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Impact of pesticide residues on the phytopharmaceutical properties of major medicinal plants of India

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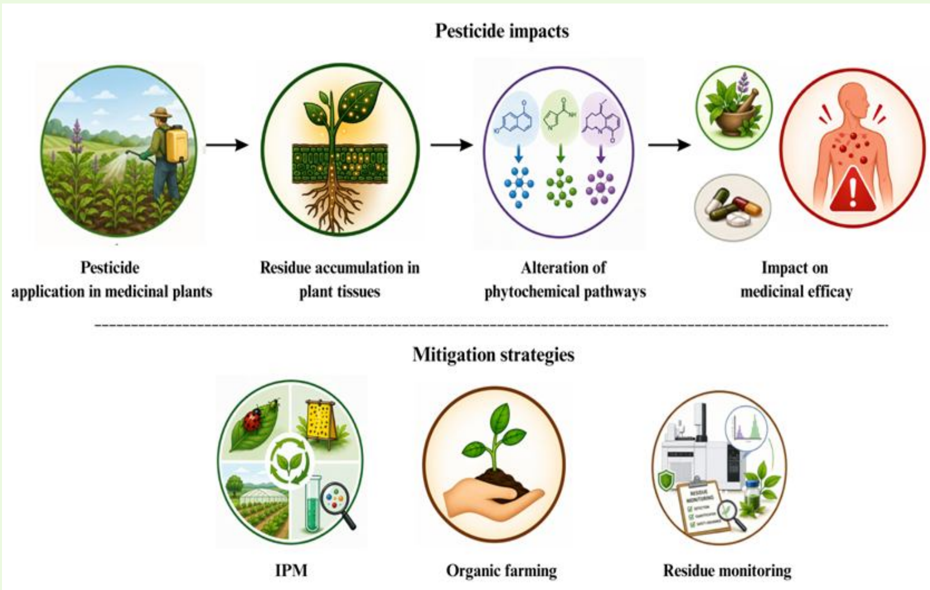
Abstract

Medicinal plants constitute the backbone of traditional healthcare systems in India and contribute significantly to global phytopharmaceutical markets. However, the extensive use of synthetic pesticides during cultivation has raised concerns regarding the accumulation of pesticide residues in medicinal plant materials. This review critically examines current evidence on the occurrence, analytical detection, and biological implications of pesticide residues in major medicinal plants of India, emphasizing the effects of pesticide residues on phytochemical composition, secondary metabolite biosynthesis, and pharmacological efficacy by interfering with metabolic pathways, inducing oxidative stress, and degrading bioactive constituents. These concerns extend beyond efficacy to significant toxicological risks for human health, while also posing challenges for regulatory frameworks aimed at ensuring the quality, safety, and standardization of herbal products. Sustainable production strategies such as integrated pest management, organic cultivation, and bioremediation approaches offer practical solutions for minimizing residues and preserving phytochemical integrity. This review highlightds the need for integrated research linking pesticide exposure with phytochemical and pharmacological outcomes, strengthened residue monitoring, and harmonized regulatory frameworks to ensure safe, residue-free medicinal plant production and sustain the therapeutic and commercial value of India's herbal resources.



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1. Introduction

About 80% of the global population depends on herbal medicinal products for primary health care. India, recognised as the "Botanical Garden of the World" (Singh, 2023), is one of the 17 megadiverse countries and possesses rich medicinal plant diversity, with nearly 15,000 documented species, of which about 8,000 are used in traditional medicine (Press Information Bureau, 2026). These botanical resources support established healthcare systems such as Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homoeopathy (Ministry of AYUSH, 2025). The Western and Eastern Ghats, Himalayas, and Aravalli range harbour nearly 70% of India's medicinal and aromatic plant species (Press Information Bureau, 2026). The global herbal medicine market is projected to reach 225 billion USD by 2033 (Verified Market Reports, 2026), driven by growing preference for plant-based therapeutics due to their minimal side effects and cost-effectiveness relative to conventional pharmaceuticals (Jadhav *et al*., 2025).

The therapeutic properties of medicinal plants arise largely from secondary metabolites such as alkaloids, flavonoids, phenolics, glycosides, and terpenoids, that are synthesised through intricate metabolic networks, including shikimate, mevalonate (MVP), and methylerythritol phosphate (MEP) pathways (Elshafie *et al*., 2023). The pharmacological efficacy of is dependent on the qualitative and quantitative integrity of their bioactive constituents. Therapeutically significant examples include curcuminoids (curcumin, dimethoxy curcumin, and bisdemethoxy curcumin) in *Curcuma longa* L., which mediate anti-inflammatory, antioxidant, and antineoplastic activities; withanolides in *Withania somnifera* (L.) Dunal, conferring adaptogenic, cytotoxic, and neuroprotective properties (Singh, 2023); and eugenol and phenylpropanoids in *Ocimum tenuiflorum* L., which provide antimicrobial, antiviral, and anti-inflammatory effects (Bhattarai *et al*., 2024).

Rising commercialisation and intensive cultivation have increased dependence on synthetic pesticides, raising concerns over residue contamination in medicinal plants. Multi-residue analyses of 1,771 cultivated herbal samples detected pesticides in 88%, with 59% exceeding European Pharmacopoeia limits and 43% containing banned toxic pesticides above maximum residue limits (MRL) (Luo *et al*., 2020). Export assessments revealed that 14.7% of raw herbal materials and 5.9% of alcoholic extracts from India exceeded European Union regulatory limits (Koshy *et al*., 2022). Beyond direct toxicological risks, persistent residues threaten environmental and human health due to long-term soil accumulation (Tzanetou and Karasali, 2022).

Pesticide residues also compromise phytopharmaceutical quality by disrupting secondary metabolism, altering phytochemical composition, and reducing therapeutic efficacy. Sublethal pesticide exposure disrupts enzymatic pathways, induces oxidative stress, and degrades bioactive compounds, thereby further diminishing pharmacological activity (Vicidomini *et al*., 2024). These effects create major challenges for quality assurance and highlight the need for rigorous standardisation and quality control. This review systematically examines the influence of pesticide residues on the phytopharmaceutical characteristics of medicinal plants, focusing on residue types and distribution, mechanisms disrupting secondary metabolite biosynthesis and bioactive integrity, associated impacts on therapeutic efficacy and toxicological risks, and sustainable mitigation strategies including integrated pest management (IPM), organic cultivation, and bioremediation approaches.

2. Major medicinal plants of India and their bioactive profiles

The pharmacological efficacy of medicinal plants depends on the concentration, stability, and bioavailability of their phytochemicals, which act on specific molecular targets and exert multi-target effects through antioxidant activity, signaling pathway regulation, and immune modulation. The major medicinal plant species, along with their key bioactive constituents and primary pharmacological activities, are detailed in Table 1.

Table 1: Key species and phytochemical constituents

Plant species	Common name	Key bioactive compounds	Pharmacological activity	References
Aegle marmelos (L.) Corrêa	Beal	Coumarins, xanthotoxol, imperatorin, aegeline, marmelosin	Antidiabetic, anticancerous, antimicrobial, immunogenic, radioprotective, wound healing	Singh, 2023
Aloe vera (L.) Burm.f.	Aloe vera	Glycoproteins, polysac-charides, anthraquinones	Hypoglycemic, wound healing, anti-inflammatory, radio-protection	Ansari *et al*., 2025; Liang *et al*., 2020
Asparagus racemosus Willd.	Shatavari	Shatavarins, flavonoids	Lactation support, fertility enhancement, anti-inflammatory	Guo *et al*., 2023; Singh, 2023
Azadirachta indica A.Juss.	Neem	Nimbidin, azadirachtin, quercetin, β-sitosterol, terpenoids, flavonoids	Antidiabetic, antihyperglycemic, wound healing, antimicrobial, anti-inflammatory, antioxidant	Elshafie *et al*., 2023; Chen *et al*., 2023
Bacopa mon-nieri (L.) Pennell	Brahmi	Bacosides, alkaloids, saponins	Neuroprotective, memory enhancer, wound healing, anti-inflammatory	Singh, 2023
Catharanthus roseus (L.) G.Don	Sadabahar	Vincristine, vinblastine	Hypoglycemic, antihyperglycemic, wound healing	Ansari *et al*., 2025; Kumar *et al*., 2022
Centella asiatica (L.) Urban	Mandookparni	Asiaticoside, asiatic acid, made-cassic acid, madecassoside	Wound healing, collagen synthesis, antioxidant, neuroprotective, memory enhancement	Ansari *et al*., 2025
Cinnamomum verum J. Presl	Cinnamon	Cinnamaldehyde, eugenol, polyphenols	Antidiabetic, antimicrobial, bronchitis treatment	Singh, 2023; Zagoskina *et al*., 2023

