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TOXICOLOGICAL SUBSTANTIATION FOR DIDECYLDIMETHYLAMMONIUM CHLORIDE OCCUPATIONAL EXPOSURE STANDARD

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ABSTRACT. *Dydetsyldymetylammonium chloride (DDAC) is used as a raw material in the chemical industry for the production of some insecticidal, fungicidal and aldehydic preparations and disinfectants in which it is an active ingredient.*
Aim of the Research. To establish a scientific substantiation for DDAC indicative safe exposure level (ISEL) in the workplace air by analyzing and summarizing the bibliographic data about the degree of DDAC danger.
Methods. *To establish a scientific substantiation for DDAC occupational exposure standard the following properties were analyzed: its physical and chemical characteristics; LD_{50} (lethal dose) for oral and dermal exposure; LC_{50} (lethal concentration) for inhalation exposure; irritant and sensitizing properties; NOAELs (no-observed adverse effect level) for DDAC were determined in sub-acute and sub-chronic experiments under different conditions of exposure as well as its long-term effects.*
The calculation of DDAC ISEL in the workplace air was performed using equations which make allowance for the toxicity properties of the preparation when it is administered to laboratory animals through different routes.
Results. *DDAC is an imported product used as an active ingredient in the production of certain pesticides and disinfectants.*
DDAC falls into the category of non-volatile substances: its vapor pressure is $<1x10^{-2}$ Pa at 20° C, at 50°C – $2,3x10^{-4}$ Pa (US ISC)
When introduced into the gastrointestinal tract, the substance is classified as moderately dangerous – Category 3 (in accordance with Globally Harmonized System of Classification and Labeling of Chemicals / GHS / United Nations, New York and Geneva, 2017) and has a mild skin-resorptive effect (Category 4, GHS). Its adverse local impact on the skin has been identified. The substance LC_{50} after inhalation exposure is 70 mg/m^3 (Category 2, GHS). DDAC produces marked irritant action on the skin and conjunctiva of rabbits (Category 1B, GHS). Erythema, crust and swelling were recorded on skin. Burns, corrosion, acute keratoconjunctivitis were observed when the substance got onto conjunctiva. No sensitizing effect of the preparation was found (not classified, GHS). The cumulative properties of the substance are incomplete. NOAELs were determined in sub-acute and sub-chronic experiments after oral, dermal and inhalation exposure. The most affected organs and systems are skin, eyes, gastrointestinal tract, liver. Mutagenic, carcinogenic, embryotoxic, teratogenic and toxic effects on the reproductive function are not limiting harmful criteria.
Calculation of the value of DDAC ISEL in the workplace air was conducted by the equations of regressive dependence, which take into consideration the parameters of acute toxicity. Making allowance for the degree of its hazard and the risk of developing the pathology of general genesis under the effect of the substance, the recommended ISEL value in the workplace air is 0.2 mg/m^3, aggregate state "a" with the mark "protection of eyes and skin is necessary".
Key Words: *dydetsyldymetylammonium chloride, DDAC, ISEL in the workplace air, insecticides, disinfectants.*

Introduction. Measures to combat synanthropic insects and pathogenic microflora are aimed at ensuring sanitary and epidemiological welfare of the population and are essential means to maintain appropriate hygienic conditions in the areas of human activities. Therefore, it is of vital importance to study how to determine the degree of safety of disinfectants which are used for their designated purposes.

At present in Ukraine dydetsyldymetylammonium chloride (DDAC) is in use. This substance has a wide spectrum of action as well as selective biological activity in fighting synanthropic insects, phytopathogenic fungi, clams and virulent pathogens. DDAC is used as a raw material in the chemical industry for the production of insecticidal, aldehydic, bactericidal and fungicidal agents. It is used to control synanthropic insects in everyday life, to protect wood and products made of wood from insects and microorganisms. It is also used to protect crops from fungal diseases as well as to destroy algae and other weeds in water bodies. DDAC is also used as a substance having bactericidal and antiviral effect. Therefore, it is contained as an active ingredient in some disinfectants (microbiostates, viricides, tuberculocides, antiseptics and deodorants) which are used to treat various surfaces in different areas of human activity, such as walls, floors, dishes, rugs, medical devices, swimming pools etc.

