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# Malathion

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# Malathion

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## MALATHION

Malathion (0,0-dimethyl-S-(1,2-bis-dicarboethoxyethyl)dithiophosphate) is a colourless oily liquid with a specific unpleasant odour. It belongs to the group of organophosphorus compounds and in the USSR is produced and marketed under the name "carbophos".

Molecular formula: $C_{10}H_{19}O_6S_2P$.

Molecular weight: 330.35

Structural formula:



Synonyms: Carbophos Ac-4049, Kiperos, malathion LV compound 4049 TM-4049, FOG-3, phosphotion, phosphotion-50, emmatos.

Melting point: 2.8 – 3.7 C.

Density: $n^{20} - 1{,}4985$.

Boiling point: 120 (0,2) °C.

Water solubility: 145 mg/1.

Commercial malathion contains minor amounts of trimethyldithiophosphate, diethylmamate and xylene [1, 2, 3, 4].

## PRODUCTION PROCESS (ES)

Malathion is mainly produced by the reaction of dimethyldithiophosphoric acid with maleic acid ether. The reaction proceeds readily in the presence of base catalysts in a medium with or without different organic solvents.

This reaction may be combined with the reaction of methylalcohol and phosphorus pentasulfide resulting in the production of dimethyldithiophosphoric acid; the reaction proceeds in a mediun of diethylmamate.

Dimethyldithiophosphoric acid and xylene are the main impurities of commercial malathion, produced by this method. The yield of malathion is more than 80% of theory but it falls when the processes of condensation and production of dimethyldithiophosphoric acid are combined [4].

The process of malathion synthesis involves 4 stages: [1] maleic acid diethyl ether is produced by the reaction of ethyl ether with maleic anhydride in a medium of xylene in the presence of a catalysts (e.g. sulfuric acid), [2] dimethyldithiophosphoric acid is produced in the same medium by the reaction

of methyl alcohol with phosphorus pentasulfide, [3] malathion is produced by the reaction of maleic acid ether with dimethyldithiophosphoric acid, and [4] malathion is mixed with OP-7 emulsifier to produce a 30% malathion preparation which is poured into bottles [5].

The preparation is offered for sale as an emulsion concentrate containing 30-60% of active substance, an emulsifier and a solvent. Xylene is used as a solvent. A 90-96% concentrate containing minute amounts of additions is used for spraying [4].

## USE

Malathion is a contact insecticide and acaricide used to fight aphid, European red mites, thrips, codling moth and other agricultural pests. The effective concentrations used are: 0.2 – 0.3% for many kinds of aphid 0.15 – 0.2 for pear louse 0.2 – 0.3 for mites, and 0.05% for louses. Malathion may be often combined with fungicides (e.g. zineb, cupric oxychloride) and acaricides (e.g. kelthan) [1, 6, 7, 8].

The following concentrations of a 30% emulsion concentrate are used: 0.5 – 2 kg/ha, to control pests feeding on cereals, food grains, maize and leguminous plants, 1 – 2 kg/ha for cotton and sugar beet, 0.8 – 1.2 kg/ha for flax, 1.6 – 4.5 kg/ha for fruit-stone or seed-bearing plants, 2 – 4.5 kg/ha for berry plantations, 1.6 – 3 kg/ha for strawberry (no spraying is allowed during fruiting), 1.8 4.5 kg/ha for vine, 4 – 6 kg/ha for open ground vegetables (provided that the produced vegetables are carefully washed), 0.4 – 1 kg/ha for bean-bearing grass, 1.6 – 3 kg/ha for tobacco planto, 0.8 – 4 kg/ha for melon plantation, 1 – 1.5 kg/ha for sunflower, mustard, rape, soy-bean, ground-nut, sesame and coriander, 1.2 – 2.4 kg/ha for oil-bearing poppy, 3.1 – 0.5 kg/ha for hop, 6 – 8 kg/ha for citrous plants, 20 – 50 g/t for food and fodder grain and 1.2 – 4.5 kg/ha to control locust.

A 50% emulsion concentrate is used to control the same pests at lower (by 20% ) consumption rate.

A 40% solution is sprayed in pasture and wild grass plantations to fight mites at the consumption rate of 1.5 l/ha. This preparation is effective to control codling moth (6 l/ha) and some other pests [1].

The following concentrations of the malation emulsion are recommended to fight maggots: 1% for liquid waste at the consumption rate of 150 – 200 ml/$m^2$ and 0.3 – 0.5% for solid waste at the consumption rate of 10 – 12 l/$m^2$. A 1.2 – 1.5% aqueous emulsion of malathion is used to fight bed at the consumption rate of 50 – 75 ml/$m^2$ [7].