Curcumin longa	Turmeric	Curcumin, turmerone, zingiberene	Wound healing, antidiabetic, anti-inflammatory, antioxidant, radioprotection	Singh, 2023
Gymnema sylvestre R. Br.	Gudmar	Gymnemic acids, gymnemosides, gurmarin	Hypoglycemic, β-cell regeneration, glucose absorption reduction, insulin secretagogue	Ansari *et al*., 2025
Ocimum tenuiflorum	Tulsi	Eugenol, ursolic acid, rosmarinic acid, orientin, vicenin, flavonoids	Hypoglycemic, antioxidant, hypolipidemic, wound healing, radioprotection, immunomodulatory, anti-inflammatory, antimicrobial	Bhattarai *et al*., 2024; Chen *et al*., 2023; Zagoskina *et al*., 2023
Piper longum L.	Long pepper	Piperine, pellitorine	Antidiabetic, respiratory health, digestive aid	Singh, 2023
Pterocarpus marsupium Roxburgh	Beejasar	Epicatechin, pterostilbene, marsupsin, flavonoids	Hypoglycemic, β-cell regeneration, insulin release enhancement	Ansari *et al*., 2025
Santalum album L.	Sandalwood	Santalol, santalene	Wound healing, skin disorders, anti-inflammatory	Singh, 2023
Withania somnifera (L.) Dunal	Ashwagandha	Withanolides, withaferin A, sitoindosides	Adaptogenic, antidiabetic, immunomodulatory, neuroprotective, stress reduction	Singh, 2023

3. Phytochemical classes and their pharmacological mechanisms

The pharmacological significance of Indian medicinal plants derives from the structural and functional diversity of their secondary metabolites. A comprehensive understanding of individual phytochemical classes is essential for evaluating how pesticide-induced disruptions may alter biosynthesis, bioactivity, and overall therapeutic efficacy.

3.1 Alkaloids

Alkaloids are nitrogen-containing heterocyclic phytochemicals with diverse pharmacological activities, including anticancer, antimalarial, antiasthmatic, and antimicrobial effects. In *C. roseus*, vincristine and vinblastine are clinically important monoterpenoid indole alkaloids that inhibit microtubule assembly and induce mitotic arrest. Their biosynthesis proceeds through secologanin and tryptamine-derived intermediates, leading to catharanthine and vindoline, which couple to form the active bis-indole alkaloids (Kumar *et al*., 2022).

3.2 Flavonoids and polyphenols

Flavonoids and polyphenols are major phenolic secondary metabolites biosynthesised through the phenylpropanoid pathway. Quercetin, present in *A. indica* and *O. tenuiflorum*, exhibits antioxidant, antimicrobial, and anti-inflammatory effects, while curcuminoids from *C. longa* contribute anti-inflammatory and antiproliferative activities (Chen *et al*., 2023). Polyphenols also participate in antiviral and immunomodulatory responses, highlighting their pharmacological significance (Zagoskina *et al*., 2023).

3.3 Terpenoids and diterpenes

Terpenoids and diterpenes are structurally diverse phytochemicals biosynthesised through the MEP and MVP pathways, yielding metabolites with significant pharmacological potential. This class includes triterpene saponins from *Astragalus membranaceus*, which exhibit immunomodulatory, anticancer, antidiabetic, and cardioprotective activities (Dong *et al*., 2023).

3.4 Phenolic acids and lignans

Phenolic acids and lignans are plant secondary metabolites biosynthesised through the shikimate and phenylpropanoid pathways, which contribute to antioxidant defense and stress adaptation (Ahlawat *et al*., 2024). They exert pharmacological effects through ROS and modulation of inflammatory and antioxidant pathways. Gallic acid, ellagic acid, and related phenolics in *Terminalia chebula* Retz. show hepatoprotective, anti-inflammatory, antifibrotic, and anticancer activities through cytokine suppression and metabolic regulation (Li *et al*., 2025).

3.5 Saponins and glycosides

Saponins and glycosides are structurally diverse amphiphilic metabolites composed of triterpenoid or steroidal aglycones linked to carbohydrate moieties. Their pharmacological effects are associated with membrane interactions, modulation of metabolic and inflammatory pathways, and antioxidant functions (Bildziukevich *et al*., 2023). Steroidal saponins from *A. racemosus* contribute immunomodulatory and adaptogenic effects (Guo *et al*., 2023), while plant glycosides from *A. vera* and saponin-rich extracts support wound healing and tissue repair (Liang *et al*., 2020). Triterpenoid saponins, including those from *Terminalia arjuna* (Roxb.) Wight and Arn., also show cardioprotective potential (Bildziukevich *et al*., 2023).

3.6 Essential oils and volatile constituents

Essential oils and volatile constituents are mixtures of terpenoids and phenylpropanoids biosynthesised through isoprenoid pathways, contributing to plant defense and pharmacological activity. Volatile constituents such as eugenol from *O. tenuiflorum* and cinnamaldehyde from *C. verum* exhibit broad antimicrobial activity, primarily through membrane disruption and related protective mechanisms (Zagoskina *et al*., 2023). Terpenoid-rich essential oils also demonstrate cytoprotective and wound healing relevance, supporting their therapeutic applications in phytomedicine and bioactive formulations (Ortiz and Sansinenea, 2023).

4. Occurrence and sources of pesticide residues

4.1 Types of pesticides

Pesticides are systematically categorised on the basis of their chemical composition, mode of action, route of entry into target organisms, and origin, with chemical classification serving as the principal framework for evaluating environmental behaviour and toxicological implications. Based on mode of entry, pesticides are categorised as contact, systemic, fumigant, stomach poison, or repellents, while origin-based classification distinguishes natural and synthetic compounds. Among these systems, classification into organochlorines, organophosphates, carbamates, and pyrethroids provides a mechanistic basis for understanding differences in persistence, target specificity, toxicodynamics, and residue behaviour (Hassaan and El Nemr, 2020).

4.1.1 Organochlorine pesticides

Organochlorine pesticides are chlorinated hydrocarbons characterized by lipophilicity, semi-volatility, and persistence in the environment due to slow degradation, promoting accumulation in soils, water, plants, and biological tissues (Jibrin *et al*., 2021). This class includes DDT, aldrin, dieldrin, lindane, heptachlor, and hexachlorobenzene, representing diphenyl aliphatic, cyclodiene, cyclohexane, and chlorinated camphene organochlorines. Their toxicity is associated with disruption of neuronal sodium and potassium ion transport, resulting in hyperexcitation, seizures, and neurotoxic effects, alongside membrane injury, reactive oxygen species generation, and apoptosis-related mechanisms linked to neurodegenerative pathways (Alehashem *et al*., 2024). Owing to their persistence and toxicological risk, several members of this class have been subjected to international regulatory restrictions.

4.1.2 Organophosphorus pesticides

Organophosphorus pesticides comprise phosphoric acid derivatives, including organothiophosphates, phosphonates, and phosphoramidates, represented by compounds such as chlorpyrifos, diazinon, malathion, parathion, and dichlorvos. These compounds exert toxicity primarily through acetylcholinesterase inhibition, disrupting cholinergic neurotransmission and causing neuromuscular paralysis and systemic effects (Tsai *et al*., 2021). Beyond acute poisoning, chronic exposure has been linked with genotoxic, neurotoxic, reproductive, developmental, hepatic, renal, and cardiovascular effects (Chen *et al*., 2024).

4.1.3 Carbamate pesticides

Carbamates are organic esters of carbamic acid, including carbaryl, carbofuran, methomyl, aldicarb, and propoxur, with toxicity varying according to structural configuration (Sajad *et al*., 2024). Similar to organophosphates, they interfere with cholinergic neurotransmission through cholinesterase inhibition, although their generally shorter persistence often makes acute intoxication more prominent than chronic accumulation (Hassaan and El Nemr, 2020). Exposure is associated with respiratory distress, gastrointestinal disorders, cardiovascular effects, and neurological impairment (Chen *et al*., 2024).

