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Medicinal plants in the management of environment-related diseases: Opportunities and challenges

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ABSTRACT

Environmental diseases pose a double threat—as such diseases affect the general population or affect only a very small segment of it-they continue to be recognized as one of the biggest health hazards in the world. Changes in respiratory disease, cardiovascular disease, cancer, and metabolic diseases all fall into this never-ending category. Diseases may be directly or indirectly caused by environmental pollution through mechanisms such as oxidative stress, inflammatory response, mitochondrial dysfunction, immune disturbance, or even epigenetic transformation. Medicinal plants and their phytochemicals offer the possibility of therapeutic treatment since their actions on physiological systems are many and varied, have been proven to be safe at appropriate doses, and almost all have been used by humans practically since the beginning of civilization for medicine. This review will cover the mechanistic basis of phytochemicals counteracting pathological responses to toxicants, examples of their incorporation into pharmacy practice, and obstacles to their enabling actual use in clinical applications.

Keywords: Plant, Environment, Toxins, Disease.
Article type: Review Article.

INTRODUCTION

Environmental factors actually profoundly contribute to human ill health and cause a large volume of diseases worldwide. The entry of synthetic chemicals into the environment coincided with industrialization and urbanization processes, thus raising sharply the level of exposure to pollution by heavy metals and pesticides, air contaminants, and industrial by-products. Studies point that these exposures do increase rates of chronic diseases, such as cardiovascular diseases, cancers of different types, respiratory diseases, diabetes, and neurodegenerative

diseases. These are environment-related diseases with a profusion of interrelated causes in oxidative stress, chronic inflammation, mitochondrial dysfunction, immune impairment, and altered gene expression. Having now higher rates of incidence and baffling biological basis, all these chronic ailments are widening sulcus as a modern public health challenge (Bolognesi *et al*. 2022). The conventional drug treatments normally target certain pathways and defined endpoints at a molecular level. However, environmental factors inducing complex disease states imply multiple interdependent origins usually obstructing the targeting of just one endpoint. For instance, pollutant exposure can hamper mitochondrial function, cause chronic inflammation, alter metabolic signalling, or simply change the gene expression through epigenetics. An approach at this scale would mean designing therapies that simultaneously target multiple pathways within one and the same condition. Thus, medicinal plants and bioactive phytochemicals would come in handy therapeutically (Bisht *et al*. 2021). Drug therapy normally targets predefined pathways and endpoints at the molecular level. But environmental factors inducing complex disease states imply multiple interdependent origins, in many cases hindering harm to just one endpoint. For example, pollutant exposure could disarm mitochondrial operation, generate chronic inflammation, disrupt metabolic signalling, or simply alter gene expression through epigenetics. Approaches at this scale would entail designing therapies to target two or more pathways for one and the same condition. Hence, medicinal plants and bioactive phytochemicals become very useful therapeutically (Mardani-Nafchi *et al*. 2025). Newly explored topics of plant medicine look at interactions with the microbiota. Increasingly, the microbiome is deemed to influence mediation and exposure to disease. Some plant metabolites or phytochemicals are metabolized by gut microbes to their bioactive and more potent forms, while others enhance microbial diversity and yield beneficial substances like short-chain fatty acids (SCFA), including butyrate and propionate. This bidirectional interaction could then become another mechanism through which one may restore health by reducing dysbiosis and systemic inflammation from toxins (Lalehgani *et al.* 2025). Despite these hope-inspiring developments, major barriers yet exist, preventing the translation of medicinal plants into usable or usable treatments upon environmental health. Variability in phytochemical content owing to geography and season, standardization issues, poor bioavailability of compounds, few controlled clinical trials, interaction with other drugs, and disparities in regulatory oversight are all worthy considerations for mention.

