Nano formulations Of Moringa Oleifera Phytoconstituents: Current Advances and Future Prospects

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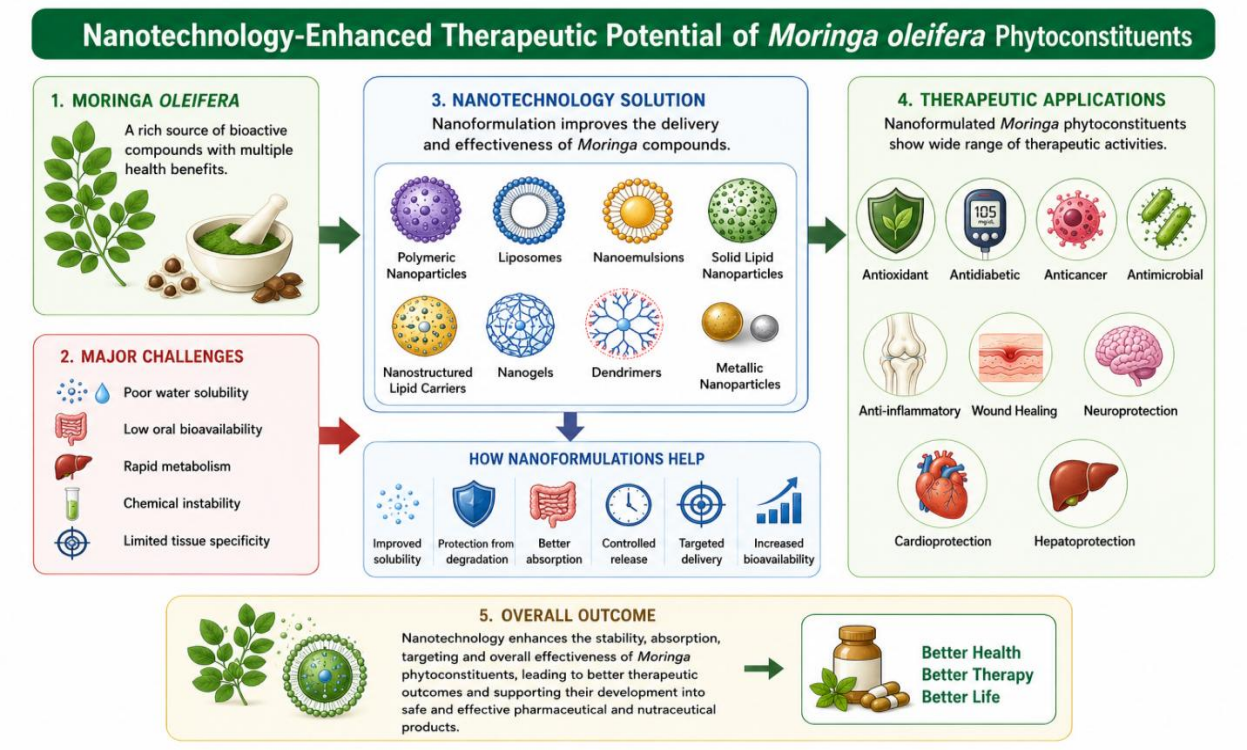
Fig.1 Graphical Abstract



***Abstract*—Moringa oleifera Lam. is a nutritionally and pharmacologically important medicinal plant widely recognized for its diverse therapeutic potential. Different parts of the plant, including leaves, seeds, flowers, pods, bark, and roots, contain numerous bioactive phytoconstituents such as flavonoids, phenolic acids, glucosinolates, alkaloids, tannins, saponins, carotenoids, vitamins, and minerals. These compounds possess antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer, hepatoprotective, cardioprotective, neuroprotective, and wound-healing properties. However, their clinical application is often restricted by poor aqueous solubility, low bioavailability, rapid metabolism, and chemical instability.**

Nanotechnology-based drug delivery systems have emerged as effective approaches to overcome these limitations by enhancing solubility, protecting phytochemicals from degradation, improving absorption, enabling controlled release, and facilitating targeted delivery. Various nanoformulations, including polymeric nanoparticles, liposomes, phytosomes, nanoemulsions, solid lipid nanoparticles, nanostructured lipid carriers, nanogels, dendrimers, and green-synthesized metallic nanoparticles, have demonstrated improved therapeutic performance of M. oleifera phytoconstituents. This review summarizes the phytochemical composition, nanoformulation strategies, therapeutic applications, recent advances, current challenges, and future prospects of nano-enabled M. oleifera, highlighting its potential for developing effective pharmaceutical and nutraceutical products.

***Index Terms*—Moringa oleifera; Nanotechnology; Nanoformulations; Phytoconstituents; Polymeric nanoparticles; Liposomes; Nanoemulsion; Drug delivery; Herbal therapeutics; Bioavailability.**

I. INTRODUCTION

Medicinal plants remain an essential source of therapeutic agents for the prevention and treatment of numerous acute and chronic diseases. According to the World Health Organization (WHO), nearly 80% of the global population depends partially on traditional herbal medicines for primary healthcare, particularly in developing countries where medicinal plants are readily available and economically affordable [1]. The growing interest in plant-derived therapeutics has stimulated extensive scientific research aimed at identifying bioactive phytochemicals with improved efficacy and safety profiles.

Among medicinal plants, Moringa oleifera Lam., belonging to the family Moringaceae, has gained remarkable scientific attention owing to its outstanding nutritional composition and diverse pharmacological activities [2]. Commonly known as the drumstick tree, horseradish tree, or miracle tree, M. oleifera is native to the Indian subcontinent but is now cultivated widely across Asia, Africa, South America, and other tropical and subtropical regions because of its rapid growth, drought tolerance, and nutritional importance [3].

Almost every part of M. oleifera possesses medicinal value. The leaves are particularly rich in proteins, essential amino acids, vitamins, minerals, carotenoids, flavonoids, and phenolic compounds. Seeds contain proteins, fixed oils, glucosinolates, and antimicrobial peptides, whereas flowers, bark, roots, and pods contain numerous secondary metabolites that contribute to the plant's therapeutic properties [4,5].

Phytochemical investigations have identified a broad range of biologically active constituents, including quercetin, kaempferol, rutin, chlorogenic acid, caffeic acid, ferulic acid, gallic acid, niazimicin, glucomoringin, benzyl isothiocyanate, β-sitosterol, saponins, tannins, alkaloids, tocopherols, carotenoids, and ascorbic acid [6,7]. These phytoconstituents exert multiple biological effects through antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer, hepatoprotective, nephroprotective, cardioprotective, neuroprotective, immunomodulatory, and wound-healing mechanisms [8].

Despite these promising pharmacological activities, many phytoconstituents suffer from poor aqueous solubility, low membrane permeability, instability under physiological conditions, rapid metabolism, and limited oral bioavailability. Consequently, conventional herbal preparations often fail to achieve adequate therapeutic concentrations at the target site, reducing their overall clinical effectiveness [9].

