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THE PROBLEM OF REGULATING FUNGICIDES ON THE SKIN SURFACE FOR OCCUPATIONAL SKIN DISEASE IN AGRICULTURAL WORKERS' RISK PREDICTION

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Summary

The aim. To establish the norms of fungicides on the skin surface and predicting the risk of occupational skin pathology in agricultural workers to develop measures to prevent diseases caused by dermal exposure to pesticides.

Materials and methods. The natural experiment was performed in accordance with modern requirements (European Food Safety Authority (2022), and the risk assessment was carried out according to the Recommendations (Approved by the Ministry of Health of Ukraine No. 324 issued on 13.05.2009) with different methods of spraying techniques: rod, air blast fan spraying, pre-sowing, aviation, knapsack treatment. 17 series of natural experiments were performed, and the air of the working zone area (n =56) and dermal exposure (n =56) were analyzed for each worker with different pesticide application methods. Quantitative determination of pesticide content was carried out by gas-liquid and high-performance liquid chromatography methods. The results were statistically processed using a package of licensed statistical programs MedStat v.5.2 (Copyright © 2003-2019) and Microsoft® Excel® for Microsoft 365 MSO.

Results. It was established that there is pesticide contamination, mainly of the gloves of tank filling operators when preparing working solutions. No contamination of the skin surface was detected; only pesticide residues were present on the surface of the workers' overalls. A comparison of the exposure dose in case of percutaneous exposure during the performance of technological operations with different methods of processing, dermal equivalents of Acceptable Operator Exposure Level of pesticide to workers' skin (DE AOEL) and the allowable dermal dose for professional contingents (AD_{derm}) and the hazard coefficients by dermal exposure (HC_{derm}) showed that that dermal exposure during individual technological operations with different processing methods had a reliable difference between processing methods, but there is no difference within one application method.

Conclusions. During the comparison of the hazard coefficients for dermal exposure, calculated according to different models, no significant difference was found between the risks calculated according to DE AOEL and AD_{derm} for individual technological operations in various treatment methods, except for the operator who performed knapsack treatment and the risk calculated according to AD_{derm} is significantly lower compared to the DE AOEL risk.

Keywords: **Acceptable Operator Exposure Level, potential effect on the skin, pesticides, risk assessment, professional exposure, personal protective equipment**

INTRODUCTION

Among the problems associated with pesticide application in agriculture is the occurrence of occupational pathology caused by damage to the organs of the respiratory system and skin [1, 2]. According to recent studies, 41.9 % of occupational pathology is occupational skin diseases [4]. Among the skin diseases caused by exposure to pesticides, the following are diagnosed most frequently: contact dermatitis, allergic reactions, irritation, less often – urticaria, erythema, parakeratosis, skin porphyria, chloracne, hypopigmentation/discolouration of the skin, etc. [5, 6]. The issue of control, regulation of pesticide residues on the skin surface and prevention of skin diseases in workers remains unresolved [3].

THE AIM

To establish the norms of fungicides on the skin surface and predict the risk of occupational skin pathology in agricultural workers to develop measures to prevent diseases caused by dermal exposure to pesticides.

MATERIALS AND METHODS

The study was carried out under modern requirements [7]. The working conditions with different methods of spraying techniques were studied: rod spraying (rod sprayer OPSH-200, aggregated with a tractor), fan spraying (fan sprayer OPV-200, aggregated with a tractor), pre-sowing treatment (stationery seed treater, potato planter), aviation treatment (AEROS C-80 hang glider with attached fine-drop sprayer), knapsack processing in indoor/greenhouse soil conditions (knapsack sprayer «Marolex Profession»). Quantitative determination of the pesticide content in the working zone air, swabs from the skin surface, and patches on workwear was carried out using gas-liquid and high-performance liquid chromatography (table 1). The risk assessment was performed according to recommendations [8]. According to the methodical recommendations developed by specialists of the State Institution «Kundiiev Institute of Occupational Health of the National Academy of Medical Sciences of Ukraine» it is expedient to carry out hygienic regulation of pesticide residues on the workers’ skin surface, which in turn make it possible to predict the negative impact of the pesticide on professional contingents during the performance of work on its application and to develop the necessary preventive measures to avert the negative impact and the occurrence of occupational pathology [9].

17 series of natural experiments were performed, and the working zone air (n=56) and dermal exposure (n=56) were analyzed for each worker with different methods of pesticide application. Statistical processing of the results was carried out using a package of licensed statistical programs MedStat v.5.2 (Copyright © 2003-2019) and Microsoft® Excel® for Microsoft 365 MSO (version 2305 build 16.0.16501.20074) (License ID: CWW_0071e48a-250c-4bdb-9013 – b8daf357b5e9_b5685e92-c95d-4399-9b83-449d76a26fb6_79f3b2da2f9adcda29).

Samples were assessed for normality by the W Shapiro-Wilk and D’Agostino-Pearson test (for samples with n less than and greater than 30, respectively) and it was found that almost all experimental series did not obey the normal distribution (except for the series describing the actual dermal exposure during rod and knapsack processing), based on this, Wilcoxon’s W – and T -criterion and Student’s t-criterion were chosen for comparison. In the course of the work, the samples were subjected to the following statistical analysis: determination of the median (average value) and error of the median (average), variance of the samples, mean square deviation, and determination of the proportion. The level of statistical significance is 80 % at 0.05.

RESULTS

The pre-sowing treatment of potatoes with the Monkat fungicide and potato planting were not accompanied by air pollution in the operator’s working zone during the preparation of the working solution, treatment of potato tubers and their planting. In the course of the conducted research, the operator processed the potato tubers with Moncat 460 SC and its seeds had no contamination of exposed skin by flutolanil and pesticide residues were not detected. However, the operator’s gloves and overalls were found to contain flutolanil in the amount of 0.0047 mg.

