Original Article

Medicinal Plants, Environmental Contaminants, and Biomedical Innovations: A Multidisciplinary Review of Natural Products in Health and Disease Management

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Abstract

Medicinal plants have been fundamental to human healthcare for millennia, serving as the primary source of therapeutic agents across diverse cultures. However, the simultaneous presence of environmental contaminants, particularly heavy metals, in these plants poses significant health risks that cannot be overlooked. This comprehensive review synthesizes findings from over 50 studies to provide a multidisciplinary perspective on the therapeutic potential of medicinal plants, the challenges posed by heavy metal contamination, and the emerging role of nanotechnology and phytoremediation in addressing these challenges. Key medicinal plants including Cichorium intybus, Ziziphora persica, Lavandula angustifolia, and Catharanthus roseus are examined for their pharmacological properties, with particular attention to anti-inflammatory, antimicrobial, and anticancer activities. The review critically evaluates the sources and health implications of heavy metal contamination in medicinal plants and food products, drawing on case studies from Northern Iran. Furthermore, it explores innovative approaches including Nano-formulations for enhanced drug delivery and phytoremediation strategies for soil decontamination. The integration of traditional knowledge with modern biotechnological tools presents unprecedented opportunities for sustainable healthcare and environmental management. This review identifies critical research gaps and proposes future directions for maximizing the therapeutic potential of medicinal plants while ensuring their safety and sustainability.

Introduction

The relationship between humans and medicinal plants represents one of the oldest and most enduring therapeutic traditions in history. Archaeological evidence suggests that plant-based medicines were utilized as early as 60,000 years ago, with written records from ancient Mesopotamian, Egyptian, Chinese, and Indian civilizations documenting sophisticated herbal pharmacopoeias [18]. Today, the World Health Organization estimates that approximately 80% of the world's population in developing countries relies primarily on herbal medicines for their basic healthcare needs, while in developed nations, plant-derived compounds form the basis of nearly 30% of all pharmaceutical drugs [25].

The enduring relevance of medicinal plants stems from their remarkable capacity to produce diverse secondary metabolites—including alkaloids, flavonoids, terpenoids, and phenolic compounds—that exhibit a wide array of pharmacological activities. These naturally occurring compounds have evolved over millions of years as defense mechanisms against herbivores, pathogens, and environmental stressors, and many have proven to be invaluable templates for drug discovery and development [28]. From the analgesic properties of morphine derived from Papaver somniferum to the antimalarial activity of artemisinin from Artemisia annua, plant secondary metabolites continue to inspire modern pharmaceutical research.

However, the therapeutic potential of medicinal plants is increasingly threatened by environmental contamination, particularly from heavy metals. Rapid industrialization, urbanization, and agricultural intensification have led to widespread contamination of soils with toxic elements including cadmium (Cd), lead (Pb), arsenic (As), and mercury (Hg). These contaminants are readily absorbed by plants and can accumulate in their tissues, posing significant health risks to consumers [14]. The situation is particularly concerning for medicinal plants, which are often harvested from wild populations or cultivated in regions with poorly regulated environmental standards.

The paradox of medicinal plants—their capacity to both heal and potentially harm—demands a multidisciplinary approach that integrates ethnopharmacology, environmental science, analytical chemistry, and biotechnology. This review aims to provide such an integrated perspective by addressing three interconnected themes. First, it examines the ethnopharmacological significance of key medicinal plants, synthesizing evidence for their therapeutic applications across various disease conditions. Second, it critically evaluates the challenge of heavy metal contamination in medicinal plants and food products, drawing on case studies from Northern Iran and other regions. Third, it explores innovative approaches including nanotechnology-based drug delivery systems and phytoremediation strategies that offer pathways toward safer and more effective utilization of plant-based therapeutics.

By synthesizing findings from over 50 original research articles and recent high-impact reviews, this work seeks to identify current knowledge gaps and propose future research directions that can advance the field while ensuring patient safety and environmental sustainability.

Ethnopharmacological Treasure: Medicinal Plants in Traditional and Modern Medicine

❖ **Phytochemical Diversity and Therapeutic Potential**

The therapeutic efficacy of medicinal plants resides in their complex phytochemical profiles, which typically contain dozens or even hundreds of bioactive compounds acting synergistically. Unlike synthetic drugs that typically target single molecular pathways, plant extracts can simultaneously modulate multiple targets, offering advantages in treating complex multifactorial diseases [29].

Flavonoids represent one of the most extensively studied classes of plant secondary metabolites, with over 9,000 structurally distinct compounds identified to date. These polyphenolic compounds exhibit potent antioxidant, anti-inflammatory, and anticancer activities through multiple mechanisms including free radical scavenging, metal chelation, and modulation of cellular signaling pathways [17]. Quercetin, kaempferol, and apigenin—flavonoids commonly found in dietary and medicinal plants—have demonstrated remarkable neuroprotective, cardioprotective, and chemopreventive effects in preclinical studies.

Alkaloids, another major class of plant-derived compounds, include some of the most potent pharmacological agents known. Vinblastine and vincristine, isolated from Catharanthus roseus, remain cornerstones of cancer chemotherapy more than half a century after their introduction. Recent research continues to identify novel alkaloids with promising therapeutic properties, including compounds with antimicrobial, analgesic, and antiarrhythmic activities [1].

Terpenoids, the largest and most structurally diverse class of plant natural products, encompass over 40,000 compounds with applications ranging from antimalarial therapy (artemisinin) to cancer treatment (paclitaxel) and cardiovascular disease management (digoxin). The structural complexity of terpenoids presents both opportunities and challenges for drug development, inspiring synthetic biology approaches for their production in heterologous hosts.

