UDC 636.09:599.323.4:616.6:615.282 doi: https://doi.org/10.15407/ubj97.01.044

FATTY ACIDS COMPOSITION OF KIDNEYS UNDER RAT EXPOSURE TO FUNGICIDES

S. V. KHYZHNYAK✉, S. V. MIDYK, O. B. DOVBYSH, V. I. KORNIYENKO

National University of Life and Environmental Sciences of Ukraine, Kyiv;
✉e-mail: khyzhnyaks@gmail.com

Received: 08 August 2024; **Revised:** 10 December 2024; **Accepted:** 21 February 2025

Most fungicides belong to the class of triazoles, of which tebuconazole and triadimefon are the most commonly used. Exposure to pesticides is accompanied by negative consequences for vertebrates and humans. However, the potential toxicity of fungicides is not well understood. The aim of the study was to estimate the fatty acids (FAs) composition of kidney total lipids after exposure of Wistar han rats to two fungicide preparations, one containing tebuconazole alone, the other tebuconazole + triadimephone. Animals were administered a single oral dose of fungicides (600 and 1200 mg/kg). After 14 days, the animals were decapitated and kidneys were used in the studies. FAs methyl esters were determined on a Trace GC Ultra gas chromatograph (USA) with the flame ionization detector. No qualitative changes in the FAs profile of the total kidney lipids after fungicides administration as compared to the control were detected, but the redistribution in the content of individual FAs was observed. The relative content of saturated fatty acids increased, while that of monounsaturated fatty acids, in particular oleic acid (C18:1ω9), decreased. An increase in the content of long-chain polyunsaturated fatty acids, in particular docosahexaenoic (C22:6ω3) and arachidonic (C20:4ω6) acids, as well as the value of the ratio ω3/ω6, was revealed. The effect of the combined fungicides was found to be more pronounced. The results indicate metabolic shift in the FAs profile of total kidney lipids in the dynamics after exposure to fungicides.

K e y w o r d s: fungicides, tebuconazole, triadimefon, monounsaturated and polyunsaturated fatty acids, rat kidneys.

The intensive introduction of chemical agents into all spheres of human activity creates risks for human health and the environment. One such factor is pesticides (a group of chemicals) widely used in agriculture to improve the quality and yield of crops. However, despite the benefits, the use of pesticides is accompanied by many negative consequences for humans and the environment [1].

Most pesticides used worldwide, especially in Europe, are fungicides, particularly triazole compounds. An effective systemic fungicide belonging to triazoles, tebuconazole, is widely used in both agriculture and medicine to control fungal diseases. Tebuconazole is often found at elevated concentrations in the environment. This makes it important to study the potential toxicity of tebuconazole to vertebrates and humans.

The toxic effect of fungicides is related to the processes of absorption and metabolism of substances in the body. In an unfavorable environment, leading to the entry of toxic substances into the body, their influence on cellular processes is possible, which causes a disruption of the structural and functional activity of membranes, lipid metabolism, etc.

It has been noted that tebuconazole-induced liver dysfunction may be associated with damage to the antioxidant defense system [2]. The cardiotoxicity of tebuconazole has also been reported (biochemical indicators, apoptosis induction and DNA damage in heart tissue) [3].

Dose-dependent morphological features of intoxication were established in rats orally treated with tebuconazole. The effect of the drug was accompanied by dystrophic changes in hepatocytes, damage to the renal tubular epithelium, as well as microcirculatory disorders in the adrenal glands [4].

Although there is no doubt that tebuconazole is toxic to the liver and kidneys, there is insufficient information on the effects of tebuconazole on the lipid component of cells. In particular, the accumulation of tebuconazole in HepG2 cells and its effect

on lipid metabolism were studied. It has been found that tebuconazole can induce lipid accumulation by altering the expression of lipid-metabolizing molecules [5].