In Ukraine, the substance is not produced, its occupational exposure standard is not developed. The urge to develop dydetsyldymetylamonium chloride ISEL in the air is due to the need to exercise control over its safe content in the workplace air while using pesticides and disinfectants developed on its base.

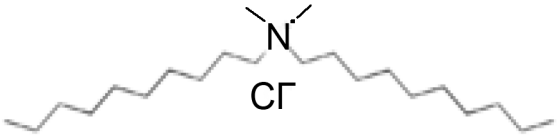
Calculations of the substance occupational exposure standard were performed on the basis of the data about DDAC toxicological properties acquired in the process of information retrieval using scholarly libraries abstract (reference) database.

The Aim of the Research. To analyze and summarize current data on the degree of DDAC danger while using it for its intended purpose; to provide a scientific basis for its ISEL in the workplace air.

Methods and Materials. Analytical review of scientific publications was performed using scholarly libraries abstract (reference) database and a text database of methodological and biological publications PubMed.

Results and Discussion. The information search of scientific publications made it possible to obtain information about DDAC physical-chemical and toxicological properties, on the basis of which calculations were made to determine its occupational exposure standard [1-22].

Physical-chemical parameters. DDAC belongs to quaternary ammonium compounds by its chemical structure [1, 2]. Chemical name – N – didecyl – N, N-dimethylammonium chloride, empirical formula $C_{22}H_{48}Cl$, structural formula



Abbreviation for didecyldimethylammonium chloride is DDAC. CAS RN 7173-51-5. Molecular weight is 362.08 g/mol. DDAC 98.2 % is a light yellow solid substance with an aromatic odor. Relative density is D_4^{20} – 0,902. Surface tension is 27.0 mN/m at 20° C (sample solution 1 g/l of aqueous solution). Vapor pressure is $<1x10^{-2}$ Pa at 20° C, at 50° C – 2.3×10^{-4} Pa. Volatility: extremely low. The octanol / water partition coefficient is log Kow = 0.41 at 20° C. Water solubility: pH 2.2 – 500 g/l at 20° C; pH 9,2 – 500 g/l at 20° C, in organic solvents (at 20° C): acetone > 600 g/l; methanol > 600 g/l; octanol > 250 g/l.

Technical DDAC (<80 %) is a lightyellow liquid substance with a characteristic odor; pH at 25° C is 6.8 - 6.9 (29.5 % aqueous solution). Density at 20° C is 0.95 g/cm^3. Solubility in water at 20° C is 650 g/l. Vapor pressure is 1.24 10^6 mm Hg at 21.6° C. Stable in organic solvents for 14 days.

Toxicological Properties. When administered through the gastrointestinal tract, DDAC belongs to moderately dangerous substances – Category 3 (according to the Globally Harmonized System of Classification and Labeling of Chemicals / GHS / United Nations, New York and Geneva, 2017). LD_{50} after oral exposure for rats is 84 mg/kg according to some data, and 238 mg/kg according to other data; for mice, it is 268 mg/kg [3, 2]. The symptoms of intoxication for rats and mice were similar: from a significant decrease in spontaneous motor activity to complete immobility. Macroscopic examination showed irritation of the intestinal mucosa. Species sensitivity is not significant.

DDAC (65%) has a skin-resorptive effect. When applied epicutaneously its LD_{50} for rabbits is 3342 mg/kg (Category 4 according to GHS). There was an adverse local effect on the skin [2]. Upon dimethylammonium chloride intake LK_{50} is 70 mg/m^3 (Category 2 according to GHS).

In the process of information retrieval, it was found that the substance is not volatile, its vapor pressure is $<1 \times 10^{-2}$ Pa at 20° C, at 50° C it is $2,3 \times 10^{-4}$ Pa (US ISC); it has high surface activity and is sprayed only in large drops of MMAD > 40 μm size [2, 3]. DDAC (80%) has marked irritant effect on the rabbits' skin and conjunctiva (Category 1 in accordance with GHS) causing burns (corrosion) [1-10]. No sensitizing effect of the compound on guinea pigs was revealed by Magnusson and Kligman method while performing skin tests (not classified according to GHS) [1-10]. The cumulative properties of the substance are not significant [2-10]. Noobserved effect levels for DDAC were determined in subacute experiment after oral, dermal and inhalation exposure [2-16]. When the substance was administered to rats through the gastrointestinal tract for 28 days NOAELwas 2.5 mg/kg. During a 90-day oral toxicity study, it was estimated that NOAEL for rats is 46 mg/kg of body weight per day. Taking technical DDAC (80.8%) with fodder at doses of 0, 30, 60 and 90 mg/kg during the period of 21 days caused in Beagle dogs impaired gastrointestinal function, and weight loss. NOEL for dogs is 60 mg/kg.

