

# ***Moringa oleifera* Leaves: A Proficient Biosynthetic Source of Myriad Nanoparticles Pertaining Biomedical Importance**

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## **Abstract**

The advent of nanotechnology has blurred the boundaries between various fields. Development of newer, efficient, and sustainable approaches for nanomaterial synthesis has become the primary focus of research in recent years. The utilization of biological molecules as matrices for nanoparticle synthesis is increasing, with bacteria, fungi, plants, agro-waste, being common choices. Among them plant extracts are favoured biological source due to their widespread availability and diverse range of primary and secondary metabolites. These antioxidant metabolites possess reducing properties, indicating the potential for plant extracts to synthesize nanoparticles with enhanced characteristics. *Moringa oleifera* is a perennial, fast growing very popular plant in Asia. Since ancient times it is an important source of natural phytochemicals employed as food and herbal medicine. *Moringa* leaves have high number of phytochemicals like flavonoids, saponins, tannins, phenolic acids, proteins, calcium, iron, vitamins, essential amino acids, omega fatty acids and antioxidants. These facilitates eco-friendliness, and cost-effectiveness for large-scale production of nanomaterials. So far, several parts have been utilised for biosynthesis such as stem, bark, seed, fruit, and leaf. Leaves are highly exploited among all other parts for synthesis of several metal (gold, silver, copper,), metal oxide (titanium, zinc, iron) and other nanoparticles. During biosynthesis process, extracted phytochemicals are added to solutions containing metal salts. They serve as both reducing and stabilizing agents for metal ions imparting biomedical functionalities. This review presents, *Moringa oleifera* mediated myriad nanoparticles and their role in various applications with special focus to healthcare and biomedical field.

**Keywords:** Biomedical Applications, Biosynthesis, *Moringa oleifera*, Nanoparticles, Plant Extract.

## **Introduction**

Nanotechnology has taken a central stage encompassing almost all areas. Engineered nanomaterials find its place in electronics, energy sector, packaging industry, cosmetics, environment, agriculture, and healthcare. Over the past few years, healthcare and biomedicine have been greatly impacted by the nanotechnology-based products. Several metal, non-metal and polymeric nanoparticles (NPs) are being used extensively for biomedical applications such as biosensors, contrast imaging agents, drug delivery systems, scaffolding material for tissue regeneration, implant materials and so on. Manipulation of size, shape, functionalization to modify surface properties has widened its potential scope. There has been a growing focus on utilizing biological organisms for synthesizing nanoparticles, driven by the need for safer nanomaterial production methods (1). Use of bacteria, algae, fungi, actinomycetes, plant extracts

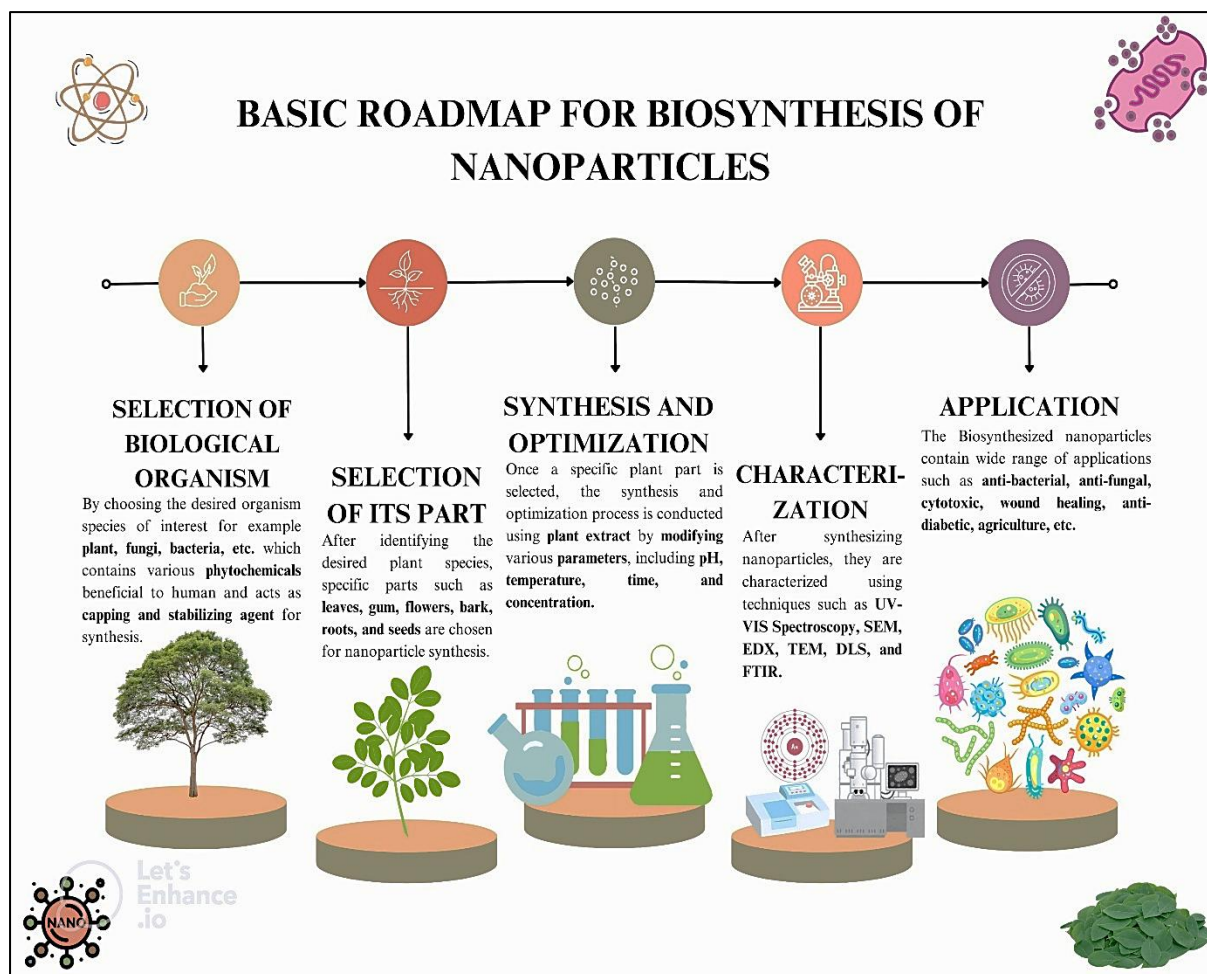
and biomolecules derived from them is reported for nano-biosynthesis (2, 3). Selection of biological source followed by thorough characterization by various techniques is necessary step before using them for several applications (Figure 1). Recently, the utilization of plant extracts for nanoparticle synthesis has emerged as a viable alternative to traditional chemical and physical approaches. Plant-mediated biological synthesis typically occurs at a faster rate compared to microorganism-based methods, resulting in nanomaterials that are more stable and exhibit a greater diversity in shape and size. Perceived advantages include quicker synthesis, eco-friendliness, and cost-effectiveness for large-scale production of nanomaterials. During this synthesis process, phytochemicals extracted from plants are added to solutions containing metal salts. These phytochemicals serve as both reducing agents for metal ions and stabilizing agents, facilitating better