4.1.4 Pyrethroid pesticides

Pyrethroids are synthetic analogues of natural pyrethrins developed for greater stability and prolonged residual activity (Sajad *et al*., 2024). They act by inducing nervous system hyperexcitation, showing high insecticidal efficiency with selective toxicity, though adverse effects are reported in aquatic organisms and at elevated vertebrate exposure (Hassaan and El Nemr, 2020).

4.2 Sources of contamination

Pesticide residues in medicinal plants arise from multiple pathways operating across the value chain. The primary source is direct application during cultivation to manage diverse pest complexes affecting medicinal crops. In India, the absence of crop-specific MRLs leads to the use of pesticide regimes designed for food crops at inappropriate doses for medicinal plants, creating safety concerns and complicating regulation and risk management. Soil is a major reservoir for persistent pesticides such as organochlorines and organophosphates, enabling continued uptake by plants even after cessation of application (Riedo *et al*., 2023). Residue levels in agricultural soils exceed 3223 ng/g dry weight (Rajput *et al*., 2022), leading to bioaccumulation in plant tissues due to the limited biodegradability and lipophilic nature of pesticides (Pririti *et al*., 2024). Pesticide residues arise from contaminated soil and irrigation water, with additional input from atmospheric drift of nearby agricultural applications, leading to accumulation in plant tissues (Bratu *et al*., 2023).

4.3 Residue distribution

Pesticide residue distribution depends on the physicochemical properties of pesticides, plant morphology, and surrounding environmental conditions. Lipophilic pesticides such as organochlorines and pyrethroids exhibit strong affinity for lipid-rich matrices in plant tissues, including waxy cuticles and roots (Xiao *et al*., 2021). In contrast, hydrophilic compounds, including organophosphates and carbamates, preferentially partition into aqueous compartments within plants, such as cell sap (Lao *et al*., 2024). Soil attributes such as organic matter, pH, and cation exchange capacity (Hua *et al*., 2024), along with temperature, climate, and seasonal variation (Pakar *et al*., 2025), regulate pesticide retention and uptake. Pesticide properties, such as persistence and degradation behaviour, determine their mobility and long-term soil residue formation (Veloso *et al*., 2025). Agricultural practices, including application method, frequency, and land use, further regulate residue distribution (Yun *et al*., 2022). Biotransformation processes, including conversion of aldrin to dieldrin and heptachlor to its epoxide, contribute to residue complexity within plant tissues (Sosan *et al*., 2020). Environmental factors further modulate residue dynamics, with wet conditions enhancing pesticide mobility and plant uptake, thereby increasing accumulation levels (Betz-Koch *et al*., 2023).

5. Analytical techniques for residue detection

5.1 Sample preparation

QuEChERS (Quick, Easy, Cheap, Effective, Rugged, Safe) is a widely used sample preparation method for multiresidue pesticide analysis in plants due to its operational simplicity, rapid processing, and cost-effectiveness. The procedure begins with the homogenization of 10 to 15 g of sample, followed by extraction using acetonitrile. Salting-out partitioning is carried out using magnesium sulfate ($MgSO_2$), sodium chloride (NaCl), and buffering salts to promote phase separation and reduce water content. Clean-up is performed through dispersive solid-phase extraction (d-SPE) using sorbents such as primary secondary amine (PSA), C18, or graphitised carbon black (GCB) to remove matrix interferences, including sugars, lipids, organic acids, and pigments. The procedure includes initial single-phase extraction followed by liquid-liquid partitioning (LLP) and d-SPE (Patel *et al*., 2024). In comparison to conventional extraction techniques such as liquid-liquid extraction, QuEChERS reduces solvent use and processing time while maintaining high recovery and accuracy (Chen *et al*., 2020). In medicinal plants, modifications to the QuEChERS protocol are necessary due to low moisture content and the presence of co-extracted compounds such as pigments and essential oils. The comparative performance of modified QuEChERS protocols used for pesticide residue extraction and clean-up in complex medicinal plant matrices is presented in Table 2. The use of alternative sorbents improves clean-up efficiency, reduces matrix interferences, and maintains analyte recovery.

Table 2: Performance of modified QuEChERS approaches for pesticide residue analysis in plant matrices

Matrix	Modification	d-SPE sorbent	Recovery (%)	RSD (%)	References
Fruits/ vegetables (High-moisture matrix)	Modified QuEChERS coupled with LC-MS/MS	PSA / GCB / C18	70.3-113.2	<6.8	Jahan *et al*., 2023
Medicinal plants (Low-moisture matrices)	Modified QuEChERS using acetonitrile extraction	MWCNT (Amino-modified)	70-120	<16.82	Fan *et al*., 2022
Medicinal plants (High-pigment matrices)	Matrix-specific clean-up modification replacing GCB with Florisil	Florisil	70.1-119.3	5.9	Slowik-Borowiec *et al*., 2022
Medicinal plants (Processed, woody root matrix)	Modified QuEChERS optimised for complex herbal matrix	Optimised d-SPE clean-up	60.4-139.3	<15	Xu X. *et al*., 2022

Abbreviations: C18, Octadecyl Silica; d-SPE, Dispersive Solid Phase Extraction; GCB, Graphitised Carbon Black; LC-MS/MS, Liquid Chromatography Tandem Mass Spectrometry; MWCNT, Multi-walled carbon nanotubes; PSA, Primary Secondary Amine; QuEChERS, Quick, Easy, Cheap, Effective, Rugged, and Safe; RSD, Relative Standard Deviation.