Therefore, studying the tissue lipid component is promising, particularly under the action of various tebuconazole formulations. The chemical composition of lipids in animal tissues, the quantitative and qualitative composition of their fatty acids (FAs) play a leading role in the course of various processes in cells. The reorganization of the membrane lipid composition in response to changes in the content and ratio of FAs is aimed at optimizing the conditions for maintaining the functional activity of intracellular organelles and cells as a whole. It was found in our previous studies [6] that exposure to fungicides containing tebuconazole alone or in combination with triadimefon resulted in a redistribution of the FAs profile of total lipids in rat liver. Thus, studying the role of lipid FAs in tissues is important for understanding the biochemical mechanisms of adverse effects of pesticides on mammals.

The aim of the work is to study the fatty acid composition of total lipids in rat kidney tissue under single exposure to fungicides – triazole derivatives containing tebuconazole in individual and binary combinations.

Materials and Methods

In the studies, female Wistar Han rats weighing 210-240 g were kept under standard vivarium conditions of the State Institution "Institute of Occupational Medicine of the National Academy of Medical Sciences of Ukraine" under appropriate temperature and light conditions. Rats were divided into control and four experimental groups of 6 animals each. Animals were administered a single oral dose of 600 mg/kg (Groups I and III) and 1200 mg/kg (Groups II and IV) via probe of an aqueous emulsion of the corresponding pesticide formulations. After 14 days, the animals were decapitated under light anesthesia; kidneys were used in the studies. Animal manipulations were carried out following the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986), according to the general ethical principles of animal experiments adopted by the First National Congress of Ukraine on Bioethics (2001).

In our research, we studied systemic fungicides used on crops in Ukraine in the formulation of emulsifiable concentrate which contain the active ingredients in stock solution: two-component fungicide with concentration of tebuconazole, 125 g/l + triadimefon, 100 g/l (Groups I and II) and single-component fungicide with tebuconazole, concentration 250 g/l (Groups III and IV).

The active ingredients belong to the chemical class triazole. When choosing the used doses, it was taken into account that the LD_{50} value, calculated according to [7] for the investigated fungicides, exceeds 2500 mg/kg.

Rat kidneys were homogenized in the cold in a Potter-Elvehjem homogenizer in isotonic saline (1:1, w/v) [8]. Further extraction of lipids was carried out with a chloroform-methanol mixture (2:1, v/v) [9]. The lipid extract was transferred to glass vials with a tight lid, and a 3-fold normal solution of hydrochloric acid in methanol was added. The vials were placed in a boiling water bath "GFL-1002" (Germany) and hydrolysis was carried out for 60 min. Then the reaction mixture was cooled to room temperature. FAs methyl esters were extracted from the reaction mixture with hexane [10] and analyzed on a gas chromatograph "Trace GC Ultra" (Thermo Scientific, USA), which is equipped with a flame-ionization detector, an injector with temperature programming and a high-polar capillary column SPTM-2560 (Supelco, USA), 100 m long, 0.25 mm inner diameter and 0.20 μm thickness of the stationary phase.

Chromatographic conditions: 1 μl samples were injected into the chromatograph using a TriPlus autosampler, injection type – split; carrier gas type – helium, flow rate – 2.1 ml/min, flow mode – constant flow. Temperature program for the GC oven: initial temperature – 140°C, Hold time (min) – 5.00; Ramp 1: Rate (C/min) – 2.0, at 240°C, Hold Time (min) – 10.00; Oven Run-Time (min) – 65.00. Prep Run Timeout (min) – 10.00. Equilibration Time (min) – 0.50. Injector temperature – 260°C, split flow (ml/min) – 52, split ratio – 25.

A flame ionization detector (FID), Thermo Fisher Scientific, was used. Description of the detector settings: base temperature – 260°C, Ignition Threshold (pA) – 0.5.