Under the conditions of subchronic exposure, the NOEL was slightly lower. It was

found that NOEL for dogs was 15mg/kg when they took DDAC for 90 days with fodder. Taking DDAC with fodder by CD-1 mice on a daily basis for 90 days at doses of 100, 300, 600 1000, and 3000 ppm caused a decrease in body weight and death of animals. NOEL for mice was determined at 600 ppm.

High doses of technical preparation (80.8%) which was administered through gastric catheter to Beagle dogs for 8 weeks (doses of 7.5, 15, 30 and 60 mg/kg) caused their death, symptoms of intoxication and defecatory disorder. There was a lot of mucus in their fecal masses. NOAEL – 7.5 mg/kg. When 0.6% aqueous solution of DDAC was applied to skin for 5 days, its NOAEL was 2.5 mg/kg. The same NOAEL value was when a compound in the form of 0.3% aqueous solution was applied to skin for 2 weeks.

Swelling, erythema, epidermitis, dermatitis, spot hemorrhage, vascular degeneration and skin ulcers were observed in Sprague-Dawley rats whose skin surface was exposed to DDAC aqueous solution in amounts of 2, 6 and 12 mg/kg for 13 weeks (6 hours exposure, 5 times a week).

After 90-day application of the preparation to the skin, NOAEL for systemic toxicity was 12 mg/kg/day, and NOAEL for local effect was 2 mg/kg/day.

Studies have been conducted to determine the DDAC toxicity when administered to the organism as aerosol through the respiratory system of Sprague-Dawley rats in concentrations of 0.15±0.15 mg/m^3, 0.58±0.40 mg/m^3, 3.63±1,56 mg/m^3 for 2 weeks. The mass median aerodynamic diameter of DDAC aerosols was 1.86 μm, and the geometric standard deviation was 2.75 μm. In groups exposed to high concentrations, a decrease in body weight of 2.6 g was observed, whereas in the control group an increase of 25.8 g after the first 3 days was observed. There were no changes in hematological and biochemical parameters of blood. There were slight changes in the amount of differentiation of bronchoalveolar cells and cell damage in the fluid of bronchoalveolar contents in groups of animals which were exposed to the preparation in high and medium concentrations. Although infiltration of inflammatory cells of interstitial pneumonia was partially observed, fibrosis in the lungs was not detected when exposed to medium and high concentrations. DDAC NOAEL for rats was determined as 0.15 mg/m^3 [11, 12].

The inhalation toxicity of DDAC aerosol was studied in Sprague-Dawley rats in chambers for 13 weeks at concentrations of 0.11, 0.36, and 1.41 mg/m^3 The mass median aerodynamic diameters of the aerosol were 0.63 μm, 0.81 μm, and 1.65 μm, while the geometric standard deviations were 1.62, 1.65, and 1.65 in groups with low (0.11± 0,06 mg/m^3), mid (0,36 ± 0,20 mg/m^3) and high (1,41±0,71 mg/m^3) concentrations of exposure respectively. The average body weight of males was 35% lower while that of females 15% lower in the high concentration group (1.41±0.71 mg/m^3) compared to the control group. While testing the fluid of bronchoalveolar lavage, it was found that the amount of albumin and lactate dehydrogenase was within the normal range. Infiltration of inflammatory cells and interstitial pneumonia, as well as lung weight increase were observed at exposures to mid and high concentrations of DDAC. However, no serious histopathological disorders in the lungs, including proteinosis and/or fibrosis, have been identified. Based on the results of changes in body weight and lungs, NOAEL for rats was defined as 0.11 mg/m^3 [13].