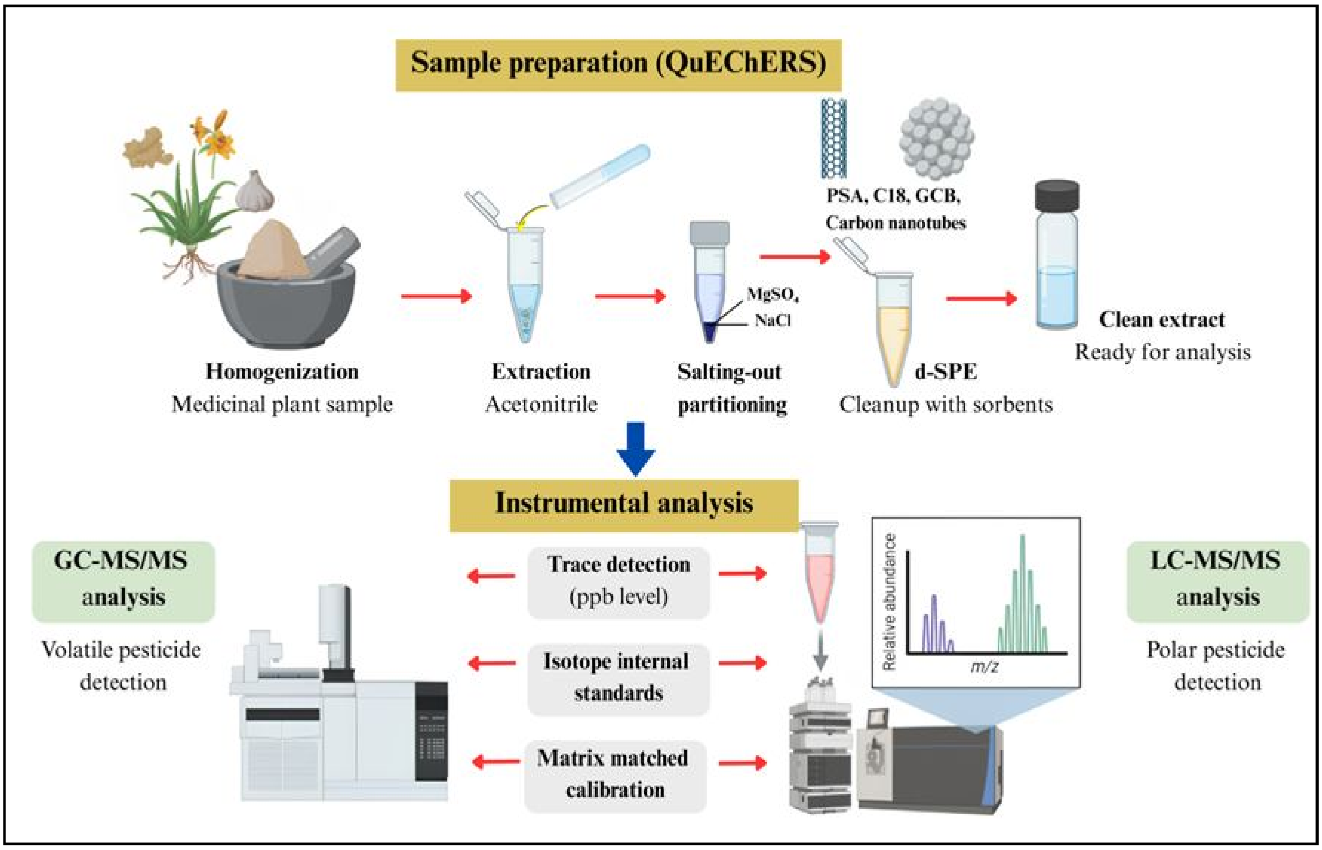

Figure 1: Schematic workflow for pesticide residue analysis in medicinal plants using QuEChERS-based sample preparation and chromatographic mass spectrometric detection. The figure illustrates sample homogenization, acetonitrile extraction, salting-out partitioning, d-SPE clean-up, and instrumental analysis by GC-MS/MS and LC-MS/MS for multiresidue pesticide detection.

5.2 Instrumental analysis

5.2.1 Gas chromatography-mass spectrometry

Gas chromatography-mass spectrometry (GC-MS) is used for quantitative and confirmatory analysis. It is also integrated with advanced analytical techniques such as liquid chromatography-mass spectrometry (LC-MS) for sensitive and selective detection of pesticide residues (Patel *et al*., 2024). Single-stage systems, such as GC-MS and LC-MS, provide basic identification, whereas tandem configurations, Gas chromatography-tandem mass spectrometry (GC-MS/MS) and Liquid chromatography-tandem mass spectrometry (LC-MS/MS), offer enhanced selectivity and sensitivity through two-stage mass analysis. GC-MS/MS is widely used for volatile and semi-volatile pesticides, enabling simultaneous multi-residue detection at trace levels with quantification limits at or below 0.01 mg kg^{-1} and reliable recovery across diverse herbal matrices (Pan *et al*., 2025).

5.2.2 Liquid chromatography-tandem mass spectrometry

LC-MS/MS is widely applied for analysis of polar, thermolabile, and non-volatile pesticides, eliminating thermal degradation associated with GC methods while ensuring high sensitivity and accurate trace-level quantification. Advanced systems such as ultra-high performance liquid chromatography (UHPLC) coupled with triple quadrupole mass analysers operating in multiple reaction monitoring (MRM) acquisition mode enable rapid, simultaneous multi-residue determination across diverse pesticide classes. Electrospray ionisation in positive and negative ion acquisition modes supports compound detection across diverse physicochemical properties, expanding the analytical scope (Li *et al*., 2020). Coupling with QuEChERS extraction improves sample preparation efficiency and supports high-throughput analysis in complex medicinal plant matrices with reduced interference. Matrix effects from co-eluting constituents still affect ionization, requiring matrix-matched calibration and internal standards for accurate results. Recent advances in hybrid and high-resolution mass spectrometry enhance selectivity and identification reliability at low concentrations, ensuring compliance with regulatory standards (Pan *et al*., 2025). The analytical workflow, from QuEChERS extraction to GC-MS/MS and LC-MS/MS detection, is illustrated in Figure 1.

5.3 Challenges in residue analysis of medicinal plant matrices

Despite these advantages, pesticide residue detection in medicinal plant matrices remains constrained by the complex and variable phytochemical composition of these materials. High levels of secondary metabolites, including phenolic acids, flavonoids, alkaloids, terpenoids, and essential oils, along with co-extracted pigments, lipids, and sugars, induce matrix effects. These effects result in ion suppression or enhancement in LC-MS/MS and altered chromatographic behaviour, thereby reducing quantification reliability (Wu and Ding, 2023). Variability also arises from analyte interactions within the injector, column, and detector systems, affecting analytical consistency. The wide polarity range of both pesticide residues and endogenous compounds complicates the development of a single, efficient extraction protocol, making multiclass, high-throughput residue analysis difficult (Pan *et al*., 2025). Analytical complexity is further increased by the diversity of medicinal plant forms encountered in commerce, including fresh samples, dried herbal materials, powders, infusions, decoctions, extracts, and polyherbal formulations, each requiring matrix-specific clean-up strategies and validation approaches (Pandey *et al*., 2024). The lack of suitable blank matrices and certified reference materials limits the use of matrix-matched calibration and hinders inter-laboratory comparability and method harmonisation. To address these constraints, current workflows rely on matrix-matched calibration, isotope-labelled internal standards, analyte protectants, and optimised clean-up techniques such as QuEChERS with dispersive sorbents to reduce matrix interference and improve analytical performance.

6. Impact of pesticide residues on phytochemical composition

Pesticide residues affect medicinal plants through a cascade of interconnected biochemical disturbances. It disrupts secondary metabolic biosynthetic pathways associated with therapeutic compounds, induces oxidative stress that exacerbates cellular damage, and destabilises phytochemical biosynthesis, ultimately leading to reductions and compositional changes in bioactive compounds. Figure 2 illustrates the mechanistic link between pesticide-induced oxidative stress, pathway disruption, and reduced bioactive metabolite production in medicinal plants.

6.1 Disruption of secondary metabolism

Pesticide residues act as chemical stressors that disrupt secondary metabolism in medicinal plants, affecting the biosynthesis of pharmacologically important metabolites such as phenolics, flavonoids, terpenoids, alkaloids, and essential oils. Major mechanisms of disruption include the following:

6.1.1 Phytohormonal imbalance

Organophosphate and pyrethroid insecticides alter jasmonic acid (JA), abscisic acid (ABA), and salicylic acid (SA) signaling, thereby affecting phenylpropanoid metabolism and essential oil biosynthesis (Lin *et al*., 2022).

6.1.2 Inhibition of precursor biosynthesis

Glyphosate inhibits 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) in the shikimate pathway, reducing synthesis of key precursors for secondary metabolites such as phenylalanine, tyrosine, and tryptophan (Ruszkowski and Forlani, 2022). This may impair biosynthesis of compounds such as rosmarinic acid in *Anthoceros* spp. and *Ocimum* spp., and terpenoid indole alkaloids in *C. roseus* (Bhattarai *et al*., 2024; Pezeshki *et al*., 2022; Kumar *et al*., 2022).

6.1.3 Disruption of terpenoid pathways

Pesticide stress affects the MVA and MEP pathways through modulation of enzymes such as 3-hydroxy-3-methylglutaryl-CoA reductase (HMGR), 1-deoxy-D-xylulose 5-phosphate synthase (DXS), and DXP reductoisomerase (DXR), influencing isoprenoid and terpenoid biosynthesis (Bergman *et al*., 2024). Reduced flux through the MVA and MEP pathways may impair biosynthesis of pharmacologically important metabolites, including withanolides associated with the adaptogenic and anti-inflammatory properties of *W. somnifera*, and curcuminoids whose accumulation relies on tightly regulated polyketide synthase-mediated pathways in *Curcuma* (Khalid *et al*., 2025; Chen *et al*., 2022).

6.1.4 Metabolic perturbations

Metabolomic analyses confirm disruption of amino acid metabolism, including phenylalanine, tyrosine, and tryptophan, which act as precursors for multiple classes of secondary metabolites (Xie *et al*., 2022).