Nanotechnology has emerged as a promising strategy to address these challenges. Nano-sized drug delivery systems generally ranging from 10 to 1000 nm improve dissolution, enhance gastrointestinal absorption, increase systemic bioavailability, protect phytochemicals from enzymatic degradation, enable controlled release, and facilitate targeted drug delivery [10]. In recent years, various nanocarriers including polymeric nanoparticles, liposomes, phytosomes, nanoemulsions, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), nanogels, dendrimers, and metallic nanoparticles have been successfully investigated for delivering herbal phytoconstituents with superior therapeutic performance [11,12].

The objective of this review is to critically summarize current advances in nanoformulations of M. oleifera phytoconstituents, discuss formulation strategies and therapeutic applications, highlight recent scientific developments, identify current challenges, and outline future prospects for clinical translation and commercialization.

II. BOTANICAL PROFILE OF MORINGA OLEIFERA

2.1 Taxonomy

Table 1. Botanical classification of Moringa oleifera.

Taxonomic Rank	Classification
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Brassicales
Family	Moringaceae
Genus	Moringa
Species	Moringa oleifera Lam.

2.2 The genus Moringa comprises thirteen recognized species, among which M. oleifera is the most extensively cultivated and scientifically investigated because of its nutritional richness and medicinal importance [13].

Botanical Description

M. oleifera is a fast-growing deciduous tree that typically reaches 8–12 m in height. It possesses a soft, corky bark; tripinnate leaves; fragrant cream-white flowers; elongated pendulous pods; and winged seeds. The plant is highly adaptable to arid and semi-arid climates and thrives in well-drained sandy or loamy soils [14].

III. PHYTOCHEMICAL COMPOSITION OF MORINGA OLEIFERA

The therapeutic efficacy of M. oleifera is attributed to its diverse phytochemical profile. More than one hundred bioactive compounds have been identified using chromatographic and spectroscopic techniques [15].

Table 2. Major phytoconstituents of Moringa oleifera and their reported pharmacological activities.

Phytochemical Class	Major Compounds	Principal Pharmacological Activities	References
Flavonoids	Quercetin, Kaempferol, Rutin	Antioxidant, anti-inflammatory, cardioprotective	[16,17]
Phenolic acids	Chlorogenic acid, Caffeic acid, Ferulic acid	Antioxidant, antidiabetic, antimicrobial	[18]
Glucosinolates	Glucomoringin	Chemopreventive, anti-inflammatory	[19]
Isothiocyanates	Moringin, Benzyl isothiocyanate	Anticancer, antimicrobial	[20]
Alkaloids	Moringinine, Spirochin	Antimicrobial, hypotensive	[21]
Saponins	Various triterpenoid saponins	Immunomodulatory, hypolipidemic	[22]
Tannins	Hydrolysable and condensed tannins	Antioxidant, antimicrobial	[23]
Carotenoids	β-Carotene, Lutein, Zeaxanthin	Antioxidant, eye health	[24]

3.1 Flavonoids

Flavonoids constitute one of the most abundant groups of secondary metabolites in M. oleifera. Quercetin and kaempferol are considered the major flavonoids and contribute significantly to antioxidant, anti-inflammatory, antihypertensive, and cardioprotective activities by scavenging reactive oxygen species, suppressing lipid peroxidation, and modulating inflammatory signaling pathways [16,17].

3.2 Phenolic Acids

Phenolic acids, including chlorogenic acid, caffeic acid, gallic acid, and ferulic acid, exhibit potent antioxidant and antidiabetic properties. These compounds inhibit oxidative stress, improve glucose metabolism, reduce inflammatory cytokine production, and protect cellular macromolecules from free radical-induced damage [18].

3.3 Glucosinolates and Isothiocyanates

M. oleifera is distinguished from many medicinal plants by its high content of glucosinolates and their hydrolysis products, particularly glucomoringin and moringin. These sulfur-containing phytochemicals exhibit chemopreventive, antimicrobial, anti-inflammatory, and anticancer activities through activation of cytoprotective enzymes, induction of apoptosis, and modulation of multiple signaling pathways [19,20].

Fig.2 Classification of the major phytoconstituents present in different parts of Moringa oleifera and their representative compounds [15–24].

IV. LIMITATIONS OF CONVENTIONAL MORINGA OLEIFERA PHYTOCONSTITUENTS

Although Moringa oleifera contains numerous pharmacologically active phytochemicals, their therapeutic application is often restricted by unfavorable physicochemical and pharmacokinetic characteristics. Many flavonoids, phenolic compounds, and isothiocyanates exhibit poor aqueous solubility, limited permeability across biological membranes, chemical instability, rapid metabolism, and extensive first-pass hepatic elimination, resulting in reduced systemic bioavailability [25,26].

Major challenges associated with conventional M. oleifera formulations include:

- Poor water solubility of hydrophobic phytoconstituents
- Low oral bioavailability
- Instability under gastrointestinal conditions
- Rapid enzymatic degradation
- Poor penetration into target tissues
- Short biological half-life
- Variable absorption due to plant matrix composition
- Lack of controlled and sustained drug release

Nanotechnology-based delivery systems have emerged as effective pharmaceutical approaches to overcome these barriers and improve therapeutic outcomes [27].

V. NANOFORMULATIONS OF MORINGA OLEIFERA PHYTOCONSTITUENTS

Nanotechnology involves the development of delivery systems with particle sizes generally ranging from 10–1000 nm. Encapsulation of herbal phytoconstituents into nanocarriers enhances their physicochemical stability, aqueous solubility, dissolution rate, intestinal permeability, cellular uptake, circulation time, and therapeutic efficacy while minimizing systemic toxicity [28].

Different nanoformulation strategies have been successfully investigated for M. oleifera phytoconstituents.

5.1 Polymeric Nanoparticles

Polymeric nanoparticles are among the most extensively investigated nanocarriers for herbal drug delivery. They are commonly prepared using biodegradable polymers such as poly (lactic-co-glycolic acid) (PLGA), chitosan, alginate, gelatin, and polycaprolactone [29].

Advantages
- Protection against degradation
- Sustained drug release
- Improved oral bioavailability
- Enhanced cellular uptake
- Better pharmacokinetic profile
- Reduced dosing frequency

Encapsulation of M. oleifera leaf extract in PLGA and chitosan nanoparticles has demonstrated enhanced antioxidant activity, improved antimicrobial efficacy, and greater cytoprotective effects compared with crude extracts [30].

5.2 Liposomes

Liposomes are phospholipid vesicles composed of one or more lipid bilayers capable of encapsulating both hydrophilic and lipophilic phytochemicals [31].