❖ **Medicinal Plants in Infectious Disease Management**

The COVID-19 pandemic reignited interest in plant-based therapies for infectious diseases, as researchers worldwide searched for effective treatments in the absence of specific antiviral drugs. A comprehensive review by Daglia et al. [18] examined the potential of medicinal plants against SARS-CoV-2, identifying numerous species with documented antiviral activity against coronaviruses. Plants including Glycyrrhiza glabra (licorice), Allium sativum (garlic), and Nigella sativa (black seed) demonstrated promising effects through multiple mechanisms including viral entry inhibition, replication blockade, and immunomodulation.

Beyond COVID-19, medicinal plants have long been employed in the management of tick-borne diseases, which pose increasing public health challenges as climate change expands the geographic range of tick vectors. Alinia-Ahandani et al. [4] documented several medicinal plants used traditionally in Northern Iran for treating tick-borne illnesses, highlighting the importance of ethnobotanical knowledge in identifying potential therapeutic agents.

Honey, one of the oldest known medicinal substances, has received renewed scientific attention for its antimicrobial properties. A comprehensive review by Riaz et al. [28] documented honey's effectiveness against a wide range of pathogens, including antibiotic-resistant bacteria, through mechanisms involving hydrogen peroxide production, osmotic effects, acidity, and the presence of antimicrobial peptides. The authors emphasized honey's potential as an adjunctive therapy in wound management and its role in combating the growing crisis of antimicrobial resistance.

❖ **Anti-Inflammatory and Immunomodulatory Properties**

Chronic inflammation underlies the pathogenesis of numerous diseases, including cardiovascular disorders, diabetes, cancer, and neurodegenerative conditions. Medicinal plants offer a rich source of anti-inflammatory compounds that may provide safer alternatives to conventional non-steroidal anti-inflammatory drugs (NSAIDs), which are associated with significant gastrointestinal and cardiovascular adverse effects.

Riaz et al. [29] systematically reviewed the anti-inflammatory activity of medicinal plants and herbs, identifying numerous species with documented effects in preclinical and clinical studies. Curcumin from Curcuma longa, boswellic acids from Boswellia serrata, and andrographolide from Andrographis paniculata emerged as particularly promising candidates, with mechanisms involving inhibition of nuclear factor-kappa B

(NF-κB), suppression of cyclooxygenase-2 (COX-2), and reduction of pro-inflammatory cytokine production.

Cichorium intybus (chicory), a plant with a long history of use in traditional medicine systems, has garnered attention for its diverse pharmacological properties. Riaz et al. [30] comprehensively reviewed the phytochemistry and pharmacology of this species, documenting its anti-inflammatory, hepatoprotective, antioxidant, and antidiabetic activities. The plant's bioactive constituents, including sesquiterpene lactones, coumarins, and flavonoids, act through complementary mechanisms that may explain its traditional uses in treating liver disorders, gastrointestinal complaints, and inflammatory conditions.

❖ **Cardiovascular and Metabolic Effects**

Cardiovascular diseases remain the leading cause of mortality globally, driving interest in plant-based approaches for prevention and management. Alinia-Ahandani et al. [17] reviewed medicinal plants used traditionally in Iran for cardiovascular conditions, identifying species with documented hypotensive, hypolipidemic, and cardioprotective effects. Garlic (Allium sativum), hawthorn (Crataegus spp.), and olive leaf (Olea europaea) were among the most frequently cited plants, with clinical evidence supporting their efficacy in reducing blood pressure and improving lipid profiles.

The relationship between medicinal plants and metabolic health extends to diabetes management, where plant-based therapies offer potential advantages in terms of safety and cost-effectiveness. Several plants used traditionally in Iranian medicine, including Triglochin maritima and Urtica dioica, have demonstrated hypoglycemic effects in experimental studies, though the authors emphasized the need for well-designed clinical trials to confirm these findings.

❖ **Hepatoprotective and Renal Protective Effects**

The liver and kidneys, as primary organs of detoxification and excretion, are particularly vulnerable to damage from xenobiotics and metabolic byproducts. Medicinal plants have been extensively studied for their hepatoprotective and renal protective properties, with several species showing promise in preventing or mitigating toxin-induced injury.

Alinia-Ahandani et al. [11] reviewed medicinal plants used traditionally for hepatitis and liver disorders, identifying species with documented hepatoprotective effects including Silybum marianum (milk thistle), Glycyrrhiza glabra, and Phyllanthus species. The mechanisms underlying these effects include antioxidant activity, membrane stabilization, stimulation of hepatic regeneration, and modulation of inflammatory responses.

The renal protective effects of medicinal plants are less extensively studied but emerging evidence suggests potential benefits. Ziziphora species, traditionally used in Iranian

medicine for various ailments, have demonstrated nephroprotective effects in experimental models, though Alinia-Ahandani et al. [10] noted that contamination with toxic metals could paradoxically increase renal risk, emphasizing the need for quality control in herbal products.

The Hidden Challenge: Heavy Metals in Medicinal Plants and Food Products

❖ **Sources and Pathways of Heavy Metal Contamination**

The contamination of medicinal plants with heavy metals represents a significant public health concern that has received insufficient attention. Unlike synthetic pharmaceutical contaminants, which can be controlled through good manufacturing practices, heavy metal contamination is often inherent to the environment in which plants are cultivated or collected.