## CONCENTRATIONS

Tractor-driven spraying of malathion on vegetable plantations results in air pollution. In the treated area of 4 hectares, malathion was detected in the air, at a distance of 500 m, in concentrations from 0.230 to 0.150 mg/$m^3$ on the day of spraying; the preparation persisted in the air for 6 days. When the area of 2 hectares was treated, malathion concentrations of 0.079 – 0.051

mg/m$^3$ were registered at a distance of 500 m on the day of spraying; the preparation persisted in the air for 4 days. At a distance of 700 m, the concentration of malathion on the day of the treatment was 0.025 – 0.010 mg/m$^3$ the preparation persisted in the air for 3 days [9].

Chemical treatment of flour in storehouses caused air pollution in the working zone: malathion level of 0.77 mg/m$^3$ was registered on the day of the treatment, 0.26 mg/m$^3$, on the 2nd day, and 0.03 mg/m$^3$ after 7 days [10].

The level of malathion in the air of the shop where carbophos is manufactured was 0.25 – 4 mg/m$^3$ and more frequently 1 – 2 mg/m$^3$. Besides, dimethyldithiophosphoric acid (0.1 – 0.7 mg/m$^3$) maleic acid diethyl ether (1 – 16 mg/m$^3$) and hydrogen sulfide (0.8 – 20 mg/m$^3$) were detected in the air [2].

After 6 – 8 chemical treatments of gardens during the vegetation period, with a mixture of 30% malathion and 80% zineb (4 –6 kg/ha and 8 kg/ha respectively), residual carbophos in soil amounted to 0.4 – 0.1 mg. In areal water filtrates malathion was found in concentrations from 0.20 – 0.05 mcg on the 5 – 6th day after treatment. After 7 – 8 months, malathion was only traced in the filtrates (0.01 g) [11].

Malathion was found in the stored flour in concentrations from 1.39 to 1.68 mg/kg on the first day; permissible residual quantities of malathion were detected after 12 days [19].

After a single spray of 0.5 and 1% aqueous emulsions of malathion on cow skins, 0.4 mg/l of the preparation was found in milk [12].

## ENVIRONMENTAL FATE TESTS

Microorganisms rapidly destroy malathion in soil which is confirmed by longer persistence of malathion in sterilized soils. Malathion is destroed completely for less than two months when its concentration in soil makes 185 mg/kg which corresponds to the consumption of 185 kg of active substance per 1 hectare [13]. Malathion is destroyed in air under the effect of light; degradation is accelerated in the presence of water and ozone [13].

Malathion is degraded mainly through hydrolysis and oxidation. These reactions proceed in air, water and soil as well as in most biological systems. The rate of hydrolysis is function of pH and ambient temperature. Dimethyldithiophosphoric acid and mercaptosuccinic acid ether are the main products of malathion hydrolysis in acid media, and dimethyldithiophosphoric acid salt and fumaric acid ether, in alkaline media. Ozone and nitric oxides accelerate malathion oxidation. A thionic sulfur atom is splitted off upon oxidation of malathion with nitric acid, and a corresponding thiophosphoric acid ether is produced [4, 13].

The pattern of absorption of malathion in sandy and subacid soils with low humus level was studied after treatment with a mixture of 30% malathion and zineb at a consumption rate of 4 – 6 kg/ha. The samples were taken from the surface and the plant root depth of the soil on the day of the treatment,

on the lst, 3rd, 5th, 8th and l0th day intervals until malathion disappeared from the soil. The kinetics of malathion was studied in the aerial water filtrates from lysimeters. The following residual quantities of malathion were found during the vegetation period to start from the 5th – 6th day after tree plantations treatment: 0.4 – 0.1 mcg in soil and 0.2 – 0.05 mcg in the aerial water filtrates. After 7 – 8 months, malathion amounted to 0.01 mcg in the aerial water filtrates taken from lysimeters placed at a depth of 1 m[11].

Persistence of malathion in soil was studied under laboratory conditions. Zink-plated metal vessels were used for the experiment. The area of the soil surface in a vessel was 623.6 $cm^2$. In the first experimental series, from 8.7 to 9.05. Persistence of malathion was studied after introducing 200 and 2 mg/kg of malathion into soil. The vessels were kept at 18 – 20°C. Soil samples were taken on the lst day of the experiment, after 15 days and then at one-month intervals until malathion was completely destroyed. It was shown that malathion introduced into soil in a concentration of 200 mg/kg was destroyed for 4 months at pH 3 – 4.6 and for 1 month at pH 8.7 – 9.6. Malathion introduced into soil in a concentration of 2 mg/kg (pH 3 – 4.6) was not traced by the end of the 3rd month of the experiment while at high initial concentration 200 mg/kg malathion persisted in soil during 4 months. The pattern of degradation of malathion was studied after introducing thereof into native and sterilized chernozem in a concentration of 200 mg/kg. The experiment was conducted at an ambient temperature of 18 – 23°C and soil moisture of 60% of total moisture capacity. The rate of malathion degradation was similar with both native and sterilized soils which is indicative of a minor role of microorganisms in this process. It is suggested that the preparation is destroyed in soil chemically as well as biologically [14].