Advantages
- Excellent biocompatibility
- Reduced toxicity
- Improved drug stability
- Enhanced intracellular delivery
- Target-specific accumulation
- Controlled drug release

Liposomal formulations containing M. oleifera flavonoids have shown increased antioxidant capacity and prolonged systemic circulation in experimental studies [32].

5.3 Nanoemulsions

Nanoemulsions are thermodynamically or kinetically stable colloidal dispersions with droplet sizes generally between 20 and 200 nm [33].

Advantages
- High solubilization capacity
- Improved gastrointestinal absorption
- Enhanced oral bioavailability
- Greater physical stability
- Ease of large-scale production

Nanoemulsions prepared from M. oleifera seed oil have demonstrated improved antimicrobial, anti-inflammatory, and antioxidant activities due to increased surface area and enhanced absorption [34].

5.4 Solid Lipid Nanoparticles (SLNs)

Solid lipid nanoparticles consist of physiologically compatible lipids that remain solid at room and body temperature [35].

Advantages
- Excellent stability
- Controlled release
- Protection from oxidation
- High drug loading
- Improved patient compliance

SLNs encapsulating M. oleifera bioactive compounds have shown improved storage stability and sustained release compared with conventional herbal formulations [36].

5.5 Nanostructured Lipid Carriers (NLCs)

Nanostructured lipid carriers are considered second-generation lipid nanoparticles containing a combination of solid and liquid lipids [37].

Advantages include:
- Higher drug loading
- Reduced drug leakage
- Enhanced stability
- Controlled release
- Improved skin permeation

NLCs have shown promise for topical delivery of M. oleifera phytochemicals in wound healing and inflammatory skin disorders [38].

5.6 Phytosomes

Phytosomes are phospholipid complexes formed by binding plant phytoconstituents with phosphatidylcholine, thereby improving membrane permeability and oral absorption [39].

Compared with conventional extracts, phytosomal formulations exhibit:
- Higher oral bioavailability
- Better gastrointestinal absorption
- Increased plasma concentration
- Improved antioxidant activity
- Enhanced therapeutic efficacy

Phytosomes are particularly suitable for delivering polyphenolic compounds such as quercetin and chlorogenic acid present in M. oleifera leaves [40].

5.7 Nanogels

Nanogels are three-dimensional cross-linked polymeric networks capable of absorbing large amounts of water while providing controlled drug release [41].

Applications include:

- Wound healing
- Burn management
- Topical antimicrobial therapy
- Transdermal drug delivery

M. oleifera-loaded nanogels have demonstrated enhanced wound contraction, collagen synthesis, antimicrobial activity, and faster epithelialization in preclinical studies [42].

5.8 Green-Synthesized Metallic Nanoparticles

One of the most rapidly expanding areas of research involves the green synthesis of metallic nanoparticles using M. oleifera extracts as reducing and stabilizing agents [43].

Common nanoparticles include:

- Silver nanoparticles (AgNPs)
- Gold nanoparticles (AuNPs)
- Zinc oxide nanoparticles (ZnO NPs)
- Iron oxide nanoparticles
- Copper oxide nanoparticles

These nanoparticles exhibit remarkable antimicrobial, anticancer, antioxidant, and catalytic activities while avoiding hazardous chemicals associated with conventional synthesis methods [44].

Table 3. Nanoformulations investigated for Moringa oleifera phytoconstituents.

Nanoformulation	Major Components	Major Advantages	Therapeutic Applications	References
Polymeric nanoparticles	PLGA, Chitosan	Sustained release, stability	Antioxidant, antimicrobial	[29,30]
Liposomes	Phospholipids	Biocompatibility, targeted delivery	Anti-inflammatory	[31,32]
Nanoemulsions	Oil-water systems	Improved bioavailability	Antimicrobial	[33,34]
Solid lipid nanoparticles	Solid lipids	Controlled release	Oral delivery	[35,36]
Nanostructured lipid carriers	Solid + liquid lipids	High drug loading	Topical therapy	[37,38]
Phytosomes	Phosphatidylcholine complexes	Improved absorption	Polyphenol delivery	[39,40]
Nanogels	Cross-linked polymers	Moist wound environment	Wound healing	[41,42]
Metallic nanoparticles	Ag, Au, ZnO	Green synthesis, multifunctionality	Anticancer, antimicrobial	[43,44]

VI. CHARACTERIZATION OF NANOFORMULATIONS

Successful development of nanoformulations requires comprehensive physicochemical characterization to ensure stability, reproducibility, and therapeutic performance [45].

Table 4. Common characterization techniques include

Parameter	Technique
Particle size	Dynamic Light Scattering (DLS)
Surface charge	Zeta potential analysis
Morphology	SEM, TEM
Crystallinity	X-ray Diffraction (XRD)
Functional groups	FTIR spectroscopy
Thermal behavior	DSC
Drug loading	UV-Visible spectroscopy / HPLC
Entrapment efficiency	HPLC / Centrifugation
In vitro drug release	Dialysis method

