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PREDICTING THE RISK OF COMBINED EXPOSURE OF WORKERS TO TRIDENT AND VG HERBICIDE

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Introduction. Since broad-spectrum herbicides are mostly ineffective for the destruction of cereal weeds, it is recommended to use tank mixtures of herbicides or combined preparations. The problem of weed resistance to herbicides is also worthy of attention. To date, 113 weed species have been registered as resistant, including almost 60 species to triazine derivatives. Every year, the agricultural market increases the supply of complex mixtures of pesticide formulations containing two or more active ingredients, which increases the likelihood of their dangerous effects on workers.

The aim of the research – is to predict the risk of occupational combined exposure to tribenuron-methyl, florasulam and flumetsulam when using their mixture to protect crops of spiked cereals.

Materials and methods of the research. Trident, VG combined herbicide, experimental studies on laboratory animals to study acute oral toxicity using the OECD method No. 423, field studies of occupational conditions when using the herbicide in the treatment of cereals; exposure doses of tribenuron-methyl, florasulam and flumetsulam, risk assessment of complex (inhalation and dermal) exposure of workers to active substances using a predictive risk assessment model; methods of expert-analytical study of scientific information on toxicological properties

Results. On the example of a mixed pesticide composition based on tribenuron-methyl (chemical class of compounds – sulfonylurea), florasulam and flumetsulam (chemical class of compounds – triazole pyrimidine derivatives), it was found that the combined effect of these substances is characterized by a potentiation effect. The potentiation coefficient for a specific mixture composition of these substances is 4.76. The combined risk of exposure to Trident, VG herbicide is permissible E = 0.296.

Conclusions. The increasing frequency of the use of multicomponent pesticide formulations poses a threat of possible potentiation as one of the most dangerous types of combined effects. The necessity of taking into account the potentiation coefficients when studying occupational conditions with the use of combined preparations based on active substances with a similar type of toxic effects is substantiated. This will increase the accuracy and reliability of the results of occupational risk assessment and will contribute to the development of preventive measures to prevent the harmful effects of pesticides on workers.

Key words: mixed insecticide, tribenuron-methyl, florasulam, flumetsulam, toxicological and hygienic assessment, combined risk prediction

Introduction

In the realm of contemporary agriculture, the efficacy of prevalent broad-spectrum herbicides in combatting grassy weeds has markedly waned. Consequently, experts advise the adoption of strategic measures such as the utilization of tank mixtures of herbicides or the incorporation of combined formulations. Moreover, the challenge of weed resistance to herbicides has emerged as a critical concern, necessitating deliberate attention. Notably, this issue has culminated in the identification of resistance in 113 weed species, a notable proportion of which showcase resistance towards triazine derivatives [1]. Each year, the agricultural market witnesses an increase in the availability of complex pesticide formulations containing two or more active substances, which

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enhances the likelihood of their hazardous impact on workers.

The toxicity of pesticides in combination usually follows the pattern predicted by knowledge of their independent effects. However, the combined effect of some pesticides is significantly greater or less than expected. The question of what effect to expect when using mixed pesticide formulations is of considerable concern [2].

When two or more active substances are combined, they can interact in different ways. The most basic toxicological interactions are synergism and antagonism. Other interactions, such as potentiation, inhibition, or masking, can also modulate possible adverse effects [3].

In recent years, the trend towards an increase in the number of complex mixtures of pesticide formulations containing two or more active ingredients has become particularly relevant in order to prevent the development of resistance mechanisms and increase the biological effectiveness of pesticides in plant protection systems. Consequently, this progression accentuates the probability of workers being exposed to compounded pesticides, thereby necessitating a comprehensive appraisal of the potential cumulative impact stemming from multiple active ingredients [4].

In 2020–2023, 2878 pesticides and agrochemicals of both domestic and foreign production were registered in the State Register of Pesticides and Agrochemicals Permitted for Use in Ukraine. Of these, 845 are combined formulations, which in turn consist of 685 two-component formulations, 154 three-component formulations, and 6 four-component formulations [5].

