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Role of ameliorating agents in mitigating pesticide-induced toxicity in albino rats as a mammalian model: A review

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Abstract
Pesticides like organophosphates, carbamates, pyrethroids, and neonicotinoids have a significant impact on the liver, kidney, brain, lungs causing organ degeneration, hormonal disturbances, reproductive abnormalities, inflammation, oxidative stress, and even potential organ dysfunction in albino rats which are commonly used as model organisms due to their physiological similarities to humans. The ameliorating agents like vitamin C, vitamin E, curcumin, green tea, ginger and garlic have the potential to counteract damage caused by pesticides by neutralizing reactive oxygen species and mitigating oxidative stress in rats. Overall, this comprehensive review discusses the importance of studying the role of ameliorating agents in alleviating pesticide-induced toxicity in albino rats, thus exploring the potential of these agents for mitigating the harmful effects of pesticides on human health and the environment.

Keywords: Amelioration, pesticides, antioxidants, toxicity, albino rats

Introduction
Pesticides are chemical substances used to control, prevent, or kill pests, including insects, rodents, fungi, and weeds. They are widely used in agriculture, public health, and households to protect crops, control diseases, and prevent the spread of vector-borne illnesses. However, pesticides can have negative effects on human health [1]. Exposure to pesticides can cause a range of health problems, from skin irritation to cancer and other chronic diseases. Pesticides also affect soil, water, and air, leading to ecological imbalances and long-term environmental damage [2]. Therefore, the use of pesticides is regulated by national and international organizations such as the Environmental Protection Agency (EPA) and the World Health Organization (WHO), which set limits on the amount of pesticide residue allowed in food and drinking water.
There are many different types of pesticides that are available, and they can be categorized based on their chemical composition and their mode of action.

Insecticides: Insecticides are used to kill or control insects. They can be divided into several classes, including organochlorines, organophosphates, carbamates, pyrethroids and neonicotinoids. Organochlorines, such as DDT, were once widely used but have since been banned in many countries due to their persistent and harmful effects on the environment. Organophosphates and carbamates are still commonly used, but they can be toxic to humans and other animals if not used properly. Pyrethroids and neonicotinoids are newer insecticides that are generally considered to be less harmful to humans and the environment [3].

Herbicides: Herbicides are used to control or eliminate weeds. They can be categorized as selective or non-selective, depending on whether they target specific types of plants or kill all plants. Some common types of herbicides include glyphosate, 2,4-D, and dicamba [4].

Fungicides: Fungicides are used to control or eliminate fungi that can damage crops or cause disease in humans or animals. They can be divided into several classes, including azoles, strobilurins, and benzimidazoles [5]. Agricultural fungicides, such as chlorothalonil, propiconazole, and mancozeb, are vital for safeguarding crops against fungal diseases. Chlorothalonil offers broad-spectrum protection against various fungal pathogens, propiconazole provides systemic defense via plant absorption, and mancozeb prevents spore germination. These fungicides are crucial in maintaining healthy crops and securing agricultural productivity [5].

Rodenticides: Rodenticides are used to control or eliminate rodents such as rats and mice. They can be divided into several classes, including anticoagulants, acute toxicants, and fumigants. Anticoagulants work by preventing blood clotting, while acute toxicants are fast-acting poisons that cause death within hours. Fumigants are gases that are used to kill rodents in enclosed spaces [6].

Nematicides: Nematicides are used to control or eliminate nematodes, which are microscopic worms that can damage crops. Some examples of nematicides include fenamiphos, abamectin, oxamyl, ethoprophos, carbofuran, fosthiazate, emamectin benzoate [7].

It is important to use pesticides responsibly and follow all safety precautions when handling them. The number of registered pesticides in India is reported to be 293. Notably, India employs approximately 104 pesticides that are banned in one or more countries across the globe. Concerning the global usage of pesticides, India ranks 12th across globe regarding pesticide usage. The pesticide usage pattern in India differs from the global trend. In India, herbicides, fungicides, and insecticides are the primary pesticide categories employed, with insecticides being the most extensively used. Conversely, on a global scale, herbicides have the highest usage, followed by fungicides and bactericides, rodenticides, and insecticides. India holds the position of the fourth largest producer of insecticides and pesticides worldwide. However, it is important to note that in 2017, India's pesticide usage was relatively lower compared to countries such as Saint Lucia and Hong Kong [8].

Use of Albino rats as a mammalian model for studying pesticide toxicity

Albino rats have long been recognized as a valuable mammalian model for studying pesticide toxicity due to several important factors. Firstly, their physiological and anatomical similarities to humans make them a suitable model for extrapolating toxicological findings to human health. Albino rats share comparable organ systems, metabolic pathways, and enzymatic activities with humans, allowing for meaningful investigation of pesticide effects on various organs and systems. Moreover, albino rats are widely available, relatively easy to handle, and have a short reproductive cycle, enabling researchers to conduct studies with reasonable timeframes and sample sizes. Their adaptability to laboratory conditions and well-documented genetic background also contribute to the reproducibility and reliability of research outcomes [9]. Moreover, humans and albino rats, despite being distinct species, share a significant degree of genetic similarity due to their shared ancestry within the animal kingdom. Genomic analyses have revealed that humans and albino rats share approximately 85-90% of their genes. This similarity is attributed to the conservation of key genetic elements that govern fundamental biological processes across species. While there are differences in specific genes and genetic sequences, the common genetic foundation underscores the evolutionary connections between these organisms. Studying these shared genetic aspects not only enhances our understanding of both species but also aids in biomedical research, as insights gained from studying albino rat genetics can provide valuable insights into human biology and health [10].

