

TERATOGENIC EFFECT OF WIDESPREAD ENVIRONMENTAL PESTICIDES ON RAT PREGNANCY

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Abstract: Pesticides are chemicals widely used in modern agriculture, and their long-term effects on human health during pregnancy and lactation pose a serious threat. They accumulate in the body and exert a harmful effect on the genotoxic, endocrine systems, leading to oxidative stress. Organophosphorus, organochlorine, carbamate, and pyrethroid pesticides negatively affect DNA synthesis, cell division, gene expression, and epigenetic processes. In particular, the passage of pesticides through the placenta to the fetus, which intensifies oxidative stress and disrupts the activity of cytochrome P450 enzymes, hinders embryonic development. In response, to reduce the risk of pesticides, there is a need to control them, protect pregnant women, and strengthen toxicological monitoring. At the same time, expanding the use of environmentally safe, low-toxicity, or biological pesticides is an important strategy. This approach is crucial for protecting human health and maintaining environmental sustainability.

Keywords: chlorpyrifos (cpf), glyphosate (gly), imidacloprid (imi), neonicotinoids, organophosphorus compounds, genotoxicity, oxidative stress

CPF (chlorpyrifos) and GLY (glyphosate) are common organophosphorus pesticides that have teratogenic and genotoxic effects by affecting endocrine system function, causing oxidative stress, and disrupting embryonic growth and development [1]. In pregnant rats, CPF affects fetal weight loss, skeletal malformations (wave-like ribs, spinal curvature), congenital defects such as microcephaly, microthiia, micromelia, as well as decreased maternal placental function, and delayed embryonic development [4]. Although this enzyme is absent in GLY animals, adverse metabolic effects have been identified. GLY increases the level of glucose, triglycerides, total cholesterol in the blood, increases the risk of insulin resistance and metabolic syndrome, an increase in liver enzymes leads to damage to the detoxification system. In the offspring of rats exposed to GLY, such conditions as weight loss, small size of the eyes and legs, and morphological anomalies (microcephaly, dysmorphogenesis) were observed. It has been experimentally proven that GLY has a teratogenic effect [1]. Studies conducted on various model animals regarding the teratogenic and genotoxic properties of pesticides show that organophosphorus compounds can be associated with embryotoxicity, DNA damage, and developmental disorders [2, 5]. For example, studies with per- and polyphloroalkyl compounds have also confirmed the detection of teratogenic and genotoxic effects in embryos and neonatal mice [5].

Indian scientists Jyoti Upadhyay, Mahendra Rana, Nidhi Tiwari, and Mohd Nazam Ansari assessed the effects of chlorpyrifos (CPF) and glyphosate (GLY) on the health of pregnant female rats and their offspring. Orally administered pesticides CPF and GLY at a dose of 10 mg/kg during gestation and lactation were associated with biochemical changes in the rat's body, disruption of the lipid profile, as well as the occurrence of morphological anomalies in offspring [1]. The research results demonstrate the teratogenic effect of pesticides and their health risks. For the experiment, 18 Wistar females weighing 200-250 g were selected, and the animals were

adapted to laboratory conditions: a 12-hour light/dark cycle, kept at a temperature of $22\pm 3^{\circ}\text{C}$ and humidity of 30-70%, provided with standard feed and water.

Rats were randomly divided into 3 groups: 1st group - control (physiological solution); 2nd group - CPF (10 mg/kg, oral); 3rd group - GLY (10 mg/kg, oral).

Females in the Proestro phase were mated with male rats. After confirmation of pregnancy through vaginal ointment, CPF and GLY were administered orally daily. At the end of gestation (21 days), a retroorbital blood sample was taken from the animals.

The body weight, gestational age, biochemical markers of the fetus (glucose, triglycerides, total cholesterol, SGOT, SGPT) and morphometric parameters (body weight, coronary-sacral length, eye length and width, leg length) are analyzed. In the groups exposed to CPF and GLY, significant changes were observed in the following biochemical markers compared to the control group: increased glucose levels; a significant increase in triglyceride and cholesterol levels; Increased levels of the enzymes CGOT and CGPT exhibited a toxic effect on the liver.

In newborn rats, the following changes were noted compared to the control group: decreased body weight and corono-sacral length; reduced eye length and width; shortened length of hind and hind limbs.

In offspring exposed to pesticides, the following anomalies were observed: microcephaly, microtsia, micromelia, dysmorphogenesis; hemorrhages in the abdominal cavity and spinal cord; In rats of the CPF group, wave-like ribs, curved spinal cord, and skeletal malformations were observed.

The results of this study showed that the pesticides CPF and GLY have a teratogenic effect on pregnant rats and their offspring. Biochemical changes are associated with metabolic disorders, while morphometric and morphological disorders indicate serious developmental problems. These effects may have been due to impaired placental function, oxygen deficiency, and oxidative stress. In vitro studies of GLY's effect on human placental cells have shown that it inhibits the activity of the aromathase enzyme, which negatively affects the balance of pregnancy and sex hormones [6]. This situation indicates that GLY can pose a direct threat to the human reproductive system. The gestational effect of the pesticides CPF and GLY causes serious disorders in fetal growth and development. Their teratogenic effect manifests itself at the morphological, skeletal, and biochemical levels. These results show that pesticide contamination poses a threat not only to the mother's body, but also to the health of the developing generation. Therefore, minimizing the effects of pesticides during pregnancy and lactation is important from an ecological and health perspective.