On the example of a mixed pesticide composition based on the herbicides tribenuron-methyl (chemical class of compounds – sulfonylurea), florasulam and flumetsulam (chemical class of compounds – triazole pyrimidine derivatives), the combined action was characterised and the potential risk of their adverse effects on the health of workers was assessed.

The aim of the study is to predict the risk of occupational combined exposure to tribenuron-methyl, florasulam and flumetsulam when using a mixture composition based on them for protection of cereal crops.

Materials and methods of the research

Objects of study: combined herbicide Traident, VG (active ingredients: tribenuron-methyl, 428 g/kg + flurasulam, 160 g/kg + flumetsulam, 137 g/kg), exposure doses of tribenuron-methyl, flurasulam and flumetsulam determined in toxicological experiments of various durations (scientific literature) and at the stage of state testing of the herbicide on cereal crops using a boom spray.

The choice of this pesticide composition for predicting the risk of occupational combined exposure is dictated by a preliminary detailed study of the scientific literature on the toxicological properties of tribenuron-methyl, florasulam and flumetsulam under different modes of their exposure to the body.

The methods used were expert analytical research of scientific information on the toxicological properties of tribenuron-methyl, flurasulam and flumetsulam, methods of toxicological experiments on laboratory animals (rats), and a predictive risk assessment model, Finney's method (1952) for taking into account the combined effect of pesticides on workers with an assessment according to the criteria of «lethal effect», which involves determining the average lethal dose (LD_{50}) of each substance under study, its percentage in the mixture, the contribution of the substance to the LD_{50} of the mixture and the percentage of this amount

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from the LD_{50} of the substance (Kagan Yu.C., 1981):

$$\frac{A}{LD_{50\,(a)}} + \frac{B}{LD_{50\,(b)}} + \frac{C}{LD_{50\,(c)}}, \qquad (1)$$

where A is the amount of substance «a» (mg/kg) included in the LD_{50} mixture;

$LD_{50(a)}$ – average lethal dose of substance «a», mg/kg;

B – the amount of substance «b» (mg/kg) included in the LD_{50} mixture;

$LD_{50(b)}$ – average lethal dose of substance «b», mg/kg;

where C is the amount of substance «c» (mg/kg) included in the LD_{50} mixture;

$LD_{50\,(c)}$ – average lethal dose of substance «c», mg/kg.

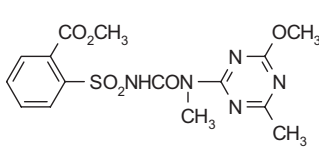
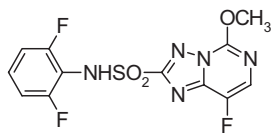
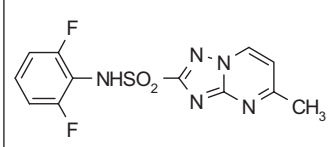
The type of combined action (summation, antagonism, potentiation) was determined based on the sum of the obtained percentages. If the sum of the percentages exceeded 100, meaning that the dose of the substances needed to achieve a lethal effect exceeded the LD_{50} when combined, then antagonism was observed. A sum of percentages less than 100 indicated potentiation, while a sum of percentages equal to 100 characterized summation [6].

Toxicological studies on the investigation of acute oral toxicity of the Traident, VG (active substance: tribenuron-methyl 428 g/kg + florasulam 160 g/kg + flumetsulam 137 g/kg) were conducted following the guidelines provided by the Organisation for Economic Cooperation and Development (OECD): Guideline for Testing of Chemical «Acute Oral Toxicity – Acute Toxic Class Method», No. 423. These toxicological studies were approved by the Bioethics Commission of the State Institution «Kundiiev Institute of Occupational Health of the National Academy of Medical Sciences of Ukraine» (protocol dated 13.06.2022, No. 1).

