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INFLUENCE OF PESTICIDES ON HEPATIC CELLS: MECHANISMS AND HEALTH IMPLICATIONS

Abdumuminov B.R.
Assistant of FMIOPH
e.mail: Abdumuminovbobur10@gmail.com.
Fergana, Uzbekistan.
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ABSTRACT

Pesticides – chemical substances used in agriculture to control pests and improve crop yields have been linked to adverse effects on human health when exposure is chronic or acute. The liver, as the principal organ responsible for xenobiotic metabolism and detoxification, is especially susceptible. Hepatic cells including hepatocytes are primary targets of pesticide-induced toxicity. This article reviews the molecular and cellular effects of pesticides on liver tissue, highlighting key mechanisms and health outcomes with scientific references.

ВЛИЯНИЕ ПЕСТИЦИДОВ НА КЛЕТКИ ПЕЧЕНИ: МЕХАНИЗМЫ И ПОСЛЕДСТВИЯ ДЛЯ ЗДОРОВЬЯ

Б.Р.Абдумуминов
Ассистент ФМИОЗ. e.mail: Abdumuminovbobur10@gmail.com.
Фергана, Узбекистан.
https://doi.org/10.5281/zenodo.18502471

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ABSTRACT

Пестициды — химические вещества, используемые в сельском хозяйстве для борьбы с вредителями и повышения урожайности, связаны с неблагоприятными последствиями для здоровья человека при хроническом или остром воздействии. Печень, как основной орган, отвечающий за метаболизм и детоксикацию ксенобиотиков, особенно восприимчива к этому. Клетки печени, включая гепатоциты, являются основными мишенями токсического воздействия пестицидов. В данной статье рассматриваются молекулярные и клеточные эффекты пестицидов на ткани печени, освещаются ключевые механизмы и последствия для здоровья с указанием научных ссылок.

Introduction. The Liver as a Target of Xenobiotic Toxicity. The liver plays a central role in converting lipophilic compounds into forms that can be excreted. It accomplishes this mainly through the cytochrome P450 (CYP450) enzyme system, but this biotransformation can paradoxically generate reactive intermediates that damage cellular structures when pesticide exposure overwhelms detoxification pathways.

Major Pesticide Classes Affecting Hepatic Cells. Various pesticide groups have demonstrated hepatotoxic potential:

- Organophosphates (e.g., chlorpyrifos, malathion)
- Pyrethroids (e.g., cypermethrin);
- Fungicides (e.g., pyraclostrobin);
- Herbicides (e.g., glyphosate-based products). These compounds differ in biochemical action but often converge on common stress pathways within the liver.

Mechanisms of Pesticide-Induced Hepatotoxicity:

1. Oxidative Stress and Redox Imbalance. Exposure to pesticides frequently results in an imbalance between pro-oxidant and antioxidant systems in hepatic cells. This oxidative stress involves the excessive generation of reactive oxygen species (ROS) and lipid peroxidation, ultimately damaging proteins, lipids, and DNA. A comprehensive review highlights that organophosphates and neonicotinoids disturb cellular redox homeostasis and increase oxidative stress biomarkers in hepatocyte models. In human liver cells exposed to natural pyrethrins, mitochondrial collapse and elevated ROS production triggered stress signaling involving the Keap1/Nrf-2 pathway, a key regulator of antioxidant responses.

2. Mitochondrial Dysfunction and Apoptotic Pathways.

Pesticides can impair mitochondrial function, reducing ATP generation and triggering cell death. Studies using HepG2 (human hepatic carcinoma) cells show that exposure to chlorpyrifos, carbofuran, and acetamiprid increased apoptosis and necrosis, accompanied by oxidative stress.

3. Altered Enzyme Activity and Detoxification Pathways.

Some pesticides inhibit critical antioxidant enzymes such as superoxide dismutase (SOD), glutathione S-transferase (GST), and catalase (CAT) in liver tissue, impairing detoxification and promoting cell injury. For example, mixtures of organophosphorus with pyrethroid insecticides significantly inhibited antioxidant enzymes in rat liver homogenates, indicating a connection between oxidative stress and enzyme inhibition.

4. Genotoxicity and Mitochondrial-DNA Damage.

Certain pesticides may produce genotoxic effects in hepatic cells, including DNA strand breaks and chromosomal aberrations. Although mechanisms vary by compound type, oxidative stress often contributes to DNA damage and can predispose liver cells to maladaptive responses.

5. Inflammation and Fibrotic Responses.

Chemical insults from pesticides can activate resident immune cells (e.g., Kupffer cells), stimulating pro-inflammatory cytokines such as TNF-α and IL-6. Chronic inflammation is a

known driver of fibrotic changes and chronic liver disease when exposures are repeated or persistent.