The study of the DDAC toxicity properties in a chronic experiment was performed on three species of animals: rats, mice and dogs [2 – 10,15]. Sprague-Dawley CD rats took the technical preparation (80.8%) with fodder for 104 weeks at doses of 300, 750 and 1500 ppm. Decrease in body weight and feed intake, as well as pathology of mesenteric lymph nodes (hemosiderosis and histiocytosis, blood in the sinuses) were noted at 1500 ppm exposure dose of DDAC. DDAC NOEL for rats in general toxicity terms is 750 ppm (27 mg/kg).

CD-1 mice took technical DDAC (80.8%) with fodder for 18 months in amounts of 100, 500 and 1000 ppm. A decrease in body weight and feed intake were observed in animals at 1000 ppm. NOEL for male and female mice in terms of systemic toxicity was defined as 500 ppm.

Clinical symptoms of intoxication (hypersalivation, vomiting, abnormal fecal masses), weight loss, periodical albumin, total protein and cholesterol decreased levels in blood serum, as well as erythrocytes, hemoglobin and hematocrit drop in peripheral blood were observed in Beagle dogs which were exposed to DDAC through catheter in the amount of 3, 10

or 30 mg/kg per day during the period of 1 year. DDAC NOAEL for dogs in terms of systemic toxicity was defined as 10 mg/kg, in terms of local reaction – 3 mg/kg.

The carcinogenic properties of DDAC have been explored in 3 animal species: rats, mice and dogs. Sprague-Dawley CD rats received the substance with fodder at doses of 300, 750, and 1500 ppm for 104 weeks. CD-1 mice were given the preparation with fodder in the amount of 100, 500 and 1000 ppm for 18 months. Beagle dogs received the substance through gastric catheter in the amount of 3, 10 or 30 mg/kg per day for 1 year. No carcinogenic effect was detected: NOAEL after chronic DDAC exposure was 32-41 mg/kg per day for rats, 76-93 mg/kg per day for mice, and 10 mg/kg per day for dogs.

The mutagenic effect of DDAC was not detected either in vitro or in vivo tests (Ames test, with or without microsomal activation / fraction S-9 / on Salmonella typhimurium; in Chinese hamster ovary cells, in rats hepatocytes of unplanned DNA synthesis, induction of chromosomal aberrations in mouse bone marrow cells and induction of micronuclei in mouse bone marrow cells).

No negative effect of DDAC (80.8%) on the reproductive function of Sprague-Dawley rats (CD) in the two generations test was found. The animals received the substance with fodder at doses of 10, 30 and 52 mg/kg. Cortical adrenal hypertrophy was observed at the maximum dose in females of the Fo generation. A decrease in body weight and an increase in spleen mass was observed in the F1 generation. No change in reproductive function was recorded. DDAC NOEL in terms of systemic toxicity was determined as 32 mg/kg [15].

When introduced through catheter into the CDBR Sprague-Dawley rats which were 6 to15 days pregnant (doses 1, 12.5 25, 37.5, and 50 mg/kg), DDAC (80.8%, solvent – Millipore deionized water) in higher doses caused respiratory malfunctions (polypnoea, dyspnoea) and decreased feed intake. There was an increase in post-implantation mortality, a decrease in fetal body weight at a dose of 50 mg/kg. NOAEL for the maternal rats was 12.5 mg/kg, for the fetus – 37.5 mg/kg. According to other authors, NOAEL for females in terms of systemic toxicity was 1.0 mg/kg [2]. When the preparation was administered to 6 to 15 days pregnant rabbits in high doses (12 and 32 mg/kg), symptoms of intoxication and abortions were observed. NOAEL for pregnant female rabbits was 4 mg/kg, for fetuses – 12 mg/kg [2, 3].

DDAC is a highly ionic compound. Studies in rats proved that 85 – 90% of the preparation is excreted within 24 hours through the gastrointestinal system, and 2.6 – 3% – through the urinary system. In animal tissues, less than 1% of the substance is found. DDAC metabolism by intestinal microflora results in the formation of hydroxylation products of an alkyl chain and involves the oxidation of 2 decyl side chains in the form of derivatives of hydroxy- and hydroxyketone compounds. In the body of females, the metabolism of the substance is faster than in males.

