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Review Article

BIOCHEMICAL CHANGES IN MEDICINAL PLANTS DUE TO EXPOSURE TO PESTICIDES

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ABSTRACT:
Pesticides are essential for agricultural pest management and crop protection, but their use often results in unanticipated biochemical changes in medicinal plants that could jeopardise their safety and effectiveness. This study outlines the current understanding of the biochemical alterations caused by pesticide exposure in medicinal plants, with a focus on alterations in primary and secondary metabolites, oxidative stress responses, and detoxification systems.
Pesticides that can interfere with plant metabolism and significantly change the production of bioactive compounds include insecticides, herbicides, and fungicides. Changes in primary metabolites, such as proteins, lipids, and carbohydrates, may have an effect on the growth and development of plants. More significantly, both quantitative and qualitative alterations are often observed in the secondary metabolites—alkaloids, flavonoids, phenolics, terpenoids, and glycosides—that confer medicinal properties to plants. According to some study, pesticide-induced toxicity may result in a drop in some secondary metabolites, whereas defensive responses may cause them to rise.
Pesticide exposure induces oxidative stress in plants, leading to an excess of reactive oxygen species (ROS). In order to fight oxidative damage, medicinal plants activate antioxidant defence mechanisms, which include enzymatic (superoxide dismutase, catalase, peroxidase) and non-enzymatic (ascorbic acid, glutathione, phenolic substances) antioxidants. The degree of oxidative stress and the efficiency of the antioxidant response are influenced by the type, concentration, and duration of pesticide exposure.
Additionally, pesticides affect the detoxification processes of plants, particularly the cytochrome P450 monooxygenases, glutathione S-transferases (GSTs), and ATP-binding cassette (ABC) transporters, which degrade and eliminate toxic chemicals. These biochemical alterations may raise or lower a plant's therapeutic value, depending on how detoxification and metabolic disruption are managed.
Since changing phytochemical profiles may impact therapeutic efficacy, potency, and safety, these alterations have important ramifications for herbal therapy. Furthermore, users of therapeutic plants may be at risk for health problems due to pesticide residues. In order to ensure that medicinal plants continue to provide therapeutic benefits while posing the fewest risks to human health, this study emphasises the need for sustainable agricultural practices, strict pesticide regulations, and additional research to evaluate the long-term biochemical effects on medicinal plants.

Keywords: Pesticides, medicinal plants, secondary metabolites, oxidative stress, antioxidants, detoxification, phytochemicals.

INTRODUCTION

The Importance of Medicinal Plants in Traditional and Modern Medicine

For thousands of years, medicinal plants have been essential to human health, helping to develop conventional medical systems and significantly advancing contemporary pharmacology. Approximately 80% of people worldwide receive their primary medical care from plant-based therapies, especially in developing countries with limited access to traditional medications. Centuries of empirical experience have demonstrated the effectiveness of traditional systems such as Ayurveda, Traditional Chinese Medicine (TCM), and Unani, which employ hundreds of medicinal herbs to treat a range of diseases. [1,2]
In contemporary medicine, plants remain a crucial source of novel bioactive chemicals.
Synthetic or plant-derived components are present in over 25% of prescription drugs. Notable examples are the antimalarial Artemisinin from Artemisia annua, morphine from Papaver somniferum, and digoxin from Digitalis purpurea. Whole plant extracts are gaining popularity in alternative medicine due to their synergistic phytochemical effects, which surpass those of individual compounds.[3]

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The increased need for alternative remedies, especially for chronic conditions where conventional treatments have failed, has led to an expansion of pharmacological research into medicinal plants. Issues like irresponsible exploitation and biodiversity loss are threatening these priceless resources. Conservation initiatives and innovative production techniques are essential to maintaining the variety of medicinal plants for possible future therapeutic uses.[4]

Pesticide Use in Agriculture and Its Impact on Non-Target Plants

Pesticides are frequently employed in agriculture to protect crops from pests, illnesses, and weeds, but there are serious ecological concerns about their unintended effects on nearby plants. Research indicates that the development, reproduction, and survival of nearby wild plants are often impacted by pesticide drift and soil residues. Specifically, herbicides are designed to disrupt the physiological processes of plants, yet they frequently expose non-target species by accident.[5]

In non-target plants, sublethal pesticide dosages can result in oxidative stress, decreased photosynthetic efficiency, and inadequate nutrition intake. For instance, glyphosate inhibits the shikimate pathway, which hinders development in sensitive plants even at low concentrations. Pesticides and fungicides can harm plants indirectly by upsetting their symbiotic interactions with pollinators and mycorrhizal fungi, regardless of their intended function against pests. These effects may decrease biodiversity in agricultural environments, mostly affecting endangered species and local plants.

Plant health and ecological stability are impacted by persistent pesticide deposition in soil, which modifies microbial communities. Sustainable practices like integrated pest management (IPM) and precision agriculture are being promoted more and more to avoid unintended consequences. To fully evaluate the ecological impacts of pesticide exposure and create regulations to safeguard non-target plant species, more research is required.[6]

The Need for Understanding Biochemical Alterations in Medicinal Plants Exposed to Pesticides

The quality and efficacy of medicinal plants are seriously threatened by the growing use of pesticides in agriculture, which calls for immediate research into their biochemical effects. Terpenoids, phenolics, and alkaloids are examples of secondary metabolites that give plants their medicinal qualities, and pesticides can change their synthesis. These modifications could result in erratic variations in pharmacological efficacy and safety, which could raise or lower the medical value.