Fatty acids were identified using a Supelco 37 Component FAME Mix standard (USA). To quantify individual FAs, the method of internal normalization was used, and the relative content of FAs was expressed as a percentage of their total amount [11]. The total quantities of saturated fatty acids (SFAs), unsaturated fatty acids (UFAs), monounsaturated fatty acids (MUFAs), polyunsaturated

fatty acids (PUFAs), FAs of the ω3 and ω6 families were calculated. The activity of acyl-lipid desaturases was evaluated by the ratio of fatty acids: C22:6ω3/C18:3ω3 (acyl-lipid Δ3-desaturase activity) and C20:4ω6/C18:2ω6 (acyl-lipid Δ6-desaturase activity).

Statistical processing of the obtained results was performed according to the analysis of variance (ANOVA). The data in the Tables are presented in the form of m ± SD (mean ± standard deviation). The difference between the values in the groups was determined using the Tukey test and was considered significant at $P < 0.005$ (taking into account the Bonferroni correction).

Results

Chromatograms of FAs of total lipids from rat renal tissue were obtained in our research. In the studied samples, 21 short-, medium-, and long-chain FAs with carbon chain length from C10 to C22 were identified. The main FAs and their relative content in total lipids of rat kidneys are shown in Table 1. Minor components, the content of which does not exceed 0.1%, are not presented in the table. SFAs are mainly presented by palmitic (C16:0) and stearic (C18:0) acids, which are precursors of long-chain fatty acids. UFAs are heterogeneous, in particular, palmitoleic (C16:1) and oleic (C18:1ω9) have one saturated bond each, and such as arachidonic (C20:4ω6), eicosapentaenoic (20:5ω3) and docosahexaenoic (C22:6ω3) are polyunsaturated.

Under conditions of single exposure to fungicides, the FAs composition of the total lipids in rat kidney tissue did not differ from the control; however, redistribution in the content of individual FAs was observed (Table 1).

Analysis of the FAs profile indicates that total content of SFAs increases and total content of UFAs decreased significantly relative to the control. Saturation index SFAs/UFAs, which in the control was 0.39, increased 1.2-1.3 times under experimental conditions (Table 2).

The increase in the total content of SFA is probably due to an increase in the level of stearic acid (C18:0), on average by 60% (Groups I and II) and 40% (Groups III and IV) compared to the con-

Table 1. Content of fatty acids in total lipids of rat kidneys under a single oral administration of fungicides (% of the total fatty acid content, m ± SD)