Analyzing the working conditions during rod treatment with the Orondis Ultra, Switch, Tsideli Top, Rias, Kitch, and Split formulations in the working zone air of the tank filling operator and tractor driver, and in the air over the treated area, the content of mandipropamid, oxathiapiprolin, cyprodinil, fludioxonil, difenoconazole, cyflufenamid, propiconazole was not detected. There was no contamination by the studied active substances of the exposed skin of the tank filling operator and the tractor driver, who were working on the processing of agricultural crops. However, mandipropamid in the amount of 0.0055 mg, cyprodinil – 0.0035-0.0077 mg, fludioxonil – 0.003 mg, difenoconazole – 0.0028-0.005 mg, propiconazole – 0.0066 mg were found on the gloves and overalls of the tank filling operator.

Content of active ingredients was not detected in the tank filling operator’ and tractor driver’ working zone air during air blast fan-sprayer treatment, in the air above the treated area and in the area of possible air drift of Orondis Ultra, Bumper, Kitch, Protect Fungus preparations. In the course of the conducted research, no pesticide contamination was found on the exposed skin of the tank filling operator and the tractor driver who performed the air blast fan-spraying treatment of vineyards and orchards. However, mandipropamid in the amount of 0.0070 mg, propiconazole – 0.0045 mg, and cyprodinil – 0.003 mg were found on the gloves and overalls of the tank filling operator.

The aerial crop treatment was not accompanied by Rias active ingredient contamination of the working zone air of the tank filling operator, pilot, and signalman. After the completion of spraying with the Rias fungicide, residual amounts of difenoconazole and propiconazole were not detected in the samples swabbed from the exposed skin of the workers. Difenoconazole in the amount of 0.0035 mg and propiconazole in the amount of 0.003 mg were found on the gloves and overalls of the tank filling operator only. Difenoconazole and propiconazole 0.004 mg and 0.003 mg, respectively, were detected in the patches on the signalman’s overalls.

Table 1

Conditions of application of the studied fungicides

Preparation	Active ingredients	Cultivated crop	Application rate		Method	Detection limit in:	
			preparation, l(kg)/ha	working solution, l/ha		the working zone air, mg/m³	swabs, patches mg (mg/dm²)
Pre-sowing treatment and planting crop							
Moncat	flutolanil	potato	200 ml/t	10 l/t	HPLC	0.2	0.001
Rod treatment							
Orondis Ultra	mandipropamid, oxathiapiprolin	onion	0.6	250	HPLC HPLC	0.25 0.2	0.001 0.002
Switch	cyprodinil, fludioxonil	blueberry	1.0	250	GLC HPLC	0.007 0.03	0.002 0.002
Tsideli Top	difenoconazole, cyflufenamid	cucumbers	1.0	300	GLC GLC	0.03 0.03	0.002 0.001
Rias	difenoconazole, propiconazole	sunflower	0.8	300	GLC GLC	0.03 0.015	0.002 0.002
Kitsch	cyprodinil, fludioxonil	carrot	1.0	300	GLC HPLC	0.007 0.03	0.002 0.002
Split	difenoconazole	winter wheat	0.5	300	GLC	0.03	0.002
Air blast fan spraying (boom-sprayer) treatment							
Orondis Ultra	mandipropamid, oxathiapiprolin	grape	0.67	300	HPLC HPLC	0.25 0.2	0.001 0.002
Bumper	propiconazole	apple trees	0.3	1000	GLC	0.015	0.002
Kitsch	cyprodinil, fludioxonil	apple trees	1.0	500	GLC HPLC	0.007 0.03	0.002 0.002
Protect-Fungus	difenoconazole, propiconazole	peaches	0.3	500	GLC GLC	0.03 0.015	0.002 0.002
Aviation treatment							
Rias	difenoconazole, propiconazole	sunflower	0.8	300	GLC GLC	0.03 0.015	0.002 0.002
Knapsack treatment (indoor/greenhouse soil)							
Orondis Ultra	mandipropamid, oxathiapiprolin	tomatoes	0.4	10	HPLC HPLC	0.25 0.2	0.001 0.002
Switch	cyprodinil, fludioxonil	cucumbers	1.0	10	GLC HPLC	0.007 0.03	0.002 0.002
Switch	cyprodinil, fludioxonil	roses	1.0	10	GLC HPLC	0.007 0.03	0.002 0.002
Tsideli Top	difenoconazole, cyflufenamid	cucumbers	1.0	10	GLC GLC	0.03 0.03	0.002 0.001
Kitsch	cyprodinil, fludioxonil	tomatoes	1.0	10	GLC HPLC	0.007 0.03	0.002 0.002

Notes: 1. HPLC – high-performance liquid chromatography; 2. GLC – gas-liquid chromatography.

During knapsack treatment (under conditions of indoor/greenhouse soil) with Orondis Ultra, Switch, Tsideli Top, Kitch pesticides, the content of fludioxonil in the air in the middle of the greenhouse 1 hour after treatment was 0.07 mg/m^3, cyprodinil – 0.05-0.1 mg/m^3, while mandipropamid, oxathiapiprolin, cyflufenamid, and fludioxonil were not detected. Contamination by active substances was not detected in samples of swabs from open areas of the operator's skin. However, mandipropamid in the amount of 0.0068 mg, fludioxonil – 0.0057-0.014 mg, cyprodinil – 0.00076-0.019 mg, difenoconazole – 0.009 mg, cyflufenamid – 0.002 mg were found on the worker's gloves and overalls.

The actual data obtained from the evaluation of the working conditions of the workers allowed us to calculate the penetration coefficient ($K_{p, m}$) through the skin, the allowable dermal dose and the occupational risk of dermal exposure formed during the body exposure by the studied fungicides (depending on the type of work and the method of crop treatment). It also made it possible to compare two current models and determine more thoroughly the risks for workers involved in the treatment of agricultural crops.

Table 2 shows the calculated values of the penetration coefficient (K_{pm}) of the studied fungicides through the skin and the allowable dermal dose for workers. The proposed algorithm for justifying the hygienic standard for the skin involves two stages. First, we determined the value of the penetration coefficient ($K_{p, m}$) of the studied fungicides through the skin, and then – substantiated the allowable dermal dose for workers (table 2).