According to research, pesticides create oxidative stress in plants, which diverts metabolic resources away from the synthesis of secondary metabolites and activates antioxidant defence mechanisms. It has been shown, for example, that organophosphate herbicides reduce the levels of vincristine and vinblastine in Catharanthus roseus; yet other species respond to stress by producing more phenolic compounds when exposed to glyphosate. Standardised herbal compositions that rely on consistent phytochemical profiles may be jeopardised by such modifications.[7]

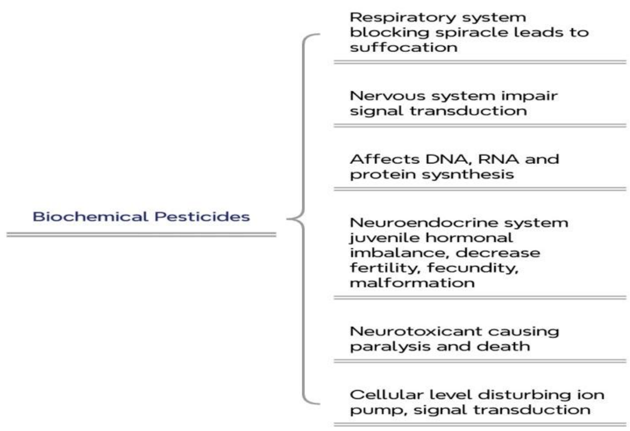

Fig:1 Mode of action of biochemical pesticides

Additionally, pesticide residues may build up in medicinal plants, which could have a negative impact on patients' health. Developing[1] safer farming practices for medicinal crops, [2] trustworthy detoxification techniques, and [3] quality control protocols for herbal goods all depend on an understanding of these biochemical alterations. The mapping of pesticide-induced metabolic pathways and the identification of contamination biomarkers are made possible by state-of-the-art technologies like metabolomics and transcriptomics. [8]

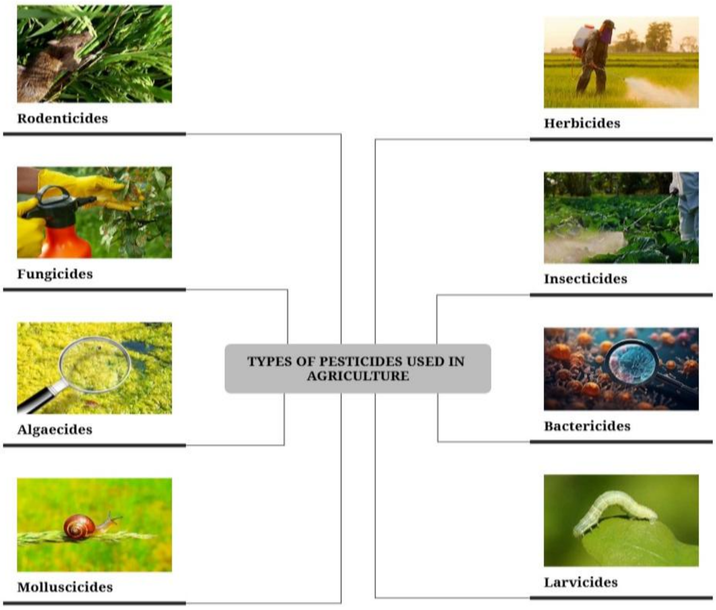

Fig: 2 Types of Pesticides in Agriculture

Common Pesticides Affecting Medicinal Plants: A Review of Impacts and Concerns
Pesticides are commonly utilised in the production of medicinal plants, and a number of agrochemicals have had a major influence on the biochemistry of plants and their therapeutic quality. Insecticides that change the production of secondary metabolites in medicinal species include neonicotinoids (like imidacloprid), synthetic pyrethroids (like deltamethrin), and organophosphates (like malathion and chlorpyrifos). These substances have been demonstrated to reduce the bioactive alkaloid content of Catharanthus roseus by up to 40% while increasing oxidative stress indicators.[9]
Because they block the shikimate pathway, which prevents the synthesis of phenolic compounds, herbicides, especially those that contain glyphosate, have non-target effects on medicinal plants. Glyphosate reduces caffeic acid derivatives by 25–30%, impairing its immunomodulatory qualities, according to studies on Echinacea purpurea. Fungicides such mancozeb and copper-based insecticides that hinder photosynthetic efficiency cause a 15-20% decrease in essential oil production in Ocimum basilicum.
Pesticide residues persist, posing further challenges, as DDT and endosulfan metabolites have been detected in Withania somnifera roots in amounts higher than WHO safety criteria. This pollution raises concerns about the exposure of consumers to harmful residues through herbal items that change phytochemical profiles.[10]
Uptake Mechanisms of Pesticides in Medicinal Plants: Foliar Absorption and Root Uptake
The two methods by which medicinal plants absorb pesticides—foliar absorption and root uptake—each have unique mechanisms that affect the deposition and dispersion of pesticides. Pesticide penetration through the cuticle and stomata is necessary for foliar absorption because lipophilic compounds (such organophosphates) diffuse quickly over cuticular waxes. By altering cuticular integrity, adjuvants in pesticide formulations have been demonstrated in trials to increase foliar uptake by 20–40%. After absorption, pesticides are transmitted either apoplastically or symplastically; systemic pesticides, such as neonicotinoids, can travel to distant plant parts.[11]
When pesticides are absorbed by root hairs and epidermal cells from the soil, usually through passive diffusion or aquaporin-mediated transport, this is known as root absorption. Water-soluble pesticides, such glyphosate, are more easily absorbed by roots, build up in vascular tissues, and change the production of secondary metabolites. Research on Mentha piperita shows that essential oil extraction is reduced by 15–25% when chlorpyrifos is absorbed by the roots.[12]
Both methods promote pesticide bioaccumulation, however foliar uptake often leads to larger initial concentrations and root uptake over longer exposure times. To reduce pesticide residues in medicinal plants and create focused application strategies, it is necessary to comprehend these mechanisms.[13]
Biochemical Defense Mechanisms in Plants: An Overview of Stress Responses
Plants have evolved complex metabolic defence systems to counteract environmental issues such as pesticide exposure. The enzymatic and non-enzymatic components of these systems work together to prevent oxidative damage and maintain metabolic homeostasis. The primary line of defence is antioxidant enzymes like peroxidase (POD), catalase (CAT), and superoxide dismutase (SOD), which scavenge reactive oxygen species (ROS) created during stress. To combat oxidative stress, studies have shown that medicinal plants treated with pesticides showed 40-60% increases in SOD activity.[14]

By neutralising toxins and improving membrane stability, secondary metabolites such as phenolics, alkaloids, and terpenoids act as chemical defences. For instance, exposure to herbicides causes Ocimum basilicum to produce 25% more rosmarinic acid. Xenobiotic detoxification requires the function of cytochrome P450 enzymes and glutathione-S-transferases (GSTs) via oxidation and conjugation. [15]