Pathophysiological mechanisms of environment-related diseases

Chronic exposure to environmental contaminants leads to diseases caused by basic exposures to elements like heavy metals, which include arsenic, lead, and cadmium. It also involves pesticides and gaseous pollutants like particulate matter, ozone, and nitrogen oxides. Endocrine-disrupting chemicals and various forms of industrial activity are additional factors. Each of these contributors disrupts normal cellular functions in complex and interconnected ways, resulting in diseases. The following sections describe the most influential disease pathways (Luthra & Roy 2022).

Oxidative stress and inflammation

An important mechanism of toxicity related to pollution is the over-generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS). Such toxins deplete glutathione and inhibit antioxidant enzymes, leading to oxidative stress, while cadmium and arsenic have been implicated in these actions. By excessive ROS being produced more, destruction can take place through oxidative damage to lipids, proteins, and nucleic acids, resulting in tissue injury and carcinogenesis enhancement levels (Rudrapal *et al*. 2024). One of the important mediator of oxidative stress is inflammatory signalling that the body initiates as a response to intervention of this stress condition. Once an oxidative stress response has been activated, environmental toxicants activate the transcription factors nuclear factor κB (NF-κB) and activator protein-1 (AP-1), which produce pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6) as a signal of stress. These environmental toxicants also cause activation of the NLRP3 inflammasome, which is one of the main intracellular multiprotein immune receptors activated by toxicants, and as a result, pro-inflammatory IL-1β and IL-18 mature to ameliorate the chronic inflammation. In parallel, activations of the oxidative stress responses also prevented the induction of the stress response characteristic of the Nrf2/Keap1 pathway that confers antioxidant exploits against the oxidative damage. Two molecular and cellular processes, oxidation and inflammation, are, therefore, the central axis or pathway in environmental health conditions that can give rise to an array of diseases (Checa & Aran 2020).

Mitochondrial dysfunction

Mitochondria are mainly targeted because of ATP generation and regulation of reactive oxygen species (ROS) and other reactive metabolites. Environmental pollutants can inhibit mitochondrial respiration, decrease ATP

production, whilst electron leakage produces excessive ROS. Environmental exposures affect mitochondrial dynamics, including fusion (via mitofusins, MFN1/2) and fission (via DRP1), thereby blocking organelle quality control. The environmental toxicants also interfere with mitophagy (selective degradation of damaged mitochondria through PINK1/Parkin signalling), promoting damaged dysfunctional mitochondria to continue and worsen oxidative injury. Environmental pollutants also affect biogenesis, i.e., the increase in mitochondrial density and the number mediated by PGC-1α-compromising the ability of cells to bounce back after toxic exposures. Each of these cellular-level deregulations finds its association with neurological disorders, metabolic syndrome, and cardiopulmonary disease due to environmental exposure (Rattan *et al*. 2017).

Xenobiotic metabolism and transport

Xenobiotic-metabolizing enzymes (XMEs) act on environmental chemicals in the body. These Phase I enzymes will mainly add some sort of functional group to the end-product to help with detoxification or activation of a procarcinogen. The Phase II enzymes will conjugate metabolites of toxins to glutathione, glucuronic acid, or sulfate to increase their solubility. Pollutants may change these pathways, resulting in low detoxification or overproduction of reactive intermediates. Antioxidant enzyme systems such as NAD(P)H:quinone oxidoreductase 1 (NQO1) are largely down-regulated, thus lowering cellular defence. Transporters such as P-glycoprotein (ABCB1), breast cancer resistance protein (ABCG2), and organic anion transporting polypeptides (OATPs) can either efflux or uptake xenobiotics. Altering the activity of these systems may cause increased toxicity, altered pharmacokinetics of a co-administered drug and site-specific toxicity to certain tissue forms (Shimada 2006).