Insecticides are among the most widely used pesticides in the world. They are used not only in agriculture, but also in the domestic, industrial, and veterinary spheres. Neonicotinoids belong to the class of modern insecticides and are widespread due to their selective effect, high toxicity to insects, and relatively low danger to mammals.

Imidacloprid (IMI) is the most commonly produced neonicotinoid, which binds to nicotine-containing acetylcholine receptors (nAChR) in a manner similar to nicotine. Nevertheless, the accumulation of IMI in soil, water, and food products poses a threat to the environment and human health. Although IMI is assessed as low toxicity, many studies have identified its hepatotoxic, nephrotoxic, neurotoxic, immunotoxic, and genotoxic effects [3].

IMI toxicity is mainly caused by free radicals and oxidizing metabolites. This leads to lipid peroxidation and a decrease in the level of antioxidant enzymes. However, the available scientific data on its teratogenic properties are still limited.

In their studies, such Egyptian scientists as Nermeen Borai El-Borai, Seham Said Hadad, and Hanem Kamal Khalifa assessed the teratogenic effects and the mechanical role of oxidative stress in this process, arising from the exposure of pregnant rats to two doses of IMI (45 and 90 mg/kg). Fifteen pregnant rats were randomly divided into three groups (control, low dose - LD-IMI, high dose - HD-IMI) and the substance was administered orally daily during organogenesis (6-15 days of pregnancy). All animals were sent for laboratory analysis on the 20th day. In the high-dose group, a significant increase in the percentage of fetal resorption, as well as a decrease

in the mass of the fetus and placenta, was revealed [7]. External morphological defects were observed only in fetuses treated with high doses, while internal (visceral) anomalies were observed in both doses. The levels of oxidative stress markers - MDA, GSH, H₂O₂, and SOD activity - changed significantly. Signs of oxidative liver damage in the mother, placenta, and fetus were detected, especially as a result of high-dose IMI exposure [7]. The results showed that high doses of IMI have a teratogenic effect at the organogenesis stage, which is mainly due to oxidative stress. This study is aimed at determining the teratogenic effect of IMI and the mechanical role of oxidative stress in this effect. The study aimed to determine the mechanisms of IMI in pregnant rats with low and high doses, leading to oxidative lesions in the tissues of the mother and fetus.

At a high dose of IMI:

- The percentage of resorption increased sharply;
- Decreased fetal and placental weight;
- Morphological and skeletal anomalies were observed;
- An increase in biomarkers of oxidative stress (MDA, H₂O₂), a decrease in the activity of GSH and SOD;

Severe oxidative injuries were observed in the fetal liver and placenta [7].

These cases indicate that IMI occurred as a result of transplacental (placental) transmission.

The study proved that IMI, especially at high doses, exhibits teratogenic properties in pregnant rats. These effects are associated with increased oxidative stress and damage observed in the tissues of the fetus and placenta. Thus, the teratogenic effect of IMI is realized through its transplacental passage, an increase in the production of ROS, and a weakening of the antioxidant defense system. This circumstance indicates the importance of antioxidant therapy, in particular, as a strategy of pharmacological protection for pregnant women exposed to IMI and other neonicotinoid insecticides.

The results of the conducted research have proven that pesticides - chlorpyrifos (CPF), glyphosate (GLY), and imidacloprid (IMI) - pose a serious threat not only to the maternal organism, but also to the health of the fetus and subsequent generations [1, 7]. They cause pathologies such as changes in biochemical parameters during the sensitive period of pregnancy, exacerbation of oxidative stress, delayed embryonic development, and skeletal malformations. In particular, impaired placental function and transplacental transfer of pesticides to the fetus increase their teratogenicity.

The harmful effects of pesticides are not limited to biological organisms - they also have a profound and multifaceted negative impact on the environment. For example:

- Negatively affects the composition of beneficial microorganisms in the soil, reduces soil fertility, and hinders the nitrogen cycle and decomposition of organic matter.
- Pesticides washed into water bodies have a toxic effect on aquatic organisms, especially plankton, fish, and amphibians, reducing their populations and leading to disruptions in the food chain.
- Non-insectively selective pesticides, especially neonicotinoids, reduce pollinating bee populations. This, in turn, negatively affects the balance of the ecosystem and agricultural productivity.
- Pesticides with persistent organic pollutant properties (e.g., CPF) persist in the environment for a long time and re-enter the human body through water, air, and the food chain, increasing the risk of cumulative poisoning.

Thus, the biological and environmental hazard of these pesticides indicates the need to develop their safe alternatives. To protect the ecosystem, preserve biodiversity, and protect human health, the transition to pest management systems based on biological, mechanical, or agroecological methods instead of chemical pesticides is a pressing task.

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