6.2 Oxidative stress induction

Pesticide-associated oxidative stress is a widely documented mechanism through which residues influence the metabolic integrity of medicinal plants. Exposure to pesticides triggers excessive generation of reactive oxygen species (ROS), including superoxide anion, hydrogen peroxide, hydroxyl radicals, and singlet oxygen, which disrupt cellular homeostasis and impair phytochemical accumulation (Vicidomini *et al*., 2024). Pesticides intensify ROS accumulation through simultaneous disruption of the shikimate pathway and photosynthetic electron transport, with similar oxidative responses reported in *Mentha arvensis* under mancozeb exposure (Muthusamy, 2025). Elevated malondialdehyde (MDA) levels in *W. somnifera* and *O. tenuiflorum* following pyrethroid and organophosphate exposure confirm enhanced lipid peroxidation and oxidative membrane damage (Muthusamy, 2025). These responses are associated with impairment of enzymatic antioxidants such as superoxide dismutase, catalase, and ascorbate peroxidase, depletion of non-enzymatic antioxidants including glutathione and ascorbate, and activation of stress signaling pathways such as MAPK (Mitogen-Activated Protein Kinase) and Nrf2 (Nuclear Factor Erythroid 2-Related Factor 2) (Jomová *et al*., 2023; Mishra *et al*., 2023). Imidacloprid and penconazole further aggravate oxidative stress by depleting glutathione (GSH) and superoxide dismutase (SOD) while increasing thiobarbituric acid reactive substances (TBARS), resulting in disruption of cellular redox balance (Lakshman *et al*., 2024). Although short-term increases in soluble sugars and antioxidant enzymes reflect adaptive responses for osmotic regulation and reactive oxygen species detoxification (Ajermoun *et al*., 2022), prolonged pesticide exposure overwhelms these defense systems, causing damage to proteins, DNA, lipids, and oxidative degradation of labile polyphenols and flavonoids, ultimately compromising the antioxidant and anti-inflammatory potential of medicinal plants.

6.3 Reduction in bioactive compounds

Pesticides can interfere with the biochemical pathways of secondary metabolites in medicinal plants, leading to changes in the concentration of these pharmacologically active substances. These effects result from disruption of enzyme activity, diversion of metabolic precursors, and ROS-driven degradation, causing both quantitative loss and qualitative modification of phytochemicals. Pesticide exposure reduces key bioactive compounds, particularly flavones such as quercetin and luteolin and phenolic acids such as caffeic acid, ferulic acid, syringic acid, and sinapic acid (Lin *et al*., 2022). A summary framework of pesticide-induced metabolic disruptions and their effects on plant bioactive compounds is listed in Table 3.

Table 3: Effects of major pesticide classes on plant physiological mechanisms and phytochemical composition

Pesticide class	Primary mechanism of action in plants	Impact on phytochemicals and efficacy	References
Organochlorines	Lipid bioaccumulation, ROS membrane damage	Labile polyphenol degradation	Jomová *et al*., 2023; Koshy *et al*., 2022
Organophosphates	JA and SA signaling disruption, reduced acetylcholinesterase inhibition	Curcuminoid reduction in *C. longa*, essential oil biosynthesis disruption	Sharma *et al*., 2019; Lin *et al*., 2022
Carbamates	Reversible enzyme inhibition, oxidative stress induction	Secondary metabolite loss, hepatotoxic carryover risk	Luo *et al*., 2020; Vicidomini *et al*., 2024
Pyrethroids	H_2O_2 and superoxide elevation, lipid peroxidation increase	Metabolite diversity reduction in *Amaranthus*, phenolic depletion	Kumar *et al*., 2025; Lin *et al*., 2022

6.3.1 Case study 1: Pesticide-induced phytochemical alteration in turmeric (*C. longa*)

Multi-residue surveys have documented the frequent occurrence of chlorpyrifos, profenofos, acephate, dimethoate, mancozeb, metalaxyl, and banned endosulfan in Indian turmeric rhizome and powder, with chlorpyrifos and profenofos often exceeding the EU MRL of 0.01 mg/kg, raising export and safety concerns (Ghosh *et al*., 2020). Such residues are particularly concerning because curcuminoid biosynthesis in turmeric depends on the phenylpropanoid pathway, initiated by phenylalanine ammonia-lyase and culminating in polyketide condensation reactions mediated by diketide-CoA synthase and curcumin synthase enzymes (Chen *et al*., 2022). Pesticides function as chemical stressors capable of disrupting this pathway through oxidative stress induction, transcriptional reprogramming, and enzymatic interference (Liu *et al*., 2025). Major regulatory enzyme in phenylpropanoid metabolism, phenylalanine ammonia-lyase, is susceptible to pesticide-induced oxidative stress and disrupted phytohormone signalling, which may adversely affect curcuminoid biosynthesis and accumulation during rhizome development (Sharma *et al*., 2019). Such disruption has implications for pharmaceutical production, as diminished curcuminoid content may reduce extraction efficiency, increase raw material demand, and elevate processing costs for standardized curcumin formulations.

6.3.2 Case study 2: Cypermethrin-induced metabolic disruption in *Amaranthus hybridus* L.

Foliar application of Cypermethrin (CYP) at the recommended dose (100 ppm) and double dose (200 ppm) induced significant physiological and metabolic alterations in *A. hybridus*. CYP exposure elevated oxidative stress markers, with H_2O_2 increasing by 9.6% and 35.5%, superoxide radicals by 33.4% and 115.5%, respectively, while lipid peroxidation (MDA) increased by 62.86% at the higher dose, indicating progressive ROS-mediated cellular damage. Pesticide stress also caused a marked decline in secondary metabolite diversity, decreasing from 138 metabolites at the recommended dose to 88 at the double dose, reflecting suppression of biosynthesis of bioactive compounds. These findings demonstrate that increasing pesticide burden disrupts cellular homeostasis, impairs secondary metabolism, and depletes pharmacologically important metabolites (Kumar *et al*., 2025).

6.3.3 Case study 3: Pesticide-induced phytochemical alteration in peppermint (*Mentha* × *piperita* L.)

Lin *et al*. (2022) reported that foliar application of insecticides, including imidacloprid, pyriproxyfen, acetamiprid, chlorantraniliprole, and chlorfenapyr, significantly altered secondary metabolism in peppermint. Pesticide stress reduced key phenylpropanoid metabolites, with quercetin declining by 50.0-78.8% and 4-hydroxybenzoic acid by 41.0-72.6%, alongside decreases in rutin, apigenin, caffeic acid, ferulic acid, syringic acid, and sinapic acid, compounds associated with the therapeutic properties of peppermint. Insecticide exposure diverted phenolic acids toward lignin biosynthesis, increasing lignin accumulation and depleting medicinally important phenolics. Elevated cinnamic acid indicated phenylpropanoid flux shifted toward defense responses, compromising phytochemical quality and therapeutic efficacy.