For the prediction and quantitative assessment of inhalation and dermal exposure levels to tribenuron-methyl, florasulam, and flumetsulam, which operators may encounter at various stages of the process (preparation of working solutions, filling of technical equipment, and spraying), a Predictive Operator Exposure Model (POEM) [7]. The chemical characteristics of tribenuron-methyl, florasulam, and flumetsulam are presented in Table 1.

Table 1

Chemical characteristics of the active substances

Indicator	Active ingredient		
	tribenuron-methyl [6]	florasulam	flumetsulam [7]
CAS RN	[101200-48-0]	[145701-23-1]	[98967-40-9]
Chemical class of compounds	Sulphonylureas	Triazole pyrimidine derivatives	Triazole pyrimidine derivatives
The empirical formula	$C_{15}H_{17}N_5O_6S$	$C_{12}H_8O_3N_5F_3S$	$C_{12}H_9F_2N_5O_2S$
Molecular mass	395.40	359.3	325.29
Structural formula			

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Results of the research

Toxicological profiles of tribenuron-methyl, florasulam, and flumetsulam are presented based on scientific literature [8–10]. Acute toxicity parameters and non-effective dose levels determined in short- and long-term experiments on laboratory animals (rats, mice, rabbits, dogs) are presented in Table 2.

Tribenuron-methyl is a selective post-emergence herbicide that inhibits the biosynthesis of branched-chain amino acids (valine, leucine and isoleucine) by blocking the substrate access to the active site of the acetolactate synthase (ALS) enzyme. Tribenuron-methyl is absorbed by roots and leaves and is easily transported in plants. Inhibition of ALS leads to growth arrest and then to plant death. Weed growth stops within a few hours after spraying. Sensitive weeds may remain green and survive, but they will not compete with cultivated plants [11].

According to the mechanism of toxic action, tribenuron-methyl is a substance of general toxicity with weakly expressed cumulative properties. In subchronic exposures in rats, the NOAEL is set at 5 mg/kg and 7 mg/kg; in experiments on dogs, the NOAEL is 500 ppm (15.1 mg/kg/day for males and 14.9 mg/kg/day for females).

Nocarcinogenic activity were detected in chronic experiments with mice; in chronic experiments with rats, the NOAEL was 25 ppm (0.95 and 1.2 mg/kg/day for males and females, respectively); in experiments with dogs, the NOAEL was 250 ppm (8.16 and 8.18 mg/kg/day for males and females, respectively). The incidence of benign and malignant mammary tumors observed in rat experiments did not differ from the «historical control» for female Sprague-Dawley rats, which suggests that tribenuron-methyl has no carcinogenic activity. Teratogenic and embryotoxic effects of tribenuron-methyl, as well as reproductive toxicity, as evidenced by the results of experiments on rats and rabbits, are detected at higher doses and are not limiting. The results of the study of the cytogenetic properties of tribenuron-methyl indicate the absence of mutagenic properties.

Based on the severe effects observed in studies on rabbits (maternal mortality in the developmental toxicity study at a dose of 80 mg/kg and histopathological changes in kidneys in a 28-day dermal toxicity study on rabbits at a dose of 1000 mg/kg), tribenuron-methyl is classified as STOT RE2 H373: «specific target organ toxicity – repeated exposure or prolonged exposure» [12].

In Ukraine, the approved Acceptable Daily Intake (ADI) for tribenuron-methyl for humans is 0.005 mg/kg, based on the results of chronic toxicity studies on rats (NOAEL – 25 ppm, equivalent to 0.95 mg/kg/day for males and 1.2 mg/kg/day for females) and an uncertainty factor (UF) of 200. In the European Union (EU), the approved ADI is set at 0.01 mg/kg, using the same NOAEL value and an uncertainty factor (UF) of 100.