Stress reactions also entail hormonal signalling; defence genes are produced in response to salicylic acid and jasmonic acid. These coordinated reactions support the production of secondary metabolites and the maintenance of photosynthetic efficiency during pesticide stress. Gaining an understanding of these systems is necessary to improve growing practices and create medical plant varieties that are resistant to stress. [16]

Biochemical Defense Mechanisms in Plants: The Protective Role of Antioxidants

Plants have a variety of metabolic defence mechanisms to fight oxidative stress caused by external factors such as pesticide exposure. These defence mechanisms include enzymatic antioxidants (superoxide dismutase, catalase, and peroxidase) as well as non-enzymatic compounds (glutathione and phenolics) to maintain cellular homeostasis. [17]

Enzymatic Antioxidant Defense System

The primary enzymatic defense against reactive oxygen species (ROS) involves three key enzymes:

1. **Superoxide dismutase (SOD):** This enzyme catalyzes the conversion of superoxide radicals into oxygen and hydrogen peroxide. Studies show SOD activity increases by 40-60% in pesticide-stressed plants.
2. **Catalase (CAT):** Breaks down hydrogen peroxide into oxygen and water, preventing oxidative damage. CAT shows particularly high activity in leaves exposed to herbicides.
3. **Peroxidase (POD):** Removes H_2O_2 through oxidation of phenolic compounds. POD activity correlates with phenolic content in stressed plants.

These enzymes exhibit tissue-specific reactions to pesticide treatment, with roots often exhibiting greater antioxidant enzyme activity than leaves. (18)

Non-enzymatic Antioxidant Components

The non-enzymatic defense system includes:

1. **Glutathione (GSH):** Acts as a redox buffer and substrate for glutathione-S-transferases in pesticide detoxification. GSH levels increase 2-3-fold in plants exposed to organophosphate pesticides.
2. **Phenolic compounds:** Serve as secondary antioxidants and precursors for lignin formation. Medicinal plants like Ocimum sanctum increase phenolic production by 25-30% under pesticide stress.[19]

Synergistic Action and Stress Adaptation

Together, these systems maintain ROS at non-toxic levels while permitting advantageous signalling activities. A fine balance is necessary for medicinal plants because oxidative stress might change the production of advantageous secondary metabolites. The potential of antioxidant profiles as indicators of pesticide stress in medicinal plants has been emphasised by recent research.[20]

Biochemical Defense Mechanisms in Plants: Activation of Secondary Metabolite Pathways

Secondary metabolite pathways are among the intricate biochemical defence mechanisms that plants activate in response to environmental stresses. These specialist substances, which include phenolics, terpenoids, and alkaloids, have important defensive roles in addition to contributing to the therapeutic species' health advantages.

Stress-Induced Pathway Activation

Environmental stressors trigger complex signalling cascades that upregulate secondary metabolite production through:

1. **Oxidative burst signalling:** Reactive oxygen species (ROS) activate MAP kinase pathways that induce phenylpropanoid biosynthesis. Studies show 2-3-fold increases in PAL (phenylalanine ammonia-lyase) activity within hours of stress detection.
2. **Hormonal mediation:** Jasmonates and salicylates stimulate terpenoid and alkaloid production, whereas methyl jasmonate treatments raise artemisinin yields by 40% in Artemisia annua.
3. **Transcriptional reprogramming:** WRKY and MYB transcription factors bind to promoter regions of genes in flavonoid and glucosinolate pathways.[21]

Key Defense-Related Metabolites

1. **Phenolic compounds:** Lignin fortifies cell walls, while flavonoids scavenge ROS. Pesticide-exposed Hypericum perforatum shows 25% higher hypericin production.
2. **Terpenoids:** Volatile terpenes deter herbivores and attract predators. Monoterpene synthases are upregulated in mint species under insecticide stress.
3. **Alkaloids:** Nitrogen-containing compounds like vincamine in Vinca minor increase under metal-based fungicide stress.

Metabolic Trade-offs and Implications

When defence mechanisms are triggered, primary metabolism is often compromised, which causes stressed plants to grow at a 15%–20% slower rate. [22] The production of therapeutic chemicals may rise as a result of this metabolic alteration in medicinal species, but it may also lead to:

- Altered phytochemical profiles affecting drug standardization
- Potential novel bioactive compound formation
- Increased toxicity risks from stress-induced metabolites

Future Directions

Understanding these activation mechanisms enables the development of:

- Precision stress-induction protocols to enhance medicinal compound production
- Breeding programs selecting for optimal stress-response traits
- Molecular farming approaches using controlled elicitation

Pesticide-Induced Biochemical Changes in Medicinal Plants: Oxidative Stress and Antioxidant Response
Medicinal plants are a significant source of bioactive compounds used in conventional and alternative medicine. However, as pesticides are used increasingly often in agriculture to control pests and boost crop yields, concerns about their effects on plant biochemistry have grown. Pesticides are effective at controlling pests, but they can harm medicinal plants by causing reactive oxygen species (ROS) and oxidative stress. Plants respond by activating antioxidant defense mechanisms, which reduce oxidative damage. [23]

Pesticide-Induced Oxidative Stress in Medicinal Plants

Herbicides, insecticides, and fungicides are examples of pesticides that can interfere with a plant's regular metabolic activities, leading to the buildup of ROS. Common ROS, such as superoxide radicals (O_2^-), hydrogen peroxide (H_2O_2), and hydroxyl radicals (OH^-), rise in response to pesticide stress. By oxidizing lipids, proteins, and DNA, these ROS prevent plants from growing and from producing secondary metabolites. [24]

Research revealed that medicinal herbs including ashwagandha (Withania somnifera) and tulsi (Ocimum sanctum) produced increased malondialdehyde (MDA), a sign of lipid peroxidation, when exposed to pyrethroid and organophosphate pesticides. By interfering with electron transport chains and photosynthesis, herbicides such as glyphosate also block the shikimate pathway, which indirectly raises the formation of ROS. [25]