The effect of malathion on the biological oxygen uptake and mineralization of organic pollutants (e.g. concentration of hydrogen ions, oxidezability and the content of the dissolved oxygen) was studied in the model water reservoirs. It was established that malathion concentrations of 0.5 to 50 mg/l did not change the parameters characterizing the dynamics of biological oxygen uptake and mineralization processes. Studies in the effects of malathion on the processes of ammonification, nitrification and nitrofication have demonstrated that 5 mg/l is a minimum concentration of malathion inhibiting the above mantioned processes [15].

## BIOCONCENTRATION /CLEARANCE TIME/ MAMMALIAN METABOLITES

Qualitative and quatntitative studies were made of the distribution of malathion in the internal rabbit organs after the administration of 1 g of the preparation. Malathion amounted to 207.5 mg in the stomach, 20.4 mg in the large intestine, 4.4 mg in the liver and 4.3 mg in the blood, as calculated per 100 g of the object [16].

The dynamics of malathion excretion in milk was studied after a single spray of 0.5 and 1.0% aqueous emulsion of malathion (1 l per animal) on cows. Milk samples were studied 1.5, 3, 6, 12 and 24 hours after spraying, and

after each morning milking until malathion excretion ceased. After a single spray of 5 and 10 g of malathion aqueous emulsion on cows, 0.4 mg/l of the preparation was excreted in milk. Maximum quantity of malathion at a dose of 5 g/animal was determined in milk during the first 3 hours. After 6 hours malation amounted to 0.02 – 0.04 mg/l; after 12 hours, the preparation was only traced and after 24 and 48 hours malathion was absent from the studied samples [12].

## MAMMALIAN TOXICITY ARRAY

Malathion is a median toxic substance. According to various researchers with intragastric administration $LD_{50}$ is 450 – 1400 mg/kg for rats, 400 – 930 mg/kg for mice, and 400 mg/kg for cats; $LD_{50}$ is 4000 – 6150 mg/kg with skin applications to rats and rabbits. Malathion is low toxic when applied to the skin [1,2]. According to classification of pesticides by their toxicity through contact with the skin, malathion is the 3rd class of danger ($LD_{50}$ ≧ 1000 mg/kg, skin and oral coefficient 3 ) which means a weak skin-resorption toxicity [18].

Malathion is a highly volatile substance and hence is dangerous in case of inhalation uptake. $LD_{50}$ is 12 mg/m$^3$ for cats; 1.3 – 2 mg/m$^3$ is a minimum concentration decreasing the activity of acetylcholinesterase of erythrocytes and cholinesterase of the blood serum of cats after 4-hour exposure [2].

Initial signs of poisoning with lethal doses manifested by depression were detected in cats after 40-60 min. After the next 30-60 min, motor excitation, hypersalivation and, sometimes, vomiting developed. Some animals exhibited tremor and clonic convulsions. Breathing was hurried and shallow. Cats died after a few hours and some of them died in the course of 2-3 days after the administration of malathion [1].

The effect of malathion on the activity of cholinesterase (acetylcholine substrate), aliesterase (methylbutyrate substrate) and arylesterase (phenylacetate substrate) was studied in experiments in vitro and in vivo.

The brain, blood serum, erythrocytes, liver, kidneys, interstine, heart and spleen of albino rats are the main sources of the enzyme. The esterases activity was determined by Hestrin's method. A correlation was revealed berween the degree of the antiesterase action of malathion in vitro and the toxicity thereof [2].

Malation is the 4th class of weak cumulation as estimated by its cumulative properties (Medved's classification); the cumulation coefficient is [5]. After daily administration of carbophos to albino rats in doses of 1/20 – 1/10 of $LD_{50}$, cumalative effect was slight; the cumulation coefficient was 6 [2].

The toxicity of malathion was studied on mice, rats and rabbits after intragastric administration during 1-2 months in doses of 180 and 40 mg/kg and during 6 months in doses of 1, 0.01 and 0.0015 mg/kg. It was shown that malathion administered in high doses of 180 and 40 mg/kg decreased considerably the working capacity of the studied mice. The pathomorphological examination of the internal organs of rabbits given 180 mg/kg of malathion during

3-4 days has revealed sharply pronounced degenerative changes in the liver, kedneys and myocardium, and inflammatory reactions in the lungs and gastrointestinal tract. The administration of malathion to rats in a dose of 40 mg/kg during 30 days did not change the latent period of the defense reflexes. With chronic (6 months) exposure to malathion in doses of 1, 0.01 and 0.0015 mg/kg no signs of poisoning were detected in rabbits [15].

After twenty-four-hour exposure of rats to malathion through inhalation (0.380 mg/m$^3$) during 3 months, cholinesterase activity was inhibited, the excretion of coproporphyrin in urine increased and that of 17-ketosteroids, decreased; pathophysiological and histochemical changes occurred in the internal organs of the experimental rats. Upon chronic inhalation of malathion in a dose of 0.075 mg/m$^3$ the above mentioned changes were less pronounced. Inhalation of malathion in a concentration of 0.014 mg/m$^3$ was harmless [9].