Approximately 0.1% of the dose of DDAC aqueous solution penetrates the skin when tested for 24 hours in human cells culture *(in vitro)*. The amount of radioactive substance in the dermis and epidermis was 9.41% of the dose applied to the skin.

Thus, analysis of the bibliographic data about DDAC toxic properties proved that DDAC produces a marked irritant effect on the skin and conjunctiva. The substance belongs to moderately toxic substances in intragastric action while it is low toxic at dermal exposure. It does not have sensitizing or cumulative properties. Mutagenic, carcinogenic, embryo toxic, teratogenic effects and toxic effect on reproductive function are not limiting harmful criteria.

The calculation of DDAC ISEL in the workplace air was performed using the equations that take into account the parameters of toxicity of the preparation depending upon different routes of its intake by laboratory animals, in accordance with the "Methodological Guidelines for Establishing Indicative Safe Exposure Levels of Harmful Substances in the Workplace Air" ("Metodicheskih ukazanij po ustanovleniju orientirovochnyh bezopasnyh urovnej vozdejstvija vrednyh veshhestv v vozduhe rabochej zony") (P. 4000-85 from 04.X1.1985) and the formulas given in the section "Substantiation for Indicative Safe Exposure Levels (ISEL) of Pesticides in the Workplace Air When They are Used in Agriculture" of Methodological Guidelines for Hygienic Evaluation of New Pesticides, Kyiv, 1988 ("Obosnovanie orientirovochnyh bezopasnyh urovnej vozdejstvija (OBUV) pes-

ticidov v vozduhe rabochej zony pri ih primenenii v sel'skom hozjajstve" (Metodicheskie ukazanija po gigienicheskoj ocenke novyh pesticidov, Kiev, 1988) [2, 3].

The formulas by which the calculation of DDAC ISEL in the workplace air was performed are given in Table 1.

The parameters in the formula were calculated in accordance with the following data: Lim_{ch} was derived from the equation: lg Lim_{ch} (mg/m^3) = 0.62 x lg CL_{50} (mg/m^3) - 1.08.

The figures given in the formula were calculated according to the following data: Lim_{ch} was determined by the equation: lg Lim_{ch} (mg/m^3) = 0,62 x lg 70 - 1,08 = 0,07 Lim_{ch} = 1,17 mg/m^3

SF is a relationship between CL_{50}/Limch and Css (species sensitivity coefficient) in accordance with MU (Recommended Practices) No. 1599-77,

Where CL50 is 70 mg/ m^3

CL_{50}/ Limch = 59.83 – corresponds to 3 points,

Css = 1.0 – correspondsto 2 points

SF = 3 x 2 = 6

According to the calculations, the value of ISEL is at 0.195 mg/m^3.

As can be seen from the above data, the value of DDAC ISEL in the workplace air is calculated by different formulas and ranges from 0.195 to 0.47 mg/m^3. The arithmetic mean of the presented ISEL values is 0.276 mg/m^3, the ISEL geometric mean is 0.246 mg/m^3. Recommended DDAC ISEL in the workplace air is 0.2 mg/m^3, aggregate state "a", marked "protection of eyes and skin is necessary". The mass concentration of DDAC in the workplace air is determined by the photometric method (the range of quantitative determination of concentrations from 0.1 mg/m^3 to 1.0 mg/m^3).

Conclusions

1. Based on DDAC toxicity parameters under different conditions of laboratory animals' exposure to the substance, it belongs to Category 1 substances in accordance with GHS.

2. The DDAC limiting harmful criteria are its marked irritant effect on the skin and conjunctiva, as well as acute inhalation action.

3. The recommended DDAC ISEL in the workplace air is 0.2 mg/m^3, aggregate state "a", marked "protection of eyes and skin is necessary".

