

Caspian Journal of Environmental Sciences

Online ISSN: 1735-3866 Print ISSN: 1735-3033

Role of medicinal plants in mitigating environmental toxin effects: Protective and detoxification mechanisms

Rustam Turakulov^{1*}, Islom Kadirov², Abdurashid Abdurakhmonov³, Abdulatif Shavazov⁴, Durdona Alikarieva⁵, Nodirakhan Nishanova⁶, Dildora Islamova⁶, Guzal Akmalova⁶, Dilnoza Khafizova⁷, Nigora Dustova⁷, Kenjabek Rozumbetov⁸, Saydali Turdiev⁹, Arsen Abdulhakimov¹⁰

- 1. Department of Internal Medicine in Family Medicine, Tashkent State Medical University, Tashkent, Uzbekistan
- 2. Department of Transport Systems, Urgench State University named after Abu Raykhan Beruni, Urgench, Uzbekistan
- 3. Department of Labour Protection, Andijan State Technical Institute, Andijan, Uzbekistan
- 4. Institute of Energy Problems of the Academy of Sciences of the Republic of Uzbekistan
- 5. Department of Ecology, Faculty of Biology and Ecology, National University of Uzbekistan named after Mirzo Ulugbek, Republic of Uzbekistan, Tashkent
- 6. Tashkent State Technical University, Tashkent, Uzbekistan
- 7. Bukhara State Medical Institute named after Abu Ali Ibn Sino, Bukhara, Uzbekistan
- 8. Department of Veterinary Diagnostics and Food Safety, Nukus Branch of Samarkand State University of Veterinary Medicine, Animal Husbandry and Biotechnology, 230100 Nukus, Uzbekistan; & Department of General Biology and Physiology, Karakalpak State University, 230100 Nukus, Uzbekistan; Bukhara State Medical Institute named after Abu Ali ibn Sino, Bukhara, Uzbekistan
- 9. Tashkent State Agrarian University, Tashkent, Uzbekistan
- 10. Department of Faculty and Hospital Surgery of Fergana Medical Institute of Public Health, Fergana, Uzbekistan

ABSTRACT

Environmental toxins—including heavy metals, organic pollutants, mycotoxins, and airborne toxicants—pose significant threats to human health by inducing oxidative stress, inflammation, mitochondrial dysfunction, and genomic damage. Current detoxification strategies are limited in efficacy and safety, creating demand for complementary approaches. This review summarizes the protective and detoxification mechanisms of medicinal plants against environmental toxins, with emphasis on molecular pathways and translational evidence. We examined experimental and clinical studies addressing the role of medicinal plants in mitigating toxin-induced damage, focusing on antioxidant activity, xenobiotic metabolism, chelation, and anti-inflammatory effects. Key phytochemicals—include silymarin (Silybum marianum), curcumin (Curcuma longa), catechins (Camellia sinensis), sulforaphane (Brassica spp.), allicin (Allium sativum), and resveratrol (Vitis vinifera)—exert protective effects via multiple mechanisms: Activation of Nrf2-ARE signaling and induction of detoxification enzymes, chelation of toxic metals (lead, cadmium, mercury), suppression of NF-κB-mediated inflammation, stabilization of mitochondria and cell membranes, and support of glutathione metabolism. Several plants, such as broccoli sprouts and garlic, show measurable benefits in human trials (e.g., increased excretion of benzene metabolites, and reduced lead burden). However, limitations include variability in phytochemical content, poor bioavailability (e.g., curcumin, and resveratrol), and potential herb-drug interactions. Medicinal plants offer promising, multitargeted strategies for mitigating the adverse health effects of environmental toxins. While robust preclinical evidence supports their use, large-scale, standardized clinical trials are essential to validate efficacy, optimize dosing, and ensure safety. Integration of phytomedicine with modern detoxification strategies may provide a sustainable approach to environmental health challenges.

 $\textbf{Keywords} \hbox{:} \ Environment, Plant, Toxins, Detoxification. \\$

Article type: Review Article.

^{*} Corresponding author's Email: rustam.turakulov@tma.uz

INTRODUCTION

Environmental pollution has emerged as one of the most pressing public health challenges of the 21st century. Industrialization, urbanization, agricultural intensification, and widespread use of synthetic chemicals have significantly increased human exposure to diverse environmental toxins (Gheibi et al. 2020). These toxins include heavy metals such as lead, cadmium, mercury, and arsenic; organic pollutants such as polycyclic aromatic hydrocarbons (PAHs), pesticides, and dioxins; naturally occurring contaminants such as mycotoxins; and airborne toxicants such as particulate matter, ozone, and volatile organic compounds (Barzi et al. 2020; Vahabi Barzi et al. 2022). Current strategies for managing environmental toxin exposure remain limited and often inadequate. Conventional chelation therapies are effective for acute heavy metal poisoning, but can cause significant side effects and are unsuitable for long-term or low-level exposure scenarios (Rahimzadeh et al. 2017). Similarly, pharmaceutical antioxidants have had limited clinical success, in part due to poor bioavailability and inability to address the complex, multi-targeted nature of toxin-induced damage. This therapeutic gap has stimulated interest in complementary and integrative approaches that harness the body's intrinsic defense systems. Among these, medicinal plants and their bioactive phytochemicals have gained considerable attention as potential modulators of toxin-induced pathophysiology (Mohammadi et al. 2024). Medicinal plants have been used for centuries in traditional systems of medicine, including Ayurveda, Traditional Chinese Medicine, and Unani, for the prevention and treatment of diseases associated with "poisoning" or systemic imbalance (Islamova et al. 2025; Jumagaliyeva et al. 2025). Modern pharmacological and toxicological research has begun to validate many of these practices, demonstrating that plant-derived compounds can directly scavenge reactive oxygen species (ROS), chelate toxic metals, modulate phase I and phase II detoxification enzymes, and regulate key signaling pathways such as the nuclear factor erythroid 2-related factor 2 (Nrf2) and nuclear factor-κB (NF-κB). Importantly, these mechanisms do not act in isolation, but often function synergistically, enabling plants to provide multi-layered protection against diverse toxic insults (Eftekhari 2020). A growing body of experimental evidence illustrates these protective roles. Silybum marianum (milk thistle), rich in silymarin, stabilizes hepatocyte membranes and activates Nrf2-dependent antioxidant defenses, reducing liver injury from aflatoxin and industrial solvents. Curcuma longa (turmeric), through curcumin and related curcuminoids, demonstrates both chelating activity against heavy metals and suppression of NF-κB-mediated inflammation, thereby mitigating damage induced by cadmium, lead, and microcystins (Jeon et al. 2021). Polyphenols from Camellia sinensis (green tea) and sulforaphane from Brassica spp. (broccoli sprouts) enhance the expression of detoxification enzymes such as glutathione S-transferases and UDP-glucuronosyltransferases, promoting clearance of benzene metabolites and other electrophiles. Garlic, Allium sativum, a widely used culinary and medicinal plant, reduces lead burden in occupationally exposed individuals, while Vitis vinifera (grapes/resveratrol) and Rosmarinus officinalis (rosemary) offer antioxidant and anti-inflammatory benefits in models of pesticide and PAH exposure. Together, these examples underscore the therapeutic promise of phytomedicine in environmental health (Alrekaby et al. 2023). Phytochemical variability due to cultivation conditions, extraction methods, and processing complicates standardization. Poor oral bioavailability of certain compounds, such as curcumin and resveratrol, limits therapeutic efficacy. Safety concerns also persist, particularly with concentrated extracts that may interact with pharmaceutical drugs or cause toxicity when consumed at high doses. These limitations highlight the need for rigorous human studies, standardized formulations, and advanced delivery systems, including nanotechnology-based carriers, to fully realize the detoxification potential of medicinal plants (Kandezi et al. 2020; Miri et al. 2025). The scientific and clinical relevance of this topic is further reinforced by global epidemiological trends. Populations in industrial and urban environments are increasingly exposed to mixtures of toxins rather than single agents, creating cumulative and synergistic risks. Vulnerable groups, including children, pregnant women, and occupational workers, are disproportionately affected. Public health systems urgently require accessible interventions that can reduce toxin burden and mitigate long-term health risks. Medicinal plants, acting through multi-targeted and adaptive mechanisms, are uniquely positioned to complement conventional strategies for environmental health protection (Sharifnia, Eftekhari & Mortazavi 2024). Given these considerations, the objective of this review is to synthesize current knowledge on the role of medicinal plants in mitigating the harmful effects of environmental toxins. Specifically, we will (i) classify the major environmental toxins and their mechanisms of toxicity, (ii) highlight the protective and detoxification pathways activated by medicinal plants, (iii) summarize experimental and clinical evidences for key species, and (iv) discuss translational challenges, safety considerations, and future research directions. By integrating mechanistic insights with evidence from preclinical and clinical studies, this review

aims to provide a comprehensive framework for understanding how phytomedicine can contribute to the prevention and management of toxin-induced diseases (Gheibi *et al.* 2020).

Medicinal Plants as Natural Defenses Against Environmental Toxins

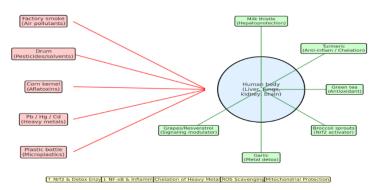


Fig. 1. Medicinal plants protect the body from environmental toxins via various mechanisms.