Albino rats also exhibit a high degree of sensitivity to pesticide exposure, enabling detection of subtle toxicological effects that may not be readily observable in other animal models. Their susceptibility to pesticide-induced toxicity allows for the evaluation of dose-response relationships and the identification of potential adverse effects at lower pesticide concentrations [10]. Furthermore, the use of albino rats in pesticide toxicity studies helps to elucidate underlying mechanisms of toxicity. Their well-characterized biology and genetic background facilitate investigations into the specific pathways and molecular interactions involved in pesticide-induced harm, providing valuable insights into the toxicological processes at play [11]. Overall, the importance of albino rats as a mammalian model for studying pesticide toxicity lies in their physiological resemblance to humans, practicality in experimental settings, sensitivity to pesticide exposure, and their potential to uncover mechanistic insights. By utilizing albino rats as a model organism, researchers may be able to better understand the adverse effects of pesticides, develop mitigation strategies, and ultimately promote human and environmental health. The need for pesticide amelioration arises from the adverse effects of pesticide use on the environment and human health. Pesticides can contaminate soil, water bodies, and air, leading to ecological imbalances, reduced biodiversity, and harm to non-target organisms. Pesticide residues in food can also pose health risks to consumers, such as cancer, reproductive problems, and neurological disorders.

Mechanism of pesticide toxicity in albino rats

Pesticides can induce alterations in albino rats through various mechanisms. Here are some common ways in which pesticides can cause changes in these animals

1. **Inhibition of Acetylcholinesterase (AChE):** Organophosphates (e.g., malathion) and carbamates (e.g., carbaryl) are characterized by their ability to inhibit the enzyme acetylcholinesterase (AChE) in the nervous system. This inhibition leads to an accumulation of acetylcholine at nerve synapses, causing continuous nerve stimulation. This overstimulation results in a range of symptoms, including muscle tremors, convulsions and paralysis. Organophosphates form a covalent bond with AChE, leading to irreversible inhibition, while carbamates form a reversible complex with the enzyme [12].
2. **Activation of Voltage-Gated Sodium Channels:** Pyrethroids, such as deltamethrin act by binding to and activating voltage-gated sodium channels in nerve cells. These channels are responsible for regulating the flow of sodium ions into nerve cells, which is essential for nerve transmission. By causing prolonged depolarization of nerve cells, pyrethroids lead to repetitive firing of nerves, resulting in muscle spasms, tremors, and paralysis [12].
3. **Interaction with Nicotine Acetylcholine Receptors (nAChRs):** Neonicotinoids like imidacloprid target the nervous system by interacting with nicotine acetylcholine receptors (nAChRs) in insects. By binding to these receptors, neonicotinoids cause continuous nerve stimulation and eventual paralysis. The specificity of neonicotinoids for insect nAChRs makes them effective against pests while posing less risk to vertebrates [13].
4. **Disruption of GABA Receptors:** Organochlorine pesticides, such as DDT, disrupt normal nerve function by affecting the balance of neurotransmitters in the brain. They prolong the activation of gamma-aminobutyric acid (GABA) receptors, which are inhibitory neurotransmitter

receptors. This leads to excessive inhibition of nerve cell firing, causing symptoms such as tremors, seizures, and impaired coordination [14].

5. **Disruption of Mitochondrial Respiration:** Fungicides like azoxystrobin inhibit enzymes in the mitochondrial electron transport chain. This disruption impairs mitochondrial respiration and energy production, causing a decrease in cellular ATP levels leading to death of the organism [12].
6. **Inhibition of Vitamin K Epoxide Reductase:** Rodenticides, designed to control rodent populations, often contain anticoagulant compounds. These compounds inhibit the enzyme vitamin K epoxide reductase, which is necessary for the activation of clotting factors involved in blood coagulation. As a result, rodents exposed to rodenticides experience bleeding disorders, leading to internal haemorrhages and death [13].
7. **Inhibition of Mitochondrial Complex I:** Acaricides target mites and ticks and humans by inhibiting enzymes in the mitochondrial electron transport chain, particularly complex I. This inhibition disrupts the production of cellular energy (ATP) and metabolic processes [13].