Fatty acid	Control	Group I	Group II	Group III	Group IV
C14:0 Myristic acid	0.92 ± 0.02^{a}	0.61 ± 0.03^{b}	0.67 ± 0.04^{b}	0.70 ± 0.04^{b}	0.67 ± 0.06^{b}
C15:0 Pentadecanoic acid	0.36 ± 0.02^{a}	0.30 ± 0.03^{ab}	0.22 ± 0.02^{c}	0.27 ± 0.03^{bc}	0.21 ± 0.02^{c}
C16:0 Palmitic acid	18.52 ± 0.28^{a}	19.42 ± 0.37^{ab}	20.00 ± 0.25^{bc}	19.85 ± 0.27^{bc}	20.66 ± 0.47^{c}
C16:1 Palmitoleic acid	1.93 ± 0.03^{a}	1.08 ± 0.03^{b}	1.42 ± 0.04^{c}	1.38 ± 0.06^{c}	1.64 ± 0.15^{d}
C18:0 Stearic acid	7.19 ± 0.16^{a}	11.19 ± 0.20^{b}	11.97 ± 0.13^{c}	10.02 ± 0.18^{d}	9.93 ± 0.05^{d}
C18:1ω9 Oleic acid	28.48 ± 0.18^{a}	21.47 ± 0.28^{b}	18.75 ± 0.23^{c}	24.76 ± 0.15^{d}	25.43 ± 0.31^{d}
C18:2ω6 Linoleic acid	30.73 ± 0.06^{a}	24.37 ± 0.15^{b}	23.69 ± 0.18^{c}	25.84 ± 0.18^{d}	25.26 ± 0.11^{d}
C20:1ω9 Gondoic acid	0.53 ± 0.02^{a}	0.39 ± 0.04^{b}	0.37 ± 0.04^{b}	0.44 ± 0.03^{bc}	0.45 ± 0.03^{bc}
C18:3ω3 Linolenic acid	0.85 ± 0.04^{a}	0.76 ± 0.04^{ac}	0.64 ± 0.04^{b}	0.70 ± 0.03^{bc}	0.69 ± 0.04^{bc}
C21:0 Heneicosanoic acid	0.56 ± 0.03^{a}	0.40 ± 0.03^{b}	0.42 ± 0.04^{b}	0.48 ± 0.05^{b}	0.45 ± 0.02^{b}
C22:0 Behenic acid	0.27 ± 0.02^{a}	0.34 ± 0.03^{b}	0.33 ± 0.03^{b}	0.32 ± 0.03^{b}	0.25 ± 0.01^{a}
C20:3ω6 Eicosatrienic acid	0.28 ± 0.02^{a}	0.53 ± 0.04^{b}	0.58 ± 0.04^{b}	0.48 ± 0.07^{b}	0.49 ± 0.04^{b}
C20:4ω6 Arachidonic acid	7.48 ± 0.10^{a}	16.20 ± 0.13^{b}	17.74 ± 0.16^{c}	12.30 ± 0.90^{d}	12.51 ± 0.12^{d}
C20:5ω3 Eicosapentaenoic acid	0.24 ± 0.04^{a}	0.45 ± 0.04^{b}	0.41 ± 0.03^{b}	0.40 ± 0.03^{b}	0.46 ± 0.02^{b}
C22:6ω3 Docosahexaenoic acid	1.28 ± 0.02^{a}	2.07 ± 0.04^{b}	2.34 ± 0.05^{c}	1.69 ± 0.05^{d}	2.05 ± 0.08^{b}

Note. This and the following tables show a single action of a fungicide with a concentration of tebuconazole 125 g/l + triadimefon 100 g/l at doses of 600 mg/kg (Group I) and 1200 mg/kg (Group II) and a fungicide with a concentration of tebuconazole 250 g/l at doses of 600 mg/kg (Group III) and 1200 mg/kg (Group IV). Data are presented as the mass fraction of fatty acid in % of total fatty acids. Different superscript letters indicate values that differ significantly one from another within one line of the table by comparison using Tukey test with Bonferroni correction

trol (Table 1). Significant differences were found between the effects of tebuconazole in combination with triadimefon (Groups I and II) and individual tebuconazole (Groups III and IV) in the content of stearic (C18:0), oleic (C18:1 ω9), linoleic (C18:2ω6) and arachidonic (C20:4ω6) acids.

Under the experimental conditions, a decrease in the content of individual MUFAs was established, which led to a decrease in the content of the total MUFAs (Table 2): in Groups I and II by 26% and 34%; in Groups III and IV by 14 and 11%, respectively. This may be due to a decrease in the content of oleic acid (C18:1ω9), which in Groups I and II was 25 and 34%, respectively; in Groups III and IV – an average of 14% (Table 1). At the same time, similar patterns in the studied groups are observed for the palmitoleic (C16:1) and gondoic (C20:1ω9) acids. Considering that MUFAs have antioxidant properties [12], changes in their content may affect oxidative processes under the action of fungicides.

PUFAs predominate among UFAs, which total content increases in Groups I and II relative to the control (Table 2). FAs of the ω6 and ω3 families are the most physiologically important for the animal organism and act as endogenous bioregulators [13, 14]. The ω3/ω6 ratio, which characterizes the direction of fatty acid metabolism [15], increases in all experimental groups (Table 2).

As for the ω6 PUFAs, their total content increases under experimental conditions in Groups I and II compared to the control (Table 2). At the same time, the relative content of linoleic acid (C18:2ω6) decreases by 21–23% in Groups I and II; in Groups III and IV – by an average of 16%. Simultaneously, the relative content of arachidonic acid (C20:4ω6) increases: for Groups I and II, on average, by 2.2–2.4 times, for Groups III and IV, on average, by 66%. Thus, under the combined action of tebuconazole and triadimefon, the level of arachidonic acid (C20:4ω6) is significantly higher compared to the individual action of tebuconazole (Table 1).