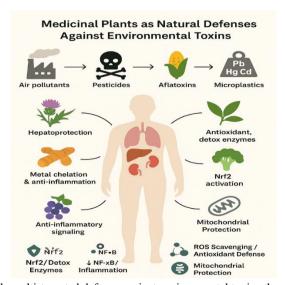


Fig. 2. Medicinal plants provide multi-targeted defense against environmental toxins through antioxidant, detoxification, chelation, and anti-inflammatory mechanisms.

Environmental toxins and their toxicity mechanisms

Human exposure to environmental toxins is virtually unavoidable in modern societies, owing to industrial processes, agricultural practices, and urbanization. These toxins exert harmful effects through diverse but overlapping molecular pathways, including oxidative stress, inflammation, mitochondrial dysfunction, and genomic damage. The following subsections summarize the major categories of environmental toxins and their mechanisms of toxicity (Amanpour *et al.* 2024).

Heavy Metals (Pb, Cd, Hg, and As)

Heavy metals are among the most pervasive environmental pollutants, with substantial evidence linking exposure to multiple chronic diseases. Lead (Pb), cadmium (Cd), mercury (Hg), and arsenic (As) are particularly concerning due to their persistence in the environment, bioaccumulation, and lack of physiological function in humans (Plaman *et al.* 2019; Amanpour *et al.* 2024).

Mechanisms of toxicity

Oxidative stress. Heavy metals catalyze the production of reactive oxygen species (ROS) through Fenton-like reactions (especially Cd and Pb indirectly), leading to lipid peroxidation, protein carbonylation, and DNA strand breaks (Zeng *et al.* 2023).

Enzyme inhibition. Metals interact with sulfhydryl groups of critical enzymes, disrupting antioxidant defenses such as glutathione peroxidase (GPx), catalase, and superoxide dismutase (SOD; van Berkel & van Delft 2018).

DNA and protein adduct formation. Arsenic and cadmium can bind to DNA and histones, altering gene expression and contributing to mutagenesis (Jumagaliyeva *et al.* 2025).

Disruption of calcium and zinc homeostasis. Lead competes with calcium in neuronal signaling, impairing synaptic function, while cadmium displaces zinc in metalloproteins, destabilizing their activity (Amanpour *et al.* 2024).

The clinical consequences include neurotoxicity (lead), nephrotoxicity (cadmium), hepatotoxicity (arsenic), and neurodevelopmental impairment (methylmercury). Chronic exposure even at low doses contributes to carcinogenesis, cardiovascular dysfunction, and metabolic disorders.

Organic pollutants (PAHs, pesticides, dioxins, and solvents)

Organic pollutants encompass a wide range of synthetic chemicals, many of which are classified as persistent organic pollutants (POPs) due to their resistance to degradation and long biological half-lives. Polycyclic aromatic hydrocarbons (PAHs), pesticides, dioxins, and industrial solvents are prominent representatives (Ramezanifar *et al.* 2023).

Mechanisms of toxicity

Carcinogenesis via DNA adduct formation. PAHs such as benzo[a]pyrene undergo bioactivation by cytochrome P450 enzymes into reactive metabolites that covalently bind DNA, leading to mutations and cancer initiation (Barzi *et al.* 2020).

Mitochondrial dysfunction. Organophosphates and solvents impair electron transport chain complexes, depleting ATP and increasing ROS production.

Endocrine disruption. Many pesticides (e.g., organochlorines, glyphosate derivatives) and dioxins interact with nuclear hormone receptors such as the estrogen receptor (ER), androgen receptor (AR), or aryl hydrocarbon receptor (AhR), leading to reproductive toxicity and altered developmental signaling (Gheibi *et al.* 2020).

Immune modulation. Dioxins, particularly TCDD, activate the AhR pathway, suppressing immune function and contributing to carcinogenesis.

The health impacts include elevated risks of lung and skin cancers, neurodegeneration, endocrine disorders, and reproductive abnormalities. Agricultural workers and populations living near industrial sites are disproportionately exposed (Amanpour *et al.* 2024).

Mycotoxins (Aflatoxin, Microcystins, Ochratoxin A)

Mycotoxins are toxic secondary metabolites produced by fungi, commonly contaminating food crops and water sources. Aflatoxin B_1 , microcystins, and ochratoxin A represent the most clinically significant mycotoxins with established links to human disease (Yu *et al.* 2022).

Mechanisms of toxicity

Hepatotoxicity and carcinogenesis. Aflatoxin B₁ undergoes metabolic activation via CYP3A4 to form an epoxide that covalently binds DNA, particularly at codon 249 of the TP53 gene, a mutational hotspot in hepatocellular carcinoma (HCC; Haider & Hussein 2022).

Inhibition of protein phosphatases. Microcystins strongly inhibit serine/threonine phosphatases (PP1 and PP2A), leading to hyperphosphorylation of cytoskeletal proteins and hepatocyte necrosis (Campos & Vasconcelos 2010). **Genotoxicity and nephrotoxicity.** Ochratoxin A induces oxidative stress, forms DNA adducts, and interferes with mitochondrial respiration, contributing to kidney injury and urothelial cancers (Khoi *et al.* 2021).

Mycotoxin exposure is of particular concern in tropical and subtropical regions, where food storage conditions favor fungal growth. Chronic intake is linked to liver cancer, kidney damage, and impaired immune function.

Airborne pollutants (PM, Benzene, Acrolein, and Ozone)

Airborne pollutants represent one of the most widespread toxin categories, contributing significantly to the global burden of non-communicable diseases. Fine particulate matter ($PM_{2.5}$ and PM_{10}), benzene, acrolein, and ozone are among the most studied toxicants in this category (Thangavel *et al.* 2022).

Mechanisms of toxicity

Oxidative and nitrosative stress. Inhaled particles generate ROS and reactive nitrogen species (RNS), overwhelming antioxidant defenses and damaging lipids, proteins, and nucleic acids.

Inflammation. Air pollutants activate toll-like receptors (TLRs) and NF- κ B signaling in airway epithelial cells and macrophages, leading to secretion of pro-inflammatory cytokines (IL-6, TNF- α , and IL-1 β ; Noshadirad *et al.* 2023).

Mitochondrial dysfunction and apoptosis. Benzene metabolites impair mitochondrial respiration, while acrolein forms adducts with proteins and DNA, triggering cell death (Hikisz & Jacenik 2023).

Immune dysregulation. Ozone exposure promotes airway hyperreactivity and exacerbates asthma through Th2-mediated immune responses (Chu *et al.* 2019).

These processes contribute to chronic respiratory diseases, cardiovascular morbidity, neurological impairment, and cancer. Notably, the World Health Organization (WHO) attributes millions of premature deaths annually to air pollution exposure, making it a leading environmental risk factor worldwide.

Emerging toxins (Nanoparticles, microplastics, endocrine disruptors)

In recent years, novel environmental contaminants such as engineered nanoparticles, microplastics, and endocrine-disrupting chemicals (EDCs) have emerged as toxins of concern. Although the field is still developing, early evidence indicates significant biological impacts.

Mechanisms of toxicity

Nanoparticles (NPs). Due to their small size and large surface area, NPs (e.g., titanium dioxide, silver nanoparticles) can penetrate biological membranes, generate ROS, and accumulate in organs, leading to oxidative stress, DNA damage, and inflammation (Kumar *et al.* 2025).

Microplastics (MPs). Microplastics and nanoplastics can translocate across the gut barrier, adsorb other pollutants (e.g., PAHs, and metals), and induce oxidative stress and inflammatory responses in the gastrointestinal and immune systems.

Endocrine disruptors. Chemicals such as bisphenol A (BPA), phthalates, and perfluoroalkyl substances (PFAS) mimic or block natural hormones by binding to estrogen, androgen, or thyroid receptors. They interfere with hormone synthesis, transport, and signaling, leading to developmental, reproductive, and metabolic disorders (Guarnotta *et al.* 2022). Although definitive human epidemiological data remain limited, the ubiquity of these emerging contaminants and their potential for bioaccumulation warrant urgent investigation.

Environmental Toxins → Mechanisms of Toxicity → Health Outcomes

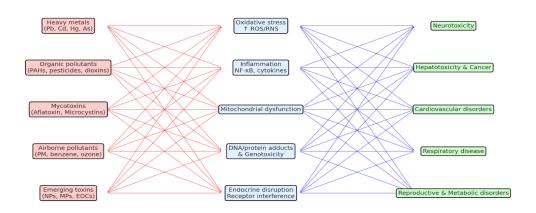


Fig. 3. A schematic diagram showing how environmental toxins trigger molecular mechanisms of toxicity (oxidative stress, inflammation, mitochondrial dysfunction, DNA damage, endocrine disruption), which ultimately lead to health outcomes such as neurotoxicity, hepatotoxicity, cancer, cardiovascular disease, and reproductive disorders.