The dependence of the toxic effect of malathion aerosol upon the degree of its dispersion was studied on male rats after a single inhalation of malathion aerosol in a concentration of 2.3 mg/m$^3$ with particles of 20, 50, 100, 200 and 300 mcm in diameter, and after chronic inhalation of the aerosol (during 3 months, daily 4-hour exposure) with particles of 20 and 300 mcm in diameter. It was established that after a single inhalation of malathion the degree of cholinesterase activity changes in the blood and internal organs was directly related to the degree of the dispersion of the aerosol with particles of 20-50 mcm. The same dependence was demonstrated in a chronic experiment. During prolonged inhalation of the malathion aerosol with particles of 20 mcm, the level of eosinophils in the blood and ascorbic acid in the adrenal glands decreased, and the alkaline reserve of the blood increased. These changes were less pronounced after the effect of aerosol with particles of 300 mcm in diameter. It is considered that particles of 100 – 200 mcm are the most adequate from the hygienic point of view [19].

In order to ascess the age-related effect of malathion on albino rats sensitivity of rats of different age (1-, 2-, 3- and 4-week rats and pubertal animals) was determined. One – week rats and adrenallectomized rats proved to be more sensitive to malathion than pubertal animals ($LD_{50}$ was 2.2 and 2.4 times respectively lower than $LD_{50}$ for pubertal rats). The sensitivity of young rats to malathion approximated that of pubertal animals eith age. It was shown that the hypophysis-adrenal system plays a much more important role in pubertal rats poisoned with malathion compared to young animals [20].

The effect of raw malathion (48-50% of malathion, 40% of xylene, and up to 10% of dimethyldithiophosphoric acid and maleic acid ether) was studied in a chronic rat experiment (5 months). After intragastric administration of malathion to rats in a dose of 1/30 of $LD_{50}$ ($LD_{50}$ = 1760 mg/kg), a decrease in the blood cholinesterase activity, dysproteinemia and growth of total SH-groups were revealed. Intragastric administration of malathion in a dose of 1/60 of $LD_{50}$ (29 mg/kg) induced the development of relative leukocytosis and growth of hemoglobin and total SH-groups [21].

The effect of raw malathion on the immune response of rats was studied after 3-month inhalation of the preparation. The disturbance of the immunobiological response of the studied animals was manifested by the

decrease in the properdin level of the blood serum and changes in the phagocytic activity of neutrophils[22].

The effect of malathion on the antibody formation in rabbits was studied after a subcutaneous injection of the preparation before and after primary immunization with a bacterial antigen and repeated administration immediately before the secondary immunization (after 50 days). It was established that the primary response of animals to the effect of carbophos was inhibited which was manifested by the prolongation of the exponential phase, delay in reaching the maximum of the antibody titers and fall of the antibody titers throughout the entire period of observation. The secondary immune response was inhibited during the first five days. In experiments on albino rats, it was demonstrated that malathionm administered before and after the injection of a tissue antigen inhibited the primary immune response of the studied animals which was manifested by the decrease in the antibody titers at the first stages of the observation. It is considered that malathion inhibits antibody formation with regard to bacterial and tissue antigens[23].

Cholinesterase activity of the cow bood was estimated 24 hours and 5 days following treatment with 1 and 2% carbophos emulsions with a prolonger (e.g. polyvinyl alcohol). No changes were detected [24].

A single 4-hour exposure and repeated 30-min exposure (at 4-hour intervals during a day) to 0.5 – 1% aqueous emulsions prepared from a 30% malathion concentrate did not induce the development of poisoning symptoms in albino mice and rats, and rabbits. When the concentration was increased up to 1.5 – 3% inhibition of the cholinesterase activity occurred and the inflammatory reactions developed in the trachea and bronchi of the experimental animals [24].

Morphological, pathomorphological and histochemical changes were studied in rats given malathion in doses of 0.380, 0.75 and 0.014 mg/m$^3$ during 24 hours in the course of 3 months. The concentration of 0.380 mg/m$^3$ caused circulation disturbances (e.g. plethora, diapedetic hemorrhages, disturbances of the permeability of the vascular wall and edema). Degenerative, proliferative and infiltration reactions of varying degree were detected in the brain, heart, liver and kidneys. The level of RNA in the cytoplasm of the parenchymal elements was high and that of DNA of their nuclei increased. Glycogen was reduced in the myocardium and hepatocytes, and sudanophil fat content of the latter increased. With a malathion concentration of 0.075 mg/m$^3$, degenerative changes in the organs of the affected animals, plethora and moderate edema were less pronounced. The level of RNA increased in the cytoplasm of muscular fibres, epithelium of the convoluted tubules and in hepatocytes. After inhalation of malathion in a concentration of 0.014 mg/m$^3$, rats did not exhibit pathohistological and histochemical changes in the internal organs [25].