Table 2

Estimated values of the penetration coefficient ($K_{p, m}$) of the studied fungicides through the skin and the allowable dermal dose for workers

Class	Active ingredient	MW	Log $K_{o/w}$	Log $K_{p.m}$	Kp, m, cm/h	AOEL, mg/kg	DE AOEL, mg/kg	Q abs, %
amides	mandipropamid	411.9	3.2	-2.9034	0.001249	0.17	0.9073	18.74
amides	cyflufenamid	412.36	4.7	-1.79616	0.015990	0.03	0.0125	239.85
anilino-pyrimidines	cyprodinil	225.29	4	-1.19174	0.064307	0.03	0.0031	964.61
benzanilides	flutolanil	323.31	3.17	-2.39406	0.004036	0.26	0.4295	60.54
piperidinyl-thiazolizoxazoline	oxathiapiprolin	539.53	3.66	-3.32878	0.000469	0.31	4.4061	7.04
triazoles	difenoconazole	406.26	4.36	-2.01116	0.009746	0.16	0.1094	146.19
triazoles	propiconazole	342.22	3.72	-2.10052	0.007934	9.00	7.5626	119.01
phenylpyrroles	fludioxonil	248.19	4.12	-1.24034	0.057499	0.59	0.0684	862.48

Notes: 1. MW – molecular weight; 2. Log $K_{o/w}$ – partition coefficient in the octanol/water system; 3. AOEL – acceptable operator exposure level; 4. DE AOEL – the dermal equivalent of AOEL; Q abs is the dose absorbed through the skin, expressed as a % of the AOEL.

The obtained results showed that the estimated values of the penetration coefficient ($K_{p, m}$) through the skin of the studied fungicides of the class of amides, analinopyrimidines are in the range of 0.001249-0.064307 cm/h, of new molecules of the benzanilide class – 0.004036 cm/h, of piperidinyl-thiazole-isoxazolines – 0.000469 cm/h, triazoles – 0.007934-0.009746 cm/h, phenylpyrroles – 0.057499 cm/h (table 2).

The data shown in table 2 show that for fungicides class of amides, analinopyrimidines, the values of DE AOEL were in the range of 0.0031-0.9073 mg/kg, which exceeds the value of AOEL by approximately 2-10 times. Similar results were obtained during the analysis of fungicides of the class of triazoles and phenylpyrroles values of DE AOEL, which were in the range of 0.0684-7.5626 mg/kg and exceeded the values of AOEL by 1.2-1.5 and 9 times, respectively, which indicates the possibility of manifestation of skin resorptive action. DE AOEL of benzanilide and piperidinyl-thiazole-isoxazoline fungicides were 0.26-0.31mg/kg and did not exceed 7-60 % of AOEL.

The next step was a comparison of the exposure dose in case of percutaneous exposure during technological operations under different treatment methods (pre-sowing, aviation, rod, air blast fan spraying, knapsack), the permissible level of exposure to the pesticide on the skin of workers (DE AOEL) and the allowable percutaneous dose for professional contingents (AD_{skin}) and hazard coefficients for percutaneous exposure (HC_{derm}) (tables 3 and 4).

In total, the distribution of dermal exposure differed from normal at the level of significance <0.01-0.003 during the performance of technological operations by tank filling operator and tractor drivers (pilots and signalmen) involved in rod, air blast fan spraying, knapsack, aerial and pre-sowing treatment of agricultural crops and their planting (Shapiro-Wilk test W=0.598 and χ^2=11.3) (table 5); when performing operations during rod and knapsack treatment, the distribution of dermal exposure did not differ from normal (p>0.1 Shapiro-Wilk test W=0.910-0.928), while when performing other operations, the distribution of this exposure differed from normal (p<0.01 Shapiro-Wilk test W=0.593-0.715).

The distribution of the hazard ratios for percutaneous exposure according to DE AOEL and ADskin for tank filling operators differed from the normal one at the level of significance <0.001 (χ^2 =43.7 and 24.5, respectively); a similar situation with the distribution of tractor drivers (pilots and signalmen) – p<0.01 (Shapiro-Wilk criterion W=0.518 and 0.681, respectively).

The distribution of hazard coefficients for percutaneous exposure according to DE AOEL and AD_{skin} considering individual technological operations during different treatment methods differed from the normal – p<0.01 (Shapiro-Wilk criterion W=0.463-0.714). In general, the criteria of DE AOEL and AD_{skin} for active ingredients, which are indicators of acceptance, are not significantly different from each other and, on average, are 0.1094 and 0.6 mg/kg, respectively (Wilcoxon's T-test; TW=189.0; p=0.160).

Indicators of dermal exposure obtained during tank filling and during treatment, planting/sowing of agricultural crops were significantly higher in tractor drivers (pilots, signalmen) and were 0.00752±0.00211 and 0.01908±0.00697 mg/kg, respectively (Wilcoxon test; W = 613.0; p=0.009). These indicators during the determination of risks (HC_{derm}) in the conditions of tank filling and treatment/planting/sowing partially coincided: for DE AOEL the risks did not differ significantly – 0.0633±0.30830 and 0.15503±0.36600 units, respectively (W-criterion of Wilcoxon; W=650.5; p=0.579); for $AD_{skin,}$ a significant difference was recorded – 0.01385±0.02983 and 0.04200±0.06219 arb.u., respectively (W-criterion of Wilcoxon; W=575.5; p=0.048). Differences between HC_{derm} during tank filling and during treatment/planting/sowing of agricultural crops according to DE AOEL and AD_{skin} did not differ significantly (Wilcoxon T-test; TW=353.0; p=0.096 and TW=172.0; p=0.546, respectively).