Protective and detoxification mechanisms of medicinal plants

Antioxidant defense. ROS scavenging and enzyme upregulation

Oxidative stress is a central mechanism of toxicity for most environmental pollutants, including heavy metals, organic xenobiotics, and airborne particulate matter. Medicinal plants provide protection by directly neutralizing reactive oxygen species (ROS) and reactive nitrogen species (RNS) through phenolics, flavonoids, carotenoids, and vitamins. Additionally, many plant-derived compounds enhance the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). For example, polyphenols from *Camellia sinensis* (green tea) and resveratrol from *Vitis vinifera* not only scavenge free radicals

but also increase enzymatic defenses, thereby reducing lipid peroxidation and DNA damage induced by toxins (Lin et al. 2022; Widoyo et al. 2022).

Activation of the Nrf2-ARE Pathway

The nuclear factor erythroid 2-related factor 2 (Nrf2) is a master regulator of antioxidant and detoxification responses. Under stress conditions, Nrf2 dissociates from its inhibitor Keap1 and translocates into the nucleus, where it binds to antioxidant response elements (ARE) in target gene promoters. Many medicinal plant constituents—including sulforaphane from broccoli sprouts, curcumin from turmeric, and silymarin from milk thistle—activate the Nrf2–ARE axis, resulting in the upregulation of cytoprotective enzymes such as heme oxygenase-1 (HO-1), NAD(P)H quinone oxidoreductase 1 (NQO1), glutathione S-transferases (GSTs), and UDP-glucuronosyltransferases (UGTs). Collectively, these enzymes enhance cellular resilience against electrophiles and oxidative damage induced by heavy metals, pesticides, and mycotoxins (Laurindo *et al.* 2023).

Chelation and binding of heavy metals

Heavy metal toxicity arises from their ability to generate ROS, displace essential metals in enzymes, and form stable complexes with DNA and proteins. Certain plant-derived molecules possess chelating properties that reduce the bioavailability and systemic burden of toxic metals. Garlic, *Allium sativum* contains sulfur compounds that bind lead and cadmium, facilitating their excretion. Polyphenols such as tannins and flavonoids also form complexes with metal ions, thereby attenuating Fenton-type reactions that generate hydroxyl radicals. This natural chelation mechanism offers a safer alternative to synthetic chelators, which may cause depletion of essential micronutrients (Mehrandish *et al.* 2019).

Modulation of xenobiotic metabolism

Medicinal plants can regulate xenobiotic-metabolizing enzymes, thereby influencing the activation and clearance of toxins. Cytochrome P450 (CYP) enzymes (phase I metabolism) are often responsible for converting procarcinogens such as benzo[a]pyrene into reactive intermediates. Phytochemicals such as curcumin, quercetin, and genistein inhibit CYP1A1 and CYP1B1, thereby reducing carcinogen activation. Conversely, phase II enzymes—including GST, UGT, and sulfotransferases—are frequently induced by phytochemicals, facilitating conjugation and elimination of electrophiles. For instance, isothiocyanates from cruciferous vegetables strongly upregulate phase II detoxification enzymes, contributing to enhanced clearance of environmental carcinogens (Nandekar & Sangamwar 2012).

Anti-inflammatory pathways

Chronic inflammation is both a consequence and amplifier of toxin-induced tissue injury. Many medicinal plants exert anti-inflammatory effects through suppression of the nuclear factor κB (NF- κB) signaling pathway, which regulates cytokine and adhesion molecule expression. Curcumin, resveratrol, and boswellic acids have been shown to inhibit NF- κB activation, reduce pro-inflammatory cytokines (TNF- α , IL-1 β , and IL-6), and enhance anti-inflammatory mediators. By limiting toxin-induced inflammation, these compounds prevent secondary damage to tissues and reduce the risk of fibrosis, cancer, and cardiovascular complications (Karaman *et al.* 2012).

Mitochondrial and membrane protection

Environmental toxins frequently impair mitochondrial structure and function, leading to reduced ATP synthesis, increased ROS leakage, and initiation of apoptosis. Polyphenols, flavonoids, and terpenoids from medicinal plants help preserve mitochondrial membrane potential, stabilize electron transport chain activity, and prevent cytochrome c release. In addition, membrane lipids are particularly vulnerable to peroxidation, a process mitigated by lipid-soluble antioxidants such as carotenoids (β -carotene, and lycopene) and vitamin E. Through these effects, medicinal plants help sustain cellular bioenergetics under toxic stress.

Epigenetic and signaling effects

Beyond classical antioxidant and anti-inflammatory mechanisms, medicinal plants also exert long-term protective effects through modulation of signaling pathways and epigenetic regulation. Resveratrol activates sirtuin 1 (SIRT1), a key regulator of mitochondrial biogenesis and cellular stress resistance. Flavonoids and polyphenols influence AMP-activated protein kinase (AMPK) and mitogen-activated protein kinase (MAPK) signaling, thereby affecting autophagy, apoptosis, and survival responses. Moreover, certain phytochemicals modulate DNA methylation, histone acetylation, and microRNA expression, offering epigenetic resilience against toxin-induced genomic instability (Bejenaru *et al.* 2024).

Medicinal plants with documented protective effects

A growing body of evidence highlights the potential of medicinal plants to counteract the adverse health impacts of environmental toxins through diverse mechanisms, including antioxidant activity, chelation, modulation of detoxification enzymes, and signaling pathway regulation. We summarize selected plants with well-documented protective effects as follows (Table 1).

Milk thistle, Silybum marianum

Milk thistle, rich in the flavonolignan complex silymarin, is among the most extensively studied hepatoprotective plants. Experimental models show its ability to protect against aflatoxin B_1 -induced hepatotoxicity by enhancing glutathione synthesis and inhibiting lipid peroxidation. Silymarin also supports regeneration of hepatocytes exposed to organic solvents, likely through upregulation of antioxidant enzymes and membrane stabilization (Valková *et al.* 2020).

Protective and Detoxification Mechanisms of Medicinal Plants → Health Benefits

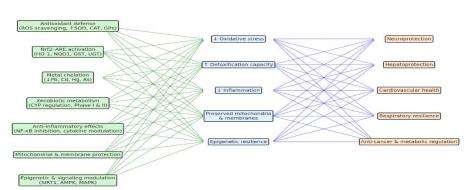


Fig. 4. The mechanistic diagram showing how medicinal plants act through antioxidant defense, Nrf2 activation, chelation, xenobiotic metabolism, anti-inflammatory effects, mitochondrial protection, and epigenetic modulation \rightarrow leading to protective processes (reduced oxidative stress, enhanced detoxification, preserved mitochondria, reduced inflammation) \rightarrow ultimately yielding health outcomes like neuroprotection, hepatoprotection, cardiovascular health, respiratory resilience, and anti-cancer effects.

Turmeric, Curcuma longa

Curcumin, the active polyphenol of turmeric, exerts pleiotropic protective effects against toxic insults. It demonstrates strong metal-chelating properties, reducing the bioavailability of cadmium and lead. Additionally, curcumin inhibits NF-κB-mediated inflammation and scavenges reactive oxygen species (ROS). These combined effects make turmeric a promising intervention against heavy metals and organic pollutant toxicity (Shakour *et al.* 2021).

Green tea, Camellia sinensis

Green tea catechins, especially epigallocatechin gallate (EGCG), exhibit both detoxification and antioxidant activity. Animal studies indicate that green tea attenuates pulmonary inflammation caused by fine particulate matter (PM_{2.5}) and reduces oxidative DNA damage from benzene exposure. Moreover, its polyphenols can chelate heavy metals such as iron and cadmium, thereby lowering systemic toxicity (Sun *et al.* 2023).

Broccoli sprouts, Brassica spp.

Broccoli sprouts are rich in glucosinolates that are metabolized to isothiocyanates, particularly sulforaphane, a potent Nrf2 activator. Human intervention studies in China demonstrated that broccoli sprout beverage enhanced urinary excretion of benzene and acrolein metabolites, indicating improved detoxification of air pollutants. Additionally, sulforaphane protects against aflatoxin-induced genotoxicity by inducing phase II detoxification enzymes such as GST and UGT (Li *et al.* 2024).

Garlic, Allium sativum

Garlic organosulfur compounds, including allicin and diallyl sulfide, provide significant protection against heavy metal toxicity. Experimental models show that garlic supplementation enhances lead excretion and restores glutathione levels in the liver and kidneys. Its sulfur compounds also support endogenous antioxidant enzymes, contributing to systemic detoxification (Eftekhari 2020).

Schisandra, Schisandra chinensis

Lignans derived from schisandra berries, such as schisandrin B, are known for their hepatoprotective properties. These compounds improve mitochondrial glutathione status, stabilize membranes, and inhibit oxidative stress caused by hepatotoxins such as carbon tetrachloride and acetaminophen. Their mitochondrial protection suggests therapeutic potential in toxin-induced organ injury (Addissouky *et al.* 2024).

Licorice, Glycyrrhiza glabra

Licorice roots contain glycyrrhizin and flavonoids that exhibit anti-inflammatory and hepatoprotective properties. Experimental studies report attenuation of dioxin-like toxicity and reduced membrane lipid peroxidation. Licorice extracts also enhance detoxifying enzyme activity, suggesting utility against persistent organic pollutants (Safdarpour *et al.* 2022; Dang *et al.* 2024).

Rosemary, Rosmarinus officinalis

Rosemary polyphenols, notably carnosic acid and rosmarinic acid, possess strong antioxidant activity. Preclinical studies show that rosemary extract mitigates benzo[a]pyrene-induced DNA adduct formation, highlighting its protective effect against PAHs. Its free radical–scavenging properties contribute to membrane stabilization and chemopreventive potential (Mohamed *et al.* 2022).