Studies of the reflex effect of malathion on a human body showed that a minimum malathion concentration which was sensed by all studied persons was 0.096 mg/m$^3$; the most susceptible patients sensed a concentration as low as 0.052 mg/m$^3$; malathion concentration of 0.044 mg/m$^3$ was not smelled. The concentration of 0.44 mg/m$^3$ impaire and 0.032 mg/m$^3$ did not affect the photosensitivity of the eyes. All five examined patients exhibited affection

of the bioelectrical activity of the brain (the method of the electrocortical reflex) at the malathion concentration of 0.032 mg/m$^3$; two of them at 0.025 mg/m$^3$ and none at 0.014 mg/m$^3$ [9].

Typical signs of poisoning humans with malathion are hupersalivation, vomition, diarrhea, dyspnea, cyanosis, hypertension and miosis [1].

Upon acute poisoning changes in cardiac activity are observed. The ECG shows sinus tachycardia, diminished wave voltage, sinus bradycardia, extrasystole, deceleration of intraventricular conduction, intraventricular block decreased S-T segment, negative T wave and increased electric systole [2].

Examination of 57 workers engaged in the manufacture of malathion (36 women and 21 men at the age of 19-40 years old handling malathion for 3 to 10 months) has revealed inhibition of blood cholinesterase activity (1/3 of the workers) and dysproteinemia (a decrease of albumins and increase of $\beta$ – and $\gamma$ – globuline fractions) which is indicative of harmful action of malathion at concentrations in the shops ranging from 0.1 to 3.0 mg/m$^3$ [5].

Examination of 230 workers engaged in manufacturing malathion (among them 97 workers were examined in dynamics) has revealed in 37 out of 87 patients progressive changes in the functional state of the nervous system and, sometimes, in the gastrointestinal tract function, and also a tendency toward hyperchromic anemia. 37 patients complained of the headache and 11 of undue fatiguability, sleep disturbance and sometimes stabbing and spasmodic pain in the heart and numbness of hands. These symptoms together with the objective signs of neurologic lesions (e.g. tremor of fingers, pronounced tendon reflexes, labile blood pressure and altered postural reflexes) indicate that neurasthenic, vegeto-neurasthenic and angiodystonic syndromes develop. It was established that the above mentioned pathologic changes were associated with a general toxic and skin-resorptive action of malathion and dimethyldithiophosphoric acid which were detected in the air of the shops in doses exceeding the maximum allowable concentration [17].

Malathion is the 3rd class of danger according to hygienic classification of pesticides (as determined by the toxicity with intragastric administration, the cumulative properties and persistence in the environment) [18].

## SPECIAL TOXICITY STUDIES

**Neurotoxicity / Behaviour.** Studies in the effect of malathion on the conditioned reflex activity showed that changes in the higher nervous system are the early signs of poisoning with malathion [2].

The phase character of the central effects was shown by the EEG. In slight poisoning with malathion (50 – 100 mg/kg), the alleviation of the nervous disorders during 1 – 2 days (the lst phase) is not followed by convulsive relaxation (the 2nd phase) and exhaustion (the 3rd phase). These phenomena are transient with carbophos doses exceeding $LD_{50}$. The signs of exhaustion of the bioelectric activity upon grave poisoning with malathion are slightly pronounced. It was shown that at the first phase of the effect of malathion the cholinesterase level in the blood serum decreased concurrently with the

changes in the activity of bioelectrical potential of the brain which was normalized as the level of cholinesterase was restored. The phase character of the effect of malathion on the visual analyser function was registered [26].

**Potentiation.** An essential potentiation of the combined effect of malathion and trichlorfon on albino rats was revealed. All the experimental animals died after the combined effect of the preparations each of which being delivered in $LD_{50}$. Animals died also after a total dose of 1/4 of $LD_{50}$, which is indicative of a reliable potentiation of the effects of malathion and trichlorfon. The total dose of both preparations inducing 50% death of the experimental animals made 40% of the calculated $LD_{50}$, i.e. there was a 2.5-fold potentiation of the effect. The potentiotion was also confirmed by the experiments on rabbits: a simultaneous intravenous injection of malathion (25 mg/kg) and trichlorfon concentration of 5 $10^{-3}$M inhibited in vitro the activity of carboxylesterase (e.g. alyesterase or CoE 3.1.1.1) of the blood serum of albino rats (methylbutyrate substrate) and, in all appearance, interferes with the processes of carboxylesterase hydrolysis of malathion [2]

The toxicity of raw malathion was studied on rats after inhalation of a mixture of malathion and xylene during 1 and 5 monts. Malathion (5 mg/m$^3$) combined with xylene (3941 mg/m$^3$) decreased cholinesterase activity of the blood, lowered the threshold of the nervous and muscular excitation, delayed the weight increase and caused pathohistological changes in the internal organs of the experimental animals: these changes were absent with a xylene concentation of 5630 mg/m$^3$ inhaled alone. In a chronic experiment, when a mixture of malathion (3 mg/m$^3$) and xylene (598 mg/m$^3$) was inhaled, cholinesterase activity of the blood increased and the blood morphology of rats changed. After inhalation of a mixture of malathion (1.4 mg/m$^3$) and xylene 97.2 mg/m$^3$), the blood morphology was impaired. Under similar conditions, xylene alone 679 mg/m$^3$ did not induce intoxication [21].