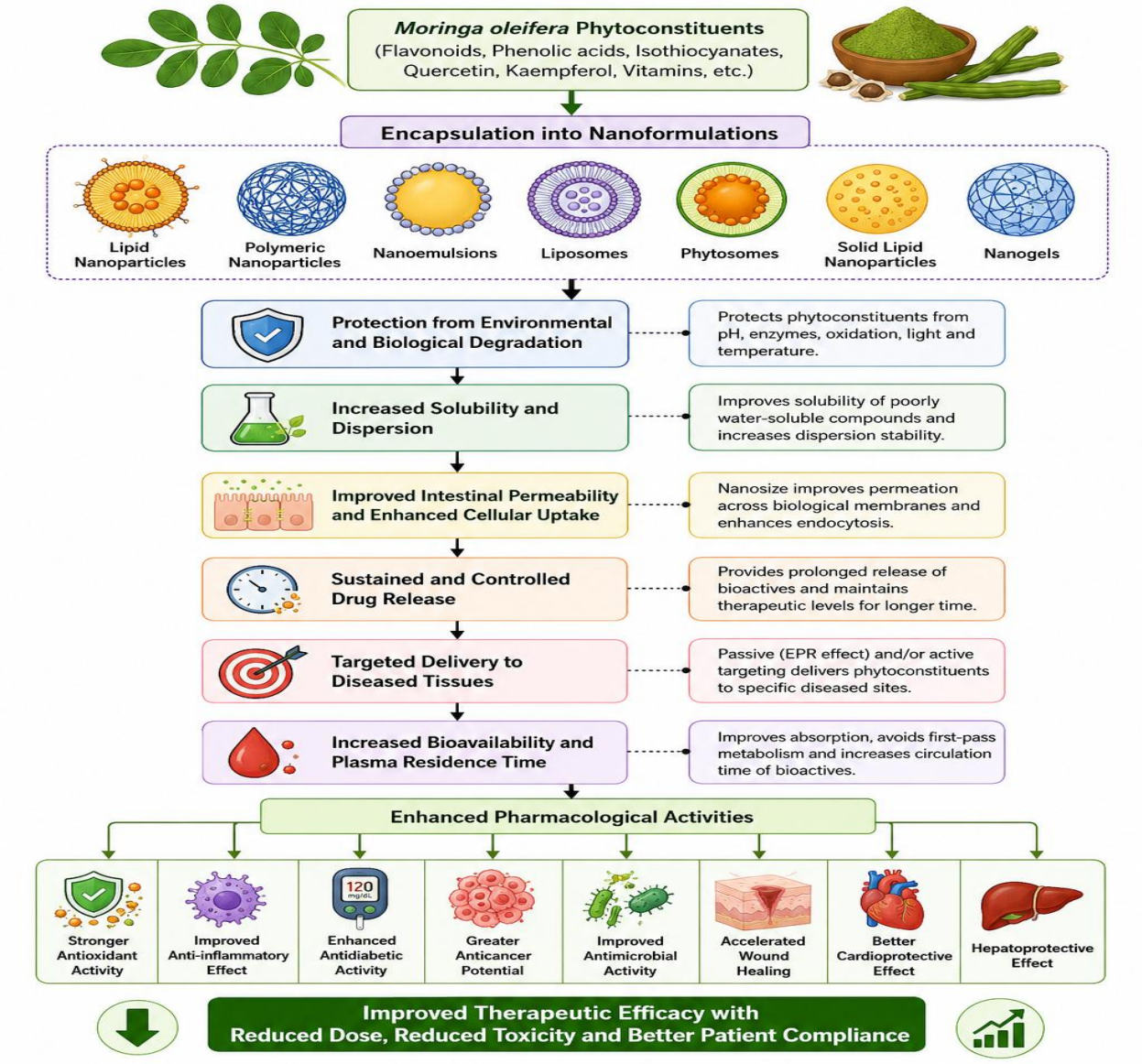


Fig.3 Schematic illustration showing how nano-formulation strategies improve the pharmacokinetic and pharmacodynamic performance of Moringa oleifera phytoconstituents [27,45].

VII. PHARMACOLOGICAL APPLICATIONS OF MORINGA OLEIFERA NANOFORMULATIONS

7.1 Antioxidant Activity

Nanoencapsulation significantly enhances the antioxidant activity of M. oleifera phytoconstituents by increasing their stability and improving intracellular delivery. Polymeric nanoparticles and liposomal formulations demonstrate greater free radical scavenging activity than conventional extracts due to enhanced bioavailability and sustained release [46].

7.2 Antidiabetic Activity

Nanoformulations improve the oral absorption of flavonoids and phenolic acids, resulting in enhanced glucose uptake, inhibition of α-amylase and α-glucosidase enzymes, improved insulin sensitivity, and reduced oxidative stress associated with diabetes mellitus [47].

7.3 Anticancer Activity

Cancer remains one of the leading causes of mortality worldwide, and the search for safer, more effective therapeutic agents continues to be an important area of

research. Numerous phytochemicals present in Moringa oleifera, particularly quercetin, kaempferol, niazimicin, benzyl isothiocyanate, glucomoringin, chlorogenic acid, and other phenolic compounds, have demonstrated significant anticancer activity through multiple molecular mechanisms [48].

These bioactive constituents suppress tumor growth by:

- Inducing apoptosis through activation of caspase-3 and caspase-9
- Arresting the cell cycle at G1/S or G2/M phases
- Inhibiting angiogenesis
- Reducing oxidative stress
- Suppressing inflammatory signaling pathways
- Modulating NF-κB, PI3K/Akt, MAPK, and p53 pathways
- Preventing metastasis by inhibiting matrix metalloproteinases (MMPs) [49].

Nanoformulations further enhance these therapeutic effects by improving intracellular uptake, increasing circulation time, and enabling selective accumulation within tumor tissues via the enhanced permeability and retention (EPR) effect. Polymeric nanoparticles and liposomal formulations encapsulating M. oleifera extracts have demonstrated superior cytotoxicity against breast, colon, liver, cervical, and lung cancer cell lines compared with conventional extracts [50].

7.4 Antimicrobial Activity

The increasing prevalence of multidrug-resistant microorganisms has intensified the search for alternative antimicrobial agents. M. oleifera exhibits broad-spectrum antibacterial, antifungal, antiviral, and antiparasitic activities due to the presence of glucosinolates, isothiocyanates, flavonoids, alkaloids, tannins, and phenolic compounds [51].

Nanoformulations significantly improve antimicrobial efficacy by:

- Increasing surface contact with microbial membranes
- Enhancing penetration into bacterial biofilms
- Sustaining drug release
- Improving intracellular delivery
- Protecting phytochemicals from degradation

Green-synthesized silver nanoparticles using M. oleifera leaf extract have shown remarkable antibacterial activity against Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae. These nanoparticles also exhibit potent antifungal activity against Candida albicans and Aspergillus species [52].

The antimicrobial mechanism involves disruption of microbial cell membranes, generation of reactive oxygen species, inhibition of DNA replication, and denaturation of essential cellular proteins [53].

7.5 Anti-inflammatory Activity

Chronic inflammation contributes to the development of diabetes, cardiovascular diseases, arthritis, neurodegenerative disorders, and cancer. Bioactive compounds from M. oleifera suppress inflammatory responses through multiple signaling pathways [54].

Major anti-inflammatory mechanisms include:

- Inhibition of cyclooxygenase (COX-2)
- Suppression of inducible nitric oxide synthase (iNOS)
- Downregulation of TNF-α
- Reduction of IL-1β and IL-6 production
- Inhibition of NF-κB activation
- Decreased prostaglandin synthesis

Nanoencapsulation further enhances anti-inflammatory activity by improving tissue penetration, increasing bioavailability, and providing sustained release at inflamed sites [55].

7.6 Wound-Healing Activity

M. oleifera possesses excellent wound-healing properties due to its antioxidant, antimicrobial, collagen-stimulating, and anti-inflammatory phytoconstituents [56].

Nanoformulations accelerate wound healing through:

- Enhanced fibroblast proliferation
- Increased collagen synthesis
- Improved angiogenesis
- Faster epithelialization
- Controlled release of phytochemicals
- Reduced microbial infection
- Maintenance of a moist wound environment

Nanogels, polymeric nanoparticles, and lipid-based nanocarriers containing M. oleifera extracts have demonstrated significantly improved wound contraction and shorter healing time in experimental animal models compared with conventional herbal formulations [57].

7.7 Neuroprotective Activity

Oxidative stress and neuroinflammation play major roles in neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease. The flavonoids and phenolic compounds of M. oleifera exhibit neuroprotective properties by reducing oxidative damage and improving neuronal survival [58].