Grapes/Resveratrol, Vitis vinifera

Resveratrol, a stilbene found in grapes, is widely studied for its ability to modulate xenobiotic metabolism and inflammatory signaling. In pesticide- and dioxin-exposure models, resveratrol reduced oxidative stress, inhibited NF-κB activation, and enhanced mitochondrial biogenesis. Its pleiotropic actions underscore its relevance in toxin-associated carcinogenesis prevention (Prud'homme *et al.* 2022).

Ginger, Zingiber officinale

Gingerols and shogaols in ginger exhibit broad detoxifying potential. Studies indicate protection against organophosphate-induced neurotoxicity, as well as reduced cadmium and arsenic accumulation in tissues. Mechanisms include ROS scavenging, improved phase II enzyme activity, and modulation of inflammatory mediators (Liew *et al.* 2020).

Table 1. Medicinal plants with documented protective effects against environmental toxins.

Medicinal Plant	Major Bioactive	Principal Mechanisms	Targeted Toxins/Models
	Compounds		
Milk thistle, Silybum	Silymarin (silibinin)	Antioxidant, hepatoprotective, Nrf2	Aflatoxin, solvents,
marianum		activation, membrane stabilization	hepatotoxins
Turmeric, Curcuma longa	Curcumin,	Metal chelation, NF-κB inhibition, ROS	Heavy metals, pesticides
	demethoxycurcumin	scavenging	
Green tea, Camellia sinensis	Catechins (EGCG), theaflavins	Antioxidant, CYP modulation, DNA protection	Air pollutants, heavy metals
Broccoli sprouts, <i>Brassica</i> spp.	Sulforaphane, indole-3-carbinol	Potent Nrf2 inducer, phase II detox enzyme activation	Aflatoxin, benzene, dioxin- like toxicants
Garlic, Allium sativum	Allicin, S-allyl cysteine	Glutathione support, chelation, antioxidant	Lead, cadmium, organophosphates
Schisandra, Schisandra chinensis	Schisandrin, lignans	Mitochondrial stabilization, antioxidant, hepatoprotective	Carbon tetrachloride, hepatotoxins
Licorice, Glycyrrhiza glabra	Glycyrrhizin, flavonoids	Membrane stabilization, CYP modulation, anti-inflammatory	Dioxins, solvents, PAHs
Rosemary, Rosmarinus officinalis	Carnosic acid, rosmarinic acid	ROS scavenging, lipid peroxidation inhibition	PAHs, oxidative pollutants
Grapes/Resveratrol, Vitis vinifera	Resveratrol, proanthocyanidins	Antioxidant, sirtuin activation, anti- inflammatory	Pesticides, dioxin models
Ginger, Zingiber officinale	Gingerols, shogaols	Anti-inflammatory, ROS scavenging, mitochondrial protection	Organophosphates, heavy metals
Cilantro, <i>Coriandrum</i> sativum	Linalool, polyphenols	Possible chelation, antioxidant	Heavy metals (controversial)
Chanca piedra, Phyllanthus niruri	Lignans, flavonoids	Antioxidant, hepatoprotection, enzyme modulation	Aflatoxin, hepatotoxins

Cilantro, Coriandrum sativum

Cilantro has been traditionally promoted for its chelating activity against heavy metals, particularly lead and mercury. While some experimental models support increased metal excretion following cilantro administration,

clinical evidence remains inconsistent. Its role in chelation therefore remains debated, though its antioxidant and anti-inflammatory effects provide additional protective value (Mehrandish *et al.* 2019).

Chanca Piedra, Phyllanthus niruri

Traditionally used in hepatobiliary disorders, *Phyllanthus niruri* demonstrates hepatoprotective effects against chemical-induced liver injury. Its polyphenols reduce lipid peroxidation and enhance antioxidant enzyme activity, while also modulating inflammatory pathways. Evidence suggests that it may protect against oxidative stress caused by xenobiotics and support hepatic detoxification (Dey *et al.* 2020).

Translational and clinical evidence

Broccoli sprouts and air pollutants

One of the most compelling examples of translational success comes from clinical trials on broccoli sprout beverages in populations exposed to airborne toxins. A landmark randomized trial in Qidong, China, demonstrated that daily consumption of broccoli sprout extract significantly increased urinary excretion of benzene and acrolein metabolites, reflecting enhanced detoxification capacity via glutathione conjugation. Subsequent follow-up studies confirmed that sulforaphane-rich preparations activate Nrf2-driven cytoprotective pathways in humans, providing strong proof-of-concept for using plant-based interventions against air pollution (Chen *et al.* 2019).

Milk thistle and aflatoxin risk

Silymarin from *Silybum marianum* has been tested in human cohorts with chronic aflatoxin exposure. In clinical studies conducted in high-risk regions of China, supplementation with silymarin reduced biomarkers of aflatoxin-induced DNA damage and liver injury. These findings are consistent with silymarin's hepatoprotective effects observed in preclinical studies and support its use in mitigating risks of hepatocellular carcinoma associated with aflatoxin exposure (Pickova *et al.* 2020).

Garlic and occupational lead exposure

Garlic supplementation has also shown translational promise in human populations. In randomized controlled trials involving workers with chronic occupational lead exposure, garlic extract significantly reduced blood lead levels and improved clinical symptoms compared to placebo. These benefits are attributed to garlic's sulfur compounds, which enhance metal chelation and glutathione synthesis (Kianoush *et al.* 2012).

Other candidates

Clinical evidence is emerging for green tea catechins in protecting DNA integrity in populations exposed to smoking and air pollution. Similarly, trials with resveratrol and curcumin have reported improvements in oxidative stress markers and inflammatory mediators, though their direct evaluation in environmental toxin exposure remains limited (Tanaka *et al.* 2022).

Bioavailability and formulation challenges

A major translational barrier in the clinical application of phytochemicals lies in their pharmacokinetic limitations. Many plant-derived compounds exhibit poor oral bioavailability, undergo rapid metabolism, and display restricted tissue distribution. Curcumin, despite extensive preclinical evidence supporting its therapeutic effects, demonstrates low systemic absorption in humans. To overcome this limitation, a variety of formulations—including nanoparticle encapsulation, liposomal delivery, and adjuvant combinations with piperine—have been explored, with some approaches yielding improved clinical outcomes (Dosoky & Setzer 2018).

Drug interactions and safety considerations

Medicinal plants with detoxification potential may also interact with drug-metabolizing enzymes and transporters, raising important safety concerns. Several phytochemicals, including curcumin, resveratrol, and garlic-derived compounds, have been shown to modulate cytochrome P450 enzymes (CYPs), thereby altering the metabolism of co-administered drugs and increasing the risk of therapeutic failure or toxicity. For example, garlic may potentiate bleeding risk when combined with anticoagulant therapies due to its intrinsic antiplatelet activity. Similarly, green tea catechins can reduce the bioavailability of drugs such as nadolol and simvastatin through interactions with intestinal transporters. Licorice, although hepatoprotective, may interfere with cortisol metabolism and disturb potassium balance, complicating treatment in patients receiving corticosteroids or

diuretics. These observations underscore the importance of carefully evaluating drug-herb interactions before recommending medicinal plants as adjunctive therapies in toxin-exposed populations (Shen & Yin 2021).

Future directions

The growing recognition of medicinal plants as modulators of toxin-induced damage underscores the need for systematic strategies to translate experimental findings into real-world applications. While substantial preclinical evidence demonstrates antioxidant, anti-inflammatory, and detoxification properties of diverse phytochemicals, several critical gaps remain. Addressing these will not only strengthen scientific understanding but also facilitate integration of plant-based interventions into public health frameworks.

Standardization of phytochemical preparations and dosing

One of the foremost challenges in advancing medicinal plants lies in the heterogeneity of preparations used across studies. Extracts often vary in composition depending on plant part, geographical origin, cultivation practices, and processing methods. Moreover, inconsistent dosing regimens hinder meaningful comparisons across clinical trials. Future research must prioritize the standardization of bioactive constituents through validated analytical techniques such as high-performance liquid chromatography (HPLC) and mass spectrometry. Establishing pharmacopeial standards for key phytochemicals (e.g., silymarin, sulforaphane, and curcumin) will enable reproducibility and comparability of results. Dose—response studies are also essential to define therapeutic windows that optimize efficacy while minimizing risks of toxicity or drug—herb interactions.

Omics approaches to elucidate detoxification mechanisms

Modern high-throughput technologies offer unprecedented opportunities to unravel the systems-level effects of medicinal plants. Integration of transcriptomics, proteomics, and metabolomics can provide comprehensive insights into how phytochemicals modulate detoxification pathways, stress responses, and cellular signaling. For instance, RNA sequencing has revealed Nrf2-driven transcriptional reprogramming following sulforaphane treatment, while metabolomics has identified shifts in glutathione conjugation and xenobiotic clearance after garlic supplementation. Multi-omics approaches can also uncover interindividual variability in response to phytochemicals, potentially driven by genetic polymorphisms, microbiome composition, or environmental factors. Such approaches will facilitate precision phytotherapy, enabling targeted interventions tailored to populations with specific toxin exposures or genetic susceptibilities.

