo pharmacokinetic research studies have shown that functionalized Moringa-SeNPs have a higher plasma retention and lower off-target accumulation, which is a step towards safer systemic application [32]. The focus of future research must be on the integrated pharmacokinetic models and biodegradation profiling to predict the long-term in vivo behavior and maximize the therapeutic dosing schedule.

8.3 Barriers to clinical and regulatory translation

In addition to technical issues, Moringa-SeNPs have very high clinical and regulatory barriers. Clinical translation is not facilitated by the lack of harmonized international standards of nanoparticle-based therapeutics. Existing regulatory systems (FDA, EMA) lack the capacity to consider the pharmacodynamics of nanoparticles and environmental toxicity, as well as the safety of their use over the long term, especially due to their biotransformation and retention in the body [58,59].

Selenium-based nanoformulations have been investigated in a limited number of preliminary clinical trials to date in cancer treatment and management of oxidative stress with promising outcomes in terms of safety and antioxidant capabilities. Yet, it is still evident that human-based evidence of the Moringa-mediated Moringa-SeNPs has not been done in detail, particularly for chronic exposure, reproductive toxicity, and immunogenicity. To fill this gap, there is a need to have multidisciplinary liaisons between nanotoxicologists, clinicians, and regulatory agencies to develop standardized testing standards, which include:

Biodistribution and elimination over a long period of time, Mechanistic toxicity tests (oxidative, genotoxic, and immunotoxic), Procedures of environmental safety and disposal, and Ethical control of nanoparticle-based pharmaceuticals.

It will be necessary to organize certain regulatory frameworks that are specific to the nano-enabled therapeutics with similarities to ISO/TR 13014 and OECD guidelines to guarantee quality control, reproducibility, and patient safety. The future effectiveness of Moringa-SeNPs in clinical practice will be linked to an integrated appraisal model that incorporates the characterization of nanomaterials, mechanistic toxicology, and clinical efficacy testing.

8.4 Future Outlook

Nevertheless, incorporation of the principles of green synthesis, especially the construction of nanoparticles by plants with the usage of Moringa oleifera, provides certain possibilities to eliminate some of the toxicity and regulation issues. The biogenic route is also intrinsically offering biocompatible capping layers, better colloidal stability, and fewer environmental risks than chemically synthesized Moringa-SeNPs. In the future, personalized nanomedicine models with systems-level approaches that bring together omics technologies, AI-based predictive toxicology, and dosage and delivery optimization can be used to ensure safe clinical use.

The mechanism of toxicity, improved pharmacokinetics, and definitive regulatory pathways will evolve Moringa-SeNPs into a viable clinical platform of nanomedicines.

9. Future Directions

The next step in the research on Moringa-SeNPs involves addressing the current limitations of selectivity, reproducibility, scalability, and clinical translation. Although Moringa-SeNPs have proven their usefulness as antioxidants, antimicrobial agents, and antidiabetics, their potential can solely be achieved with the employment of prudent materials science, molecular biology, and regulatory policy. The future research must aim at producing clinically adaptable, safe, and sustainable nanotherapeutic formulations that are able to be customized to meet the needs of individual patients and health conditions that are prevalent in the world.

The new surface-engineering techniques, such as ligand functionalization, polymeric encapsulation, and biomimetic coating, promise to improve the selectivity and minimize off-target acquisition [58,60]. These functionalization methods allow site-directed targeting where peptides, antibodies, or polysaccharides are conjugated to the surface of Moringa-SeNPs, enhancing cellular internalization and tissue selectivity with reduced systemic cytotoxicity. Also, predictive information about nanoparticle biodistribution, clearance dynamics, and molecular interactions can be achieved using computational modelling and pharmacokinetic profiling, which contributes to the control of dosage and therapeutic precision [61,62].

It is important to develop standardized systems of toxicity testing in the long term and pharmacovigilance to make them reproducible and compliant with regulations. Convergence of green chemistry, clinical nanomedicine, and data-driven modeling can speed up the safe transfer of Moringa-SeNPs out of bench to bedside.