Studies in the effect of raw malathion delivered alone or in a combination with xylene, on the immunobiological response of female rats have demonstrated that a mixture of malathion and xylene decreased the activity of cholinesterase, induced phase changes in the total threshold index and affected markedly the immunobiological response of the organism (e.g. decreased the level of properdin in the blood serum and altered the phagocytic activity of neutrophils). When malathion and xylene were inhaled separately reticulocytosis developed and changes in the immunobiological response of the organism occurred which were less pronounced than in the case of combined application of the preparations [22].

In experiments on albino rats, a study was made of the toxicity of a mixture of malathion with some of its intermediates. The mixture was composed of malathion (1 part,), dimethyldithiophosphoric acid (3 parts), maleic acid diethyl ether (5 parts), xylene 300 parts and methanol (30 parts). The effect of these combination on rats was estimated by determining $LD_{50}$ of each component and $LD_{50}$ of the mixture. The values of $LD_{50}$ were calculated by different methods: 2000-2015 mg/kg for malathion, 1300-1500 mg/kg for dimethyldithiophosphoric acid, 9010-9340 mg/kg for xylene, 1833-2141 mg/kg for maleic acid diethyl ether, and 6121 mg/kg for methanol.

$LD_{50}$ of the mixture was 6000-6340 mg/kg. The clinical picture of poisoning by the mixture is similar to that induced by xylene. Animals died on the 1st-4th day after poisoning. It was established that the studied combination has an additive effect on albino rats [27].

A study was made of the effect of per os administration (during 21 and 45 days) of malathion to rabbits in a dose of 1/25 of $LD_{50}$ and of the mixture of malathion and polychloropinen (cumulative dose of 1/25 of $LD_{50}$) on the rate of oxyhemoglobin dissociation, ascorbic acid level in the blood, liver, kidneys, adrenal glands and brain, thiamine level in the blood, brain, muscles and liver, and copper, manganese and iron content of the blood, liver, kidneys, adrenal glands and brain. The administration of malathion decelerated oxyhemoglobin dissociation, increased the ascorbic acid level in the brain and blood, and the copper content of the brain, kidneys and blood. Exposure to a mixture of malathion and polychloropinen decelerated oxyhemoglobin dissociation, increased the level of vitamin C in the blood, manganese, in the kidneys, and iron in the crossestriated muscle. It was established that the effect of the mixture of malathion and polychloropinen varied from that of carbophos alone [28].

It was demonstrated that a slight poisoning of albino mice with malathion (subcutaneous injection of a 2% aqueous emulsion in a dose of 120 mg/kg) enhanced the narcotic effect of hexenal, helithiamine, chloroform and ether. The increased narcotic sensitivity of mice persisted for the first 24 hours after the administration of malathion and manifested itself reliably during the first 6 hours of poisoning. There was no complete parallelism between the increase in the narcotic effect and growth of the toxicity of narcotics [29].

Intramuscular injection of TMB-4 (a clolinesterase reactivator) to mice in a dose of 15 mg/kg 30 min after the administation of malathion in a dose of 100 mg/kg reactivated the inhibited cholinesterase and normalized cholinesterase activity 8 days after poisoning (against 18 days in the nontreated animals). TMB-4 reduced pachyemia in experimental mice. The treated animals did not exhibit paralyses and throphicity disorders. Atropine administered intraperitoneally to mice in a dose of 2 mg/kg after the exposure to malathion in doses of 500 and 25 mg/kg did not prevent the animal death but prolonged the lifespan from 1-3 to 24 hours. DAM (150 mg/kg) and 2 PAN (30 mg/kg), the reactivators of cholinesterase, administered intraperitoneally to mice after exposure to malathion in a dose of 25 mg/kg did not essentially influence the course of poisoning [30].

A study was made of the effect of cholinesterase reactivators, dipiroxime and isonitrosine on the bioelectric activity of the rabbit rain (e.g. a change in the total EEG and the rhythms composing thereof) after subcutaneous injection of malathion in doses of 100 and 600 mg/kg. Dipiroxime in doses from 2 to 15 mg/kg administered intravenously and intramuscularly reactivated the inhibited cholinesterase of the blood and improved the clinical picture of the experimental animals but failed to influence the bioelectric activity of the brain affected by malathion. The EEG was temporarily normalized after subarachnoid and intraventricular administration of dipiroxime in a dose of 1 mg/kg as was normalised the follow-up reaction in the visual region of

the cortex. In grave cases (e.g. the affection by malathion in a dose of 500 mg/kg), dipiroxime facilitated the assimilation of low-frequency rhythms in the visual analyser. Isonitrosin, injected intravenously in a dose of 5-20 mg/kg, somewhat inhibited the assimilation of the photostimulation rythms, relieved by malathion in the first phase of its action. In cases of severe intoxication isonitrosin markedly inhibits the standard Q – rythm and syncronises $\delta$ – potentials [31].

