1. Introduction

It is known that the most of vegetable crops are almost impossible to grow without protective measures. Scientists convinced, that, using the necessary amount of pesticides, the farmer could potentially save from 1 hectare of field around 95 centners of sugar beet, 40 centners of potato and 15 centners of fruits [1, 2]. This is one of the reasons for the annual expansion of the pesticides and agrochemicals assortment, a large part in the structure of which takes fungicides formulations used on vegetable crops [3]. However, the presence of pesticide active substances residual amounts in food and raw materials can lead to violations in the health of consumers [4, 5].

In Ukraine, the maximum allowable level is calculated based on the value of residues in harvests of agricultural crops, acceptable daily dose, risk assessment considering acceptable daily intake and daily real intake from all crops in which the substance is registered [6]. In other European countries [7, 8], Canada [9], USA [10], the value of residues in harvests of crops and estimated values of the relative risks in the results obtained are taking into account primarily.

That is why assessing the risk associated with the consumption of products containing pesticide residues is a vital and integral part of regulatory processes.

Aim of research: forecasting and comparative estimation of hazard to a person at consumption of agricultural products contaminated with triazole, amide, piperidinyl, thiazole, isoxazoline and oxazole classes of fungicides.

FORECASTING OF TRIAZOLE, AMIDE, PIPEREDINYLE THIAZOL ISOXAZOLINE, OXAZOLE FUNGICIDES HAZARDOUS EFFECT ON HUMAN HEALTH IN CONSUMPTION OF VEGETABLES GROWED IN THEIR APPLICATION

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Abstract: The chemical plant protection products application is an integral part of intensive crop production technologies. However, scientists have proven that the increase in chemical pollution of the environment in 2 times increases the general level of morbidity of the adult population by 25 %. That is why the risk assessment of pesticide-contaminated products consumption is an important part of the regulatory process.
Methods. The parameters of fungicides difenoconazole, tebuconazole, cyflufenamid, oxathiapiprolin, famoxadone persistence in agricultural crops were studied in the field experiments. For the integrated assessment of the potential risk of pesticide-contaminated products consumption for human (RPCPC), a methodology developed on the basis of the Institute of Hygiene and Ecology was used. The acceptable daily intake (ADI), the half-life period ($\tau 50$) in plants and the average daily consumption of the product have been evaluated using four-graded scale.
Results. According to the persistency in tomatoes and potatoes, fungicides difenoconazole, cyflufenamid, famoxadone are pertained to 3 classes of hazard (5–14 days); tebuconazole – to 2 class (15–30 days); oxathiapiprolin – to 4 class (less than 5 days). After the addition of all the obtained points, the RPCPC value (tomatoes and potatoes) for difenoconazole, cyflufenamid, famoxadone amounted 8 points ($2+2+2\times 2$ and $2+2+4$, respectively); tebuconazole – 8 points ($3+1+2\times2$ or $3+1+4$, respectively); oxathiapiprolin – 6 points ($1+1+2\times2$ or $1+1+4$, respectively).
Discussion. Thus, the studied compounds belong to the 3rd class of hazard according to pesticide-contaminated products consumption for human index value. The results obtained by us correlate with the studies carried out in the previous stage. The exception was only difenoconazole, which was classified as hazard class 2 due to its high toxicity for human.
Keywords: fungicide, daily food intake, vegetables, hazard, risk, food products contamination.

the harvest. For comparison, before the crop treatment, control samples of the vegetables were taken. In the control samples, the studied active substances were not detected.

Determination of the active ingredients (a. i.) content of in vegetables and green mass of plants was carried out using high-performance liquid (HPLC) and gas chromatography (GHG) methods.

In studying the behavior of the studied fungicides in agricultural crops, a mathematical modeling method was used to calculate the half-life (τ_{50}) and almost total destruction (τ_{95}) periods in the green mass of plants, which involves the estimated reproduction of pesticide destruction processes based on actual data, which allows predicting their persistence.

For the classification of substances according to studied pesticides persistency in plants (receiving from field experiments), the Ukrainian classification of pesticides by the degree of hazard was used [11]. This classification foresees the division of substances into 4 classes: 1 – highly persistent (τ_{50} more than 30 days), 2 – persistent (15–30 days), 3 – moderately persistent (5–14 days), 4 – not persistent (less than 5 days).