Industrial activities, including mining, smelting, and manufacturing, release substantial quantities of toxic metals into the environment. Atmospheric deposition of industrial emissions can contaminate soils at considerable distances from emission sources, while industrial wastewater can introduce metals into irrigation water and agricultural soils [14]. Agricultural practices themselves contribute to contamination through the application of phosphate fertilizers, which often contain significant cadmium concentrations, and sewage sludge, which may contain various toxic metals.

Traffic-related contamination represents another significant source, particularly for plants growing near roads. Alinia-Ahandani et al. [10] investigated heavy metal concentrations in roadside soils in Rasht, Iran, finding elevated levels of lead, cadmium, and zinc that correlated with traffic volume. Plants growing in these locations can accumulate metals through root uptake and foliar deposition, potentially exceeding safety limits even when cultivated far from obvious contamination sources.

Geological factors also influence heavy metal content in medicinal plants. Regions with naturally elevated background concentrations of certain elements may produce plants with inherently high metal content, regardless of anthropogenic contamination. This is particularly relevant for selenium, which can accumulate to toxic levels in plants growing on seleniferous soils, and for arsenic in regions with arsenic-rich geological formations.

❖ **Case Studies from Northern Iran**

Northern Iran, with its diverse climate and rich botanical heritage, has been the focus of extensive research on heavy metal contamination in medicinal plants and food products. These studies provide valuable insights into the magnitude and patterns of contamination in a region where traditional

medicine remains widely practiced and where environmental pressures are increasing.

Alinia-Ahandani et al. [10] assessed toxic metal concentrations in Ziziphora persica obtained from local markets in Lahijan, Northern Iran. Analysis revealed detectable levels of lead, cadmium, and arsenic in all samples, with some exceeding permissible limits established by the World Health Organization and national regulatory authorities. The authors noted that regular consumption of contaminated herbal products could pose significant health risks, particularly for vulnerable populations including pregnant women, children, and individuals with chronic diseases.

Soil contamination studies in the region have identified multiple hotspots of heavy metal pollution. Alinia-Ahandani et al. (2020) assessed soil in Roodsar, finding elevated concentrations of several toxic metals that exceeded background levels and, in some cases, regulatory guidelines. Similarly, Ahandani et al. [14] evaluated soil in Langerud, documenting contamination patterns that reflected both industrial activities and geological factors.

The transfer of contaminants from soil to food products was documented by Sheydaei et al. [34], who analyzed heavy metals in different parts of consumed chickens in Lahijan city. The study found detectable levels of lead and cadmium in chicken tissues, with concentrations varying by tissue type and potentially reflecting contamination of feed and water sources. These findings highlight the complexity of contaminant transfer through food chains and the importance of comprehensive monitoring programs.

❖ Health Risk Assessment

The presence of heavy metals in medicinal plants and food products raises important questions about the magnitude of associated health risks. Traditional approaches to risk assessment compare measured concentrations with established safety standards, but more sophisticated methods incorporate exposure estimates and toxicological data to provide quantitative risk characterizations.

Alinia-Ahandani et al. [14] conducted a systematic review of toxic elements in medicinal plants, synthesizing data from multiple studies to assess patterns of contamination and associated health risks. The review identified lead and cadmium as the most frequently detected contaminants, with concentrations varying widely based on plant species, geographical origin, and cultivation practices. The authors emphasized the need for harmonized regulatory standards and improved quality control measures to protect consumers.

Quantitative health risk assessment typically employs parameters including the Target Hazard Quotient (THQ), Hazard Index (HI), and Cancer Risk (CR). THQ values below 1 indicate acceptable levels of non-carcinogenic risk, while values above 1 suggest potential health concerns. Studies on contaminated medicinal plants have occasionally reported THQ values exceeding 1 for individual metals, with HI values indicating cumulative risks from multiple contaminants.

The carcinogenic risks associated with chronic exposure to arsenic, cadmium, and lead are particularly concerning. Arsenic, classified as a Group 1 carcinogen by the International Agency for Research on Cancer, has been detected in medicinal plants from various regions, with some samples exceeding acceptable cancer risk levels. The long latency period for carcinogenic effects means that current contamination levels may not manifest as disease for decades, complicating efforts to establish causal relationships.

❖ Regulatory Framework and Quality Control

The regulation of heavy metals in medicinal products varies considerably across jurisdictions, creating challenges for international trade and consumer protection. The World Health Organization has established guidelines for maximum permissible levels of selected metals in medicinal plants, but these are not binding and many countries have developed their own standards.

In the European Union, regulations establish maximum levels for lead, cadmium, and mercury in food supplements, including herbal products. The United States Pharmacopeia provides voluntary standards for heavy metal limits in herbal ingredients, while the Chinese Pharmacopoeia includes mandatory limits for selected metals in specific herbal materials.

Despite these regulatory efforts, significant gaps remain in the coverage and enforcement of heavy metal standards for medicinal plants. Many countries lack comprehensive monitoring programs, and even where standards exist, testing capacity may be insufficient to ensure compliance. The proliferation of herbal products through internet sales further complicates regulatory oversight, as products may be manufactured in jurisdictions with weak controls and sold directly to consumers across borders.

Quality control measures for heavy metals in medicinal plants require validated analytical methods, appropriate sampling strategies, and consideration of the complex factors influencing metal content. Sample preparation is particularly critical, as metals may be distributed unevenly within plant tissues and contamination can occur during processing and storage. Analytical techniques including atomic absorption spectroscopy, inductively coupled plasma mass spectrometry, and X-ray fluorescence spectrometry offer varying combinations of sensitivity, specificity, and cost-effectiveness.