Nanoformulations improve neuroprotection by:

- Enhancing blood-brain barrier penetration
- Increasing antioxidant enzyme activity
- Reducing neuronal apoptosis
- Decreasing neuroinflammation
- Improving sustained drug delivery

These findings suggest that nanoformulated M. oleifera phytoconstituents may serve as promising candidates for future neuroprotective therapies [59].

VIII. RECENT ADVANCES IN NANOFORMULATIONS OF MORINGA OLEIFERA

During the past decade, substantial progress has been achieved in the development of nano-enabled delivery systems for M. oleifera phytoconstituents. Recent investigations have focused on improving formulation stability, increasing drug-loading capacity, optimizing release kinetics, and enhancing therapeutic efficacy [60].

Major research trends include:

- Green synthesis of metallic nanoparticles using aqueous M. oleifera extracts
- Polymeric nanoparticle systems for oral delivery
- Liposomal encapsulation of flavonoids
- Phytosome-based enhancement of polyphenol bioavailability
- Nanostructured lipid carriers for topical wound-healing applications
- Nanoemulsions containing M. oleifera seed oil for antimicrobial therapy
- Smart nanocarriers with pH-responsive drug release
- Combination nanoformulations incorporating multiple phytoconstituents [61].

Several studies have reported enhanced antioxidant, antidiabetic, anticancer, antimicrobial, and wound-healing activities following nanoencapsulation compared with crude plant extracts [62].

Table 4. Recent studies on nanoformulations of Moringa oleifera phytoconstituents.

Nanoformulation	Encapsulated Material	Major Findings	References
PLGA nanoparticles	Leaf extract	Improved antioxidant activity and sustained release	[30,60]
Chitosan nanoparticles	Polyphenol-rich extract	Enhanced antimicrobial efficacy and stability	[30,61]
Liposomes	Flavonoid fraction	Increased cellular uptake and anti-inflammatory activity	[32,55]
Nanoemulsion	Seed oil	Improved oral bioavailability and antimicrobial activity	[34,62]
Solid lipid nanoparticles	Leaf phytochemicals	Controlled release and enhanced stability	[36]
Nanostructured lipid carriers	Polyphenols	Better skin penetration and wound healing	[38,57]
Silver nanoparticles	Leaf extract	Potent antibacterial and anticancer activity	[52,63]
Gold nanoparticles	Leaf extract	Enhanced biocompatibility and antioxidant activity	[64]

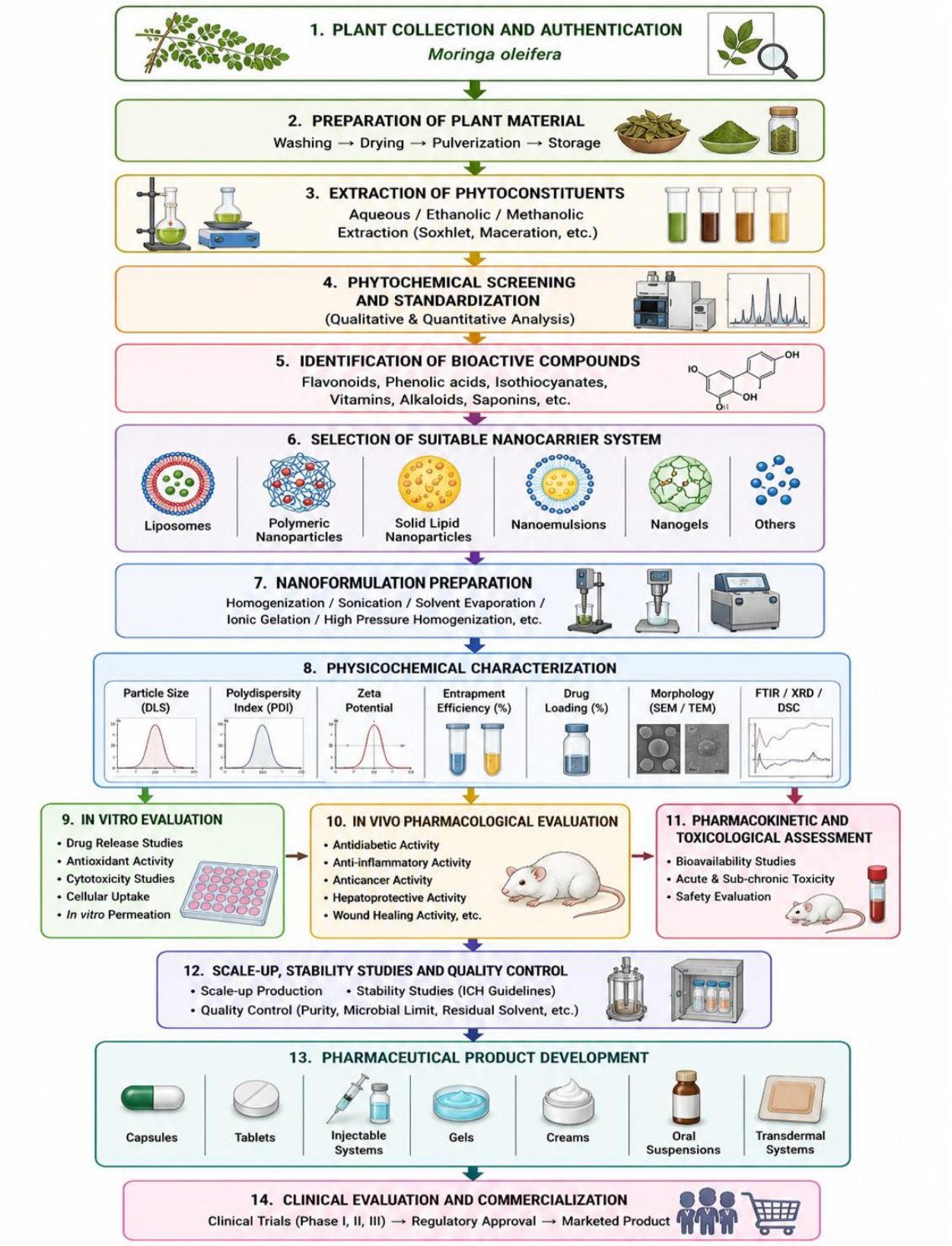


Fig.4 General workflow involved in the development of nanoformulations of Moringa oleifera phytoconstituents from plant extraction to pharmaceutical product development [45,60–64].