Endocrine and metabolic disruption

Numerous pollutants have properties similar to endocrine-disrupting chemicals (EDCs) because they mimic or block natural hormones. Dioxins, bisphenol A (BPA), and phthalates interact with estrogen, androgen, and thyroid receptors. This interaction ultimately changes reproductive and developmental pathways. Additionally, environmental exposures can affect the actions of peroxisome proliferator-activated receptors (PPARs), which help regulate lipid and glucose metabolism. Importantly, disrupting insulin signalling pathways leads to insulin resistance and type 2 diabetes. It often disrupts the AMPK-mTOR axis, an important energy sensing pathway. This disruption can result in altered cellular growth, increased autophagy, and disrupted metabolic balance. These broader changes contribute to obesity, diabetes, and metabolic syndrome as a whole (Barzi *et al*. 2020; Gheibi *et al*. 2023).

Epigenetic Reprogramming

Environmental toxicants cause lasting changes in gene expression through epigenetic mechanisms. Elements like arsenic and cadmium alter DNA methylation patterns, which can silence tumour suppressor genes or activate oncogenes. Histone modifications are influenced by histone acetyltransferases (HATs), deacetylases (HDACs), and sirtuins. This disruption affects chromatin structure and alters transcriptional activity. Pollutants also affect microRNAs (miRNAs). These small noncoding RNAs regulate mRNA stability and translation. Abnormal miRNA levels can lead to inflammation, fibrosis, and cancer. Importantly, these epigenetic changes can be inherited, raising concerns about the impact of environmental exposures on future generations (Barzi *et al*. 2020; Vahabi Barzi *et al*. 2022).

Immune Dysregulation and Barrier Function

The immune system is very sensitive to environmental stressors. Pollutants damage the epithelial barrier in the gut and lungs, elevating permeability and leading to systemic inflammation. Pollutants also disrupt mucosal immunity, weakening the body's defence against pathogens. At the systemic level, pollutants alter T cell differentiation, disrupting the balance between regulatory T cells (Tregs) and Th17 cells. This imbalance promotes chronic inflammation, autoimmunity, and allergic diseases. This immune disruption is behind the rising cases of asthma, autoimmune disorders, and cancers linked to the environment (McCombe & Pittock 2022; Amanpour *et al*. 2024).

Microbiome Disturbance

Our interactions with the environment are strongly influenced by our gut microbiota. Environmental pollutants can change the diversity of our microorganisms. They can reduce beneficial bacteria and encourage harmful ones. Short-chain fatty acids (SCFAs), such as butyrate, are vital for supporting the immune system and maintaining gut health. Their production may drop due to this imbalance. Additionally, pollutants disrupt bile acid metabolism

and signalling through receptors like FXR and TGR5. This can lead to metabolic and liver problems. Changes in the microbiome also hinder the enterohepatic cycling of toxins, which might extend their time in the body. Therefore, disruptions in the microbiome are a key link between environmental exposure and systemic disease (Lin *et al*. 2024).

Phytochemicals and medicinal plants with protective roles (Table 1 and Fig. 1)

Polyphenols. (e.g., resveratrol, curcumin, and epigallocatechin gallate) restore redox balance and inhibit NF-κB (MARTINS *et al*. 2023).

Terpenoids and alkaloids. (e.g., ginsenosides, and berberine) modulate mitochondrial and metabolic signalling.

Sulfur-containing compounds. (e.g., sulforaphane from broccoli) activate Nrf2 and detoxification enzymes (Liew *et al.* 2020).

Traditional medicinal plants. with strong evidence include:

Curcuma longa: anti-inflammatory via NF-κB inhibition.

Camellia sinensis: antioxidant and cardioprotective.

Ginkgo biloba: neuroprotective effects in oxidative stress.

Silybum marianum: hepatoprotective against xenobiotics.

Nigella sativa: immunomodulatory and anti-cancer potential.

Table 1. Traditional medicinal plants with evidence-based protective effects.