❖ Impact on Rhizosphere Microorganisms and Plant Quality

The effects of heavy metal contamination extend beyond direct toxicity to consumers, influencing the complex interactions between plants and their associated microorganisms. Recent research has revealed that heavy metals significantly impact rhizosphere microbial communities, with consequences for plant health and the production of bioactive secondary metabolites.

A comprehensive review by Ahmad et al. [2] examined the ecotoxicological impacts of heavy metals on medicinal plant quality and rhizosphere microbial communities. The authors documented that metal stress alters the composition and diversity of rhizosphere microorganisms, reducing beneficial populations while selecting for metal-tolerant strains. These microbial changes can affect nutrient cycling, plant growth promotion, and the induction of plant defense responses.

The relationship between metal stress and secondary metabolite production is complex and context-dependent. Moderate metal stress can stimulate the production of phenolic compounds and other defense-related metabolites, potentially enhancing the pharmacological activity of medicinal plants. However, severe stress can overwhelm plant defense systems, reducing growth and compromising the quality of herbal materials.

Rhizosphere microorganisms play a crucial role in mediating plant responses to metal stress through mechanisms including metal chelation, precipitation, and transformation. Arbuscular mycorrhizal fungi, in particular, can reduce metal uptake by plants while improving nutrient acquisition, offering potential applications in the cultivation of medicinal plants on contaminated soils.

Bridging Nature and Nanotechnology: Modern Drug Delivery Systems

❖ **Limitations of Conventional Herbal Formulations**

Despite the remarkable therapeutic potential of plant-derived compounds, their clinical application has been limited by several inherent physicochemical and biopharmaceutical challenges. Poor aqueous solubility, limited permeability across biological membranes, rapid metabolism, and extensive first-pass elimination substantially reduce the oral bioavailability of many promising phytochemicals.

Curcumin, the principal curcuminoid in turmeric (Curcuma longa), exemplifies these challenges. Despite extensive documentation of its anti-inflammatory, antioxidant, and anticancer activities, clinical translation has been hampered by extremely poor oral bioavailability. Following oral administration, curcumin concentrations in plasma and tissues remain below therapeutic levels due to limited absorption, rapid metabolism, and rapid systemic elimination [19].

Similar challenges affect other valuable phytochemicals including silymarin from milk thistle, quercetin from various dietary sources, and paclitaxel from the Pacific yew tree. The development of effective formulations that can overcome these limitations represents a critical priority for translating the therapeutic potential of medicinal plants into clinical practice.

❖ **Nanoformulation Strategies for Phytochemicals**

Nanotechnology offers powerful tools for addressing the biopharmaceutical limitations of phytochemicals while potentially enhancing their therapeutic efficacy and reducing adverse effects. Nanoformulations can improve solubility, protect compounds from degradation, enhance permeability across biological barriers, enable targeted delivery, and provide controlled release profiles.

Liposomes, spherical vesicles composed of phospholipid bilayers, were among the first nanocarrier systems to achieve clinical translation and remain widely used for phytochemical delivery. The amphiphilic nature of liposomes enables encapsulation of both hydrophilic and hydrophobic compounds, while surface modification with polyethylene glycol (PEG) can prolong circulation time and improve targeting. Liposomal formulations of curcumin have demonstrated substantially enhanced bioavailability compared to unformulated compound, with some studies reporting increases of up to 9-fold in animal models [28].

Polymeric nanoparticles, fabricated from biodegradable polymers including polylactic acid (PLA), poly (lactic-co-glycolic acid) (PLGA), and natural polymers such as chitosan, offer advantages including high drug loading capacity, controlled release kinetics, and versatile surface functionalization. Sheydaei and Alinia-Ahandani [33] extensively reviewed the role of polymer carriers in cancer treatment, documenting applications ranging from targeted delivery of chemotherapeutic agents to the development of theranostic systems combining therapy and imaging.

Solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) represent alternative platforms that combine the advantages of polymeric nanoparticles with the biocompatibility of lipid-based systems. These carriers are particularly suitable for lipophilic phytochemicals and have demonstrated enhanced oral bioavailability for compounds including piperine, with some studies reporting increases of 2.5-fold compared to conventional formulations [19].

Nanoemulsions, thermodynamically stable dispersions of oil and water stabilized by surfactants, offer advantages including ease of preparation, scalability, and enhanced mucosal penetration. These systems have been extensively investigated for topical and oral delivery of phytochemicals, with applications including antimicrobial, anti-inflammatory, and wound healing formulations.

❖ **Applications in Cancer Therapy**

The application of nanotechnology to phytochemical-based cancer therapy has emerged as a particularly active research area, reflecting both the urgent need for improved cancer treatments and the rich potential of plant-derived anticancer agents.

Catharanthus roseus alkaloids, including vincristine and vinblastine, have been mainstays of cancer chemotherapy for

decades, but their clinical use is limited by neurotoxicity, narrow therapeutic windows, and the development of drug resistance. Nanoformulations of these agents offer the potential to improve tumor targeting, reduce systemic toxicity, and overcome resistance mechanisms. Aftab et al. (2023) reviewed recent advances in Catharanthus roseus phytochemistry and pharmacology, noting that nanoformulated vinca alkaloids are under active investigation in preclinical models.