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control over nanoparticle crystal growth (1). *Moringa oleifera* (MO) is a tropical plant very popular in Asia and cultivated worldwide. Since ancient times it is used as an important source of natural polysaccharides. It has good biological properties such as improving the activity of digestive enzyme, antioxidant, antidiabetic, immunomodulatory, pharmacological effect as well as it has capacity to cure different diseases like high blood pressure, hypercholesterolemia, cancer, anemia, headaches, and migraine (4). It is a powerpack of nutrients often called as 'Miracle tree.' The beneficial phytochemicals present in MO have 7-times higher vitamin C contents than in citrus, 10-times higher vitamin A contents than in carrot, 17-times higher calcium contents than in milk and this plant has highest amount of protein, potassium, and iron. Malnutrition in body can be naturally treated with consumption of leaves and drumsticks (5). *Moringa* leaves have high amount of phytochemical like flavonoids, saponins, tannins, phenolic acids, proteins, calcium, iron, vitamins, essential amino acids, omega fatty acids

and antioxidant because of this they are center of attraction (6). Certain studies have shown protective function of various plants parts in improving metabolism, reducing toxicity caused due to various factors or as an anticancer therapy. A study on supplementation of *Moringa* leaf extract, revealed the improvement in overall metabolism, reproductive health of rabbit doe at various stages. Nano formulations were effective even at lower dosage suggesting better bioavailability (7). While, titanium dioxide toxicity inducing brain damage in rats was alleviated by seed extract affecting cellular gene expression and reducing oxidative damage (8). Isothiocyanates extracted from the *Moringa*, encapsulated in liposomes were tested for dermal delivery. They had reduced ultra violet (UV) induced photoaging in HaCaT cell lines, and improved skin permeation *in vivo* (9). Whereas, MO leaf polyphenols in phytosomes have been reported for its anticancer activity against 4T1 (mouse breast cancer) cell line (10).