Plant	Key Effects	Mechanisms
Curcuma longa	Anti-inflammatory	Inhibits NF-κB signalling
Camellia sinensis (green tea)	Antioxidant, cardioprotective	Reduces ROS, enhances endothelial function
Ginkgo biloba	Neuroprotective	Mitigates oxidative stress in neurons
Silybum marianum (milk thistle)	Hepatoprotective	Protects against xenobiotic-induced liver injury
Nigella sativa	Immunomodulatory, anti-cancer	Modulates immune response and induces apoptosis in cancer cells

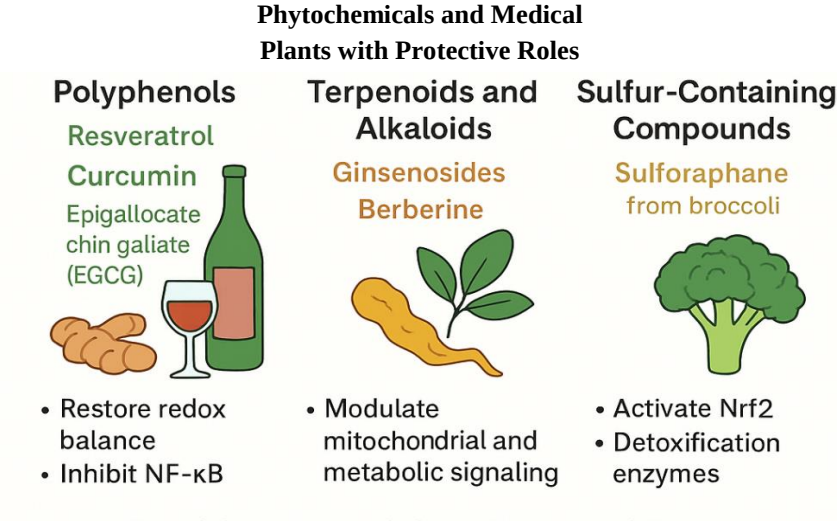

Fig. 1. Medicinal plants and their protective roles.

Mechanistic crosstalk between toxicants and phytochemicals

Environmental toxicants and phytochemicals are different in structure and function, but they often influence the same molecular signalling pathways. This interaction is called mechanistic crosstalk. In this context, phytochemicals can counteract or alter the harmful effects of toxicants by targeting similar areas in cellular regulation. Understanding these connections is important for identifying treatment possibilities for medicinal plants in dealing with environmentally related diseases (Afsharnezhad *et al*. 2017).

Redox–inflammation axis

Toxicants such as heavy metals, polycyclic aromatic hydrocarbons, and fine particulate matter induce oxidative stress by generating ROS and suppressing endogenous antioxidant systems. This promotes activation of NF-κB

and AP-1, leading to chronic inflammation, and stimulates the NLRP3 inflammasome, further amplifying pro-inflammatory signalling (Kumar *et al*. 2021).
Phytochemicals such as curcumin, resveratrol, sulforaphane, and quercetin counteract these effects by:
Activating Nrf2/Keap1 signalling, upregulating antioxidant enzymes (HO-1, NQO1, GSTs).
Inhibiting NF-κB/AP-1 transcriptional activity, thereby reducing cytokine release.
Suppressing NLRP3 inflammasome activation, mitigating pyroptotic cell death and inflammation (Checa & Aran 2020).

Mitochondrial homeostasis
Environmental pollutants impair mitochondrial respiration, alter dynamics (fusion/fission), and disrupt mitophagy, resulting in energy deficits and apoptotic signalling (Meyer *et al.* 2017).
Phytochemicals restore mitochondrial function by:
Enhancing biogenesis via activation of PGC-1α and SIRT1.
Normalizing fusion–fission balance through regulation of DRP1 and mitofusins.
Promoting mitophagy via PINK1/Parkin pathways to remove dysfunctional mitochondria.
For example, ginsenosides, polyphenols, and berberine improve mitochondrial efficiency and attenuate toxicant-induced apoptosis.