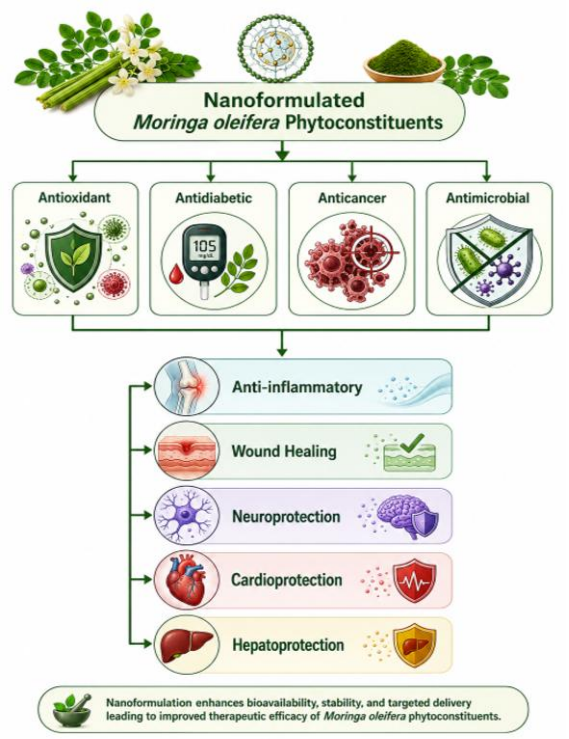


Fig.5 Major pharmacological applications reported for nano formulations of Moringa oleifera phytoconstituents [46–64].

IX. CHALLENGES AND LIMITATIONS

Despite encouraging preclinical findings, several challenges continue to limit the clinical translation of Moringa oleifera nanoformulations.

9.1 Variability in Plant Material

The phytochemical composition of M. oleifera varies with geographical location, climate, soil conditions, harvesting season, and extraction method. Such variability can influence nanoparticle loading efficiency, stability, and therapeutic efficacy [60].

9.2 Standardization Issues

Many studies use crude extracts without proper standardization of marker compounds such as quercetin, chlorogenic acid, or glucomoringin. Lack of standardization creates difficulties in reproducibility and comparison among studies [61].

9.3 Scale-Up and Manufacturing

Laboratory-scale nanoformulations may not retain identical characteristics during industrial-scale production. Factors such as particle size distribution, zeta potential, encapsulation efficiency, and batch-to-batch consistency require strict process control [62].

9.4 Safety and Toxicological Concerns

Although M. oleifera is generally regarded as safe, the long-term toxicity, biodistribution, and clearance of nanoformulations remain insufficiently investigated. Comprehensive toxicological evaluation is necessary before clinical application [63].

9.5 Regulatory Challenges

Herbal nanoformulations often fall between conventional herbal medicines and nanomedicines, creating regulatory uncertainty. Clear guidelines for quality control, safety assessment, and clinical evaluation are still evolving in many countries [64].

X. FUTURE PERSPECTIVES

Future research should focus on translating promising laboratory findings into clinically useful products.

Important future directions include:

- Standardized extracts: Development of chemically characterized extracts with defined marker compounds.
- Targeted nanocarriers: Surface-modified nanoparticles capable of targeting tumor tissues, inflamed sites, or specific organs.
- Stimuli-responsive systems: pH-, temperature-, or enzyme-responsive nanocarriers for controlled release.
- Combination therapy: Co-delivery of M. oleifera phytoconstituents with conventional drugs to achieve synergistic effects.
- Clinical studies: Well-designed human trials evaluating efficacy, pharmacokinetics, and safety.
- Nutraceutical applications: Development of nano-enabled functional foods and dietary supplements with enhanced bioavailability.
- Sustainable manufacturing: Green synthesis approaches using plant extracts as reducing and stabilizing agents for metallic nanoparticles [60–64].

Integration of nanotechnology with herbal medicine offers a promising platform for developing safer, more effective, and patient-friendly therapeutic systems.

XI. CONCLUSION

Moringa oleifera is a nutritionally rich medicinal plant containing diverse bioactive phytoconstituents, including flavonoids, phenolic acids, glucosinolates, isothiocyanates, alkaloids, tannins, and carotenoids. These compounds exhibit antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer, hepatoprotective, neuroprotective, and wound-healing activities. However, poor solubility, limited bioavailability, rapid metabolism, and instability restrict their therapeutic performance in conventional formulations.

Nanotechnology-based delivery systems such as polymeric nanoparticles, liposomes, nanoemulsions, solid lipid nanoparticles, nanostructured lipid carriers, phytosomes, nanogels, and green-synthesized metallic nanoparticles provide effective strategies to overcome these limitations. Nanoformulations improve solubility, protect phytochemicals from degradation, enhance absorption, prolong circulation time, and enable controlled and targeted delivery. Preclinical studies consistently demonstrate superior pharmacological activity for nanoformulated M. oleifera phytoconstituents compared with crude extracts.

Although several challenges remain regarding standardization, large-scale manufacturing, safety evaluation, and regulatory approval, the available evidence indicates substantial potential for the development of M. oleifera-based nanomedicines and nutraceuticals. Future research combining advanced nanocarrier design, phytochemical standardization, and clinical evaluation may facilitate successful translation from laboratory investigations to commercial pharmaceutical products.

REFERENCES

[1] Leone, A. Spada, A. Battezzati, A. Schiraldi, J. Aristil, and S. Bertoli, "Cultivation, genetic, ethnopharmacology, phytochemistry and pharmacology of *Moringa oleifera* leaves: An overview," *International Journal of Molecular Sciences*, vol. 16, no. 6, pp. 12791–12835, 2015, doi: 10.3390/ijms160612791.

[2] F. Anwar, S. Latif, M. Ashraf, and A. H. Gilani, "*Moringa oleifera*: A food plant with multiple medicinal uses," *Phytotherapy Research*, vol. 21, no. 1, pp. 17–25, 2007, doi: 10.1002/ptr.2023.

[3] L. Gopalakrishnan, K. Doriya, and D. S. Kumar, "*Moringa oleifera*: A review on nutritive importance and its medicinal application," *Food Science and Human Wellness*, vol. 5, no. 2, pp. 49–56, 2016, doi: 10.1016/j.fshw.2016.04.001.

[4] M. Vergara-Jimenez, M. M. Almatrafi, and M. L. Fernandez, "Bioactive components in *Moringa oleifera* leaves protect against chronic disease," *Antioxidants*, vol. 6, no. 4, Art. no. 91, 2017, doi: 10.3390/antiox6040091.

[5] J. W. Fahey, "*Moringa oleifera*: A review of the medical evidence for its nutritional, therapeutic, and prophylactic properties. Part 1," *Trees for Life Journal*, vol. 1, p. 5, 2005.

[6] Waterman *et al*., "Stable, water extractable isothiocyanates from *Moringa oleifera* leaves attenuate inflammation," *Phytochemistry*, vol. 103, pp. 114–122, 2014, doi: 10.1016/j.phytochem.2014.03.028.

[7] R. K. Saini, I. Sivanesan, and Y. S. Keum, "Phytochemicals of *Moringa oleifera*: A review of their nutritional, therapeutic and industrial significance," *3 Biotech*, vol. 6, Art. no. 203, 2016, doi: 10.1007/s13205-016-0526-3.