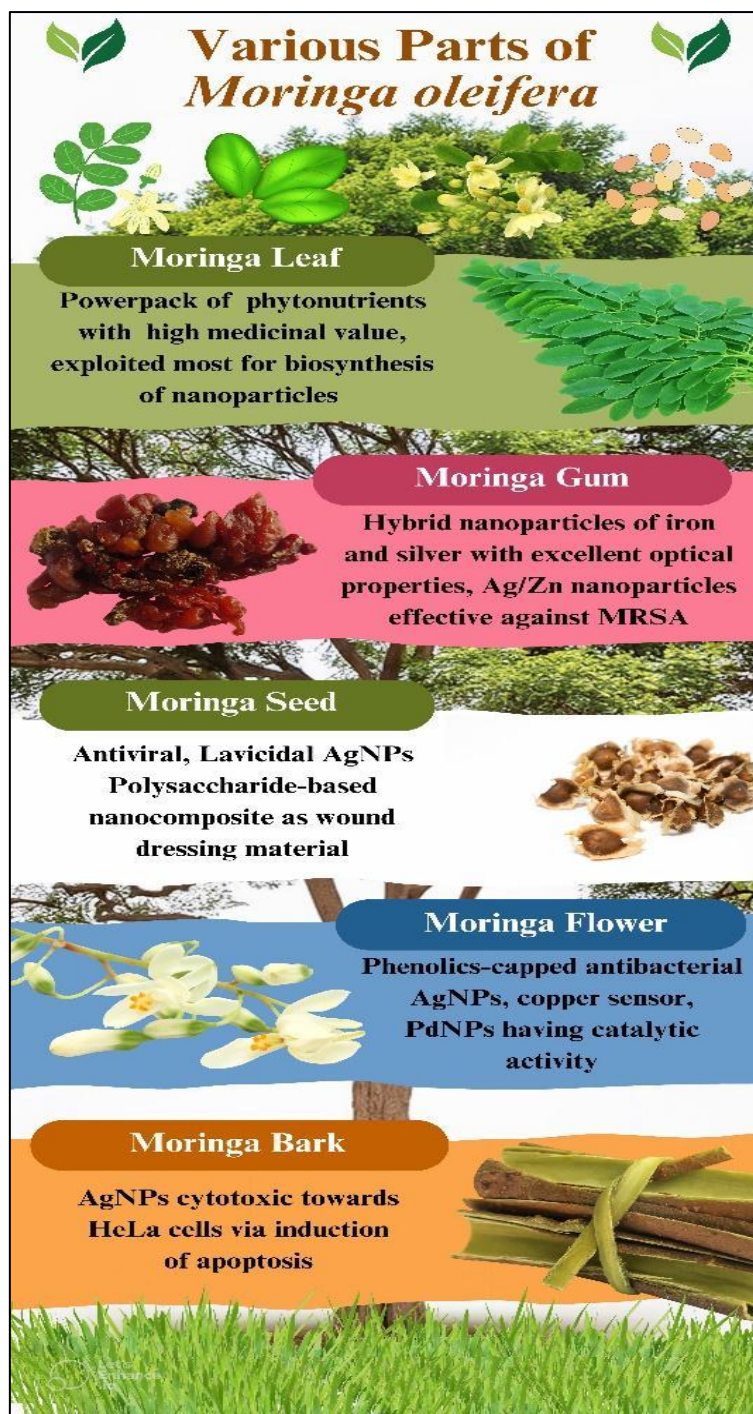
**Figure 1:** A Sequential Flow of Nano-biosynthesis, Characterization and Applications

These functionalities of *Moringa* makes them suitable as an important nano-biosynthetic source. Previous efforts have been made by a few research groups to review the biogenic nanoparticles using *Moringa oleifera* plant. Some of them have focused on a single type of nanoparticles such as silver or gold nanoparticles mentioning their synthesis, antimicrobial and antiproliferative properties (11, 12). While others focused on Nobel metal based/other nanoparticles' synthesis, their characterization, and applications (13, 14). *Moringa* seed cake, a byproduct after oil extraction and its utilization for green nano-synthesis as a sustainable choice has been reviewed (15). Occurrence of polyphenols, their importance in nanoparticle synthesis and applications was thoroughly reviewed recently (16). *Moringa* is fast growing tropical plant and can be seen growing easily with profuse foliage throughout the year. Their abundance, availability, and simple pre-processing before utilizing them for nanoparticle biosynthesis makes them better source as compared to other plant parts such as bark, fruit, gum, and seed. Although this topic is explored extensively before, in the present review, we attempt to update the nanoparticle biosynthesis especially using *Moringa oleifera* leaves and highlight their role in various applications with special focus to healthcare and biomedical field.

### ***Moringa oleifera*: A Good Biosynthetic Source of Nanoparticles**

*Moringa* plant parts such as flower, seed, stem bark, fruit, gum, and leaves are rich in terms of their phytonutrient contents. All these parts were exploited for nanoparticle biosynthesis has been reviewed earlier (17). Although focus of this review is leaf-mediated nanoparticles from *Moringa*, it is noteworthy to discuss few of the articles making use of various parts as biosynthetic machinery (Figure 2). Silver nanoparticles (AgNPs) from flower extract containing phenolic contents tested against bacterial pathogens and could

inhibit growth which is evident from zone of inhibition. These spherical 8nm NPs were also able to detect copper ions up to 12mM concentration by optical sensor (18, 19). Multiple application of biogenic palladium nanoparticles from MO flower extract have been reported. They exhibited anticancer, antimicrobial, antioxidant property, tested for safety assay on *Artemia salina*, and shown catalytic degradation of p-nitrophenol, methylene blue (20). Fruit pulp was utilized for bimetallic NPs synthesis of silver and copper metal with antimicrobial function (21). Hybrid NPs of ferrite and silver were synthesized using *Moringa* Gum, formed of unique shape of spherical with cubical spinal structures. These unusual shaped NPs may be useful for various applications in the biomedical field owing to their optical properties (22). Antibiotic resistance is a burning issue and nanomaterials provide alternatives to the conventional antimicrobial therapy. *Moringa oleifera* gum-based silver and zinc oxide nanoparticles exhibited antibacterial activity against methicillin resistant *Staphylococcus aureus* (MRSA) (23). Seed extract synthesized AgNPs showed antiviral activity in Vero cells infected with dengue serotype DEN-2. In addition, AgNPs were found highly effective against its vector *Aedes aegypti*, in both larval and pupal stages (24). This research group also synthesized carbon nanoparticles along with AgNPs. These NPs could show larvicidal and pupicidal activity against another vector *Culex quinquefasciatus* responsible for filariasis (25). A nanocomposite of seed polysaccharide and AgNPs have shown excellent properties as wound dressing material promoted wound contraction and internal tissue growth (26). Thin nanosheets of zinc nanoparticles from seed extract find its utility in spectrum of applications, including energy devices and nanofluids seeds (27). When AgNPs were synthesized using MO stem bark, it showed a cytotoxic effect on HeLa cell lines via oxidative damage that resulted into induction of apoptosis and inhibiting cell replication (28).