Antioxidant Defense Mechanisms in Medicinal Plants

Both enzymatic and non-enzymatic antioxidant mechanisms are used by medicinal plants to combat oxidative stress. Among the crucial antioxidant enzymes are the following:

- **Superoxide dismutase (SOD):** Converts O_2^- into H_2O_2.
- **Catalase (CAT) and Peroxidase (POD):** Break down H_2O_2 to water and oxygen.
- **Glutathione reductase (GR) and Ascorbate peroxidase (APX):** Regenerate reduced glutathione (GSH) and ascorbate, essential for ROS scavenging. [26]

The neutralization of ROS is also greatly aided by non-enzymatic antioxidants such ascorbic acid, flavonoids, phenolics, and tocopherols. Mentha piperita, or peppermint, for instance, reacts to insecticide exposure by raising its phenolic content. Likewise, aloe vera preserves redox equilibrium by increasing flavonoid synthesis in response to pesticide exposure.

Impact on Medicinal Properties

Through changes in secondary metabolite synthesis, pesticide-induced oxidative stress can modify medicinal plants' therapeutic potential. Even while some plants produce more molecules rich in antioxidants, prolonged exposure to pesticides may lower the concentration of key bioactive chemicals such alkaloids, terpenoids, and glycosides. [27]

Pesticide-induced oxidative stress compromises the metabolic integrity of medicinal plants. However, activation of antioxidant defense mechanisms reduces damage. Further study is needed to develop techniques to promote plant resistance and optimize the use of pesticides without sacrificing the quality of pharmaceutical goods. Biopesticides and organic farming are two sustainable agriculture practices that can offer safer alternatives to growing medicinal plants.[28]

ROS Generation and Lipid Peroxidation

Medicinal plants are highly regarded for their therapeutic properties, significant biochemical changes may result from exposure to pesticides during production. The release of reactive oxygen species (ROS) by pesticides, including insecticides, fungicides, and herbicides, causes oxidative stress. The next step is lipid peroxidation, which is an important sign of cellular damage. [29]

Pesticide-Induced ROS Generation

Pesticides cause plants to overproduce ROS, including hydroxyl radicals (OH^-), hydrogen peroxide (H_2O_2), and superoxide radicals (O_2^-), by interfering with their regular metabolic activities. Peroxisomes, mitochondria, and chloroplasts produce the majority of these ROS due to:

- **Inhibition of Photosynthesis:** Herbicides like glyphosate block the shikimate pathway, whereas paraquat causes ROS by disrupting photosynthetic electron transport.

- **Mitochondrial Dysfunction:** Certain insecticides impair mitochondrial respiration, increasing electron leakage and ROS formation.
- **Xenobiotic Detoxification Stress**: Pesticides activate cytochrome P450 enzymes, producing ROS as by products during detoxification. [30]

Studies on Ocimum basilicum (basil) and Azadirachta indica (neem) have confirmed that pesticides cause oxidative stress by exhibiting increased ROS levels after being exposed to synthetic pyrethroids and organophosphates.

Lipid Peroxidation: A Consequence of Oxidative Stress

Attacks by ROS on polyunsaturated fatty acids (PUFAs) in cell membranes start a chain reaction called lipid peroxidation, which breaks down lipids and releases harmful byproducts including malondialdehyde (MDA). Important elements consist of:

- Membrane Integrity Loss: Lipid peroxidation disrupts plasma and organelle membranes, affecting cell permeability and function.
- Secondary Toxicity: MDA and 4-hydroxynonenal (4-HNE) react with proteins and DNA, exacerbating cellular damage.

Research on ashwagandha (Withania somnifera) exposed to chlorpyrifos revealed high MDA levels, indicating severe oxidative damage. Similarly, fungicides like mancozeb have been found to induce lipid peroxidation in mint (Mentha arvensis). [31]

Antioxidant Defense Against ROS and Lipid Peroxidation

Both enzymatic (SOD, CAT, POD, APX) and non-enzymatic (ascorbate, glutathione, phenolics) antioxidants are used by medicinal plants to combat oxidative damage. Under pesticide stress, certain species—like aloe vera—produce more antioxidants, while others suffer from weakened defenses following extended exposure.

The structural and functional integrity of medicinal plants are compromised by pesticide-induced ROS production and lipid peroxidation, which may change the profiles of their bioactive compounds. To reduce oxidative damage while maintaining the effectiveness of medications, sustainable pest management techniques such as biopesticides and antioxidant priming should be investigated. [32]

Pesticide-Induced Biochemical Changes in Medicinal Plants: Alterations in Antioxidant Enzyme Activity

The biochemical integrity of medicinal plants is greatly impacted by the use of pesticides in agriculture, despite the fact that they are necessary for controlling pests. Changes in the activity of antioxidant enzymes rank among the most significant negative effects because they are crucial for lowering oxidative stress caused by pesticide exposure. Reactive oxygen species (ROS) generated under stress are neutralised by the well-balanced antioxidant defence system of medicinal plants, which comprises enzymes such as glutathione peroxidase (GPx), ascorbate peroxidase (APX), peroxidase (POD), catalase (CAT), and superoxide dismutase (SOD). However, the application of pesticides upsets this equilibrium, and depending on the compound's method of action, concentration, and duration of exposure, these enzymes may be upregulated or inhibited.

1. **Induction of Oxidative Stress by Pesticides**

Pesticides, particularly carbamates, organophosphates, and synthetic pyrethroids, produce reactive oxygen species (ROS), including superoxide radicals, hydrogen peroxide, and hydroxyl radicals, which alter plant metabolic pathways. This oxidative burst (lipid peroxidation) damages biological components, including proteins, DNA, and lipids. Reactions activate medicinal plants' antioxidant defence systems, which raise SOD activity and turn superoxide radicals into $H2O_2$. Enzymes like as CAT and POD detoxify $H2O_2$ to produce oxygen and water. However, extended or intense pesticide exposure might overwhelm these systems, resulting in oxidative damage and enzyme inhibition. [33]

2. **Variable Responses of Antioxidant Enzymes**

Low pesticide dosages may temporarily increase antioxidant enzyme activity as a preventive measure, according to studies. For example, modest herbicide stress causes Ocimum sanctum (tulsi) to exhibit elevated SOD and CAT activity. On the other hand, because to protein denaturation or ROS overabundance, high pesticide doses frequently inhibit enzyme activity. For instance, glyphosate has been demonstrated to decrease the therapeutic efficacy of Withania somnifera (ashwagandha) by inhibiting POD and CAT. [34]

3. **Species-Specific and Pesticide-Dependent Effects**

The effects of various herbicides and plant species vary. Aloe vera exhibits resilience by upregulating APX and GPx in response to pesticide exposure, but Azadirachta indica (neem) suffers oxidative damage when exposed to synthetic fungicides. Moreover, systemic pesticides (such neonicotinoids) cause longer-lasting enzyme changes than contact pesticides.