Florasulam is a systemic herbicide of the triazolpyrimidine derivatives class, an ALS inhibitor with a mechanism of action similar to tribenuron-methyl. Florasulam has a high selectivity of action, which is achieved by a high metabolic rate in cultivated plants compared to weed species; it penetrates plants through leaves and roots, and does not penetrate grain [13].

The toxicokinetics data of florasulam have shown high bioavailability after oral administration, a large distribution without bioaccumulation, and rapid elimination, primarily through the urine. In short-term studies, side effects were observed in the blood (anemia), liver, and kidneys. The impact on the kidneys was considered adaptive or spontaneous, but it cannot be ruled out as study-related.

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Table 2

Results of toxicological studies of tribenuron-methyl, florasulam and flumetsulam

Indicator	Active ingredient		
	tribenuron-methyl [8]	florasulam [9]	flumetsulam [10]
Acute oral toxicity	LD_{50} for rats > 5000 mg/kg	LD_{50} tor rats > 5000 mg/kg for male and female; LD_{50} for male and female mice > 5000 mg/kg	LD_{50} tor rats > 5000 mg/kg for males and females
Subacute oral toxicity	NOEL for rats: 5000 ppm	NOAEL for rats for systemic toxicity: 1000 mg/kg; NOAEL for local irritant effect: 500 mg/kg; NOAEL for dogs: 5 mg/kg; NOAEL for mice: 100 mg/kg	NOAEL for rats for systemic toxicity >1000 mg/kg; NOAEL for rabbits: >1000 mg/kg
Subchronic oral toxicity	NOEL for mice: 500 ppm – 70 mg/kg for males and 90 mg/kg for females; NOEL for rats: 5 mg/kg and 7 mg/kg, for males and females, respectively; NOAEL for dogs: 500 ppm – 15.1 mg/kg/day for males and 14.9 mg/kg/day for females)	NOEL for rats: 100 mg/kg; NOEL for dogs: 5 mg/kg; NOEL for mice: 100 mg/kg	NOAEL for rats: 250 mg/kg for males and females; NOAEL for mice: 1000 mg/kg for males and females
Chronic toxicity	NOEL for rats: 5 ppm – 0.95 mg/kg and 1.2 mg/kg for males and females, respectively; NOAEL for rats for carcinogenic activity: 250 ppm (10 mg/kg); NOEL for mice: 20 ppm (2.5 mg/kg for males); NOEL for dogs: 250 ppm (8.16 and 8.18 mg/kg/day for males and females, respectively)	NOAEL for mice: 50 mg/kg; NOAEL for rat: 10 mg/kg; NOAEL for dogs: 5 mg/kg	NOAEL for rats (based on signs of systemic action – 500 mg/kg for males and 1000 mg/kg for females; NOAEL for mice – 1000 mg/kg; NOAEL for dogs (systemic effects) – 100 mg/kg
Teratogenic and embryotoxic effects	NOAEL for rats for systemic toxicity to the mother: 20 mg/kg; NOAEL for rat fetal development: 20 mg/kg; NOAEL for rabbits for maternal body: 20 mg/kg; NOAEL for rabbit fetal development: 20 mg/kg	NOAEL for rats for maternal body: 250 mg/kg; NOAEL for rat for fetal development: 750 mg/kg; NOAEL for rabbits for maternal and fetal development: 500 mg/kg	NOAEL for rats for maternal systemic toxicity: 5000 mg/kg; NOAEL for rat fetal development > 1000 mg/kg; NOAEL for rabbits for maternal systemic toxicity: 100 mg/kg; NOAEL for rabbit fetal development > 700 mg/kg
Reproductive toxicity	NOEL for rats: 25 ppm – 1.9–2.28 mg/kg and 2.15—2.64 mg/kg for males and females for the parental and offspring generations, respectively)	NOEL for systemic toxicity: 100 mg/kg; NOEL for reproductive toxicity: 500 mg/kg	NOEL for rats for the parental generation and offspring: 1000 mg/kg

Notes. NOAEL – no observed adverse effect level, NOEL – no observed effect level (no action level)
According to the literature.