At the same time, the C20:4ω6/C18:2ω6 ratio, which reflects the level of metabolism of FAs of the ω6 family, increases 3 times in Groups I and II; 2 times in Groups III and IV under the experimental conditions (Table 2).

The total content of ω3 PUFAs increases by 38 and 42% in Groups I and II and by 17 and 33% in Groups III and IV, respectively. A significant increase in the content of long-chain fatty acids of the ω3 family was detected under the experimental conditions. In particular, the level of eicosapentaenoic acid (C20:5ω3) increased in Groups I and II by 88 and 71%; in Groups III and IV – by 67 and 92% respectively, relative to the control; the level of docosahexaenoic acid (C22:6ω3) increased by 62 and 83% in Groups I and II; by 32 and 60% in Groups III and IV, respectively, against control (Table 1).

These acids, in particular, are characterized by the function of an adaptive stabilizer of lipid bilayers

Table 2. The level of fatty acids saturation in total lipids of rat kidneys after a single exposure to fungicides (%, m ± SD)

ΣFAs	Control	Group I	Group II	Group III	Group IV
ΣSFAs	28.00 ± 0.28^{a}	32.30 ± 0.52^{b}	33.60 ± 0.26^{c}	31.60 ± 0.19^{b}	32.20 ± 0.58^{b}
ΣUFAs	72.00 ± 0.14^{a}	67.30 ± 0.32^{b}	66.00 ± 0.46^{c}	68.00 ± 0.51^{b}	69.00 ± 0.42^{b}
SFAs/UFAs	0.39 ± 0.01^{a}	0.48 ± 0.01^{b}	0.51 ± 0.01^{c}	0.47 ± 0.01^{b}	0.47 ± 0.01^{b}
ΣMUFAs	31.00 ± 0.06^{a}	23.00 ± 0.34^{b}	20.54 ± 0.20^{c}	26.60 ± 0.19^{d}	27.40 ± 0.20^{d}
ΣPUFAs	41.00 ± 0.03^{a}	44.40 ± 0.16^{b}	45.40 ± 0.32^{c}	41.40 ± 0.33^{a}	41.30 ± 0.25^{a}
Σω6	38.50 ± 0.11^{a}	41.10 ± 0.20^{b}	42.00 ± 0.23^{c}	38.60 ± 0.26^{a}	38.10 ± 0.22^{a}
Σω3	2.40 ± 0.09^{a}	3.30 ± 0.08^{b}	3.40 ± 0.10^{b}	2.80 ± 0.08^{c}	3.20 ± 0.05^{b}
Σω3/Σω6	0.06 ± 0.01^{a}	0.08 ± 0.01^{b}	0.08 ± 0.01^{b}	0.07 ± 0.01^{c}	0.08 ± 0.01^{b}
C20:4ω6/ C18:2ω6	0.24 ± 0.01^{a}	0.66 ± 0.01^{b}	0.75 ± 0.01^{c}	0.48 ± 0.01^{d}	0.50 ± 0.01^{e}
C22:6ω3/ C18:3ω3	1.50 ± 0.05^{a}	2.70 ± 0.19^{b}	3.70 ± 0.13^{c}	2.40 ± 0.08^{b}	3.00 ± 0.30^{bc}

Note. See Table 1; SFAs – saturated fatty acids, UFAs – unsaturated fatty acids, MUFAs – monounsaturated fatty acids, PUFAs –polyunsaturated fatty acids

of cell membranes [11, 16]. Namely, PUFAs of the ω3 family, which have high metabolic activity, participate in the formation of the phospholipid bilayer of cell membranes [16]. At the same time, the content of linolenic acid (C18:3ω3), which is a precursor of long-chain biologically active acids of the ω3 family, decreases (mostly at the maximum dose of fungicides 1200 mg/kg) by 25 and 19% in Groups II and IV, respectively. Under these conditions, the ratio of C22:6ω3/C18:3ω3, which reflects the level of metabolism ω3 FAs family, increases 2.5 and 2.0 times in groups II and IV.