Effect of Pesticides on health parameters in albino rats

- Biochemical and metabolic alterations: Pesticides can disrupt normal biochemical and metabolic processes in albino rats. They may affect enzyme activities, interfere with cellular signaling pathways, and disturb the balance of various biochemical compounds. These alterations can lead to changes in energy metabolism, nutrient utilization, and overall physiological homeostasis [15].
- Oxidative stress: Pesticides can induce oxidative stress in albino rats by generating reactive oxygen species (ROS) and impairing antioxidant defense mechanisms. This oxidative stress can cause damage to lipids, proteins, and DNA in various tissues, leading to cellular dysfunction and tissue injury [15].
- Inflammation and immune response: Pesticides can trigger inflammatory responses in albino rats. They may activate immune cells, induce the release of pro-inflammatory cytokines, and promote the infiltration of inflammatory cells into affected tissues. Prolonged or excessive inflammation can contribute to tissue damage, impair organ function, and potentially lead to chronic inflammatory conditions [16].
- Neurotoxicity: Many pesticides have neurotoxic effects on albino rats. They can target the central nervous system, leading to alterations in neuronal function, neurotransmitter imbalances, and disruption of neural pathways. These effects can manifest as changes in behaviour, cognitive deficits, and neurological abnormalities [17].
- Reproductive and developmental alterations: Pesticides can interfere with the reproductive and developmental processes in albino rats. They may disrupt hormone signaling, affect gamete quality, impair fertility, and cause adverse effects on pregnancy, foetal development, and offspring health [18].
- Genotoxicity and DNA damage: Some pesticides have genotoxic potential and can induce DNA damage in albino rats. They may cause DNA strand breaks, DNA adduct formation, or interfere with DNA repair mechanisms. These genetic alterations can increase the risk of mutations, chromosomal abnormalities, and potential carcinogenic effects [19, 20].

It's important to note that the specific alterations induced by pesticides can vary depending on the type of pesticide, its chemical properties, dosage, duration of exposure, and the susceptibility of albino rats. Additionally, the effects may vary among different organs and tissues in the rats' bodies (Table 1).

Table 1: Effect of Pesticides reporte on different organs of albino rats

Organ	Pesticide	Effect on organs	References
Liver	Thiram, Chlorpyrifos, Cypermethrin, and Imidacloprid, Mancozeb, Paraquat	Hepatotoxicity (liver damage), alteration of liver enzyme activity, oxidative stress, Mitochondrial dysfunction, inflammation, fibrosis.	[21, 22]
Kidneys	Paraquat, Imidacloprid, Hexaflumuron, Malathion, Carbaryl	Nephrotoxicity (kidney damage), impaired renal function, oxidative stress, inflammation, renal failure.	[23, 24]
Brain	Chlorpyrifos, Malathion, Delthamethrin	Neurotoxicity, alterations in behavior, cognitive deficits, oxidative stress, neuronal damage, neuroinflammation.	[25, 26]
Heart	Carbaryl, Imidacloprid, methomyl, Chlorpyrifos	Cardiotoxicity, changes in cardiac function, oxidative stress, inflammation, arrhythmias, cardiac cell damage.	[27, 28]
Lungs	Chlorothalonil, fipronil, Endosulfan	Pulmonary toxicity, lung inflammation, decreased lung function, oxidative stress, lung tissue damage.	[29, 30]
Intestine	Atrazine, imidacloprid	Gastrointestinal toxicity, intestinal epithelial cell damage, inflammation, changes in gut microbiota.	[31, 32]

Effects of ameliorating agents against pesticide toxicity in albino rats

Pesticide toxicity in albino rats can be mitigated by using various ameliorating chemicals. The present review focuses on the discussion and evaluation of the following ameliorating agents in the context of mitigating pesticide-induced toxicity in albino rats. These ameliorating agents have been studied extensively for their potential to counteract the adverse effects of pesticides and promote the well-being of living organisms are described below.

Vitamin C

Vitamin C is recognized as a potent water-soluble antioxidant, assumes a critical role in shielding cells from oxidative stress and preserving overall health. As the widespread utilization of pesticides persists, concerns have arisen regarding their unintended repercussions on non-target organisms, particularly albino rats. Pesticide exposure triggers the generation of reactive oxygen species (ROS), contributing to cellular damage and toxic effects. Vitamin C acts as a potent ROS scavenger, neutralizing these harmful molecules and

preventing oxidative damage to cellular components, including lipids, proteins, and DNA. Furthermore, its ability to regenerate other antioxidants, such as vitamin E, amplifies its protective effects [33]. Through these mechanisms, vitamin C not only safeguards cellular integrity but also modulates pathways influencing haematological parameters, hepatic function, neural health, renal integrity, histopathological changes, reproductive outcomes, and genotoxicity[34]. The multifaceted involvement of vitamin C underscores its potential to mitigate a diverse array of pesticide-induced toxicities, making it a vital ally in preserving the health and well-being of albino rats subjected to pesticide exposure. Recent investigations have thus sought to harness vitamin C's potential in mitigating the adverse effects of pesticide exposure on albino rats.

Exposure to pesticides, including organophosphates, often triggers significant haematological imbalances in albino rats, encompassing disruptions in red and white blood cell counts, as well as haemoglobin levels. Addressing these concerns, researchers have explored the simultaneous administration of vitamin C alongside pesticide treatments. For instance, experiments involving albino rats subjected to malathion at a dose of 15 mg/kg b.w. revealed that concurrent vitamin C supplementation at 200 mg/kg b.w. led to notable enhancements in haematological parameters including red blood cell count, haemoglobin levels, and haematocrit values [35]. In another research, indoxacarb (100 mg/kg b.w. treatment resulted in a notable increase in red blood cells (RBC), haemoglobin content (Hb), haematocrit value (Hct), mean corpuscular volume (MCV), white blood cells (WBC). However, the administration of vitamin C (200 mg/Kg b.w.), known for its potent antioxidant properties, has shown promise in mitigating the adverse impacts of indoxacarb by alleviating the adverse impacts caused by Indoxacarb [36].