**Sensitization.** Malathion can induce allergic affections manifested by allergic dermatitis, asthmatic bronchitis and other disease. The allergic reaction to malathion is related to the ability of carbophos to react with functional groups of different proteins [2].

**Embryotropic action.** A study was made of the embryotropic effect of malathion administered to rat stomach in doses of 10, 1 and 0.1 mg/kg troughout the entire period of pregnancy. It was shown that malathion did not affect the course of pregnancy, did not decrease the fertility and did not change the mortality of embryos. The studied carbophos doses did not elicit external and internal abnormalities in the development of fetus organs. The newborn rats developed normally during the first month after birth (the period of observation). It is concluded that malathion applied in the studied doses has no embryotropic effect [32].

**Primary irritation.** Examination of 230 workers engaged in the manufacture of malathion has revealed conjunctivitis and occupational dermatoses (e.g. epidermitis, dermatitis and chemical vurns) which is ascribed to the irritant effect of malathion, xylene and hydrogen sulfide. Malathion was found in the water used by the workers for washing hands in concentrations from 0.11 to 2.5 mg/dm$^2$, and on the overalls in concentrations from 0.24 to 0.72 mg/dm$^2$; 0.06 – 0.1 mg/dm$^2$ of malathion were detected on the overalls even after washing thereof [17, 33].

## EFFECT ON ORGANISMS IN THE ENVIRONMENT

Studies of the effect of malathion on fishes have revealed high sensitivity of embryos. The effect of malathion in a concentration of 1 mcg/l causes a 16-34 hour delay in hatching. The hatched fishes are weak, adynamic and anemic with slow heart action. The resistance of fishes to poisons increases with age [34].

It was established that $LD_{50}$ is 0.12 mcg/fly for female sinanthropic flies (upon application of malathion), 4.1 mcg/female for German cockroaches and 0.35 mcg/m$^2$ for bed bugs (on contacting glass surface). All bugs died after 15-min exposure to malathion dose of 0.2 g/m$^2$ placed on the glass object and 3.0 – 4.0 g/m$^2$ placed on the absorbing matter (e.g. wall paper or plywood). $LD_{50}$ was 0.0075% for louses placed into an aqueous emulsion of malathion and exposed therein for 5 minutes; $LD_{50}$ was 0.0006% for louses contaction during 24 hours with coarse calico treated with the malathion emulsion. All louses died after a 15-min exposure in a 0.005% malathion emulsion or after 3-hour contact with coarse calico treated with the emulsion at the consump-

tion rate of 0.23 g/m$^2$. Louse eggs were killed with 0.05% aqueous emulsion of carbophos after a 15-min exposure [6. 7] .

The insecticide efficiency of malathion was studied on mosquito. After one-hour exposure to malathion, $LD_{50}$ for mosquito was 0.0006 g/m$^2$. The insicticide effectiveness of malathion was 1.75 g/m$^2$ as determined after a 5-min exposure of mosquito population [35].

A study of malathion as an acaricide showed that $LD_{50}$ for ticks (I. persulcatus) was 0.0085 g/m$^2$ after a 12-hour exposure. There was a 4-fold decrease in the number of insects on the grass layer treated with a 10% dust at a dose of 0.3 g/m$^2$ and the consumption rate of 30 kg/ha, as determined on the first day after treatment. After 10 days the number and specific composition of insects were normalized [8] .

It was demonstrated that selectivity in the effect of malathion on some insect species is related to different rate of the processes of activation and detoxication of malathion. It was established that carboxylesterase, promoting breakdown of malathion to nontoxic products, is more active in warm – blooded animals that in insects; that is why malathion is less toxic for humans. The selectivity coeffecient ($C_S$) of malathion (the ratio of $LD_{50}$ for warm-blooded animals to $LD_{50}$ for insects) is 16.

$$C_s = \frac{LD_{50} \text{ for mouse (450 mg/kg)}}{LD_{50} \text{ for Musca domestica (28 mg/kg)}} \qquad (1, 2)$$

## SAMPLING /PREPARATION/ ANALYSIS

Malathion is identified in air by thin layer chromatography. The method is based on the separation and quantitative determination of organophosphorus pesticides in a thin layer of alumina or silica gel. The sensitivity of the method is 3 mcg [36] .

The colorimetric method is used for determining malathion in air by total phosphorus. The method is based on extracting malathion from the sample by an organic solvent (e.g. ammonium persulfate) and subsequent colorimetric identification by a blue phsopho-molybdic heteropolycomplex. The sensitivity of the method: 3-5 mcg of malathion in an air sample [36] .

Gas-liquid chromatography is used to identify malathion in air. The method is based on the absorption of malathion from the sample by dimethylmethylformamide, re-extraction by hexane and subsequent identification thereof by gas-liquid chromatography. The sensitivity of the method: 0.05 mg/m$^3$ [36] .