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The subacute oral toxicity for dogs resulted in a NOAEL of 5 mg/kg body weight per day. Available genotoxicity studies did not show any signs of genotoxic potential for florasulam. After prolonged exposure, the kidneys were the main target organ, exhibiting cell hypertrophy in collecting ducts (in rats and mice), tubular degeneration with regeneration (in rats), papillary necrosis or mineralization (in rats), without kidney tumor formation. For reproductive toxicity based on systemic toxicity, the NOAEL is 100 mg/kg body weight per day.

In the developmental toxicity study on rats NOAEL for the maternal organism was 250 mg/kg body weight per day, and the NOAEL for fetal development was 750 mg/kg body weight per day (high dose). For rabbits, the NOAEL for the maternal organism and fetal development was 500 mg/kg body weight per day (high dose). Acute and one-year neurotoxicity studies on rats did not show specific neurotoxic effects. In chronic studies, critical effects were related to overall parameters such as body weight decrease and signs of nephrotoxicity [9].

In Ukraine, the approved ADI for florasulam for humans is 0.05 mg/kg, based on the non-effective dose for dogs in the chronic experiment (NOEL – 5 mg/kg) and an UF of 100. The same value for the acceptable daily dose is approved in the European Union.

Flumetsulam is a systemic herbicide belonging to the class of triazolopyrimidine derivatives. It inhibits the activity of ALS (acetolactate synthase) and has a broad application range, from early seedling to the appearance of the first trifoliate leaf. Additionally, it can control broadleaf weeds in later stages of development and suppress those species that may exhibit resistance to other herbicides. It does not leave any residual effects on subsequent crops.

Flumetsulam does not exhibit skin-resorptive effects: when applied to the skin of rabbits in a subacute experiment, the NOEL is > 1000 mg/kg. In subchronic studies on rats, the NOAEL is 250 mg/kg. In chronic experiments conducted on dogs (1 year), the NOAEL is 100 mg/kg. At a higher dose of 500 mg/kg, a decrease in body weight and signs of inflammatory and atrophic changes in the kidneys were observed. In toxicity/carcinogenicity studies on rats, the systemic NOAEL for males is 100 mg/kg, and for females, it is 1000 mg/kg. Flumetsulam did not exhibit carcinogenic effects. No signs of reproductive toxicity were observed, and the NOAEL for rats is 1000 mg/kg. Teratogenicity and embryotoxicity studies established the NOEL for systemic toxicity in rats at 500 mg/kg, and the NOEL for embryotoxicity was > 1000 mg/kg (highest dose tested). For rabbits, the NOEL for systemic toxicity is 100 mg/kg, and the NOEL for embryotoxicity is ≥ 700 mg/kg (highest dose tested). Flumetsulam does not demonstrate mutagenic activity.

In Ukraine, the ADI for flumetsulam in humans is approved at 0.2 mg/kg. In EU countries, the ADI is set at 1 mg/kg based on the NOEL established for male rats in chronic experiments for systemic effects and uncertainty factor (UF 100).

It can be considered that under the combined influence of tribenuron-methyl, florasulam, and flumetsulam on the organism, there may be manifestations of potentiation of their toxic effects. The assessment of the combined impact was conducted based on the LD_{50} values established for the Traident, VG preparation, and its active substances during the study of acute oral toxicity.

The acute oral toxicity study was conducted according to OECD Test Guideline No. 423 [14, 15]. The test substance, in the form of a 30 % aqueous solution, was administered to female

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Wistar Han rats (n = 3 at each of the two stages) via a metal probe directly into the stomach at a single dose of 2000 mg/kg body weight. No deaths of animals were observed during the study. Clinical signs of intoxication (lethargy, reduced motor activity, decreased appetite, nasal hemorrhage, pathological secretion from the urogenital system) were noted during the first two days of the experiment, but the condition of the test subjects returned to normal afterward. The body weight of the animals showed slight positive dynamics throughout the observation period, with an average weight gain of 5.83 grams at the end of the study. No macroscopic changes in the internal organs were detected.