Paclitaxel, originally isolated from the Pacific yew tree (Taxus brevifolia), represents one of the most successful plant-derived anticancer drugs. Commercial formulations including Abraxane®, albumin-bound paclitaxel nanoparticles, have demonstrated improved efficacy and reduced toxicity compared to conventional formulations, validating the potential of nanotechnology to enhance phytochemical-based therapies.

Beyond established anticancer agents, nanoformulations are enabling the development of novel phytochemical combinations that target multiple cancer hallmarks simultaneously. Polyherbal formulations, incorporating extracts from multiple plants with complementary mechanisms of action, can be co-encapsulated in nanocarriers to provide synergistic effects while simplifying administration and improving patient compliance.

❖ Antimicrobial and Wound Healing Applications

The increasing prevalence of antimicrobial resistance has renewed interest in plant-derived antimicrobial agents, which often act through multiple mechanisms that may be less susceptible to resistance development than conventional antibiotics. Nanotechnology offers approaches to enhance the antimicrobial activity of phytochemicals while addressing formulation challenges.

Green-synthesized silver nanoparticles, produced using plant extracts as reducing and stabilizing agents, have demonstrated potent antimicrobial activity against a wide range of pathogens. Fatima et al. [20] explored the therapeutic potential of green-synthesized silver nanoparticles in psoriasis, documenting effects on epidermal hyperproliferation and inflammation that suggest applications beyond infectious diseases. The combination of plant-derived bioactive compounds with the unique properties of silver nanoparticles creates opportunities for multifunctional therapeutic systems.

Wound healing applications of phytochemical nanoformulations leverage both the regenerative properties of plant compounds and the wound-healing promoting characteristics of nanocarrier systems. Chitosan-based nanoparticles, in particular, offer advantages including hemostatic activity, antimicrobial effects, and promotion of tissue regeneration. Nanoformulated plant extracts have demonstrated accelerated wound closure, reduced inflammation, and improved cosmetic outcomes in preclinical wound healing models.

❖ Market Trends and Future Directions

The global market for natural product nanoformulations is experiencing rapid growth, driven by increasing consumer demand for natural products, advances in nanomanufacturing technologies, and expanding clinical evidence for efficacy. Recent market analyses project the sector to reach approximately $19 billion USD by 2035, with applications spanning pharmaceuticals, nutraceuticals, cosmetics, and functional foods.

Despite this growth, significant challenges remain in the clinical translation and commercialization of phytochemical nanoformulations. Scale-up from laboratory to industrial production remains difficult for many nanocarrier systems, and regulatory pathways for complex nanoformulated products are not yet well established. Quality control is particularly challenging for polyherbal formulations, where multiple bioactive compounds must be characterized and standardized.

Future research directions include the development of targeted nanocarriers that can deliver phytochemicals to specific tissues or cell types, reducing systemic exposure and enhancing therapeutic effects. Active targeting strategies employing ligands including antibodies, peptides, and aptamers can direct nanocarriers to receptors overexpressed on diseased cells, offering the potential for precision medicine approaches with plant-derived therapeutics.

The integration of artificial intelligence and machine learning with nanotechnology and natural product research presents unprecedented opportunities for accelerating discovery and development. AI algorithms can predict phytochemical-nanocarrier interactions, optimize formulation parameters, and identify novel combinations with synergistic effects, potentially transforming the field of phytochemical-based therapeutics.

Environmental Sustainability and Soil Remediation

❖ Phytoremediation: Principles and Mechanisms

Phytoremediation, the use of plants to remove, degrade, or stabilize environmental contaminants, offers a sustainable and cost-effective approach to managing heavy metal pollution. This green technology harnesses the natural capabilities of plants to extract, sequester, or transform toxic elements, providing an alternative to energy-intensive and environmentally disruptive conventional remediation methods.

Hajipour et al. [22] comprehensively reviewed phytoremediation potential and methods, documenting the diverse mechanisms by which plants interact with metal contaminants. Phytoextraction involves the uptake of metals from soil and their translocation to harvestable plant tissues, enabling removal of contaminants through biomass harvesting. Phytostabilization reduces metal mobility and bioavailability through root uptake, precipitation, and adsorption, minimizing off-site migration. Phytovolatilization

converts metals to volatile forms that are released to the atmosphere, applicable primarily to mercury and selenium.

The effectiveness of phytoremediation depends on complex interactions between plant characteristics, soil properties, metal speciation, and environmental conditions. Ideal plants for phytoextraction should exhibit high biomass production, extensive root systems, efficient metal translocation to shoots, and tolerance to elevated metal concentrations. Hyperaccumulator plants, defined as species capable of accumulating metals to concentrations exceeding 100 mg/kg for cadmium or 10,000 mg/kg for zinc and nickel, have been identified for various elements and form the basis of many phytoremediation applications.

Brassica juncea (Indian mustard) has demonstrated remarkable cadmium accumulation capacity, with documented uptake exceeding 200 mg/kg in shoot tissues under optimal conditions. Pteris vittata (Chinese brake fern) can accumulate arsenic to concentrations as high as 20,000 mg/kg, representing one of the most extreme examples of hyperaccumulation documented. These and other hyperaccumulator species have been extensively studied for their potential in phytoremediation applications.

❖ Medicinal Plants in Phytoremediation

The use of medicinal plants for phytoremediation presents both opportunities and challenges. On one hand, the cultivation of high-value medicinal species on contaminated soils could generate economic returns while providing environmental remediation services. On the other hand, metal accumulation in harvestable plant tissues raises concerns about the safety of products derived from remediated plants.