Gas-liquid chromatography is used to detect malathion in potatoes, carrots beet, water and apples of an early ripeness variety. The method is based

on extracting malathion by n-hexane. The chromatograph with a thermo-ion detector is used for quantitative measurements. The sensitivity of the method: 0.02 mg/kg for fruits and vegetables, and 0.005 mg/l for water [36].

Malathion is identified in water, vegetables and fruits by thin-layer chromatography. The method is based on extraction carbophos by diethyl ether or chloroform and subsequent thin-layer chromatography using silica gel. The sensitivity of the method: 0.01 mg/l in water and 0.1 mg/kg in vegetables and fruits. Extraction: 92 ±7.3% [36].

The method is discribed for determining malathion in juices and compotes using "Tsvet-6-69A" chromatograph with the detector of the recombination rate constant, malathion is extracted by n-hexane derivatives or acetone and hexane. The sensitivity of the method: 1-3 mcg/50 g sample. Extraction: 80-90% [37].

Malathion content in the internal organs of rabbits was studied by qualitative reactions and quantitative determination after extraction thereof from the organs. Malathion was extracted by benzene and mineralized in the acid, then phosphorus was identified by the formation of phospho-molybdic heteropoly acid. Qualitative reactions involved microcrystalloscopic reaction with 0.8% iodine solution and production of 0,0-dimethyldithiophosphorous copper complex. The results of the quantitative determination of malathion and of the analysis of the rabbit internal organs by qualitative reactions were similar [16].

Thin-layer chromatography may be used for identifying malathion in organs and tissues of animals. Malathion is extracted by an 80% aqueous solution of acetone acidified by 2N solution of hydrochloric acid. The extract is placed on the chromatographic plate. Chloroform-hexane (10:1) is a mobile solvent [38].

The method of gas-chromatography is used to determine malathion in the blood of patients and in the dialyzating liquid obtained by operation of peritoneal dialysis in acute cases. The chromatograph "Tsvet-106" with a thermo-ion detector is used. The sensitivity of the method: 0.01 mg/% in the blood.

## TREATMENT OF POISONING

Treatment of acute poisoning with malathion involves the following measures: intensive resuscitation, removal of the poison from the organism (e.g. a gastric lavage with a probe, forced diuresis and peritoneal dialysis) and active complex specific therapy. Specific therapy of acute poisoning with malathion involves a combined application of cholinolytics (e.g. atropine) and cholinesterase reactivators. Intensive atropinization is necessary during the first hour of the treatment until all symptoms of the muscarinic action of carbophos are coped. Cholinesterase reactivators (e.g. dipiroxime and isonitrosine) can restore the activity of inhibited cholinesterase and exert a direct antidotal effect. Symptomatic therapy is also applied [1, 2, 40].

## REMOVAL

The overalls polluted with malathion should be shaken and soaked in a soap-and-soda solution for 6-8 hours. Then the overalls must be washed 2-3 times in a hot soap-and-soda solution and rinsed carefully.

Containers are decontaminated with 5% caustic or washing soda (300-500 g per 10 litres of water). The containers are filled with this solution, kept for 6-12 hours, then washed with ample water. If soda is not at hand, wood ash may be used instead [1].

## RECOMMENDATION / LEGAL MECHANISMS

Adolescents (up to 18), pregnant and lactating women, men over 55 and women over 50 are not allowed to work with malathion. The personnel should undergo annual medical examination.

Prior to and during the work (once a week)the workers handling malathion should be examined for cholinesterase activity of the blood. Those who exhibited a 25% (and over) decrease in cholinesterase activity must be dismissed from work with malathion until the activity of the enzyme is normalized.

The workers handling malathion should be provided with individual protective means: respirators with catridges, protective goggles, an overall made of dense or waterproof cloth, rubberized or PVC apron, rubber boots and gloves.

During aerial spraying, the pilot should carefully avoid settlements, water bodies, irrigation ditches and other objects [1].

The terms of the last chemical treatment of agricultural plants before gathering in a crop are as follows: 20 days for all kinds of plants, 7 days for tabacco, and 2-3 days for cucumbers in hothouses (provided that the produced vegetables are carefully washed).

Men are allowed to enter the forest aerially treated with malathion: after 4 days to work therein (e.g. to control over the efficiency of the chemical treatment), after 7 days to rest if there are no berries and fruits [1].

In the Soviet Union the maximum allowable concentration of malathion (MAC) in the air of the working zone is 0.5 $mg/m^3$ (vapour + aerosol) which signifies the second class of danger [1, 2, 18].

MAC in the air of settlements: maximum single dose – 0.015 $mg/m^3$, calculated mean daily dose – 0.006 $mg/m^3$ [1, 2, 18].

Maximum residual quantities of malathion in food: 1.0 mg/kg for vegetables and fruits. Allowable residual concentrations of malathion are: 2.0 mg/kg for domestic animals (dairy cattle and egg-lying poultry) and 5.0 mg/kg for fattened cattle and poultry [1, 2, 18].