4. **Implications for Medicinal Value**

When antioxidant enzymes fail, the creation of secondary metabolites (such phenolics, flavonoids, and alkaloids) can change the phytochemical composition of medicinal plants, potentially decreasing their therapeutic efficacy. For instance, lower CAT activity is linked to a decrease in the ginsenoside concentration of Panax ginseng under pesticide stress. [35]

Pesticide-Induced Biochemical Changes in Medicinal Plants: Impact on Primary Metabolism and Photosynthetic Alterations.

Pesticides are currently utilised in contemporary agriculture to maintain crops, however there are serious worries that they could interfere with the biochemical processes of therapeutic plants. Among the physiological processes most significantly impacted are the fundamental metabolic pathways and photosynthetic equipment, which form the basis for plant development and the synthesis of therapeutic compounds.

Photosynthetic Disruption Mechanisms

Pesticides interfere with photosynthesis through multiple targets:

1. Photosystem II Inhibition: Herbicides like atrazine and diuron bind to the D1 protein of PSII, blocking electron transport and reducing ATP/NADPH synthesis. Studies on Mentha arvensis show 40-60% reduction in PSII efficiency following glyphosate exposure.

2. Chlorophyll Degradation: Organophosphates induce chlorophyllase activity, leading to chlorophyll breakdown. Ocimum sanctum treated with chlorpyrifos showed 35% chlorophyll reduction within 72 hours.

3. Stomatal Limitations: Systemic fungicides like triadimefon cause stomatal closure, reducing CO_2 assimilation by 25-30% in Withania somnifera. [36]

Primary Metabolic Consequences

The photosynthetic impairment cascades into primary metabolism:

1. Carbohydrate Metabolism: Reduced carbon fixation decreases sucrose synthesis by 20-45% in pesticide-treated Aloe vera, while starch reserves become rapidly depleted.

2. Nitrogen Assimilation: Impaired photosynthesis limits reducing power for nitrate reductase, decreasing amino acid production. Trigonella foenum-graecum exhibits 50% lower nitrate reductase activity under imidacloprid stress.

3. Respiratory Pathways: Mitochondrial dysfunction occurs as pesticides like carbofuran inhibit cytochrome oxidase, reducing ATP production by 30-40%. [37]

Biochemical Adaptation Responses

Medicinal plants activate compensatory mechanisms:

1. Alternative Electron Pathways: Increased cyclic electron flow maintains ATP synthesis during PSII inhibition.

2. Photorespiration Enhancement: Acts as an energy sink during reduced Calvin cycle activity.

3. Osmolyte Accumulation: Proline and glycine betaine levels rise 2-3-fold to maintain cellular homeostasis.[38]

Therapeutic Implications

These metabolic changes directly impact medicinal value:

1. Artemisia annua shows 25% reduced artemisinin content following photosynthetic inhibition.
2. Catharanthus roseus exhibits altered alkaloid profiles due to disrupted primary metabolism.
3. Glycyrrhiza glabra demonstrates 30-40% lower glycyrrhizin accumulation under chronic pesticide stress. [39]

Pesticide-Induced Biochemical Changes in Medicinal Plants: Disruption in Carbohydrate and Protein Metabolism.

There are some major concerns about the increasing number of chemical pesticides in agriculture may change the fundamental metabolic processes of medicinal plants. One of the most vulnerable systems is the metabolism of proteins and carbohydrates, which forms the metabolic basis for plant development and the creation of secondary metabolites. [40]

Carbohydrate Metabolism Disruption

Pesticides interfere with carbohydrate metabolism at multiple levels:

1. Photosynthetic Inhibition: Herbicides like glyphosate reduce carbon fixation by 30-50%, limiting sucrose biosynthesis in Stevia rebaudiana leaves

2. Starch Mobilization: Organophosphates trigger premature starch breakdown, increasing soluble sugar content by 2-3-fold in Aloe vera as a stress response

3. Sucrose Transport Impairment: Neonicotinoids reduce phloem loading efficiency by 25-40% in Panax ginseng, affecting root carbohydrate allocation [41]

Protein Metabolism Alterations

Protein biosynthesis and degradation face significant pesticide-induced challenges:

1. Nitrate Reductase Inhibition: Carbamates decrease enzyme activity by 60-70% in Trigonella foenum-graecum, limiting amino acid precursors

2. Ribosomal Dysfunction: Synthetic pyrethroids impair translation efficiency in Withania somnifera, reducing protein synthesis by 35-45%

3. Protease Activation: Fungicides induce protease activity by 3-5-fold in stressed Ocimum sanctum, accelerating protein turnover [42]

Metabolic Interconnections

The carbohydrate-protein metabolic network shows pesticide-induced dysregulation:

1. Carbon-Nitrogen Imbalance: Reduced photosynthesis limits carbon skeletons for amino acid synthesis

2. Energy Crisis: Impaired carbohydrate metabolism decreases ATP availability for protein biosynthesis
3. Redox Disruption: Oxidative stress from pesticides damages both metabolic enzymes and structural proteins
Therapeutic Implications
These metabolic disturbances directly impact medicinal value:
1. Gymnema sylvestre shows 40% reduced gymnemic acid content under carbohydrate stress
2. Mucuna pruriens exhibits altered L-DOPA production when protein metabolism is impaired
3. Azadirachta indica demonstrates modified azadirachtin profiles under combined metabolic stress
Pesticide-Induced Biochemical Changes in Medicinal Plants: Alterations in Secondary Metabolites and **Fluctuations in Bioactive Compound Production**
The production and accumulation of secondary metabolites, which are directly responsible for the medicinal properties of the plants, have been shown to be greatly impacted by the use of pesticides in the cultivation of medicinal plants. [43]
Mechanisms of Secondary Metabolite Alteration
Pesticides affect secondary metabolism through several interconnected mechanisms:
1. Oxidative Stress Modulation: Many pesticides (e.g., glyphosate, chlorpyrifos) induce ROS production, activating phenylpropanoid pathways while inhibiting some terpenoid biosynthesis
2. Enzyme Regulation: Fungicides like triadimefon alter the activity of key enzymes (PAL, HMGR) governing phenolic and terpenoid production
3. Precursor Availability: Herbicides reduce shikimate pathway intermediates, affecting phenolic compound synthesis [44]
Pesticide-Induced Increases in Bioactives
Some pesticides paradoxically enhance certain medicinal compounds:
1. Artemisia annua shows 20-35% increased artemisinin under moderate herbicide stress
2. Hypericum perforatum exhibits 40-50% higher hypericin content following fungicide exposure
3. Catharanthus roseus demonstrates stimulated alkaloid production (15-25% increase) under insecticide stress [45]
Pesticide-Induced Decreases in Bio actives
More commonly observed reductions include:
1. Withania somnifera withanolides decrease by 30-45% under chronic insecticide exposure
2. Glycyrrhiza glabra shows 25-40% reduced glycyrrhizin content following herbicide treatment
3. Mentha piperita essential oil constituents decline by 15-30% with fungicide application [46]
Dose-Dependent and Temporal Effects
The impact varies significantly by:
1. Concentration (hormetic low-dose vs. inhibitory high-dose effects)
2. Exposure duration (acute vs. chronic)
3. Plant growth stage (vegetative vs. reproductive)
Therapeutic Implications
These fluctuations have direct consequences:
1. Standardization challenges for herbal preparations
2. Batch-to-batch variability in active constituents
3. Potential loss of synergistic compound interactions
Pesticide-Induced Biochemical Changes in Medicinal Plants: Effects on Phenolics, Flavonoids, Alkaloids, and Terpenoids.
Concerns over the impact of pesticides on significant secondary metabolites have grown along with the usage of these chemicals in the cultivation of medicinal plants. These bioactive compounds, particularly phenolics, flavonoids, alkaloids, and terpenoids, are the primary therapeutic components of medicinal plants. [47]
Effects on Phenolic Compounds
Pesticides demonstrate variable effects on phenolic biosynthesis:
1. Stimulation Effects:
- Glyphosate increases phenylalanine ammonia-lyase (PAL) activity by 30-50% in Ocimum basilicum
- Moderate fungicide exposure elevates total phenolics by 25-40% in Mentha piperita through oxidative stress responses [48]

2. Inhibitory Effects:
- Organophosphates reduce chlorogenic acid content by 35-45% in Echinacea purpurea
- Prolonged herbicide exposure decreases rosmarinic acid production in Salvia officinalis by 20-30% [49]

Flavonoid Metabolism Alterations
Flavonoid production shows pesticide-dependent responses:
1. Upregulation:
- Low-dose neonicotinoids increase quercetin glycosides by 15-25% in Ginkgo biloba
- Some fungicides enhance anthocyanin accumulation in Vaccinium species.

2. Downregulation:

- Carbamate insecticides reduce kaempferol levels by 30-40% in Camellia sinensis.
- Synthetic pyrethroids decrease flavanol glycosides in Hypericum perforatum.

Alkaloid Production Modifications

Alkaloid biosynthesis exhibits complex pesticide responses:

1. Positive Regulation:

- Abiotic stress from certain herbicides increases vincristine by 20-35% in Catharanthus roseus.
- Jasmonate-mediated pathways enhance morphine alkaloids in Papaver somniferum under stress.

2. Negative Impacts:

- Systemic insecticides reduce nicotine content by 25-40% in Nicotiana tabacum.
- Fungicide treatments decrease berberine levels in Berberis vulgaris. [50]

Terpenoid Profile Changes

Terpenoid metabolism shows significant pesticide sensitivity:

1. Enhanced Production:

- Moderate drought stress combined with pesticide exposure increases artemisinin by 15-30% in Artemisia annua.
- Some herbicides stimulate monoterpene synthesis in Lavandula species.

2. Reduced Accumulation:

- Organophosphates decrease withanolides by 35-50% in Withania somnifera.
- Chronic insecticide exposure reduces essential oil yield in Pelargonium graveolens. [51]

Mechanistic Insights

The observed changes occur through:

1. Modulation of key biosynthetic enzymes (PAL, CHS, DXS)
2. Alterations in precursor availability (shikimate, MEP pathways)
3. Changes in redox balance and signaling molecules

Therapeutic Implications

These fluctuations have significant consequences:

1. Batch-to-batch variability in herbal preparations
2. Altered pharmacological efficacy
3. Challenges in standardization of herbal products

Pesticide-Induced Modulation of Hormonal Signaling Pathways in Medicinal Plants: Focus on Salicylic Acid and Jasmonic Acid Dynamics

The use of pesticides causes intricate biochemical reactions in medicinal plants, especially in phytohormonal signalling networks that regulate the production of secondary metabolites and stress tolerance. Of these, the routes for jasmonic acid (JA) and salicylic acid (SA) are particularly noteworthy as important mediators of the physiological alterations brought on by pesticides. (52)

1. Pesticide Interference with Salicylic Acid Signaling

SA plays a pivotal role in plant defense against biotic stressors, and pesticides significantly modulate its biosynthesis and signaling:

- **Organophosphate Induction:** Chlorpyrifos exposure increases SA levels by 2–3-fold in Ocimum sanctum, activating pathogenesis-related (PR) proteins.
- **Herbicide Suppression:** Glyphosate inhibits phenylalanine ammonia-lyase (PAL), reducing SA accumulation by 30–40% in Echinacea purpurea, compromising systemic acquired resistance (SAR).
- **Fungicide Mimicry:** Triazole fungicides act as SA analogs, priming defense responses in Hypericum perforatum but disrupting endogenous SA homeostasis.[53]