Synergistic plant combinations and dietary interventions

Traditional medicine systems have long emphasized polyherbal formulations, where multiple plants act synergistically to enhance therapeutic outcomes. Emerging evidence suggests that combining phytochemicals may provide broader protection against diverse classes of toxins. For example, combining turmeric and green tea catechins enhances antioxidant defenses more robustly than either compound alone, while garlic and cilantro together may improve heavy metal clearance. Similarly, diets rich in cruciferous vegetables, berries, and spices may provide cumulative benefits that surpass isolated supplements. Future studies should systematically evaluate synergistic interactions, both at the molecular level (e.g., complementary activation of detox enzymes) and clinical level (e.g., combined effects on toxin excretion). Designing dietary interventions that incorporate protective plants into culturally acceptable foods may also represent a cost-effective strategy for at-risk populations (Bahmani *et al.* 2014).

Nanotechnology and advanced delivery systems

A major translational bottleneck for many phytochemicals is their poor bioavailability. Advances in delivery technologies provide promising strategies to address this limitation. Nanoparticles and liposomes have been employed to encapsulate compounds such as curcumin, resveratrol, and silymarin, resulting in significant improvements in absorption, stability, and tissue distribution. Similarly, solid lipid nanoparticles and polymer-based carriers enable controlled release, thereby reducing the requirement for high oral doses. More recently, targeted delivery systems, including mitochondria-directed nanoparticles, have emerged as particularly valuable for counteracting toxin-induced mitochondrial dysfunction. Nanotechnology-enabled formulations not only optimize pharmacokinetics but also broaden therapeutic potential by directing phytochemicals to vulnerable organs such as the liver, lungs, and brain. However, clinical validation of these platforms remains essential to translate laboratory advances into tangible public health benefits (Safdarpour *et al.* 2022; Sharifnia *et al.* 2023).

Integration with public health strategies

Finally, the future of plant-based detoxification should progress beyond individual interventions and move toward population-level health strategies. Environmental toxin exposure disproportionately affects vulnerable groups, including industrial workers, agricultural communities, and residents of highly polluted urban regions. Incorporating medicinal plant-based approaches into public health frameworks may involve nutritional programs that encourage the consumption of detoxifying foods such as broccoli, garlic, and green tea. In addition, occupational health initiatives could provide phytochemical supplements to workers in high-risk sectors, such as mining and pesticide application. Community-based interventions in toxin-endemic areas, for example in regions prone to aflatoxin contamination, may rely on affordable and locally sourced plant preparations. At a broader scale, policy-level support is essential for promoting the evidence-based use of medicinal plants as complementary tools in environmental health management. Achieving this goal requires close collaboration among biomedical researchers, nutritionists, policymakers, and public health agencies to ensure that plant-based detoxification strategies are implemented effectively and equitably.

CONCLUSION

In conclusion, medicinal plants represent a multifaceted and sustainable strategy to counteract the adverse health impacts of environmental toxins. They bridge traditional knowledge and modern biomedical science, offering not only therapeutic promise but also preventive potential in vulnerable populations. While challenges remain in standardization, bioavailability, and clinical validation, the convergence of phytochemistry, biotechnology, and public health policy can pave the way for evidence-based integration of medicinal plants into global environmental health strategies. Ultimately, harnessing the detoxification and protective power of medicinal plants may provide a vital tool in reducing the global health burden of environmental toxins in the 21st century.

REFERENCES

- Addissouky, TA, El Sayed, IET, Ali, MMA, Alubiady, MHS & Wang, Y 2024, Schisandra chinensis in liver disease: exploring the mechanisms and therapeutic promise of an ancient Chinese botanical. *Archives of Pharmacology and Therapeutics*, 6(1): 27-33.
- Alrekaby, FFM, Alkhatib, AJ, Abubakar, H & Shokri, S 2023, Evaluation of phytochemical properties and antioxidant activity of methanol extract of *Ziziphus spina-christi*, *Satureja khuzistanica*, and *Salvia rosmarinus* using FT-IR method. *Journal of Biochemicals and Phytomedicine*, 2(2): 47-53.
- Amanpour, P, Eftekhari, Z, Eidi, A & Khodarahmi, P 2024, Ameliorative mechanism of dietary vitamin d and magnesium on newborn's pulmonary toxicity induced by cadmium. *Journal of Trace Elements in Medicine and Biology: Organ of the Society for Minerals and Trace Elements (GMS)*, 84: 127469.
- Bahmani, M, Saki, K, Rafieian-Kopaei, M, Karamati, SA, Eftekhari, Z & Jelodari, M 2014, The most common herbal medicines affecting Sarcomastigophora branches: a review study. *Asian Pacific Journal of Tropical Medicine*, 7: S14-S21, viewed https://www.sciencedirect.com/science/article/pii/S199576451460198X.
- Barzi, NV, Eftekhari, Z, Doroud, D & Eidi, A 2020, DNA methylation changes of apoptotic genes in organogenesis stage of mice embryos by maternal chlorpyrifos induction. *Environmental Toxicology*, 35: 794-803.
- Bejenaru, LE, Biţă, A, Belu, I, Segneanu, A-E, Radu, A, Dumitru, A, Ciocîlteu, MV, Mogoşanu, GD & Bejenaru, C 2024, Resveratrol: A review on the biological activity and applications. *Applied Sciences*, 14(11): 4534.
- van Berkel, SS & van Delft, FL 2018, Enzymatic strategies for (near) clinical development of antibody-drug conjugates. *Drug Discovery Today*. *Technologies*, 30: 3-10.
- Campos, A & Vasconcelos, V 2010, Molecular mechanisms of microcystin toxicity in animal cells. *International Journal Of Molecular Sciences*, 11: 268–287.
- Chen, J-G, Johnson, J, Egner, P, Ng, D, Zhu, J, Wang, J-B, Xue, X-F, Sun, Y, Zhang, Y-H, Lu, L-L, Chen, Y-S, Wu, Y, Zhu, Y-R, Carmella, S, Hecht, S, Jacobson, L, Muñoz, A, Kensler, K, Rule, A, Fahey, J, Kensler, T & Groopman, J 2019, Dose-dependent detoxication of the airborne pollutant benzene in a randomized trial of broccoli sprout beverage in Qidong, China. *The American Journal of Clinical Nutrition*, 110: 675-684.
- Chu, Y-H, Kao, S-W, Tantoh, DM, Ko, P-C, Lan, S-J & Liaw, Y-P 2019, Association between fine particulate matter and oral cancer among Taiwanese men. *Journal of investigative Medicine: The Official Publication of the American Federation for Clinical Research*, 67: 34-38.
- Dang, L, Jin, Y, Yuan, Y, Shao, R & Wang, Y 2024, The king of Chinese medicine—Glycyrrhiza glabra