**Figure 2:** Different Plant Parts of *Moringa oleifera* Utilized for Biosynthesis

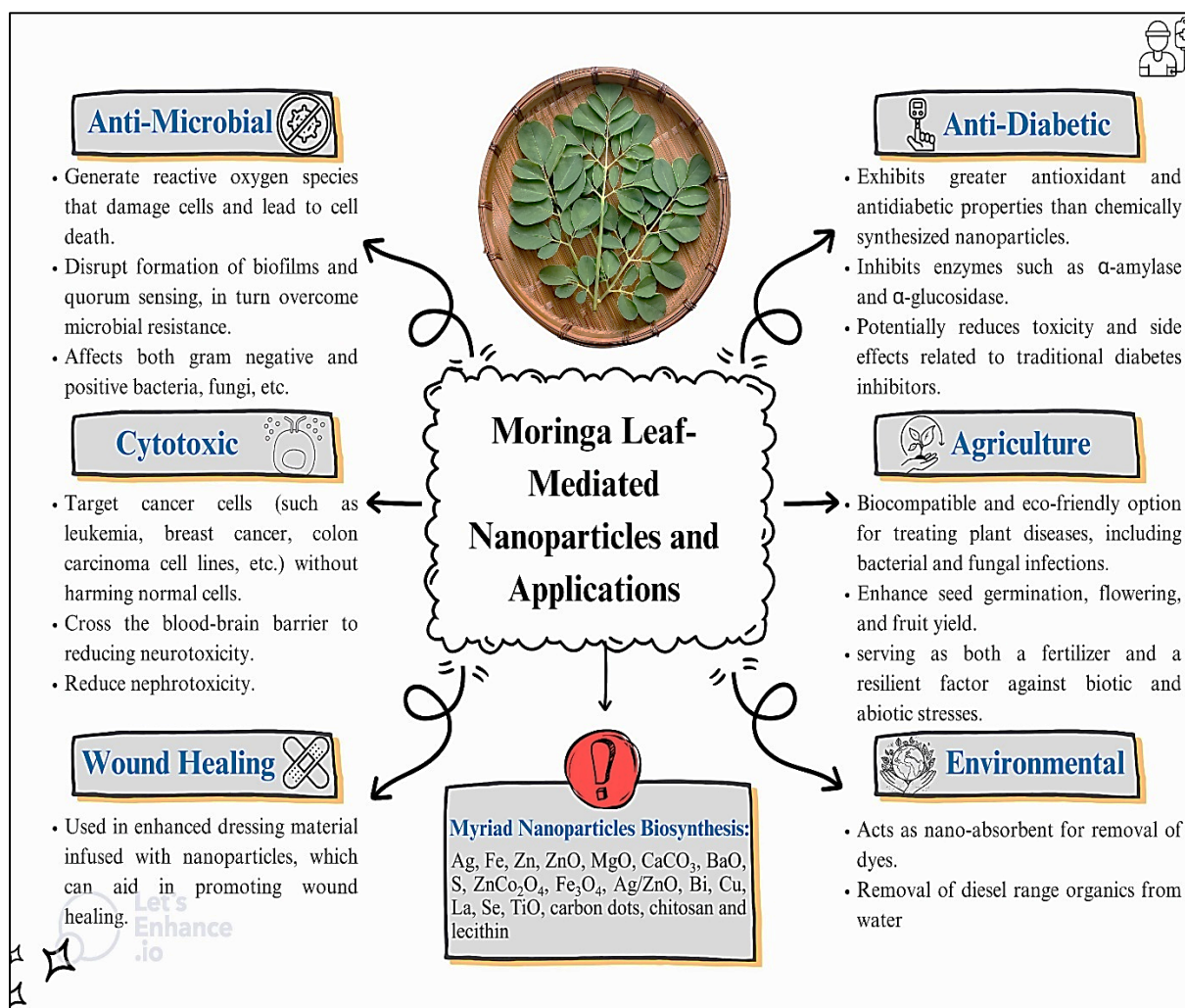
### ***Moringa* Leaves: A Widely Explored Plant Part for Nano-Biosynthesis**

Leaves of *Moringa* being edible can be consumed directly as a food. Its powder is available commercially in the form of tablets or leaf tea mixture providing a good nutritional supplement. Aqueous and ethanolic extracts of leaves have been studied for mapping range of phytochemicals.

Flavonoids, polyphenols, steroids, tannins, saponins, carbohydrates, alkaloid, and amino acids are present in varying amounts depending on the extraction procedure (29). Therapeutic nature of these biomolecules attribute anticancer, anti-inflammatory, antidiabetic, and antioxidant properties to the leaves. These bio-reductants acts as capping agents facilitating synthesis of various types of nanoparticles. Their abundance, accessibility, rich phytonutrient content and eco-friendliness makes *Moringa* leaves a promising

candidate and used widely in nanobiotechnology as compared to other plant parts (Figure 3). Bolade and group have presented a thorough analytical data based on Fourier-transform infrared and gas chromatography analysis on MO leaf extracts along with three other plants (*Azadirachta indica*, *Canna indica*, *Magnifera indica*). These datasets provide valuable information on bioactive components and their applications in nano-biosynthesis. Among phenolics, cannabidiol and 4-hydroxy-bezoic acid were present in abundant quantity in MO leaf extracts (30). Leaves being rich source of phytonutrients have been exploited by researchers to make myriad metal, metal oxide and other nanoparticles. *Moringa* leaves contain a plethora of bioactive compounds that can be used to