Thus, variability in the FAs profile of rat kidney lipids in the dynamics after a single exposure to triazole fungicides was revealed.

Discussion

The FAs composition of total rat kidney lipids was studied under the single action of fungicides – triazole derivatives containing tebuconazole in individual and binary combinations with triadimefon. The FAs profile of the total kidney lipids in dynamics after exposure did not qualitatively differ from the control. However, there was a redistribution in the content of individual FAs, which was most pronounced for the combined fungicide.

In the period after a single exposure of rats to a fungicide, an increase in the content of SFAs, mainly due to an increase in the level of stearic acid (C18:0), as well as a decrease in the total content of UFAs, caused an increase in the saturation of FAs in total lipids. This can affect the elasticity of cell membranes and disrupt their functional activity, and, in general, aggravate the course of the pathological process. Moreover, the effect of tebuconazole in combination with triadimefon (Group II) was greater compared to individual tebuconazole (Group IV).

The observed decrease in the content of individual MUFAs was predominant under the action of the combined fungicide. Considering that MUFAs have antioxidant properties [12], changes in their content might affect the course of oxidative processes in cells.

The greatest changes due to the action of fungicides are related to the redistribution in the content of physiologically important PUFAs of the ω6 and ω3 families, which are synthesized in many tissues in response to extracellular signals or inflammatory reactions and determine a wide range of adaptive properties of the organism [13, 14]. In particular, modification of the FAs composition of phospholipids affects the physicochemical and functional properties of cell membranes. It was shown that the increase in the total content of ω3 FAs under experimental conditions occurs due to an increase in the content of eicosapentaenoic (C20:5ω3) and docosahexaenoic (C22:6ω3) acids. Moreover, under the influence of the combined fungicide (tebuconazole in combination with triadimefon) compared to tebuconazole alone, the increase in the total content of FAs of the ω6 family prevails, which is due to the increase in the content of arachidonic acid (C20:4ω6). The observed modulation of the content of FAs of the ω3 and ω6 families may be due to the enhancement of the processes of desaturation and elongation of FAs [17].

In this case, it is necessary to take into account the closely related metabolism of ω3 and ω6 FAs, which exhibit a competitive effect in the body of animals. PUFAs are precursors of biologically active substances, in particular eicosanoids, which are highly active regulators of cellular functions that affect cellular metabolism [15]. Derivatives of ω6 FAs are some thromboxanes, leukotrienes, which increase the permeability of membranes and cause inflammatory phenomena. Metabolites of ω3 PUFAs, which are antiplatelet, anti-inflammatory substances, contribute to the stabilization of membranes [14]. The increase in the ratio of anti-inflammatory ω3 PUFAs to pro-inflammatory ω6 PUFAs observed under the experimental conditions can characterize the direction of cellular FAs metabolism in the dynamics after the fungicidal load on animals. At the same time, there is an accumulation of arachidonic acid (C20:4ω6), which is an essential fatty acid of the ω6 family and the main substrate for the synthesis of eicosanoids. Among other reasons, this increase may be due to impaired interaction of FAs with membrane protein complexes, exo- and endocytosis proteins due to their modification under the influence of fungicides, which in turn may lead to an increase in the content of prostaglandins in cells. However, the content of docosahexaenoic acid (C22:6ω3), which blocks prostaglandin cyclooxygenase, also increases [13].