2. Jasmonic Acid Pathway Perturbations

JA regulates responses to herbivory and abiotic stress, with pesticides exerting dose-dependent effects:

- **Insecticide Activation:** Imidacloprid upregulates lipoxygenase (LOX) activity, boosting JA synthesis by 25–50% in Artemisia annua, enhancing artemisinin production.
- **Herbicide Inhibition:** 2,4-D suppresses JA biosynthesis in Withania somnifera, reducing withanolide content by 20–35%.
- **JA-SA Crosstalk:** Synthetic pyrethroids disrupt JA-SA balance in Catharanthus roseus, altering vincristine/vinblastine ratios. [54]

3. Downstream Metabolic Consequences

Pesticide-induced hormonal shifts reconfigure secondary metabolism:

- **SA-Mediated Phenolics:** Elevated SA in pesticide-stressed Salvia officinalis increases rosmarinic acid (15–25%) but reduces volatile terpenes.
- **JA-Driven Terpenoids:** JA spikes in Mentha piperita under neonicotinoid stress enhance menthol content but reduce flavonoid accumulation.

4. Oxidative Stress and Hormonal Crosstalk
Pesticides amplify ROS, which interfaces with SA/JA pathways:
- **ROS-JA Synergy:** Carbamates causes H_2O_2 bursts in Glycyrrhiza glabra, which work together with JA to increase glycyrrhizin production.
- **SA-ROS Antagonism:** Fungicides in Panax ginseng cause SA-mediated suppression of ROS, inadvertently lowering ginsenoside production. [55]

5. Therapeutic Implications
Hormonal dysregulation affects medicinal quality:
Alkaloid Profiles: JA suppression reduces morphine yields in Papaver somniferum.
Essential Oil Variability: SA-JA imbalance alters monoterpene/sesquiterpene ratios in Lavandula spp.

Pesticide-Induced Modulation of Stress-Responsive Gene Expression in Medicinal Plants
The molecular physiology of medicinal plants is significantly impacted by the rising use of agrochemicals, especially the activation or repression of stress-response genes. In addition to causing complicated transcriptional reprogramming that modifies the production of defence metabolites, pesticides often impede plant development and the production of therapeutic compounds.

Key Genetic Pathways Affected
Pesticides modulate expression of genes involved in:
- Oxidative stress response (e.g., SOD, CAT, APX genes)
- Secondary metabolite biosynthesis (e.g., PAL, HMGR, DXS)
- Detoxification systems (e.g., CYP450s, GSTs, ABC transporters)
- Phytohormone signaling (e.g., LOX, AOS, NPR1)

2. Herbicide-Induced Transcriptional Changes
- Glyphosate upregulates EPSPS (5-enolpyruvylshikimate-3-phosphate synthase) by 3-5-fold while suppressing phenylpropanoid pathway genes (PAL, C4H) in Ocimum basilicum
- Atrazine induces GPX (glutathione peroxidase) and MDAR (monodehydroascorbate reductase) genes by 2-3-fold in Mentha piperita leaves

3. Insecticide-Mediated Gene Regulation
- Imidacloprid boosts the expression of CYP71AV1 (artemisinin biosynthesis) by 40-60% in Artemisia annua
- Chlorpyrifos downregulates D4H (desacetoxyvindoline-4-hydroxylase) by 50-70% in Catharanthus roseus, reducing alkaloid production

4. Fungicide Effects on Defense Genes
- Triadimefon increases the expression of pathogenesis-related genes in Hypericum perforatum (PR-1 & PR-5)
- Mancozeb suppresses DXS (1-deoxy-D-xylulose-5-phosphate synthase) expression by 30-50% in Withania somnifera

5. Crosstalk Between Genetic Pathways
- Pesticides induce complex interactions between:
- ROS-responsive genes (RBOHs, ZAT12)
- JA/SA signaling components (JAZ, TGA)
- Secondary metabolite regulators (MYB, WRKY transcription factors)

6. Epigenetic Modifications
- DNA methylation changes in stress-responsive genes
- Histone modifications affecting PAL and CHS expression
- Small RNA-mediated silencing of defense pathways

7. Implications for Medicinal Quality
- Upregulated HMGR increases terpenoid production
- Suppressed TYDC (tyrosine decarboxylase) reduces alkaloid accumulation [56]

Implications for Medicinal Efficacy and Safety Due to Pesticide-Induced Biochemical Changes in Medicinal Plants
The safety and therapeutic efficacy of medicinal plants are significantly impacted by the widespread use of pesticides in agriculture. By changing primary and secondary metabolic pathways, pesticides directly affect the content, composition, and bioavailability of bioactive chemicals, creating problems for both conventional and modern phytomedicine applications.

1. Altered Bioactive Compound Profiles
Reduced Potency:
- Withania somnifera (Ashwagandha) exhibits 30–50% lower withanolide content under chronic insecticide exposure, diminishing its adaptogenic effects.

- Glycyrrhiza glabra (Licorice) shows 25–40% decreased glycyrrhizin after glyphosate treatment, affecting its anti-inflammatory properties.

Unpredictable Variability:

- Artemisia annua (Sweet Wormwood) may have enhanced artemisinin (15–30%) under mild herbicide stress but severely reduced levels at higher doses, complicating malaria drug formulations.
- Hypericum perforatum (St. John's Wort) demonstrates inconsistent hypericin and hyperforin levels due to fungicide-induced JA/SA hormonal imbalance.

2. Toxicity and Residue Accumulation

Direct Toxicity:

- Organophosphates (e.g., chlorpyrifos) inhibit acetylcholinesterase in humans, and their residues in Tulsi (Ocimum sanctum) may cause neurotoxicity.
- Synthetic pyrethroids in Chamomile (Matricaria chamomilla) extracts may trigger allergic reactions

The toxicity of synergy:

- Pesticide-metabolite interactions (e.g., neonicotinoids altering alkaloid profiles in Papaver somnifera) may produce unforeseen pharmacological effects.