9.1 Combination of Moringa-SeNPs and Precision Nutrition and Lifestyle Medicine

Precision nutrition and lifestyle medicine is a positive paradigm shift due to the integration of Moringa-SeNPs into disease prevention and metabolic optimization at a personal level. In comparison to the traditional selenium supplements, Moringa-SeNPs are characterized by higher bioavailability, controlled release, and lower systemic toxicity, which makes them the perfect choice in nutraceutical and therapeutic nutrition [18].

There are targeted delivery system types that enable Moringa-SeNPs to mediate redox homeostasis, regulate insulin sensitivity, and enhance antioxidant defense, which are essential to the prevention of oxidative stress-related diseases, which include diabetes, cardiovascular diseases, and neurodegeneration. Indicatively, nanoformulated selenium-fortified diets have been shown to have a positive control on glycemic and mitochondrial activities in preclinical metabolic disease models.

Clinical validation as an aspect of the future research needs to be focused on the development of synergistic formulations involving Moringa-SeNPs with polyphenols, vitamins, or probiotics to improve the gut-microbiome balance and metabolic resilience. SeNP-based interventions administered as functional foods and lifestyle therapeutics have the potential to provide scalable and sustainable health solutions to genetic and dietary diversity.

9.2 Hybrid Nanoplatforms: A favorite combination of phytochemicals and metallic elements

A new way to multifunctional nanomedicine is the development of hybrid nanoplatforms that integrate Moringa-SeNPs with phytochemicals found in plants or other metallic moieties. These hybrid systems utilize the synergistic antioxidant, anti-inflammatory, and antimicrobial activities of selenium and bioactives like flavonoids, terpenoids, and phenolic acids [63,64].

Hybrid SeNP-phytochemical systems have a dual therapeutic effect, which is mechanistically observed: Natural polyphenol capping of redox stabilizing against oxidative degradation Reducing oxidative degradation. Specialized signalling regulation of oxidative and inflammatory pathways, such as Nrf2 and NF-κB. Metal incorporation of gold, silver, or iron expands its uses to cancer theranostics, biosensing, antimicrobial coatings, and smart drug delivery systems due to added functionalities of magnetic responsiveness, photothermal activation, and catalytically boosted functionality. The recent preclinical research that has been conducted on Au-SeNP and Ag-SeNP composites has shown increased tumor-specific cytotoxicity and high biocompatibility, which demonstrates the translational potential of hybrid nanoplatoons. This said, these complex systems require serious toxicology and pharmacokinetic as well as environmental checks to make them safe and sustainable in their application.

9.3 Sustainable Production and Health Applications in the World

Sustainable manufacture of the Moringa-SeNPs constitutes an ethical and technological requirement of global health. Green methods to synthesize them with Moringa oleifera, agricultural waste, or microbiological systems limit the amount of hazardous by-products, use less energy, and increase the biocompatibility of the nanoparticle [7,65].

The biggest problem is with scalability; hence, subsequent attempts should be made at creating continuous-flow bioreactors and low-cost, renewable bio-reduction methods that could be used in the production of nanoparticles on a large scale. The inclusion of the synthesis of SeNP in the framework of the circular bioeconomy may facilitate the environmentally friendly production pipelines in accordance with the UN Sustainable Development Goals (SDGs).

Outside of the medical field, Moringa-SeNPs have been shown to have promising uses in agriculture and food security, including: Improving the stress resiliency and nutrient absorption in crops, Justification of selenium biofortification of soils and edible plants, and used as antioxidant preservatives in after-harvest systems [66,67].

These two biomedical-agricultural uses have the potential to reduce the health inequalities and malnutrition due to poor diets, especially in the resource-constrained areas. Integrating the creation of Moringa-SeNPs into sustainable, localized production systems can align health, nutrition, and environmental objectives transforming Moringa-SeNPs into an agent of equal opportunity health innovation in the world [68].