LD_{50} > 2000 mg/kg.

As reported in the literature, toxicometric parameters for a single oral administration to rats have been elucidated: LD_{50} of tribenuron-methyl, florasulam and flumetsulam are established at 5000 mg/kg [8–10].

The tested preparation contains the following relative content of active substances: tribenuron-methyl – 42.8 %, florasulam – 16 %, flumetsulam – 13.7 %. The total sum of the ratios of the content of each active substance to their LD_{50} is 21.025 %, which corresponds to a potentiation of the combined toxic effect of the preparation with a potentiation factor of 4.76.

The next step of the study involves the risk assessment procedure for potential cumulative occupational exposure to tribenuron-methyl, florasulam, and flumetsulam among workers, using the Predictive Operator Exposure Model (POEM) for risk assessment [7].

In the exposure calculation algorithm of the herbicide Traident, VG, the following factors were taken into account: the stage of the production process (mixing/filling and spraying); the method of application and the type of sprayer used; the formulation type (water-soluble granules); the application rate of the preparation/working solution (35 g/ha in 300 liters of water); the concentrations of active substances in the preparation, and the availability of personal protective equipment (PPE+).

The acceptable operator exposure level (AOEL) for tribenuron-methyl is 0.05 mg/kg, based on a subchronic study on rats with a defined NOAEL value of 7 mg/kg, an uncertainty factor (UF) of 100, and an oral absorption factor of 67 %. Dermal absorption of tribenuron from concentrated solutions is 23 %, and from diluted solutions is 75 % [8].

The AOEL value for florasulam is also 0.05 mg/kg, based on the NOEL established in a subchronic experiment on dogs (NOEL – 5 mg/kg) and an UF of 100. Dermal absorption of florasulam from the formulation (PRIMUS SC) is 12 %, and from diluted water solutions is 23 % [9].

The AOEL for flumetsulam is 100 mg/kg. The dose absorbed through the skin was assumed to be 100 % due to the lack of experimental data [10, 16].

The absorbed dose of the substance when it enters the body by inhalation is 100 % of the maximum exposure dose.

The assessment of working conditions was carried out based on the indicator of the degree of influence (E), which is calculated as the ratio of the total absorbed dose to the acceptable operator exposure level (AOEL). The risk is considered acceptable if $E \leq 1$.

The calculation of exposure and absorbed dose is presented in Table 3.

From the given data, it appears that the predicted risk of combined (inhalation and dermal) exposure, calculated using the POEM model, will be as follows for tribenuron-methyl – 0.228, for florasulam – 0.068, for flumetsulam – 0.0000216. These predicted risk values do not exceed their respective Acceptable Operator Exposure Levels (AOEL).

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Table 3

Potential risk of exposure of workers to tribenuron-methyl, florasulam and flumetsulam when applying Traident, VG by boom spraying (Predictive Operator Exposure Model model)