synthesize various types of nanoparticles, including metallic (e.g., silver, gold), semiconductor (e.g., zinc oxide), and polymer nanoparticles. It is a fast-growing, drought-tolerant tree that can be cultivated easily. Using *Moringa* extracts for nanoparticle synthesis is cost-effective and environmentally friendly, reducing hazardous waste and pollution. *Moringa*-mediated nanoparticles are biocompatible, non-toxic, and often exhibit improved properties, such as increased stability, controlled release, and enhanced therapeutic efficacy making them suitable for biomedical applications. *Moringa oleifera* is a sustainable and renewable source of nanoparticles.



**Figure 3: Moringa Leaf as a Nano-Biosynthetic Source and their Myriad Applications**

### Metal Nanoparticles

Bacterial infections in plants affect growth, fruit quality and overall crop yield that ultimately linked to economic losses. Biogenic silver

nanoparticles have been studied in this respect to mitigate these infections. Aqueous leaf extracts mediated synthesis of AgNPs of size around 74nm were studied in developing a formulation for plant

disease management. These NPs were demonstrated as a biocompatible and environmentally benign alternative to treat a plant disease Huanglongbing, in Kinnow plants. Dosage variation and studying different biochemical parameters of plant have shown promising results. 75 mg/L AgNPs were found to be most effective concentration that improved the plants' physiological status as carotenoid content, fruit weight, peel diameter, total sugar, and total soluble solids (31). Bacterial Canker disease management using AgNPs in Tomato plant was also shown better performance. Foliar application of AgNPs improved morphological, biochemical, and physiological parameters in plants. 30 ppm concentration of AgNPs was found to be optimum, that decreased the disease severity index (32). Although spherical shape is the most common, a dendritic AgNPs was synthesized by changing concentration of extract and addition of copper ions during the reaction. Dendritic AgNPs formed were of size ~300nm while spherical AgNPs were of ~100nm. Utilizing greener approach in synthesizing a nanomaterial of different morphologies and their ability to degrade dye, antimicrobial potential was studied. Comparatively, dendritic AgNPs performed better as against spherical NPs suggestive of influence of shapes in activity (33). Apart from bacterial diseases, fungal infections are also responsible for the crop losses affecting productivity in agriculture sector. Chemical pesticides may be effective control agents, affect soil health and beneficial microorganism badly. Leaf and flower-mediated AgNPs found inhibitory to the fungal plant pathogen *Pestalotiopsis mangiferae* which was isolated from coconut palm (34). A protection during ultraviolet exposure via fabrics could provide additional safeguard measure. Composites of cellulosic fabric was developed by using aqueous and ethanolic extracts of *Moringa* leaves. Addition of biogenic AgNPs to the fabric further improved mechanical properties, giving better ultraviolet protection. This group also noted that, pH and extraction method could be the driving factor influencing biosynthesis and size of NPs (35). Zinc is an important micronutrient and addition of zinc during agriculture practices could improve its content in food. For fortification, zinc nanoparticles (ZnNPs) were synthesized as hexagonal crystals of 23.69 nm size. Parameters

such as seed germination, plant height and biomass content in amaranth were observed after foliar application of NPs. Zinc content and its efficiency was found optimum at 10ppm under the study, which could be developed into spray for large scale use (36). Ethanolic leaf extract was used to develop a nano-absorbent in another report. A zerovalent iron particles was employed for removal of diesel range organics from water that cause environmental concerns due to oil spillage (37). Metal NPs such as silver, zinc, and iron from aqueous or ethanolic leaf extracts find its potential in plant disease management, as nano fertilizers, in functional fabrics protecting from UV exposure, for water treatment.

#### **Metal oxide Nanoparticles**

The oxides of zinc, magnesium, calcium have been studied in agriculture to promote plant growth, mineral content in fruits and improvement in germination potential of seeds. Zinc oxide NPs when applied directly to soil had amended flowering and in turn number of fruits. The optimum concentration was reported to be 25ppm for tomato plants. Foliar application had influenced sodium, magnesium, and calcium mineral content of fruits. These act as nano fertilizers, work in lesser quantity which may lead to reduction in traditional use of fertilizers (38). In another study (39), Zinc oxide NPs revived the seed germination potential that have been hampered due to aging process. This proves to be a good technique to prevent losses caused due to low germination rate in agriculture. Up-regulation in antioxidants, cell cycle regulatory genes, and aquaporins when NPs applied within permissible amounts, improve overall crop yield of *Cajanus cajan* seeds (39). Moreover, magnesium oxide (MgO) and calcium carbonate NPs could be advised as a nano-fertilisers. They significantly enhanced groundnut production via growing biomass following weekly foliar application of MgO and calcium carbonate nanoparticles. 50mg/L of MgO and 100mg/L calcium carbonate is optimized concentration that affected yield and nodulation positively among several treatment groups (40). Although nutrient supplementation is important for crop development, shielding crops from various diseases is still a challenge. Spot blotch disease is caused by a fungus *Bipolaris sorokiniana* in plants which affects the quality and the yield. Biogenic titanium dioxide NPs from *Moringa* leaf

was applied in different concentration to wheat plants. It was found effective in alleviating stress due to fungal exposure to plants and improved various morphological and physiological parameter. 40mg/L was the optimum concentration for foliar spraying titanium dioxide NPs that improved biomass and chlorophyll content and overall disease resistance capacity (41). Effect of radiations on biosynthesised nanoparticles is underexplored area of research. Islam and group have taken up this study on MO leaf-mediated barium oxide NPs for evaluation of structural characteristics on gamma irradiation. Results suggested higher stability and absorption intensity for gamma radiation in NPs their potential use in gamma exposed conditions (42).