Likewise, biochemical hepatotoxicity, a frequent outcome of exposure to pesticides such as pyrethroids, manifests through disturbances in liver enzymes and heightened oxidative stress. Herein, vitamin C emerges as a potent hepatoprotective agent, capable of attenuating oxidative stress and preserving liver function. Notably, studies involving albino rats exposed to deltamethrin (2 mg/kg b.w.) showed that simultaneous administration of vitamin C at 150 mg/kg b.w. resulted in reduced hepatic enzyme levels such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), along with decreased lipid peroxidation. These hepatic enzymes, ALT and AST, are indicative of liver damage and their elevation signifies hepatotoxicity. This highlights vitamin C's potential in mitigating the pesticide-induced hepatotoxicity [37].

Further, neurotoxicity induced by certain pesticides, notably organochlorines, poses a risk to neurological health in albino rats, causing behavioural and neurological aberrations. In this context, vitamin C's neuroprotective attributes come to the fore. Its ability to scavenge free radicals and mitigate oxidative damage in neural tissues has been observed in experiments where albino rats exposed to lindane (10 mg/kg) demonstrated improved neurobehavioral parameters upon concurrent administration of vitamin C (100 mg/kg b.w.) [38].

Nephrotoxicity, a consequence often induced by pesticides poses a significant risk by impairing renal function and leading to tissue damage. In this intricate process, exposure to pesticides exacerbates the generation of reactive oxygen species (ROS) within renal tissues, resulting in oxidative stress and subsequent cellular damage. Vitamin C emerges as a compelling candidate for mitigating nephrotoxic effects due to its robust antioxidant capabilities at 100 mg/kg b.w., signifying its potential in alleviating nephrootoxicity caused by pesticides. Experiments involving albino rats exposed to glyphosate at a dose of 50 mg/kg b.w. demonstrated the profound impact of concurrent vitamin C co-treatment at 250 mg/kg b.w. [38]. The administration of vitamin C led to a discernible reduction in kidney damage markers such as serum creatinine and blood urea nitrogen levels, reflecting its potential role in counteracting pesticide-induced nephrotoxicity.

Pesticide exposure frequently gives rise to histopathological changes in various organs, necessitating interventions to minimize tissue damage. With its anti-inflammatory and antioxidant properties, vitamin C becomes a potential candidate for this purpose. For instance, when albino rats were exposed to diazinon (5 mg/kg b.w.), co-administration of vitamin C at 200 mg/kg b.w. led to diminished histopathological abnormalities in the liver and brain, signifying its potential in alleviating tissue damage caused by pesticide exposure [39]. Further, Vitamin C at 100 mg/kg b.w. demonstrated its efficacy in restoring the histological damage caused by quinalphos (2 mg/kg b.w.) in the ileal enterocytes of albino rats. The histological and ultrastructural analysis of the ileal cells upon quinalphos exposure was characterized by a lack of well-defined microvilli structure, prominent vacuolation within the microvilli, disrupted nuclei exhibiting chromatin margination, disoriented mitochondria, and an increased intercellular space [40]. The absorptive columnar cells displayed numerous intracellular vacuoles with microvilli herniation, while the goblet cells appeared morphologically normal. However, in the quinalphos plus Vitamin C group, the ileal mucosal architecture closely resembled that of the healthy control group, indicating that vitamin C supplementation successfully counteracted the detrimental effects of quinalphos. This restorative effect of vitamin C suggests its potential as a therapeutic agent in ameliorating ileal dysfunction induced by quinalphos.

Further, Reproductive toxicity, linked to pesticides like carbamates, can adversely impact fertility and offspring development in albino rats. Vitamin C's antioxidative and hormonal modulating effects position it as a potential mitigator of reproductive disruptions. A study involving albino rats exposed to carbaryl (3 mg/kg b.w.) revealed that supplementation with vitamin C at 100 mg/kg b.w. resulted in notable improvements in sperm parameters, including enhanced sperm count, motility, and morphology. Additionally the co-administration of vitamin C demonstrated a significant reduction in embryo toxicity, as evidenced by decreased rates of developmental abnormalities and malformations observed in the offspring [41].

Pesticide-induced genotoxicity, often causing DNA damage and mutations, can be counteracted by vitamin C's antioxidative properties. When albino rats were subjected to cypermethrin at a dose of 4 mg/kg b.w., simultaneous administration of vitamin C at 150 mg/kg b.w. bled to reduced levels of DNA damage markers, indicating vitamin C's potential in mitigating pesticide-induced genotoxicity[42]. In determining the effectiveness of vitamin C in mitigating pesticide toxicity, careful consideration of dosages is essential. Different pesticides exhibit varying toxicities, necessitating thorough dose-response studies to ascertain optimal vitamin C dosages for specific pesticides.

Vitamin E

Vitamin E, a fat-soluble antioxidant, holds a pivotal role in safeguarding cellular health by countering oxidative stress by reducing the production of free radicals. These pesticides encompass a spectrum of toxicities, spanning haematological, biochemical hepatotoxicity, neurotoxicity, nephrotoxicity, histopathological alterations, reproductive toxicity, and genotoxicity. In response, recent research has focused on harnessing the potential of vitamin E to mitigate the deleterious effects of pesticide exposure on albino rats. Exposure to pesticides like organophosphates can induce significant haematological alterations in albino rats, affecting red and white blood cell counts, as well as haemoglobin levels [43]. In studies aimed at addressing this, simultaneous administration of vitamin E alongside pesticide treatments has shown promise. For instance, when albino rats were subjected to chlorpyrifos at a dose of 10 mg/kg b.w., the co-administration of vitamin E at 100 mg/kg b.w. resulted in observable improvements in haematological parameters. This underlines vitamin E's capacity to counteract haematological toxicity induced by pesticides [44].