For the integrated assessment of the potential risk of pesticide-contaminated products consumption for human (RPCPC), a methodology developed on the basis of the Institute of Hygiene and Ecology was used. The acceptable daily intake (ADI), the half-life period (τ_{50}) in plants and the average daily consumption of the product have been evaluated using four-graded scale [12] (**Table 1**).

2. Methods

Fungicides of the following chemical classes were investigated: triazoles (difenoconazole, tebuconazole), amides (cyflufenamid), piperidinyl thiazole isoxazolines (oxathiapiprolin), oxazoles (famoxadone).

The parameters of studied fungicides persistence in agricultural crops were studied in the field experiments in soil and climatic conditions of Ukraine. During study we determined the actual content of the compounds in the vegetable crops. The samples were taken from the date of the last treatment and, after certain periods, 3-6 times during the growing season until

If the pesticide is used on different crops, its average daily consumptions are added and the total average daily consumption is estimated in points.

After adding all the points, the integral index of the potential risk of pesticide-contaminated products consumption (RPCPC) is evaluated as follows: if the value is 3–5 points – substance is hazardous for human (class 4), 6–8 – moderately hazardous (class 3), 9–11 – hazardous (class 2), 11–12 – extremely hazardous (class 1).

Statistical processing of the results was performed using the statistical suite of statistical software IBM SPSS StatisticsBase

v.22. The results are processed by the methods of variation statistics with the calculation of the arithmetic mean, mean square deviation. The reliability of the discrepancies (checking the hypothesis of the equality of the mean of two independent samples) is estimated according to the Student's t-criterion (with the Bonferroni correction) or non-parametric criteria in the case of a difference in the distribution of the normal distribution (Kruskal-Wallis). The adequacy of the developed techniques was evaluated by the correlation coefficient of coherence, the criterion of coherence and the Kronbach alpha.

Table 1

Scale of the potential risk of pesticide-contaminated products consumption for human (RPCPC) estimation

Index	Score (points), depends on index value			
	1	2	3	4
τ_{50} in plants, day[1]	<5	5–14	15–30	>30
ADI, mg/kg	>0.02	0.0051–0.02	0.002–0.005	≤0.002
average daily consumption of the product, g/day	<100	100–200	201–300	>300

Note: If the product is consumed raw or used as a baby food, the half-life period is doubled

3. Results

The results obtained in the course of field studies in different soil-climatic zones of Ukraine, and the use of the mathematical modeling method allowed to calculate the persistency parameters (τ_{50}) of the studied compounds in vegetative crops (vegetables) (**Table 2**).

The mathematical processing of the results obtained during a field study of the residual amounts of studied fungicides dynamics showed that the process of their degradation in agricultural crops was subject to exponential dependence.

Differences in the k, τ_{50} and τ_{95} values of the same class substances was not significant (p>0.05). This allowed us to calculate the averaged indices values for each class of fungicides. According to persistency in agricultural crops, tebuconazole is pertained to 2 class of hazard (moderately persistent), difenoconazole, cyflufenamide, oxathiapiproline – to 3 class (persistent), famoxadone – to 4 class of hazard (non-persistent) (**Table 3**).

After the addition of all the obtained points, the RPCPC value (tomatoes and potatoes) for difenoconazole, cyflufenamid, famoxadone amounted 8 points (2+2+2× 2 and 2+2+4, respectively); tebuconazole – 8 points (3+1+2×2 or 3+1+4, respectively); oxathiapiprolin – 6 points (1+1+2×2 or 1+1+4, respectively) (**Table 3**).

Table 2

Assessment of the risk of adverse effects of fungicides on human health when consuming vegetable products grown in their application

Chemical class	Active ingredient	ADI, mg/kg	Crop	Average daily consumption, g/day	Half-life period (τ_{50}), day M±m	M±m	Total daily consumption, g/day	RPCPC value	RPCPC class
Triazoles	tebuconazole	0.030	tomato	120	15.27±0.44	18.79±1.56	740	8 (1+4+3)	3
			cabbage	100	26.08±3.29				
			carrot	50	17.18±1.31				
			potato	470	16.64±2.01				
	difenoconazole	0.002	tomato*	120	11.39±0.84	7.48±0.52	840	9 (3+4+2)	2
			cucumber	50	8.13±0.70				
			tomato*	120	6.79±0.61				
			potato*	470	7.70±0.27				
			potato*	470	5.57±0.15				
			tomato*	120	5.31±0.18				
Amides	cyflufenamid	0.01	tomato	120	10.56±2.26	10.32±1.17	640	8 (2+4+2)	3
			cucumber	50	12.37±5.90				
Piperidinyl thiazole isoxazolines	oxathiapiprolin	0.1	tomato	120	4.57±0.65	11.46±2.87	640	7 (1+4+2)	3
			onion	50	2.17±0.00				
			potato	470	2.17±0.00				
Oxazoles	famoxadone	0.01	tomato	120	14.53±1.17	3.61±0.69	640	7 (2+4+1)	3
			onion	50	7.10±0.32				
			potato	470	9.33±0.58				