Indicator	Values for active substance		
	tribenuron-methyl	florasulam	flumetsulam
Mixing/filling stage: Dermal exposure			
Hand skin contamination, mg a.s./day	4.28428	1.6016	1.37137
Use of PPE	*Gloves*		
Absorption	1%		
Dermal exposure to herbicide, mg/day	0.04284	0.016016	0.013714
Inhalation exposure			
Inhalation exposure, mg/day	0.026814	0.0010024	0.00858
Use of PPE	–		
Absorption	100 %		
Absorbed inhalation dose, mg/day	0.026814	0.010024	0.00858
At the stage of spraying: Dermal exposure			
Working fluid consumption rate, 1/ha	300		
Contamination levels, ml/h	10		
Total dermal exposure to the working solution, ml/day	6.45		
Absorbed dose through the skin, mg/day	0.24155	0.2769	0.10309
Inhalation exposure during spraying			
Inhalation exposure to working solution, ml/h	0.01		
Inhalation exposure to a.s., mg/day	0.002996	0.00112	0.00959
Percent absorption	100%		
Absorbed inhalation dose, mg/day	0.002996	0.00112	0.00959
Total absorbed dose, mg/day	0.281217	0.000679	0.002106
Operator body weight	60 кг		
Total absorbed inhalation/dermal dose, mg/kg b.w./day	0.0072/0.0042	0.00029/0.0005	0.00016/0.002
Risk assessment			
AOEL, мг/кг	0.05	0.05	100
$E_{inhal} = I_{adsorb}$: AOEL	0.144	0.058	0.0000016
$E_{derm} = D_{absorb}$: AOEL	0.084	0.01	0.00002
$E_{total} = E_{inhal} + E_{derm}$	0.228	0.068	0.0000216
$E_{TRIDENT, VG} = E_{tribenuron\text{-}methyl} + E_{florasulam} + E_{flumetsulam}$	0.296		

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The combined risk of the effects of Tribenuron-methyl, Florasulam, and Flumetsulam on workers, calculated by summing up the risks of each individual active substance, will be 0.296, which is considered acceptable (E < 1).

The potentiation factor is 4.76, then inhalation risk is exceeded by 4.96 times, and the dermal risk is exceeded by 4.85 times.

To reduce the potential inhalation exposure for workers, it is necessary to use universal respirators that meet the requirements and have a maximum protection factor of 0.05. It is possible to reduce the potential dermal exposure of workers by using protective gloves with an exposure attenuation factor of 0.1.

When considering the potentiation coefficient, the effectiveness of evaluating working conditions is increased, and a plan of measures to reduce the combined and complex impact of the mixed herbicide composition is determined.

To ensure occupational health and safety and industrial sanitation when working with Traident, VG, it is necessary to comply with the requirements of the developed instructions for safe use and adhere to generally accepted occupational health and safety requirements for working with pesticides.

Discussion

At the Hygiene and Ecology Institute of Bogomolets National Medical University, a combined risk was established when using the mixed fungicide Switch 62.5 WG, with a risk level of 0.062 u.o. when applying the preparations sequentially in the strawberry chemical protection system – 0.452 u.o., which does not exceed the acceptable risk (1) [17]. The combined risk of the herbicide Traident, VG (containing tribenuron-methyl 428 g/kg + florasulam 160 g/kg + flumetsulam 137 g/kg) determined by us is E = 0.296 (E < 1), which is considered permissible. The interest of specialized researchers from various institutions in the issue of combined risk testifies to the relevance of this direction and the potential harm it poses to workers' health, creating prerequisites for improving methodological approaches and systematizing the knowledge already acquired.

Conclusions

1. One of the most perilous manifestations of combined effects on the human body is potentiation, a phenomenon that can arise due to the use of combinations of distinct active substances within pesticide formulations.
2. On the example of a mixed pesticide composition based on the herbicides tribenuron-methyl (chemical class of compounds – sulfonylurea), florasulam and flumetsulam (chemical class of compounds – triazole pyrimidine derivatives), the type of their combined toxic effect was determined, which is characterised by a pronounced potentiation effect, when taken into account in the identification of hazard according to the prognostic risk assessment model, the inhalation exposure to the active substances exceeded the permissible level by almost 5 times.
3. Enhancing the precision and dependability of occupational risk assessments for workers mandates the inclusion of potentiation factors when studying working conditions involving combined formulations comprising active substances with comparable toxic effects.
4. The work environment ensures a satisfactory level of safety for workers, provided that it adheres to established labor protection standards concerning pesticide handling. The permissible combined risk of exposure to the herbicide Traident VG is within acceptable limits, indicated by a value of E = 0.296.

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