- (Licorice): All-round inquiry in its chemical composition, pharmacodynamics, traditional and medicinal value. *Acupuncture and Herbal Medicine*, LWW, pp. 10–1097.
- Dey, D, Chaskar, S, Bhatt, N & Chitre, D 2020, Hepatoprotective activity of BV-7310, a proprietary herbal formulation of *Phyllanthus niruri*, *Tephrosia purpurea*, *Boerhavia diffusa*, and *Andrographis paniculat*a, in alcohol-induced HepG2 cells and alcohol plus a haloalkane, CCl4, induced liver damage in rats. *Evidence-Based Complementary and Alternative Medicine*, *Wiley Online Library*, 2020: 6428906.
- Dosoky, NS & Setzer, WN 2018, Chemical composition and biological activities of essential oils of curcuma species. *Nutrients*, vol. 10, no. 9, Switzerland.
- Eftekhari, Z 2020, Garlic: A brief overview of its interaction with chemical drugs. *Plant Biotechnology Persa*, 2 (2): 31-32.
- Gheibi, P, Eftekhari, Z, Doroud, D & Parivar, K 2020, Chlorpyrifos effects on integrin alpha v and beta 3 in implantation window phase. *Environmental Science and Pollution Research*, 27: 29530–29538.
- Guarnotta, V, Amodei, R, Frasca, F, Aversa, A & Giordano, C 2022, Impact of chemical endocrine disruptors and hormone modulators on the endocrine system. *International Journal of Molecular Sciences*, 23 (10), Switzerland.
- Haider, AA & Hussein, HZ 2022, Efficiency of biologically and locally manufactured silver nanoparticles from Aspergillus niger in preventing Aspergillus flavus to produce aflatoxin B1 on the stored maize grains. *Caspian Journal of Environmental Sciences*, 20: 765-773, viewed https://cjes.guilan.ac.ir/article 5760.html>.
- Hikisz, P & Jacenik, D 2023, The tobacco smoke component, acrolein, as a major culprit in lung diseases and respiratory cancers: molecular mechanisms of acrolein cytotoxic activity. *Cells*, 12: 879.
- Islamova, ST, Nazarova, MA, Burkhanov, AU, Khamraev, F, Isagova, BU, Xamdamov, S, Nazarova, NS, Zubaydov, FF, Khursandova, DS & Badriddinov, OU 2025, Antibacterial and antioxidant effects of Punicalagin extracts from Punica granatum peels. *Caspian Journal of Environmental Sciences*, 23: 579-586, viewed https://cjes.guilan.ac.ir/ article_8570.html>.
- Jeon, HH, Yang, CY, Shin, MK, Wang, J, Patel, JH, Chung, CH & Graves, DT 2021, Osteoblast lineage cells and periodontal ligament fibroblasts regulate orthodontic tooth movement that is dependent on Nuclear Factor-kappa B (NF-kB) activation. *The Angle orthodontist*, 91: 664-671.
- Jumagaliyeva, A, Tungushbayeva, Z, Raushan, D, Tashenova, G, Baigutty, A, Tatarinova, G & Batyrova, K 2025, Gonadoprotective potential of *Taraxacum officinale* on testicular tissue damage induced by cadmium chloride. *Caspian Journal of Environmental Sciences*, 23: 595-603, viewed https://cjes.guilan.ac.ir/article 8910.html>.
- Kandezi, N, Mohammadi, M, Ghaffari, M, Gholami, M, Motaghinejad, M & Safari, S 2020, Novel insight to neuroprotective potential of curcumin: A mechanistic review of possible involvement of mitochondrial biogenesis and PI3/Akt/ GSK3 or PI3/Akt/CREB/BDNF signaling pathways TT -ijmcmed, 9: 1-32, viewed http://ijmcmed.org/article-1-1245-en.html.
- Karaman, M, Firinci, F, Cilaker, S, Uysal, P, Tugyan, K, Yilmaz, O, Uzuner, N & Karaman, O 2012, Anti-inflammatory effects of curcumin in a murine model of chronic asthma. *Allergologia et Immunopathologia*, 40: 210-214, viewed https://www.sciencedirect.com/science/article/pii/S0301054611002424.
- Khoi, C-S, Chen, J-H, Lin, T-Y, Chiang, C-K & Hung, K-Y 2021, Ochratoxin A-induced nephrotoxicity: up-to-date evidence. *International Journal of Molecular Sciences*, 22 (20), Switzerland.
- Kianoush, S, Balali-Mood, M, Mousavi, SR, Moradi, V, Sadeghi, M, Dadpour, B, Rajabi, O & Shakeri, MT 2012, Comparison of therapeutic effects of garlic and d-Penicillamine in patients with chronic occupational lead poisoning. *Basic & Clinical Pharmacology & Toxicology*, 110 (5): 476-481.
- Kumar, R, Kumar, A, Bhardwaj, S, Sikarwar, M, Sriwastaw, S, Sharma, G & Gupta, M 2025, Nanotoxicity unveiled: Evaluating exposure risks and assessing the impact of nanoparticles on human health. *Journal of Trace Elements and Minerals*, 13: 100252, viewed https://www.sciencedirect.com/science/article/pii/S2773050625000436.
- Laurindo, LF, de Maio, MC, Minniti, G, de Góes Corrêa, N, Barbalho, SM, Quesada, K, Guiguer, EL, Sloan, KP, Detregiachi, CRP, Araújo, AC & de Alvares Goulart, R 2023, Effects of medicinal plants and phytochemicals in Nrf2 pathways during inflammatory bowel diseases and related colorectal cancer: A comprehensive review. *Metabolites*, 13 (2), Switzerland.

- Li, L, Ma, P, Nirasawa, S & Liu, H 2024, Formation, immunomodulatory activities, and enhancement of glucosinolates and sulforaphane in broccoli sprouts: A review for maximizing the health benefits to human. *Critical Reviews in Food Science and Nutrition*, 64: 7118-7148.
- Liew, KY, Hafiz, MF, Chong, YJ, Harith, HH, Israf, DA & Tham, CL 2020, A review of Malaysian herbal plants and their active constituents with potential therapeutic applications in sepsis. *Evidence-Based Complementary and Alternative Medicine*, 2020: 8257817, viewed https://doi.org/10.1155/2020/8257817>.
- Lin, S, Wang, X, Tang, RW-L, Lee, HC, Chan, HH, Choi, SSA, Dong, TT-X, Leung, KW, Webb, SE, Miller, AL & Tsim, KW-K 2022, The extracts of *Polygonum cuspidatum* root and rhizome block the entry of SARS-CoV-2 wild-type and omicron pseudotyped viruses via inhibition of the S-protein and 3CL protease. *Molecules (Basel, Switzerland)*, 27 (12), Switzerland.
- Mehrandish, R, Rahimian, A & Shahriary, A 2019, Heavy metals detoxification: A review of herbal compounds for chelation therapy in heavy metals toxicity. *Journal of Herbmed Pharmacology*, 8: 69-77.
- Miri, ZS, Bagheri, H, Amani, A & Karami, H 2025, Anti-tumor effects of curcumin and ABT-737 in combination therapy for glioblastoma in vivo. *International Journal of Molecular and Cellular Medicine*, 14 (1), viewed http://ijmcmed.org/article-1-2480-en.html>.
- Mohamed, ME, Younis, NS, El-Beltagi, HS & Mohafez, OM 2022, The synergistic hepatoprotective activity of rosemary essential oil and curcumin: The role of the MEK/ERK pathway. *Molecules*, 27 (24): 8910.
- Mohammadi, Z, Pishkar, L, Eftekhari, Z, Barzin, G & Babaeekhou, L 2024, Evaluation of the antimicrobial and cytotoxic activity of cultivated *Valeriana officinalis*. *Plant Science Today*, 11: 145-155.
- Nandekar, PP & Sangamwar, AT 2012, Cytochrome P450 1A1-mediated anticancer drug discovery: In silico findings. *Expert Opinion on Drug Discovery*, 7 (9): 771-789.
- Noshadirad, E, Parivar, K, Motesaddi Zarandi, S, Mortazavi, P & Gorbani Yekta, B 2023, Gaseous pollutants and PM_{2.5} co-exposure induces BCL2/Bax apoptosis pathway activation in rat Sertoli cells: Implication of GATA4 and GATA6 interaction. *Caspian Journal of Environmental Sciences*, pp. 1–7, viewed https://cjes.guilan.ac.ir/article_7102.html>.
- Pickova, D, Ostry, V, Toman, J & Malir, F 2020, Presence of mycotoxins in milk thistle (Silybum marianum) food supplements: A review. *Toxins*, 12 (12): 782.
- Plaman, BA, Chan, WC & Bishop, AC 2019, Chemical activation of divergent protein tyrosine phosphatase domains with cyanine-based biarsenicals. *Scientific Reports*, 9: 16148.
- Prud'homme, GJ, Kurt, M & Wang, Q 2022, Pathobiology of the klotho antiaging protein and therapeutic considerations. *Frontiers in Aging*, 3: 931331.
- Rahimzadeh, Mehrdad Rafati, Rahimzadeh, Mehravar Rafati, Kazemi, S & Moghadamnia, A 2017, Cadmium toxicity and treatment: An update. *Caspian Journal of Internal Medicine*, 8: 135.
- Ramezanifar, S, Beyrami, S, Mehrifar, Y, Ramezanifar, E, Soltanpour, Z, Namdari, M & Gharari, N 2023, Occupational exposure to physical and chemical risk factors: A systematic review of reproductive pathophysiological effects in women and men. *Safety and Health at Work*, 14: 17-30, viewed https://www.sciencedirect.com/science/article/pii/S2093791122001457.
- Safdarpour, S, Eftekhari, Z, Eidi, A & Doroud, D 2022, Encapsulated saponin by ferritin nanoparticles attenuates the murine pneumococcal pneumonia. *Microbial Pathogenesis*, 172: 105731.
- Shakour, N, Cabezas, R, Santos, JG, Barreto, GE, Jamialahmadi, T, Hadizadeh, F & Sahebkar, A 2021, Curcumin can bind and interact with CRP: an in silico study. *Pharmacological Properties of Plant-Derived Natural Products and Implications for Human Health*, pp. 91–100.
- Sharifnia, M, Eftekhari, Z & Mortazavi, P 2024, Niosomal hesperidin attenuates the M1/M2-macrophage polarization-based hepatotoxicity followed chlorpyrifos-induced toxicities in mice. *Pesticide Biochemistry and Physiology*, 198: 105724.
- Sharifnia, M, Eftekhari, Z & Mortazavi, P 2023, Niosomal hesperidin attenuates the M1/M2-macrophage polarization-based hepatotoxicity followed chlorpyrifos-induced toxicities in mice. *Pesticide Biochemistry and Physiology*, p. 105724.
- Shen, X & Yin, F 2021, The mechanisms and clinical application of traditional Chinese medicine Lianhua-Qingwen capsule. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, 142: 111998.
- Sun, J, Yu, J, Niu, Xinyi, Zhang, X, Zhou, L, Liu, X, Zhang, B, He, K, Niu, Xiaofeng & Ho, KF 2023, Solid fuel