Histopathological and Functional Outcomes. Experimental studies in animal models and cell cultures show pesticide exposure leading to classic hepatotoxic changes, such as:

- Hepatocyte swelling and vacuolization
- Increased lipid peroxidation
- Mitochondrial disruption and apoptosis
- Inflammatory infiltration
- Early signs of steatosis (fat accumulation)

For example, histopathological analysis in rats exposed to common pesticides revealed significant liver degeneration and biochemical indicators of cellular stress.

Health Implications and Epidemiological Evidence.

In various populations with occupational pesticide exposure, researchers have observed abnormalities in liver function biomarkers such as ALT, AST, GGT, and bilirubin, correlating with increased risk of metabolic disorders like non-alcoholic fatty liver disease (NAFLD) and fibrosis.

Protective Strategies and Future Research. Mitigating liver damage from pesticides involves multiple strategies:

- Reducing occupational and environmental exposure
- Promoting the use of less toxic alternatives
- Enhancing dietary antioxidant defenses
- Developing hepatoprotective agents

Recent studies on natural antioxidants (e.g., curcumin nano-lipid carriers) demonstrate potential hepatoprotective effects against pesticide-induced oxidative and inflammatory changes in animal models.

The Liver and Its Role in Detoxification. The liver is the main metabolic hub of the body, responsible for biotransformation and elimination of xenobiotics, including pesticides. Hepatocytes contain enzyme systems such as cytochrome P450 (CYP450) that convert lipophilic compounds into more water-soluble metabolites for excretion. While this process is protective, it can also generate reactive intermediates that damage liver cells when exposure is excessive or prolonged.

Types of Pesticides Affecting Hepatic Cells. Several classes of pesticides have been implicated in liver toxicity:

- Organophosphates (e.g., chlorpyrifos, malathion);
- Organochlorines (e.g., DDT);
- Carbamates;
- Pyrethroids;
- Herbicides (e.g., paraquat, glyphosate).

These compounds differ in chemical structure but often share common toxicological pathways in hepatic tissue.

Mechanisms of Hepatotoxicity. Oxidative Stress. One of the primary mechanisms of pesticide-induced liver injury is oxidative stress. Many pesticides increase the production of reactive oxygen species (ROS), overwhelming the antioxidant defense systems of hepatic cells. Excess ROS can damage cellular lipids, proteins, and DNA, leading to lipid peroxidation and membrane instability.

Mitochondrial Dysfunction. Pesticides may disrupt mitochondrial function by impairing the electron transport chain. This results in reduced ATP production

and increased ROS generation, ultimately triggering cell death pathways such as apoptosis or necrosis in hepatocytes.

Inflammation. Exposure to pesticides can activate Kupffer cells (resident liver macrophages), leading to the release of pro-inflammatory cytokines such as TNF-α and IL-6. Chronic inflammation contributes to progressive liver damage and may promote fibrosis.

Enzyme Dysregulation. Pesticides can alter liver enzyme activity, including CYP450 enzymes. This dysregulation may impair normal detoxification processes and increase susceptibility to other toxins or drugs, compounding hepatic injury.

Genotoxicity and Carcinogenic Potential. Some pesticides exhibit genotoxic effects, causing DNA damage and chromosomal abnormalities in hepatic cells. Long-term exposure has been associated with an increased risk of liver tumors in experimental models, raising concerns about their carcinogenic potential in humans.

Histopathological Changes in Hepatic Cells. Microscopic examination of pesticide-exposed liver tissue often reveals:

- Hepatocyte swelling and vacuolization
- Fatty degeneration (hepatic steatosis)
- Cellular necrosis and apoptosis
- Inflammatory cell infiltration
- Fibrotic changes in chronic exposure

These alterations compromise liver architecture and function.

Health Implications. Damage to hepatic cells can lead to impaired metabolism, reduced detoxification capacity, and altered bile production. Clinically, this may manifest as elevated liver enzymes, jaundice, metabolic disorders, or progression to chronic liver diseases such as fibrosis or cirrhosis. Occupational exposure among agricultural workers represents a significant risk factor.

Prevention and Protective Strategies. Reducing the harmful effects of pesticides on hepatic cells involves:

- Limiting exposure through protective equipment and safe handling practices;
- Promoting the use of less toxic or biodegradable pesticides;
- Strengthening antioxidant defenses through diet and lifestyle;
- Regulatory monitoring and stricter safety guidelines.

Research into hepatoprotective agents, including natural antioxidants, is ongoing and shows promise in mitigating pesticide-induced liver damage.

Conclusion. Pesticides exert a wide range of detrimental effects on hepatic cells through oxidative stress, enzyme disruption, mitochondrial dysfunction, and inflammatory signaling. These mechanisms compromise liver function and pose significant health risks, particularly for individuals with chronic or high-level exposure. Continued research is essential for refining safety standards and protective interventions.

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