Additionally, biochemical hepatotoxicity, frequently observed in response to different pesticides, involves disruptions in liver enzymes and lipid peroxidation. In this context, vitamin E emerges as a potent hepatoprotective agent, capable of attenuating oxidative stress and preserving liver function. Notably, when albino rats were exposed to endosulfan (5 mg/kg b.w.), concomitant administration of vitamin E at 200 mg/kg b.w. exhibited a marked reduction in hepatic enzyme levels (Superoxide dismutase, Catalase, Glutathione reductase) and lipid peroxidation, highlighting its hepatoprotective potential [45].

Neurotoxicity induced by certain pesticides, notably organophosphates, can trigger neurological abnormalities and behavioral changes in albino rats. Here, vitamin E's role in mitigating such adverse effects becomes evident. By scavenging free radicals and mitigating oxidative damage within neural tissues, vitamin E demonstrates neuroprotective capabilities. When albino rats were exposed to diazinon at a dose of 8 mg/kg b.w., co-treatment with vitamin E at 150 mg/kg b.w. led to measurable improvements in neurobehavioral parameters, further substantiating its neuroprotective attributes [46].

Nephrotoxicity, associated with pesticides like glyphosate, can induce renal dysfunction and tissue damage. Vitamin E's antioxidative prowess has shown promise in counteracting such nephrotoxic effects by mitigating oxidative stress and preserving renal function. In experimental setups involving albino rats exposed to glyphosate (50 mg/kg b.w.), concurrent administration of vitamin E at 100 mg/kg b.w. demonstrated a notable reduction in kidney damage markers *viz* urea and creatinine in serum of treated albino rats, suggesting its utility in safeguarding against pesticide-induced nephrotoxicity [47].

Histopathological changes, a common outcome of pesticide exposure, can affect various organs including the liver, kidneys, and brain. Here, vitamin E's anti-inflammatory and antioxidant properties prove beneficial. In cases where albino rats were exposed to malathion at a dose of 20 mg/kg b.w., co-treatment with vitamin E at 300 mg/kg b.w. yielded diminished histopathological abnormalities in both the liver, brain and kidneys, highlighting vitamin E's capacity to alleviate tissue damage resulting from pesticide exposure [48].

Pesticide-induced reproductive toxicity, linked to compounds like pyrethroids, can have adverse effects on fertility and offspring development in albino rats. Vitamin E's ability to enhance reproductive outcomes is attributed to its modulation of oxidative stress and reproductive hormone balance. Notably, in studies involving albino rats exposed to deltamethrin (2 mg/kg b.w.), supplementation with vitamin E at 100 mg/kg b.w. led to improved fertility parameters and reduced embryo toxicity, suggesting its potential in ameliorating reproductive toxicity [49].

The genotoxicity stemming from pesticide exposure, often causing DNA damage and mutations in albino rats, can be countered by vitamin E's antioxidant properties. Through neutralizing reactive oxygen species, vitamin E plays a pivotal role in safeguarding DNA integrity. In experiments where albino rats were subjected to cypermethrin at a dose of 3 mg/kg b.w., concurrent treatment with vitamin E at 150 mg/kg b.w. displayed a reduction in DNA damage markers, signifying its potential in mitigating pesticide-induced genotoxicity [50].

Vitamin E's multifaceted involvement in mitigating pesticide-induced toxicity stems from its potent antioxidant properties and ability to counteract oxidative stress. As pesticides trigger the generation of reactive oxygen species (ROS) within tissues, vitamin E acts as a radical scavenger, intercepting and neutralizing these harmful molecules. This antioxidative prowess enables vitamin E to maintain cellular integrity and prevent oxidative damage to biomolecules like lipids, proteins, and DNA[51]. Moreover, vitamin E's anti-inflammatory characteristics further contribute to its protective role, as it dampens the cascade of inflammatory responses often provoked by pesticide exposure. By engaging in these mechanisms, vitamin E not only safeguards cellular structures but also modulates various pathways related to haematological, hepatic, neural, renal, histopathological, reproductive, and genotoxic outcomes. This multifaceted involvement underscores vitamin E's capacity to ameliorate a wide spectrum of pesticide-induced toxicities in albino rats, offering a holistic approach to counteracting the deleterious effects of pesticide exposure.

Curcumin

Curcumin, a natural compound derived from the turmeric plant (*Curcuma longa*), has gained significant attention for its potential protective effects against pesticide-induced toxicity. Curcumin, as a potent antioxidant, counteracts the detrimental effects induced by pesticides by effectively scavenging ROS and preventing oxidative damage to essential cellular constituents, including lipids, proteins, and DNA [52]. Furthermore, curcumin's capacity to modulate intricate molecular pathways reinforces its impact, influencing hematological parameters, hepatic function, neural integrity, renal health, histopathological changes, reproductive outcomes, and genotoxicity [53]. Through these mechanisms, curcumin emerges as a formidable candidate in safeguarding the health and well-being of albino rats subjected to pesticide exposure. Recent studies are increasingly exploring the potential of curcumin to alleviate pesticide-induced toxicities in these organisms.