Table 1

Formulas for calculating DDAC ISEL

Equation	**ISEL mg/m^3**
1. ISEL = 0.002 x LD_{50} per os	0.47
2. lg ISEL = 0.58 lg LD_{50} per os - 1.96	0.26
3. lg ISEL = 0.47 lgLD_{50} per os + 0.11 lgLD_{50} derm - 2.02	0.36
4. lg ISEL = 0.52 lgLD_{50} per os + 0.04 lgLD_{50} derm + 0.04 Ccum - 2.13	0.2
5. 0.467 lgLD_{50} per os + 0.06 lgLD_{50} derm + 0.04 Ccum - 2.12	0.25
6. Y = exp (0.58 lnLD_{50} per os - 4.51)	0.26
7. Y = exp (0.47 lnLD_{50} per os + 0.11 lnLD_{50} derm - 4.66	0.30
8. Y = exp (0.52 lnLD_{50} per os + 0.1 Ccum - 4.9	0.21
9. Y = exp (0.46 lnLd_{50} per os + 0.06lnLD_{50} derm + 0.1 Ccum - 4.87)	0.26
Where: LD_{50} per os = 238 mg/kg LD_{50} derm = 3342 mg/kg Ccum > 5	

The calculation of DDAC ISEL in the workplace air was performed using a formula for organic substances which have general toxic effect:

10. ISEL = estimated Limch/ SF (SF – safety factor).

The autors declare that there are no conflicts of interest.

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ТОКСИКОЛОГІЧНЕ ОБҐРУНТУВАННЯ ГІГІЄНІЧНОГО НОРМАТИВУ ДИДЕЦИЛДИМЕТИЛАМОНІЙ ХЛОРИДУ У ПОВІТРІ РОБОЧОЇ ЗОНИ

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РЕЗЮМЕ. Вступ. *Дидецилдиметиламоній хлорид (DDAC) використовується в якості сировини в хімічній промисловості при виробництві деяких інсектицидних, фунгіцидних, альдегідних препаратів і дезинфікуючих засобів як діюча речовина.*
Мета досліджень. *На основі аналізу та узагальнення даних літературі щодо ступеня небезпечності DDAC науково обґрунтувати його орієнтовно-безпечний рівень впливу (ОБРВ) у повітрі робочої зони.*
Матеріали і методи. *Для обґрунтування гігієнічного нормативу DDAC у повітрі робочої зони аналізували його фізико-хімічні характеристики, $ЛД_{50}$ за пероральної та дермальної дії, $ЛК_{50}$ при інгаляційному надходженні до організму, подразнюючі та сенсибілізуючі властивості, встановлені NOAEL речовини в підгострому і субхронічному експериментах за різних шляхів надходження до організму, віддалені ефекти.*
Розрахунок величини ОБРВ DDAC у повітрі робочої зони проведено за рівняннями, які враховують параметри токсичності препарату за різних шляхів надходження до організму лабораторних тварин.
Результати. *DDAC – імпортована продукція, використовується як діюча речовина при виробництві деяких пестицидних та дезинфікуючих засобів.*
DDAC відноситься до нелетких речовин: тиск парів $<1x10^{-2}$ Па при 20 ℃, при 50℃ - $2,3 x 10^{-4}$ Па (US ISC).
При введенні в шлунково-кишковий канал він класифікований як помірно небезпечний – 3 категорія (згідно з Globally Harmonized System of Classification and Labeling of Chemicals /GHS/ United Nations, New York and Geneva, 2017), володіє слабовираженою шкірно-резорбтивною дією (4 категорія, GHS). Виявлено його несприятливий місцевий вплив на шкіру. ЛК50 речовини при інгаляційному шляху надходження до організму – 70 мг/м^3 (2 категорія, GHS). DDAC проявляє виражену подразнюючу дію на шкіру і слизові оболонки очей кролів (1В категорія, GHS). На шкірі відмічали появу еритеми, струпи, набряк. Опіки, корозію, гострий кератокон'юнктивіт спостерігали при потраплянні на слизові оболонки очей. Не виявлено сенсибілізуючої дії препарату (не класифікується, GHS). Кумулятивні властивості речовини не виражені. Встановлені NOAEL у підгострому і субхронічному експериментах при пероральному, дермальному та інгаляційному шляхах надходження до організму. Найбільш уражені органи та системи – шкіра, очі, шлунково-кишковий тракт, печінка. Мутагенний, канцерогенний, ембріотоксичний, тератогенний ефекти та токсична дія на репродуктивну функцію не є лімітуючими критеріями шкідливості речовини.
Розрахунок величини ОБРВ DDAC у повітрі робочої зони проведено за рівняннями регресійної залежності, що враховують параметри гострої токсичності. Беручи до уваги ступінь його небезпеки, ризик розвитку патології загального генезу за дії речовини, рекомендована величина ОБРВ в повітрі робочої зони на рівні 0,2 мг/м^3, агрегатний стан «а», з позначкою «потребує захисту очей і шкіри».
Ключові слова: *дидецилдиметиламоній хлорид, DDAC, ОБРВ у повітрі робочої зони, інсектициди, дезінфікуючі засоби.*