[8] N. Z. Abd Rani, K. Husain, and E. Kumolosasi, "*Moringa* genus: A review of phytochemistry and pharmacology," *Frontiers in Pharmacology*, vol. 9, Art. no. 108, 2018, doi: 10.3389/fphar.2018.00108.

[9] K. Dhakad *et al*., "Biological, nutritional and therapeutic significance of *Moringa oleifera* Lam.," *Phytotherapy Research*, vol. 33, no. 11, pp. 2870–2903, 2019, doi: 10.1002/ptr.6475.

[10] M. Lin, J. Zhang, and X. Chen, "Bioactive flavonoids in *Moringa oleifera* and their health-promoting properties," *Journal of Functional Foods*, vol. 47, pp. 469–479, 2018.

[11] M. Mbikay, "Therapeutic potential of *Moringa oleifera* leaves in chronic hyperglycemia and dyslipidemia," *Frontiers in Pharmacology*, vol. 3, Art. no. 24, 2012, doi: 10.3389/fphar.2012.00024.

[12] Tiloke, A. Phulukdaree, and A. A. Chuturgoon, "The antiproliferative effect of *Moringa oleifera* crude aqueous leaf extract on

cancerous human alveolar epithelial cells," *BMC Complementary and Alternative Medicine*, vol. 13, Art. no. 226, 2013, doi: 10.1186/1472-6882-13-226.

[13] S. J. Stohs and M. J. Hartman, "Review of the safety and efficacy of *Moringa oleifera*," *Phytotherapy Research*, vol. 29, no. 6, pp. 796–804, 2015, doi: 10.1002/ptr.5325.

[14] J. L. Rockwood, B. G. Anderson, and D. A. Casamatta, "Potential uses of *Moringa oleifera* and an examination of antibiotic efficacy conferred by *Moringa oleifera* seed and leaf extracts," *African Journal of Biotechnology*, vol. 12, no. 37, pp. 6077–6089, 2013.

[15] S. Sreelatha and P. R. Padma, "Antioxidant activity and total phenolic content of *Moringa oleifera* leaves in two stages of maturity," *Plant Foods for Human Nutrition*, vol. 64, no. 4, pp. 303–311, 2009, doi: 10.1007/s11130-009-0141-0.

[16] W. Nouman, M. T. Siddiqui, S. M. A. Basra, I. Afzal, and H. Rehman, "Enhancement of the nutritional value of *Moringa oleifera* leaves through optimized cultivation practices," *Turkish Journal of Agriculture and Forestry*, vol. 38, pp. 1–8, 2014.

[17] G. M. Chodur *et al*., "Wild and domesticated *Moringa oleifera* differ in glucosinolate content and bioactivity," *Journal of Agricultural and Food Chemistry*, vol. 66, no. 9, pp. 2263–2272, 2018.

[18] Y. Xiong *et al*., "Virucidal and immune-modulatory properties of *Moringa oleifera* bioactive compounds," *Food Chemistry*, vol. 338, Art. no. 128034, 2021.

[19] S. Bhatnagar, A. Kumar, and M. Bhatnagar, "Evaluation of antioxidant and antimicrobial activities of *Moringa oleifera* extracts," *Journal of Medicinal Plants Research*, vol. 5, no. 19, pp. 4798–4805, 2011.

[20] V. Sharma, R. Paliwal, P. Janmeda, and S. Sharma, "Renoprotective effects of *Moringa oleifera* against drug-induced nephrotoxicity: A review," *Journal of Ethnopharmacology*, vol. 142, no. 2, pp. 317–322, 2012.

[21] J. K. Patra *et al*., "Nano based drug delivery systems: Recent developments and future prospects," *Journal of Nanobiotechnology*, vol. 16, no. 1, Art. no. 71, 2018, doi: 10.1186/s12951-018-0392-8.

[22] Khan, K. Saeed, and I. Khan, "Nanoparticles: Properties, applications and toxicities," *Arabian Journal of Chemistry*, vol. 12, no. 7, pp. 908–931, 2019, doi: 10.1016/j.arabjc.2017.05.011.

[23] B. Pelaz *et al*., "Diverse applications of nanomedicine," *ACS Nano*, vol. 11, no. 3, pp. 2313–2381, 2017, doi: 10.1021/acsnano.6b06040.

[24] V. P. Torchilin, "Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery," *Nature Reviews Drug Discovery*, vol. 13, no. 11, pp. 813–827, 2014.

[25] Kumari, S. K. Yadav, and S. C. Yadav, "Biodegradable polymeric nanoparticles based drug delivery systems," *Colloids and Surfaces B: Biointerfaces*, vol. 75, no. 1, pp. 1–18, 2010.

[26] M. Danaei *et al*., "Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems," *Pharmaceutics*, vol. 10, no. 2, Art. no. 57, 2018.

[27] N. Naseri, H. Valizadeh, and P. Zakeri-Milani, "Solid lipid nanoparticles and nanostructured lipid carriers: Structure, preparation and application," *Advanced Pharmaceutical Bulletin*, vol. 5, no. 3, pp. 305–313, 2015.

[28] O. Elzoghby, "Gelatin-based nanoparticles as drug and gene delivery systems," *Journal of Controlled Release*, vol. 172, no. 3, pp. 1075–1091, 2013.

[29] Rani and A. Sharma, "Chitosan nanoparticles as promising carriers for herbal drug delivery," *International Journal of Biological Macromolecules*, vol. 183, pp. 1770–1782, 2021.

[30] S. Jain, N. Patel, and S. Lin, "Phytosome technology for herbal drug delivery: A review," *Drug Delivery and Translational Research*, vol. 10, no. 3, pp. 797–817, 2020.

[31] G. Bozzuto and A. Molinari, "Liposomes as nanomedical devices," *International Journal of Nanomedicine*, vol. 10, pp. 975–999, 2015.

[32] Akbarzadeh, R. Rezaei-Sadabady, S. Davaran, S. W. Joo, N. Zarghami, Y. Hanifehpour, *et al*., "Liposome: Classification, preparation and

applications," *Nanoscale Research Letters*, vol. 8, p. 102, 2013.

[33] J. McClements, "Nanoemulsions versus microemulsions: Terminology, differences and similarities," *Soft Matter*, vol. 8, pp. 1719–1729, 2012.

[34] Shakeel, W. Ramadan, and M. A. Ahmed, "Investigation of true nanoemulsions for transdermal drug delivery," *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, vol. 315, pp. 29–34, 2009.

[35] R. H. Müller, M. Radtke, and S. A. Wissing, "Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and pharmaceutical dermal products," *Advanced Drug Delivery Reviews*, vol. 54, Suppl. 1, pp. S131–S155, 2002.

[36] S. A. Wissing, O. Kayser, and R. H. Müller, "Solid lipid nanoparticles for parenteral drug delivery," *Advanced Drug Delivery Reviews*, vol. 56, no. 9, pp. 1257–1272, 2004.