Investigations have delved into the concurrent administration of curcumin alongside pesticide treatments. For instance, experiments involving albino rats exposed to chlorpyrifos at a dose of 2 mg/kg b.w. unveiled that concurrent curcumin supplementation at 100 mg/kg b.w. elicited improvements in haematological parameters such as red blood cell count, haemoglobin levels, and haematocrit values [54].

Biochemical hepatotoxicity, a common outcome of pesticide exposure, often manifests through disruptions in liver enzymes and exacerbated oxidative stress. Curcumin's potent hepatoprotective attributes have been demonstrated in studies involving albino rats exposed to cypermethrin (3 mg/kg b.w.) and cyfluthrin (4 mg/kg b.w.). In these studies, co-administration of curcumin at doses ranging from 100 mg/kg b.w. to 200 mg/kg b.w. resulted in reduced hepatic enzyme levels, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), coupled with decreased lipid peroxidation. These outcomes underscore curcumin's potential in mitigating the hepatic damage triggered by pesticide exposure [55].

Neurotoxicity induced by pesticides poses significant risks to neurological health, leading to behavioral and neurological aberrations in albino rats. Curcumin's neuroprotective capabilities are evident in studies where albino rats exposed to imidacloprid at a dose of 1 mg/kg b.w. demonstrated improved neurobehavioral parameters upon concurrent curcumin administration at 50 mg/kg b.w[55]. Nephrotoxicity, a consequence often induced by pesticides, impairs renal function and causes tissue damage. In experiments involving albino rats exposed to glyphosate at 100 mg/kg b.w., co-treatment with curcumin at 150 mg/kg b.w. resulted in decreased kidney damage markers such as serum creatinine and blood urea nitrogen levels, highlighting curcumin's potential in mitigating pesticide-induced nephrotoxicity [56].

Additionally, research has focused on protective effects of curcumin on reproductive parameters also. In a study, albino rats subjected to the reproductive toxicant carbaryl at a dosage of 3 mg/kg b.w. exhibited compromised sperm parameters, including diminished count, motility, and morphology, alongside perturbed hormonal profiles encompassing luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone. However, concurrent administration of curcumin at 100 mg/kg b.w. showcased remarkable improvements, reinstating sperm quality and hormonal balance[56]. This was evident in notable enhancements in sperm count, motility, and morphology, coupled with the reestablishment of LH, FSH, and testosterone levels. Furthermore, in a separate study focusing on fenvalerate-induced reproductive toxicity, curcumin intervention at 150 mg/kg exhibited comparable auspicious outcomes, effectively mitigating the adverse impact on sperm parameters and hormonal equilibrium. These studies collectively underline curcumin's potential to counteract reproductive toxicity by harmonizing hormonal dynamics, safeguarding sperm quality, and preserving reproductive health in albino rats exposed to pesticide stress [57].

Further, histopathological changes induced by pesticide exposure underscore the need for interventions to minimize tissue damage. Curcumin's anti-inflammatory and antioxidant properties position it as a candidate for this purpose. When albino rats were exposed to malathion at a dose of 5 mg/kg b.w., co-administration of curcumin at 100 mg/kg led to diminished histopathological abnormalities in the liver *viz*. hepatocellular damage, vacuolation, infilteration and Kupffer cell damage alongwith various abnormalities induced in the kidney like tubular degeneration, damage to interstitial tissue, jnfilteration suggesting its potential in alleviating pesticide-induced tissue damage [58].

Green tea extract

Green tea extract (GTE) is a popular natural remedy that has gained significant attention for its potential health benefits. It is derived from the leaves of the *Camellia sinensis* plant and is known for its rich content of bioactive compounds, particularly polyphenols. These polyphenols, including catechins like epigallocatechin gallate (EGCG), have been associated with a wide range of health-promoting properties, including antioxidant, anti-inflammatory, anti-cancer, and neuroprotective effects [59].

Several recent studies have investigated the potential ameliorative effects of green tea extract (GTE) on pesticide-induced toxicity in albino rats. In a study, albino rats were exposed to lambda cyhalothrin at a dosage of 5 mg/kg b.w., resulting in significant reductions in body weight gain over a 4-week period. However, concurrent administration of green tea extract at a dose of 200 mg/kg b.w. mitigated this effect, leading to a noticeable improvement in body weight gain. Moreover, the adverse impact of lambda cyhalothrin on brain weight, evidenced by a decrease in brain-to-body weight ratio, was attenuated with GTE supplementation [60].

In the context of neurotoxicity induced by deltamethrin in the rat brain, the potential role of green tea extract as a mitigating agent against oxidative damage and apoptosis has garnered significant attention. Deltamethrin, a synthetic pyrethroid insecticide, has been linked to neural oxidative stress and apoptotic phenomena. In contrast, green tea extract, abundant in polyphenolic compounds like catechins and flavonoids, boasts notable antioxidant and neuroprotective properties. In a focused investigation, the effects of green tea extract on deltamethrin-induced neurotoxicity were studied, employing doses of 15 mg/kg b.w. for deltamethrin and 150 mg/kg b.w. for green tea extract. Results indicated that green tea extract administration led to a reduction in oxidative damage (decreased SOD and CAT) through the scavenging of free radicals, reinforcement of endogenous antioxidants, and modulation of intracellular signaling pathways[61]. Moreover, green tea extract exhibited an inhibitory influence on apoptosis, potentially attributed to its interaction with Bcl-2 family proteins and caspases, reducing DNA fragmentation as well as suppressing the expression of the TP53 and COX2 genes [62].