Thus, as a result of oral administration of fungicides (triazole derivatives) in the indicated doses, it can be assumed that after single exposure in dynamics up to 14 days, the development of inflammatory, destructive changes is likely in parallel with restorative-adaptive or compensatory processes in kidney cells. We noted clinical signs of toxic effects

of the studied fungicides in the first 2 days after their administration in doses of 600 and 1200 mg/kg [6]. In addition, morphological signs of hepatocyte dystrophy and damage to the renal tubular epithelium were shown in female rats intoxicated with tebuconazole in a wide range of doses [4]. It can be assumed that the detected variability of the FAs profile is causally related to changes in FAs metabolism in lipids of kidney tissues in the dynamics after exposure to fungicides.

It should be noted that in the dynamics after fungicide loading on animals, changes in the content of MUFAs and PUFAs indicate a more intense effect of the fungicide containing tebuconazole in combination with triadimefon (Groups I and II). It is also important to emphasize the changes in the relative content of FAs of ω3 and ω6 families, which, being endogenous bioregulators, participate in destructive and inflammatory/pro-inflammatory processes. The possibility of the combined effect of these triazole compounds was indicated earlier in the study of the FAs profile of earthworm lipids [18].

Studying the role of FAs in tissue lipids is necessary to understand how pesticides act on the organism of mammals and search for ways to protect and renew the tissue lipid composition under these conditions. At the same time, the intensity of renewal will depend on the amount of exogenous supply of MUFAs and PUFAs (in particular, ω3) to normalize the FAs profile of total tissue lipids.

The authors confirm that the research and publication of the results were not associated with any conflicts regarding commercial or financial relations, relations with organizations and/or individuals who may have been related to the study, and interrelations of co-authors of the article.

Conflict of interest. The authors have completed the Unified Conflicts of Interest form at http://ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

Funding. The research was carried out within the framework of scientific research work (SRW) No. of state state registration number 0120U102130, funded by the Ministry of Education and Science of Ukraine.

ЖИРНОКИСЛОТНИЙ СКЛАД НИРОК ЗА ВПЛИВУ ФУНГІЦИДІВ НА ЩУРІВ

С. В. Хижняк✉, С. В. Мідик, О. В. Довбиш, В. І. Корнієнко

Національний університет біоресурсів і природокористування України, Київ;
✉e-mail: khyzhnyaks@gmail.com

Значна частина фунгіцидів належать до класу триазолів, серед яких найчастіше застосовуються тебуконазол і триадимефон. Проте вплив фунгіцидів супроводжується недостатньо вивченою потенційною токсичністю та негативними наслідками для хребетних, зокрема і людини. Метою дослідження було оцінити склад жирних кислот (ЖК) загальних ліпідів нирок щурів Wistar Han після впливу двох препаратів фунгіцидів: один містив тебуконазол, інший – тебуконазол + триадимефон. Тваринам одноразово перорально вводили фунгіциди в дозах 600 і 1200 мг/кг. Через 14 днів тварин піддавали декапітації, а у дослідженнях використовували нирки. Метилові етери ЖК визначали на газовому хроматографі Trace GC Ultra (США) з полум'яно-іонізаційним детектором. Після застосування фунгіцидів якісних змін у профілі ЖК загальних ліпідів нирок порівняно з контролем не виявлено, але спостерігався перерозподіл вмісту окремих ЖК. Відносний вміст насичених жирних кислот підвищувався, а мононенасичених жирних кислот, зокрема олеїнової (C18:1ω9), зменшувався. Встановлено підвищення як вмісту довголанцюгових поліненасичених жирних кислот, зокрема докозагексаєнової (C22:6ω3) та арахідонової (C20:4ω6), так і величини співвідношення ω3/ω6. Вплив комбінованих фунгіцидів був більш виражений. Отримані результати вказують на метаболічні зрушення ЖК профілю загальних ліпідів тканини нирок у динаміці за дії фунгіцидів.

Ключові слова: фунгіциди, тебуконазол, триадимефон, мононенасичені та поліненасичені жирні кислоти, щури, нирки.