- derived PM2. 5 induced oxidative stress and according cytotoxicity in A549 cells: The evidence and potential neutralization by green tea. *Environment International*, 171: 107674.
- Tanaka, KI, Nakaguchi, S, Shiota, S, Nakada, Y, Oyama, K, Sakakibara, O, Shimoda, M, Sugimoto, A, Ichitani, M & Takihara, T 2022, Preventive effect of epigallocatechin gallate, the main component of green tea, on acute lung injury caused by air pollutants. *Biomolecules*, 12 (9): 1196.
- Thangavel, P, Park, D & Lee, Y-C 2022, Recent insights into particulate matter (PM_{2.5})-mediated toxicity in humans: An overview. *International Journal of Environmental Research and Public Health*, 19 (12), Switzerland.
- Vahabi Barzi, N, Eftekhari, Z, Doroud, D & Eidi, A 2022, Maternal exposure during organogenesis to chlorpyrifos insecticide induce apoptosis process. *The Journal of Maternal-Fetal & Neonatal Medicine: The Official Journal of The European Association of Perinatal Medicine, The Federation of Asia and Oceania Perinatal Societies, The International Society of Perinatal Obstetricians*, 35 (20): 3845-3852.
- Valková, V, Ďúranová, H, Bilčíková, J & Habán, M 2020, Milk thistle (*Silybum marianum*): A valuable medicinal plant with several therapeutic purposes. *The Journal of Microbiology, Biotechnology and Food Sciences*, 9 (4): 836.
- Widoyo, H, Mohammed, ZY, Ramírez-Coronel, AA, Iswanto, AH, Thattarauthodiyil, U, S Alkhayyat, A, Karimi, M, Bahmani, M & Eftekhari, Z 2022, Herbal therapy in Covid-19: A systematic review of medicinal plants effective against Covid-19. *Caspian Journal of Environmental Sciences*, pp. 1-10.
- Yu, J, Hennessy, DA, Tack, J & Wu, F 2022, Climate change will increase aflatoxin presence in US Corn. *Environmental Research Letters*, vol. 17, no. 5.
- Zeng, Y, Luo, Y, Wang, L, Zhang, K, Peng, J & Fan, G 2023, Therapeutic Effect of Curcumin on Metabolic Diseases: Evidence from Clinical Studies. *International Journal of Molecular Sciences*, 24 (4), Switzerland.

Addissouky, TA, El Sayed, IET, Ali, MMA, Alubiady, MHS & Wang, Y 2024, Schisandra chinensis in liver disease: exploring the mechanisms and therapeutic promise of an ancient Chinese botanical. *Archives of Pharmacology and Therapeutics*, 6(1): 27-33.

Alrekaby, FFM, Alkhatib, AJ, Abubakar, H & Shokri, S 2023, Evaluation of phytochemical properties and antioxidant activity of methanol extract of *Ziziphus spina-christi, Satureja khuzistanica*, and *Salvia rosmarinus* using FT-IR method. *Journal of Biochemicals and Phytomedicine*, 2(2): 47-53.

Amanpour, P, Eftekhari, Z, Eidi, A & Khodarahmi, P 2024, Ameliorative mechanism of dietary vitamin d and magnesium on newborn's pulmonary toxicity induced by cadmium. *Journal of Trace Elements in Medicine and Biology: Organ of the Society for Minerals and Trace Elements (GMS)*, 84: 127469.

Bahmani, M, Saki, K, Rafieian-Kopaei, M, Karamati, SA, Eftekhari, Z & Jelodari, M 2014, The most common herbal medicines affecting Sarcomastigophora branches: a review study. *Asian Pacific Journal of Tropical Medicine*, 7: S14-S21, viewed https://www.sciencedirect.com/science/article/pii/S199576451460198X.

Barzi, NV, Eftekhari, Z, Doroud, D & Eidi, A 2020, DNA methylation changes of apoptotic genes in organogenesis stage of mice embryos by maternal chlorpyrifos induction. *Environmental Toxicology*, 35: 794-803.

Bejenaru, LE, Biţă, A, Belu, I, Segneanu, A-E, Radu, A, Dumitru, A, Ciocîlteu, MV, Mogoşanu, GD & Bejenaru, C 2024, Resveratrol: A review on the biological activity and applications. *Applied Sciences*, 14(11): 4534.

van Berkel, SS & van Delft, FL 2018, Enzymatic strategies for (near) clinical development of antibody-drug conjugates. *Drug Discovery Today*. *Technologies*, 30: 3-10.

Campos, A & Vasconcelos, V 2010, Molecular mechanisms of microcystin toxicity in animal cells. *International Journal of Molecular Sciences*, 11: 268–287.

Chen, J-G, Johnson, J, Egner, P, Ng, D, Zhu, J, Wang, J-B, Xue, X-F, Sun, Y, Zhang, Y-H, Lu, L-L, Chen, Y-S, Wu, Y, Zhu, Y-R, Carmella, S, Hecht, S, Jacobson, L, Muñoz, A, Kensler, K, Rule, A, Fahey, J, Kensler, T & Groopman, J 2019, Dose-dependent detoxication of the airborne pollutant benzene in a randomized trial of broccoli sprout beverage in Qidong, China. *The American Journal of Clinical Nutrition*, 110: 675-684.

Chu, Y-H, Kao, S-W, Tantoh, DM, Ko, P-C, Lan, S-J & Liaw, Y-P 2019, Association between fine particulate matter and oral cancer among Taiwanese men. *Journal of investigative Medicine : The Official Publication of the American Federation for Clinical Research*, 67: 34-38.

Dang, L, Jin, Y, Yuan, Y, Shao, R & Wang, Y 2024, The king of Chinese medicine——*Glycyrrhiza glabra* (Licorice): All-round inquiry in its chemical composition, pharmacodynamics, traditional and medicinal value. *Acupuncture and Herbal Medicine*, LWW, pp. 10–1097.

Dey, D, Chaskar, S, Bhatt, N & Chitre, D 2020, Hepatoprotective activity of BV-7310, a proprietary herbal formulation of *Phyllanthus niruri*, *Tephrosia purpurea*, *Boerhavia diffusa*, and *Andrographis paniculata*, in alcohol-induced HepG2 cells and alcohol plus a haloalkane, CCl4, induced liver damage in rats. *Evidence-Based Complementary and Alternative Medicine*, *Wiley Online Library*, 2020: 6428906.

Dosoky, NS & Setzer, WN 2018, Chemical composition and biological activities of essential oils of curcuma species. *Nutrients*, vol. 10, no. 9, Switzerland.

Eftekhari, Z 2020, Garlic: A brief overview of its interaction with chemical drugs. *Plant Biotechnology Persa*, 2 (2): 31-32.

Gheibi, P, Eftekhari, Z, Doroud, D & Parivar, K 2020, Chlorpyrifos effects on integrin alpha v and beta 3 in implantation window phase. *Environmental Science and Pollution Research*, 27: 29530–29538.

- Guarnotta, V, Amodei, R, Frasca, F, Aversa, A & Giordano, C 2022, Impact of chemical endocrine disruptors and hormone modulators on the endocrine system. *International Journal of Molecular Sciences*, 23 (10), Switzerland. Haider, AA & Hussein, HZ 2022, Efficiency of biologically and locally manufactured silver nanoparticles from Aspergillus niger in preventing Aspergillus flavus to produce aflatoxin B1 on the stored maize grains. *Caspian Journal of Environmental Sciences*, 20: 765-773, viewed https://cjes.guilan.ac.ir/article 5760.html>.
- Hikisz, P & Jacenik, D 2023, The tobacco smoke component, acrolein, as a major culprit in lung diseases and respiratory cancers: molecular mechanisms of acrolein cytotoxic activity. *Cells*, 12: 879.
- Islamova, ST, Nazarova, MA, Burkhanov, AU, Khamraev, F, Isagova, BU, Xamdamov, S, Nazarova, NS, Zubaydov, FF, Khursandova, DS & Badriddinov, OU 2025, Antibacterial and antioxidant effects of Punicalagin extracts from Punica granatum peels. *Caspian Journal of Environmental Sciences*, 23: 579-586, viewed https://cjes.guilan.ac.ir/article_8570.html>.
- Jeon, HH, Yang, C-Y, Shin, MK, Wang, J, Patel, JH, Chung, C-H & Graves, DT 2021, Osteoblast lineage cells and periodontal ligament fibroblasts regulate orthodontic tooth movement that is dependent on Nuclear Factor-kappa B (NF-kB) activation. *The Angle orthodontist*, 91: 664-671.
- Jumagaliyeva, A, Tungushbayeva, Z, Raushan, D, Tashenova, G, Baigutty, A, Tatarinova, G & Batyrova, K 2025, Gonadoprotective potential of *Taraxacum officinale* on testicular tissue damage induced by cadmium chloride. *Caspian Journal of Environmental Sciences*, 23: 595-603, viewed https://cjes.guilan.ac.ir/article_8910.html>.
- Kandezi, N, Mohammadi, M, Ghaffari, M, Gholami, M, Motaghinejad, M & Safari, S 2020, Novel insight to neuroprotective potential of curcumin: A mechanistic review of possible involvement of mitochondrial biogenesis and PI3/Akt/ GSK3 or PI3/Akt/CREB/BDNF signaling pathways TT *-ijmcmed*, 9: 1-32, viewed http://ijmcmed.org/article-1-1245-en.html>.
- Karaman, M, Firinci, F, Cilaker, S, Uysal, P, Tugyan, K, Yilmaz, O, Uzuner, N & Karaman, O 2012, Anti-inflammatory effects of curcumin in a murine model of chronic asthma. *Allergologia et Immunopathologia*, 40:. 210-214, viewed https://www.sciencedirect.com/science/article/pii/S0301054611002424.
- Khoi, C-S, Chen, J-H, Lin, T-Y, Chiang, C-K & Hung, K-Y 2021, Ochratoxin A-induced nephrotoxicity: up-to-date evidence. *International Journal of Molecular Sciences*, 22 (20), Switzerland.
- Kianoush, S, Balali-Mood, M, Mousavi, SR, Moradi, V, Sadeghi, M, Dadpour, B, Rajabi, O & Shakeri, MT 2012, Comparison of therapeutic effects of garlic and d-Penicillamine in patients with chronic occupational lead poisoning. *Basic & Clinical Pharmacology & Toxicology*, 110 (5): 476-481.
- Kumar, R, Kumar, A, Bhardwaj, S, Sikarwar, M, Sriwastaw, S, Sharma, G & Gupta, M 2025, Nanotoxicity unveiled: Evaluating exposure risks and assessing the impact of nanoparticles on human health. *Journal of Trace Elements and Minerals*, 13: 100252, viewed https://www.sciencedirect.com/science/article/pii/S2773050625000436.
- Laurindo, LF, de Maio, MC, Minniti, G, de Góes Corrêa, N, Barbalho, SM, Quesada, K, Guiguer, EL, Sloan, KP, Detregiachi, CRP, Araújo, AC & de Alvares Goulart, R 2023, Effects of medicinal plants and phytochemicals in Nrf2 pathways during inflammatory bowel diseases and related colorectal cancer: A comprehensive review. *Metabolites*, 13 (2), Switzerland.
- Li, L, Ma, P, Nirasawa, S & Liu, H 2024, Formation, immunomodulatory activities, and enhancement of glucosinolates and sulforaphane in broccoli sprouts: A review for maximizing the health benefits to human. *Critical Reviews in Food Science and Nutrition*, 64: 7118-7148.
- Liew, KY, Hafiz, MF, Chong, YJ, Harith, HH, Israf, DA & Tham, CL 2020, A review of Malaysian herbal plants and their active constituents with potential therapeutic applications in sepsis. *Evidence-Based Complementary and Alternative Medicine*, 2020: 8257817, viewed https://doi.org/10.1155/2020/8257817.
- Lin, S, Wang, X, Tang, RW-L, Lee, HC, Chan, HH, Choi, SSA, Dong, TT-X, Leung, KW, Webb, SE, Miller, AL & Tsim, KW-K 2022, The extracts of *Polygonum cuspidatum* root and rhizome block the entry of SARS-CoV-2 wild-type and omicron pseudotyped viruses via inhibition of the S-protein and 3CL protease. *Molecules (Basel, Switzerland)*, 27 (12), Switzerland.
- Mehrandish, R, Rahimian, A & Shahriary, A 2019, Heavy metals detoxification: A review of herbal compounds for chelation therapy in heavy metals toxicity. *Journal of Herbmed Pharmacology*, 8: 69-77.
- Miri, ZS, Bagheri, H, Amani, A & Karami, H 2025, Anti-tumor effects of curcumin and ABT-737 in combination therapy for glioblastoma in vivo. *International Journal of Molecular and Cellular Medicine*, 14 (1), viewed http://ijmcmed.org/article-1-2480-en.html>.