Further, histopathological alterations *viz*. congestion, desquamated epithelium in bronchi and bronchioles peribronchial and perivascular edema, thickening of interalveolar septa by inflammatory cells has also been found to improve upon treating the female albino rats with green tea extract (100 mg/kg b.w.) after the exposure of fenitrothion (10 mg/kg b.w.) [63].

The role of Green Tea Extract (GTE) in mitigating hepatotoxicity induced by fenitrothion is of considerable importance, particularly concerning histopathological alterations in the liver and associated biochemical parameters. In a targeted investigation, GTE's efficacy was examined against fenitrothion-induced hepatotoxicity, employing doses of 150 mg/kg b.w. for green tea extract and 20 mg/kg b.w. for fenitrothion[64]. Notably, GTE administration demonstrated a significant reduction in hepatocellular damage, as evidenced by lowered levels of serum transaminases and bilirubin. Moreover, histopathological evaluation revealed that GTE attenuated fenitrothion-induced alterations in liver architecture, such as hepatocyte degeneration, inflammatory infiltrates, and necrosis. Additionally nephroprotective impact of green tea extract, were evidenced by decreased levels of serum creatinine and urea. Furthermore, histopathological examination demonstrated that GTE attenuated fenitrothion-

induced changes in kidney architecture, including glomerular congestion, tubular necrosis, and inflammatory infiltrates [65].

Ginger

Ginger (*Zingiber officinale*), derived from the rhizomes of the ginger plant, is a well-recognized herbal remedy known for its diverse bioactive constituents, primarily gingerols and related compounds. The bioactive constituents of ginger, including gingerols and shogaols, play a pivotal role in conferring certain protective effects. These compounds act as potent antioxidants, effectively scavenging free radicals and reactive oxygen species, thereby mitigating oxidative stress and preventing cellular damage. Additionally, ginger modulates intracellular signaling pathways related to inflammation and apoptosis, leading to the suppression of pro-inflammatory gene expression and the inhibition of apoptotic processes[66]. These bioactive constituents have attracted significant scientific interest due to their potential health-enhancing properties, including anti-inflammatory, antioxidant, antimicrobial, and antiemetic effects.

Recent investigations have explored the potential ameliorative effects of ginger on pesticide-induced toxicity in albino rats. In a controlled study, albino rats were subjected to exposure to cypermethrin, a synthetic pyrethroid insecticide, at a dosage of 3 mg/kg b.w., leading to substantial decreases in body weight gain over a designated 3-week period. However, concurrent administration of ginger at a dose of 100 mg/kg b.w. showed promising outcomes, mitigating the adverse impact on body weight gain and exhibiting a noticeable improvement in the observed decline [67]. Furthermore, the negative influence of cypermethrin on brain parameters, as indicated by a decrease in brain-to-body weight ratio, was counteracted through supplementation with ginger.

Considering the neurotoxic effects induced by chlorpyrifos in the rat brain, ginger's potential role as a mitigating agent against oxidative stress and neuronal damage warrants scientific scrutiny. Chlorpyrifos, an organophosphorus pesticide, has been implicated in eliciting neural oxidative stress and degenerative phenomena. In contrast, ginger, enriched with bioactive constituents like gingerols and shogaols, possesses substantial antioxidative and neuroprotective attributes. In an in-depth investigation, the effects of ginger on chlorpyrifos-induced neurotoxicity were meticulously explored, employing doses of 10 mg/kg b.w. for chlorpyrifos and 150 mg/kg b. w. for ginger [68]. Results demonstrated that ginger administration led to a reduction in oxidative damage, evident through the restoration of antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT), achieved through the scavenging of free radicals, fortification of endogenous antioxidants, and modulation of intracellular signaling pathways [69]. Additionally, ginger exhibited a repressive effect on neuronal degeneration, potentially attributed to its interaction with key apoptotic regulators like Bcl-2 family proteins and caspases, thereby curtailing DNA fragmentation and suppressing the expression of pro-inflammatory genes.

Moreover, ginger role in alleviating histopathological deviations, including bronchial congestion, epithelial desquamation, peribronchial and perivascular edema, and interalveolar septal thickening, was unveiled through an experimental intervention involving female albino rats. After exposure to fenitrothion at a dose of 10 mg/kg b.w., ginger administration at a dosage of 100 mg/kg b.w. exhibited noteworthy improvements in these histopathological markers, reflecting its potential to counteract pesticide-induced pulmonary alterations [70].

The potential of Ginger in mitigating hepatotoxicity induced by fenitrothion holds significant scientific significance, especially concerning liver histopathological changes and associated biochemical indicators. In a targeted study, the efficacy of ginger was investigated against fenitrothion-induced hepatotoxicity, utilizing doses of 200 mg/kg b.w. for ginger and 25 mg/kg b.w. for fenitrothion[71]. Remarkably, ginger administration demonstrated a substantial reduction in hepatocellular injury, manifested by decreased levels of serum transaminases and bilirubin. Furthermore, histopathological assessment disclosed that ginger ameliorated fenitrothion-induced disruptions in hepatic architecture, encompassing hepatocyte degeneration, inflammatory infiltration, and necrosis. Notably, the nephroprotective impact of ginger was also evident, with diminished serum creatinine and urea levels. Histopathological analysis corroborated this finding by revealing that ginger attenuated fenitrothion-associated alterations in kidney structure, encompassing glomerular congestion, tubular necrosis, and inflammatory infiltration.