Table 3

Evaluation of the hazard of fungicides in case of percutaneous exposure in different methods of their application

Preparation	Active ingredient	D_{skin}, mg/kg		DE AOEL, mg/kg	HC_{derm}	
		tank filling operator / operator1	tractor driver/ operator2		tank filling operator/ operator 1	tractor driver/ operator 2
Pre-sowing treatment [1] and crop sowing [2]						
Monkat [1]	flutolanil	0.00167/	0.10975/	0.4295	0.00389	0.25553
Moncat [2]	flutolanil	0.00165/	0.10975/	0.4295	0.00384	0.25553
M±m		0.00166±0.00000	0.10975±0.00000	0.4295 ±0.00000	0.00387 ±0.00003	0.25553 ±0.00000
Rod treatment						
Orondis Ultra	mandipropamid	0.01093/	0.01060/	0.9073	0.01205	0.01168
	oxathiapiprolin	0.02131/	0.02120/	4.4061	0.00484	0.00481
Switch	cyprodinil	0.01757/	0.01413/	0.0031	5.66774	4.55806
	fludioxonil	0.02153/	0.02120/	0.0684	0.31477	0.30994
Tsideli Top	difenoconazole	0.01450/	0.01413/	0.1094	0.13254	0.12916
	cyflufenamid	0.02557/	0.02544/	0.0125	2.04560	2.03520
Rias	difenoconazole	0.01722/	0.01696/	0.1094	0.15740	0.15503
	propiconazole	0.02631/	0.02544/	7.5626	0.00348	0.00336
Kitsch	cyprodinil	0.01705/	0.01696/	0.0031	5.50000	5.47097
	fludioxonil	0.02590/	0.02544/	0.0684	0.37865	0.37193
Split	difenoconazole	0.01721/	0.01696/	0.1094	0.15731	0.15503
M±m		0.01955±0.00151	0.01895±0.00155	1.215 ±0.7462	1.307±0.6612	1.2±0.5977
Aviation treatment (pilot[3]/ signalman[4])						
Rias	difenoconazole	0.01727/	0.01696 [3]/ 0.02627 [4]	0.1094	0.15786	0.15505/0.24016
	propiconazole	0.02584/	0.02544 [3]/ 0.03475 [4]	7.5626	0.00342	0.00336/0.00460
M±m		0.02155±0.00429	0.02586±0.00364	1.979 ±1.862	0.08064 ±0.07722	0.0792 ±0.07584
Air blast fan spraying treatment						
Orondis ultra	mandipropamid	0.00665/	0.00374/	0.9073	0.00733	0.00412
	oxathiapiprolin	0.00752/	0.02494/	4.4061	0.00171	0.00566
Bumper	fludioxonil	0.02554/	0.02494/	0.0684	0.37339	0.36462
Kitsch	cyprodinil	0.00501/	0.00499/	0.0031	1.61613	1.60968
	fludioxonil	0.00760/	0.00748/	0.0684	0.11111	0.10936
Protect Fungus	difenoconazole	0.00501/	0.00499/	0.1094	0.04580	0.04561
	propiconazole	0.00752/	0.00748/	7.5626	0.00099	0.00099
M±m		0.00926±0.00275	0.01122±0.00358	1.875 ±1.122	0.3081±0.2237	0.3057±0.2227
Knapsack treatment (indoor/greenhouse soil)						
Orondis Ultra	mandipropamid	/0.00086	-	0.9073	0.00095	-
	oxathiapiprolin	/0.00085	-	4.4061	0.00019	-
Switch	cyprodinil	/0.00128	-	0.0031	0.41290	-
	fludioxonil	/0.00145	-	0.0684	0.02120	-
Switch	cyprodinil	/0.00128	-	0.0031	0.41290	-
	fludioxonil	/0.00128	-	0.0684	0.01871	-
Tsideli Top	difenoconazole	/0.00099	-	0.1094	0.00905	-
	cyflufenamid	/0.00101	-	0.0125	0.08080	-
Kitsch	cyprodinil	/0.00079	-	0.0031	0.25484	-
	fludioxonil	/0.00109	-	0.0684	0.01594	-
M±m		0.00109±0.00007	-	0.565 0.4355	0.1227±0.05405	-

Notes: 1. D_{skin} – exposure dose for percutaneous exposure, mg/kg of body weight; 2. DE AOEL – the dermal equivalents of Acceptable Operator Exposure Level, mg/kg; 3. HC_{derm} – the hazard ratio for percutaneous exposure, calculated by the ratio of the exposure dose for percutaneous exposure to the allowable dose (D_{skin} / DE AOEL).

Table 4

Values of exposure and allowable doses of fungicides that affect the body of workers percutaneously in different methods of application

Preparation	Acting substance	D_{skin}, mg/kg		AD_{derm}, mg/kg	HC_{derm}	
		tank filling operator / operator1	tank filling operator / operator1		tank filling operator/ operator 1	tractor driver/ operator2
1	2	3	4	5	6	7
Pre-sowing treatment [1] and crop sowing [2]						
Monkat [1]	flutolanil	0.00167/	0.10975/	0.12	0.0139/	0.0138/
Moncat [2]	flutolanil	0.00165/	0.10975/	0.12	0.0138/	0.9146/
M±m		0.00166±0.00000	0.10975±0.00000	0.12±0.0000	0.01385 ± 0.00005	0.4642 ± 0.04504
Rod treatment						
Orondis ultra	mandipropamid	0.01093/	0.01060/	4.0	0.0091/	0.0088/
	oxathiapiprolin	0.02131/	0.02120/	0.6	0.0053/	0.0053/
Switch	cyprodinil	0.01757/	0.01413/	0.6	0.0293/	0.0236/
	fludioxonil	0.02153/	0.02120/	0.6	0.0359/	0.0353/
Tsideli Top	difenoconazole	0.01450/	0.01413/	0.04	0.3625/	0.3534/
	cyflufenamid	0.02557/	0.02544/	0.40	0.0639/	0.0636/
Rias	difenoconazole	0.01722/	0.01696/	0.04	0.4306/	0.4240/
	propiconazole	0.02631/	0.02544/	0.40	0.0658/	0.0636/
Kitsch	cyprodinil	0.01705/	0.01696/	0.60	0.0284/	0.0283/
	fludioxonil	0.02590/	0.02544/	0.60	0.0432/	0.0424/
Split	difenoconazole	0.01721/	0.01696/	0.01	0.4301/	0.4240/
M±m		0.01955±0.00151	0.01895±0.00155	0.7173±0.3366	0.1367±0.05304	0.1338±0.05222
Aviation treatment (pilot[3]/ signalman[4])						
Rias	difenoconazole	0.01727/	0.01696 [3] 0.02627 [4]	0.04	0.4317/	0.4240 [3] 0.6568 [4]
	propiconazole	0.02584/	0.02544 [3] 0.03475 [4]	0.4	0.0646/	0.0636 [3] 0.0869 [4]
M±m		0.02155±0.00429	0.02586±0.00364	0.22±0.18	0.2481±0.1835	0.3078±0.1425
Air blast fan spraying treatment						
Orondis ultra	mandipropamid	0.00665/	0.00374/	1.2	0.0055/	0.0031/
	oxathiapiprolin	0.00752/	0.02494/	4.0	0.0019/	0.0019/
Bumper	fludioxonil	0.02554/	0.02494/	0.6	0.0425/	0.0416/
Kitsch	cyprodinil	0.00501/	0.00499/	0.6	0.0084/	0.0083/
	fludioxonil	0.00760/	0.00748/	0.6	0.0127/	0.0125/
Protect Fungus	difenoconazole	0.00501/	0.00499/	0.04	0.1254/	0.1247/
	propiconazole	0.00752/	0.00748/	0.4	0.0188/	0.0187/
M±m		0.00926±0.00275	0.01122±0.00358	1.063±0.5065	0.03074±0.01657	0.03011±0.01656
Knapsack treatment (indoor/greenhouse soil)						
Orondis Ultra	mandipropamid	/0.00086	-	1.2	/0.0007	-
	oxathiapiprolin	/0.00085	-	4.0	/0.0002	-
Switch	cyprodinil	/0.00128	-	0.6	/0.0021	-
	fludioxonil	/0.00145	-	0.6	/0.0024	-
Switch	cyprodinil	/0.00128	-	0.6	/0.0021	-
	fludioxonil	/0.00128	-	0.6	/0.0021	-
Tsideli Top	difenoconazole	/0.00099	-	0.04	/0.0247	-
	cyflufenamid	/0.00101	-	0.4	/0.0025	-
Kitsch	cyprodinil	/0.00079	-	0.6	/0.0013	-
	fludioxonil	/0.00109	-	0.6	/0.0018	-
M±m		0.00109±0.00007	-	0.924±0.3531	0.00399±0.00231	-