#### **Alternative Types of Nanoparticles**

Along with single element containing metal and metal oxide nanoparticles, several studies have biosynthesized bimetallic alloy NPs, heterometallic spinel, magnetite and a non-metal sulphur nanoparticle using leaf extracts. Silver and zinc oxide alloy (Ag/ Zinc oxide) nanoparticles have been synthesized using leaf extracts of *Moringa*. These NPs were subjected to wheat plant for evaluation of various morphological and physiological parametric tests. When these Ag/ Zinc oxide nanoparticles were used along with a urea fertilizer for external application, results obtained indicative of increase in chlorophyll, water content, plant weight and height. Bimetallic nature facilitated larger surface area with excellent functional quality (43). Nanoforms release micronutrients in efficient ways promoting growth of plant when compared to their bulk counter parts. Green synthesized Sulphur nanoparticles were also employed as a nano-fertilizer. These NPs had dual functional role as a fertilizer and abiotic stress resilient factor in faba beans. Sulphur NPs reduced salt stress related harmful effects on the plants by affecting oxidative stress biomarkers. Expression of stress responsive genes were upregulated in Sulphur NPs treated plant group (44). Co-precipitation method was used while preparing zinc-cobalt nanoparticles. Pomegranate peel, *Moringa* leaf, green coffee beans and *Camellia sinensis* extracts were used for this purpose. Comparative analysis of biosynthesized zinc-cobalt particles on photocatalysis of Rhodamine B was performed for potential use in water remediation. In addition, antimicrobial assessment

showed antibacterial activity against pathogenic *Bacillus* strains (45). The issue of antibiotic contamination in water bodies is addressed earlier. Magnetite (Fe<sub>3</sub>O<sub>4</sub>) nanoparticles from aqueous leaf extract was demonstrated for removal of the drug levofloxacin. These NPs had adsorbent property with size of 14.34nm and suggestive chemisorption and diffusion mechanism for removal. Multiple use of these nano-adsorbent was possible as results showed around 85% removal efficiency after four cycles (46).

### **Biomedical Applications of *Moringa* Leaves - Mediated Nanoparticles**

Biocompatibility is a prerequisite for any nanomaterial intended to use in biomedical or healthcare sector. Bio-fabrication techniques are preferred in such settings, so the researchers are trying to synthesize nanoparticles and working on their applications. Following section emphasizes, the nanoparticles as antimicrobial, anticancer, antidiabetic, antioxidant, wound healing material or their suitability for related biomedical applications.

#### **Antimicrobial and Anticancer Nanoparticles**

Emerging drug resistance has become a major concern due to improper, frequent, and illegitimate use of antibiotics. Treating infectious diseases requires alternate and effective antibiotics for its control. Antibacterial activity of silver nanoparticles from *Moringa* leaf extract was demonstrated earlier. Nano conjugated form of antibiotics levofloxacin and ciprofloxacin may reduce the use of antibiotics providing larger surface area as compared to bulk counter parts (47). Nanomaterials could disrupt formation of biofilms and quorum sensing, in turn overcome microbial resistance. Bio-assisted AgNPs from MO leaf have shown efficacy against test pathogenic bacteria by decreasing the production of prodigiosin, a red pigment linked with quorum sensing. Biofilm inhibition by affecting virulence factors have attributed their potential use in implants and other medical devices as coating agents (48). Biogenic copper and bismuth nanoparticles were also found to be effective against bacterial pathogens as well as fungal species such as *Aspergillus niger* and *Candida albicans* (49, 50). Biogenic NPs have been explored

for its anticancer potential on various cell lines. Silver nanoparticles synthesized from the leaf extract exhibited selective cytotoxicity to leukemia cell lines (Kasum-1 cells) and breast cancer cell line MCF-7. While AgNPs were found safe on normal CD4+ and HUVEC cell lines (51, 52). Cytotoxic assessment on various human cell lines (T47D, HepG2, A549, and Wi38) using biogenic metal nanoparticles such as silver, lanthanum, copper, iron, zinc was investigated. *In vitro* studies showed time and dose dependent anticancer effect that can be used as an alternative to current therapy (53).