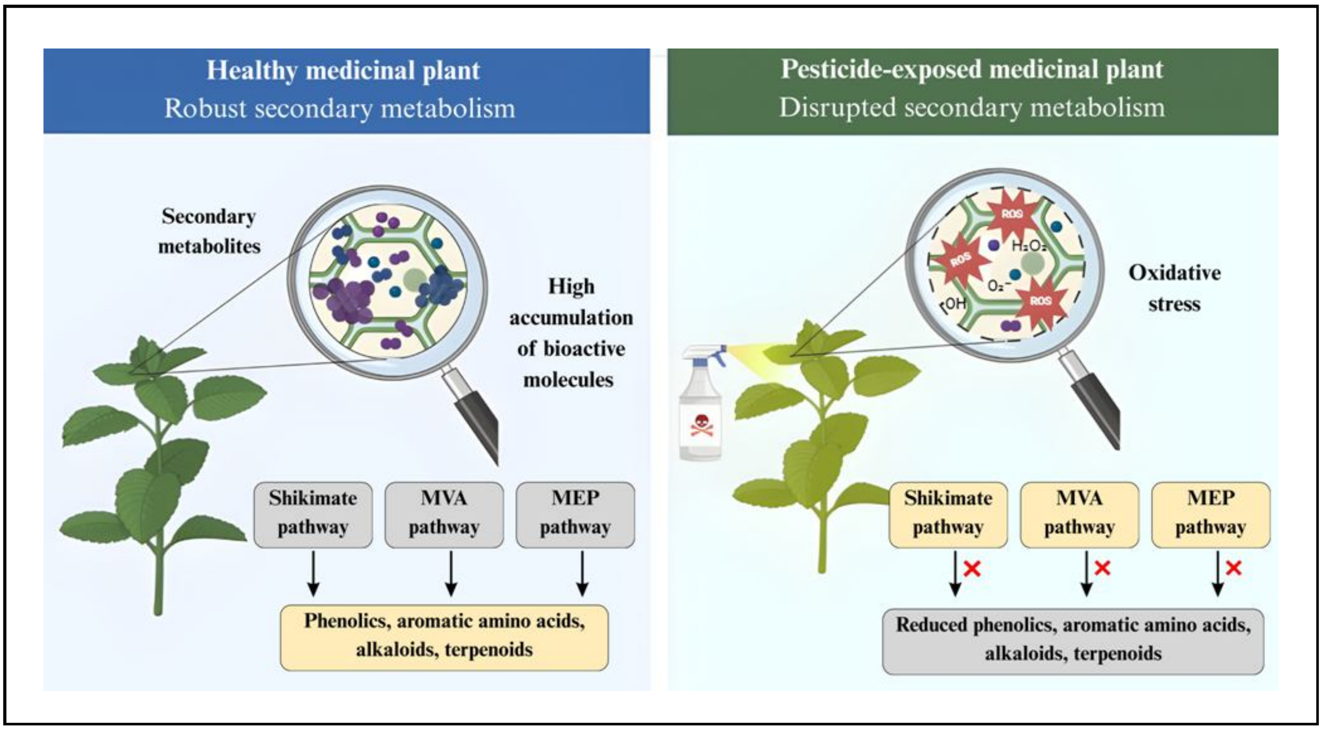

Figure 2: Overview of pesticide residue effects on medicinal plants, illustrating oxidative stress, disruption of shikimate, MVA, and MEP pathways, and reduced accumulation of bioactive secondary metabolites.

7. Impact on medicinal and pharmacological properties

7.1 Decline in therapeutic efficacy

Pesticide exposure disrupts the medicinal value of plants by altering the composition, interactions, and metabolic fate of bioactive compounds. Oxidative stress induced by pesticides modifies key phytochemicals, which are essential for therapeutic efficacy in complex herbal systems. Altered phytochemical profiles affect absorption and metabolism, including cytochrome P450 3A (CYP3A) enzyme activity, reducing bioavailability, disrupting synergism, and lowering pharmacological efficacy in medicinal plants (Chen *et al*., 2021). Pesticide-induced metabolic disruption reduces the therapeutic efficiency of medicinal plants by depleting and modifying bioactive compounds, despite no visible morphological injury (Lin *et al*., 2022). The resultant reduction in phenolics, flavonoids, and other secondary metabolites directly impairs antioxidant, antimicrobial, and anticancer activities that define the therapeutic value of medicinal plant preparations (Sun and Shahrajabian, 2023). Alterations of curcuminoids may impair modulation of key molecular targets, including nuclear factor kappa B (NF-κB), cyclooxygenase 2 (COX-2), IκB kinase 1 (IKK1), and 5-lipoxygenase (5-LOX), thereby reducing anti-inflammatory and neuroprotective activities. Moreover, depletion of phenols and curcuminoids has been associated with reduced acetylcholinesterase and lipoxygenase (LOX) inhibitory potential, reinforcing the decline in therapeutic efficacy of medicinal plants under pesticide stress (Perez *et al*., 2025).

7.2 Toxicological concerns

Pesticide residues in medicinal plants pose toxicological risks through both direct human exposure and deterioration of phytopharmaceutical quality. Chronic exposure to low-dose residues through medicinal plant preparations has been associated with hepatotoxic, nephrotoxic, neurotoxic, carcinogenic, developmental, reproductive, immunological, and endocrine-related effects (Chen *et al*., 2024; Luo *et al*., 2020). The exposure routes and their corresponding systemic health impacts, illustrating the multifaceted toxicological burden imposed by pesticide-contaminated medicinal plant products, are depicted in Figure 3. These risks are intensified by widespread multi-residue contamination, where concurrent occurrence of multiple pesticides increases cumulative and synergistic toxicity potential. Particularly, organophosphates, carbamates, and organochlorines such as chlorpyrifos, phorate, omethoate, and DDT have been implicated in genotoxic and neurotoxic outcomes, with some residues reported above regulatory thresholds (Luo *et al*., 2020).

Beyond systemic toxicity, pesticide contamination can compromise medicinal quality by altering phytochemical integrity, disturbing biochemical synergy, and affecting the pharmacological reliability of plant-based therapeutics. Evidence from Indian medicinal plants further supports these concerns, where residues detected in raw materials and alcoholic extracts demonstrated contaminant carryover into herbal products, and hazard quotient values exceeding one for dieldrin in *O. tenuiflorum* and hexachlorocyclohexane in *Glycyrrhiza glabra* L. indicated specific toxicological risks (Koshy *et al*., 2022). The combined effects of phytochemical depletion, disrupted biochemical synergy, altered pharmacokinetics, and direct human toxicity undermine the safety, quality, and clinical reliability of plant-based therapeutics, highlighting the need for stringent residue monitoring and cultivation practices.

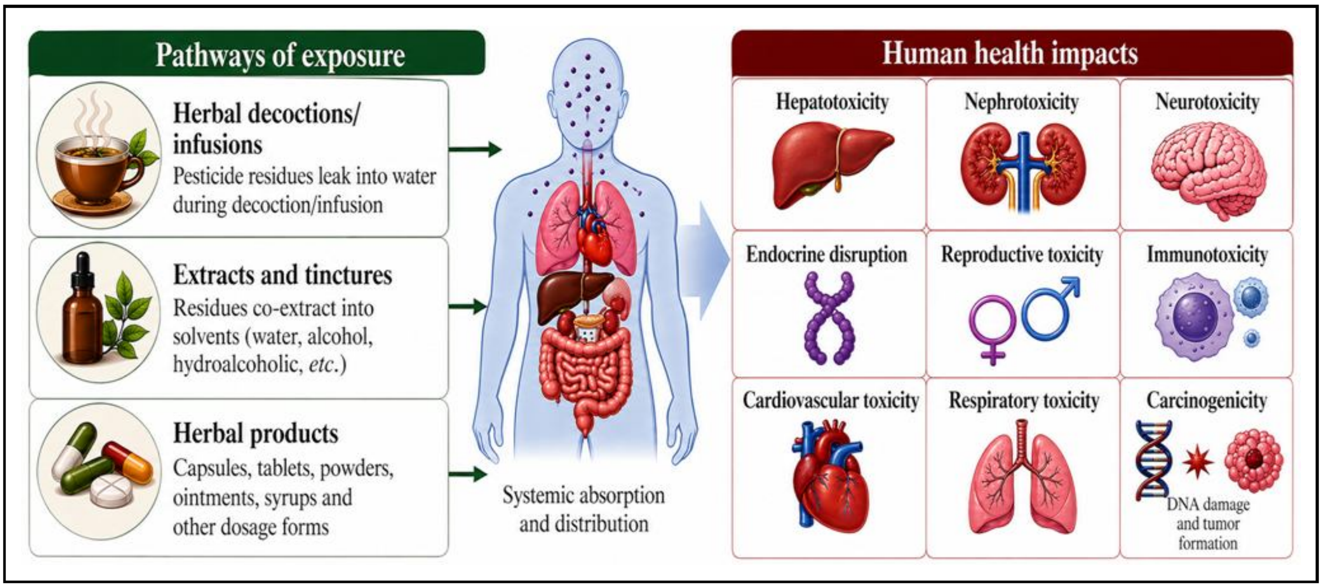

Figure 3: Pathways of human exposure to pesticide residues in medicinal plant products and their associated toxicological health impacts.

7.3 Interaction with bioactive compounds

Pesticide residues interact with plant bioactive compounds through metabolic, physicochemical, and pharmacokinetic mechanisms, leading to significant alterations in phytochemical functionality and therapeutic performance. Systemic insecticides can reduce phenylpropanoid metabolites, including rutin, quercetin, caffeic acid, ferulic acid, syringic acid, and sinapic acid, while redirecting phenolic precursors toward lignin biosynthesis, a process further modulated by JA, SA, and ABA signaling, potentially altering phytochemical composition and pharmacological activity (Lin *et al*., 2022; Moradi *et al*., 2020). Pesticides can alter the pharmacological behaviour of medicinal plant compounds through modulation of cytochrome P450 enzymes that regulate xenobiotic metabolism. Induction or inhibition of CYP isoforms by pesticides affects metabolic pathways and pharmacokinetic interactions. Evidence indicates that the key metabolic enzyme (CYP3A4) modulated by pesticides affects the biotransformation and systemic availability of secondary metabolites such as alkaloids and polyphenols (Hernández-Lorca *et al*., 2025). Although direct evidence in medicinal plants is limited, established findings on herb-drug and xenobiotic interactions support the potential for CYP-mediated effects under co-exposure conditions. In *Cannabis* systems, chlorpyrifos modifies CYP-mediated metabolism of delta-9-tetrahydrocannabinol, while cholinergic contaminants alter pharmacodynamic responses, indicating combined pharmacokinetic and pharmacodynamic effects (Silva and Kwok, 2022).