ТОКСИКОЛОГИЧЕСКОЕ ОБОСНОВАНИЕ ГИГИЕНИЧЕСКОГО НОРМАТИВА ДИДЕЦИЛДИМЕТИЛАММОНИЯ ХЛОРИДА В ВОЗДУХЕ РАБОЧЕЙ ЗОНЫ

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РЕЗЮМЕ. Введение. *Дидецилдиметиламмоний хлорид (DDAC) используется в качестве сырья в химической промышленности при производстве некоторых инсектицидных, фунгицидных, альдегидних препаратов и дезинфицирующих средств в качестве действующего вещества.*
Цель исследований. *На основе анализа и обобщения данных литературы о степени опасности DDAC научно обосновать его ориентировочно безопасный уровень воздействия (ОБУВ) в воздухе рабочей зоны.*
Материалы и методы. *Для обоснования гигиенического норматива DDAC в воздухе рабочей зоны анализировали его физико-химические свойства и токсикологическую характеристику ($ЛД_{50}$ при пероральном и дермальном действии, $ЛК_{50}$ при ингаляционном поступлении в организм, раздражающие и сенсибилизирующие свойства, NOAEL вещества в подостром и субхроническом и хроническом экспериментах при различных путях поступления в организм, отдаленные эффекты).*
Расчет величины ОБУВ DDAC в воздухе рабочей зоны проведен по уравнениям регрессионной зависимости, которые учитывают параметры токсичности препарата при различных путях поступления в организм лабораторных животных.
Результаты. *DDAC – импортированная продукции, используемая в качестве действующего вещества при производстве некоторых пестицидных и дезинфицирующих средств. DDAC относится к нелетучих веществам. Давление пара $<1x10^{-2}$ Па при 20 ℃, при 50 ℃ – $2,3 x 10^{-4}$ Па (US ISC). При введении в желудочно-кишечный канал он классифицирован как умеренно опасный – 3 категория (согласно Globally Harmonized System of Classification and Labeling of Chemicals / GHS / United Nations, New York and Geneva, 2017), обладает слабовыраженным кожно-резорбтивным действием (4 категория, GHS). Выявлено его неблагоприятное воздействие на кожу. $ЛК_{50}$ вещества при ингаляционном пути поступления в организм – 70 мг/м^3 (2 категория, GHS). DDAC оказывает выраженное раздражающее действие на кожу и слизистые оболочки глаз кроликов (1В категория, GHS). На коже отмечали появление эритемы, струпья, отек. Ожоги, коррозию, острый кератоконъюнктивит наблюдали при поступлении DDAC на слизистые оболочки глаз. Не выявлено сенсибилизирующего действия (не классифицирован, GHS). Кумулятивные свойства вещества не выражены. Установлены NOAEL в подостром и субхроническом эксперименте при пероральном, дермальном и ингаляционном путях поступления в организм. Наиболее чувствительные органы и системы кожа, глаза, желудочно-кишечный тракт, печень. Мутагенный, канцерогенный, эмбриотоксический, тератогенный эффекты и токсическое действие на репродуктивную функцию не являются лимитирующими критериями вредности вещества.*
Расчет величины ОБУВ DDAC в воздухе рабочей зоны проведено по уравнениям регрессионной зависимости, учитывающих параметры острой токсичности. Принимая во внимание степень его опасности, риск развития патологии общего генеза при воздействии вещества ОБУВ в воздухе рабочей зоны, рекомендуется на уровне 0,2 мг/м^3, агрегатное состояние «а», с пометкой «нуждается в защите глаз и кожи».
Ключевые слова: *дидецилдиметиламмоний хлорид, DDAC, ОБУВ в воздухе рабочей зоны, инсектицидные средства, дезинфицирующие средства.*

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