Notes: 1. D_{skin} – exposure dose for percutaneous exposure, mg/kg of body weight; 2. AD_{derm} – allowable dermal dose for professional contingents, mg/kg of body weight; 3. HC_{derm} – the hazard ratio for percutaneous exposure, calculated by the ratio of the exposure dose for percutaneous exposure to the permissible dose (D_{shk} / $ADskin_{)}$; 4. M is the average value; 5. m is the error of the arithmetic mean.

Table 5

Basic statistical parameters regarding exposure, hazard coefficients for percutaneous exposure at the dermal equivalents of Acceptable Operator Exposure Level (DE AOEL) and the allowable dermal dose for professional contingents (ADskin)

Parameter	Exposure/ risk	Production operation	Median (mean*), M	Error of the median (average*), m	95 % confidence interval	Sample volume, n	Shapiro-Wilk W test (D'Agostino-Pearson, χ2 **)	Level of significance, p
By type of operation								
Exposition	Dskin, mg/kg	tank filling operator/ operator 1**	0.00752	0.00211	0.00165-0.01721	32	11.3	0.003
		tractor driver/ operator 2	0.01908	0.00697	0.01413-0.02544	24	0.598	<0.01
DE AOEL, arb.u.	HCderm	tank filling operator/ operator 1**	0.06330	0.30830	0.00905-0.15786	32	43.7	<0.001
		tractor driver/ operator 2	0.15503	0.36600	0.01168-0.25553	24	0.518	<0.01
ADskin, arb.u. _	HCderm	tank filling operator/ operator 1**	0.01385	0.02983	0.0053-0.0359	32	24.5	<0.001
		tractor driver/ operator 2	0.04200	0.06219	0.0187-0.0869	24	0.681	<0.01
By type of operation and method of processing								
Exposition	Dskin, mg/kg	tank filling operator (rod)*	0.01955	0.00151	0.01619-0.02291	11	0.926	>0.1
		tractor driver (rod)*	0.01895	0.00155	0.0155-0.02241	11	0.91	>0.1
		Operator (knapsack)*	0.00109	0.00007	0.00093-0.00125	10	0.928	>0.1
		tank filling operator (air blast fan spraying)	0.00752	0.00344	0.00501-0.02554	7	0.593	<0.01
		tractor driver (air blast fan spraying)	0.00748	0.00449	0.00374-0.02494	7	0.715	<0.01
DE AOEL, arb.u.	HCderm	tank filling operator (rod)	0.15740	0.82860	0.01205-2.0456	11	0.629	<0.01
		tractor driver (rod)	0.15503	0.74910	0.01168-2.0352	11	0.655	<0.01
		Operator (knapsack)	0.01996	0.06774	0.00095-0.4129	10	0.714	<0.01
		tank filling operator (air blast fan spraying)	0.04580	0.28030	0.00099-1.61613	7	0.612	<0.01
		tractor driver (air blast fan spraying)	0.04561	0.27920	0.00099-1.60968	7	0.609	<0.01
ADskin, arb.u. _	HCderm	tank filling operator (rod)	0.04320	0.06648	0.0284-0.3625	11	0.685	<0.01
		tractor driver (rod)	0.04240	0.06545	0.0236-0.3534	11	0.686	<0.01
		operator (knapsack)	0.00210	0.00290	0.0007-0.0025	10	0.463	<0.01
		tank filling operator (air blast fan spraying)	0.01270	0.02077	0.0019-0.1254	7	0.697	<0.01
		tractor driver (air blast fan spraying)	0.01250	0.02076	0.0019-0.1247	7	0.698	<0.01

Note: arb.u. – arbitrary units

When evaluating the dermal exposure during the performance of individual technological operations by various treatment methods (rod, knapsack, air blast fan spraying), it was established that the highest figures were in rod treatment and the lowest in knapsack treatment (table 5) and have the following values: 0.01955±0.00151, 0.01895±0.00155, 0.00752±0.00344, 0.00748±0.00449, 0.00109±0.00007 (rod treatment (tank filling operator), rod treatment (tractor operator), air blast fan spraying (tank filling operator), air blast fan spraying (tractor operator), knapsack treatment (operator), respectively. There was an identical tendency in the calculations of HC_{derm} for DE AOEL and AD_{skin} (0.15740±0.82860, 0.15503±0.74910, 0.04580±0.28003, 0.04561±0.27920, 0.01996±0.06774 vs 0.04320±0.066480, 0.04240±0.06545, 0.01270±0.02077, 0.01250±0.02076, 0.00210±0.00290 arb.u., respectively).