Notably, in a comprehensive investigation, albino rats subjected to the reproductive toxicant imidacloprid at a dosage of 2 mg/kg b.w. displayed perturbed reproductive parameters, encompassing compromised sperm quality and perturbed hormonal profiles, particularly follicle-stimulating hormone (FSH) and testosterone. However, concurrent supplementation of ginger at 150 mg/kg b.w. mitigated these detriments, manifesting as substantial enhancements in sperm count, motility, and morphology, along with the reestablishment of FSH and testosterone levels[72]. Correspondingly, in a separate study involving fenvalerate-induced reproductive toxicity, ginger intervention at 100 mg/kg b.w. showed similar auspicious outcomes, effectively ameliorating the deleterious impact on sperm quality and hormonal equilibrium, including luteinizing hormone (LH). These investigations collectively underscore ginger's potential to counteract reproductive toxicity by harmonizing hormonal dynamics and safeguarding against oxidative stress-induced impairments, thus fostering the preservation of reproductive well-being in albino rats [73].

Garlic

Garlic (*Allium sativum*) is a well-recognized herbal remedy known for its rich bioactive constituents, primarily allicin and related compounds. These constituents contribute significantly to garlic's protective effects. Acting as potent antioxidants, allicin and its derivatives effectively scavenge free radicals and reactive oxygen species, thereby attenuating oxidative stress and preserving cellular integrity. Moreover, garlic modulates intricate intracellular signaling pathways associated with inflammation and apoptosis, leading to the suppression of pro-inflammatory gene expression and inhibition of apoptotic processes. The multifaceted attributes of garlic's bioactive constituents have sparked substantial scientific interest due to their potential health-enhancing properties, including anti-inflammatory, antioxidant, antimicrobial, and cardioprotective effects [74].

Recent scientific inquiries have sought to uncover the potential ameliorative effects of garlic on pesticide-induced toxicity in albino rats. In a study, albino rats were exposed to deltamethrin, a synthetic pyrethroid insecticide, at a dosage of 5 mg/kg b.w., resulting in substantial reductions in body weight gain over a stipulated 4-week period. However,

concurrent administration of garlic at a dose of 150 mg/kg b.w. demonstrated promising outcomes, mitigating the observed decline in body weight and showing a discernible improvement [75]. Moreover, the detrimental impact of deltamethrin on brain parameters, as evidenced by a decrease in brain-to-body weight ratio, was effectively counteracted through supplementation with garlic.

Considering the neurotoxic ramifications instigated by malathion in the rat brain, garlic's potential as a mitigating agent against oxidative stress and neuronal damage demands comprehensive exploration. Malathion, an organophosphorus pesticide, is known to induce neural oxidative stress and degenerative changes. In contrast, garlic, enriched with bioactive compounds like allicin, exhibits robust antioxidative and neuroprotective properties. In a comprehensive investigation, the effects of garlic on malathion-induced neurotoxicity were meticulously scrutinized, employing doses of 15 mg/kg b.w. for malathion and 200 mg/kg body weight for garlic [76]. Findings elucidated that garlic administration led to a notable reduction in oxidative damage, evidenced by the restoration of antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT), achieved through the scavenging of free radicals, reinforcement of endogenous antioxidants, and modulation of intracellular signaling cascades. Furthermore, garlic exhibited suppressive effects on neuronal degeneration, potentially attributed to its interaction with pivotal apoptotic regulators like Bcl-2 family proteins and caspases, thereby mitigating DNA fragmentation and suppressing the expression of pro-inflammatory genes [77].

Moreover, the potential of garlic in ameliorating histopathological perturbations, including bronchial congestion, epithelial desquamation, peribronchial and perivascular edema, and interalveolar septal thickening, has been unveiled through a controlled study involving female albino rats. Following exposure to cypermethrin at a dose of 10 mg/kg b.w., garlic administration at a dosage of 100 mg/kg b.w. exhibited notable improvements in these histopathological markers, underscoring its capacity to mitigate pesticide-induced pulmonary alterations. As an herbal ameliorating agent, garlic's intricate mechanisms hold promise in safeguarding albino rats from pesticide-induced toxicities [78].

Conclusion

The ameliorating agents – namely, vitamin C, vitamin E, green tea, ginger, and garlic have exhibited remarkable capabilities in attenuating the adversities imposed by pesticides on a spectrum of bodily organs. These ameliorating agents have potent antioxidant attributes in mitigating oxidative stress evoked by pesticides by reducing the production of free radicals and thus, reinforcing the endogenous antioxidant defense mechanisms by maintaining the activities of antioxidant enzymes *viz*. SOD, CAT, Glutathione reductase thereby affording protection against oxidative damage. While the promise of these ameliorating agents is compelling, further investigation is warranted to decipher their precise mechanisms of action, optimize dosages, and unveil potential interactions.

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