A critical meta-analysis by Pandey et al. [27] examined the potential of energy, aromatic, and medicinal plants for remediation of metal-contaminated agricultural soils. The authors documented that aromatic plants including lavender (Lavandula angustifolia), mint (Mentha species), and rosemary (Rosmarinus officinalis) can accumulate substantial metal concentrations in their tissues while producing essential oils that remain largely free of metal contamination. This finding has important implications for the safe utilization of remediated biomass, as essential oil distillation can separate valuable products from metal-laden plant materials.

Selamoglu et al. [31] reviewed the medicinal properties of lavender and methods for enhancing its effective compounds, noting that moderate metal stress can stimulate the production of volatile oils and other secondary metabolites. This observation suggests that carefully managed cultivation on contaminated soils might simultaneously achieve remediation goals and enhance the quality of essential oil products.

Hajipour et al. [22] assessed the effects of nanoparticles in phytoremediation, documenting that engineered nanomaterials can influence plant metal uptake through multiple mechanisms. Nanoparticles can adsorb metals from soil solution, reducing bioavailability and uptake, or can be taken up by plants themselves, potentially translocating to shoots and influencing metal distribution. The complex interactions between nanoparticles, metals, and plants in contaminated systems require careful investigation to optimize remediation outcomes.

❖ Soil Decontamination with Natural Sorbents

Complementary approaches to phytoremediation involve the use of natural sorbents for soil decontamination. Bentonite, a clay mineral with high adsorption capacity for metal cations, has been investigated for its potential to immobilize contaminants and reduce their bioavailability.

Sunakbaeva et al. [35] examined decontamination of soil with natural sorbents bentonite, documenting effective reduction in the bioavailability of several toxic metals following bentonite application. The authors noted that bentonite amendment could complement phytoremediation approaches by reducing the immediately available metal fraction while plants gradually extract more strongly bound contaminants over multiple growing seasons.

Other natural sorbents including zeolites, biochar, and compost have demonstrated effectiveness in metal immobilization, with the choice of amendment depending on soil characteristics, contaminant types, and remediation objectives. Combinations of multiple amendments may provide synergistic benefits, addressing the complex challenges of heterogeneous contamination.

❖ Enhancing Phytoremediation Efficiency

Despite its promise, phytoremediation faces limitations including slow remediation rates, limited effectiveness for strongly bound contaminants, and challenges in managing contaminated biomass. Research efforts are therefore focused on strategies to enhance phytoremediation efficiency.

Genetic engineering approaches, particularly using CRISPR/Cas9 technology, offer the potential to develop plants with improved metal accumulation, tolerance, and translocation characteristics. Genes involved in metal uptake (e.g., ZIP family transporters), translocation (e.g., heavy metal ATPases), and sequestration (e.g., metallothioneins, phytochelatins) represent targets for modification to enhance phytoremediation performance [23].

Microbial-assisted phytoremediation harnesses the capabilities of plant-associated microorganisms to improve metal availability, enhance plant growth, and reduce metal toxicity. Plant growth-promoting bacteria can produce siderophores that solubilize metals, synthesize phytohormones that stimulate root development, and induce systemic tolerance to metal stress. Mycorrhizal fungi can

extend the effective root surface area for metal uptake while improving plant nutrition and stress tolerance.

Agronomic practices including soil amendments, irrigation management, and harvesting strategies can be optimized to enhance phytoremediation outcomes. The application of chelating agents can increase metal solubility and uptake, though careful management is required to avoid off-site migration. Intercropping of hyperaccumulator species with high-biomass crops may provide economic returns during remediation while maintaining remediation progress.

❖ Circular Economy Approaches

The integration of phytoremediation with circular economy principles offers opportunities to transform contaminated biomass from a disposal problem into a resource for valuable products. Metal-enriched plant biomass can be processed for metal recovery (phytomining), converted to bioenergy, or utilized for production of bio-based materials.

Phytomining, the recovery of valuable metals from hyperaccumulator biomass, has been demonstrated for nickel, thallium, and other elements with economic value. The incineration of harvested biomass produces bio-ore with metal concentrations substantially higher than those in typical ores, enabling recovery through conventional metallurgical processes. For elements with high market values, phytomining could potentially offset remediation costs and generate economic returns.

Bioenergy production from contaminated biomass offers an alternative valorization pathway that isolates metals in concentrated byproduct streams while generating renewable energy. Anaerobic digestion, pyrolysis, and combustion each present advantages and limitations depending on biomass characteristics and metal behavior during processing.

Hajipour et al. [22] discussed the potential of nano-particles in phytoremediation within a circular economy framework, noting that engineered nanomaterials could both enhance remediation and enable novel approaches to biomass valorization. The integration of multiple technologies within systems-level approaches will be essential for realizing the full potential of phytoremediation as a sustainable solution to heavy metal contamination.

Reproductive Health, Pregnancy, and Women's Wellness

❖ Traditional Uses and Scientific Validation

Medicinal plants have played central roles in women's healthcare throughout history, with traditional medical systems documenting numerous species used for conditions including menstrual disorders, infertility, pregnancy complications, and menopausal symptoms. The scientific validation of these traditional uses represents an active area of research with implications for both drug discovery and the safe use of herbal products.

Alinia-Ahandani et al. [4] reviewed new approaches of herbs used for reproductive issues globally, documenting traditional uses and emerging scientific evidence for plants including Vitex agnus-castus (chasteberry), Actaea racemosa (black cohosh), and Tribulus terrestris. The authors emphasized that while some traditional uses are supported by clinical evidence, many others require rigorous investigation to establish efficacy and safety.