Xenobiotic metabolism and transport
Toxicants interfere with Phase I and II enzymes (CYP450s, UGTs, SULTs, and GSTs) and modulate drug transporters (P-gp/ABCB1, BCRP/ABCG2, and OATPs). This can either impair detoxification or generate harmful intermediates (F Martins *et al*. 2022).
Phytochemicals influence these same systems by:
Modulating CYP activity (e.g., green tea catechins inhibit CYP1A1, reducing activation of procarcinogens).
Inducing detoxification enzymes (e.g., sulforaphane enhances GSTs and NQO1 expression).
Regulating efflux transporters, limiting intracellular accumulation of toxicants.

Endocrine and metabolic signalling
Toxicants often act as endocrine disruptors, altering PPARs, insulin signalling, and nuclear hormone receptors, while disturbing energy sensing via AMPK–mTOR (Shi *et al*. 2020).
Phytochemicals provide regulatory balance by:
Activating AMPK, improving insulin sensitivity and metabolic homeostasis (e.g., resveratrol, and berberine).
Modulating PPARs, restoring lipid metabolism.
Influencing estrogen, androgen, and thyroid receptors, thereby counteracting endocrine disruption.

Epigenetic programming
Environmental exposures cause long-term gene expression changes via DNA methylation, histone modifications, and dysregulation of microRNAs.
Phytochemicals act as epigenetic modulators (Barzi *et al*. 2020):
EGCG and curcumin influence DNA methyltransferases, restoring normal methylation patterns.
Sulforaphane and butyrate inhibit HDACs, enhancing histone acetylation and gene expression of protective enzymes.
Multiple phytochemicals regulate miRNAs involved in inflammation, apoptosis, and tumorigenesis.

Barrier function and immunity
Toxicants compromise intestinal tight junctions and mucosal integrity, leading to leaky gut and systemic inflammation. They also skew immune balance, reducing Tregs and promoting Th17 polarization (Wu & Meydani 2019).
Phytochemicals such as polyphenols and flavonoids help restore barrier integrity by:
Strengthening tight junction proteins (occludin, and claudins).
Enhancing mucosal immunity and anti-inflammatory cytokine production.
Restoring Treg/Th17 balance, promoting immune tolerance.

Microbiome–metabolome axis
Environmental pollutants alter gut microbial diversity, impair SCFA production, and disrupt bile acid metabolism (Zhang *et al*. 2022).

Phytochemicals interact closely with the microbiome:
Many (e.g., flavonoids, and lignans) are biotransformed by gut bacteria into bioactive metabolites with enhanced activity.
Promoting production of SCFAs such as butyrate, which support epithelial and immune health.
Influencing bile acid signalling through FXR and TGR5, counteracting toxicant-induced metabolic disturbances.

Opportunities

Integration into preventive medicine. Using phytochemicals as dietary supplements or functional foods to reduce disease risk.
Nanotechnology and formulation advances. Enhancing bioavailability of poorly soluble phytochemicals such as curcumin.
Multi-omics and artificial intelligence. Identifying phytochemical-target interactions for precision medicine.
Global health impact. Affordable, culturally acceptable interventions for populations at high risk of environmental exposures.

Challenges

Standardization: Variability in plant composition due to geography, cultivation, and processing.
Pharmacokinetics: Limited absorption, rapid metabolism, and low bioavailability of many phytochemicals.
Drug Interactions: Potential modulation of drug-metabolizing enzymes (e.g., CYP450).
Clinical Evidence: Scarcity of large-scale, randomized controlled trials.
Regulatory Frameworks: Lack of harmonized guidelines for medicinal plant use.

CONCLUSION

Medicinal plants provide bioactive compounds that can help treat environment-related diseases with complex mechanisms that are hard to understand. The phytochemicals influence oxidative stress, mitochondrial balance, immune response, and epigenetic changes. This suggests they can be used for prevention and treatment. To fully realize their potential in modern medicine, we first need to tackle issues of standardization, pharmacokinetics, and clinical validation.

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