[37] B. Souto and R. H. Müller, "Lipid nanoparticles: Effect on bioavailability and pharmacokinetic changes," in *Handbook of Experimental Pharmacology*, vol. 197, pp. 115–141, 2010.

[38] S. Ahmed, M. Ahmad, B. L. Swami, and S. Ikram, "Green synthesis of silver nanoparticles using plant extracts and their antimicrobial activities," *Journal of Advanced Research*, vol. 7, no. 1, pp. 17–28, 2016.

[39] S. Iravani, "Green synthesis of metal nanoparticles using plants," *Green Chemistry*, vol. 13, no. 10, pp. 2638–2650, 2011.

[40] Hussain, V. Sharma, M. A. Khan, *et al*., "Green synthesized metallic nanoparticles from medicinal plants and their biomedical applications," *Biomedicine & Pharmacotherapy*, vol. 158, Art. no. 114123, 2023.

[41] V. Mishra, K. K. Bansal, A. Verma, N. Yadav, S. Thakur, K. Sudhakar, *et al*., "Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems," *Pharmaceutics*, vol. 10, no. 4, p. 191, 2018.

[42] Puglia and F. Bonina, "Lipid nanoparticles as novel delivery systems for cosmetics and dermal pharmaceuticals," *Expert Opinion on Drug Delivery*, vol. 9, no. 4, pp. 429–441, 2012.

[43] Yadav, S. Suri, A. A. Choudhary, M. Sikender, Hemant, N. M. Beg, *et al*., "Novel approach: Herbal remedies and natural products in pharmaceutical science as nano drug delivery systems," *International Journal of Pharmaceutical Investigation*, vol. 1, no. 3, pp. 131–139, 2011.

[44] B. V. Bonifácio, P. B. da Silva, M. A. S. Ramos, K. M. S. Negri, T. M. Bauab, and M. Chorilli, "Nanotechnology-based drug delivery systems and herbal medicines: A review," *International Journal of Nanomedicine*, vol. 9, pp. 1–15, 2014.

[45] R. P. Singh, H. V. Gangadharappa, and K. Mruthunjaya, "Phytosome complexed herbal drug delivery system for enhanced therapeutic applications: A review," *Journal of Drug Delivery Science and Technology*, vol. 38, pp. 15–23, 2017.

[46] M. Lu, Q. Qiu, X. Luo, X. Liu, J. Sun, C. Wang, *et al*., "Phyto-phospholipid complexes (phytosomes): A novel strategy to improve the bioavailability of herbal extracts," *Drug Discovery Today*, vol. 24, no. 7, pp. 1474–1482, 2019.

[47] V. Sanna and M. Sechi, "Nanoparticle therapeutics for prostate cancer treatment," *Nanomedicine*, vol. 7, no. 7, pp. 1091–1106, 2012.

[48] P. K. Mukherjee, R. K. Harwansh, S. Bahadur, S. Banerjee, A. Kar, J. Chanda, *et al*., "Evidence-based validation of herbal medicines: Pharmacokinetic and pharmacodynamic approaches," *Phytotherapy Research*, vol. 31, no. 4, pp. 505–529, 2017.

[49] V. P. Chavda, L. K. Vora, and A. K. Pandya, "Nanoherbal medicines: A comprehensive review," *Phytomedicine Plus*, vol. 2, no. 1, Art. no. 100203, 2022.

[50] M. J. Ansari, M. N. Alomary, S. AlYahya, *et al*., "Green synthesis of metallic nanoparticles using medicinal plant extracts and their biomedical applications," *Molecules*, vol. 27, no. 17, p. 5523, 2022.

[51] M. M. Ibrahim, "Green synthesis and characterization of silver nanoparticles using *Moringa oleifera* leaf extract and evaluation of

antimicrobial activity," *Scientific Reports*, vol. 10, p. 6391, 2020.

[52] S. Moodley, S. B. N. Krishna, K. Pillay, and P. Govender, "Green synthesis of silver nanoparticles from *Moringa oleifera* leaf extracts and their antimicrobial properties," *Journal of Nanomaterials*, vol. 2018, pp. 1–8, 2018.

[53] M. E. El-Naggar and T. I. Shaheen, "Preparation and characterization of antibacterial silver nanoparticles using *Moringa oleifera* extracts," *Carbohydrate Polymers*, vol. 210, pp. 264–272, 2019.

[54] M. E. Abd El-Hack, M. Alagawany, A. S. Elrys, *et al*., "Nutritional value, medicinal applications and future perspectives of *Moringa oleifera*: A review," *South African Journal of Botany*, vol. 146, pp. 1–12, 2022.

[55] B. Falowo, F. E. Mukumbo, E. M. Idamokoro, J. M. Lorenzo, A. J. Afolayan, and V. Muchenje, "Multi-functional application of *Moringa oleifera* in nutrition and health: An overview," *Food Research International*, vol. 106, pp. 317–334, 2018.

[56] R. K. Saini and Y. S. Keum, "Bioactive compounds of *Moringa oleifera*: A review of extraction, isolation and biological activities," *Food Chemistry*, vol. 245, pp. 502–515, 2018.

[57] S. Kumar and A. K. Pandey, "Chemistry and biological activities of flavonoids: An overview," *The Scientific World Journal*, vol. 2013, Art. no. 162750, 2013.

[58] B. Nair and S. Jacob, "A simple practice guide for dose conversion between animals and humans," *Journal of Basic and Clinical Pharmacy*, vol. 7, no. 2, pp. 27–31, 2016.

[59] P. Rajendran, T. Rengarajan, J. Thangavel, *et al*., "The vascular protective effects of flavonoids and polyphenols," *Nutrients*, vol. 6, no. 9, pp. 3915–3932, 2014.

[60] Khan, H. Ullah, M. Aschner, W. S. Cheang, and E. K. Akkol, "Neuroprotective effects of quercetin and related flavonoids: Mechanistic review," *Biomedicine & Pharmacotherapy*, vol. 126, Art. no. 110012, 2020.

[61] V. M. Patil, S. Das, and K. Balasubramanian, "Quantum dots and nano-enabled delivery systems in herbal medicine," *Drug Discovery Today*, vol. 25, no. 10, pp. 1969–1982, 2020.

[62] P. Kumari, B. Ghosh, and S. Biswas, "Nanocarriers for cancer-targeted drug delivery," *Journal of Drug Targeting*, vol. 24, no. 3, pp. 179–191, 2016.

[63] World Health Organization, *WHO Global Report on Traditional and Complementary Medicine 2019*. Geneva, Switzerland: World Health Organization, 2019.

[64] World Health Organization, *WHO Monographs on Selected Medicinal Plants*, vol. 1. Geneva, Switzerland: World Health Organization, 1999.