❖ Plants for Lactation and Pregnancy

The use of galactagogues—substances that promote milk production—has a long history in traditional medicine, with numerous plants employed to support breastfeeding women. Alinia-Ahandani (2018) reviewed milk-increasing medicinal plants, documenting species including Foeniculum vulgare (fennel), Trigonella foenum-graecum (fenugreek), and Galega officinalis (goat's rue) with traditional uses supported by preliminary scientific evidence.

Pregnancy sickness, affecting up to 80% of pregnant women, represents another condition where medicinal plants are frequently employed. Alinia-Ahandani et al. [17] examined medicinal plants used for pregnancy sickness, noting that ginger (Zingiber officinale) has the strongest evidence base, with clinical trials supporting its efficacy and safety. Other traditionally used plants including peppermint (Mentha piperita) and chamomile (Matricaria chamomilla) require additional study to establish safety profiles during pregnancy.

❖ Safety Considerations in Pregnancy and Lactation

The use of medicinal plants during pregnancy and lactation raises particular safety concerns, as developing fetuses and nursing infants may be especially vulnerable to toxic effects. Limited safety data for most herbal products, combined with the potential for contamination with heavy metals or other toxic substances, demands caution in recommending herbal therapies to pregnant or breastfeeding women.

Alinia-Ahandani et al. [13] provided an overview of raspberry leaves and cohosh as partus preparatory agents, documenting traditional uses while emphasizing the need for quality control and safety assessment. Caulophyllum thalictroides (blue cohosh), in particular, has been associated with adverse effects including neonatal myocardial infarction, highlighting the potential risks of inadequately studied herbal products.

The transfer of heavy metals from contaminated herbal products to breast milk represents a poorly characterized but potentially significant exposure pathway. Lead, cadmium, and mercury can accumulate in breast milk, exposing nursing infants to toxic metals during critical developmental windows. The absence of routine testing for heavy metals in most herbal products marketed to pregnant and breastfeeding women represents a significant gap in consumer protection.

❖ Future Research Directions

Research priorities for medicinal plants in reproductive health include rigorous clinical trials to establish efficacy for specific indications, comprehensive safety assessments including

developmental toxicity studies, and development of quality control measures that ensure product safety and consistency.

The integration of traditional knowledge with modern analytical and pharmacological methods offers opportunities for identifying novel therapeutic agents while ensuring that traditional uses are appropriately validated. Collaborative approaches involving traditional healers, ethnobotanists, pharmacologists, and clinicians can facilitate the responsible development of plant-based therapies for women's health.

Discussion and Conclusion

This comprehensive review has examined the multifaceted relationships between medicinal plants, environmental contaminants, and biomedical innovations, synthesizing findings from over 50 original research articles and recent high-impact reviews. Several key themes emerge from this synthesis, with important implications for research, clinical practice, and public health policy.

❖ **The Therapeutic Potential of Medicinal Plants**

The evidence summarized in this review reaffirms the remarkable therapeutic potential of medicinal plants across diverse disease conditions. From the anti-inflammatory effects of Cichorium intybus to the anticancer activity of Catharanthus roseus alkaloids and the antimicrobial properties of honey, plant-derived compounds continue to demonstrate value in both traditional and modern medical contexts.

The diversity of phytochemical structures and mechanisms of action positions medicinal plants as valuable sources of new therapeutic agents, particularly for complex multifactorial diseases where single-target synthetic drugs may be inadequate. The synergy between multiple compounds within plant extracts offers advantages that are increasingly recognized in the development of multi-target therapeutic approaches.

However, the translation of this therapeutic potential into clinical practice requires rigorous scientific validation, standardization of herbal products, and careful consideration of safety issues including contamination with toxic elements. The gap between traditional knowledge and evidence-based medicine remains substantial for many plant species, representing both a challenge and an opportunity for future research.

❖ **The Challenge of Heavy Metal Contamination**

The documentation of heavy metal contamination in medicinal plants and food products from Northern Iran and other regions raises serious concerns about the safety of herbal products and the adequacy of current regulatory frameworks. The presence of toxic elements including lead, cadmium, and arsenic in commonly used medicinal plants represents a public health issue that demands urgent attention.

The sources of contamination are diverse and include industrial activities, agricultural practices, traffic-related pollution, and geological factors. This complexity complicates efforts to control contamination and requires multifaceted approaches addressing environmental management, cultivation practices, and post-harvest handling.

Health risk assessments indicate that contaminated herbal products can contribute significantly to toxic metal exposure, with potential for both non-carcinogenic and carcinogenic effects. The cumulative risks from multiple contaminants and multiple exposure sources are particularly concerning and are inadequately addressed by current regulatory approaches that consider contaminants in isolation.

❖ **The Promise of Nanotechnology**

Nanotechnology offers powerful tools for addressing the limitations of conventional herbal formulations while potentially enhancing therapeutic efficacy and reducing adverse effects. Nanoformulations of phytochemicals can improve solubility, protect against degradation, enhance bioavailability, enable targeted delivery, and provide controlled release profiles.

The clinical translation of phytochemical nanoformulations is progressing, with some products already achieving market approval and many others in development. Liposomal, polymeric, and lipid-based nanocarriers have demonstrated particular promise for a range of phytochemicals, with applications spanning cancer therapy, antimicrobial treatment, and wound healing.

Challenges remain in scale-up, quality control, and regulatory approval, but the rapid growth of the natural product nanoformulation market reflects both commercial interest and scientific progress. Future developments in targeted delivery, combination therapies, and AI-optimized formulations are likely to further expand the therapeutic potential of plant-derived compounds.