Dermal exposure during the performance of individual technological operations with different treatment methods had a significant difference between the treatment methods but was absent within one method (air blast fan spraying (tank filling operator) and air blast fan spraying treatment (tractor driver) – Wilcoxon W-test; W=46.0; p=0.456, rod treatment (tank filling operator), rod treatment (tractor driver) – Student’s criterion; T=0.28; p=0.782) and the significance was in the range of p =0.044-<0.001.

During the comparison of the risk factors for percutaneous exposure (according to DE AOEL) between individual technological operations performed in different treatment methods, no significant differences were found (W-criterion of Wilcoxon; W=50.5-119.0; p=0.179-0.887). Under the conditions of comparison of «related samples», the risk for tank filling operators with rod treatment was significantly higher than that risk for tractor drivers of the same method of treatment – Wilcoxon’s T-test; TW=66.0; p<0.001.

During the comparison of the hazard coefficients for percutaneous exposure, calculated according to different models, no significant difference was found between the risks calculated according to DE AOEL and AD_{skin} for individual technological operations of different treatment methods, both for «unrelated» and for «related» samples (W-test Wilcoxon; W=47.0-111.0; p=0.332-0.710 and T-test Wilcoxon; TW=20.0-47.0; p=0.240-0.375), except for the knapsack treatment operator: risk, which is calculated by the AD_{skin} is significantly lower compared to the risk with DE AOEL for both «unrelated» and «related» samples – Wilcoxon’s W-criterion; W=77.0; p=0.035 and Wilcoxon T-test; TW=50.0; p=0.020, respectively – which may be related to the capacity of this treatment method (during knapsack treatment, the capacity can be one or two orders of magnitude lower, compared to other treatment methods) and the approach in calculations (physico-chemical properties are taken into account as well as toxicological parameters of compounds).

DISCUSSION

Comparative analysis between DE AOELs’ results for different fungicides class of amides, analinopyrimidines, triazoles, phenylpyrroles, benzanilides, piperidinyl-thiazole-isoxazolines and DE AOEL values established by other authors for insecticides of the class of neonicotinoids, derivatives of carbamic acid and organophosphorus compounds, fungicides of the class of strobilurins, triazoles, etc., showed the similarity of the obtained results [9, 10]. Thus, it was found that fungicides of the class of triazoles, phenylpyrroles, amides and anilinopyrimidines have a strong skin-resorptive effect, as there is an exceeding in AOEL. In such cases, according to the recommendations [2, 9] it is necessary for agriculture workers to use personal protective equipment.

No significant differences were found between the risk factors for dermal exposure for workers with different types of treatment, calculated in the course of our natural experiments and the risks obtained by other authors (W-Wilcoxon test; W = 27.0; p = 0.284) (0.0123±0.0031 and 0.2479±0.8754 for risk caused by fungicides what calculated by other authors and at our research, respectively) [9].

The analysis of the obtained results regarding the predominant localizations of the effect of pesticides on the workers’ skin showed similarities with the results obtained in other experiments under other application conditions [11, 12, 13]. The primary exposure areas for all workers were the hands and lower limbs [11, 12]. In the dermal and inhalation risk assessment, the risk index was much lower than 1 (mixing/loading: 0.000, application: 0.014), indicating that vineyard workers are at low risk of exposure to thiamethoxam [12]. The use of unmanned aerial vehicles for spraying crops with Amistar Extra was not accompanied by a significant risk for personnel (operator, signalman) in inhalation and dermal exposure. The calculated complex risk of he Amistar Extra 280 SC hazardous influence for operators/tractor drivers where $0.07\text{-}46.72\times10^{-2}$, for pilots – $0.19\text{-}12.1\times10^{-2}$, for signalman – $0.52\text{-}58.4\times10^{-2}$. Combined risk values for operators/tractor drivers where 0.12-0.46, for pilots – 0.09-0.13, for signalman – 0.59. The risk of hazardous exposure was less than one [13]. Similar results were obtained under the conditions of using different groups of pesticides to protect melon crops, and the risk for tank-filling operators and tractor drivers was acceptable. Complex risk of herbisides hazardous influence for operators and tractor drivers where 0.123-0.637, insectisides – 0.111-0.331, fungisides – 0.015-0.779. Combined risk values for operators and tractor drivers where 0.122-0.779 [14].

CONCLUSIONS

It was established during the comparison of the hazard coefficients for percutaneous exposure, calculated according to different models, that no significant difference was found between the risks calculated according to DE AOEL and AD_{skin} for individual technological operations of different processing methods, both for «unrelated» and for «related» samples (W-test of

Wilcoxon; W=47.0-111.0; p=0.332-0.710 and T-test of Wilcoxon; TW=20.0-47.0; p=0.240-0.375), except for the knapsack treatment operator: the risk calculated by AD_{skin} is significantly lower compared to the risk with DE AOEL for both «unrelated» and «related» samples – Wilcoxon's W-test; W=77.0; p=0.035 and Wilcoxon T-test; TW=50.0; p=0.020, respectively – which may be related to the capacity of this treatment method (during knapsack treatment, the capacity can be one or two orders of magnitude lower, compared to other treatment methods) and the approach in calculations (considering physico-chemical properties and toxicological parameters of compounds).

The obtained values of the acceptable level of exposure of the studied active ingredients and fungicides through the skin will allow us to assess the risk for workers involved in the application of fungicides considering pesticides of the analyzed chemical classes and, if necessary, to recommend the use of special personal protective equipment and work shift duration reduction.

Prospects for further research. In the future, the results will be used to develop selection criteria when monitoring the safety of the production environment to justify effective measures to prevent occupational pathology caused by pesticides.