9.4 Methodological and Analytical Reflections

To develop further SeNP research, one must pay careful attention to the methodological reproducibility and analytical accuracy. Sample preparation differences (e.g., drying process, aggregation in storage, remnant biomaterials) may change the morphology of nanoparticles and size distribution analysis (TEM, SEM, DLS, etc.). In a similar manner, the inabilities to obtain the surface chemistry and oxidation state may be ambiguous when the spectra are obtained using calibration failures in the instrumental calibration and overlapping signals in both FTIR and XPS.

It should be the priority in the future work: Procedures of standard synthesis and characterization, Stock materials of nanoparticles to be used in inter-laboratory validation, and automated pipelines in analytics based on AI-assisted spectral deconvolution and image recognition to increase the precision and reproducibility. These improvements will allow equally potent structure-function correlation mapping, enhance comparability with other studies, and allow

regulatory validation. Finally, the translation of the safe, reproducible, and transparent translation of SeNP-based nanomedicines will be supported by harmonized standards of analysis.

9.5 Outlook

The future development of the SeNP studies will be based on the balancing of therapeutic innovation and risk management. Although the use of Moringa-mediated Moringa-SeNPs has great potential, based on its green synthesis, biocompatibility, and versatility, unresolved issues, including dose-related toxicity, biodistribution, and persistence in the environment, have to be dealt with critically.

Future studies ought to aim at: Extensive clinical studies of efficacy and chronic safety, System-level toxicology modelling with genomics, metabolomics, and proteomics, Regulatory frameworks Standardized regulatory frameworks on nanoparticle assessment, and Socioeconomic impact Research on the access and fair implementation in low-resource areas. Moringa-SeNPs can be used to transform experimental materials into scalable, clinically relevant, and ethically controlled solutions by integrating nanotechnology, sustainability, and global health systems. Moringa-mediated Moringa-SeNPs, specifically, are an example of how bioinspired innovation can facilitate sustainable nanomedicine that can solve both disease-related and planet-related health issues.

10. Conclusion

The review highlights that Moringa-SeNPs are among the most potentially effective nanomaterials in the areas of biomedicine, nutrition, and sustainable agriculture. Their distinct physicochemical properties, especially nanoscale crystal size and morphology (depending on shape), are ultimately decisive in regulating antioxidant and antidiabetic action. Smaller crystallites provide a higher reactivity of the surface and electron-transfer capacity, whereas the uniform cellular uptake and biomolecular interaction of the spherical Moringa-SeNPs can enhance therapeutic outcomes.

Moringa-SeNPs synthesized out of Moringa oleifera and other phytogenic systems have synergistic biological activity because of phytochemical capping materials that guarantee colloidal stability and biocompatibility. Nevertheless, to scale laboratory discoveries into practice in nanomedicine and food, future research will need to combine standardized synthesis procedures, sophisticated toxicology assessments, and regulatory frameworks that will comply with the concepts of green chemistry and Safe-and-Sustainable-by-Design.

With the help of environmental and health ethics, sustainable production and hybrid nanoplatforms will be developed to make sure that the Moringa-SeNPs are not only contributing to human wellness but also to the sustainability of the planet. The future of Moringa-SeNPs, as highlighted in this review, is in the integration of structural optimization, mechanistic knowledge, and eco-friendly innovation in achieving the full potential of the nanoparticles in holistic medicine and sustainable technology development. The interaction between crystal size and morphology through sphericity determines important biological determinants of the Moringa-mediated Moringa-SeNPs. These discoveries reveal the direct relationship between manipulating physical aspects at the synthesis stage to control redox modulation, enzyme inhibition, and cellular compatibility to constitute the scientific basis of biomedical and nutraceutical biomedical applications in the future.

Conflict of Interest

The author declares that he has no conflict of interest regarding this publication.

Generative AI Statement

The authors declare that no Gen AI was used in the creation of this manuscript.

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