#### *In vivo* Assessment of Nanoparticles

Insights taken from *in vitro* studies, further extended for several *in vivo* evaluation of biogenic nanoparticles making them relevant in biomedical setup. Nano extract of *Moringa* leaves and silver nanoparticles were tested against human colon carcinoma cell lines. This study was carried out further *in vivo* using chemically induced cancer rat models. Azoxymethane induced colon cancer in the animals were treated with nano extract which showed decrease in the levels of tumour and inflammatory markers. Biochemical, histopathological studies suggested reduction of the colon cancer induced chemically (54, 55). Nephrotoxicity model was developed by induction of melamine in male rats. Role of Selenium nanoparticles (SeNPs) in such condition was evaluated when administered orally for 28 days. Impaired renal function due to oxidative stress, histological alterations and resulting murine nephropathy was reduced significantly. Both leaf extract and SeNPs were found to be effective in protecting the renal function caused due to melamine toxicity (56). Rotenone is used as insect control agent as well as fungicide. Its harmful metabolites can cause toxicity in other animals. To address this issue zinc nanoparticles were tested as a potential remedy in rotenone induced neurotoxicity model. MO leaf mediated ZnNPs could cross the blood brain barrier, reduce oxidative stress, and stabilize neuronal proteins. This nano therapy regulated hypothalamus-pituitary-testicular axis by affecting acetylcholinesterase activity and other functions (57). In another study, acrylamide-associated adverse effects on reproductive health of male rats were investigated. ZnNPs were able to reduce the damage caused, by restoring cellular functions,

gene regulation and histopathological changes. These NPs also improved steroidogenesis and sex hormones by suppressing oxidative stress (58). Further mechanism of action of biogenic ZnNPs were deciphered by a group of researchers that affected expression of miRNAs. MiRNA profiling of rats after exposure to acrylic amide suggested downregulation of 223-3 P and 325-3 P miRNAs which are associated with inflammatory pathways in lung tissues. Nanoparticles treatment could elevate the levels of these miRNAs, reduce inflammation, and pulmonary fibrosis (59). A comparative study on both chemically synthesized and *Moringa* leaf-mediated ZnNPs highlighted the hepatoprotective role. Biosynthesized NPs could restore normal liver and kidney function efficiently in Wistar Albino male rats exposed to carbon tetrachloride (60). Biomolecular fraction of MO entrapped in biodegradable polycaprolactone polymer as a nano-delivery system. *In vitro* photothermal transduction efficacy against retinoblastoma cell lines was evaluated, this nano delivery system could to inhibit the heat shock response in these cell lines (61).

#### **Antidiabetic, Antioxidant, and Wound healing Nanoparticles**

The research aims to evaluate the  $\alpha$ -amylase and  $\alpha$ -glucosidase activities of ZnNPs produced from natural sources, offering a potential reduction in the toxicity and side effects associated with traditional diabetes inhibitors. ZnNPs nanoparticles synthesized using MO leave extract demonstrated higher antioxidant and antidiabetic properties in comparison with chemically synthesized NPs (62). Biosynthesis of SeNPs was carried out using leaf extract by varying parameters for obtaining optimum conditions. There spherical SeNPs with size of 20–250 nm, had antioxidant and antidiabetic activities evident from inhibition of enzymes  $\alpha$  amylase and  $\alpha$  glucosidase (63). The therapeutic effect of the leaf nanoparticles was evaluated based on *in vitro* anti diabetic assays and cytotoxicity assay on MCF-7 and HepG-2. A profound therapeutic efficacy of MO leaf nanoparticles suggest treatment using nano formulation than the *Moringa* leaf extract (64). Wounds may result from various pathophysiologic factors, infections, surgeries, or trauma caused due to accidents. Managing wounds is critical in preventing nosocomial infections in hospital settings. Biosynthesized titanium dioxide



nanoparticles using *Moringa* leaves extract was evaluated in excision wound rat models for its wound healing capacity. Results revealed the better closure to nanosized titanium dioxide particles than microsized particles (65). An improved dressing material containing bacterial cellulose (BC) impregnated with biogenic AgNPs was developed. It could inhibit bacterial pathogens *Staphylococcus aureus* and *Pseudomonas aeruginosa* with at 1.25 mg/mL as minimum inhibitory concentration. BC-AgNP composite had good holding efficiency could be further evaluated for detailed study (66).

### **Nanoparticles in other Biomedical**

#### **Applications**

Metal and metal oxide nanoparticles are commonly synthesized nanomaterials using plant extracts especially *Moringa* leaves as evident from present article. Leaf-mediated synthesis of carbon dots showed excellent antioxidant, anti-inflammatory, hypoglycemic, and antibacterial properties. To best of our knowledge there is a single report on carbon dots as a potential nanomaterial for biomedical technologies (67). *Moringa oleifera* leaf extract loaded in starch-bovine serum albumin hydrogel nanoparticles had shown hepatoprotective activity in Bisphenol induced toxicity rat models. This study reveals the protective role of these hydrogels from environmental exposure to such toxic chemicals (68). Dental restorative procedures make use of adhesive compounds such as glass ionomer cement. Addition of biogenic hydroxyapatite nanoparticles enhanced mechanical compressive strength and biocompatibility of glass ionomer cement (69). Improved dentin remineralization was observed when samples were photoactivated along with *Moringa* extract (70). A study on, chitosan and lecithin nanoparticles synthesized using ethanolic *Moringa* leaves extract showed anti-otomycotic activity. Promising results *in vitro* on pathogenic fungi further led to clinical trial with patients having ear infection. They show improvement in the condition and may hold an important future place in Otolaryngology (71). Some research suggests other applications of biogenic AgNPs in the development of herbal hand sanitizer (72), whereas Zinc nanoparticles for anti-acne purposes (73).