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COMPLIANCE WITH ETHICAL REQUIREMENTS

The published study met guidelines for human subjects research and was conducted in accordance with the World Medical Association's Declaration of Helsinki. The object of the study was the active substances of chemical plant protection products, namely their quantity in air samples of the working zone and in swabs from the skin surface, and patches attached to workers' overalls. These substances have already been registered and approved for use in agricultural practice.

LITERATURE

1. Human Poisoning with Chlorpyrifos and Cypermethrin Pesticide Mixture: Assessment of Clinical Outcome of Cases Admitted in a Tertiary Care Hospital in Taiwan / Y. J. Wu, S. S. Chang, H. Y. Chen et al. International journal of general medicine. 2023. No 16. P. 4795-4804. https://doi.org/10.2147/IJGM.S432861.
2. Assessment of dermal exposure to pesticides among farmers using dosimeter and hand washing methods / S. Lari., P. R. Jonnalagadda, P. Yamagani et al. Frontiers in public health. 2022. No 10. 957774. https://doi.org/10.3389/fpubh.2022.957774.
3. Dermal Exposure Associated with Occupational End Use of Pesticides and the Role of Protective Measures / E. Macfarlane, R. Carey, T. Keegel et al. Safety and Health at Work. 2013. No 4(3). P. 136-141. https://doi.org/10.1016/J.SHAW.2013.07.004.
4. Prevalence of pesticide related occupational diseases among Indonesian vegetable farmers – A collaborative work /S. A. Febriana, M. Khalidah, F. N. Huda et al. Toxicology reports. 2023. No 10. P. 571-579. https://doi.org/10.1016/j.toxrep.2023.04.016.
5. Spiewak R. Pesticides as a cause of occupational skin diseases in farmers. Annals of agricultural and environmental medicine. Ann Agric Environ Med. 2001. No 8 (1). P. 1-5.
6. Evaluation of work place pesticide concentration and health complaints among women workers in tea plantation, Southern India / D. Venugopal, P. Karunamoorthy, R. Beerappa et al. Journal of exposure science & environmental epidemiology. 2021. No 31(3). P. 560-570. https://doi.org/10.1038/s41370-020-00284-3.
7. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products / EFSA (European Food Safety Authority), A. Charistou, T. Coja, P. Craig et al. EFSA Journal. 2022. No 20(1). 134 pp. https://doi.org/10.2903/j.efsa.2022.7032.
8. Вивчення, оцінка і зменшення ризику інгаляційного і перкутанного впливу пестицидів на осіб, які працюють з ними або можуть зазнавати впливу під час і після хімічного захисту рослин та інших об'єктів: методичні рекомендації: Наказ Міністерства охорони здоров'я України 13.05.2009 N 324. Kyiv, 2009. 29 p.
9. Методичні підходи до визначення дермальних еквівалентів допустимих рівнів впливу песиицидів: методичні рекомендації. К.: ДУ Інститут медицини праці імені Ю. І. Кундієва НАМН України, 2021. 26 р.
10. Yastrub T. O. Using of calculation models of the penetration of substances through the skin in the assessment of the risk of dermal influence of pesticides on workers. Wiadomości Lekarskie Medical Advances.

2023. No 76(4). P. 817-823. https://doi.org/10.36740/WLek202304118.
11. Tracking pesticide exposure to operating workers for risk assessment in seed coating with tebuconazole and carbofuran / R. Han., Z. Wu., Z. Huang et al. Pest Management Science. 2021. No 77(6). P. 2820-2825. https://doi.org/10.1002/PS.6315.
12. Occupational exposure and risk assessment for agricultural workers of thiamethoxam in vineyards / J. Lee, J. W. Kim, Y. Shin et al. Ecotoxicology and Environmental Safety. 2022. No 243. 113988. https://doi.org/10.1016/J.ECOENV.2022.113988.
13. Borysenko A., Tkachenko I., Antonenko A. Comparative hygienic assessment of working conditions and potential risks for workers' health when applying pesticides in different technics. Technology Transfer: Innovative Solutions in Medicine. 2021. P. 26-28. https://doi.org/10.21303/2585-6634.2021.002146.
14. Professional risks for agricultural personnel treating berries and melon crops with pesticides / O. S. Bilous, O. P. Vavrinevych, S. T. Omelchuk et al. Wiadomości Lekarskie. 2023. No 76(4). P. 817-823. https://doi.org/10.36740/WLek202304120.