*Note: M – mean value: m – mean value deviation; ADI – acceptable daily intake, mg/kg; RPCPC – the integral index of the potential risk of pesticide-contaminated products consumption; * – active ingredient applicate in form of different formulations*

4. Discussion

Thus, the studied compounds of amide class (cyflufenamid), piperidinyl thiazole isoxazoline (oxathiapiproline), oxazole (famoxadone), and triazoles (tebuconazole) belong to the 3 classe of hazard by RPCPC value (**Table 3**) – moderately hazardous. The exception is only difenoconazole, which is classified as hazard class 2 (hazardous) due to its high, compared with other studied compounds, toxicity for warm-blooded animals and humans (low ADI value).

The results obtained by us correlate with the studies carried out in the previous stage. Thus, when developing a method for assessing the integral index of the potential risk of pesticide-contaminated products consumption, it was found that pyrazolecarboxamide class fungicides (isopyrazam, penthiopyrade, sedaxan, fluxapyroxad) belong to the 3 class of hazard by the RPCPC value – moderately hazardous [12].

The obtained results should be taken into account when deciding on the expansion of the application scope of fungicides of the studied amides, piperidinyl thiazole isoxazolines, oxazoles and triazoles classes.

We also plan to further evaluation, using proposed RPCPC calculation method, of the potential risk of pesticide-contaminated products consumption for active ingredients of the most common in Ukraine and in the world herbicides and insecticides. The results obtained will be compared with the indices values for already studied fungicides.

References

1. Popp, J., Pető, K., Nagy, J. (2012). Pesticide productivity and food security. A review. Agronomy for Sustainable Development, 33 (1), 243–255. doi: https://doi.org/10.1007/s13593-012-0105-x

2. Mahmood, I., Imadi, S. R., Shazadi, K., Gul, A., Hakeem, K. R. (2016). Effects of Pesticides on Environment. Plant, Soil and Microbes, 253–269. doi: https://doi.org/10.1007/978-3-319-27455-3_13

3. List of pesticides and agrochemicals authorized for use in Ukraine (Official edition) (2018). Kyiv: Univest Media, 1039.

4. Aktar, W., Sengupta, D., Chowdhury, A. (2009). Impact of pesticides use in agriculture: their benefits and hazards. Interdisciplinary Toxicology, 2 (1), 1–12. doi: https://doi.org/10.2478/v10102-009-0001-7

5. Damalas, C. A., Eleftherohorinos, I. G. (2011). Pesticide Exposure, Safety Issues, and Risk Assessment Indicators. International Journal of Environmental Research and Public Health, 8 (5), 1402–1419. doi: https://doi.org/10.3390/ijerph8051402

6. Guidelines for the hygienic assessment of new pesticides. MG No. 4263-87. (1988). Ministry of health of USSR, 210.

7. Maximum Residue Levels. URL: https://ec.europa.eu/food/plant/pesticides/max_residue_levels_en

8. Maximum Residue Limits (MRLs) List of Agricultural Chemicals in Foods. Available at: http://www.m5.ws001.squarestart.ne.jp/foundation/search.html

9. Health Canada. Maximum Residue Limits for Pesticides. Available at: http://pr-rp.hc-sc.gc.ca/mrl-lrm/index-eng.php

10. Codex Alimentarius. Codex Pesticides Residues in Food Online Database. Available at: http://www.fao.org/fao-who-codexalimentarius/standards/pestres/pesticides/en/

11. Pesticides. Classification according to the degree of danger: 8.8.1.002-98. (2000). Kyiv, 9 (1), 249–266.

12. Antonenko, A. M., Vavrinevych, O. P., Omelchuk, S. T., Korshun, M. M. (2018). Hygienic substantiation of forecasting model of hazard for human when consuming agricultural products contaminated with pesticides (on pyrazolecarboxamide class fungicides example). The unity of science, 46–48.