❖ **Environmental Sustainability and Phytoremediation**

Phytoremediation presents a sustainable approach to managing heavy metal contamination that aligns with circular economy principles and offers potential economic returns through biomass valorization. The use of medicinal and aromatic plants for remediation is particularly attractive, as essential oil production can separate valuable products from metal-laden biomass.

Advances in genetic engineering, microbial-assisted remediation, and agronomic optimization are enhancing the efficiency and applicability of phytoremediation. The integration of phytoremediation with complementary approaches including natural sorbent amendments and advanced biomass processing technologies offers pathways

toward comprehensive solutions for metal-contaminated sites.

❖ Research Gaps and Future Directions

Several critical research gaps emerge from this review that should inform future research priorities:

First, the mechanisms by which heavy metal contamination affects the biosynthesis of pharmacologically active secondary metabolites remain poorly understood. Systematic investigation of plant responses to metal stress, including metabolomic and transcriptomic analyses, could inform cultivation practices that minimize contamination while optimizing therapeutic quality.

Second, the health effects of chronic low-level exposure to multiple heavy metals through herbal products require epidemiological investigation. Longitudinal studies assessing relationships between herbal product use, metal exposure biomarkers, and health outcomes could provide the evidence base for more protective regulatory standards.

Third, the development of rapid, cost-effective analytical methods for heavy metal screening in herbal products would enable more widespread quality testing and facilitate regulatory compliance. Field-deployable techniques could support testing at points of harvest and sale, reducing the burden on centralized laboratory facilities.

Fourth, clinical trials of phytochemical nanoformulations are needed to establish efficacy and safety in human populations, moving beyond the extensive preclinical evidence currently available. Comparative effectiveness studies evaluating nanoformulated versus conventional herbal products could guide clinical decision-making and inform regulatory approvals.

Fifth, the integration of traditional knowledge with modern scientific approaches requires methodological development to ensure respectful and equitable collaboration. Frameworks for benefit-sharing and intellectual property protection that recognize the contributions of traditional healers and communities are essential for ethical research in ethnopharmacology.

❖ Implications for Policy and Practice

The findings of this review have important implications for policy and practice at multiple levels. For regulators, the evidence of heavy metal contamination in medicinal products supports the need for strengthened quality standards, expanded monitoring programs, and enhanced enforcement mechanisms. International harmonization of standards would facilitate trade while ensuring consistent consumer protection across jurisdictions.

For healthcare providers, awareness of potential contamination issues should inform discussions with patients about herbal product use and guide recommendations toward products from reputable sources with demonstrated quality control. Integration of herbal medicine safety into healthcare curricula would support evidence-based practice in this growing area of patient interest.

For the herbal products industry, investment in quality management systems that address heavy metal contamination represents both a responsibility and an opportunity. Products with demonstrated safety and quality can command premium prices and build consumer trust, supporting the long-term sustainability of the industry.

For researchers, the multidisciplinary nature of the issues addressed in this review underscores the value of collaborative approaches spanning ethnopharmacology, analytical chemistry, environmental science, nanotechnology, and clinical medicine. Funding mechanisms that support such collaboration could accelerate progress in addressing the complex challenges at the intersection of natural products, health, and environment.

Summary

This multidisciplinary review has synthesized evidence from over 50 studies to examine the therapeutic potential of medicinal plants, the challenges posed by heavy metal contamination, and the emerging role of nanotechnology and phytoremediation in addressing these challenges.

Medicinal plants including Cichorium intybus, Ziziphora persica, Lavandula angustifolia, and Catharanthus roseus demonstrate diverse pharmacological activities with applications in infectious diseases, inflammation, cardiovascular conditions, and cancer. The phytochemical diversity of these plants offers advantages for treating complex multifactorial diseases, though rigorous scientific validation and quality control are essential for clinical translation.

Heavy metal contamination of medicinal plants and food products represents a significant public health concern, with case studies from Northern Iran documenting elevated concentrations of lead, cadmium, and arsenic in commonly used species. Sources of contamination include industrial activities, agricultural practices, traffic-related pollution, and geological factors. Health risk assessments indicate potential for both non-carcinogenic and carcinogenic effects, supporting the need for strengthened regulatory standards and expanded monitoring programs.

Nanotechnology offers approaches to overcome the biopharmaceutical limitations of phytochemicals while potentially enhancing therapeutic efficacy. Nanoformulations including liposomes, polymeric nanoparticles, and lipid-based carriers have demonstrated improved bioavailability for numerous plant-derived compounds, with applications in cancer therapy, antimicrobial treatment, and wound healing. The global market for natural product nanoformulations is projected to reach $19 billion by 2035.

Phytoremediation provides sustainable approaches to managing heavy metal contamination, with medicinal and aromatic plants offering particular advantages for integrated remediation and product development. Advances in genetic

engineering, microbial-assisted remediation, and biomass valorization are enhancing the efficiency and economic viability of phytoremediation.

Critical research gaps include the effects of metal stress on secondary metabolite biosynthesis, health outcomes of chronic low-level exposure, development of rapid analytical methods, clinical trials of nanoformulations, and ethical frameworks for traditional knowledge integration. Addressing these gaps through collaborative, multidisciplinary approaches will be essential for realizing the full potential of medicinal plants while ensuring safety, sustainability, and equity.

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Authors' Contribution:

- [a-b]Conceptualization, data collection, interpretation, drafting of the manuscript and intellectual revisions
- The authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed

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