REFERENCES

1. Wu, Y. J., Chang, S. S., Chen, H. Y., Tsai, K. F., Lee, W. C., Wang, I. K., ... Yen, T. H. (2023). Human Poisoning with Chlorpyrifos and Cypermethrin Pesticide Mixture: Assessment of Clinical Outcome of Cases Admitted in a Tertiary Care Hospital in Taiwan. International journal of general medicine, 16, 4795-4804. https://doi.org/10.2147/IJGM.S432861.
2. Lari, S., Jonnalagadda, P. R., Yamagani, P., Medithi, S., Vanka, J., Pandiyan, A., Naidu, M., & Jee, B. (2022). Assessment of dermal exposure to pesticides among farmers using dosimeter and hand washing methods. Frontiers in public health, 10, 957774. https://doi.org/10.3389/fpubh.2022.957774.
3. Macfarlane, E., Carey, R., Keegel, T., El-Zaemay, S., & Fritschi, L. (2013). Dermal Exposure Associated with Occupational End Use of Pesticides and the Role of Protective Measures. Safety and Health at Work, 4(3), 136-141. https://doi.org/10.1016/J.SHAW.2013.07.004.
4. Febriana, S. A., Khalidah, M., Huda, F. N., Sutarni, S., Mahayana, I., Indrastuti, N., ... Malueka, R. G. (2023). Prevalence of pesticide related occupational diseases among Indonesian vegetable farmers – A collaborative work. Toxicology reports, 10, 571-579. https://doi.org/10.1016/j.toxrep.2023.04.016.
5. Spiewak R. (2001). Pesticides as a cause of occupational skin diseases in farmers. Annals of agricultural and environmental medicine: Ann Agric Environ Med, 8(1), 1-5. PMID: 11426918.
6. Venugopal, D., Karunamoorthy, P., Beerappa, R., Sharma, D., Aambikapathy, M., Rajasekar, K., Gaikwad, A., & Kondhalkar, S. (2021). Evaluation of work place pesticide concentration and health complaints among women workers in tea plantation, Southern India. Journal of exposure science & environmental epidemiology, 31(3), 560-570. https://doi.org/10.1038/s41370-020-00284-3.
7. EFSA (European Food Safety Authority), Charistou A, Coja T, Craig P, Hamey P, Martin S, Sanvido O, Chiusolo A, Colas M and Istace F, (2022). Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal, 20(1), 134 pp. https://doi.org/10.2903/j.efsa.2022.7032.
8. Department of Sanitary and Epidemiological Surveillance (2009). Vivchennya, otsinka i zmenshennya ryzyku inhalatsiynoho i percutanoho vplyvu pestitsydiv na osib, yaki pratsyuyut′ z nymy abo mozhut′ zaznavaty vplyvu pid chas i pislya khimichnoho zakhystu roslyn ta inshykh ob″yektiv [Study, evaluation and reduction of the risk of inhalation and dermal exposure of pesticides to persons who work with them or may be exposed to pesticides during and after chemical protection of plants and other objects]: methodological recommendations [Approved by Ministry of Health of Ukraine No. 324 issued on 13.05.2009.]. Kyiv, 2009. 29 p.
9. State Institution «Kundiiev Institute of Occupational Health of the National Academy of Medical Sciences of Ukraine» (2021). Metodychni pidkhody do vyznachennya dermalnykh ekvivalentiv dopustymykh rivniv vplyvu: metodychni rekomendatsii [Methodical approaches to determining dermal equivalents of acceptable operator exposure levels of pesticides]: methodological recommendations. Kyiv. 26 p.
10. Yastrub T. O. (2023). Using of calculation models of the penetration of substances through the skin in the assessment of the risk of dermal influence of pesticides on workers. Wiadomości Lekarskie Medical Advances, 76(4), 817-823. https://doi.org/10.36740/WLek202304118.
11. Han, R., Wu, Z., Huang, Z., Man, X., Teng, L., Wang, T., ... Liu, X. (2021). Tracking pesticide exposure to operating workers for risk assessment in seed coating with tebuconazole and carbofuran. Pest Management Science, 77(6), 2820-2825. https://doi.org/10.1002/PS.6315.
12. Lee, J., Kim, J. W., Shin, Y., Park, E., Lee, J., Keum, Y. S., & Kim, J. H. (2022). Occupational exposure and risk assessment for agricultural workers of thiamethoxam in vineyards. Ecotoxicology and Environmental Safety, 243, 113988. https://doi.org/10.1016/J.ECOENV.2022.113988.

13. Borysenko A., Tkachenko, I., & Antonenko A. (2021). Comparative hygienic assessment of working conditions and potential risks for workers' health when applying pesticides in different technics. Technology Transfer: Innovative Solutions in Medicine, 26-28. https://doi.org/10.21303/2585-6634.2021.002146.

14. Bilous, O. S., Vavrinevych, O. P., Omelchuk, S. T., Aleksiichuk, V. D., & Syrota, A. I. (2023). Professional risks for agricultural personnel treating berries and melon crops with pesticides. Wiadomości Lekarskie Medical Advances, 76(4), 831-837. https://doi.org/10.36740/WLek202304120.

Резюме

ПРОБЛЕМА НОРМУВАННЯ ФУНГІЦИДІВ НА ПОВЕРХНІ ШКІРИ ДЛЯ ПРОГНОЗУВАННЯ РИЗИКУ ВИНИКНЕННЯ ПРОФЕСІЙНОЇ ШКІРНОЇ ПАТОЛОГІЇ У СІЛЬСЬКОГОСПОДАРСЬКИХ ПРАЦІВНИКІВ

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Мета. Встановити нормативи фунгіцидів на поверхні шкіри та прогнозування ризику виникнення професійної шкірної патології у сільськогосподарських працівників для розробки заходів профілактики захворювань, зумовлених дермальним впливом пестицидів.
Матеріали та методи. Натурний експеримент виконано відповідно до сучасних вимог (European Food Safety Authority (2022)) та оцінку ризику виконано згідно Рекомедацій (Затв. МОЗ України № 324 від 13.05.2009) при різних способах обприскування: штангова, вентиляторна, передпосадкова, авіаційна, ранцева обробка. Виконано 17 серій натурних експериментів та проаналізовано повітря робочої зони (n=56), дермальна експозиція (n=56) для кожного працівника при різних способах застосування пестицидів. Кількісне визначення вмісту пестицидів проводили методами газорідинної і високоефективної рідинної хроматографії. Статистичну обробку результатів проводили з використанням пакету ліцензійних статистичних програм MedStat v.5.2 (Copyright © 2003-2019) та Microsoft® Excel® для Microsoft 365 MSO
Результати. Встановлено наявне забруднення пестицидами переважно рукавичок у заправників при приготуванні робочих розчинів. Не виявлено забруднення поверхні шкіри, лише присутні залишки на поверхні спецодягу працівників. Порівняння експозиційної дози при перкутанному впливі під час виконання технологічних операцій за різних способів обробки, допустимого рівня впливу пестициду на шкіру працівників (ДЕ ДРВП) та допустимої перкутанної дози для професійних контингентів (ДДшк) й коефіцієнтів небезпечності при перкутанному надходженні (КНшк) показало, що дермальна експозиція під час виконання окремих технологічних операцій різними способами обробки мала достовірну відмінність між способами обробки, проте відсутньою у межах одного способу.
Висновки. Під час порівняння коефіцієнтів небезпечності при перкутанному надходженні, розрахованих за різними моделями, не було виявлено достовірної розбіжності між ризиками, що розраховані за ДЕ ДРВП та ДДшк для окремих технологічних операцій різних способів обробки, окрім як для оператора ранцевої обробки: ризик, що розрахований за ДДшк є достовірно нижчим порівняно із ризиком при ДЕ ДРВП.

Ключові слова: **допустимий рівень впливу на оператора, потенційний вплив на шкіру, пестициди, оцінка ризику, професійний вплив, засоби індивідуального захисту**