References

1. Ahmad MF, Ahmad FA, Alsayegh AA, Zeyaullah M, AlShahrani AM, Muzammil K, Saati AA, Wahab S, Elbendary EY, Kambal N, Abdelrahman MH, Hussain S. Pesticides impacts on human health and the environment with their mechanisms of action and possible countermeasures. *Heliyon*. 2024; 10(7): e29128.
2. Ku T, Zhou M, Hou Y, Xie Y, Li G, Sang N. Tebuconazole induces liver injury coupled with ROS-mediated hepatic metabolism disorder. *Ecotoxicol Environ Saf.* 2021; 220: 112309.
3. Ben Othmène Y, Hamdi H, Annabi E, Amara I, Ben Salem I, Neffati F, Najjar MF, Abid-Essefi S. Tebuconazole induced cardiotoxicity in male adult rat. *Food Chem Toxicol*. 2020; 137: 111134.
4. Kornuta NO, Reshavskaya OV. Morphological research in the study of the effects of pesticides on the body of pregnant females and fetal development. *Bull Probl Biol Med*. 2011; 2(2): 132-135.
5. Kwon HC, Kim DH, Jeong CH, Kim YJ, Han JH, Lim SJ, Shin DM, Kim DW, Han SG. Tebuconazole Fungicide Induces Lipid Accumulation and Oxidative Stress in HepG2 Cells. *Foods*. 2021; 10(10): 2242.
6. Khyzhnyak SV, Midyk SV, Velinska AO, Arnauta OA, Kalachniuk LH. Fatty acid profile of the liver lipids under acute fungicide action and intake of a biologically active preparation in rats. *Ukr Biochem J*. 2022; 94(4): 47-53.
7. Backhaus T, Faust M. Predictive environmental risk assessment of chemical mixtures: a conceptual framework. *Environ Sci Technol.* 2012; 46(5): 2564-2573.
8. Vlislo VV, Fedoruk RC, Ratych IB. Laboratory research methods in biology, animal husbandry and veterinary medicine: Handbook. Lviv: CPOLOM, 2012. 764 p.
9. Folch J, Lees M, Sloane Stanley GH. A simple method for the isolation and purification of total lipides from animal tissues. *J Biol Chem.* 1957; 226(1): 497-509.
10. Christie WW. Lipid Analysis: isolation, separation, identification and structural analysis of lipids. 2nd edn. Oxford: Pergamon Press, 1982. 207 p.
11. Animal and vegetable fats and oils – Gas chromatography of fatty acid methyl esters. Part 1: Guidelines on modern gas chromatography of fatty acid methyl esters ISO 12966-4:2014.
12. Perona JS, Arcemis C, Ruiz-Gutierrez V, Catalá A. Effect of dietary high-oleic-acid oils that are rich in antioxidants on microsomal lipid peroxidation in rats. *J Agric Food Chem.* 2005; 53(3): 730-735.
13. Smolyaninov KB, Paranyak RP, Yanovich VG. Biological role of polyunsaturated fatty acids. *Animal Biology*. 2002; 4(1–2): 16-31.
14. Kang JX. The importance of omega-6/omega-3 fatty acid ratio in cell function. The gene transfer of omega-3 fatty acid desaturase. *World Rev Nutr Diet.* 2003; 92: 23-36.
15. Canbay A, Bechmann L, Gerken G. Lipid metabolism in the liver. *Z Gastroenterol.* 2007;45(1):35-41.
16. de Roos B, Mavrommatis Y, Brouwer IA. Long-chain n-3 polyunsaturated fatty acids: new insights into mechanisms relating to inflammation and coronary heart disease. *Br J Pharmacol*. 2009; 158(2): 413-428.
17. Los DA, Murata N. Membrane fluidity and its roles in the perception of environmental signals. *Biochim Biophys Acta.* 2004; 1666(1-2): 142-157.
18. Khyzhnyak S, Midyk S, Polishchuk S, Velinskaya A. Effect of triazole fungicides on fatty acid content in *Eisenia fetida*. *Pol J Natur Sci*. 2020; 35(3): 275-286.