### **Mode of Action**

Myriad nanoparticles mediated by *Moringa* and their applications are discussed in the above sections. Phytochemicals such as flavonoids, phenolic acids like gallic acid, salicylic, illicic acid, and ferulic acid etc. are found in *Moringa* leaves. These metabolites act as electron donors to reduce the metal ions and provide capping facilitating nucleation reaction while biosynthesis. Role of polyphenols responsible for aggregation, stabilization via redox reaction during synthesis is also accounted (16). Efforts have been made by many researchers to find out the mechanism by which these nanoparticles act in carrying out several functions. Reduction in cancer progression by decreasing the expression of TNF- $\alpha$ , HSP27, and IL-10 after treating the rats with *Moringa* nanoparticles was reported (74). Cytotoxicity towards leukemia cell line (Kasumi-1) was due to cell cycle arrest and upregulation of proapoptotic proteins thereby inducing apoptosis (51). Altering acetylcholinesterase activity and by regulating oxidative stress, biogenic zinc-oxide nanoparticles reduced rotenone induced neuroendocrine toxicity (57). Toxicity caused due cadmium stress in linseed was alleviated by synergistic application of ZnNPs and *M. oleifera* leaf extract. Substantial increase in the enzymatic activity of several antioxidant enzymes such as superoxide dismutase, peroxidase, catalase, and ascorbate peroxidase were noted (75). Aging in seed affects germination efficiency which was restored by leaf-mediated ZnNPs. Administration of biogenic NPs could maintain cellular redox homeostasis, hormonal signalling and prevented alteration in expression patterns of cell cycle regulatory genes (39). Removal of pollutants such as chromium was possible due to presence of cationic protein in extract as biosorbent, while other dyes might be due to electrostatic interaction and reduction process. Breakage of azo-bond, deamination found to be associated with copper NPs mediated dye degradation (76). Phytochemicals in the plant extracts leading to the reduction of Fe<sup>2+</sup> ions to Fe<sup>0</sup> atoms thereby stabilizing the synthesized zerovalent iron nanoparticles. They oxidise wide range of organics in presence of dissolved oxygen, could be used as a decontamination agent.

### **Future Viewpoints**

Nanomaterials made up from biological sources have gained a front seat in the biomedical research.

Number of biomolecules present in them with varying compositions impart unique features to the nanoparticles thereby increasing their applicability. Especially plants, among all the biological sources have the great capacity for synthesizing biomolecules in the form of primary and secondary metabolites. This makes them a candidate of choice for biosynthesis. *Moringa oleifera* a long known medicinal herb has the intrinsic ability to treat certain health conditions and used as a food for its nutritional value. Bioactive compounds present in them act as capping and reducing agents imparting additional properties to the nanomaterials. Silver nanoparticles are synthesized most followed by other metal nanoparticles. Biomedical applications of these nanoparticles range from being antibacterial, antifungal, antioxidants to hepatoprotective, neuroprotective and nephroprotective. Several NPs could be excellent coating materials for implants, wound dressings, acts as dental restorative material by changing mechanical properties promoting tissue growth. Although plant extract improve biocompatibility of nanoparticles are associated with certain issues. Potential of *Moringa*-leaf mediated nanoparticles could be explored in the drug delivery applications. Mechanistic pathways affecting cellular function could be taken up by the experts to further deepen the knowledge in this regard. Metallic nanoparticles synthesized extensively using *Moringa* for their antibacterial, biocompatible and antioxidant properties. This review provides extensive breadth of nanoparticle biosynthesis using *Moringa* leaves, further studies on NPs may be taken up for sensing applications and nano fortification. Energy sector is less explored area when it comes to *Moringa* mediated nanoparticles. In addition, a comparative analysis of different plant parts as a biosynthetic source is lacking. This may provide future cues to choose a plant part according the application under the study. Since most reports suggest nontoxic and biocompatible nature of these nanoparticles, certain studies have shown toxic effect of AgNPs in fishes (*Oreochromis niloticus*). At the same time SeNPs from *Moringa* could reduce the toxicity caused due to AgNPs exposure by restoring oxidative balance (77). *Moringa* leaves mediated zinc nanoparticles reduce the level of cadmium accumulation in linseed plants, ultimately minimizing the chance of

oxidative stress. It protected photosynthesis, increased concentration of zinc by reducing damage due to cadmium stress. This approach could be a more environmentally friendly way to replace traditional techniques used to reduce Cd levels in plants and, eventually, in humans (75).

## Conclusion

In conclusion, *Moringa* leaf holds a great potential as a cost effective biocompatible, cheap biosynthetic precursor for scale up purposes in healthcare and other sectors. *Moringa oleifera*'s abundance, making it a sustainable and renewable source of nanoparticles that help reduce the generation of hazardous waste and pollution associated with conventional nanoparticle production. Ability to produce diverse nanoparticles with enhanced properties make it a highly efficacious alternative for nanoparticles of biomedical relevance.

## Abbreviations

Iron: Fe, Magnesium oxide: MgO, Magnetite: Fe<sub>3</sub>O<sub>4</sub>, Methicillin Resistant *Staphylococcus aureus*: MRSA, *Moringa oleifera*: MO, Nanoparticles: NPs, Selenium nanoparticles: SeNPs, Silver nanoparticles: AgNPs, Ultra violet: UV, Zinc nanoparticles: ZnNPs.

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## Author Contributions

Tahsin Bennur: conceptualization, writing - review and editing, resources. Nutan Bankar: initial draft, resources. Mohammed Saif: initial draft, figures. Insha Suleman: figures editing.

## Conflict of Interest

All the authors agree to the present manuscript for publication and declare no conflict of interest.

## Ethics Approval

Not applicable.

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