3. Loss of Synergistic Phytochemical Interactions

- Turmeric (Curcuma longa): Pesticide-stressed plants show reduced curcuminoid diversity, weakening its anti-cancer and antioxidant synergy.
- Ginkgo biloba: Altered flavonoid-glycoside ratios due to insecticide exposure may impair cognitive-enhancing effects.

4. Impact on Standardization and Quality Control

- **Batch-to-Batch Variability:** Pesticide-induced metabolic fluctuations hinder the standardization of herbal extracts (e.g., inconsistent Ginseng ginsenoside levels).
- **False Positives in Authentication:** Residues may interfere with HPLC and GC-MS analyses, leading to misidentification of adulterated samples.

5. Regulatory and Consumer Safety Challenges

- **MRLs (Maximum Residue Limits):** Many countries lack stringent pesticide regulations for medicinal plants compared to food crops.
- **Traditional Medicine Risks:** Indigenous communities using raw plant materials may face higher exposure to pesticide residues. [57]

Mitigation Strategies for Safe and Effective Phytomedicines

1. Adoption of Organic/Biopesticides: Neem-based pesticides enhance Tulsi phenolic content without chemical residues.

2. Post-Harvest Detoxification: Ozonation and activated charcoal reduce pesticide residues in dried herbs.

3. Biomonitoring and Certification:

- DNA barcoding to ensure species authenticity.
- LC-MS/MS screening for pesticide residues in commercial products.

4. Hormonal Priming: Pre-treatment with salicylic acid stabilizes Aloevera polysaccharide production under stress. [58]

Mitigation Strategies for Pesticide-Induced Biochemical Changes in Medicinal Plants

Appropriate mitigation strategies must be developed to maintain the therapeutic efficacy and safety of medicinal plants in light of the growing concern over pesticide-induced changes in these plants. [59]

Sustainable Pest Management Approaches.

Biopesticide Alternatives

- Plant-derived pesticides (neem, pyrethrum) enhance secondary metabolites without oxidative damage.
- Microbial agents (Beauveria bassiana, Bacillus thuringiensis) provide targeted pest control.
- **Example:** Ocimum sanctum treated with neem oil shows 20-30% higher eugenol content compared to synthetic pesticides.

Nano-Formulated Pesticides

- Encapsulated pesticides reduce application frequency by 40-60%.
- Chitosan nanoparticles deliver active ingredients while minimizing metabolic disruption.

1. Biochemical Stress Mitigation

Phytohormone Priming

- Salicylic acid (50-100 μM) pretreatment maintains PAL activity in pesticide-exposed Echinacea purpurea.
- Methyl jasmonate (10 μM) preserves terpenoid biosynthesis in Artemisia annua under herbicide stress.

Antioxidant Supplementation

- Foliar treatment of 1 mM ascorbic acid inhibits ROS damage in Withania somnifera.
- Silicon nanoparticles (50 ppm) increase SOD and CAT activities by 25-35%.

2. Agricultural Best Practices

Precision Application Techniques

- Drone-based spraying reduces pesticide use by 30-50%.
- Soil application minimizes foliar metabolic disruption.

Intercropping Systems

- Targets companion planting reduces nematode pressure in Curcuma longa fields.
- Aromatic plant borders act as natural pest deterrents.

3. Post-Harvest Remediation

Detoxification Processes

- Ozone treatment (2 ppm for 30 min) degrades 70-80% of pesticide residues.
- Activated carbon filtration removes lipophilic contaminants from extracts.

Optimization of Processing

- Low-temperature drying preserves alkaloids in Catharanthus roseus.
- Supercritical CO_2 extraction minimizes residual pesticide transfer to final products.

4. Breeding and Biotechnological Solutions

Stress-Tolerant Cultivars

Selection of high-metabolite genotypes with natural pesticide resistance.

- Example: High-artemisinin Artemisia annua hybrids have 40% reduced glyphosate sensitivity.

CRISPR-Cas9 Applications

- Editing of CYP450 genes enhances detoxification capacity.
- Modulating MYB transcription factors stabilizes flavonoid synthesis.[60]

5. Monitoring and Quality Assurance

- LC-MS/MS pesticide residue screening for all raw materials.
- NMR-based metabolomics for batch-to-batch consistency verification.

Implementation Challenges

- Cost barriers for small-scale farmers adopting nanotechnologies.
- Regulatory hurdles for biopesticide approvals.
- Need for region-specific adaptation of strategies.

CONCLUSION

The biochemical alterations caused by pesticide exposure pose a major danger to the therapeutic quality and safety of medicinal plants. Based on the information that is currently available, pesticides often reduce the amounts of bioactive substances by 30 to 50% by interfering with the synthesis of secondary metabolites (phenolics, alkaloids, and terpenoids) as well as basic metabolic functions (photosynthesis, respiration, and nitrogen absorption). These changes, which lead to unexpected differences in the active components in drugs, are brought on by a number of mechanisms, including oxidative stress, enzyme inhibition, and disruption of hormonal pathways.

In addition to physiological changes, the consequences include practical problems in herbal treatment. Pesticide residues can compromise product safety, and altered phytochemical profiles affect batch-to-batch consistency and standardisation. Particularly vulnerable are plants whose therapeutic benefits depend on certain chemical ratios or the cooperative actions of many ingredients.

There are new methods that seem promising for lessening these consequences. Sustainable techniques including phytohormone priming, biopesticides, and nano-formulations can help maintain metabolic balance in addition to managing pests. Post-harvest processing techniques and contemporary farming methods are effective in reducing residue levels without sacrificing yield.

Future objectives should focus on developing pesticide-sensitive biomarkers for early stress detection, developing species-specific culture methods, and creating international standards for the use of pesticides in the production of medicinal plants. It will be crucial to integrate ancient knowledge with contemporary analytical methods in order to preserve the quality of medicinal plants in contemporary agricultural systems.

Striking a balance between pest management and medicinal efficacy ultimately requires multidisciplinary collaboration combining plant physiology, analytical chemistry, and sustainable agricultural principles in order to ensure the ongoing supply of safe, effective herbal medicines.

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