8. Regulatory standards and quality control

8.1 International frameworks

International frameworks governing the quality, safety, and functional efficacy of medicinal plants have evolved through contributions from multiple regulatory bodies. The World Health Organization (WHO) has developed comprehensive guidelines, including good agricultural practices (GAP) and good agricultural and collection practices (GACP), to regulate cultivation, collection, and post-harvest handling of medicinal plants. The WHO-GACP integrates ethical, legal, biodiversity, and conservation considerations, ensuring global applicability (Zhang *et al*., 2021). These guidelines address quality assessment with emphasis on contaminants and residues, supported by standards from the United States Pharmacopoeia and the European Pharmacopoeia to safeguard safety, efficacy, and standardisation of herbal medicines (Marcelino *et al*., 2023). Regional frameworks, including European Union good agricultural and collection practices (EU-GACP), China good agricultural practices (China-GAP), and American Herbal Products Association good agricultural and collection practices (AHPA-GACP), further regulate cultivation, collection, and processing to uphold medicinal plant quality and safety (Zhang *et al*., 2021). Regarding pesticide regulation, the Codex Alimentarius Commission has established MRLs for pesticides in spices. However, MRLs for medicinal plants specifically remain undefined under Codex standards, highlighting a critical regulatory gap that compromises consistent quality and safety enforcement in international herbal trade. Despite these frameworks, the lack of harmonisation across countries affects consistent enforcement of pesticide residue standards in medicinal plants, influencing quality and safety. Regulatory systems also address worker safety, toxicity labelling, and environmental impacts associated with agrochemical use, though gaps persist in some regions. Global efforts focus on the convergence of pharmacopeial and regulatory standards, emphasizing harmonised limits for contaminants and residues to ensure consistent phytopharmaceutical quality and safety of herbal products.

8.2 Indian regulations

India regulates medicinal plants and herbal products through the Drugs and Cosmetics Act, 1940, with the AYUSH coordinating approval of classical formulations. Agencies such as the Ministry of AYUSH and the National medicinal plants board (NMPB) handle regulation, quality control, and policy functions. The Ministry of AYUSH regulates traditional medicine systems, develops policies, promotes research and education, and ensures quality control of drugs through pharmacopoeial standards and regulatory frameworks (Ministry of AYUSH, 2025). NMPB focuses on conservation, cultivation, and sustainable supply of medicinal plants, promotes GAP and GACP, and supports quality raw material production and supply chains (NMPB, 2026). India has established permissible limits for pesticides in medicinal plants broadly aligned with WHO GAP and GACP principles, with government bodies such as AYUSH actively supporting implementation and promoting growth of the herbal sector (Metta *et al*., 2021). A critical regulatory gap persists in pesticide residue control, as India largely relies on food-crop MRLs rather than medicinal plant-specific thresholds, which limits alignment with stringent EU market requirements and affects export competitiveness (Dixit, 2023; Chaudhari and Paul, 2025). Similarly, the Indian Pharmacopoeia has fewer documented monographs than the European and United States Pharmacopoeias, constraining standardisation and international acceptance (Metta *et al*., 2021). Despite initiatives such as the Ayush Export Promotion Council, the absence of harmonised quality, safety, and efficacy criteria continues to impede global acceptance of Indian herbal products (Chaudhari and Paul, 2025).

8.3 Limitations

Quality assurance of medicinal plants is constrained by the absence of uniform MRLs and weak monitoring systems. The lack of globally defined MRLs has led to reliance on food-based standards, resulting in inconsistency and limited scientific validity. Inadequate harmonisation of GAP and GACP further restricts quality consistency and international trade. Regulatory disparities are also evident in documentation requirements across EU, China, WHO, and AHPA frameworks, with only China mandating comprehensive quality evaluation records (Zhang *et al*., 2021). At the production level, excessive pesticide use, insufficient farmer training, and poor implementation of GAP contribute to contamination risks and variable product quality (Dixit, 2023). Limited access to advanced analytical methods and low research capacity further constrain effective quality control. Unregulated practices, including unregistered products and non-standardised crude formulations, continue to compromise safety. At the global level, the absence of a dedicated monitoring authority and weak regulatory enforcement, particularly in developing regions, results in inadequate supply chain surveillance. Additionally, lack of mandatory safety and efficacy evaluation, scarcity of certified raw materials, and poor supply chain transparency hinder standardisation and regulatory compliance (Chaudhari and Paul, 2025). Policy priorities include the development of medicinal plant-specific MRLs, expansion of pharmacopoeial monographs, and greater harmonisation of Indian standards with international regulatory frameworks. Strengthening residue surveillance, certification systems, and routine integration of advanced analytical techniques into regulatory monitoring would improve quality control, support standardisation, and enhance global acceptance of Indian herbal products.

9. Implications for trade and public health

9.1 Export challenges and market access

Global trade in herbal medicines and medicinal plant products is constrained by regulatory asymmetries, quality inconsistencies, and supply chain inefficiencies, which collectively limit market access and competitiveness. Stringent residue standards imposed by major markets such as the EU, the US, and Japan, combined with the absence of harmonised global frameworks, frequently result in border rejections of Indian exports. Non-compliance with pesticide residues reflects gaps in contaminant monitoring across cultivation and post-harvest stages, where inadequate control of residues and other contaminants compromises product safety and quality. These failures generate direct financial losses through rejected consignments and associated costs, along with indirect impacts such as reputational damage and stricter inspection regimes, disproportionately affecting small and medium enterprises. Further constraints arise from fragmented regulatory systems, a lack of standardised quality benchmarks, and weak supply chain coordination. Limited clarity on permissible plant species, inadequate recognition of traditional medicine systems, and the absence of consistent pharmacopeial standards restrict international acceptance. Variability in raw material quality due to inconsistent germplasm, suboptimal cultivation practices, and excessive pesticide use further undermines therapeutic reliability and export competitiveness (Zhang *et al*., 2021). Tariffs and non-tariff barriers, coupled with inefficient certification and distribution systems, increase transaction costs and delay market entry. In response, the sector is transitioning toward value-added phytopharmaceutical products supported by improved cultivation and quality assurance practices. Adoption of GAP and GACP and related standards is critical for ensuring quality consistency and facilitating international trade (Zhang *et al*., 2021). Strengthening globally harmonised quality management frameworks remains essential for improving compliance, reducing trade barriers, and enhancing the long-term competitiveness of the herbal medicines sector.

9.2 Consumer safety implications

Pesticide contamination in medicinal plants arises primarily from agricultural practices and persists through processing, posing risks to consumer safety. Large-scale evidence shows that a high proportion of samples contain pesticide residues, often with multiple compounds and occasional exceedance of regulatory limits. The presence of banned and highly toxic pesticides, including organochlorines and carbamates, indicates gaps in monitoring and enforcement, with associated risks such as carcinogenic, hepatotoxic, and reproductive effects (Luo *et al*., 2020). Although, average exposure levels are often within acceptable limits, cumulative effects of multiple residues and concentration during processing raise concerns regarding long-term exposure (Chen *et al*., 2024). Consumer safety is closely linked to raw material quality and regulatory consistency across markets. Variations in classification and oversight of herbal products across countries result in uneven safety standards, while the absence of harmonised quality, safety, and efficacy benchmarks limits effective regulation and trade (Dixit, 2023). Strengthening residue monitoring, improving cultivation practices, and aligning regulatory frameworks are critical for ensuring the safety and reliability of phytopharmaceutical products.

9.3 Economic impact on the herbal industry and production systems

Plant-based therapeutics contain diverse bioactive compounds, which makes quality control and standardisation difficult. Pesticide residues reduce product quality and economic significance (Luo *et al*., 2020). Studies on Indian herbal materials show pesticide residue levels above international limits, which affects export acceptance and product reliability (Koshy *et al*., 2022). These contaminants alter plant metabolism and create variation in phytochemical profiles, with reports of pesticides such as organochlorines and organophosphates in medicinal plants. Strong cultivation practices, routine residue monitoring, and aligned regulations improve consistency and support economic stability.