Mohamed, ME, Younis, NS, El-Beltagi, HS & Mohafez, OM 2022, The synergistic hepatoprotective activity of rosemary essential oil and curcumin: The role of the MEK/ERK pathway. *Molecules*, 27 (24): 8910.

Mohammadi, Z, Pishkar, L, Eftekhari, Z, Barzin, G & Babaeekhou, L 2024, Evaluation of the antimicrobial and cytotoxic activity of cultivated *Valeriana officinalis*. *Plant Science Today*, 11: 145-155.

Nandekar, PP & Sangamwar, AT 2012, Cytochrome P450 1A1-mediated anticancer drug discovery: In silico findings. *Expert Opinion on Drug Discovery*, 7 (9): 771-789.

Noshadirad, E, Parivar, K, Motesaddi Zarandi, S, Mortazavi, P & Gorbani Yekta, B 2023, Gaseous pollutants and PM_{2.5} co-exposure induces BCL2/Bax apoptosis pathway activation in rat Sertoli cells: Implication of GATA4 and GATA6 interaction. *Caspian Journal of Environmental Sciences*, pp. 1–7, viewed https://cjes.guilan.ac.ir/article-7102.html.

Pickova, D, Ostry, V, Toman, J & Malir, F 2020, Presence of mycotoxins in milk thistle (Silybum marianum) food supplements: A review. *Toxins*, 12 (12): 782.

Plaman, BA, Chan, WC & Bishop, AC 2019, Chemical activation of divergent protein tyrosine phosphatase domains with cyanine-based biarsenicals. *Scientific Reports*, 9: 16148.

Prud'homme, GJ, Kurt, M & Wang, Q 2022, Pathobiology of the klotho antiaging protein and therapeutic considerations. *Frontiers in Aging*, 3: 931331.

Rahimzadeh, Mehrdad Rafati, Rahimzadeh, Mehravar Rafati, Kazemi, S & Moghadamnia, A 2017, Cadmium toxicity and treatment: An update. *Caspian Journal of Internal Medicine*, 8: 135.

Ramezanifar, S, Beyrami, S, Mehrifar, Y, Ramezanifar, E, Soltanpour, Z, Namdari, M & Gharari, N 2023, Occupational exposure to physical and chemical risk factors: A systematic review of reproductive pathophysiological effects in women and men. *Safety and Health at Work*, 14: 17-30, viewed https://www.sciencedirect.com/science/article/pii/S2093791122001457.

Safdarpour, S, Eftekhari, Z, Eidi, A & Doroud, D 2022, Encapsulated saponin by ferritin nanoparticles attenuates the murine pneumococcal pneumonia. *Microbial Pathogenesis*, 172: 105731.

Shakour, N, Cabezas, R, Santos, JG, Barreto, GE, Jamialahmadi, T, Hadizadeh, F & Sahebkar, A 2021, Curcumin can bind and interact with CRP: an in silico study. *Pharmacological Properties of Plant-Derived Natural Products and Implications for Human Health*, pp. 91–100.

Sharifnia, M, Eftekhari, Z & Mortazavi, P 2024, Niosomal hesperidin attenuates the M1/M2-macrophage polarization-based hepatotoxicity followed chlorpyrifos-induced toxicities in mice. *Pesticide Biochemistry and Physiology*, 198: 105724.

Sharifnia, M, Eftekhari, Z & Mortazavi, P 2023, Niosomal hesperidin attenuates the M1/M2-macrophage polarization-based hepatotoxicity followed chlorpyrifos-induced toxicities in mice. *Pesticide Biochemistry and Physiology*, p. 105724.

Shen, X & Yin, F 2021, The mechanisms and clinical application of traditional Chinese medicine Lianhua-Qingwen capsule. *Biomedicine & Pharmacotherapy = Biomedecine & Pharmacotherapie*, 142: 111998.

Sun, J, Yu, J, Niu, Xinyi, Zhang, X, Zhou, L, Liu, X, Zhang, B, He, K, Niu, Xiaofeng & Ho, K-F 2023, Solid fuel derived PM2. 5 induced oxidative stress and according cytotoxicity in A549 cells: The evidence and potential neutralization by green tea. *Environment International*, 171: 107674.

Tanaka, K-I, Nakaguchi, S, Shiota, S, Nakada, Y, Oyama, K, Sakakibara, O, Shimoda, M, Sugimoto, A, Ichitani, M & Takihara, T 2022, Preventive effect of epigallocatechin gallate, the main component of green tea, on acute lung injury caused by air pollutants. *Biomolecules*, 12 (9): 1196.

Thangavel, P, Park, D & Lee, Y-C 2022, Recent insights into particulate matter (PM_{2.5})-mediated toxicity in humans: An overview. *International Journal of Environmental Research and Public Health*, 19 (12), Switzerland. Vahabi Barzi, N, Eftekhari, Z, Doroud, D & Eidi, A 2022, Maternal exposure during organogenesis to chlorpyrifos insecticide induce apoptosis process. *The Journal of Maternal-Fetal & Neonatal Medicine : The Official Journal of The European Association of Perinatal Medicine, The Federation of Asia and Oceania Perinatal Societies, The International Society of Perinatal Obstetricians*, 35 (20): 3845-3852.

Valková, V, Ďúranová, H, Bilčíková, J & Habán, M 2020, Milk thistle (*Silybum marianum*): A valuable medicinal plant with several therapeutic purposes. *The Journal of Microbiology, Biotechnology and Food Sciences*, 9 (4): 836.

Widoyo, H, Mohammed, ZY, Ramírez-Coronel, AA, Iswanto, AH, Thattarauthodiyil, U, S Alkhayyat, A, Karimi, M, Bahmani, M & Eftekhari, Z 2022, Herbal therapy in Covid-19: A systematic review of medicinal plants

effective against Covid-19. Caspian Journal of Environmental Sciences, pp. 1-10.

Yu, J, Hennessy, DA, Tack, J & Wu, F 2022, Climate change will increase aflatoxin presence in US Corn. *Environmental Research Letters*, vol. 17, no. 5.

Zeng, Y, Luo, Y, Wang, L, Zhang, K, Peng, J & Fan, G 2023, Therapeutic Effect of Curcumin on Metabolic Diseases: Evidence from Clinical Studies. *International Journal of Molecular Sciences*, 24 (4), Switzerland.