10. Mitigation strategies

GAP is a certified farming method that ensures safe and sustainable production with a focus on quality, environmental protection, economic viability, and worker welfare. In medicinal plants, GAP as per WHO guidelines integrates soil, seed, climate, water, and pH management with proper cultivation, harvesting, and post-harvest handling to maintain quality, while use of organic inputs, crop diversification, and environmentally sustainable practices such as bioformulations, neem-based control, biochar, agroforestry, and IPM reduces chemical use and improves productivity and sustainability.

10.1 Organic farming

Organic farming eliminates synthetic pesticide residues by avoiding chemical inputs and promoting soil health, biodiversity, and ecological balance. Empirical evidence shows that organic systems significantly reduce pesticide contamination, with residue levels 70-90% lower than in conventional systems (Silva *et al*., 2021). Organic management using castor cake, vermicompost, biofertilizers, microbial consortia, and bioaugmented amendments improves soil fertility, plant growth, and yield in Ashwagandha, while increasing key bioactive compounds such as withaferin A, withanone, and withanolide A (Basak *et al*., 2020). Enriched organic amendments, including enriched compost and biochar fortified minerals, improved herbage yield, sennoside content, and soil microbial activity in Senna (*Cassia angustifolia*) compared with conventional fertilization (Kumar *et al.,* 2024).

10.2 Natural farming

Natural farming systems such as zero budget natural farming (ZBNF) provide a chemical-free and resource-efficient alternative by relying on locally available bio-inputs such as Beejamrit, Jeevamrit, and Ghanajeevamrit, along with agroecological practices including mulching and crop diversification, which enhance soil fertility, microbial activity, and crop resilience. In India, ZBNF and related natural farming approaches are actively promoted through national initiatives such as Paramparagat krishi vikas yojana (PKVY), the national mission on natural farming (NMNF), and the Andhra Pradesh community managed natural farming programme (APCNF), reflecting strong policy support due to their economic feasibility and adaptability for smallholder farmers (Chandravanshi *et al*., 2024). For medicinal plants, organic and sustainable cultivation approaches improve quality, safety, and biodiversity by reducing pesticide use and maintaining ecological balance, as demonstrated across multi-site evaluations involving 76 field locations (Jiang *et al*., 2022), while recommended good practices across cultivation, harvesting, and processing stages support sustainable resource use and long-term productivity (Marcelino *et al*., 2023).

10.3 Integrated pest management

Integrated pest and disease management is essential in medicinal plant cultivation to maintain yield and phytochemical quality while minimising pesticide residues due to their role in traditional and modern medicine (Zhang *et al*., 2025). Improper pesticide application increases residue levels and reduces bioactive compound content (Kang *et al*., 2025), whereas agronomic practices and balanced fertilization with organic inputs further improve secondary metabolite content (Zhang *et al*., 2025). Cultural practices such as crop rotation, field sanitation, planting time adjustment, and canopy management disrupt pest life cycles, while cropping system diversification enhances soil microbial communities and supports natural pest suppression. Biological control through natural enemies and microbial processes further reduces dependence on chemical inputs (Greff *et al*., 2023). Plant-based products, especially neem-derived extracts, offer effective, eco-friendly, and economical pest and disease control in medicinal plants and can be integrated into crop protection strategies. Research is needed for medicinal crops to develop pest and disease management strategies aimed at producing clean, pesticide-free raw material.

10.4 Bioremediation

Bioremediation integrates microbial ecology and soil management to sustainably reduce pesticide residues, improve soil health, and enhance the quality of medicinal plants by utilizing the biochemical and metabolic potential of rhizosphere microorganisms (Karimi *et al*., 2022). Diverse microbial taxa, including *Pseudomonas*, *Bacillus*, *Arthrobacter*, *Sphingomonas*, *Burkholderia*, *Aspergillus*, and *Trichoderma*, degrade major pesticide classes such as organophosphates, pyrethroids, and carbamates, thereby reducing environmental pollution and associated health risks (Datta *et al*., 2024; Kumar *et al*., 2021). Rhizosphere microorganisms further enhance soil health, suppress pathogens, promote plant development and synthesis of secondary metabolites (Wang *et al*., 2022). Experimental evidence highlights the efficiency of microbial systems, where consortia such as PCS-1, consisting of *Pseudomonas*, *Enterobacter*, *Aspergillus*, and *Rhodotorula*, effectively degraded multiple pesticides in soil and water, reducing residues in roots, stems, and leaves of Medicago sativa (Li *et al*., 2020). Similarly, in *Andrographis paniculata* (Burm.f.) Nees, inoculation with *Bacillus* reduces pesticide stress and enhances physiological and biochemical attributes, including secondary metabolite production (Wang *et al*., 2022). The integration of plant growth-promoting rhizobacteria enhances pesticide degradation, reduces phytotoxicity, and improves crop productivity in contaminated soils (Shahid *et al*., 2023). Additionally, biochar-based immobilised microbial systems improve degradation efficiency by adsorbing pesticide residues and providing favourable microhabitats for microbial activity (Xiang *et al*., 2022).

11. Research gaps and future perspectives

Pesticide residues are widely reported in medicinal plants, yet existing studies focus mainly on occurrence and human health risk, with limited attention to system-level effects on plant metabolism and pharmacological efficacy (Luo *et al*., 2020). Research specifically addressing the effects of pesticide residues in medicinal plants also remains limited compared with food crops, creating a major knowledge gap in understanding impacts on phytochemical integrity and therapeutic value. Bridging this gap requires linking pesticide exposure with alterations in biosynthetic pathways that determine phytochemical composition and therapeutic value. Systems biology tools such as transcriptomics, proteomics, and metabolomics provide a structured approach to identify pesticide-induced metabolic disruptions and biomarkers of phytochemical stress (Wang *et al*., 2024). In addition, controlled field studies across agroclimatic regions are needed to establish dose-response relationships and to evaluate pesticide metabolite interactions and adduct formation that influence efficacy (Chen *et al*., 2024).

Assessment of cumulative and mixture toxicity remains limited and requires the application of mixture toxicology models for realistic risk evaluation. Strengthening monitoring systems depends on rapid, field-deployable detection tools such as immunoassays, enzyme-linked immunosorbent assay (ELISA), and portable spectroscopic devices (Xu L. *et al*., 2022). Emerging approaches, including nano-remediation and precision agriculture, provide additional pathways to reduce contamination, though further field validation is required. Adoption of these strategies is closely linked to farmer behaviour, knowledge gaps, and resource constraints, highlighting the need for socioeconomic research and targeted policy support. Overall, future efforts must integrate agronomy, phytochemistry, toxicology, and data-driven technologies to ensure safe and effective medicinal plant production.

12. Conclusion

Pesticide residue contamination in Indian medicinal plants represents a critical challenge affecting phytochemical quality, consumer safety, regulatory compliance, and economic sustainability. At the molecular level, pesticide exposure disrupts biosynthetic pathways and oxidative balance, reducing key bioactive compounds and pharmacological activity, which increases toxicological risk through chronic exposure. Analytical capacity for multi-residue detection using GC-MS/MS and LC-MS/MS is well established. However, critical gaps persist in crop-specific MRLs. Limited monitoring infrastructure and inconsistent enforcement continue to weaken quality assurance and contribute to export rejections and reputational losses. Mitigation strategies, including IPM, organic cultivation, botanical pesticides, and microbial bioremediation, provide effective approaches for reducing pesticide residues, while enhancing phytochemical content, with implications for therapeutic quality and market value. Adoption remains limited due to economic, technical, and institutional constraints, requiring targeted policy support. The economic burden extends across the value chain, including reduced farm gate prices, higher compliance costs, and restricted market access, highlighting the need for investment in sustainable production and farmer capacity building. Future progress requires integrated research linking pesticide exposure with phytochemical and pharmacological outcomes, along with harmonised regulations and stronger monitoring systems. Residue-free production is essential to maintain therapeutic quality, protect public health, and sustain India's competitiveness in the global herbal market.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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